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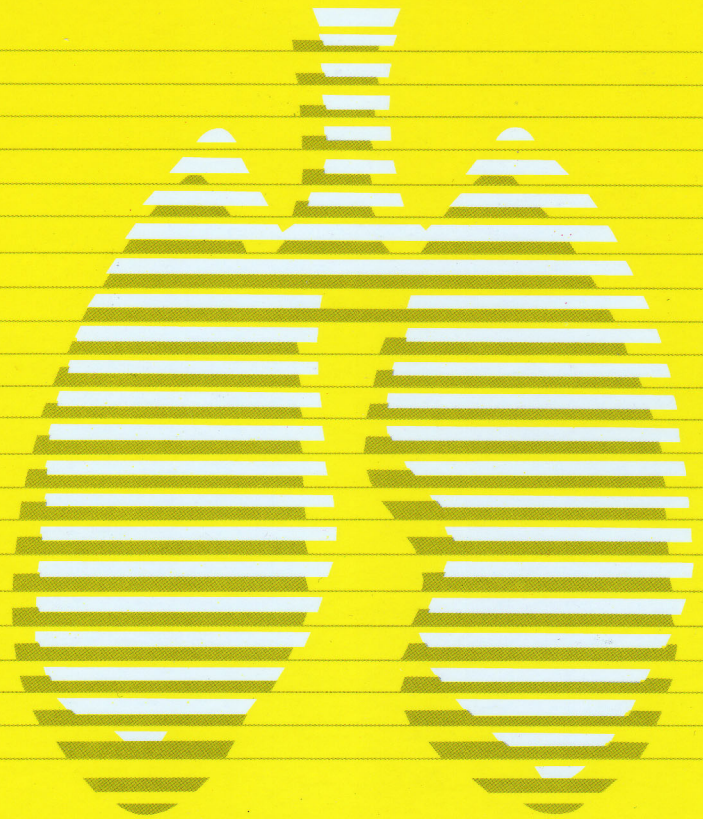

台灣胸腔暨重症加護醫學會

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原著

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Orginial Articles

Case Reports

Outcome and Predictors of Prolonged Mechanical Ventilation in Patients with Heart Failure

Hung-Yu Huang*, Li-Fu Li*,**, Chung-Shu Lee***, Chee-Jen Chang****, Ning-Hung Chen*,**

Introduction: Cardiac dysfunction is 1 of several common factors related to prolonged mechanical ventilation (PMV). We investigated the weaning success rate of patients with heart failure (HF), who received PMV and the factors associated with weaning success in these patients.

Methods: This was a retrospective observational study on patients with HF who received PMV in a 24-bed respiratory care center (RCC) between January 2011 and December 2013. The main outcome was weaning success, which was defined as more than 7 days entirely free from mechanical ventilator support.

Results: In total, 117 patients with HF and 634 patients without HF treated in the RCC during the study period were included. The HF group had a significantly lower rate of weaning success (40.2% vs. 51.7%, $P<0.05$) and a higher rate of in-hospital mortality (46.2% vs. 37.5%, $P=0.11$). In the HF group, the left ventricular ejection fraction and B-type natriuretic peptide were similar in patients with successful weaning and in those with unsuccessful weaning. The successfully-weaned patients with HF had a higher Glasgow coma scale (GCS) score, required less hemodialysis support, exhibited a high serum albumin level, and fewer of them having received a coronary artery bypass graft (CABG). Multivariable analysis revealed the most crucial predictor for weaning success was a high GCS score ($P<0.001$). Other clinically important predictors were higher albumin level ($P=0.047$) and decreased hemodialysis support ($P=0.047$). The successfully-weaned patients in the HF group had a significantly lower in-hospital mortality rate (23.4% vs. 61.4%, $P<0.001$).

