Inhalation of Nitric Oxide in Acute Respiratory Distress Syndrome

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Inhalation of nitric oxide (INO) selectively vasodilates ventilated lung regions with increased vascular tone. The oxygenation of nonventilated regions often improves due to a reduction in relative blood flow. Most effects of NO are mediated by cyclic GMP (cGMP) resulting from the activation of adenylate cyclase by NO. Selective pulmonary vasodilation by INO in acute respiratory distress syndrome (ARDS) reduced pulmonary artery pressure (PAP) with increased PaO_2/FiO_2 as the shunt decreased, lowered right ventricle end-diastolic volume (RVEDV) and right ventricle end-systolic volume (RVESV), and increased the right ventricle ejection fraction (RVEF), but the mean artery pressure (MAP) and cardiac index (CI) did not change. With INO, there was a rapid improvement in PaO_2/FiO_2, and this effect was immediately lost on discontinuation. INO may reduce hydrostatic forces in pulmonary capillaries by decreasing pulmonary venous tone. INO may also reduce pulmonary capillary permeability by inhibiting oxidant injury, and INO acts as a free radical scavenger and attenuates oxidative damage. Management of ARDS was not standardized between groups, and survival benefits to small subgroups were lost within large groups of heterogenous ARDS patients. Improvement in gas exchange was variable and may not be meaningful. A favorable response is related to baseline pulmonary vascular tone, alveolar recruitment, high initial venous admixture, increased cardiac output (CO), and ABO blood type. The combination of INO with other agents that increase pulmonary vascular tone or prolong or accentuate the effect of INO may lead to better results than INO. INO may improve new modalities, such as high frequency ventilation and partial liquid ventilation (PLV), to ventilate ARDS patients.
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Key words: acute respiratory distress syndrome, nitric oxide, shunt

The initial studies of inhaled nitric oxide (INO) in the laboratory [1] and in adult with primary pulmonary hypertension [2] were published in 1991. In selected groups of hypoxic patients, INO improves PaO_2 and reduces pulmonary arterial hypertension (PAH). The definite indications for INO include hypoxic respiratory failure of the new-born and the evaluation of pulmonary vascular activity in patients with pulmonary hypertension. The potential use of INO is for managing patients with acute respiratory distress syndrome (ARDS), lung and cardiac transplant, congenital and acquired heart disease, PAH, and sickle cell disease.

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Endogenous nitric oxide

Endogenous nitric oxide is produced in macrophages, nonadrenergic noncholinergic neurons, mast cells, and pulmonary vascular, endothelial, and smooth muscle cells. Migrating neutrophils and platelets also can produce and release NO. Endogenous NO is synthesized from L-arginine and O_2 by a set of enzymes called NO synthases [3]. NO has high lipid solubility allowing it to diffuse across the cell membrane, and high affinity for the heme chemicals, including guanylate cyclase and hemoglobin; therefore it can perform the modulation of vascular tone, neurotransmission, and inhibition of platelet aggregation and cell cytotoxicity. In addition, endogenous NO can combine with superoxide to form the peroxynitrate anion and enhance lipid oxidation. The metabolism of NO binds to hemoglobin by conversion to nitrites and nitrates, and then it is excreted in the urine [4].

Inhalation of nitric oxide

After inhalation, NO diffuse across the epithelial surface of ventilated alveoli and into vascular cells. Excess NO is inactivated by hemoglobin when it diffuses into the lumen of the pulmonary capillary. INO selectively vasodilates ventilated lung regions with increased vascular tone. The oxygenation of nonventilated regions often improves due to a reduction in relative blood flow.

Mechanism of action of inhalation of nitric oxide

Most effects of NO are mediated by cyclic GMP (cGMP) resulting from the activation of adenylate cyclase by NO [5]. The actions of cGMP are regulated by cyclic nucleotide phosphodiesterase (PDE). PDE1 exists in the brain, heart, lung, and testis, and PDE5 can be inhibited by zaprinast or dipyridamole [6].

Effects of inhalation of nitric oxide on pulmonary vascular tone

Right ventricle ejection fraction (RVEF) reduction with RV dilation and increased right ventricle end-diastolic volume (RVEDV) and right ventricle end-systolic volume (RVESV) in ARDS is caused by acute pulmonary hypertension (PHTN) [7]. Selective pulmonary vasodilation by INO in ARDS reduced pulmonary artery pressure (PAP) with increased PaO_2/FiO_2 as the shunt decreased, lowered RVEDV and RVESV, and increased RVEF, but the mean artery pressure (MAP) and cardiac index (CI) did not change [8]. Prostacyclin in ARDS reduced PAP with decreased PaO_2/FiO_2 as the shunt increased, but MAP fell and CI rose [9]. (Figure 1)

Inhibition of endogenous NO synthesis augments acute hypoxic pulmonary vasoconstriction

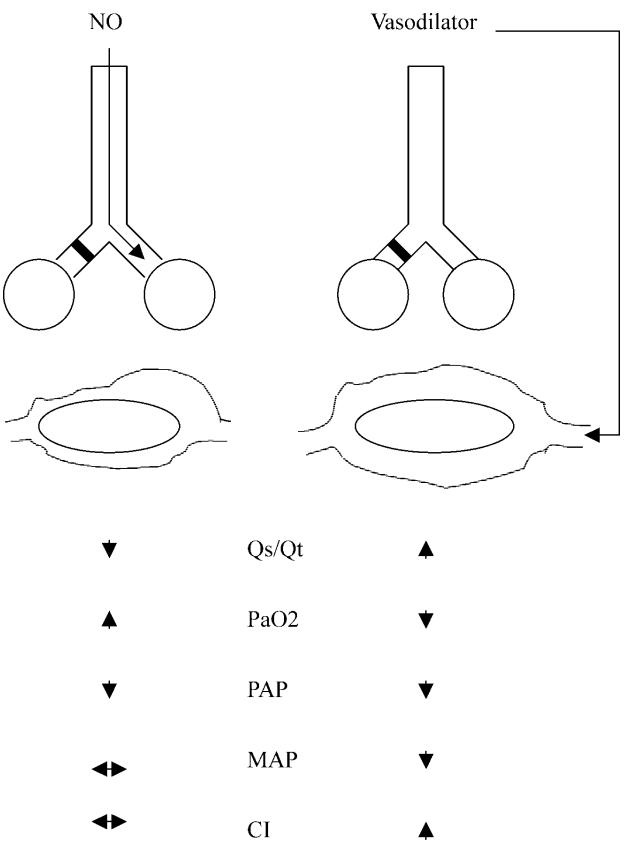

Fig. 1. Although intravenous vasodilators increase blood flow through shunting blood vessels (right), INO selectively dilates pulmonary vessels in contact with ventilating alveoli (left). This effect decreases the shunt and increases oxygenation. CI=cardiac index, INO=inhaled NO, MAP=mean artery pressure, PAP=pulmonary artery pressure, Qs/Qt=shunt.

and the pulmonary vasoconstrictor effects of agents like endothelin-1, angiotensin II, and thromboxane [10]. INO has no effect in healthy adults, but it is a vasodilator when pulmonary circulation is vasoconstricted [11].

INO lowers PAP in patients with hypoxic PHTN caused by acute respiratory illnesses like pulmonary embolism, after pneumonectomy or thromboembolectomy, and acute lung injury [12]. INO has a pulmonary vasodilator effect in patients with chronic PHTN, such as primary pulmonary hypertension, chronic obstructive pulmonary disease (COPD), and idiopathic pulmonary fibrosis [13].

Effects of inhalation of nitric oxide on gas exchange

The most striking effect of INO may be its ability to improve pulmonary oxygenation, but not pulmonary hemodynamics. INO is delivered only to the ventilated lung, and this delivery results in better ventilation/perfusion (V/Q). INO increases flow to the area of normal V/Q by redistributing blood flow from a poorly ventilated to a well-ventilated area of the lung [14].

The beneficial effect of INO on oxygenation happens in a high degree of perfusion to areas of low V/Q or shunt such as acute lung injury [14]. INO causes little improvement or even worsens oxygenation in V/Q mismatches with little shunt such as COPD [15].

With the initiation of INO, there was a rapid improvement of PaO_2/FiO_2, but this effect was immediately lost on discontinuation [16]. Prolonged INO failed to result in tachyphylaxis [16]. INO also has a relaxant effect on bronchial smooth muscles and improves ventilation.

Effects of inhalation of nitric oxide on pulmonary capillary permeability and inflammation

INO may reduce hydrostatic forces in pulmonary capillaries by decreasing pulmonary venous tone [17]. INO may reduce pulmonary capillary permeability by inhibiting oxidant injury, and INO acts as a free radical scavenger and attenuates oxidative damage [18].

INO can inhibit the inflammatory response in the lung, including those by hydrogen peroxide, CD11b/CD18, and IL6/IL8 by bronchial alveolar lavage [19]. INO reduces platelet aggregation with normal bleeding time and decreases platelet and neutrophil sequestration [20].

Failure of inhalation of nitric oxide to improve acute respiratory distress syndrome

PAH, but not hypoxic respiratory failure contributes to mortality in ARDS, and reducing PAP or pulmonary vascular resistance (PVR) with INO may improve the outcome [21]. Most studies titrated the dose of INO (5 ppm) to optimize oxygenation, but not a maximal decrease in PAP (3 to 4 mmHg), and correlated this with the outcome [22]. Higher INO (35 ppm) increased cardiac output (CO)(> 20%) in a recent study in 8 patients from a total of 12 patients with ARDS and hemodynamic instability [23].

Reducing FiO_2, positive end-expiratory pressure (PEEP), or mean airway pressure for adequate oxygenation with INO may improve the outcome in ARDS. PEEP was below 10 cmH_2O and FiO_2 was below 0.6 in most studies, and the FiO_2 was above 0.9, and PEEP was above 15 cmH_2O for selected patients in one recent study [24].

The management of ARDS is not standardized between groups, and survival benefits to small subgroups are lost within large groups of heterogenous ARDS patients. The brief favorable effect of INO on oxygenation may not be long enough to affect outcome. Increasing or prolonging the beneficial effects of INO to affect underlying disease, or identifying selected groups (rapidly progressive hypoxia, severe PHTN, or right ventricle failure), may improve survival with ARDS.

Improving response to inhalation of nitric oxide

Improvement in gas exchange is variable and may not be meaningful. A favorable response is related to baseline pulmonary vascular tone, alveolar recruitment, high initial venous admixture, increased CO, and ABO blood types [25].

Increasing the amount of ventilated lung should potentiate the pulmonary vasodilating effect of INO. INO improves oxygenation by encouraging blood flow to the well-ventilated lung, and is determined by the balance of pulmonary blood flow to the ventilated and nonventilated lung.

INO may fail to improve oxygenation with increased endogenous pulmonary vasodilators, as in pneumonia or sepsis [26]. Persistent perfusion of the nonventilated lung caused by local vasodilators in the affected area may result in a significant shunt fraction, and may explain the lower rate of INO response in these patients [26].

Oxygenation can be enhanced by adding pulmonary vasoconstrictors such as almitrine; its vasoconstrictor effect is greater in the nonventilated lung, decreasing the shunt fraction when given with INO [27]. The administration of norepinephrine and INO in patients with ARDS and sepsis has similar results [28].

Most biological effects of INO are mediated through increased intracellular cGMP levels; cGMP is degraded by PDE [29]. Hyporesponsive-ness to INO has been associated with increased PDE activity, and the addition of PDE inhibitors to INO increases the duration of the INO effect, prevents rebound PHTN after INO discontinuation, and facilitates weaning from INO [30].

Combination therapies with inhalation of nitric oxide

Limitation of inspiratory plateau pressures causes hypercapnia, increased CO and PVR, and resulting PAH [31]. INO in hypercapnia decreased PVR, slightly decreased PAP, and improved oxygenation with an unchanged shunt [32].

PEEP that increases lung alveoli recruitment should potentiate NO-induced improvement in arterial oxygenation at a traditional dose of INO [33]. The optimal effects of INO in ARDS rely on an optimization of PEEP for alveolar recruitment [34].

Oxygenation improvement is slightly better in a prone position than with INO, and this may be caused by a better matching of V/Q when dependent, atelectatic lung zones are moved to the dorsal position [35]. Response to one modality did not predict response to the other [36]. The beneficial effects of each modality on oxygenation seem to be additive.

Neonates with respiratory failure treated with INO and high frequency oscillatory ventilation were more likely to have a favorable response than with either modality alone [37]. A patient with bilateral bronchopleural fistula and ARDS following pneumoplasty for bullous emphysema became hypoxic on high frequency jet ventilation, but improved on high frequency jet ventilation with INO [38].

Animal studies showed that a INO and partial liquid ventilation (PLV) combination may improve oxygenation more effectively in acute lung injury than either modality alone [39]. PLV may achieve better alveolar recruitment than conventional ventilation, and make the more ventilated lung accessible to INO. PLV may also be more efficient in delivering INO to the poorly ventilated lung.

Future consideration

The combination of INO with other agents that increase pulmonary vascular tone or prolong or accentuate the effect of INO may lead to better results than INO alone. INO may improve new modalities, such as high frequency ventilation and PLV, to ventilate ARDS patients.

When favorable conditions or beneficial groups are identified, we can recommend the routine use of INO. The lack of serious adverse effects associated with INO and its ability to cause pronounced and immediate beneficial effects on gas exchange and pulmonary hemodynamics in most patients without increasing airway pressure make INO a unique therapy.

Abbreviations

ARDS	acute respiratory distress syndrome
cGMP	cyclic GMP
CI	cardiac index
CO	cardiac output
COPD	chronic pulmonary obstructive disease
INO	inhaled NO
MAP	mean artery pressure
PAH	pulmonary artery hypertension
PAP	pulmonary artery pressure
PDE	phosphodiesterase
PEEP	positive end-expiratory pressure
PHTN	pulmonary hypertension
PLV	partial liquid ventilation
PVR	pulmonary vascular resistance
RVEDV	right ventricle end-diastolic volume
RVEF	right ventricle ejection fraction
RVESV	right ventricle end-systolic volume

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成人呼吸窘迫症候群患者吸入一氧化氮

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一氧化氮吸入選擇性擴張具高血管張力的可通氣肺部。非通氣肺部的氧合作用常因為相對血流減少而改善。一氧化氮的大部分效應是經由激發腺嘌呤環酵素所產生的 CGMP 所媒介。成人呼吸窘迫症候群病患吸入一氧化氮（選擇性肺部血管擴張劑），減少肺部動脈血壓及增加氧合作用，因為分流減少，減少右心室舒張末期和收縮末期容積，增加右心室收縮分率，但平均全身血壓及心臟指數並不改變。一氧化氮吸入能夠迅速增加氧合作用，一旦停止使用，這個效應馬上消失。一氧化氮吸入能夠因為減少肺部靜脈血管張力，而減少肺部微血管的靜水壓力。一氧化氮吸入能夠因為抑制氧化傷害，而減少肺部微血管的通透性，一氧化氮吸入能夠扮演自由基清除者，而減少氧化傷害。成人呼吸窘迫症候群病患的處理並不一致，少數特殊病患的生存，不容易在多數異質病患發現。氣體交換的改善並不一致，可能也不具意義。良好反應常和基礎肺部血管張力、肺泡容積增加、初期分流增加、心輸出量增加、和 ABO 血型有關。一氧化氮吸入結合增加肺部血管張力或增加一氧化氮吸入效應的方法，可能得到比一氧化氮吸入更好的結果。一氧化氮吸入可能改善成人呼吸窘迫症候群病患通氣的新方案，例如高頻通氣和液體通氣。***（胸腔醫學 2003; 18: 385-391）***

關鍵詞：成人呼吸窘迫症候群，一氧化氮吸入，分流

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Ultrasonographic Hemidiaphragmatic Weakness in Acute Respiratory Failure: Impact on Extubation Outcome

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Background: The impact of hemidiaphragmatic weakness on the extubation outcome is unclear.

Methods: We performed ultrasonographic evaluations of the hemidiaphragms of patients with acute respiratory failure treated in the medical ICU. The patients were intubated and mechanically ventilated. At the beginning of a spontaneous breathing trial before extubation, the movements of the liver and spleen, which represented the hemidiaphragmatic movements, as well as conventional weaning parameters, were measured. Clinical data, radiographic findings, weaning parameters, and ultrasonographic findings were analyzed.

Results: During a study period of six months, 58 patients completed ultrasonographic study. Among them, 14 (24%) patients had unilateral hemidiaphragmatic weakness and 3 (5%) had bilateral weakness. The mean values of liver and spleen displacement did not correlate well with P_{Imax} and V_{Tspon} (R square = 0.19 and 0.16, respectively). In patients with unilateral hemidiaphragmatic weakness, 67% showed radiographic evidence of hemidiaphragmatic elevation, and only 17% showed abdominal paradoxical movements. The extubation failure rate for all patients was 41%. We found that bilateral hemidiaphragmatic weakness, but not unilateral hemidiaphragmatic weakness, is associated with a poor extubation outcome.

Conclusion: Unilateral hemidiaphragmatic weakness does not have significant impact on the extubation outcome of patients with acute respiratory failure. Ultrasonographic measurements of liver and spleen displacement during spontaneous breathing is a feasible method for evaluating hemidiaphragmatic movement. ***(Thorac Med 2003; 18: 392-401)***

Key words: Liver and spleen movements, Hemidiaphragmatic weakness, Extubation outcome, Ultrasonography

Introduction

Diaphragmatic weakness may impair the pulmonary function and increase the incidence of pneumonia [1]. In patients with respiratory failure, weaning failure may result from respiratory muscle fatigue due to excessive ventilatory demand [2]. Since the diaphragm is the major contributor to the inspiration effort, an evaluation of its function may be important in patients undergoing weaning from the ventilator. Although hemidiaphragmatic weakness (HDW) may be occasionally seen in the

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clinical setting, its impact on extubation outcome remains unclear. Previously, the evaluation of HDW was difficult because of a lack of accessibility to the diaphragmatic movements. In earlier reports, several modalities were introduced, such as fluoroscopy, pulmonary function tests, phrenic nerve stimulation, and the measurement of transdiaphragmatic pressure (Pdi). However, the use of these methods is limited by their invasive nature or the dependency on the maximal voluntary efforts of the patients [4], therefore they might provide incomplete information concerning diaphragmatic function, especially in patients with unilateral HDW. Recently, several reports have demonstrated the use of ultrasonography in the evaluation of the hemidiaphragm [5-8]. As these studies directly visualized the hemidiaphragm and directly traced its movements, their reproducibility might be limited by the difficulty in localizing a reference point to the hemidiaphragm and the possible presence of discordant movements in different parts of the diaphragm [9].

The movements of the diaphragm displace the abdominal organs adjacent to the hemidiaphragm, such as the liver and spleen. A study employing MRI showed that abdominal organs primarily undergo translational motion in a superior-inferior direction, and the motion of the organs correlates well with hemidiaphragmatic movement [10]. Similar observations of the cranio-caudal movements of the liver, spleen, and kidneys during the respiratory cycle, evaluated by ultrasound, have also been reported [11-13]. For impaired diaphragmatic movements, ultrasound can also detect possible disorders in the pleural or abdominal cavity [14].

The impact of HDW on the weaning outcome remains unclear. Since ultrasound is a noninvasive tool to evaluate the diaphragm, we performed an observational study by using ultrasound to evaluate the hemidiaphragmatic movements via measuring the extent of liver and spleen movements in patients who were prepared for extubation. We hypothesized that HDW is associated with extubation failure.

Methods

From July to December 2002, we studied the ultrasonographic features of the liver and spleen movements of patients who were preparing for extubation. The institutional ethics committee approved the study.

Patients

We evaluated the intubated and mechanically ventilated patients in the medical intensive care unit (MICU) for their eligibility to enter this study. The decision to extubate was made by the attending physicians of the patients. Before extubation, eligible patients were enrolled in the study after informed consent had been obtained from them or their surrogate decision-makers. Patients were included if they fulfilled all of the following criteria: age ≥ 20 years; use of oxygen with a fraction (F_1O_2) of 0.4 or less; use of positive end-expiratory pressure (PEEP) at 5 cm H_2O or less; use of pressure support at 8 cm H_2O or less from the ventilator; and a duration of continuous mechanical ventilation of 30 days or less. Patients were excluded if they met one or more of the following criteria: intubated with mechanical ventilation for elective surgery; intubated due to upper airway obstruction; unstable hemodynamic status at the time of the study; inability to undergo a spontaneous breathing trial; mechanical ventilation via a tracheostomy tube; history of peritonitis or abdominal surgery; or a history of pleural empyema or pleurodesis. Figure 1 shows the flow chart of the inclusion of patients into the study.

Study protocol

Weaning parameters, including V_{Tspon} and P_{Imax}, were measured within 6 hours before a spontaneous breathing trial (SBT), which was followed by extubation. Two well-trained experts in ultrasonography measured the displacement distance of the liver (LD) and spleen (SD) in a real-time fashion. Each operator performed the ultrasonography twice with an interval of 5 minutes. An ultrasound scanner (Aloka Echo Camera SSD-1400, Aloka, Zug, Switzerland) equipped with a 3.5 MHz sonar probe was used. While a patient was lying in the supine position, the probe was placed on the abdominal

wall along the right anterior and left posterior axillary lines. The LD and SD were then measured in the cranio-caudal aspect (Figure 2) at the beginning of the SBT with a T-piece before extubation. A maximal LD and SD of ten respiratory cycles were recorded. A patient was considered as having HDW if the LD or SD value was less than one standard deviation below the mean. These patients were divided into three groups, namely, good LD/SD, unilateral HDW (UHDW), and bilateral HDW (BHDW).

Extubation was performed for all patients. Those patients who received reintubation or noninvasive positive pressure ventilation (NIPPV) within 72 hours after extubation were defined as extubation failures. The decision to re-institute ventilatory support was made by the attending physicians based on the presence of symptoms and signs of respiratory failure. The mean of the LD and SD (MD) was calculated from the mean of the LD and SD of the two measurements (with intervals of 5 minutes) from each operator.

Data collection

In addition to the values of the ultrasonographic measurements, the following clinical data were obtained: demographic data, including age, sex, and race; underlying disease or comorbidity; admission diagnosis and reason for mechanical ventilation; duration of mechanical ventilation use; physical examination findings; chest radiograph report; weaning methods and weaning parameters; outcome of extubation, including duration of NIPPV use; and outcome of ICU discharge and hospital discharge. Hemidiaphragmatic elevation on the chest X-ray (CxRDE) was defined by the presence of either of the following two findings: 1) the left hemidiaphragm was higher than the right; or 2) the right side was higher than the left by a distance of more than one intercostal space.

Statistical analysis

Measured data were expressed as mean ± SD. Intra- and inter-observer variations were analyzed by a paired samples t test. An independent samples t test was used for evaluating the difference between the LD and the SD. Linear regression analysis was performed for the LD with the SD, the MD with the pressure of maximal inspiration (P_{Imax}), and the MD with the volume of spontaneous breathing (V_{Tspon}). The differences among the three groups (good LD and SD, UHDW and BHDW) and between any two among them for the extubation outcome, abdominal paradoxical movement (AP), and diaphragmatic elevation over the chest radiography (CxRDE), were analyzed by an ANOVA test and independent samples t test. A p value of less than 0.05 was considered statistically significant.

Results

During the study period, 205 patients were evaluated for entry into the study (Figure 1). Sixty-five patients did not complete the ultrasonography, the reasons for which included unavailable consent for 46 patients, poor cooperation in 13, poor image quality in four, and an irregular breathing pattern in two. The failure rate for the ultrasonographic measurement, including patient non-cooperation was 13%, and the pure rate of technical failure, due to poor image quality or an irregular breathing pattern, was 4%. All of the 205 patients were extubated eventually.

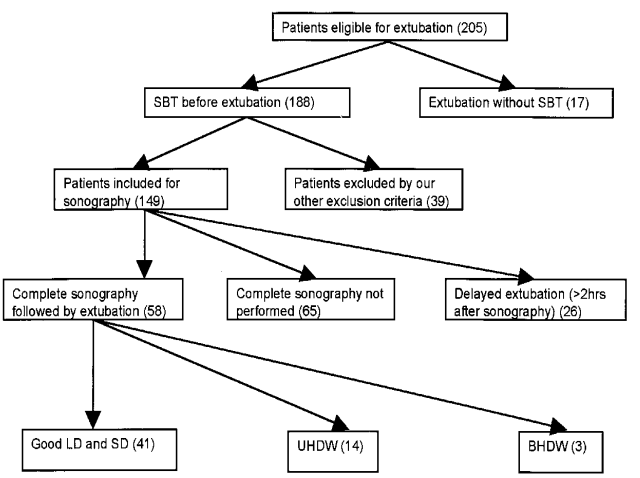

Fig. 1. Flow chart of the inclusion of patients in this study (SBT: spontaneous breathing trial; LD: liver displacement; SD: spleen displacement; UHDW: unilateral hemidiaphragmatic weakness; BHDW: bilateral hemidiaphragmatic weakness).

The mean age of the 58 analyzable patients was 67 years (range, 33 to 87), and 28 of the patients (48%) were men (Table 1). Five (9%) patients had a history of respiratory failure requiring mechanical ventilation prior to this study. During the patients' ICU course of respiratory failure, 15 (26%) had been extubated once, five (9%) extubated twice, and one (2%) extubated three times prior to the ultrasonographic study. Overall, 22 (38%) had experienced recurrent respiratory failure or extubation failure with reintubation. Of the patients, 45 (78%) had underlying co-morbidity. The most common cause of acute respiratory failure was pneumonia (32 patients, 55%). The duration of mechanical ventilation before extubation was 11 ± 6 days (range, 2 to 26 days). The rate of successful extubation was 59%; it was higher in patients with congestive heart failure (CHF)-related acute respiratory failure (ARF) and less in patients with underlying chronic obstructive lung diseases (COLD, including chronic obstructive pulmonary disease, asthma, and bronchiectasis) or malignancy, or those suffering from ARF due to COLD. The mean values of LD and SD were 1.15 ± 0.62 cm and 1.26 ± 0.73 cm, respectively. Figure 3 shows that the differences in the LD and SD were not significant, and the correlation

Table 1. Baseline data of patients

Baseline parameters	Results	Successful extubation, n (%)
Age, yr (range)	67 (33-87)	34 (59%)[c]
Male, n (%)	28 (48%)	17
Comorbidity*, n (%)	45 (78%)	22 (49%)
Malignancy, n	5	2 (40%)
COLD[a], n	13	6 (46%)
Diabetes mellitus, n	9	7 (78%)
Renal insufficiency, n	11	7 (64%)
Liver cirrhosis, n	1	1 (100%)
CAD/CHF, n	12	9 (75%)
Neurological diseases[b]	18	10 (56%)
Causes of MV used*		
COLD[a], n	11	5 (45%)
Neurological diseases[b], n	6	4 (67%)
Pneumonia /ARDS, n	32	17 (53%)
CHF, n	8	7 (88%)
Others, n	3	2 (67%)
Duration of MV	11±6 (2-26)	
ARF episodes prior to this admission, n (%)	5 (9%)	3 (60%)
Extubation failures previous to this admission, n (%)	21 (36%)	11 (52%)
Once, n (%)	15 (26%)	8 (53%)
Twice, n (%)	5 (9%)	2 (40%)
Three times, n (%)	1 (2%)	0 (0%)

Definition of abbreviations: ARDS: acute respiratory distress syndrome; CHF: congestive heart failure; MV: mechanical ventilation; COLD: chronic obstructive lung diseases. [a]Including chronic obstructive pulmonary disease, asthma and bronchiectasis; CAD: coronary artery disease; ARF: acute respiratory failure. [b]Including cerebrovascular accident, consciousness disturbance, central or peripheral neural system or neuromuscular disorder. [c]34 (59%) of all 58 patients were extubated successfully, among them, 17 were male. Age is expressed as mean followed by range, duration of MV is expressed as mean ± 1 standard deviation followed by range, and other data are expressed as case numbers and percentage.