Conclusions: Patients with HF who received PMV had lower weaning and higher mortality rates than did patients without HF. Patients with HF who had an enhanced consciousness level, reduced hemodialysis use, and no history of receiving a CABG were more likely to be weaned from mechanical ventilation. ***(Thorac Med 2016; 31: 311-322)***

Key words: prolonged mechanical ventilation, heart failure, weaning outcome

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Background

Heart failure (HF) is a clinical syndrome characterized by inadequate systemic perfusion to meet the body's metabolic needs [1]. The incidence and prevalence of HF are considerably high in an aging population [2]. At least 10% of hospital admissions of people aged ≥65 years are due to HF, and the ICU admission rate for such patients ranges from 10% to 45% [3-5]. Mechanical ventilation (MV) support is the main reason for ICU transfer [3]. The outcome of patients with HF in the ICU is poor and the 30-day mortality rate was reported to be from 4.5-27% [6].

During the weaning process, patients with HF are more susceptible to hemodynamic change, and cardiac dysfunction has been identified as the primary cause of unsuccessful weaning [7]. A proportion of patients with HF in the ICU require prolonged mechanical ventilation (PMV), which is commonly defined as continuous MV for more than 21 days [8]. Several factors contribute to PMV, including old age, multiple comorbidities, cardiovascular disease, COPD, poor nutritional status, and muscle weakness [9]. However, previous studies have not focused specifically on the outcomes of patients with HF or the effects of cardiac function on PMV because of relatively small sample sizes [10-12].

PMV is associated with increased hospital treatment costs, more MV-related complications, and higher mortality rates [13]. Studies on clinical characteristics and outcomes of patients with HF who received PMV are limited and few studies have focused on management of the weaning process in ventilator-dependent patients with HF. Therefore, we investigated the effects of HF on the main outcomes, including weaning failure and mortality and identified the predictive factors for prolonged weaning.

Materials and Methods

Patients and inclusion criteria

The respiratory care center (RCC) is a 24-bed unit in Linkou Chang Gung Memorial Hospital in Taiwan. It was designed to care for patients with PMV. Patients in the ICU are eligible for RCC transfer if they have been maintained on MV for more than 21 days with unsuccessful weaning attempts. The transfer criteria include stable hemodynamics, no vasoactive or sedative drug use, and stable oxygen requirements (fraction of inspired oxygen less than 45%, and positive end-expiratory pressure less than 10 cm H_2O).

Patients were included in this study if they were diagnosed with HF before being transferred to the RCC between January 2011 and December 2013. Clinical physicians diagnosed HF on the basis of clinical HF signs and symptoms by using modified Framingham criteria, regardless of the value of the left ventricular ejection fraction (-LVEF) [14]. LVEF was determined during hospitalization using echocardiography, and reduced systolic function was defined as LVEF<50%. HF was classified as "chronic" if patients had a history of HF and "de novo" if patients did not.

This study was approved by the Institutional Internal Review Board (IRB) for Human Studies at Chang Gung Memorial Hospital (permit number: 104-1140B). According to the rules of the IRB, no consent was needed for this retrospective study.

Weaning process

Specialists in pulmonary and critical care

medicine evaluated the clinical condition and set the daily weaning process target. Spontaneous breathing trials (SBTs) were started when ventilatory support was gradually reduced to pressure support mode. Translaryngeal intubated patients were ready to be extubated if they had no signs of weaning failure during a 2-hour T-piece trial.

For tracheostomized patients, SBTs was carried out via gradually increasing the duration of use of a Venturi tracheostomy mask from 2 hours to 24 hours. Patients were liberated from ventilatory support after the 24-hour SBT.