*A patient may have more than one comorbid disease or cause of MV.

between these two measurements was poor. As defined by the criteria mentioned earlier, patients with LD ≤ 0.5 cm or SD ≤ 0.5 cm were considered as having UHDW; those with LD ≤ 0.5 cm and SD ≤ 0.5 cm were defined as BHDW. The correlation between MD and P_{Imax} or that between MD and V_{Tspon} was poor (Figure 4a and 4b). During the ultrasonographic evaluation, none of the patients was shown to have paradoxical movements of the liver and spleen. There was a good correlation of measured data between and within the observers (0.988 and 0.952 respectively), and the variations were not significant (p = 0.157 and 0.10 respectively).

We found that 41 (71%) were in the good LD and SD group, 14 (24%) were in the UHDW group, and 3 (5%) in the BHDW group. Thirty-four patients were extubated successfully, 11 underwent reintubation within 72 hours after extubation, and 13 were not reintubated but treated with noninvasive positive pressure ventilation (NIPPV) (BiPAP®, Model S/T 30, Respironics Inc., Murrysville, PA, USA), with a mean duration of 26.1 hours within 72 hours after extubation. Ten of these patients were free from NIPPV within 72 hours, and three received intermittent NIPPV for more than three days. Conditions associated with reintubation included respiratory distress (7 patients), profuse airway secretion (5), altered mental status (3), and hemodynamic instability (4). None of the patients showed evidence of upper airway obstruction.

The extubation failure rate differed significantly among these three groups (P = 0.04), but there was no significant difference in the extubation failure rate between the good LD/SD group and the UHDW group (P=0.134) (Table 2). AP and CxRDE also differed significantly among these three groups (P=0.007 and 0.013 respectively), but CxRDE did not differ significantly between the good LD/SD group and the BHDW group (P=0.125) or the UHDW and the BHDW group (P=0.487). The causes of ARF, P_{Imax} and V_{Tspon} did not differ significantly among these three groups. The prevalence of UHDW in patients with CxRDE and AP was 31% (4/13) and 7% (1/15), respectively. Of the 15 patients with AP, 14 (93%) suffered from poor bilateral hemidiaphragmatic weakness. On the other hand, among the patients with UHDW, 67% showed

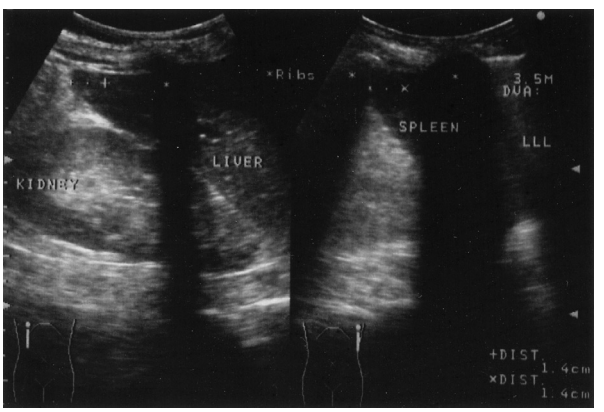

Fig. 2. Liver/spleen displacements (LD/SD) in the cranio-caudal aspect during quiet spontaneous breathing, measured by 2D real time ultrasound.

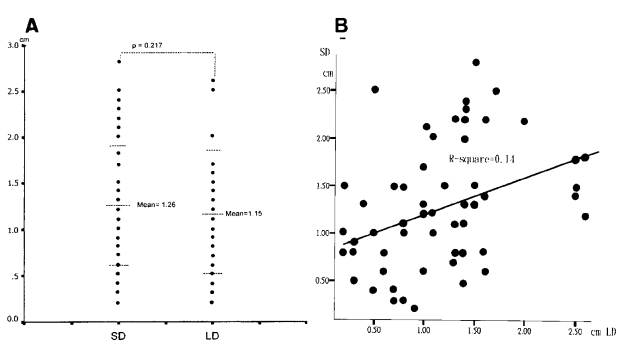

Fig. 3. 3A: Distribution of liver and spleen displacements (LD and SD) with mean and standard deviation; 3B: No significant difference or correlation between LD and SD.

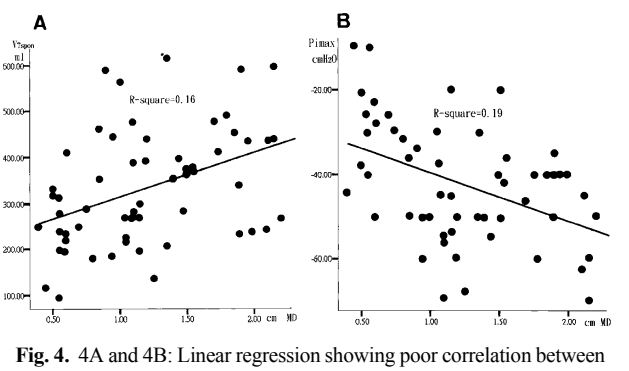

Fig. 4. 4A and 4B: Linear regression showing poor correlation between MD (mean displacement) and VTspon (tidal volume of spontaneous breathing), and between MD and PImax (pressure of maximal inspiration).

Table 2. Causes of ARF, extubation outcomes, AP, CxRDE, P_{Imax} and V_{Tspon} in three groups

	Good LD and SD (41)	UHDW (14)	BHDW (3)	P value
Comorbidity/causes of ARF				
COLD[a], n	11	2	0	0.408
Neurological diseases[b], n	14	4	0	0.469
Pneumonia/ARDS, n	19	11	2	0.106
CHF, n	10	2	0	0.493
Others, n	2	0	1	0.061
Extubation failure rate*, %	34	57	100	0.04
AP*, n	6	7	2	0.007
CxRDE*, n	6	7	3	0.013
P_{Imax}, cm H_2O	43	41	30	0.27
V_{Tspon}, ml	328	355	318	0.775

Definition of abbreviations: LD: liver displacement; SD: spleen displacement; UHDW: unilateral hemidiaphragmatic weakness; BHDW: bilateral hemidiaphragmatic weakness; AP: abdomen paradoxical movement; CxRDE: unilateral diaphragm elevation in the chest radiograph (right side higher than the left side by more than one intercostal space or left side higher than the right side); ARF: acute respiratory failure; CAD: coronary artery disease; ARF: acute respiratory failure; P_{Imax} : pressure of maximal inspiration; V_{Tspon} : tidal volume of spontaneous breathing. [a]Including chronic obstructive pulmonary disease, asthma and bronchiectasis. [b]Including cerebrovascular accident, consciousness disturbance, central or peripheral neural system or neuromuscular disorder. Good LD and SD is defined as both LD and SD > 0.5 cm; UHDW is defined as one of LD or SD ≤ 0.5 cm; BHDW is defined as both LD and SD ≤ 0.5 cm. Extubation failure rate is expressed as percentage, causes of ARF is expressed as number, P_{Imax} and V_{Tspon} are expressed as mean values of respective groups. *$p < 0.05$ by ANOVA test.

CxRDE, and 17% showed AP. Six patients with good LD and SD, however, also showed AP. Among them, three (50%) had extubation failure. Of the patients with AP in the UHDW and BHDW groups, extubation failures were 4 (57%) and 2 (100%), respectively.

Discussion

Various diseases or disorders may result in weakness of the diaphragm. Diagnosis of isolated diaphragmatic weakness, however, may be difficult, and the most frequent diagnosis is idiopathic, due to the difficulty in accessibility [1]. Clinical symptoms may include dyspnea, orthopnea, a rapid shallow breathing pattern and paradoxical inward motion of the abdomen (AP) during inspiration; the latter symptom is more specific and may been seen in patients lying in a supine position with marked diaphragmatic weakness [1, 15]. Unilateral hemidiaphragmatic paralysis (UHDP) may result in a modest reduction in vital capacity, to approximately 75% of predicted value, but the lung volumes may be normal in chronic UHDP, as a result of compensation by the chest wall and abdominal muscles [16]. Pdi remains the standard for the diagnosis of bilateral hemidiaphragmatic paralysis [17]; but previous studies have demonstrated that the values of Pdi in normal subjects may also vary widely [18], therefore this method appears to be not sensitive for the diagnosis of diaphragmatic weakness, especially mild UHDW.

In our study, the correlation of the MD with V_{Tspon} or with P_{Imax} was not good. An explanation is that V_{Tspon} and P_{Imax} are a result of contributions by all inspiratory muscles, whereas MD is contributed to mainly by the diaphragm. As poor endurance may be the most difficult to predict, an evaluation of the diaphragmatic movements by ultrasonography may be an important tool to assess the endurance of the patient, especially in patients who show normal P_{Imax} and V_{Tspon} as a result of compensation by other inspiratory muscles [16].

Previous studies have shown that in healthy

subjects, the hemidiaphragmatic movement was better in the right side. In our studies of patients with ARF, however, there was no significant difference or correlation between SD and LD. Diaphragmatic movement is a result of diaphragmatic contraction against the chest and abdominal organs. The chest and abdominal conditions may be altered by various disease processes, such as space-occupying lesions, gas distension, edema, inflammation, fibrotic contraction, and surgery; all may cause either unilateral or bilateral HDW, as seen in the patients in our study.

Chest radiographs and fluoroscopy have been commonly used to assess UHDW, but 6% of normal subjects have paradoxical motion of the hemidiaphragm in the fluoroscopic examination [20]. The methods are limited by appreciable false positive and false negative rates for HDW [1], especially in the case of BHDW or paralysis [17]. Radiation exposure is another concern. Electrophysiological studies are useful to determine the level and causes of diaphragmatic weakness and as a monitoring method for the recovery of a paralyzed diaphragm, but its use in the evaluation of the severity of diaphragmatic weakness remains limited. Gottesman and colleagues used ultrasound to measure diaphragm thickness below the chest-phrenic angle, and showed that the thickness and its change in the respiratory cycle are good predictors of diaphragm paralysis [17]. However, this technique is useful only for the diagnosis of hemidiaphragmatic paralysis, rather than weakness, because the small change (1.3 to 3.9 mm) poses difficulty in quantifying the severity of weakness.

The technique used in this study is reproducible because the reference points are easier to find, as compared with direct ultrasonographic visualization of the diaphragm. Mild rotation of the spleen and the liver were occasionally detected during the respiratory cycle, but this was considered to contribute little to the lung volume change, and therefore could be neglected. The reproducibility for this method was reliable, confirming that it can be used as a method for analyzing LD and SD repeatedly, and by different operators.

The rate of successful extubation in this study was 59%, a value less than previously reported in the literature [19]. Explanations include advanced age, a high prevalence of co-morbidities, a history of respiratory failure or extubation failure, and the definition of extubation failure as any use of positive pressure ventilation including NIPPV within 72 hours after extubation in this study. Since the criteria for applying NIPPV were not uniform in this study, an interventional study with definite criteria for NIPPV and reintubation is needed to determine the extubation success rate more precisely. It seems that a successful extubation rate is higher in patients with CHF-related ARF, and lower in patients with underlying obstructive lung diseases (including COPD, asthma, bronchiectasis), or malignancy, or those suffering from ARF due to obstructive lung diseases. ARF in patients with CHF is usually due to an acute episodic fluid overload or other reversible factor. None of our patients suffered from acute myocardial infarction or other factor that would lead to a permanent deterioration of the cardiac function. The rate of extubation failure in the good LD/SD group still was 34%. This can be explained by the diverse causes of ARF (Table 2).

The difference in extubation outcome was only significant between the UHDW and BHDW groups or between the good LD/SD and BHDW groups, but there was no significant difference between the patients with good LD/SD and those with UHDW ($p=0.134$). In patients with UHDW, the UHDW did not affect the extubation outcome. The measured P_{Imax} and V_{Tspon} were also not significantly decreased in patients with UHDW, as compared to patients with good LD/SD (Table 2). The P_{Imax}, not the pressure measured during spontaneous breathing, is effort-dependent and has a large patient-to-patient variation [1]. The P_{Imax} is also contributed by respiratory muscles other than the diaphragm, and was therefore not well correlated with HDW in our study (Figure 4). However, if an abrupt decrease in P_{Imax} occurs, especially after a cardiothoracic operation, the possibility of HDW or paralysis is high. Unilateral hemidiaphragmatic dysfunction does not dramatically compromise ventilation in patients

with baseline normal lung function [21]. In infants with UHDW, paradoxical movement of bilateral hemidiaphragms may occur, with shifts in the mediastinal structure, and a reduced function in the contralateral lung [22, 23]. This effect may be less in adults; no paradoxical movement of the hemidiaphragms was noticed in our patients. However, atelectasis of the lung may occur after the patients have been weaned from positive pressure ventilation, increasing the risk of extubation failure and morbidity; therefore diagnosis of UHDW may remain important in patients with respiratory failure. Ultrasound evaluation of liver and spleen displacement during SBT, as described earlier, may be an adequate diagnostic modality.

Abdominal paradoxical movement usually occurs in patients with diaphragmatic weakness or respiratory distress. The prevalence of AP and CxRDE is significantly greater in patients with UHDW than in patients with good LD and SD. However, only 31% and 7% of patients with CxRDE and AP, respectively, suffered from pure UHDW, and 93% of patients with AP suffered from BHDW. Therefore CxRDE and AP may not be specific for UHDW. Only 67% and 17% of patients with UHDW suffered from CxRDE and AP, respectively, suggesting that CxRDE and AP are also not sensitive for UHDW.

In conclusion, clinical symptoms and radiological findings are not sensitive and specific for the diagnosis of UHDW. In patients with suspected UHDW, measurement of liver and spleen displacement by ultrasound is a feasible method for evaluating diaphragmatic movement. Patients with acute respiratory failure, who show bilateral HDW, rather than unilateral HDW, have a greater chance of extubation failure.

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在急性呼吸衰竭之病患，以超音波評估單側橫膈膜肌無力之情形：分析其對拔管預後之影響

江榮人　鄭之勛　楊泮池

背景：單側橫膈膜肌無力對於呼吸衰竭病人拔管失敗率的影響目前仍不明。

方法：本研究以超音波對內科加護病房內急性呼吸衰竭之病患評估其橫膈膜肌收縮之情形，病患均接受氣管內插管及呼吸器輔助呼吸。以肝臟及脾臟的移動代表橫膈膜的移動，我們測量其於病患自主性呼吸時移動的情形，並測量傳統的呼吸器脫離指標，並將病患之臨床資料、影像學表現、傳統呼吸器脫離指標及超音波測量結果納入研究分析。

結果：在六個月期間，共有58位病患被完整地收案，其中，14位病患（24%）為單側橫膈膜肌無力；3位病患（5%）為雙側橫膈膜肌無力。肝臟和脾臟之移動平均值和吸氣最大壓力值（P_{Imax}）及自主性呼吸潮氣量（V_{Tspon}）的相關性不佳。在所有的單側橫膈膜肌無力病患中，僅67%病患在影像上顯示單側橫膈升高，而只有17%的病患的理學檢查發現有腹部矛盾性呼吸的情形。所有的病患中，拔除氣管內插管脫離呼吸器的失敗率為41%。本研究發現，雙側橫膈膜肌無力與拔管失敗率有相關，但單側橫膈膜肌無力和拔管失敗率並沒有統計學上的相關性。

結論：在我們的研究結果中，單側橫膈膜肌無力對急性呼吸衰竭病患之拔管失敗率無決定性的影響。以超音波測量肝臟及脾臟於自然呼吸下的移動來評估橫膈肌收縮是實用可行的方法。***（胸腔醫學 2003; 18: 392-401）***

關鍵詞：肝臟及脾臟移動、單側橫膈膜肌無力、拔管預後、超音波

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Analysis of Bronchoscopic Findings in Patients Suspected of Having Upper Airway Obstruction

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Young-Fa Lai, Sui-Liong Wong

Background: A great variety of the conditions affecting the upper airway from the naso-pharynx to the tracheal carina can cause upper airway obstruction (UAO). It is important to make an early diagnosis of UAO, because it may lead to severe respiratory problems or respiratory failure. The purpose of this study is to explore the bronchoscopic findings in patients suspected of having upper airway obstruction.

Materials and Methods: We retrospectively analyzed a series of 108 patients with suspected UAO who had undergone bronchoscopic examination from February 1998 to March 2003 at Kaohsiung Chang Gung Memorial Hospital. The medical records of these patients were subsequently reviewed.

Results: The overall positive rate of the bronchoscopic findings exceeded 80%. The most frequent symptom or sign was dyspnea, followed by stridor. The most common obstruction location was the trachea, followed by the vocal cord. The most common etiology was tracheal stenosis as a complication of translaryngeal intubation or tracheostomy (50.3%). However, no relationship among gender, age, percentage of stenosis, indication for intubation, type of stenosis, and length of time between intubation and bronchoscopy was noted. We also found other etiologies of UAO, such as a neoplasm causing vocal cord paralysis.

Conclusions: We need frequently to remind ourselves of the possibility of UAO in every patient complaining of dyspnea. Chest roentgenograms of good quality interpreted with a high degree of suspicion, particularly when the patient has the risk of UAO, will lead to earlier diagnosis.
(Thorac Med 2003; 18: 402-408)

Key words: upper airway obstruction, bronchoscopy, stridor

Introduction

The upper airway can be considered as the conduit for inspired and expired gas from the external nares or the lips to the tracheal carina. It is important to make an early diagnosis of upper airway obstruction (UAO), because it may lead to severe respiratory problems or respiratory failure.

A number of examinations are used to confirm the presence of upper airway obstruction and estimate its magnitude. Direct bronchoscopic visualization is the gold standard for confirming the presence of airway obstruction and also aids in discerning its underlying etiology. Over the past few years a considerable number of studies have been done in interventional pulmonology [1]. The

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purpose herein was to explore a little further into the bronchoscopic findings of patients suspected of having UAO. We also wanted to find the relationship between the type of stenosis, percentage of stenosis, and other variables. Under what conditions should we become suspicious of UAO, and can we detect UAO earlier?

Materials and Methods

Reports of bronchoscopies performed at Kaohsiung Chang Gung Memorial Hospital from February 1998 to March 2003 (a total of 6640) were retrospectively reviewed to determine which patients had suspected upper airway obstruction. The medical records of these patients were subsequently reviewed for the following information: age, gender, medical history, symptoms and signs and their duration, treatment, radiographic findings, and pulmonary function test findings, if available. We also reviewed the chest roentgenograms retrospectively.

A total of 108 patients with 124 fiberoptic bronchoscope procedures for suspected UAO were recorded. Typically, clinical suspicion was raised because of abnormal radiographic findings, and symptoms or signs, although not specific, accompanied by a history of endotracheal intubation or tracheostomy. Some bronchoscopic procedures were performed to exclude UAO for other reasons, such as unexplained dyspnea while the tracheostomy tube was still in place. After excluding patients with negative findings, which meant no stenosis observed during the bronchoscopy, 91 patients were enrolled. The reduction of the airway area was measured retrospectively from the photographs taken during the bronchoscopic examination.

Pearson correlation coefficients were performed to assess the relationships between gender, age, percentage of stenosis, indication for intubation, types of stenosis, and the length of time between intubation and bronchoscopy. Statistical results were considered to be significant at $P \leq 0.05$. The SPSS for windows software package was used for statistical analysis.

Results

The study group included 55 men (60.4%) and 36 women (39.6%), with an average age of 55.7 ±17 years (range: 19 to 85). The characteristics of the 91 patients are summarized in Table 1. The median duration of symptoms or signs before bronchoscopy was 7 days (range: 1 day to ten years). There was one patient with a moth-eaten epiglottis and vocal cord narrowing who complained of stridor for 10 years. The most frequent symptom or sign recorded as the chief complaint in the medical charts of the patients was dyspnea (75.9%), followed by stridor (27.5%). Nevertheless, it is not uncommon for a patient to present with more than 2 symptoms or signs (25.3%).

The most common obstruction location was the trachea, followed by the vocal cord. A laryngeal lesion was found in 7 (7.7%) patients. The etiologies are listed in Table 2. The most common etiology was tracheal stenosis, followed by tracheostomy or prolonged endotracheal intubation. The etiologies may be divided into (1) post translaryngeal intubation, (2) post tracheostomy, and (3) tracheostomy tube still in place. Two types of stenosis can be

Table 1. Characteristics of patients # with upper airway obstruction

Variable	No. of patients	(%)
Gender		
Male	55	(60.4)
Female	36	(39.6)
Obstruction location		
Larynx	7	(7.7)
Vocal cord*	10	(11)
Trachea+ vocal cord	10	(11)
Tracheal	64	(70.3)
Symptoms/signs		
Dyspnea	69	(75.9)
Stridor	25	(27.5)
Hoarseness	11	(12.1)
Cough	11	(12.1)
Wheezing	5	(5.5)

Includes patients with positive findings only

* Refers to vocal cord paralysis

Table 2. Etiologies of upper airway obstruction

Variable	No. of patients	(%)	Male/female
Post-intubation	15	16.5	10/5
Post-tracheostomy	6	6.6	4/2
Tracheostomy tube still in place	25	27.3	13/12
Vocal cord palsy	10	11	5/5
Tracheal tumor	5	5.5	5/0
External compression	3	3.3	3/0
Direct extension of neoplasm	12	13.2	6/6
Laryngeal cancer	6	6.6	6/0
Other	9	9.9	3/6

observed. First, the so-called web-like stenosis is a short (<1 cm), membranous stenosis without damage to the cartilage. Second is the complex tracheal stenosis, longer, with circumferential hour glass-like contraction, scarring, or malacia [2]. If the bronchoscope could not pass through the stenostic area, we also measured the length of stenosis from adjuvant radiographs. The post-translaryngeal intubation group included 15 patients. The shapes of stenosis in this group included web-like stenosis (Figure 1) in 6, and complex stenosis in 9. The average stenosis percentage was 72.4 ±19.5%, excluding 1 patient with 10% stenosis. The stenosis occurred 1 to 5 cm below the vocal cord and was 0.5 cm to 3 cm in length. The indications for intubation included respiratory failure in 7, and operations in 8. The median delay between the tracheal intubation and the bronchoscopy was 67 days (range: 20 days to 5 years). There was no relationship among gender, age, percentage of stenosis, indication for intubation, types of stenosis, and length of time between intubation and bronchoscopy.

The post-tracheostomy group included 6 patients. The shapes of stenosis in this group included web-like stenosis in 1, and complex lesions in 5. Tracheal strictures occurred at the level of the stoma in 5, and subglottis in 1 patient (Figure 2) who had undergone translaryngeal intubation before tracheostomy. One patient was associated with vocal cord palsy. The average stenosis percentage was 61.6% (range: 30 to 90%).

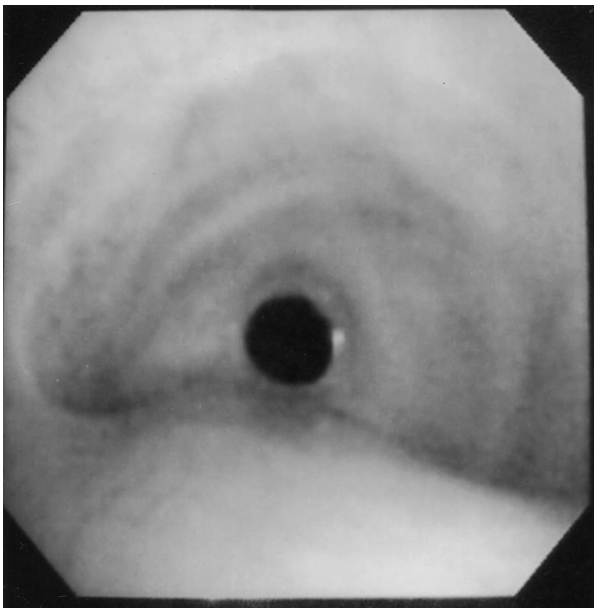

Fig. 1. Web-like stenosis, 3 cm below the vocal cord.

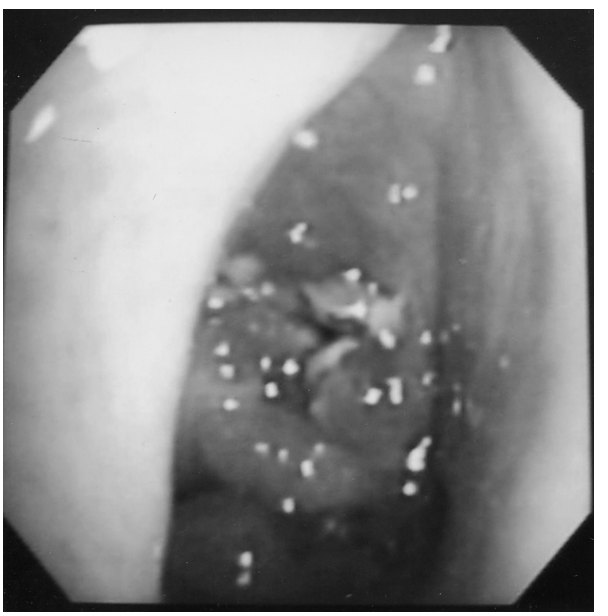

Fig. 2. Subglottic stenosis due to granulation formation with nearly total occlusion of the tracheal lumen.

Obstructive symptoms developed while the tracheostomy tube was still in place in 25 patients. Six (24%) patients were secondary to granulation forming at the tip of the tube. But we could find tracheal strictures occurring at the level of the stoma

in 8, subglottis in 8 with previous histories of translaryngeal intubations, and in a combination of the stoma and tip in 3. The causes of dyspnea in patients whose tracheostomy tubes were patent were their underlying diseases, such as pneumonia and others, and they were not suited for removal of their tracheostomy tubes. A characteristic flattening of the flow-volume loop was noted in 5 patients with tracheal stenosis as a complication of translaryngeal intubation or tracheostomy, with a reduction of the tracheal area by at least 70%.

Eight of the 10 patients who had developed upper airway obstruction solely due to vocal cord paralysis had a cardiovascular accident. The remaining 2 patients had malignancies including thyroid carcinoma in one patient and lung cancer in the other.

The causes of tracheal external compression in our study included goiters in 2, and mediastinal lymphadenopathy in 1. Five primary tracheal tumors were found, all of which were squamous cell carcinoma, with a mean initial reduction of the tracheal area by 48.8%. The etiologies of the direct extension of the neoplasm into the trachea included thyroid papillary carcinomas in 7, esophageal carcinomas in 4, and lung carcinoma in 1. Of these 12, seven were associated with vocal cord paralysis.

Six patients were diagnosed with laryngeal carcinoma (Figure 3), and were transferred to the ENT department for further treatment. Other relatively rare etiologies in our study included post-stent granulation, tracheal tuberculosis (TB), vocal cord TB, moth-eaten epiglottis combined with vocal cord narrowing, lung cancer post radiotherapy, mucopolysaccharidosis, and hypopharyngeal carcinoma post reconstruction surgery.

Among 17 patients with negative bronchoscopic findings, one patient had chronic parasinusitis complaining of stridor for 1 year, three patients had asthma history, 4 patients had chest roentgenograms because of a suspicion of having UAO, and the other patients were suspected of having UAO due to their symptoms or signs and a history of endotracheal intubation.

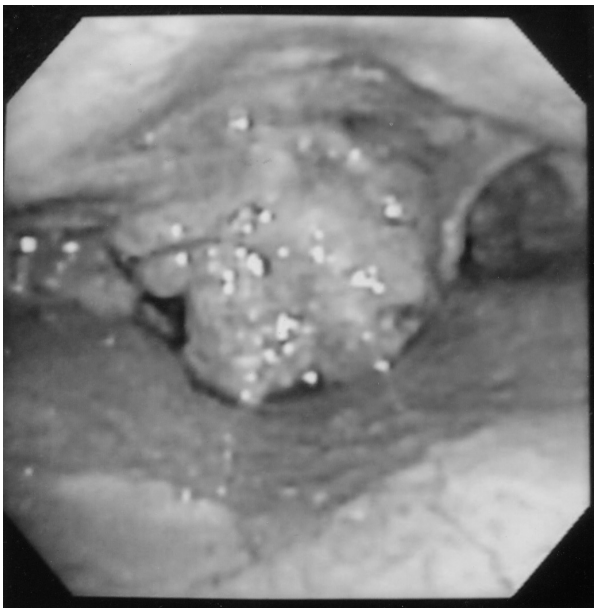

Fig. 3. Hypopharyngeal tumor causing nearly total occlusion of the vocal cord.

Discussion

A great variety of conditions affecting the upper airway, from the nasopharynx to the tracheal carina, can cause UAO. Minor obstruction is often asymptomatic, since airflow limitation is mild. However, rapid deterioration may occur if swelling or secretion increases the degree of luminal impingement during a respiratory tract infection.Reversible laryngeal edema and inflammation are the major causes of the stricture after extubation [3] Acute UAO occurs most commonly in infants and young children because of the small intraluminal caliber and greater compliance of their upper airways. The cause is often apparent from the history. The principal causes of acute UAO are infection, edema, hemorrhage, and foreign body aspiration. In contrast to acute UAO, it is not uncommon for patients with subcritical lesions to be misdiagnosed as suffering from an exacerbation of asthma or chronic obstructive pulmonary disease while the true etiology is anatomic airway obstruction [4]. Most of our patients belong to the category of chronic UAO. This is not to say that patients with negative bronchoscopic findings absolutely have no UAO. Obstructive sleep

apnea syndrome is one of the exceptions to the rule.

The symptoms and signs of UAO vary with the nature of the underlying lesions. It may be worth pointing out that 25 patients complaining of stridor had a reduction of the tracheal area by at least 50%, but 3 patients complaining of stridor had negative findings during bronchoscopy in our series. In addition, we found some patients with tracheal stenosis of less than 30% complaining of dyspnea. Their symptoms were attributed to other etiologies, such as congestive heart failure. Flow-volume curves are of interest but of little practical use in the face of a severe stenosis. Only 18 patients in our series completed this examination. It is also unsuited for patients with tracheostomy tubes in place, and is an insensitive test for UAO. Data from Miller and Hyatt suggest that a lesion must narrow the tracheal lumen to less than 8 mm before abnormalities can be detected [5]. Of the 13 patients with characteristic UAO flow-volume curve patterns in our series, all had a reduction of the tracheal area by at least 70%, or bilateral vocal cord paralysis.

The routine chest radiography usually is unrevealing. For example, one patient with 80% tracheal stenosis occurring 5 cm below the vocal cord, with a lesion about 3 cm in length was overlooked. In the post-translaryngeal intubation and post-tracheostomy groups, tracheal stenosis was detected on the chest radiograph of only 6 (28%) patients by radiologist who were not informed of the possibility of UAO, whereas the stenosis could be identified retrospectively in 15 (71%) patients. Adequate visualization of the tracheal stenosis requires the use of high kilovolts and the paying of particular attention to this region. In the group of patients with the tracheostomy tube still in place, we could not detect tracheal stenosis on the plain film because the tube itself would splint the stenosis [6] In addition, plain radiography plays a limited role in the assessment of patients who have pharyngeal or laryngeal abnormalities. Chest CT may detect airway compromise, but the test as generally performed is not sensitive. If an airway lesion is suspected, and time permits, a high resolution CT with three-dimensional airway reconstruction can prove helpful [7]. Internal rendering of 3-D reconstruction images of the airway, also referred to as virtual bronchoscopy, provides an intraluminal perspective. Virtual bronchoscopy may play a complementary role to bronchoscopy in the assessment of patients with high-grade airway stenosis, particularly with regard to assessing the patency of the airway beyond the site of a stenosis. However, this technique is limited by a high false-positive rate due to the difficulty in differentiating retained secretions from true airway lesions. This technique also has difficulty in distinguishing mucosal from submucosal disease [8].

Tracheal stenosis was present in 10% to 19% of patients after intubation in two prospective studies [9, 10], but was only symptomatic in 1% of patients [9]. The common factor in the origin of these lesions is pressure necrosis by the endotracheal tube, the tracheostomy tube, or their attached cuffs at varying points in the upper airway [11]. Although the most common cause of UAO is tracheal stenosis following tracheostomy or prolonged translaryngeal endotracheal intubation, we cannot omit other possibilities. In spite of their history of intubation, some patients suffer from UAO due to other etiologies.

A patient with severe UAO requires initial stabilization to rescue ventilation and oxygenation. Detailed bronchoscopy should be performed after the airway has been secured and appropriate gas exchange documented. Then we can plan further interventions aimed at opening the airway and maintaining patency. The treatment of choice for tracheal stenosis is surgical resection with end-to-end anastomosis. In many cases this may not be feasible because of the site and the general condition of the patient. Nonsurgical palliative methods have been developed to deal with airway stenosis. For example, endobronchial brachytherapy was used for the palliation of symptoms related to tracheal stenosis in 2 patients with tracheal tumors in our series. A greater than 50% improvement in patency has been noted post-brachytherapy without serious complication. An expandable metallic stent was introduced with a flexible bronchoscope into the stenosed

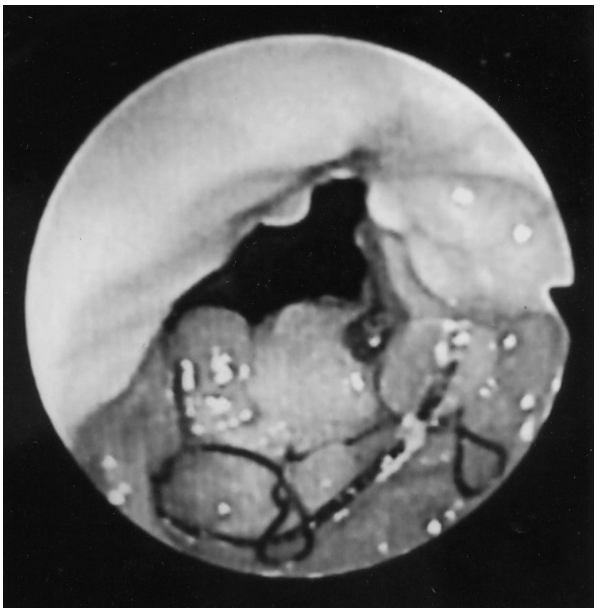

Fig. 4. Formation of granulation tissue at the proximal end of the metal stent.

trachea of a patient , which was caused by previous tracheostomy. The first follow-up bronchoscopy after stent placement was performed 1 month later. No recurrence of obstruction or stent migration was noted. But, the formation of granulation tissue at the proximal end of the metal stent (Figure 4) was noted during a meticulous follow-up. Endoscopic interventions, including electrocautery and balloon dilation, were used to restore airway patency.

During the 5-year study period, over 80% patients with suspected UAO had positive bronchoscopic findings. The early diagnosis of UAO depends on the initial complete history-taking and the detailed physical examination accompanied by attention paid to the possibility of UAO. The most common cause of UAO is tracheal stenosis occurring as a complication of translaryngeal endotracheal intubation or tracheostomy. Every patient who has been intubated or had a tracheostomy in place, and who develops dyspnea, difficulty in clearing secretions, or stridor, must be suspected of having an organic obstruction until proved otherwise. Chest roentgenograms of good quality, interpreted with a high degree of suspicion, particularly when the patient has the risk of UAO, will lead to earlier diagnosis. And we need frequently to remind ourselves of the possibility of UAO in every patient complaining of dyspnea.

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疑有上呼吸道阻塞病患之支氣管鏡檢查結果分析

方文豐　吳沼漪　王逸熙　吳自成　賴永發　王瑞隆

前言：很多侵犯鼻咽至氣管隆凸間呼吸道的狀況會造成上呼吸道阻塞。及早診斷出上呼吸道阻塞是很重要地，因為它可能會導致嚴重的呼吸問題甚至呼吸衰竭。本文目的在探討於疑有上呼吸道阻塞病患之支氣管鏡檢查結果分析。

材料與方法：我們回溯性分析自從 1998 年 2 月到 2003 年 3 月間，在高雄長庚紀念醫院因為疑似有上呼吸道阻塞之病患而來接受支氣管鏡檢查之檢查結果，一共有 108 位病患。並且由病歷中分析其相關資料。

結果：支氣管鏡檢查有所發現者超過八成。最常見之症狀或徵兆為呼吸困難，其次為喘鳴。最常見之阻塞部位在氣管，其次在聲帶。最常見之病因是因為曾經接受氣管內插管，或氣管造口術之氣管狹窄後遺症（佔 50.3%）。然而，在年齡、性別、氣管狹窄之比率、接受氣管內插管之原因、氣管狹窄之形狀、接受氣管內插管和接受支氣管鏡檢查之時距上並無相關性存在。我們也注意到其他造成上呼吸道阻塞的病因，例如因為腫瘤而導致聲帶麻痺等等。

結論：對於抱怨會喘的病患，我們應該常常保持警覺性，看看病患是否有上呼吸道阻塞。當病患有上呼吸道阻塞的可能性時，品質良好的胸部X光並且仔細判讀可以幫助提早診斷。***(胸腔醫學 2003; 18: 402-408)***

關鍵詞：上呼吸道阻塞，支氣管鏡術，喘鳴

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Experience with Pigtail Tube Drainage Treatment for Spontaneous Pneumothorax With and Without a Water Seal

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Yi-Chang Cheng*, Wei-Kung Chen*, Te-Chun Hsia, Wu-Huei Hsu

We report our experience with pigtail tube drainage in the treatment of spontaneous pneumothorax, including the use of the pigtail with a one-way-valve bag only and with the water-sealed bottle system, and compare this to the traditional chest tube thoracotomy. One hundred and seventy patients were included and analyzed. One hundred and three patients were treated with the pigtail tube (82 patients were treated with a pigtail tube connected to a one-way-valve bag, and 21 with an underwater seal), and 67 patients were treated with the traditional chest tube. The extubation time, mean hospital stay, evacuation rate, and total cost were similar, without significant statistical difference. In the chest tube group (success rate, 78%), fifteen patients underwent surgical intervention due to delayed resolution, hemopneumothorax, and personal considerations; and in the pigtail group (success rate, 70%), thirty-one patients underwent other procedures for pneumothorax, including chest tube insertion and surgical intervention. This verifies our initial suspicion that the pigtail drainage system is effective but not superior to the chest tube system. Between the two subgroups using the pigtail drainage system (one with a one-way-valve bag and one with an underwater-sealed bottle), the extubation time, mean hospital stay, and evacuation rate were similar, but the total cost was higher in the underwater seal group. Therefore, when considering ambulatory ability and good patient compliance, pigtail tube drainage with a one-way-valve bag system can be considered the initial treatment of choice for spontaneous pneumothorax. ***(Thorac Med 2003; 18: 409-418)***

Key words: chest tube, pigtail, spontaneous pneumothorax

Introduction

The term pneumothorax was first coined in 1803 by Itard, and its clinical features were described by Laennec in 1819 [1]. Pneumothorax is defined as air accumulation in the pleural cavity with secondary lung collapse. Primary spontaneous pneumothorax is idiopathic, and often occurs in healthy patients. In a recent study, spontaneous pneumothorax was shown to affect over 20,000 patients per year in the United States, and accounted for nearly $130 million in health-care expenditures [2]. Hospital admissions for pneumothorax occurred at an overall incidence of 16.7/100,000 persons per

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year, and at 5.8/100,000 for men and women in England [1]. Even so, there are no demonstrable guidelines for treating spontaneous pneumothorax, and management tends to differ, based on the experience of the physician.

The initial management for symptomatic and large-sized spontaneous pneumothorax is to evacuate air from the pleural space. The underwater-sealed chest tube has been the treatment of choice for decades [3,4]. However this modality requires the patient to stay in bed almost all day, and carries the possible risks of effusion reflux due to bottle elevation, breakage, and leakage from the connections of the bottle system. Therefore, alternative devices for improving compliance, such as the Heimlich flutter valve system [5,6] and the small-bore catheter (including the pigtail tube), have been developed and promoted [7-13]. In recent studies, some researchers have demonstrated the successful evacuation of spontaneous pneumothorax with a small-bore catheter [7,12]. However, it is not known whether this system is as good as the chest tube. Questions regarding efficacy, hospital days, extubation days, total expense, and recurrence, compared with the conventional large-bore chest tube, have remained unanswered thus far. Even in recent studies regarding the small-lumen catheter draining system for pneumothorax, controversy has persisted regarding the tube size, attachment to the Heimlich flutter valve [13,17], active aspiration [8,10,12,16], the underwater seal [14], and whether or not to use suction. And most importantly, is the pigtail catheter a reliable device for all spontaneous pneumothorax patients? Can it be used more confidently attached to a water seal?

Herein, we report our experience and results in using a small-bore catheter (pigtail) connected both to a one-way-valve drainage bag system and to a water-sealed bottle system, and also compare the outcome and clinical efficacy of pigtail drainage and the standard water-sealed chest tube in the treatment of spontaneous primary pneumothorax.

Patients

We retrospectively collected and reviewed the data of patients with spontaneous pneumothorax treated at China Medical College Hospital from January 1997 to September 2002. The study population was determined by reviewing the charts of patients who were discharged with the diagnosis of spontaneous pneumothorax (International Classification of Diseases code 512.8), excluding congenital and traumatic diseases, tuberculosis, and current lung disease. The individual patient's chart and chest X-ray (CXR) were carefully reviewed. Only symptomatic patients with a confirmed diagnosis, an adequate follow-up CXR, and initial treatment with a chest tube or pigtail, were included in the final study population.

In all, 223 patients with spontaneous pneumothorax, including 175 males and 48 females, were screened in our series. Fifty-three were excluded from analysis for the following reasons: observation only (n=21, the average size of the pneumothorax was 21.8%); and direct operation (n=32, 31 patients with recurrent pneumothorax, and one case due to personal reasons). After screening, only 170 patients were enrolled in our series, including 134 (78.8%) males and 36 (21.2%) females. The mean age was 27 (range, 14 to 80). One hundred and three patients were initially treated with a pigtail (82 with a one-way-valve bag and 21 with a water seal), and 67 received conventional chest tubes.

Methods

Tube Intubation

The choice of treating spontaneous pneumothorax patients with observation, tube insertion, or operation was assessed and determined by clinical physicians. In patients undergoing pigtail drainage, a chest echo was performed first for guidance, then the pigtail (8, 10 Fr) with a trocar system was inserted into the superior part of the 4th rib at the middle axillary line, after a local anesthesia had been injected, and dilated with a surgical blade, with the patient in a sitting position. The catheter was then connected to a one-way-valve drainage bag or water-sealed bottle collection system. Air, and even

pleural effusion, was released from the bag when full, or directed from the collection bottle, and the patient was closely followed up with a CXR (after almost 8 hrs, 24 hrs, and 48 hrs). Once there was no longer air drainage from the pigtail system, and the lung had reached almost full expansion, as revealed by CXR, the pigtail was extubated. Patients were discharged when there were no more clinical symptoms and no air accumulated in the pleural space, as determined by close observation and follow-up CXR. The chest tube group followed the conventional procedure [3,4]. The timing of the follow-up CXR, and the decision-making regarding extubation and discharge, were similar to the pigtail group.

Data Collection and Statistics

The clinical data and information gathered for each patient included gender, age, initial symptoms, the size of the pneumothorax according to the CXR (using the Light index) [3,4,18], the involved side, treatment methods, the follow-up pneumothorax size, days of hospital stay, extubation time, complications, reasons for changing treatment, and total expense. Extubation time was calculated from the date and time of tube insertion.

Multivariate analysis was done with one-way ANOVA (SPSS statistical software for Windows; statistical significance = $p<0.05$).

Results

Among the 170 enrolled patients, clinical symptoms included chest pain (N=138, 81.2%), dyspnea (N=19, 11.2%), and tachypnea (N=26, 15.3%). Seventy-one patients (41.8%) had right-side pneumothorax and 98 patients (57.6%) had left-side pneumothorax. No significant differences were found between the two groups with respect to the demographic characteristics shown in Table 1. In the subgroups, 82 patients underwent pigtail tube drainage with a one-way-valve bag system and 21 patients used a water seal. The subgroup data are shown in Table 2.

Table 1. Demographic characteristics of spontaneous pneumothorax patients treated with a chest tube and with a pigtail

	Treated with Chest Tube (%)	Treated with Pigtail (%)	All (%)
Numbers	67	103	170
Gender			
Male	55 (82.1)	79 (76.7)	134 (78.8)
Female	12 (17.9)	24 (23.3)	36 (21.2)
Mean age (Mean ± SD)	25.7 ± 10.7	27.2 ± 13.9	26.6 ± 12.7
Range	14-73	14-80	14-80
Area			
Left	39 (58.2)	60 (58.3)	98 (57.6)
Right	28 (41.8)	43 (41.7)	71 (41.8)
Hx of penumothorax			
First	53 (79.1)	79 (76.7)	132 (77.6)
Recurrent	14 (20.9)	24 (23.3)	38 (22.4)
Symptom			
Chest pain	50 (74.6)	88 (85.4)	138 (81.2)
Dyspnea	5 (7.5)	14 (13.6)	19 (11.2)
Tachypnea	7 (10.4)	19 (18.4)	26 (15.3)
Mean size of pneumothorax (Mean ± SD)*	55.1 ± 26.6	55.9 ± 23.5	55.6 ± 24.7

* The sizes of the pneumothorax were calculated using the Light index [3,4,18].

Table 2. Demographic characteristics of spontaneous pneumothorax patients treated with a pigtail one-way-valve bag system and with a pigtail underwater-sealed bottle system.

	Treated with Pigtail-bag System (%)	Treated with Pigtail-underwater Bottle System (%)	All (%)
Numbers	82	21	103
Gender			
Male	62 (75.6)	17 (81)	79 (76.7)
Female	20 (24.4)	4 (19)	24 (23.3)
Mean age (Mean ± SD)	26.6 ± 12.7	29.7 ± 18.0	27.2 ± 13.9
Range	16-76	14-80	14-80
Area			
Left	47 (57.3)	13 (61.9)	60 (58.3)
Right	35 (42.7)	8 (38.1)	43 (41.7)
Hx of penumothorax			
First	65 (79.3)	14 (66.7)	79 (76.7)
Recurrent	17 (20.7)	7 (33.3)	24 (23.3)
Symptom			
Chest pain	64 (78.0)	20 (95.2)	84 (81.6)
Dyspnea	15 (18.3)	6 (28.6)	21 (20.4)
Tachypnea	11 (13.4)	8 (38.1)	19 (18.4)
Mean size of pneumothorax (Mean ± SD)*	54.9 ± 24.4	59.9 ± 19.7	55.9 ± 23.5

* The sizes of the pneumothorax were calculated using the Light index [3,4,18].

We examined various data associated with the two major procedures. The results (summarized in Table 3) were as follows: patients using the pigtail catheter had fewer extubation days, but more hospital days and total cost, and the resolution rate with the pigtail was slower. None of these differences reached statistical significance. Fifty-two of 67 patients who underwent a chest tube procedure obtained full expansion in the affected lung and successful discharge (success rate, 78%). Fifteen of 67 patients receiving chest tube treatment underwent a further operation due to delayed resolution (N=5), hemopneumothorax (N=2), or personal reasons (N=8).

Seventy-two of the 103 patients whose initial treatment was pigtail decompression obtained full expansion in the affected lung and successful discharge (success rate, 70%). In the two subgroups (pigtail with one-way-valve bag and pigtail with an underwater-sealed bottle system), data were calculated and the results were as follows (summarized in Table 4): fewer extubation days, shorter hospital stay, and lower total cost were noted in the pigtail with one-way-valve bag group. A faster evacuation rate was also noted in this group. Only in total cost was there a significant difference. Thirty-one of 103 patients in the pigtail-treated group were changed to other procedures. In one subgroup (pigtail with one-way-valve bag, N=82), 22 patients underwent a further procedure due to delayed resolution (N=11), recurrent pneumothorax (N=3), hemopneumothorax (N=2), bil. pneumothorax (N=1), or personal reasons (N=5). Five of 16 patients received a chest tube instead of the pigtail due to delayed resolution, and were discharged when they had finally reached full expansion. Eleven of 16 patients were changed to chest tube drainage and then referred to chest surgery for operation due to persistent bronchopleural fistula (N=5), bilateral pneumothorax (N=1), hemopneumothorax (N=1),

Table 3. Comparison of lengths of extubation, evacuation rate, days of hospital stay, and total cost in spontaneous pneumothorax patients treated with a pigtail catheter and a chest tube*.

	Pigtail (N=103)	Chest tube (N=67)	p-value
Extubation days	5.3	5.6	0.052
Evacuation rate* (% per hour)	10.6	14.5	0.168
Hospital stay	8.6	8.1	0.811
Total cost	NT$32683	NT$23946	0.350

* The evacuation rate is the absorption percentage per hour, and is calculated by comparing the pneumothorax size as seen in the series of CXRs [3, 4,18].

Table 4. Comparison of lengths of extubation, evacuation rate, days of hospital stay, and total cost in spontaneous pneumothorax patients treated with the pigtail one-way-valve bag and pigtail with underwater seal*.

	Pigtail with one-way-valve bag (N=82)	Pigtail with underwater sealed (N=21)	p-value
Extubation days	5.1	5.5	0.682
Evacuation rate* (% per hour)	12.8	9.2	0.607
Hospital stay	8.5	8.9	0.862
Total cost	NT$22229	NT$55525	0.001

* The evacuation rate is the absorption percentage per hour, and is calculated by comparing the pneumothorax size as seen in the series of CXRs [3, 4,18].

or personal considerations (N=4). The other six patients were directly changed to operation due to recurrent pneumothorax (N=3), delayed resolution (N=1), hemopneumothorax (N=1), and personal considerations (N=1).

In the next subgroup (pigtail with an underwater-sealed bottle system, N=21), one of two patients received a chest tube instead of the pigtail due to delayed resolution, and was discharged when he had finally reached full expansion. The other patient had received pigtail treatment, but was changed to chest tube intubation, and finally underwent an operation due to delayed resolution. Seven patients were referred to the chest surgeon for operation due to delayed resolution (N=4), recurrent pneumothorax (N=2), and a giant bleb noted on the CXR (N=1).

Other variable factors of the pigtail and chest tube groups, such as the involved lung (left or right side), and first episode or recurrence, were analyzed. These results are listed in Table 5 and Table 6. The data revealed a shorter extubation time in the pigtail group. The admission stay and total costs were higher in patients treated with the pigtail. The pigtail resolution rate was still lower than that of the chest tube. In right-side and first episode pneumothorax, the extubation rate in the chest tube group was higher than in the pigtail group, and reached statistical significance.

Discussion

The goals of treatment in patients with pneumothorax are relief of pain and relief of respiratory distress in the acute phase. This is accomplished by air evacuation and re-expansion of the lung. In asymptomatic patients and patients with a small amount of pneumothorax (often less than 20%) [3, 4], observation and a close follow-up is often sufficient. However, in patients with a large amount of pneumothorax (over 25%), evacuation of the pleural air is needed. Treatments include simple needle aspiration, chest tube thoracostomy with or without the instillation of a sclerosing agent, negative pressure suction, thoracoscopy with the stabi-

Table 5. Comparison of the lengths of extubation, evacuation rate, days of hospital stay, and total cost between the two lung fields*.

	Right side Pneumothorax			Left side Pneumothorax		
	Pigtail	Chest tube	p-value	Pigtail	Chest tube	p-value
Extubation	5.4	6.2	0.263	5.0	6.2	0.082
Evacuation rate* (% per hour)	8.5	17.1	0.028	14.1	18.1	0.552
Hospital stay	9.7	8.2	0.534	7.9	8.6	0.560
Total cost	NT$26238	NT$22890	0.601	NT$32499	NT$25817	0.362

* The evacuation rate is the absorption percentage per hour, and is calculated by comparing the pneumothorax size as seen in the series of CXRs [3, 4,18].

Table 6. Comparison of the lengths of extubation, evacuation rate, days of hospital stay, and total cost between the first episode and recurrence*.

	First episode of pneumothorax			Recurrent pneumothorax		
	Pigtail	Chest tube	p-value	Pigtail	Chest tube	p-value
Extubation	5.3	5.7	0.139	6.0	8.1	0.227
Evacuation rate*(% per hour)	9.3	18.2	0.030	19.6	13.7	0.659
Hospital stay	8.2	7.9	0.838	10.4	10.4	0.993
Total cost	NT$23654	NT$22508	0.497	NT$43510	NT$36368	0.506

* The evacuation rate is the absorption percentage per hour, and is calculated by comparing the pneumothorax size as seen in the series of CXRs [3, 4,18].

lizing of blebs and instilling of a sclerosing agent or pleural abrasion, and open thoracotomy.