Assessed Variables

Medical records were retrospectively reviewed. We recorded demographics, reasons for initiating MV, length of ICU stay prior to RCC admission, length of RCC stay, age, gender, Glasgow coma scale (GCS) score at initial hospital admission (maximum score was 15), LVEF, B-type natriuretic peptide (BNP), EKG rhythm, renal replacement therapy (RRT) needs, body mass index (BMI), co-morbidities (presence or absence of end-stage renal disease (ESRD), hypertension, diabetes mellitus, stroke, chronic respiratory disorders), coronary artery bypass graft (CABG, current CABG was defined as receiving a CABG during this admission), tracheostomy, RCC and in-hospital mortality. Maximum inspiratory negative pressure (Pimax) and rapid shallow breathing index (RSBI) were recorded when we began SBT. The following variables were recorded within 24 hours of admission to the RCC: GCS scores (verbal score = 1 for those who were intubated and the maximum score was 11), Acute Physiology and Chronic Health Evaluation II (APACHE II) score, serum albumin, blood creatinine level, and ventilator mode.

Definition of outcomes

The main outcome was successful weaning from MV support for 7 consecutive days and nights [8,12]. Other outcomes included length of hospital stay, RCC mortality and in-hospital mortality. Ventilator dependence was defined as being unable to be weaned from the ventilator in the RCC after rigorous effort for more than 42 days. Patients with weaning failure included those who expired in the RCC and those who were regarded as ventilator-dependent.

Statistical analysis

Continuous data are expressed as the mean ± standard deviation (SD) and categorical data are expressed as the count (percentage, %). The data were then compared between patients with weaning failure and those with successful weaning using the *t*-test for continuous variables and Chi-square tests for categorical variables. Univariate and multivariate logistic regression analyses were used to identify the risk factors associated with weaning failure. SPSS Statistics for Windows, version 17.0, was used for data analysis.

Results

Patient characteristics

During the study period, 751 patients were admitted to the RCC for PMV (Figure 1), The overall successful RCC weaning and RCC mortality rates were 49.9% and 24.9%, respectively (Table 1). Among the 751 patients receiving PMV, 117 were diagnosed with HF (prevalence of 15.6%). Compared with the patients without HF, the patients with HF had a long-term RCC stay, received long-term MV, and had high APACHE II scores. The 2 groups were comparable in age, sex and GCS scores. Compared

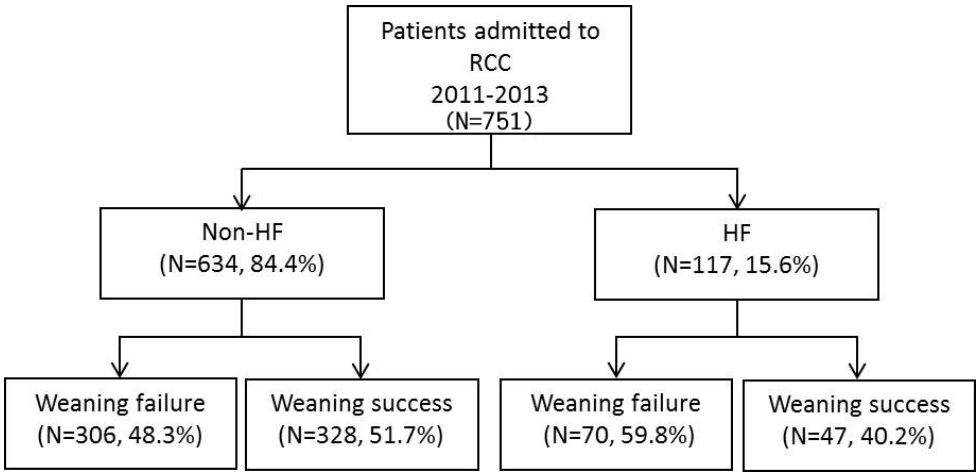

Fig. 1. Schematic Representation of the Studied Population
Acronyms: RCC: respiratory care center, HF: heart failure, non-HF: non-heart failure

Table 1. Demographics of Patients in RCC during 2011~2013

	ALL (N=751)	Non-HF (N=634, 84.4%)	HF (N=117, 15.6%)	*p*-value
Age, years	71.2 ± 16.2	70.8 ± 16.2	73.3 ± 16.2	0.130
Gender, Male (%)	405 (53.9%)	341 (53.8%)	64 (54.7%)	0.885
APACHE II	20.5 ± 5.9	20.3 ± 6.0	21.7 ± 5.7	0.015*
GCS score	8 ± 3	8 ± 3	8 ± 3	0.586
RRT				
No	515 (68.6%)	444 (70.0%)	71 (60.7%)	0.014*
ESRD under regular RRT	57 (7.6%)	51 (8.0%)	6 (5.1%)	
RRT During admission	179 (23.8%)	139 (21.9%)	40 (34.2%)	
Tracheostomy	405 (53.9%)	344 (54.3%)	61 (52.1%)	0.672
Hospital stay, days	90.8 ± 70.0	91.4 ± 73.9	87.7 ± 43.3	0.605
RCC stay, days	27.1 ± 31.1	26.8 ± 32.5	28.5 ± 21.6	0.601
ICU stay, days	29.7 ± 22.6	29.4 ± 22.9	31.0 ± 21.4	0.503
RCC mortality	187 (24.9%)	151 (23.8%)	36 (30.8%)	0.079
In-hospital mortality	292 (38.9%)	238 (37.5%)	54 (46.2%)	0.110
Weaning				
Failure	376 (50.1%)	306 (48.3%)	70 (59.8%)	0.022*
Success	375 (49.9%)	328 (51.7%)	47 (40.2%)	

Continuous data expressed as mean±SD, and categorical data expressed as number (%). *Indicates a statistically significant between-group difference (P<0.05).
GCS score: Glasgow coma scale score, ESRD: end stage renal disease, RRT: renal replacement therapy

with the non-HF group, the patients with HF showed a significantly lower successful weaning rate (40.2% vs 51.7%, *P*=0.035) and a higher in-hospital mortality rate (46.2% vs 37.5%, *P*=0.11).

Chronic HF was diagnosed in 58.1% of the patients and de-novo HF was diagnosed in 41.9% of them. Ischemic heart disease (47.9%), valvular heart disease (17.1%), and hypertension (18.8%) were the most common etiologies of HF. The baseline characteristics including mean LVEF, BNP, and comorbidities, were similar between the weaning success and weaning failure groups. The patients with weaning failure had a significantly higher rate of undergoing a CABG (*P*=0.021) (Table 2).

The clinical data of the patients with HF immediately after they were transferred to RCC were similar, except that the group with successful weaning had high GCS scores, a high estimated glomerular filtration rate (eGFR), and high albumin levels (*P*<0.05 for all). Similarly, the causes of initiating MV, including cardiovascular diseases (acute myocardial infarction, congestive heart failure, and pulmonary embolism), infection (pneumonia and sepsis), and cerebrovascular disease (acute stroke) were comparable. The patients with weaning failure showed a high rate for receiving RRT during ICU or RCC admission (44.3% vs 19.1%, *P*= 0.014).

The lengths of stay in the ICU before transferring to the RCC and the lengths of hospital stay were similar between the 2 groups. Patients with successful weaning had a significantly lower mortality rate than did those with weaning failure (23.4% vs 61.4%, *P*<0.001) (Table 4).

Factors predicting weaning failure

Univariate analysis revealed associations between several variables and prolonged weaning (Table 5). Multivariate analysis showed that RRT during admission [odds ratio (OR)=2.88, 95% confidence interval (CI)=1.02-8.16, *P*=0.047] and having received CABG [OR=3.29, 95% CI=0.91-11.9, *P*=0.070] were risk factors for weaning failure. In contrast, a high GCS score in the RCC [OR=0.75, 95% CI=0.63-0.87, *P*<0.001] and high serum albumin [OR=0.35, 95% CI=0.12-0.99, *P*=0.047] were protectors against weaning failure.