The frequently used initial treatment method is standard chest tube thoracostomy with an underwater-sealed chest tube. However, this treatment limits the patient's ambulatory ability, and increases possible leaking risk in the tube connection. The more sophisticated methods have included the Heimlich flutter valve [5], in which one side is connected to the chest tube and the opposite side is open to the air. The flutter valve allows the escape of air in the pleural cavity and prevents air reflux. However, this method is limited in use when the air is mixed with pleural effusion in the tube. Sargent and Turner (1970) also described a catheter technique for pneumothorax, which results in less pain and a smaller wound, allows patients to be ambulatory, and is an easy way for doctors to perform pneumothorax treatment. Even so, the use of small-bore catheter drainage for pneumothorax is not widespread. In recent years, many studies have revealed that pneumothorax can be treated with a small-bore catheter only, with full expansion later [7-17]. Investigators have found that the usefulness of the small-bore catheter is no less than that of the chest tube, especially regarding patient convenience, hospital stay, and health care costs [16]. These results are consistent with our clinical experience. We have also succeeded in treating iatrogenic and secondary spontaneous pneumothorax with this method.

In our series, the pigtail catheters (8, 10 Fr) were inserted with echo guidance. A chest echo was performed at bedside before the procedure for the following reasons: 1., to confirm the diagnosis of pneumothorax with an echo finding (with an absence of a pleural gliding sign or a comet-tail sign [19]), and 2., to evaluate the presence of pleural effusion and locate the solid organ position.

A few technical factors have been noted in the placement of the chest tube and pigtail. In theory, if the opening of the catheter is too low, it will not adequately drain the pleural air from the pleural apices, and will probably induce loculated pneumothorax. The classical opening has been the 2nd intercostal space. However we placed the pigtail at

the 4th intercostal space and mid-axillary line. It was not attached to the apex. The results showed there was no significant difference between the pigtail tube and the chest tube. It is worthy of note that this insertion location decreased the possibility of injury to the internal thoracic artery. A rapid expansion of the lung parenchyma could be related to ipsilateral or bilateral pulmonary edema. This has happened in patients with a prolonged presence of pneumothorax when a high negative pressure suction was used [3]. Most physicians agree that negative pressure suction is an alternative treatment when patients have persistent symptoms and a failed lung expansion [2]. None of our patients suffered severe symptoms of re-expansion pulmonary edema. Only subcutaneous emphysema (N=5) and wound bleeding (N=1) were noted.

In our series, there was no significant difference among the 170 cases we studied with regard to the disturbance, average, and severity of pneumothorax. In earlier years, most patients received chest tube decompression therapy. We began treating spontaneous pneumothorax with a pigtail catheter in 1997. From Sep 2001 to Sep 2002, 68 patients were included in our study after the initial results that the pigtail tube drainage system for spontaneous pneumothorax was not less effective than the chest tube, were made known [20]. Fifteen patients underwent chest tube intubation decompression drainage, and the other 53 patients received a pigtail tube drainage system (including all 21 patients who received a pigtail tube with a water seal).

During this time, we found that it was difficult to encourage some weak patients and some elderly patients to cough or do respiratory exercises. Most clinical physicians may choose to perform manual aspiration with a 20 cc syringe or a one-way-valve bag attached to the negative pressure suction. The amount of drained air is easy to calculate with the one-way-valve bag, but the bag still needs frequent manual deflection. Some physicians may choose pigtail tube drainage with an underwater-sealed bottle system as an initial treatment, when considering reliability and continuous evacuation. However, after this procedure and with limited ambulation, does it really work better than the one-way-valve bag alone?

Among all our patients treated for pneumothorax, we found no significant difference between the chest tube and the pigtail as an initial treatment method for spontaneous pneumothorax. The time required until extubation was shorter in the pigtail group, however the admission days and total costs were higher, but with no statistically significant difference. The evacuation rate was also lower in the pigtail group. The single pigtail drainage system's successful evacuation rate was 70.0%. Regarding the treatment failure patients who initially received the pigtail catheter, 18 underwent chest tube insertion and only six of the 18 patients attained a complete evacuation of air. Twelve of them ultimately needed an operation. In the beginning of the study, we arranged chest tube decompression for poorly evacuated pneumothorax patients treated initially with a pigtail. We found no significant difference between those patients who initially underwent pigtail tube drainage, but whose drainage had failed and were later shifted to a chest tube, and those patients who received a chest tube as initial treatment. In the latter period of our study, 13 patients who failed to evacuate the pneumothorax directly underwent an operation and attained a complete evacuation.

In the pigtail with a one-way-valve bag and with a water seal subgroups, the results were noteworthy. Originally, we considered that the underwater-sealed group may be better in evacuation and have a shorter admission stay and lower total cost. The data revealed that patients who underwent a pigtail with a water seal needed a longer time until extubation, longer hospital stays, and higher total cost. We then added the time factor as a dependent variable (since the water seal method was used for only one year), but the results remained the same. One possible reason was that the patient number was not high enough, and another reason was that physicians tended to chose more severe patients, often with limited ambulation, to receive the water seal method of treatment, and who underwent operations ultimately when there was delayed evacuation

or a persistent air leak. In conclusion, the use of the water seal did not show an increasingly significant effectiveness in our study. These results are pending further large group surveys.

The benefits of the pigtail method include its ease of performance, fewer clinical procedures for physicians, less trauma and discomfort for the patient, and no ambulatory limitation. This method provides immediate relief for the patient, and may even be considered on an outpatient basis. When treating weak and severe patients, the manual aspiration method, or using an underwater seal attached to a vacuum, is suggested. However, the issue of the effectiveness of the pigtail compared to the chest tube is pending further exploration. In addition, there was no significant difference in the effectiveness of the one-way-valve bag group and the underwater-sealed bottle group. Interpretation of the current literature has been difficult due to various issues, such as small patient numbers, and the principle issue of a lack of prospective randomized trials comparing the two methods of treatment. These issues require further investigation, preferably in the context of a large randomized, prospective trial.

In conclusion, our results showed that the pigtail with one-way-valve bag drainage appears to be a safe and promising technique in the treatment of spontaneous pneumothorax. We recommend that pigtail tube drainage be considered as the initial treatment of choice in patients with spontaneous pneumothorax.

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自發性氣胸以豬尾巴管治療包括單向閥門引流袋及水下引流之處理經驗

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在此我們報告以豬尾巴管治療治療原發性自發性氣胸之經驗，包括以豬尾巴管連接單向閥門引流袋及連接水下引流瓶系統，並與傳統胸管引流術作比較。從 1997 年 1 月到 2002 年 9 月，我們分析了 170 位原發性自發性氣胸之病人，其中 103 人接受豬尾巴管引流治療（82 位病人接受豬尾巴管連接單向閥門引流袋治療，21 位接受以豬尾巴管連接水下引流瓶系統），其餘 67 位接受傳統胸管引流術治療。在拔管時間、住院日、吸收速度、及住院費用比較上接近，並無顯著差異。以傳統胸管引流之成功率為 78%，15 位病人因吸收效果不佳、發生血胸或個人因素後續接受手術治療；而以豬尾巴管治療之成功率為 70%，有 31 位病人亦因相同原因後續接受其他治療包括以胸管引流或手術治療。在豬尾巴管連接單向閥門引流袋治療及連接水下引流瓶系統之間的比較上：水下引流瓶組在拔管時間、住院日、吸收速度未呈現明顯優勢，而住院費用反而較高。以豬尾巴管治療原發性自發性氣胸是明顯有效，但並未優於傳統胸管引流術，這與我們起初的假設符合，但加上考慮簡易技術施行、病人行動方便性、較小的傷口及病人舒適性，以豬尾巴管連接單向閥門引流袋可以考慮當作原發性自發性氣胸的第一線治療。***（胸腔醫學 2003; 18: 409-418）***

關鍵詞：氣胸，胸管，豬尾巴管

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High-Frequency Oscillatory Ventilation in Adult Patients With Acute Respiratory Distress Syndrome Plus Air-Leak Syndrome

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Objective: There have been a limited number of studies on the improvement of gas exchange in adult patients with acute respiratory distress syndrome (ARDS) through the use of high-frequency oscillatory ventilation (HFOV). The aim of this study was to evaluate the efficacy of HFOV as a rescue therapy in adult patients with ARDS complicated by air-leak syndrome.

Method: From January 1999 to August 2002, 17 adult ARDS patients with air leakage were diagnosed in the medical intensive care unit (ICU). Four patients underwent HFOV due to refractory hypoxemia and/or hypercapnia under conventional ventilation (CV). The other 13 patients continued CV support. The changes in gas exchange and ICU mortality were analyzed. All of the data are expressed as mean ± SEM.

Results: In all subjects, positive end-expiratory pressure and peak inspiratory pressure were significantly lower one day after air leakage (p=0.005 and p=0.033, respectively). $PaCO_2$ and PaO_2/FiO_2 (oxygenation index, OI) showed insignificant change 3 days after air leakage. In the HFOV group, the mean duration from air-leakage to the initiation of HFOV was 10.8 ± 4.3 days. The percentages of change in OI and $PaCO_2$ on the third day of HFOV use were 69.7 ± 56.3%, and -13.7 ± 7.1%, respectively, compared to pre-HFOV use. Two HFOV patients (50%) from the ICU survived. Twelve of 13 CV patients (92.3%) had significant deterioration in gas exchange before mortality, and expired in the course of their stay in the ICU, with a mean of 16.5 ± 3.5 days after air leakage.

Conclusion: The study suggests that HFOV may be used as a rescue ventilatory modality when conventional ventilation cannot maintain adequate gas exchange in patients with ARDS with air-leak syndrome. ***(Thorac Med 2003; 18: 419-426)***

Key words: High-frequency oscillatory ventilation, acute respiratory distress syndrome, barotrauma, pneumothorax, air leakage

Introduction

Acute respiratory distress syndrome (ARDS), induced by various local or systemic inflammatory processes, causes a pulmonary complication with high mortality and morbidity. All patients suffer from a severe impairment of pulmonary gas exchange, and as such, mechanical ventilatory support

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plays an important role in the management of ARDS. The study results of ARDS Network provided a so-called *lung protective strategy* – i.e, low tidal volume and high positive end-expiratory pressure (PEEP) with a plateau airway pressure of no more than 35 cmH_2O [1]. This ventilatory strategy could protect patients from further barotrauma that might be induced by the preceding high tidal volume setting.

However, despite this lung protective principle, air leak syndromes, such as pulmonary interstitial emphysema, pneumothorax, subcutaneous emphysema, and pneumomediastinum, still commonly complicate the course of ARDS. Although Weg et al suggested that air leaks were not associated with a poor prognosis [2], air leaks will make ventilatory management difficult. Airway pressure must be decreased for the healing of the pneumothorax and a decrease in the air leak. In the meantime, high PEEP is often needed to maintain adequate oxygenation with ARDS. Therefore, there is a dilemma between what is needed for the management of air leaks and adequate oxygenation in ARDS.

In theory, high-frequency oscillatory ventilation (HFOV) is a ventilatory mode in accordance with the current lung protective strategy. In addition, HFOV yields a lower peak air pressure and a smaller tidal volume than does conventional ventilation, which is possibly more beneficial in terms of managing air leaks. The experience with HFOV in neonatal respiratory distress syndrome (RDS) and pediatric air leaks is promising [3-7]. Recently, a randomized controlled prospective trial has proven HFOV to be an effective and safe mode in the ventilatory support of ARDS [8]. However, reports regarding the use of HFOV for adults with ARDS and air-leak syndrome are lacking. The aim of this study was to present our experience at National Taiwan University Hospital in the use of HFOV to treat adult patients with ARDS complicated with air leaks.

Method

The study population was selected from the medical intensive care unit (ICU) of National Taiwan University Hospital. From January 1999 to August 2002, 66 adult patients (older than 18 years of age) were diagnosed with ARDS, and 17 of these patients (25.8%) were complicated with air-leak syndrome. The medical records were reviewed. The diagnosis of ARDS was made based on the definition of the American-European Consensus Conference: (1) acute onset, (2) pulmonary artery wedge pressure less than 18 mmHg or no evidence of left atrial hypertension, (3) bilateral infiltrates in the chest radiograph, and (4) $PaO_2/FiO_2 \leq 200$mmHg [9]. Air-leak syndrome was defined as any air extrusion outside the tracheobronchial tree, including pulmonary interstitial emphysema, pneumothorax, subcutaneous emphysema, and pneumomediastinum.

Four patients (the HFOV group) underwent HFOV (3100B, Sensormedics, Yorba Linda, CA) as a rescue therapy due to refractory hypoxemia and/or hypercapnia, under conventional ventilation and adequate medical treatment. The definition of refractory hypoxemia was blood oxygen saturation that could not be kept more than 88%-90% in the fraction of oxygen (FiO_2) below 0.6. Meanwhile refractory hypercapnia was defined as $PaCO_2$ more than 50 mmHg, with pH ≤ 7.30. Thirteen patients (the CV group) were kept under conventional ventilatory support during the course of their ICU stay.

The primary end-point was the change in gas exchange (PaO_2/FiO_2 and arterial blood gas). The arterial blood gas data before the air-leak syndrome and HFOV use and those 3 days after the air-leak syndrome and HFOV use, were recorded. The levels of positive end-expiratory pressure (PEEP) and peak inspiratory pressure (PIP) during these periods were also recorded. The secondary end-point was the ICU outcome.

All of the data were expressed as mean ± standard error (SEM). The comparison of the parameters of arterial blood gas after the air-leak syndrome and HFOV was made using a non-parametric test – the Wilcoxon Signed Ranks test. The differ-

ences between the CV and HFOV groups were also made using another non-parametric test – the Mann-Whitney test. A value of $p < 0.05$ was taken as statistically significant.

Results

The demographic and baseline characteristics are illustrated in Table 1. The causes of ARDS were pneumonia (14/17), urosepsis (1/17), transfusion-related acute lung injury (1/17), and acute interstitial pneumonitis (1/17). There was no significant difference in the APACHE II scores, airway pressure levels (PIP and PEEP) before air leakage, and the parameters of gas exchange, between the two groups.

The occurrence of the air leak was 8.3 ± 2.7 days after ARDS (range: 1-42 days). In 10 patients (8 in the CV group and 2 in the HFOV group), air leaks persisted throughout the whole ICU course. An upward trend for $PaCO_2$ developed after air leakage occurred, as shown in Figure 1. In the HFOV group, the arterial blood gas parameters before launching HFOV deteriorated in comparison with the 3rd day after the air leak (Figure 1). The PEEP level 3 days after the air leak was significantly lower than before the event ($p = 0.005$, 0.004, and 0.008 on days 1, 2, and 3, respectively). PIP on the first day after the air leak was also significantly lower, though it did not achieve statistical significance on the 2nd and 3rd day after the air leak ($p = 0.033$, 0.261, and 0.113, respectively), as illustrated in Figure 2. The physician's adjustment of the ventilator setting played a major role in lowering PIP and PEEP. The decrement of airway pressure after the air-leak syndrome could be explained by the attempt to decrease and further heal the air leaks.

The demographic and clinical characteristics of the HFOV group are shown in Table 2. The mean duration from air leak to the initiation of HFOV was 10.8 ± 4.3 days. The period of HFOV use was 4.8 ± 1.5 days. No complications associated with HFOV were noted in these four cases. The parameters of arterial blood gas and their percent of change within 3 days after HFOV use are illustrated in Table 3 and Figure 3.

Cases 1 and 2 showed beneficial gas exchange responses to HFOV. Though delayed improvement in blood gas was observed till the 7th day of HFOV in Case 3 (the percent of change in the oxygenation index (OI) on the 7th day of HFOV was +17.5%), subcutaneous emphysema improved soon after HFOV was initiated. The mean percent of change

Table 1. Demographic data and baseline characteristics of the subjects.

	Total (n=17)	Group CV (n=13)	Group HFOV (n=4)
Age	70.5 ± 3.9	68.9 ± 5.0	75.5 ± 3.4
Sex (M/F)	10/7	7/6	3/1
Preexisting lung diseases (n)	6	3	3
Malignancy (n)	5	4	1
APACHE II	24.6 ± 1.8	23.9 ± 1.7	26.8 ± 5.8
Baseline PaO_2/FiO_2 (mmHg)	114.1 ± 8.0	107.2 ± 9.4	136.3 ± 9.5
Baseline $PaCO_2$ (mmHg)	40.7 ± 2.8	40.2 ± 3.5	42.5 ± 2.8
The onset of air leak (Days)	8.3 ± 2.7	9.6 ± 3.5	4 ± 2.1
PIP before air leak (cmH_2O)	34.5 ± 1.9	36.1 ± 1.9	30.8 ± 4.3
PEEP before air leak (cmH_2O)	9.8 ± 0.9	10.6 ± 0.9	7.0 ± 2.3

Data represent means ± SEM

CV = conventional ventilation. HFOV = high-frequency oscillatory ventilation. APACHE II = Acute Physiology and Chronic Health Evaluation II. PIP = peak inspiratory pressure. PEEP = positive end-expiratory pressure.

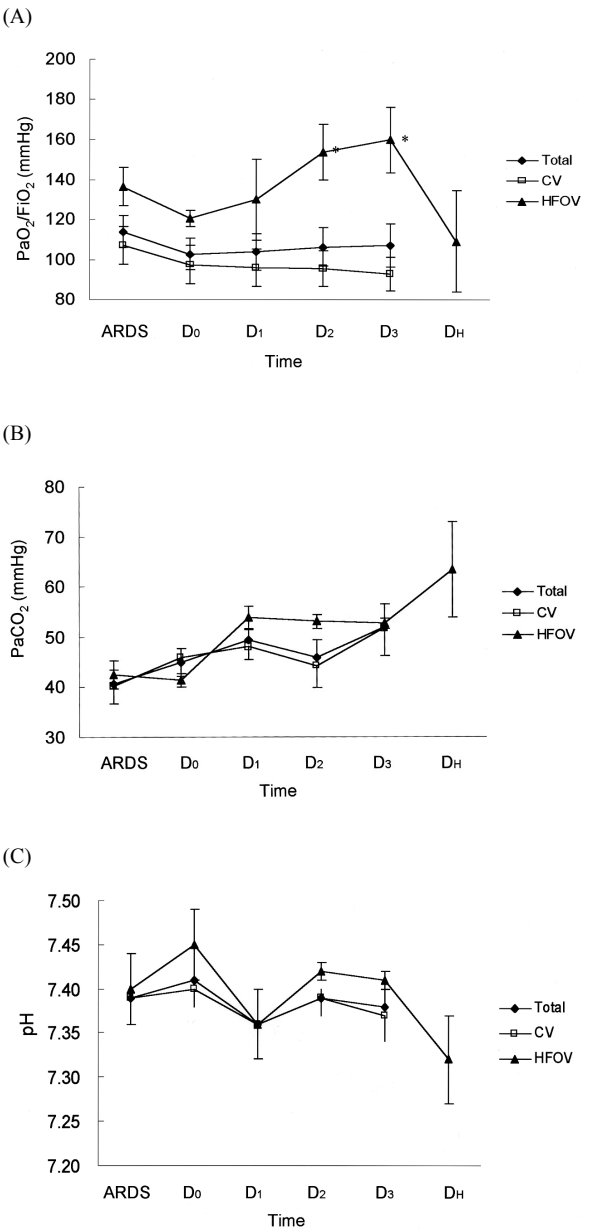

Fig. 1. Changes in the parameters of arterial blood gas before and within 3 days after the air-leak syndrome. (A) PaO_2/FiO_2 (B) $PaCO_2$ (C) pH. ARDS = the day that subjects were diagnosed as acute respiratory distress syndrome; CV = conventional ventilation; HFOV = high-frequency oscillatory ventilation; D_0 = the day before the air-leak syndrome. D_1, D_2, and D_3 represent the first, second, and third day after the air-leak syndrome. D_H = the day before launching HFOV. In the total population and the subgroups, air-leak syndrome didn't cause significant changes in gas exchange except a trend toward a $PaCO_2$ increment. PaO_2/FiO_2 on the second and third day after air leakage in the HFOV group was significantly higher than the CV group. Though not achieving significance, gas exchanges tended to deteriorate before initiating HFOV. Error bars are meant to be ± SEM.

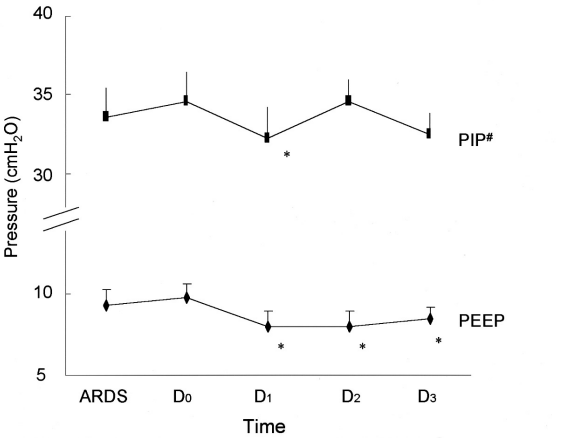

Fig. 2. Mean positive end-expiratory pressure and peak airway pressure in the total population. PEEP = positive end-expiratory pressure. PIP = peak airway pressure. ARDS = the day that subjects were diagnosed as acute respiratory distress syndrome; D_0 = the day before the air-leak syndrome. D_1, D_2, and D_3 represent the first, second, and third day after the air-leak syndrome, respectively. PEEP was significantly lower during the 3 days after the air-leak syndrome than before it. PIP only on the first day after the air leak was lower than before.
#: PIP data were gotten from 13 patients only.
*: $p < 0.05$, compared to D_0.
Error bars are meant to be ± SEM.

in OI and $PaCO_2$ on the 3rd day of HFOV, in comparison with the pre-HFOV, showed a trend toward improvement, though without statistical significance.

The overall ICU mortality rate in the study population was 82.4%. Two ICU patients (50%) in the HFOV group survived. Twelve patients in the CV group (92.3%) had significant deterioration in gas exchange before mortality, and expired in the course of their stay at the ICU, with a mean of 16.5 ± 3.5 days after the air leak began.

Discussion

The results of the study showed favorable responses in gas exchange, air leaks, and ICU outcome whenever HFOV was used to rescue patients with ARDS complicated with air-leak syndrome unresponsive to conventional ventilation.

The ventilatory management of pneumothorax is to reduce PEEP and the pressure gradient in

Table 2. Demographic and clinical characteristics of the four subjects in the HFOV group.

	Case I	Case II	Case III	Case IV
Age/Sex	66/M	76/M	78/F	82/M
Diagnosis	Pneumonia, COPD	Pneumonia, IPF	Pneumonia, IPF	IP, NHL, pneumonia
APACHE II	27	43	20	17
Duration from air leak to HFOV use (Day)	1	7	21	14
Duration of CV before HFOV (Day)	2	14	30	22
Duration of HFOV use (Day)	6	4	8	<1
Persistent air leak	No*	Yes	No**	Yes
ICU outcome	Survival, ViD	Expired	Survival, VD	Expired

HFOV = high-frequency oscillatory ventilation. APACHE II = Acute Physiology and Chronic Health Evaluation II. ICU = intensive care unit. COPD = chronic obstructive pulmonary disease. IPF = interstitial pulmonary fibrosis. IP = interstitial pneumonitis. NHL = non-Hodgkin lymphoma. ViD = ventilator independent. VD = ventilator dependent.

*: Pneumothorax was treated by video-assisted thoracoscopy. **: Only subcutaneous emphysema without apparent pneumothorax was noted. It improved after HFOV use.

Table 3. Mean values and percent of change in the parameters of arterial blood gas before and after high-frequency oscillatory ventilation (HFOV).

	Pre-HFOV	HFOV D_1	HFOV D_2	HFOV D_3
PaO_2/FiO_2 (mmHg)	109.1 ± 25.3	105.9 ± 17.5	135.5 ± 34.3	146.3 ± 30.4
△ PaO_2/FiO_2% (%)		4.65 ± 25.5	54.2 ± 55.7	69.7 ± 56.3
$PaCO_2$ (mmHg)	63.4 ± 9.5	56.7 ± 12.1	53.9 ± 7.2	57.0 ± 9.7
△ $PaCO_2$% (%)		-16.0 ± 7.3	-17.3 ± 7.4	-13.7 ± 7.1
PH	7.32 ± 0.05	7.40 ± 0.05	7.40 ± 0.02	7.41 ± 0.03

Pre-HFOV = before starting HFOV. HFOV D1, D2, and D3 represent the 1st, 2nd, and 3rd day after HFOV use, respectively. △ PaO_2/FiO_2%, △ $PaCO_2$%, and △ PH% = the percent of change in PaO_2/FiO_2, $PaCO_2$, and PH in reference to the pre-HFOV data.

Data represent mean ± SEM.

pressure-limited ventilation. In our study, PEEP and PIP were lowered after the occurrence of the air leaks. However, this is contrary to the lung protective strategy for ARDS — high PEEP and low tidal volume. From animal and human studies, more evidence has been collected about the effects of mechanical ventilation on multiple organ dysfunction [10]. Low PEEP and high tidal volume might cause more injury to the lung and extrapulmonary organs [11]. Moreover, the oxygen fraction must be increased to compensate for the effect of lowering PEEP in oxygenation. The two factors of lower PEEP and a higher oxygen fraction might cause more damage to the lungs and contribute to a higher mortality rate.

In theory, HFOV fluctuates pressure changes around a selected mean airway pressure and delivers a very small tidal volume with a high respiratory rate, resulting in the maintenance of ventilation and in preventing the lung from over-distending and collapsing [12]. HFOV accomplishes many of the goals of the lung protective strategy. Furthermore, the minimal swing of alveoli pressure and a peak airway pressure lower than conventional ventilation

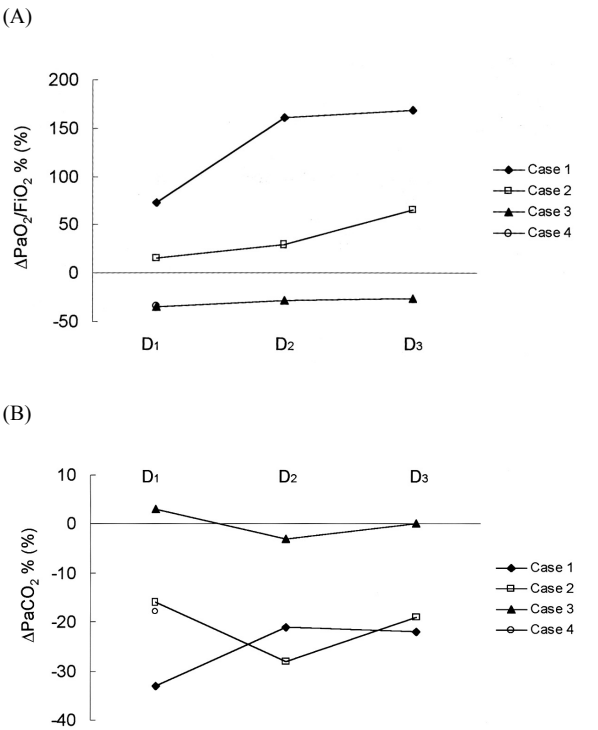

Fig. 3. Percent of change in the parameters of gas exchange within 3 days after high-frequency oscillatory ventilation (HFOV), in comparison with pre-HFOV. (A) the percent of change in PaO_2/FiO_2 ($\triangle PaO_2/FiO_2$%) (B) the percent of change in $PaCO_2$ ($\triangle PaCO_2$%). D_0 = before initiation of HFOV. D_1, D_2, and D_3 represent the first, second, and third days after HFOV use, respectively. Two of four cases were responsive to HFOV in the arterial blood gases.
*: the data were obtained at 8hr after HFOV, due to less than one day of HFOV use in case 4.

possibly promote the healing of the air leaks [5, 13]. Hence, HFOV may theoretically be a novel therapy for patients with ARDS complicated with air-leak syndrome.