Discussion

Patients receiving PMV are increasing in number and have high resource utilization [15]. Patients with HF are a difficult-to-treat subgroup of patients who receive PMV. Our results revealed that patients with HF who received PMV had substantially less successful weaning and increased requirements for RRT compared with the other patients in our RCC. In the HF group, patients with successful weaning had significantly higher RCC and in-hospital survival rates than did those with weaning failure.

The weaning and RCC survival rates of patients who received PMV in our RCC were 49.9% and 75.1%, respectively, which is consistent with reported weaning rates and hospital survival rates of 40-60% and 50-90%, respectively [11-12]. The common reasons for undergoing PMV are acute or chronic lung injury, neurological diseases, cardiovascular disease, and musculoskeletal diseases. After PMV, the characteristics of the patients admitted to our RCC were heterogeneous. Some recent reports have focused on analyzing the outcomes of patients with COPD, an older age, and ESRD who received PMV [16-18]. However, data that could reveal the influence of cardiac function

Table 2. Clinical Characteristics of Heart Failure Patients with PMV

	ALL (N=117)	Weaning failure (N=70, 59.8%)	Weaning success (N=47, 40.2%)	*p*-value
Age, years	73.3 ± 16.2	75.5 ± 14.9	69.9 ± 17.6	0.065
Sex, Male (%)	64 (54.7%)	38 (54.3%)	26 (55.3%)	0.912
Chronic HF	68 (58.1%)	44 (62.8%)	24 (51.1%)	0.252
De novo HF	49 (41.9%)	26 (37.2%)	23 (48.9%)	0.252
HFrEF	89 (76.7%)	51 (73.9%)	38 (80.9%)	0.385
LVEF %	42.6 ± 10.6	42.5 ± 11.1	42.6 ± 9.9	0.968
<30%	11 (9.4%)	8 (11.4%)	3 (6.4%)	0.359
≥30%	106 (90.6%)	62 (88.6%)	44 (93.6%)	
BNP	1457.4 ± 1381.4	1505.1 ± 1428.3	1384.0 ± 1320.8	0.672
Etiology of HF				0.479
Ischemic heart disease	56 (47.9%)	32 (45.7%)	24 (51.1%)	
Valvular heart disease	20 (17.1%)	12 (17.1%)	8 (17.0%)	
Hypertension	22 (18.8%)	15 (21.4%)	7 (14.9%)	
Post cardiac resuscitation	3 (2.6%)	3 (4.3%)	0 (0%)	
Sepsis	8 (6.8%)	3 (4.3%)	5 (10.6%)	
Others	8 (6.8%)	5 (10.6%)	3 (4.3%)	
EKG rhythm				0.363
Sinus	63 (53.8%)	34 (48.6%)	29 (61.7%)	
Atrial fibrillation	47 (40.2%)	31 (44.3%)	16 (34.0%)	
Pacemaker	7 (6.0%)	5 (7.1%)	2 (4.3%)	
Hypertension	87 (74.4)	53 (75.7%)	34 (72.3%)	0.682
Diabetes mellitus	45 (38.5%)	25 (35.7%)	20 (42.6%)	0.456
Chronic respiratory disorders	34 (29.1%)	19 (27.1%)	15 (31.9%)	0.577
Stroke	23 (19.7%)	15 (21.4%)	8 (17%)	0.556
Chronic kidney disease	65 (55.6%)	42 (60.0%)	23 (48.9%)	0.238
CABG	19 (16.2%)	16 (22.8%)	3 (6.4%)	0.012*
Previous CABG	7 (6.0%)	6 (8.6%)	1 (2.1%)	
Current CABG	12 (10.2%)	10 (14.3%)	2 (4.3%)	

Continuous data expressed as mean±SD, and categorical data expressed as number (%). *Indicates a statistically significant between group difference (P<0.05).PMV: prolonged mechanical ventilation, HF: heart failure, HFrEF: heart failure with reduced ejection fraction, LVEF: left ventricular ejection fraction, BNP: B-type natriuretic peptide, CABG: coronary artery bypass graft, ACEi: angiotensin-converting-enzyme inhibitor, ARB: angiotensin receptor blocker

on successful weaning rates and hospital survival outcomes are scant. In the report by Wu *et al* (2009), patients with cardiovascular disease had a lower weaning rate than the other groups (48.1% vs 58.4%, P=0.202) [12]. However, we confirmed that patients with HF had significantly lower weaning rates and a trend toward lower survival rates compared to patients with-

Table 3. Clinical Characteristics of Patients with Heart Failure after Transfer to the RCC

	ALL (N=117)	Weaning failure (N=70, 59.8%)	Weaning success (N=47, 40.2%)	*p*-value
Body mass index	23.8 ± 5.4	23.6 ± 4.7	24.0 ± 6.5	0.780
APACHE II	21.7 ± 5.7	22.4 ± 5.8	20.7 ± 5.5	0.107
Tracheostomy	61 (52.1%)	38 (54.3%)	23 (48.9%)	0.570
Reasons for initiating MV				
Cardiovascular	54 (46.2%)	36 (51.4%)	18 (38.3%)	0.260
Infection	37 (31.6%)	22 (31.4%)	15 (31.9%)	
Cerebrovascular	9 (7.7%)	3 (4.3%)	6 (12.8%)	
Others	17 (14.5%)	9 (12.9%)	8 (17.0%)	
GCS score				
Hospital admission	12 ± 3	12 ± 4	12 ± 4	0.938
RCC	8 ± 3	7 ± 3	10 ± 2	<0.001*
eGFR (ml/min/1.73 m^2)				
Hospital admission	51.6 ± 34.7	49.0 ± 34.6	55.6 ± 35.0	0.317
RCC	43.3 ± 37.8	33.5 ± 26.8	60.3 ± 47.6	0.013*
RRT				
ESRD under RRT	6 (5.1%)	4 (5.7%)	2 (4.3%)	0.014*
RRT since admission	40 (34.2%)	31 (44.3%)	9 (19.1%)	
Serum albumin (g/dL)	2.7 ± 0.5	2.6 ± 0.5	2.9 ± 0.5	0.012*
Pimax (cm H_2O)	59.7 ± 52.0	58.3 ± 54.2	61.4 ± 49.8	0.771
RSBI	97.4 ± 66.9	111.8 ± 75.8	80.7 ± 50.8	0.020*
MV Mode at RCC transfer				
Pressure Support (PS)	90 (76.9%)	54 (77.1%)	36 (76.6%)	0.945
Pressure Control (PC)	27 (23.1%)	16 (22.9%)	11 (23.4%)	

Continuous data expressed as mean±SD, and categorical data expressed as number (%). *Indicates a statistically significant between group difference (P<0.05). MV: mechanical ventilation, LVEF: left ventricular ejection fraction, BNP: B-type natriuretic peptide, eGFR: estimated glomerular filtration rate, RRT: renal replacement therapy, Pimax: maximum inspiratory negative pressure, RSBI: rapid shallow breathing index

Table 4. Clinical Outcomes of HF Patients Who Were Successfully vs. Unsuccessfully Weaned from Prolonged Mechanical Ventilation

	ALL (N=117)	Weaning failure (N=70, 59.8%)	Weaning success (N=47, 40.2%)	*p*-value
Hospital stay, days	87.7 ± 43.3	83.5 ± 45.1	94.0 ± 40.0	0.197
RCC stay, days	28.5 ± 21.6	31.0 ± 23.5	24.7 ± 18.0	0.109
ICU stay, days	31.0 ± 21.4	33.3 ± 23.1	27.3 ± 18.3	0.136
RCC mortality	36 (30.8%)	36 (51.4%)	0 (0.0%)	<0.001*
In-hospital mortality	54 (46.2%)	43 (61.4%)	11 (23.4%)	<0.001*

Continuous data expressed as mean±SD, and categorical data expressed as number (%). *Indicates a statistically significant between group difference (P<0.05).