In animal studies, the use of HFOV for air leaks improved the healing of pneumothorax and decreased the amount of air leaks [14,15]. Seller et al demonstrated the successful management of persistent air leaks in pediatric patients using HFOV [6]. This study showed the favorable responses in the gas exchanges of half of the HFOV group. There was also significant improvement in the subcutaneous emphysema of another patient, which suggests of the safety and efficacy of HFOV in managing ARDS with air leaks.

The loss of a substantial portion of inspired air may alter the intrapulmonary distribution of ventilation, ventilation-perfusion matching, and the arterial blood gases. Gagnon et al found that the partial pressure of CO_2 in the air measured from bronchocutaneous fistula was similar to that of the alveoli in HFOV, as seen in an animal model [16]. Thereafter, in addition to the possible decrement of the air leak and the maintenance of the lung opening by HFOV, another contributor in the improvement of gas exchange might be the greater alveolization of the air leak in HFOV than in conventional ventilation, due to specific mechanisms of gas exchange in the alveoli, using HFOV [16, 17]. HFOV might further minimize the impact of air loss, causing by barotrauma, on the blood gas.

Though the protocol of HFOV management in adult ARDS has been proposed in various studies [8,18], the optimal manipulation of HFOV in air-leak syndrome remains unclear. By using an animal model, Ellsbury et al suggested the use of low amplitudes, short inspiratory times, low mean airway pressures, and higher frequencies for healing air leaks with HFOV [19]. A standardized management of air leaks by HFOV may be necessary before further randomized, prospective studies may be conducted.

The main limitation of this study was the very small number of cases. In addition, underlying idiopathic pulmonary fibrosis (IPF) comprised a major component in the HFOV group. Whether or not these results can be extrapolated into the general population is questionable. However, even though the prognosis of IPF on admission to the ICU is poor [20,21], one subject from this study was successfully treated by HFOV, suggesting a possible role for HFOV in managing IPF with pneumonia. But more cases and a controlled study are needed to reach any further conclusion.

Conclusion

In summary, this study shows a favorable response in terms of gas exchange and ICU outcome in ARDS with air leak syndrome after HFOV. This

might have resulted from both the lung protective strategy and the decrement of the air leaks. From this study, it is suggested that HFOV might be used as a rescue therapy for patients with ARDS and air leak syndrome whenever conventional ventilation fails.

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高頻振盪呼吸器在成人急性呼吸窘迫症併發肺部漏氣之應用

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簡介：根據目前的研究發現高頻振盪呼吸器用於治療罹患急性呼吸窘迫症的成人病患，可以改善肺部氣體交換，這篇研究的目的在於評估高頻振盪呼吸器用在罹患急性呼吸窘迫症的成人病患併發肺部漏氣之效果。

方法：自 1999 年一月至 2002 年八月，一共有 17 位成年病人罹患急性呼吸窘迫症併發肺部漏氣，其中四人因為使用傳統呼吸器並無法維持適當的氣體交換，而改用高頻振盪呼吸器，其餘 13 人持續使用傳統呼吸器，動脈血氧分析的變化及加護病房的死亡率加以紀錄及分析。

結果：在肺部漏氣之後，呼氣末正壓壓力有顯著的下降，但血液的二氧化碳分壓及氧氣指數（PaO_2/FiO_2）並沒有受到肺部漏氣的影響。在改用高頻振盪呼吸器後，病患血液的二氧化碳分壓及氧氣指數（PaO_2/FiO_2）有改善的趨勢。在兩組病人的死亡率而言，使用高頻振盪呼吸器的是 50%，而使用傳統呼吸器的是 92.3%。

結論：當成人急性呼吸窘迫症併發肺部漏氣，同時傳統呼吸器無法維持適當的氣體交換時，高頻振盪呼吸器似乎是一種可以嘗試的一種治療方法。***（胸腔醫學 2003; 18: 419-426）***

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Primary Pulmonary Lymphoma — A Case Report

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Primary pulmonary lymphoma is a rare lung disease. The most common histological subtype is the well-differentiated B-cell tumor with a low-grade lymphoproliferative process. This appears to arise from bronchus-associated lymphoid tissue (BALT). We report a patient with primary pulmonary lymphoma, with the presentation of nonproductive cough and body weight loss. The chest radiograph showed left lingular consolidation. Transbronchial biopsy revealed lymphocytic interstitial pneumonitis. Open lung biopsy with immuno-histochemistrical stains confirmed the diagnosis of a marginal zone B-cell lymphoma. There was no evidence of involvement of the bone marrow, stomach, or other organs. After 3 courses of chemotherapy with cyclophosphamide, vincristine and prednisolone (COP), the patient's symptoms greatly improved. This primary lung lymphoma presented with diagnostic and therapeutic problems, but was not associated with a similar grave prognosis as found in non-Hodgkin's lymphomas of other sites. ***(Thorac Med 2003; 18: 427-432)***

Key words: primary pulmonary lymphoma, lymphocytic interstitial pneumonitis, chemotherapy

Introduction

Malignant lymphomas presenting within the lung are rare. [1] Tumors localized to extranodal parenchymal tissues (stomach, salivary gland, lung, skin, etc.) tend to remain restricted to these sites with a potential for cure, in striking contrast to most low-grade lymphomas. [2] Lymphomas of the lung might be primary without identifiable extrapulmonary disease. The precise pathogenesis of primary pulmonary lymphomas is unknown. The majority of extranodal non-Hodgkin's lymphomas arise in sites of mucosa-associated lymphoid tissue (MALT). MALT lymphomas are more frequently found in the stomach, and rarely in the lung, which comprises less than 1% of all non-Hodgkin's lymphomas. [2,3] MALT is known as bronchus-associated lymphoid tissue (BALT) in the lung. Congenital and acquired immunodeficiency states, including acquired immunodeficiency syndrome (AIDS), solid organ transplantation, and allogeneic bone marrow transplantation, especially with T-cell-depleted allogeneic marrows, are associated with the development of lymphoproliferative disorders. Some large cell lymphomas might represent Epstein-Barr virus-associated lymphoproliferative disorders. Primary pulmonary lymphomas of B-cell origin are not associated with EB virus infection. [4]. Specific chromosome abnormalities have been reported in distinct subgroups of lymphomas. [5,6] These chromosome abnormalities are associated with the activation and rearrangement of certain cellular oncogenes located in the involved chromosomes, and are considered to be related closely to the

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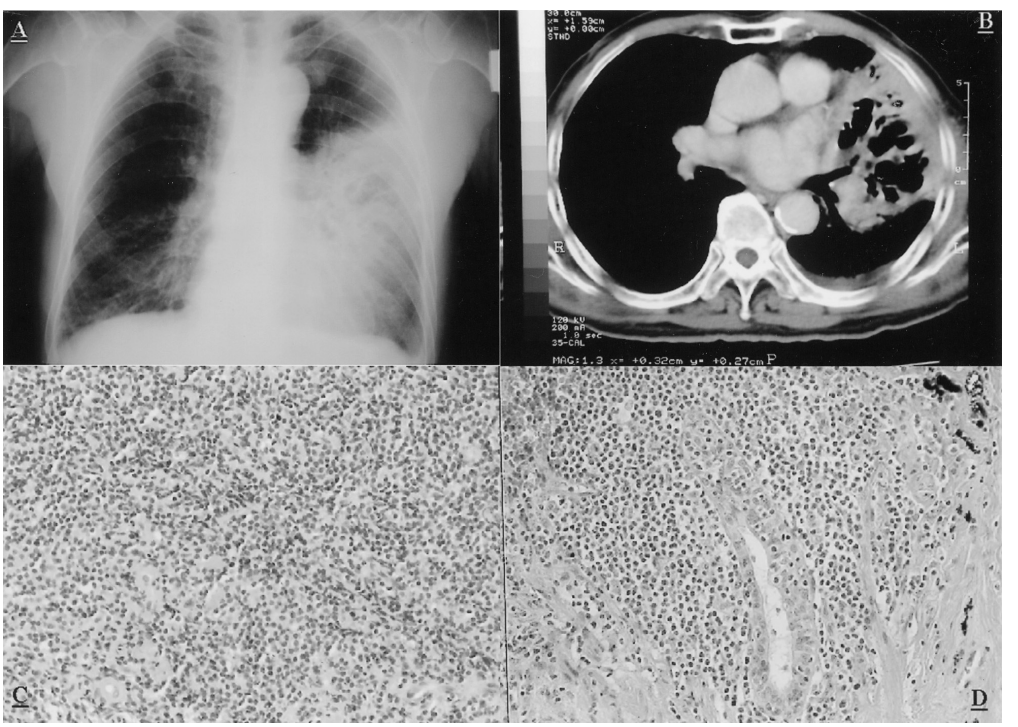
pathogenesis of disease. The clinical features of primary pulmonary lymphoma vary. Most patients are asymptomatic at presentation. The disease is discovered on a screening chest radiograph. In the typical asymptomatic patient, lung lesions are usually seen on routine chest films incidentally. Respiratory complaints predominate in symptomatic patients, with dyspnea, cough, chest pain, and weight loss described most commonly. [1] The radiological features of non-Hodgkin's lymphoma might be a solitary nodule, mass, or pulmonary infiltrate. The lesions are most frequently found in the lower lobes. [7] CT scans are very useful for patients with lymphoma in determining the extent of intrathoracic disease and invasion into contiguous structures, such as the chest wall, pericardium, and esophagus. Herein, we present a case of primary lymphoma of the lung with a brief review of the literature.

Case Report

A 76-year-old male patient, a retired civil servant, had no history of systemic disease. In May, 2001, a nonproductive cough developed, and progressed without dyspnea. He had suffered from anorexia with a body weight loss of 5 kg in 3 weeks when just prior to admission. There was no fever, fatigue, or night sweats. His body temperature was 36.3℃, with the pulse rate at 72/min, respiratory rate at 20/min, and blood pressure at 120/80 mmHg. Physical examination revealed no palpable lymphadenopathy, clubbing of the fingers, or hepatosplenomegaly. The breathing sounds revealed diffusely fine crackles in the left lung without wheezes. Routine laboratory examinations, including complete blood count, blood creatinine, and liver biochemistrical tests, were all within normal limits. His anti-HIV antibody was negative, and the thyroid function tests (T3, T4, TSH) were normal. The chest



Figures. A. Chest radiograph in Jun 2001, in which patchy infiltrates in the left lung were first noted. B. A CT scan shows consolidation at the lingular segment of the left upper lobe, with an airbronchogram and angiogram. C. High power view (400X) of the lung lesion from the transbronchial lung biopsy showing bronchial tissue heavily infiltrated by small lymphocytes. D. High power view (400X) of the lung lesion from the wedge resection showing a heavy interstitial infiltration of monotonous small lymphocytes with marked interstitial fibrosis.

radiography (Figure A) and chest computerized tomography (CT) (Figure B) revealed lobar consolidation with air-bronchogram and angiogram evidence within the consolidation at the lingual segment of the left upper lobe. No bacterial, fungal or viral pathogens were isolated from the sputum or the fluid of the bronchoalveolar lavage. The results of sputum smears for acid-fast bacilli were negative. Transbronchial biopsies (Figure C) with H.E. staining showed bronchial tissues heavily infiltrated by small lymphocytes, suggestive of lymphocytic interstitial pneumonitis. A resection of the lingual segment of the left upper lobe was performed for the definite diagnosis. The histology of the resected lung (Figure D) revealed lung tissue with a heavy interstitial infiltration of monotonous small lymphocytes, and marked interstitial fibrosis. Immunostains (L26+, CD10-, CD5-, cyclin D1-) confirmed this was a marginal zone B-cell lymphoma. A series of studies, including of bone marrow biopsy, panendoscopy, and CT scan of the abdomen, revealed no evidence of involvement of the bone marrow, stomach, or abdominal organs. The patient received COP chemotherapy, including an intravenous infusion of 800 mg of cyclophosphamide and 2 mg of vincristine, and 7 days' oral prednisolone at the dose of 45 mg per day. After 3 courses of chemotherapy, the dry cough and anorexia greatly improved. The chest radiograph revealed no marked change in the lung lesion. He has been followed up at the hematology department throughout chemotherapy.

Discussion

In symptomatic patients with primary pulmonary lymphoma, respiratory symptoms, including cough, dyspnea, chest pain, and hemoptysis, are more common than systemic symptoms. [8] Constitutional symptoms, when present, might include body weight loss, fever, night sweats, or fatigue. Our patient presented with nonproductive cough and body weight loss, which are not usually seen in most patients with primary pulmonary lymphoma.

The radiological features of localized or multiple areas of consolidation are seen in about one fourth of patients. Diffuse alveolar and interstitial infiltrates are seen in less than 10% of cases. Airbronchograms within the mass on CT scan have been commonly demonstrated in up to 51% of cases. [8] Our case revealed lobar consolidation with airbronchograms at the lingular segment of the left upper lobe, and no involvement of contiguous structures. These findings are compatible with those of most patients with primary pulmonary lymphoma. However, more common diseases, including pneumonia due to atypical pathogens, obstructive pneumonitis due to an endobronchial lesion, and bronchoalveolar cell carcinoma, should be ruled out. In addition, bronchiolitis obliterans-organizing pneumonia (BOOP) has been reported as the presenting manifestation of primary pulmonary lymphoma. [9]

The diagnosis of lymphoma should be made by tissue biopsy. Lymphocytic interstitial pneumonitis was suggestive in this patient from the transbronchial lung biopsies with H.E. staining. The patient had the clinical and radiological features of lymphoid interstitial pneumonitis. Lymphoid interstitial pneumonitis has been nearly unique to children with AIDS, occurring in up to 28% of this population and rarely in adults. [10] Lymphoid interstitial pneumonitis might be associated with Sjögren's syndrome, Hashimoto's thyroiditis, human immunodeficiency virus (HIV) infection, chronic active hepatitis, primary biliary cirrhosis, or other disorders. [11] Epstein-Barr virus infection might also play a role in the pathogenesis of these lesions. [12] Small lymphocytic lymphomas of the lung were not reported to be related to Epstein-Barr virus infection. [4] Immunodeficiency-associated lymphomas frequently originate from extranodal and unusual anatomic sites. These tumors are often of high-grade B-cell lineage with rapid progression, and are frequently associated with Epstein-Barr virus infection. [13] The case we have presented here was an adult with an euthyroid function, who was not in an immunodeficient state, and who had no evidence of autoimmune diseases, HIV, or

Epstein-Barr virus infection. The possibility of lymphocytic interstitial pneumonitis was less than that of pulmonary lymphoma in this case. It is difficult to distinguish lymphomas and lymphoid interstitial pneumonitis simply based on a histopathologic examination without immunohistochemstrical stains.

The treatment of choice for primary pulmonary lymphoma is based on the histologic subtype of the neoplasm, tumor bulk, and comorbid general medical conditions. Non-Hodgkin's lymphomas can regress spontaneously. Observation is the initial treatment of choice for asymtomatic patients. [8, 14] Most patients have remained stable over long periods, with little radiographic change and no evidence of extrapulmonary spread. [6] Symptomatic patients with localized low-grade non-Hodgkin's lymphoma may be treated with local radiotherapy or a combination of chemotherapy and radiotherapy. [15,16] Radiotherapy produces permanent pulmonary injury, so its use should be restricted to small volumes of the lung. Chemotherapy includes single-agent, daily oral chlorambucil or intravenously administered COP (cyclophosphamide, vincristine, and prednisolone). Because our patient was elderly, symptomatic, and had a bulky lymphoma, surgical treatment and radiotherapy were not considered. The patient underwent treatment with COP chemotherapy. Although the tumor did not resolve, the symptoms subsided during the course of treatment. His response was similar to that reported previously. [14,17]

Primary pulmonary lymphoma is generally an indolent disease with a more favourable outcome than nodal non-Hodgkin's lymphoma. Five percent of patients can develop aggressive large cell or immunoblastic lymphomas which herald a dismal outcome even with chemotherapy. [14,18] The critical period of recurrence is in the first thirty months, in which it commonly appears in the lungs, pleura, and mediastinum. According to the REAL/WHO classification [19], this patient was a case of extranodal marginal zone B-cell lymphoma of the MALT type. The overall 5-year survival rate with this type of lymphoma is greater than 70%. Frequent follow-up during the first 3 years after chemotherapy is warranted.

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原發性肺淋巴瘤—病例報告

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原發性肺淋巴瘤是一種罕見的肺部疾病，其中最常見的組織學型態為分化良好的B細胞腫瘤併有低程度淋巴增生，可能來自支氣管相關的淋巴組織。我們報告一例以乾咳、體重減輕為最初表現的原發性肺淋巴瘤男性病患，其胸部X光檢查呈現左舌葉實質化，經支氣管鏡生檢的病理報告是淋巴球間質肺炎，開胸手術取得的組織切片用特殊染色證實這是一例B細胞淋巴瘤。經過一系列檢查後，未發現侵犯到骨髓、胃及其它器官的證據。這個病患接受三次化學藥物治療後，原先的症狀很顯著的改善。原發性肺淋巴瘤在診斷與治療方面仍有許多問題尚待進一步研究，不過和其它部位的非何杰金氏淋巴瘤比起來，預後沒有那麼差。*(胸腔醫學 2003; 18: 427-432)*

關鍵詞：原發性肺淋巴瘤，淋巴球間質肺炎，化學藥物治療

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Catamenial Pneumothorax Caused By Diaphragmatic Endometriosis

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Catamenial pneumothorax is a rare disease. The etiology and pathogenesis of this syndrome has remained enigmatic. Many hypotheses have been proposed including anatomical, physiological, and metastatic models. Each hypothesis has been criticized because of a lack of a unifying source for each report in the literature. We report a 39-year-old woman presenting with monthly right thoracic pain occurring before menstruation. Thoracic endometriosis was confirmed histologically after a thoracotomy with biopsy. ***(Thorac Med 2003; 18: 433-436)***

Key words: catamenial pneumothorax, endometriosis

Introduction

Although spontaneous pneumothorax is relatively common in young and healthy men, it is 4~10 times less common in women.[1] Recurrent spontaneous pneumothorax associated with menstruation is rare, and accounts for 2.8% to 5.6% of all episodes in women.[2] This condition was first described by Maurer and associates [3] in 1958. Lillington and colleagues [4] introduced the term "catamenial pneumothorax" in 1972. The physiological mechanism remains unclear, though various theories exist. We present a case of catamenial pneumothorax in which systemic endometriosis was confirmed histologically.

Case Report

A 39-year-old woman, gravida 2, para 2 was referred to our hospital in November 2001 for recurrent right-sided pneumothorax. She had been in excellent health before and had no history of pelvic endometriosis. The first episode occurred in October 2001, in which sudden onset, right-side chest pain and tightness developed 2 days before menstruation. Dyspnea and a sensation of "air rolling" in her right chest persisted, and she accepted a tube thoracostomy at another hospital.

In November 2001, the same signs and symptoms developed 2 days before menstruation again, and the chest X-ray film showed pneumothorax of the right side. She was then referred to our hospital. The results of the physical examination were unremarkable. The gynecologic examination and pelvic sonogram revealed no signs of endometriosis externa. The CA125 was normal. The high resolution computed tomography of the chest showed a bleb in the right lung apex. Video-assisted thoracoscopy surgery was performed, the bleb was stapled with an Endo-GIA 60 (USSC, Auto Suture International, Norwalk, CT), and a mechanical pleurodesis was done.

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Two months later, the same signs and symptoms developed again, and chest radiography revealed basal pneumothorax on the right side. Conservative treatment with oxygen inhalation and bed rest was suggested, and an oral contraceptive was started. Since the dull pain in the right chest and sub-phrenic region occurred after beginning contraceptives, and the chest X ray showed a normal finding, she stopped the medication 2 months later, on her own due to the above symptoms bothering her so much. Unfortunately, she was admitted again because of recurrent spontaneous pneumothorax associated with menstruation. A right thoracotomy was performed in May, 2002, due to the incomplete expansion of the right lung. On the posterior parietal pleura, the pericardium, and the tendinous part of the diaphragm, many blue-purple spots were seen intraoperatively (Figure 1). Several biopsies were taken, and a chocolate-like fluid leaked from the specimen. The decortication and mechanical pleurodesis were then completed.

Postoperative recovery was uneventful and therapy with danazol was started following the gynecologist's suggestion. The pathological examination showed chronic inflammation in the peel and fibrosclerotic tissue, macrophages with iron pigment, and endometrial glands surrounded by endometrial stroma in the parietal pleura and diaphragm (Figure 2).

Discussion

According to the literature, catamenial pneumothorax is a recurrent syndrome of pneumothorax that occurs between 48 to 72 hours after menstruation. However, in this case, the patient could predict her menstruation when the chest discomfort began.

Most women affected with catamenial pneumothorax are in the third or fourth decade of their lives [5-6], and the right pneumothorax is affected in 90% to 95% of cases. [5-6]

The pathogenesis of catamenial pneumothorax is unclear, and several theories have been put forward:

(1) The anatomical model [1, 3]: Loss of the cervical mucus plug during the menstrual phase assists the movement of air into the peritoneum, and through the congenital fenestration, mainly on the right side, causing a pneumothorax.

(2) The physiological model [7]: High serum levels of prostaglandin F2α in menstruating women may cause severe vasospasm and bronchoalveolar constriction producing alveolar damage, which results in a pneumothorax.

(3) The metastatic hypothesis [8-9]: This best fits the pathologic evidence. The endometrial implants travel across the fenestration or lymphatic channels to the surface of the pleura and diaphragm.

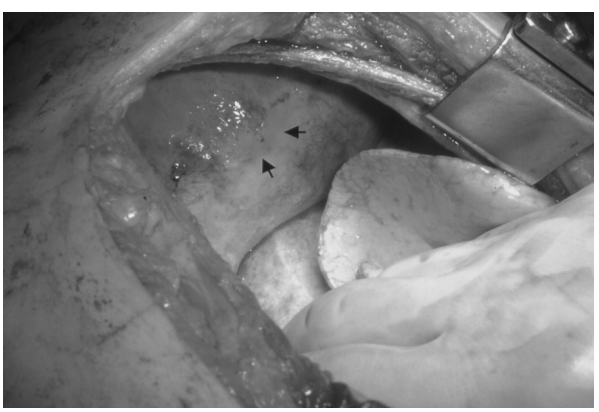

Fig. 1. Many blue-purple spots (arrow) were present on the tendinous part of the diaphragm.

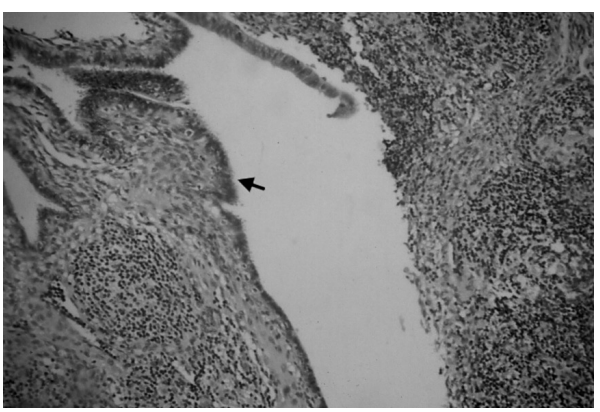

Fig. 2. Microphotograph showing endometrial glands (arrow) and stroma in a biopsy specimen of the diaphragm (Hematoxylin and eosin, original magnification x 100)

The desquamation during menstruation causes a focal defect and leads to pneumothorax.

Each hypothesis has been criticized because of the lack of a unifying source for each report in the literature. Clinical or pathological endometriosis is identified in only 22% to 37% of patients [10]. The pleural and diaphragmatic endometrial implants are seen in between 23% and 35% of published reports [10]. In our report, there was neither diaphragmatic fenestration nor lung parenchymal abnormality. The thoracic endometriosis was thought to cause the catamenial pneumothorax.

Elevation of serum CA125 in thoracic endometriosis in patients with catamenial pneumothorax has been discussed in the literature [11], but in our case, the level of serum CA125 was normal.

The initial treatment of catamenial pneumothorax is managed in exactly the same way as other types of pneumothorax. Oral contraceptives, danazol, or gonadotropin-releasing hormone analogue can be adminstered for 6 months if there are no contraindications. [8,12-13] In patients who no longer desire children, tubal ligation or hysterectomy can be considered, base on the above-mentioned hypotheses.[6] When these are unsuccessful, thoracotomy or a thoracoscopic procedure is the next logical step to biopsy and excising the abnormal lesions. The partial pleurectomy or chemical pleurodesis should be performed completely.

More than one hundred cases of catamenial pneumothorax have been described in the literature, but most doctors are not thoroughly aware of this disease. The etiology, pathogenesis, and treatment are totally different from those of spontaneous pneumothorax. We should consider the entity in all premenopausal women who have pneumothorax, especially with recurrence.

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因橫膈子宮內膜異位症所造成之月經性氣胸

黃俊雄　程永隆　李世俊　于承平*

月經性氣胸是一個臨床上相當少見的疾病，不論在好發年齡，性別，體型，以及主要發生在右側等特性均與一般之自發性氣胸有所不同。迄今在英文文獻報告上僅有一百多例。造成月經性氣胸的原因及致病機轉至今仍是難以理解，目前有許多假說被學者們所提出，包括有：解剖學上模式，生理學的模式，以及轉移的模式。每一種假說均有其理論基礎，但沒有一種假說能解釋所有病人的情形。所以至今仍無定論。

本篇文章我們介紹一個病例為 39 歲女性每次月經來時常合併右側胸痛，經開刀處理及病理切片後，證實為胸腔之子宮內膜異位症所引發之自發性氣胸。經治療後至今未再復發。同時希望藉由本篇文章之討論能引起更多臨床醫師的注意，以期能揭開月經性氣胸之神秘面紗。***(胸腔醫學 2003; 18: 433-436)***

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Rectus Sheath Hematoma, a Rare Complication of Asthma — A Case Report

Chin-Kai Su, Hong-Chung Wang, Min-Hsi Lin, Jau-Yeong Lu

Hematoma of the rectus sheath is a rare complication of asthma. We describe a case of rectus sheath hematoma caused by severe coughing during an exacerbation of asthma. This 65-year-old male patient had been a victim of asthma for more than 8 years. He suffered an acute attack of asthma and was treated at a local hospital five days before this admission. Two days later, a sudden onset of severe cough followed by abdominal pain occurred. The physical examination found an ecchymosis measuring 10x12 cm in size at the periumbilical area of the abdomen. Computed tomography of the abdomen revealed a well-defined soft tissue mass with contrast media enhancement in the left rectus sheath, consistent with rectus sheath hematoma. The aspirate from an ultrasound-guided diagnostic tapping also showed the blood clot. The patient received bronchodilators, corticosteroids, antitussive agents, and local heat packing for this abdominal wall lesion. The clinical condition of the patient improved gradually and he was discharged 2 weeks after admission. Failure to suspect the presence of a rectus sheath hematoma as a cause of acute abdominal pain may result in unnecessary invasive diagnostic studies or laparotomy. ***(Thorac Med 2003; 18: 437-441)***

Key words: asthma, rectus sheath hematoma

Introduction

Severe cough is a common presentation of the acute exacerbation of asthma and may contribute to serious complications such as pneumothorax and pneumomediastinum [1-3]. Occasionally, costochondral strain, subconjunctival hemorrhage, or cough syncope may occur as a result of repetitive cough in association with an acute episode of asthma [2, 3]. Rectus sheath hematoma is a rare complication [4,5], and its clinical recognition is often more difficult since it may simulate an acute abdominal emergency or retroperitoneal hemorrhage.

Case Presentation

This 65-year-old male patient had suffered from intermittent dyspnea, nocturnal dyspnea and cough for more than 8 years. He was diagnosed with bronchial asthma based on the typical clinical symptoms and the results of spirometry and a bronchodilator test. He received regular anti-asthmatic therapy at a local hospital. About 5 days before this admission, aggravated shortness of breath with cough developed. He was admitted to a local hospital with the diagnosis of asthma with acute exacerbation, and received inhalation bronchodilator therapy and intravenous glucocorticoid there. Two days later, a sudden onset of severe abdominal pain struck him

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after an episode of severe coughing. The pain was tearing in character and localized at the periumbilical area. Under the impression of an acute abdomen, he was referred to our hospital.

At the emergency room, he complained of diffuse abdominal pain. His temperature was 36.4 ℃, blood pressure: 167/90 mmHg, respiration rate: 24/min, and heart rate: 137/min. Diffuse expiratory wheezing was heard throughout the chest. Mild abdominal pain without obvious rebounding tenderness was present in the mid-abdomen along with an ecchymosis measuring about 10×12 cm in size (Figure 1). The laboratory data at the emergency room demonstrated the following: hematocrit, 39.2%; hemoglobin, 13.8 g/dL; and white blood cell count, 10,840/cumm with 69% segment cells, 1% bands, 20% lymphocytes, and 5% monocytes. Serum amylase was within the normal range. The platelet count, prothrombin time, partial prothrombin time, liver function, and renal function profiles were all within the normal limits.

After admission, he was treated with salbutamol and ipratropium inhalation therapy via a Hudson's nebulizer, intravenous hydrocortisone and aminophylline, and oxygen therapy. Antitussive agents were also prescribed. A computerized tomograph of the abdomen (Figure 2) revealed a well-defined soft tissue mass with contrast media enhancement in the left rectus sheath, compatible with a hematoma. The aspirate from an ultrasound-guided diagnostic tapping also showed the blood clot. Conservative treatment with heat packing was prescribed for the abdominal wall hematoma. The clinical condition of the patient gradually improved, and he was discharged 2 weeks after admission. At the time of discharge, the area of ecchymosis had decreased in size and the patient was free of abdominal symptoms.

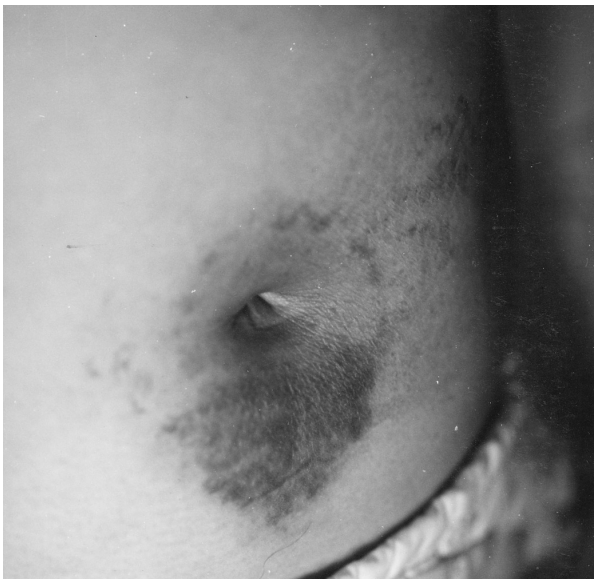

Fig. 1. The photograph taken 2 days after admission demonstrating large ecchymosis in the periumbilical area.

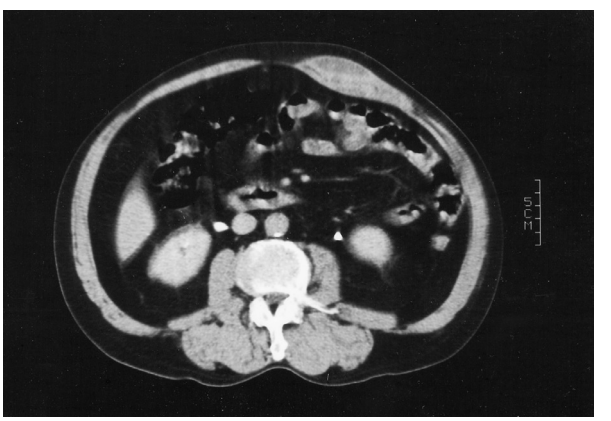

Fig. 2. Computerized tomograph of the abdomen showing a well-defined soft tissue mass with contrast media enhancement in the left rectus sheath, compatible with hematoma.

Discussion

Rupture of the rectus abdominis muscle with a resulting tear of the epigastric arteries and the subsequent development of a hematoma of the rectus sheath often mimic serious intra-abdominal disorders. Asthma as the inciting factor of rectus sheath hemorrhage has been reported previously [4, 5]. We describe another case of rectus sheath hematoma caused by a severe cough during an exacerbation of asthma.

Several review articles have listed the factors that predispose to hemorrhage within the rectus sheath. These factors include 1) direct trauma to the abdomen, 2) pregnancy, labor, and puerperium, 3) cardiovascular disease (congestion heart failure, arteriosclerosis, or hypertension), 4) degenerative

muscle disease, associated with infections (particularly typhoid), obesity, leukemia, or cancer, 5) sudden vigorous, uncoordinated muscular contractions (coughing, defecation, urination and sexual intercourse), and 6) blood dyscrasia and anticoagulant therapy [4,6]. In this patient, there were no major risk factors of rectus sheath hematoma, other than the sudden onset of severe cough and dyspnea.

The superior epigastric artery (a branch of the internal mammary artery) and the inferior epigastric artery (a branch of the external iliac artery) supply the rectus abdominis. Two sets of veins accompary each artery. The source of blood loss from hematomas of the rectus sheath may be ruptured fibers of the rectus abdominis or a tear in the epigastric vessels [7]. If the rectus sheath is torn, it is not unusual to see an early bluish discoloration of the abdomen. Even with an intact sheath, enough blood may leak around the site of the repair to produce a bluish discoloration three or four days after the injury. However, the skin discoloration does not commonly extend to the flank, since bleeding into the retroperitoneal space is unusual. In our case, there were no Cullen's or Gray Turner's signs found in the physical examination. In many instances, the history of a sudden onset of severe abdominal pain coupled with the findings of tenderness and peritoneal signs may initially suggest the presence of acute abdominal emergence.

The correct diagnosis may be suggested by a detailed history-taking and the detection of the abdominal mass. Two clinical signs may be helpful in diagnosing rectus sheath hematoma. The first sign of a rectus sheath hematoma is a palpable abdominal mass during voluntary tensing of the abdominal musculature and when in the sitting position (Fothergill's sign) [8]. Further, the mass should not be movable from side to side because of the restriction imposed upon it by the rectus sheath. The second sign is that the swelling of the hematoma should be limited to the rectus abdominis muscle and its sheath, and should not extend beyond the abdominal mid-line or the lateral borders of the muscle. Laboratory data is often nonspecific. In the early phase of a hemorrhage, leukocytosis with a left shift in the differential count occurs. If bleeding is sufficient, hemoglobin and hematocrit may decrease by the second or the third day. Diagnostic needle aspiration has been suggested, but may be contraindicated if the differential diagnosis includes incarcerated hernia. The rectus muscle is not visible in the anterior-posterior view of the abdomen or lower chest. Herzan reported that with acute hematoma of the rectus sheath, a "placental" or ovoid or spindle-shaped mass may be seen in lateral views of the abdomen [9]. However, the mass must be large and fortuitous in location to be visible on plain abdominal radiographs. Kaftori et al presented 5 cases of rectus sheath hematoma, with the diagnosis confirmed by ultrasonography, in which the hematomas appeared to be spindle-shaped on longitudinal sections and ovoid on transverse sections of the ultrasound views [10]. However, as can be seen in figure 2, computed tomograph scanning clearly demonstrated the rectus sheath hematoma as an anatomically distinct entity; the ultrasonography study was not initially diagnostic, and only retrospectively was helpful and confirmatory. The computed tomograph is an accurate noninvasive method of evaluating the presence, nature, location, size, and extent of abdominal masses, particularly obscure masses such as rectus sheath hematomas. In most cases, including our patient, conservative treatment is appropriate. Considerable acute depletion of intravascular volume caused by the hemorrhage may ocurr, resulting in hypotension and even death. Therefore, initial observation in a hospital is advisable. Intravenous volume repletion may be required. In a minority of cases, surgical ligation of the ruptured epigastric vessels may have to be undertaken because of an expanding hematoma; usually, tamponade of the bleeding vessel arrests the hemorrhage as the hematoma increases in size.

When asthma with severe cough is the precipitating factor, the usual management for bronchospasm should be initiated, including the appropriate use of corticosteroids, beta-2 agonists, and anticolingaergic agents. Small doses of antitussive medications may also be used cautionsly in initial management if required, although the cough may

be expected to subside as the bronchospasm is reversed. It is important that physicians who treat patients with asthma be aware of the features of this disorder, since failure to suspect the presence of rectus sheath hematoma as a cause of acute abdominal pain may result in unnecessary invasive studies or laparotomy.

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氣喘併發腹直肌血腫—病例報告

蘇經凱　王鴻昌　林旻希　盧朝勇

腹直肌血腫是氣喘病的一種罕見的併發症。我們報告一老年男性因氣喘發作而嚴重咳嗽導致腹直肌血腫之病例。一名年齡六十五歲之病人患有間歇性呼吸困難及夜間咳嗽，被診斷有氣喘病八年，在外院接受氣管擴張劑與類固醇之治療。在住院前五日，氣喘發作時併有嚴重咳嗽而住院接受治療，兩天後因急性腹痛而轉至本院。理學檢查發現腹部有一 10 × 12 公分大之紫斑。我們安排腹部電腦斷層檢查，結果發現在施打顯影劑後，左側腹直肌有顯影情形，與腹直肌血腫相符。我們亦利用超音波導引在腹部病灶處抽出少量血塊，這更進一步幫我們確定診斷。之後病患接受止咳藥物、氣管擴張劑與類固醇以及在腹部病灶給予熱敷等內科治療，病患氣喘狀況改善且腹部病灶縮小，兩週後病患出院。***(胸腔醫學 2003; 18: 437-441)***

關鍵詞：氣喘病，腹直肌血腫

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Acute Respiratory Distress Syndrome due to *Chlamydia pneumoniae* Infection In A Healthy Young Adult — A Case Report and Literature Review

Chun Hui, Ming-Cheng Chan, Chieh-Liang Wu, Juet-Chuang Tzeng*, Chun-Wen Chang**, Chi-Der Chian

Chlamydia pneumoniae is one of the common pathogens in community-acquired pneumonia (CAP). The clinical presentation is usually mild or even unrecognized. Severe CAP due to *C. pneumoniae* is usually found in the elderly or in patients with underlying diseases. Herein, we report a previously healthy young adult, who developed severe CAP with rapid progression to acute respiratory distress syndrome (ARDS) due to *C. pneumoniae* infection. With aggressive treatment, the patient recovered well without residual pulmonary function impairment. If a patient presents with ARDS without a clear-cut etiology, *C. pneumoniae* infection should be included in the differential diagnosis, even in the healthy young adult. ***(Thorac Med 2003; 18: 442-448)***

Key words: *C. pneumoniae*, community-acquired pneumonia, acute respiratory distress syndrome

Introduction

Chlamydia pneumoniae is one of the common causes of pneumonia worldwide [1,2]. It accounts for 10.9% of CAP in Taiwan [3]. The clinical course is generally mild and self-limited, but it may cause severe pneumonia in the elderly or in patients with underlying disease [3,4]. To the best of our knowledge, very few articles regarding ARDS resulting from *C. pneumoniae* in previously healthy adults have been published [5,6]. Herein, we present a patient who contracted severe CAP with rapid progression to ARDS as a result of *C. pneumoniae* infection, and briefly review the current literature.

Case Report

A 20-year-old man, a soldier with previously good health, was transferred from a local hospital due to progressive dyspnea. He had been serving at a military camp. Ten days before this admission, he had a fever, runny nose, and abdominal discomfort, which were followed by a non-productive cough and sore throat. Three other soldiers at the same camp demonstrated similar upper respiratory symptoms at the same time. After initial treatment as a common cold, the other soldiers recovered well, but not our patient.

He was admitted to a local hospital three days later. The chest radiograph (CXR) showed alveolar infiltration in the left lower lung. Community-

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acquired pneumonia was suspected and was treated with antibiotics, including minocyclin, and then changed to clarithromycin. As the dyspnea got more severe and progressed to respiratory failure, he was intubated and transferred to our hospital.

On admission, physical examination revealed a very ill man in marked respiratory distress. A pulse rate of 117/min, blood pressure 112/46 mmHg, and respiratory rate 24/min, were noted. Bronchial breathing sounds and crackles were heard at the base of both lungs. A CXR showed diffuse bilateral opacification. Arterial blood gas analysis on 100% oxygen revealed PaO_2 71 mmHg and $PaCO_2$ 32.5 mmHg, with a pH of 7.43. A diagnosis of ARDS was made after pulmonary artery catheterization with a pulmonary capillary wedge pressure of 7 mmHg, a cardiac index of 2.78 l/min/m^2, and a systemic vascular resistance index of 1554 dynes · m^2/cm^5. The acute lung injury had a score of 3. (The laboratory data is displayed in Table 1.) He was put on empirical treatment for severe community-acquired pneumonia including intravenous (i.v.) maxipime 2 g, amikacin 750 mg i.v. and erythromycin 4 g i.v., daily. Follow-up arterial blood gas analysis on 100% oxygen revealed PaO_2 47 mmHg, $PaCO_2$ 36.5 mmHg, with a pH of 7.43, and oxygenation saturation 83% by pulse oximeter. Due to refractory hypoxemia, the patient was placed in a prone position after heavy sedation. The ventilator was adjusted to a volume-controlled mode, and was kept in a lung-protective strategy with a low tidal volume (450ml) and a high positive end-expiratory pressure (PEEP) 14 cm H_2O. On the second hospital day, thoracocentesis of the left pleural effusion yielded lactic dehydrogenase (LDH) 4,188U/l and protein 3,700mg/dl. A tube thoracostomy was then performed to drain the complicated parapneumonic effusion. The infiltration on the chest radiographs subsided (Figure 1-3), and the fraction of oxygen was tapered gradually.

Both the pneumococcal and Legionella antigen of the urine were negative. The Gram's stain of the

Table 1. Laboratory data

Parameters	Values	
	Day 1	Day 8
Hemoglobin (g/dl)	15.6	13.7
Platelet (per cu mm)	208,000	444,000
White blood count (per cu mm)	10,100	8,300
Differential count (%)		
Neutrophil	95.4	87.8
Lymphocyte	3.7	8.4
Monocyte	0.8	3.5
Eosinophil	0.1	0.2
Urea nitrogen (mg/dl)	14	-
Creatinine (mg/dl)	1.1	-
Sodium (mEq/liter)	134	140
Potassium (mEq/liter)	4.6	4.2
Alanine aminotransferase (U/liter)	65	-
Aspartate aminotransferase (U/liter)	140	-
Bilirubin (mg/dl)		
total	2.5	-
direct	1.1	-
Alkaline phosphatase (U/liter)	165	-
Lactate dehydrogenase (U/liter)	1,920	641

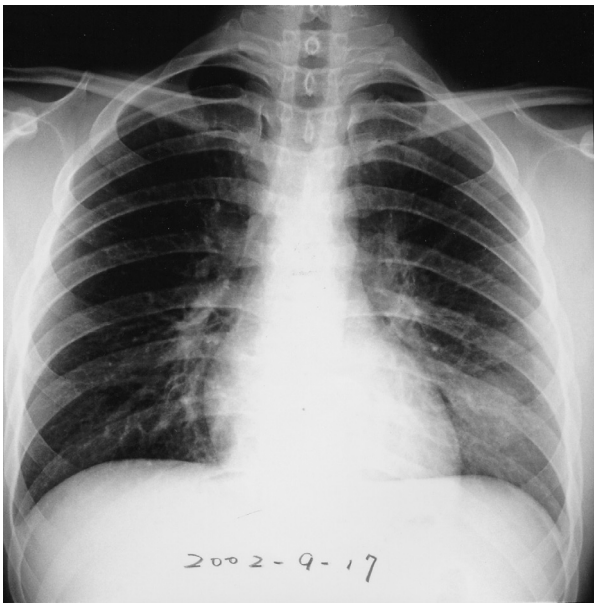

Fig. 1. The initial chest radiograph taken at a local hospital shows infiltration in the left lower lung field.

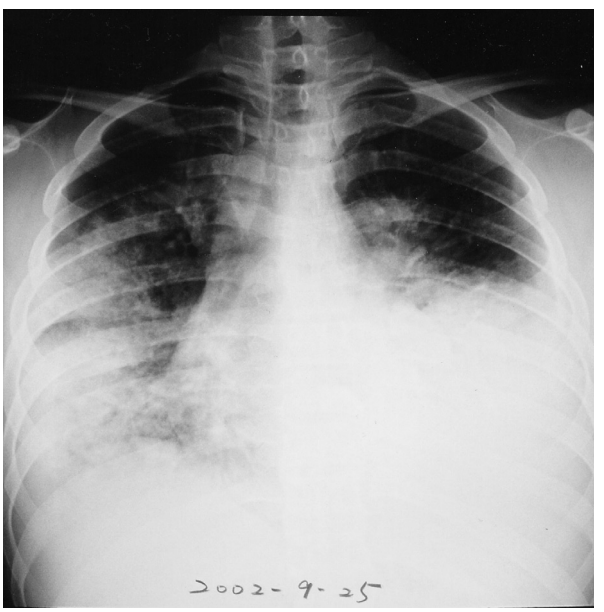

Fig. 2. The chest radiograph shows diffuse bilateral opacification and left pleural effusion on admission.

sputum revealed many polymorphonuclear leukocytes without bacteria. The serology data of Chlamydia IgM antibody to *Mycoplasma pneumoniae* and *Legionella* were all negative. The tests for Coxsackie virus (B1-B6), enzyme-linked immunosorbent assay for human immunodeficient virus (HIV-ELISA), and the Weil-Felix test were all negative. Two sets of blood culture and the bacterial culture of the pleural effusion revealed no growth, although the sputum grew oxacillin-resistant *Staphylococcus aureus*, the colony count of the bronchoalveolar lavage was less than 1,000 per milliliter. We reported this case to the Center for Disease Control (CDC), due to for the unknown etiology of ARDS. One week after admission, the CDC reported a very high serum titer of Chlamydia IgG >1:1,000 by indirect immunofluorescence, with no rise in IgM. In addition, one of the other three soldiers revealed a high serum titer for Chlamydia IgG >1:1,000, and Chlamydia IgG >1:100 was found in the remaining two. All of them denied any exposure to birds either recreationally or occupationally, and had no history of recent urethritis.

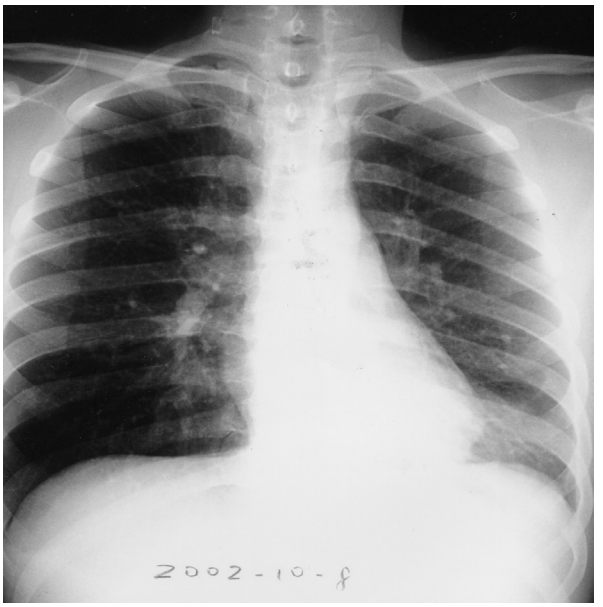

Fig. 3. The chest radiograph shows marked resolution before discharge.

Our patient was turned to the supine position on the 7th hospital day. He was extubated and the chest tube was removed on the 10th hospital day. Two weeks after this admission, he was discharged. The pulmonary function test 6 weeks after discharge was normal, with a forced vital capacity (FVC) of 4.77 l (105% of predicted value), a forced expiratory

volume in 1 second (FEV_1) of 4.21 l (108% of predicted value), FEV_1/FVC 88.3%, and a total lung capacity (TLC) of 5.52 l (90% of predicted value).

Discussion

C. pneumoniae is the most commonly occurring intracellular bacterial pathogen. It is frequently involved in respiratory tract infection and, to a lesser degree, in extrapulmonary diseases. According to seroepidemiologic surveys, *C. pneumoniae* infection seems to be both endemic and epidemic. Such studies indicate that *C. pneumoniae* infection is widespread, with frequent reinfection during a lifetime [7]. Isolation of *C. pneumoniae* from throat swabs serves as the "gold standard" for the diagnosis of infection. Polymerase chain reaction (PCR) and antibody detection provide more rapid and highly sensitive and specific means of identifying infection, and are coming into greater use. Diagnoses using PCR or cultures are only performed by a few laboratories and are not universally available. With serological examination, the diagnosis can be established by a single IgM titer ≧ 1:16, or a single IgG titer ≧ 1:512, or a fourfold rise in the titer of IgG antibody during convalescence [8]. Our patient was a case of re-infection with a high IgG titer rather than an acute infection, because the IgM titer appeared low. Previous studies have shown that re-infection may be associated with a milder illness than the primary infection [5,9], which is not consistent with our case. Some reports [7,10-12] anecdotally stated the close relationship between the antibody titers and respiratory symptoms. Grayston [8] considered that illness with cough developed more frequently in persons with a rise in the antibody titer. Ferrari et al [13] also found that *C. pneumoniae* antibodies were more common in patients with higher titers. We therefore inferred that the high serum IgG titer was probably associated with the clinical severity.

C. pneumoniae is a common pathogen for CAP. *C. pneumoniae* infection accounts for 10.9% of the identified agents of CAP in Taiwan [3]. Most reports rank *C. pneumoniae* as the third most common etiologic pathogen of CAP, with an incidence ranging from 6% to 25% [7]. In the report of a 500-member military camp, subclinical infection was estimated to be as high as 49% of healthy people, and only 7% of patients with *C. pneumoniae* infection had clinical symptoms of pneumonia [12]. The true incidence in a closed community will thus be underestimated.

The clinical presentations of *C. pneumoniae* infection are quite variable. Some patients demonstrate a gradual onset of symptoms: a sore throat and hoarseness followed by a cough or a subclinical presentation, while others may develop severe pneumonia and even ARDS. In one study, the most common clinical manifestations include fever (92%), productive cough (52%), leukocytosis (56%), and bilateral pulmonary infiltrates (60%) [3]. The clinical symptoms are usually mild with short-term disability, but a serious life-threatening illness due to *C. pneumoniae* usually occurs in the elderly or in patients with underlying comorbid conditions [4]. An age above 60 years is a risk factor for *C. pneumoniae* infection [3]. Our patient was a previously healthy young man. He had an acute lung injury score of 3, which means a severe lung injury [14]. The other soldier with the same high Chlamydia IgG titer had only minimal symptoms and was treated at the outpatient department. Sporadic cases of severe CAP due to *C. pneumoniae* infection in young adults have been reported [5,6,11]. Panagou et al reported a 42-year-old man of previously good health who suffered from ARDS and encephalitis. Marik et al [6] reported a previously healthy 24-year-old woman who developed multisystem organ failure with oligo-anuria, requiring continuous veno-veno hemodialysis, rhabdomyolysis, disseminated intravascular coagulation, and hepatic dysfunction. Mofredj et al [11] reported a 42-year-old alcoholic who developed status epilepticus and ARDS. Our patient was a 20-year-old man who contracted ARDS complicated with parapneumonic effusion. With adequate ventilatory support and rigorous antibiotic treatment, all patients, including our patient, recover fully without any sequelae.

One possible pathogenic mechanism involved

in severe *C. pneumoniae* infection has been proposed. The pathogen resides in alveolar macrophages and vascular endothelial cells. These cells can be induced to release cytokines, including IL-1, IL-6 and TNF-alpha, subsequently leading to organ dysfunction and systemic inflammatory response [15].

The radiographic appearance of *C. pneumoniae* infection begins predominantly with unilateral alveolar infiltrates. McConnel et al have observed that in patients with primary infection, alveolar opacities with an unilateral distribution were common, whereas in patients with re-infection, interstitial opacities with a bilateral distribution were more common on admission [16]. In our case, we failed to observe this association. In fact, the radiographic appearance of *C. pneumoniae* infection could not be differentiated from that due to other common respiratory tract pathogens. Small- to medium-sized pleural effusions occur commonly, and most are present early in the course of illness [16]. In the seven-year experience of Monno et al, ten percent of patients with *C. pneumoniae*-induced pneumonia had been reported to have pleural effusion [17]. However, massive complicated parapneumonic effusion is rare. In this case, complicated pleural effusion was noted on the second day of admission. We performed an adequate drainage using a chest tube, and the effusion regressed gradually.

C. pneumoniae is an intracellular pathogen. Acute or chronic infection due to this pathogen might induce superimposed bacterial colonization and infection because of this pathogen's harmful effects on neutrophils and alveolar macrophages [17]. In this case, the sputum and bronchial washing cultures yielded oxacillin-resistant *Staphylococcus aureus* (ORSA), which was unlikely to be the pathogen of severe pneumonia, because the quantitative bacterial culture of the bronchoalveolar lavage was less than 10^3 colony-forming units per milliliter. The ORSA might have been due to colonization after a stay in the previous local hospital. In addition, the prior antibiotics usage at a local hospital and the broad-spectrum antibiotics coverage immediately after admission might have influenced the results of the bacterial cultures. The initial therapeutic regimen contained an erythromycin plus a fourth-generation cephalosporin for broad-spectrum antibiotic coverage, however, as the clinical condition improved without any treatment aimed at the ORSA, and the colony count was quite low on culture, the possibility of ORSA infection was quite low. The ARDS may have been directly due to *C. pneumoniae* infection.

Use of the prone position improved oxygenation in this case with refractory hypoxemia. The fraction of oxygen was tapered from 100% to 55% in 2 days. Despite the fact that there are no studies showing improvement in mortality rate or organ dysfunction, there is evidence suggesting that prone position ventilation may be of the most benefit in more severely ill patients [18,19]. Although respiratory impairment of a restrictive pattern is a common finding after recovery from an episode of ARDS [20], this patient recovered well without any residual pulmonary function impairment.

In conclusion, our case illustrates that *C. pneumoniae* can be a cause of severe pneumonia with rapid progression to ARDS. If patients present with ARDS without a clear-cut etiology, *C. pneumoniae* infection should be included in the differential diagnosis, even in the healthy young adult.

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Chlamydia pneumoniae 感染所引起之急性呼吸窘迫症候群—病例報告及文獻回顧

惠 群 詹明澄 吳杰亮 曾瑞壯* 張瓊文** 江自得

C. pneumoniae 是社區型肺炎常見的病原菌之一，大部份的病人病情都很輕微甚至沒有症狀，而因為 *C. pneumoniae* 感染造成嚴重社區型肺炎的病人多是老年人或合併有其他疾病。我們報告一位健康年輕成人，因為 *C. pneumoniae* 感染造成急性呼吸窘迫症候群，經積極治療復元狀況良好，沒有肺功能障礙。如果病人罹患不明原因的急性呼吸窘迫症候群，即使是年輕成人，*C. pneumoniae* 感染都應該要列入鑑別診斷。***(胸腔醫學 2003; 18: 442-448)***

關鍵詞：*Chlamydia pneumoniae* ，社區型肺炎，急性呼吸窘迫症候群

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Severe Critical Illness Polyneuropathy Resulting in Tetraplegia: A Complication of Sepsis and Multiple Organ Dysfunction Syndrome — A Case Report

Ming-Jhieh Chang, Yao-Kuang Wu, Meng-Chih Lin, Ying-Huang Tsai

Sepsis is a major infection-induced syndrome that promotes the failure of various organs such as the lung, heart, brain, liver, gastrointestinal tract, and kidney. In addition, sepsis can cause damage to or dysfunction of the peripheral nerves and skeletal muscles, leading to conditions called critical illness polyneuropathy (CIP) and critical illness myopathy (CIM). CIP is an acute, diffuse neuropathy due to axonal dysfunction appearing in critically ill patients with sepsis or multiple organ dysfunction syndromes. We report a 75-year-old male with pneumonia, sepsis, and heart and respiratory failure. He developed paralysis in the four extremities with flaccid muscle 5 days after admission to the intensive care unit (ICU), and delayed weaning once the sepsis was under control. Meticulous examinations had been performed to look for the cause of the tetraplegia before electrodiagnosis confirmed critical illness polyneuropathy. Before the weaning trial, the maximal inspiratory pressure (MIP) was -10 cmH_2O. After 2 months of aggressive pulmonary rehabilitation exercise and sepsis treatment, the MIP reached -38 cmH_2O. His muscle power recovered slowly but steadily. Nocturnal use of a positive airway pressure ventilator was still needed 3 months after discharge. We conclude that CIP should be suspected when a patient presents with decreased peripheral muscle power or difficulty weaning after controlling the underlying critical condition in the ICU. A confirmed diagnosis and rehabilitation training are necessary for these patients. ***(Thorac Med 2003; 18: 449-454)***

Key words: sepsis, critical illness polyneuropathy, multiple organ dysfunction syndrome

Introduction

Sepsis is a major infection-induced syndrome that promotes the failure of various organs such as the lung, heart, brain, liver, gastrointestinal tract, and kidney [1]. In addition, sepsis can cause damage to or dysfunction of the peripheral nerves and skeletal muscles, leading to conditions called critical illness polyneuropathy (CIP) and critical illness myopathy (CIM) [2-3]. It has been recognized that these are responsible for the muscle weakness and wasting that occurs during the care of critically ill patients. However, many retrospective investigations of CIP may have underestimated its rate of occurrence due to the complexity of the diagnosis and clinicians' past unfamiliarity with the syndrome. It is usually diagnosed by clinical presentation (delayed weaning from the ventilator, muscle weakness, and prolongation of the mobilization phase) and electrophysiological findings (nerve

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conduction and needle electromyography). Recovery is rapid and mostly complete in patients with mild to moderate neuropathy; survivors of severe neuropathy with a prolonged stay in the intensive care unit (ICU) may show a slow and incomplete recovery and reduced quality-of-life scores [4]. Herein we present a patient with sepsis leading to multiple organ dysfunction who developed tetraplegia and difficulty weaning during the ICU stay.

Case Report

This 75-year-old man had a history of arrhythmia and hypertension, for many years, without regular medication control. One week before admission, he had an episode of intermittent fever and productive cough with shortness of breath. He was brought to our hospital due to progressive dyspnea. On admission, the vital signs were, blood pressure: 96/63mmHg; pulse rate: 79/min; respiratory rate: 24/min; and body temperature: 39.9℃. The hemogram showed leukocytosis (WBC: 18,000/mm^3, neutrophil: 85%). Biochemistry tests were within normal limits, except the creatinine value was 2.2 mg/dl. Physical examination showed an ill-looking man with jugular vein engorgement and bilateral legs pitting edema. There were diffuse crackles in the bilateral lung fields and an irregular heartbeat on auscultation. A arterial blood gas showed hypoxemia with hypercapnia (pH: 7.244, PaO_2: 53.6 mm-Hg, $PaCO_2$: 75.2mm-Hg, Sat: 80.9%). He was intubated soon thereafter because of consciousness change with lip cyanosis. The chest X-ray (Figure 1) revealed cardiomegaly with a ground-glass appearance in the right lower lung field. Diagnostic thoracentesis with 2-dimensional echocardiography showed transudative effusion with moderate mitral and tricuspid regurgitation, while the ejection fraction was 57%. An inotropic agent was administered to control his unstable hemodynamic status. Under the impression of septic shock due to pneumonia with acute respiratory and heart failure, he was transferred to the ICU for further management.

Antibiotics with ceftriaxone 500 mg q12h were administered to treat his pneumonia. The inotropic

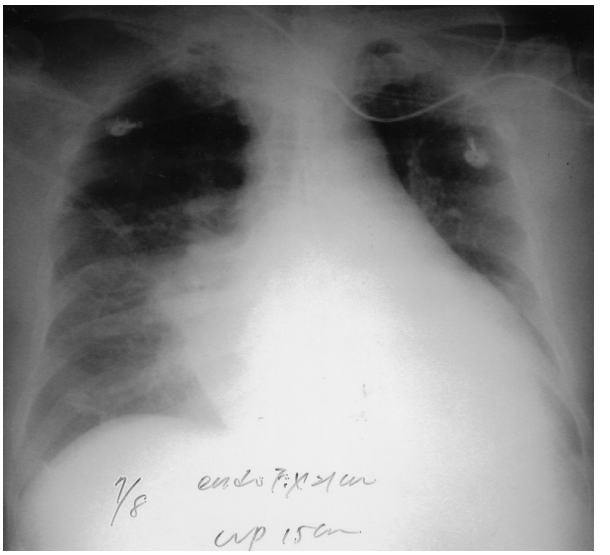

Fig. 1. The chest roentgenogram reveals cardiomegaly with a ground-glass appearance in the right lower lung field.

agent was gradually withdrawn and a right pig-tail was inserted to facilitate weaning. Four-extremity paralysis with flaccid muscles was found on day 5 after ICU admission. The fever subsided initially, but rose after 2 weeks of antibiotics. The follow-up chest X-ray (Figure 2) showed increased right lower lung infiltration. Sputum culture yielded oxacillin-resistant *staphylococcus aeruginosa*. The antibiotic was then changed to vancomycin. The patient was in stable condition except for the persistent tetraplegia and difficult weaning. There was no electrolyte abnormality (Na: 142 meq/L, K: 4.5 meq/L, Ca: 8.0 mg/dL, P: 3.0 mg/dL) or use of neuromuscular blocking agents during this period. The brain computerized tomography revealed no organic lesion. An electrophysiological study was performed, and revealed that the sensory and motor nerve conduction velocity (NCV) showed severely decreased compound muscle action potentials (CMAP) and no pick-up of sensory nerve action potentials (SNAP) amplitude on all nerves tested. The electromyography (EMG) reported fibrillation and a peak wave with reduced motor unit recruitment and increased motor unit action potential duration in the left biceps, anterior tibialis, and vastus medialis muscle, which was compatible with the diagnosis of critical illness polyneuropathy. A tracheostomy

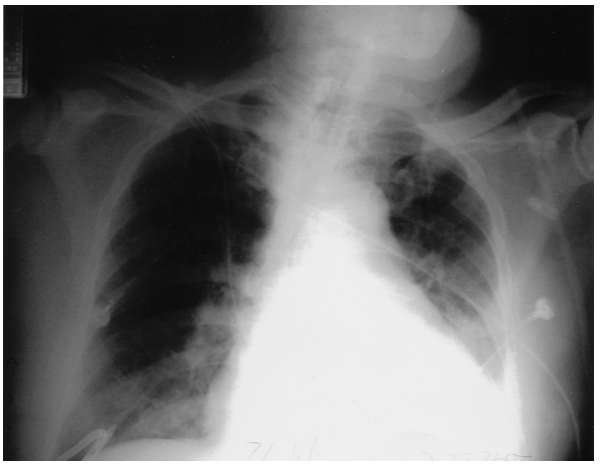

Fig. 2. The chest roentgenogram shows a right lower lobe infiltration increase and good positioning of the small caliber chest tube in the right hemithorax.

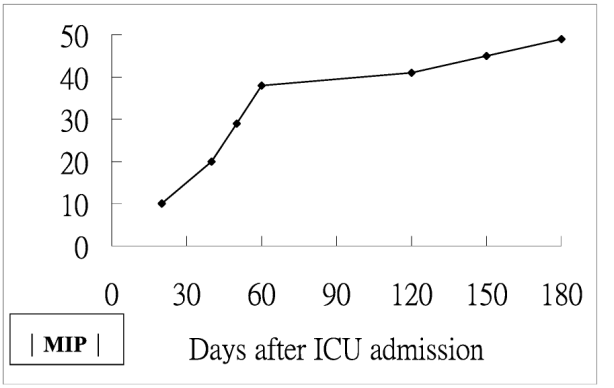

Fig. 3. The absolute value of maximal inspiratory pressure (|MIP|, cmH_2O) of the patient was measured and plotted based on the days after ICU admission. Initial MIP was -10cmH_2O and increased to -38cmH_2O before discharge. Steadily elevated MIP was noted after discharge; the maximal MIP was -49cmH_2O.

was performed on day 30 after ICU admission for long-term care. The maximal inspiratory pressure (MIP) was -10 cmH_2O when tetraplegia was noted and gradually improved after aggressive pulmonary rehabilitation exercise and sepsis treatment. We planned range-of-motion of the four extremities and reconditioning exercises to prevent joint contractures and muscle wasting. We avoided the use of steroids, neuromuscular blocking agents, and aminoglycosides. The electrolytes were monitored regularly. Due to respiratory muscle dysfunction, nocturnal positive pressure ventilator support was needed. The MIP increased to -38 cmH_2O (Figure 3) on day 60 after ICU admission. On his visit to the outpatient department three months after ICU discharge, the maximal MIP was -49 cmH_2O. His muscle power also gradually recovered (upper extremity: grade 3-4, lower extremity: grade 1-2 symmetrical).

Discussion

Diffuse axonal polyneuropathy, later termed critical illness polyneuropathy (CIP), has been described simultaneously by French, Canadian, and American authors as the cause of weaning failure and muscle weakness [5]. CIP emerges with an acute onset following the development of respiratory insufficiency in patients with sepsis and multiple organ dysfunction. CIP occurs primarily in adults, although a few cases has been reported in children [6]. In prospective studies, some 70-80% of patients with severe sepsis and multiple organ failure developed CIP [7-9]. However, we may underestimate CIP occurrence due to the complexity of the diagnosis and clinicians' unfamiliarity with the syndrome.

Patients with CIP are commonly men over 50 years of age admitted to an ICU for various causes who develop respiratory failure and sepsis and remain in the ICU for more than 5 days. Primary conditions on admission to the ICU include infection, trauma, surgery, and burns [10]. Delayed weaning from the ventilator not explained by pulmonary or cardiovascular findings is the most frequent reason for neurology consultation in patients with CIP [4]. On neurologic examination, these patients have muscular atrophies, severe flaccid tetraparesis, and slight sensory disturbances. Tendon reflexes are usually decreased or absent, but may be normal in one third of patients [11-12]. Even in patients with concurrent central nervous system disease, tendon reflexes may be augmented [13]. Since physical examination of the severely ill patient is often unreliable during the acute stage of the disease, because of encephalopathy, sedation, or the

critical condition of the patient, the demonstration of neuropathy relies on electrodiagnosis. In addition, many conditions may contribute to muscle weakness in critically ill patients: myopathy, neuromuscular junction defects, motor neuron disease, demyelinating polyneuropathy, axonal polyneuropathy, or a combination of any of these conditions [14]. Thus, before weakness and weaning failure are attributed to CIP, a thorough differential diagnosis (such as drug-induced weakness, myasthenia gravis, myopathy, disuse atrophy, Guillain-Barré syndrome, and polyneuropathy caused by heavy metal intoxication) should be made [10]. In our case, we had excluded all the possibilities of muscle weakness such as electrolyte imbalance, brain lesion or drug induced tetraplegia, by biochemistry, image study, and history taking.

Severe CIP may complicate the weaning from mechanically-assisted ventilation in patients with sepsis or MODS [15-16]. When there is a paucity of clinical symptoms, diagnosis must be made by electrophysiological studies. CIP has been diagnosed when signs of acute axonal injuries were present: reduction in CMAP and SNAP amplitudes with minor change in conduction velocities and distal latencies in combination with fibrillation potentials (signs of denervation) in at least one of the explored muscles [3,17]. In our case, the diagnosis of CIP was confirmed by the electrophysiological studies. A muscle biopsy was not performed due to the family's refusal, therefore we could not ascertain whether the CIP was combined with critical illness myopathy (CIM) or not.

The pathophysiology of this axonopathy is poorly understood. Many factors have been claimed to be involved in the pathogenesis of CIP, including malnutrition, hyperalimentation, vitamin depletion, hyperglycemia, and hyperosmolality, but none has been definitely proven so far [7,18-19]. Many authors have suggested that factors mediating the systemic effects of sepsis, i.e. the systemic inflammatory response syndrome (SIRS), are responsible for the axonal degeneration of CIP [3]. These factors include the release of tumor necrosis factor, histamine and arachidonic acid metabolites, activation of the complement and cell adhesion systems, and formation of local free radicals. Therefore, disturbances in the microcirculation of the peripheral nerve has been suggested [3]. In this viewpoint, CIP is just another organ failure during sepsis or SIRS. Recently, Garnacho-Montero J and coworkers conducted a cohort study in septic patients to determine the risk factors and clinical consequences of CIP. They found that CIP is associated with the duration of mechanical ventilation and in-hospital mortality [17]. Hyperosmolality, parenteral nutrition, nondepolarizing neuromuscular blockers, and neurologic failure can enhance CIP development [17]. In our case, we did not find any drugs (muscle relaxant or steroid) or medical treatment that might have aggravated the severity of CIP.

Weaning is delayed and hospital stay is lengthened for patients with CIP, potentially leading to increased resource use and associated costs. Mortality ranged from 26-71% in patients with CIP evaluated in prospective studies. Rehabilitation with complete recovery within weeks or months occurs frequently in patients with mild-form CIP who survive the ICU stay [20]. Unusually severe forms may be associated with incomplete recovery, resulting in persistent motor handicaps [21]. In our case, the length of ICU and hospital stay was 60 and 80 days, respectively. This was longer than the average ICU and hospital stay in our hsopital.

This case brought to our attention the diagnosis of CIP due to difficult weaning with persistent quadriplegia without central nervous system or spinal cord organic lesion. Superimposed nosocomial infection may have precipitated his CIP severity and delayed recovery. Treatment of CIP includes supportive care and attention to suspected underlying causes. Additionally we must plan appropriate physical positions for these patients to prevent additional nerve damage, and administer drugs (such as muscle relaxants, corticosteroids, and other agents with effects on neuromuscular transmission) at the lowest doses possible [4]. Since sepsis often occurs in patients with CIP, therapies directed at the pathophysiology of sepsis may reduce the frequency of CIP. Treatment with intravenous

immunoglobulin has been suggested if therapy is started immediately after the onset of sepsis [22]. However, prospective studies are necessary to confirm the usefulness of this treatment.

In conclusion, CIP is difficult to diagnose due to the complexity of critically ill patients. The accurate diagnosis relies on electrophysiological studies. Since pulmonary physicians may be not familiar with the syndrome, we have reported this case and reviewed the literature to remind physicians to add CIP to the differential diagnosis of acute weakness and weaning failure. A thorough survey should be made before CIP is diagnosed. Prolonged mechanical ventilation and a lengthened hospital stay are the negative outcomes linked to CIP. Nevertheless, the long-term prognosis appears promising. Although there is no effective therapy for CIP now, pulmonary rehabilitation is necessary to improve the outcome of CIP.

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嚴重的重症疾病併多發性神經病變導致四肢癱瘓：敗血症及多重器官失調症候群之併發症—病例報告

張明哲　吳燿光　林孟志　蔡煥煌

敗血症主要是由於感染引發之症候群，它會促進各不同器官的衰竭，如肺臟、心臟、腦部、肝臟、腸胃道及腎臟。此外，敗血症也會使週邊神經和骨骼肌受到損傷或功能異常而導致重症疾病併多發性神經病變及重症疾病併肌肉病變。重症疾病併多發性神經病變是指在敗血症或多重器官失調症候群的重症病人，所併發的急性瀰漫性軸突功能異常。我們在此報告一個患肺炎、敗血症及心臟和肺臟衰竭的 75 歲男性病人。在入加護病房住院第五天時發現四肢癱瘓及肌肉無力而且當敗血症已控制後卻仍然難以脫離呼吸器。為了找尋四肢癱瘓的原因我們做了詳盡的檢查，神經電氣生理學檢查確診為重症疾病併多發性神經病變。在嘗試脫離呼吸器之前的最大吸氣壓力為負 10 公分水柱。經過兩個月積極的肺部復原運動及治療敗血症，最大吸氣壓力到達負 38 公分水柱。病患的肌力緩慢而穩定的恢復。在出院後三個月，夜間仍需正壓呼吸器的使用。結論：當病患在加護病房的病危狀況受到控制後若仍有週邊肌力減弱及難以脫離呼吸器，此時我們應懷疑是否為重症疾病併多發性神經病變。確定診斷以及進行復健訓練對這些病人是必須的。***（胸腔醫學 2003; 18: 449-454）***

關鍵詞：敗血症，重症疾病併多發性神經病變，多重器官失調症候群

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Primary Lymphoepithelioma-Like Carcinoma of the Lung Associated With Hypertrophic Osteoarthropathy — A Case Report

Chuan-Sheng Wang, Kun-Bow Tsai*, Jong-Rung Tsai, Chau-Chyun Sheu, Jen-Yu Hung, Te-Hung Hsu, Ming-Shyan Huang

Lymphoepithelioma-like carcinoma of the lung, an Epstein-Barr virus (EBV) -associated undifferentiated carcinoma, is a rare entity of pulmonary malignancy, and only a few cases have been reported in the literature. Herein, we report a 42-year-old man who was admitted to our hospital with the chief complaint of symmetrical pain, swelling, and hyperemia of the knees, elbows, and wrists, associated with clubbing of the toes and fingers. The chest roentgenogram and computed tomography (CT) of the thorax revealed a soft tissue mass in the upper lobe of the right lung. Radiographs of the joints and long bones and a ^{99m}Tc MDP whole body bone scan revealed hypertrophic osteoarthropathy. The patient underwent surgical resection of the primary pulmonary lesion. From the histological characteristics and positive signals for EBV-encoded RNA-1(EBER-1) found by *in situ* hybridization, the diagnosis of lymphoepithelioma-like carcinoma of the lung was made. After the operation, he received adjuvant chemotherapy and radiotherapy. A follow-up examination nine months later showed the patient to be free of joint symptoms and without evidence of relapse or metastasis. ***(Thorac Med 2003; 18: 455-460)***

Key words: Primary lymphoepithelioma-like carcinoma (LELC) of the lung, hypertrophic osteoarthropathy (HOA)

Introduction

Lymphoepithelioma-like carcinoma (LELC) arising primarily in the lung is rare, but it is a distinct entity that has recently been recognized and included in the 1999 Histological Classification of Lung Tumors formulated by the World Health Organization [1]. LELC, best known to occur in the nasopharynx, can arise in a variety of sites, such as the salivary gland, thymus, lung, cervix, stomach, and skin [2]. Primary LELC of the lung is an Epstein-Barr virus-associated undifferentiated carcinoma with prominent lymphoid stroma and ultrastructural features of squamous cell carcinoma [2]. Primary LELC of the lung tends to affect young non-smoking Asians and is often resectable [3]. From the limited available data, the behavior of LELC of the lung is highly variable, ranging from apparent curability by excision (particularly for localized disease) to highly aggressive, extensive disease at presentation [4].

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Case Report

A 42-year-old man was admitted to our hospital in August 2001 with a six-month history of symmetrical pain, swelling, and hyperemia of the knees, elbows, and wrists, associated with clubbing of the toes and fingers. He had been quite well and had no previous smoking history. The tumor markers, including carcinoembryonic antigen (CEA), tissue plasmin antigen (TPA), and squamous cell carcinoma antigen (SCC), were all within normal limits. Chest roentgenogram demonstrated a well-defined soft tissue shadow in the upper lobe of the right lung (Figure 1). Computed tomography (CT) of the thorax revealed a homogenous soft tissue mass with a spiculate margin in the upper lobe of the right lung, and a thickened adjacent bronchovascular bundle involving the right pulmonary hilum, with a small lymph node at the pretracheal region of the mediastinum. Radiographs of the joints and long bones showed the characteristic periosteal new bone formation that is diagnostic of hypertrophic osteoarthropathy (Figure 2). A ^{99m}Tc methylene disphosphonate whole body bone scan revealed an intense cortical uptake in the long bones of the four limbs compatible with hypertrophic osteoarthropathy.

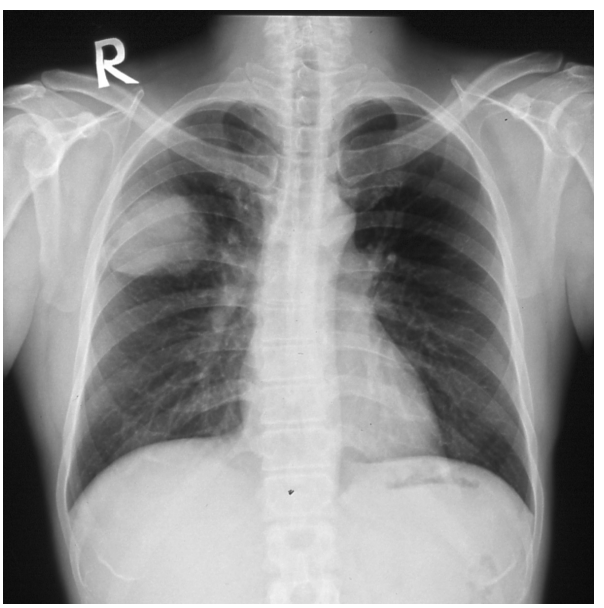


Fig. 1. Chest roentgenogram at admission shows a well-defined soft tissue shadow in the upper lobe of the right lung.

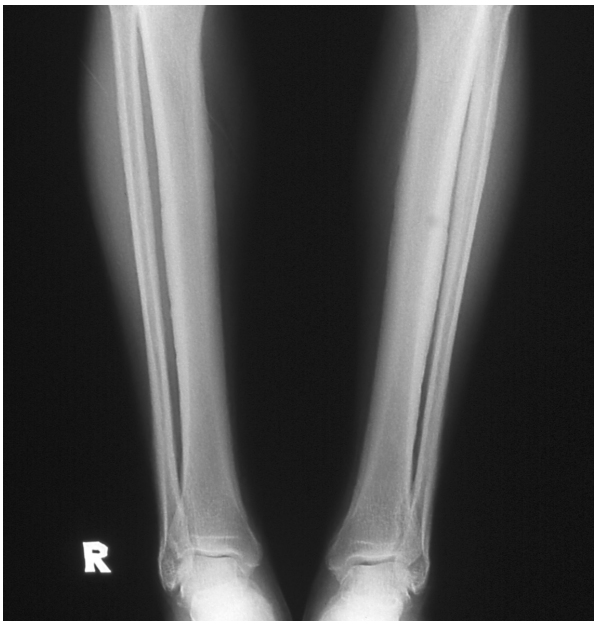


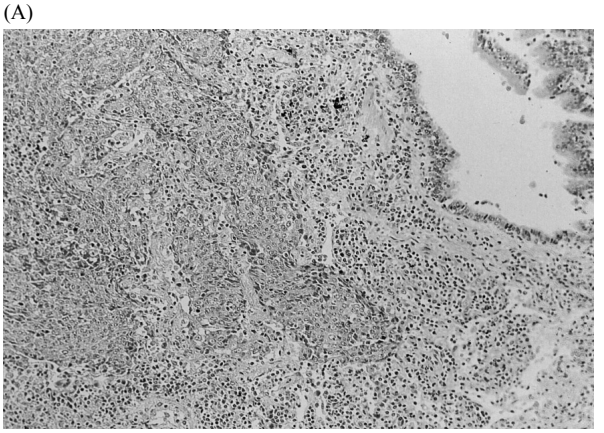
Fig. 2. Radiographs of bilateral lower legs show characteristic periosteal new bone formation that is diagnostic of hypertrophic osteoarthropathy.

Clinical history-taking and a complete nasopharyngeal examination, including a nasopharyngoscopy, were carried out to exclude the possibility of a primary nasopharyngeal lesion. In view of the possibility of a primary lung tumor, a right posterolateral thoracotomy, right upper lobe lobectomy, and mediastinal lymph node dissection were performed. The gross appearance of the surgical specimen showed a well-demarcated mass, 4.0 x 3.0 x 9.0 cm in size, with a grayish-white cut surface. Several hilar lymph nodes were obtained. Histologically, the tumor was composed of poorly differentiated neoplastic cells which had large vesicular nuclei with prominent nucleoli and scanty cytoplasm, mainly arranged in a syncytial growth pattern, and a heavy lymphocytic infiltration. The features simulated undifferentiated carcinoma of the nasopharynx. Immunohistochemical staining revealed positive staining for cytokeratin. A strong expression of EBV-encoded RNA-1(EBER-1) presented in the nuclei of the large undifferentiated neoplastic cells, but was absent in the surrounding

lymphocytic infiltrates, as determined by *in situ* hybridization (Figure 3). From the histological characteristics and positive signals for EBER-1 found by *in situ* hybridization, the diagnosis of lymphoepithelioma-like carcinoma of the lung was made. Regional lymph nodes showed reactive hyperplasia with marked anthracosis.

The patient subsequently received adjuvant chemotherapy and radiotherapy. A follow-up examination in May 2002 showed the patient to be free of joint symptoms and without evidence of relapse or metastasis.

(A)



(B)

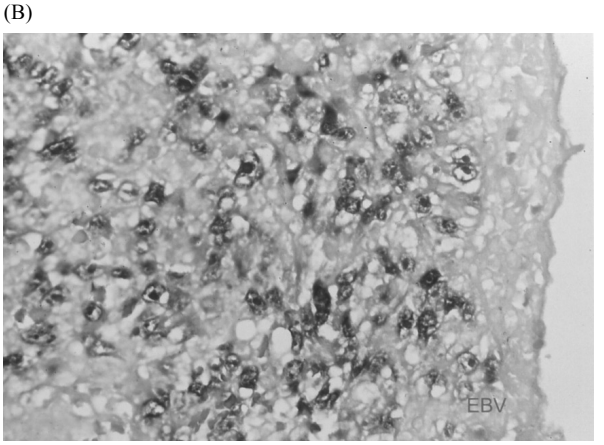


Fig. 3. Histophathology of the resected lung tissue shows *A,* several cohesive nests of cancer cells within abundant inflammatory stroma (hematoxylin and eosin stain; original magnification X20). *B,* a strong EBER RNA expression present in the nuclei of large undifferentiated cancer cells but absent in the surrounding lymphocytic infiltrates (*in situ* hybridization, original magnification X80).

Discussion

Hypertrophic osteoarthropathy (HOA) characterized by the subperiosteal formation of new cancellous bone at the distal ends of the long bones, especially the radius and ulna (80%) and tibia and fibula (74%), is clearly linked to clubbing, particularly in patients with bronchogenic carcinoma [5]. HOA may be suspected by its clinical features: pain and swelling of the neighboring soft tissues and occasional joint effusions, erythema, and warmth, often simulating inflammatory arthritis. The diagnosis of HOA is made by the radiographic demonstration of characteristic periosteal new bone formation. Bone scans using ^{99m}Tc-labeled imaging agents, which concentrate in sites of increased osteoblast activity, may reveal new bone formation before it is detectable radiographically [6]. When newly discovered, the presence of clubbing, with or without HOA, warrants a chest roentgenogram to look for a pulmonary neoplasm. If the plain film is unrevealing, a CT of the thorax is indicated. HOA can rapidly disappear after resection of the primary tumor [7]. This is the first reported case of primary lymphoepithelioma-like carcinoma (LELC) of the lung associated with HOA.

Primary LELC of the lung is a rare and clinicopathologically distinctive neoplasm that was first described in 1987 by Begin et al., and to date, there have been a total of about 100 cases [3,8-9]. The great majority of cases are found in Asian patients, particularly those residing in southern China, Hong Kong, and Taiwan [3]. The incidence of LELC ranges from 0.15-3.6% of all lung cancers among the different reports [12-13]. The patients, in general, are characterized by an equal sex ratio and a conspicuous absence of a history of smoking. The age of the patients has varied from 8 to 78 years, with a mean of 53 years [3,14-16]. LELC has been reported in pharyngeal and fore-gut derivatives, including the oral cavity, salivary gland, thymus, lung, cervix, skin, and stomach. Similar to nasopharyngeal carcinoma, LELC of the lung is strongly associated with Epstein-Barr virus (EBV) infection in Asian patients, but there is controversy over

whether an association exists in Caucasians [4,9, 17].

Radiographically, most tumors usually present as a solitary, white, firm, and well circumscribed subpleural nodule with right-side predominance [9]. The imaging study in our case revealed a soft tissue mass in the upper lobe of the right lung.

The distinctive cytologic features consist of nests, sheets, and cords of a syncytial-like growth pattern of anaplastic cells with prominent eosinophilic nucleoli. There is a moderate to heavy lymphoplasma cell infiltration, and the lymphoid component is seen even in metastatic sites. Immunohistochemical study, performed on the cell block preparation, has revealed strong positive staining of these tumor cells for epithelial markers [2,4,9, 15,18]. The differential diagnosis of LELC of the lung includes metastasis from nasopharyngeal carcinoma, malignant lymphoma, and malignant melanoma. Histologically, primary LELC of the lung cannot be distinguished from a metastatic nasopharyngeal carcinoma, but the diagnosis can be established on the basis of clinical history and the absence of a primary lesion in the nasopharynx [9]. Numerous techniques have been used to demonstrate the virus, including *in situ* hybridization for EBV-encoded small nuclear ribonucleic acids, the demonstration of EBV deoxyribonucleic acid in the tumor cells, and the expression of latent membrane protein-1 by immunohistochemistry [2,12.19]. In our case, the morphology under light microscopy revealed poorly differentiated neoplastic cells which had large vesicular nuclei with prominent nucleoli and scanty cytoplasm mainly arranged in a syncytial growth pattern, and a heavy lymphocytic infiltration. Immunohistochemical studies disclosed positive staining for cytokeratin. A strong expression of EBV-encoded RNA-1(EBER-1) was present in the nuclei of the large undifferentiated neoplastic cells, but was absent in the surrounding lymphocytic infiltrates using *in situ* hybridization.

LELC of the lung often confers a better prognosis than the other types of non-small cell lung cancer in reports comprising patients with mainly early-stage disease [4,10-11]. The few available case reports appear to suggest that pulmonary LELC may be curable by resection, which is the recommended treatment of choice. Pulmonary LELC is a tumor that is very often sensitive to both chemotherapy and radiotherapy, with prolonged survival achievable by multimodality treatment, even in advanced stages not amenable to curative surgery. Clearly, chemotherapy and/or radiotherapy are essential tools in managing the advanced or inoperable cases comprising up to 30-40% of all patients in some reports [2-3,8,14,20-21]. In our case, the patient received multimodality treatment, including surgical resection of the primary pulmonary lesion, adjuvant chemotherapy, and radiotherapy. A follow-up examination nine months later showed the patient to be free of joint symptoms and without evidence of relapse or metastasis.

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肺原發淋巴上皮瘤樣癌合併肥大性骨關節病變之一病例報告

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肺原發淋巴上皮瘤樣癌是一個 EB 病毒相關的未分化癌，它占肺癌的極少部分，只有一些病例曾見諸於文獻。在此我們報告一位 42 歲男性病患主訴雙側膝部，肘部及腕部紅腫疼痛合併手指及腳指杵狀變形而住進我們醫院治療。胸部 X 光及胸部電腦斷層掃描發現在右上肺部中有一顆軟組織腫瘤，關節及長骨的 X 光和 ^{99m}Tc MDP 骨骼掃描攝影顯示肥大性骨關節病變。他接受肺原發病變區域的外科切除手術，根據組織特徵及原位染交 EBER-1 陽性訊號，確定診斷為肺淋巴上皮瘤樣癌。在手術之後，他繼之接受輔助性化學藥物及放射治療，九個月後的追蹤檢查顯示這位病人並無關節症狀，而且沒有復發或轉移的證據。 ***（胸腔醫學 2003; 18: 455-460）***

關鍵詞：肺原發淋巴上皮瘤樣癌，肥大性骨關節病變

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A Huge CervicomeDiastinal Hemangioma Enveloping the Right Subclavian Vessels and Extending into the Intraspinal Canal — A Case Report

Chien-Chung Lin, Lili Cheng**, Yueh-Fon Tsai*, E-Jian Lee*, Wu-Wei Lai*

Benign hemangiomas account for less than 0.5% of mediastinal masses. While a preoperative diagnosis is difficult using noninvasive means, an MRI study proved useful for suggesting the correct diagnosis.

We report a 27-year-old patient with a huge cervicomediastinal mass (25X15X15 cm) with compression of the entire right lung, extending into the spinal canal and the neck, and enveloping the right subclavian vessels. Total excision of the tumor was done by a neurosurgeon and chest surgeon, using both posterior and anterior approaches.

A hemangioma, even though very rare, may present as a mass in the neck, and should be considered in the differential diagnosis of neck and mediastinal masses. ***(Thorac Med 2003; 18: 461-466)***

Key words: cervicomediastinal mass, hemangioma, intraspinal canal extension

Introduction

Mediastinal hemangiomas are rare and typically occur in young patients; approximately 75% manifest before the age of 35 years. One-third to one-half of patients have no symptoms at presentation, and the remaining patients present with symptoms or signs that are the result of infiltration into adjacent structures, or a mass in the neck [1]. Mediastinal hemangiomas usually arise in the anterior mediastinum; the next most common site is the posterior mediastinum. Isolated involvement of the middle mediastinum is rare [2]. At histological examination, these tumors are composed of large, interconnecting vascular spaces lined by a flattened cuboidal epithelium. The tumors have varying amounts of interposed stromal elements (fat, myxoid, and fibrous tissue) and focal areas of organized thrombus. Various authors have stated that diagnostic techniques may provide some clues specific to mediastinal hemangioma [1]. However, others have concluded that diagnostic surgical resection and histology of parts of the tumor seem to be the only reliable diagnostic strategies for suspected mediastinal hemangioma [3].

We report the case of a patient with a huge cervicomediastinal hemangioma. A neck mass was her first presenting sign. This large tumor compressed the entire right lung, displaced the mediastinal structures, extended into the neck and intras-

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pinal canal, and enveloped the subclavian vessels.

Case Report

A 27-year-old patient was hospitalized with the chief complaint of progressive dyspnea and right back pain for the previous 6 months. She noticed a mass in her neck when she was 16 years old (Figure 1A). A neck and chest CT at that time revealed innumerable hypodense nodular lesions in the right supraclavicular area, thoracic inlet, and mediastinum. Sonography disclosed multiple channels communicating with each other in the right lower neck, and a hemangioma was strongly suspected. However, the pathologic report from the neck incision biopsy revealed fibroadipose tissue; the angiography was normal. She underwent a CT-guided biopsy again, but only normal ganglion cells and nerve fibers were found microscopically. Surgical intervention was suggested, but she hesitated and decided to take Chinese herbal medicine instead. Eleven years later, she came to our outpatient clinic again with dyspnea on exertion and right upper back pain. A chest X-ray (Figure 1B) showed 2nd-3rd rib destruction, tracheal deviation, elongation of the right main bronchus, a shifting of the mediastinum to the left side, and a total collapse of the right lung.

On physical examination, her original neck mass was still there and larger than before, measuring 6.5 x 4 cm, with prominent engorged superficial veins. Though the patient complained of discomfort in the right upper back, no local tenderness or focal neurological sign could be detected in this area or in the right upper extremities. Most of this patient's laboratory data were within normal limits except for tumor marker C125 (84.6; normal < 33). An MRI examination (Figure 2A) revealed a huge cervicomediastinal tumor with multiple cystic structures with fluid-fluid levels that suggested different stages of blood content. Right lung compression, mediastinal structure shift, neck extension with envelopment of the right subclavian vessels, and intraspinal canal extension at the level of C6-T3, were also depicted. The preoperative tentative diagnosis was mediastinal neurogenic tumor with intraspinal canal and neck extension, based on the previous pathologic report and MRI findings.

Total excision of the tumor was performed through the cooperation of a neurosurgeon and chest surgeon (Figure 1C). The whole procedure could

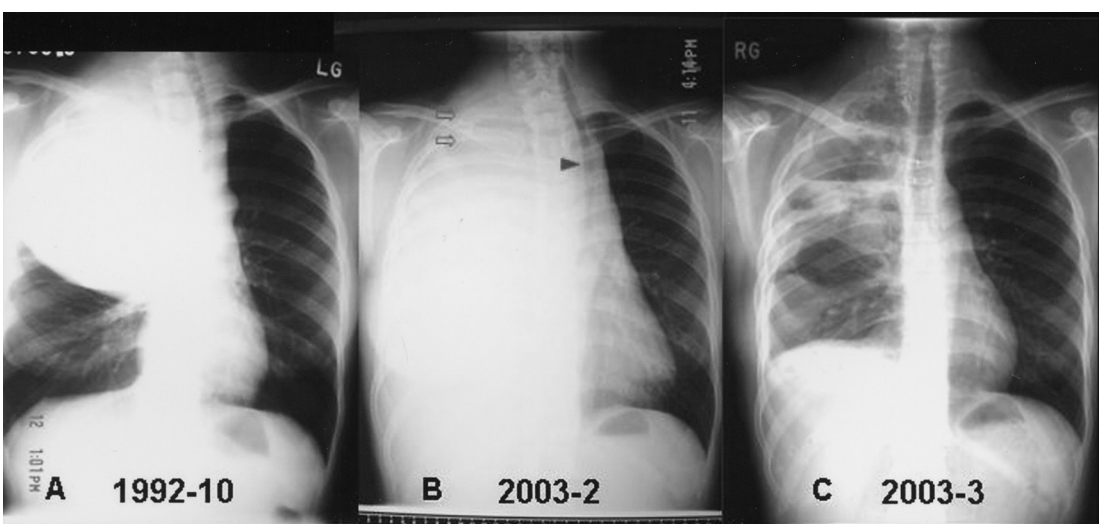

Fig. 1. Chest PA radiography shows a progressing mass (A → B) lesion in right lung field with 2nd and 3rd rib destruction (hollow arrow), tracheal deviation, and a left-shifting mediastinum (arrowhead). C, Postoperative chest PA radiography is shown. The 2nd and 3rd ribs were not removed because the hemangioma could be separated from the chest wall without difficulty during operation.

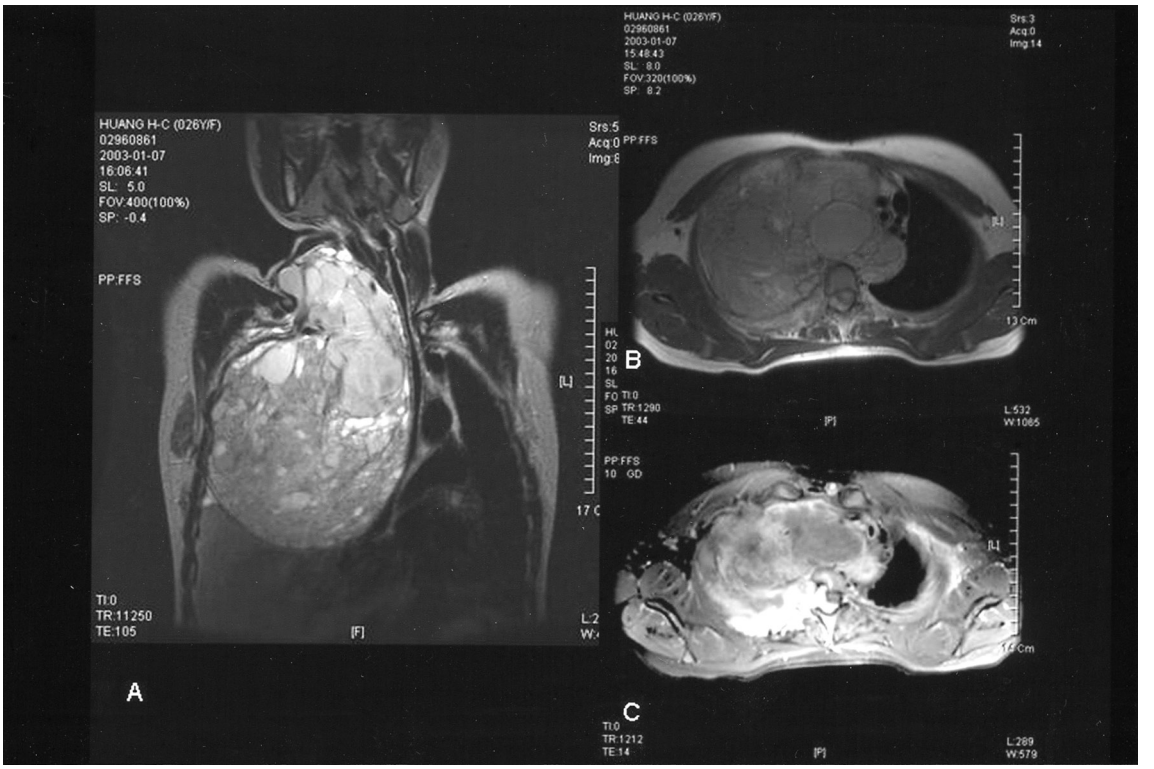

Fig. 2. MRI pictures of the hemangioma. A, T2-weighted coronal image in the chest MRI reveals a huge heterogeneous cervicomediastinal mass with multiple thin-walled cysts, a left-shifting mediastinum, and envelopment of the right subclavian artery. The density of the hemangioma was considerably higher than that of skeletal muscle and was slightly more intense than fat. B, T1-weighted cross section image shows multiple fluid-fluid levels in the cysts. The hemangioma was homogenous and significantly less intense than fat. C, Gd-enhanced fatsat T1-weighted cross section image in the chest MRI demonstrates that the spinal canal is involved, with spinal cord compression (hollow arrow). There is also a marked peripheral enhancement.

be divided into a posterior and an anterior phase. In the posterior phase (Figure 3A), the patient was put in the left lateral position. A laminectomy of C6-T3 for removal of the intraspinal canal lesion and a thoracotomy to debulk the intrathoracic part were done via a high posterolateral thoracotomy. When the patient was put in the supine position, the anterior transmanubrial-thoracic approach (Figure 3B), as described by Grunenwald et al [4], was performed to spare the subclavian artery, phrenic nerve, and recurrent laryngeal nerve, and to remove the neck and intrathoracic residual tumor. The mass measured 25 x 15 x 15 cm (Figure 4A), and it took 13 hours to complete the whole procedure. The final pathological diagnosis was venous hemangioma. Grossly, it appeared as a soft compressible mass and had many small to large cavities with a hemorrhagic appearance (Figure 4A, insert). Microscopically (Figure 4B), the mass was characterized by large, thick-walled vessels with dilated lumens and well-developed muscular walls. An admixture of some small-to-medium-sized vessels was also apparent. There was no evidence of malignancy.

The postoperative course of this patient was unremarkable except that a neck collar was needed for head support in the first few days postoperatively. The patient was discharged with a minimal sequela: numbness of the right forearm along the T1 distribution.

Discussion

Hemangiomas are rare tumors of the mediastinum and account for less than 0.5% of mediastinal

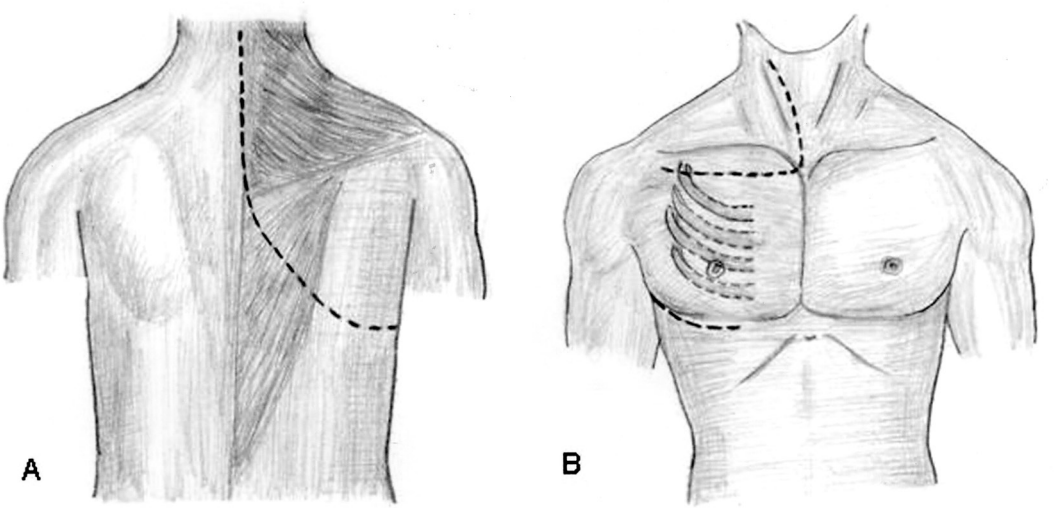

Fig. 3. Posterior (A) and anterior (B) phase of the surgical approach to the tumor over the cervicomediastinal region.

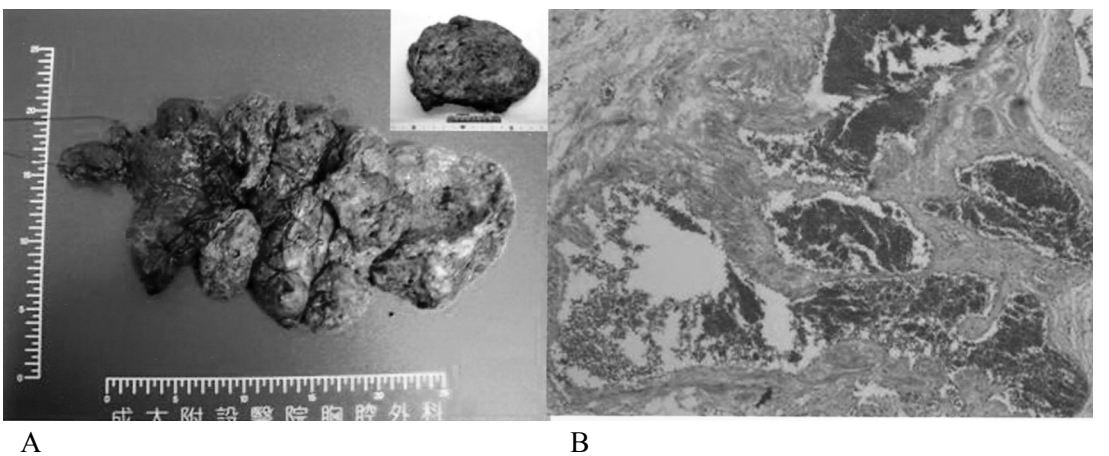

Fig. 4. Both macro- and microscopic findings of the hemangioma. A, The tumor measured around 25 x 15 x 15 cm. It was spongy and had many small to large vascular channels (cross section: insert) with a hemorrhagic appearance. B, Groups of dilated vascular channels with some fibrous tissue and well-developed muscular walls. No evidence of malignancy can be seen (hematoxylin-eosin; x 40).

masses. Only 103 cases had been reported in the literature up to 1987 [5]. They are usually discovered by a routine chest X-ray examination, often in asymptomatic patients. However, the mediastinal hemangioma may extend into the neck as a first presenting sign, as in the case we report here. The tumor presented in this case report behaved like a cervicomediastinal lymphangioma (cystic hygroma): it grew slowly but enveloped or compressed the adjacent structures [2].

Phleboliths (calcified thrombi), which can usually be demonstrated on CT, but not on chest radiographs, are believed to be a specific finding of mediastinal hemangiomas. However, these have been seen in only 10-30% of cases with hemangioma [1-2,5]. According to McAdams et al. [1], dynamic CT study-contrast opacification is another useful tool for diagnosing mediastinal hemangioma, because when a well-circumscribed heterogeneous mediastinal mass appears on unenhanced CT scans, injection of a bolus of contrast material may show enhancement peripherally in the beginning and then

filling in the center gradually. However, neither of these specific image findings were the case here.

Hemangiomas often have a homogeneous internal structure, but they may be heterogeneous in the presence of hemorrhage or a thrombus related to a different stage. Although we did not get an accurate preoperative diagnosis from our MRI study, our MRI images were consistent with the findings of Worthy et al. [6], that on T1-weighted images, hemangiomas are homogenous and significantly less intense than fat (Figure 2B). On T2-weighted images they are of considerably higher intensity than skeletal muscle and are slightly more intense than fat (Figure 2A). On Gd-enhanced fatsat T1-weighted images, there is heterogeneous peripheral enhancement (Figure 2C). In addition to the information mentioned above, MRI and CT scans demonstrated the extent of spinal and neck invasion clearly, especially the former. In agreement with Cohen et al. [5] and Schurawitzki et al. [3], we found that transthoracic needle biopsy of mediastinal hemangiomas is of little diagnostic value for the establishment of the diagnosis because the specimen is too small.

Surgical excision of a mediastinal hemangioma remains the recommended choice of treatment for both diagnosis and symptom relief. Even Cohen et al. [5] suggested that subtotal resection is a therapeutic option in these cases because it avoids the increased morbidity and mortality of an extensive mediastinal resection. We believe, however, that total excision with few sequelae is possible for mediastinal hemangiomas once they are well circumscribed. For the tumor-involved cervicomediastinal region, we agree with Grunenwald et al. [4] that combined anterior and posterior approaches allow safe control and resection of the thoracic inlet structure. In cases of simultaneous intraspinal canal extension, the vertical component of the posterior approach incision could be placed in the midline of the lower neck and upper back, just overlying the spinous processes. The incision then curves into a sloping transverse line that sweeps forward to become a standard high posterolateral thoracotomy. Laminectomy can be done posteriorly through the vertical portion of the incision, and thorcotomy can be performed laterally in the same wide incision. The anterior transmanubrial-thoracic approach provided us excellent exposure of the right recurrent laryngeal and right phrenic nerves, as well as safe control of the right subclavian artery and its branches. This approach did not involve the resection of the clavicle and muscular sacrifice; therefore, shoulder girdle movement was fully maintained.

Mediastinal hemangioma, especially when both the neck and mediastinum are involved, remains a challenge for both diagnosis and treatment. It is difficult to establish a definite diagnosis with a noninvasive survey or even a needle biopsy [3]. Consequently, a well-planned surgical intervention seems to be the only convincing method for both diagnosis and therapy.

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縱膈腔血管瘤合併頸部及脊椎侵犯—病例報告

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良性血管瘤只佔縱膈腔腫瘤中百分之 0.5 ，因為表現並無特異性且由非侵襲性的檢查不易診斷出來，開刀前往往無法確定診斷。我們報告一位 27 歲血管瘤的病人，手術時發現：整個血管瘤約 25 × 15 × 15 公分，侵犯到脊椎及頸部並壓迫大血管及整個右肺。在胸腔外科及神經外科合作下，整個腫瘤仍可完全取出。

在縱膈腔腫瘤中血管瘤雖然極為罕見，仍須列入鑑別診斷之一。***（胸腔醫學 2003; 18: 461-466）***

關鍵詞：縱膈腔腫瘤，血管瘤，脊椎侵犯

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