Table 5. Univariate and Multivariate Analysis of Predictors of Prolonged Weaning

	Univariate analysis		Multivariate analysis	
	OR (95%CI)	*p*-value	Adjusted OR (95% CI)	*p*-value
GCS score at RCC	0.71 (0.61-0.84)	<0.001	0.75 (0.63-0.87)	<0.001*
Serum albumin	0.35 (0.15-0.81)	0.015	0.35 (0.12-0.99)	0.047*
RRT				
no	1		1	
ESRD under regular RRT	2.61 (0.23-29.4)	0.438	1.12 (0.13-9.81)	0.916
RRT during admission	2.76 (0.87-8.79)	0.086	2.88 (1.02-8.16)	0.047*
CABG	4.70 (1.29-17.1)	0.019	3.29 (0.91-11.90)	0.070

Data were tested using logistic regression analysis and are presented as odds ratio (OR) and 95% confidence interval (CI). *Indicates a statistically significant predictor (P<0.05).

out HF.

Cardiac dysfunction is 1 of the most common causes of unsuccessful weaning [7]. When the use of MV support is gradually reduced, respiratory distress may manifest because of the increase in the work of breathing, sympathetic tone, or myocardial oxygen demand [19]. During spontaneous breathing, ventilator support is shifted from positive to negative pressure ventilation, and this decrease in intrathoracic pressure may increase the pre- or afterload of left ventricle, or decrease in left ventricle compliance [20]. Patients with prior coronary artery disease, congestive heart failure, or COPD are particularly at risk of weaning-induced cardiac dysfunction [21].

Cardiac dysfunction negatively affects the weaning of patients receiving PMV. However, a reliable marker for predicting the weaning outcome before SBTs is not available. Similar to some studies [22-23], markers of HF such as LVEF and BNP did not correlate with the weaning success of our patients who received PMV. Although BNP is a prognostic marker of mortality in patients receiving RRT, the value is confounded by residual renal function and is not a precise marker of volume status [24]. In the regression model, receiving a CABG previously or currently was determined to be a risk factor for PMV in patients with HF. Patients that use MV for more than 72 hours immediately after receiving a CABG had higher in-hospital mortality and lower future survival rates even after surviving the initial postoperative period for up to 5 years [25]. This would be due to poor cardiac function and more difficulty with postoperative pulmonary rehabilitation. However, the impact of previous CABG on weaning from mechanical ventilation in patients with HF remains unclear. Future large-scale study would be needed to confirm the effect of previous CABG on PMV.

The prevalence of chronic kidney injury was >40% in patients with HF, and those with weaning failure were at a higher risk of receiving RRT in our study (34.2% vs 21.9%, P=0.014). HF is a critical risk factor for acute kidney injury in patients admitted to the ICU [26]. Another study revealed that, after ICU hospitalization, acute kidney injury developed in more than half of the study patients with HF (150/251) who had normal renal function on ad-

mission, and 30 patients subsequently received RRT [27]. Acute or acute-on-chronic kidney injury in patients admitted to the ICU increases the duration of ventilator weaning and the mortality rate [28]. Moreover, renal failure with RRT is considered to be an unfavorable indicator of patients with chronic respiratory failure. Kao *et al* (2011) associated RRT for patients receiving PMV with lower weaning and survival rates compared with those not receiving RRT [17]. Our study affirmed that RRT is also a strong predictor of poor weaning in patients with HF (OR= 2.88; *P*=0.047). A heart with impaired contractility is sensitive to fluctuation of body fluids, especially during the SBT, and the imbalance of body fluid may precipitate pulmonary edema.

We found that high GCS scores and serum albumin were predictors of weaning success. Albumin can reflect the nutrition status, and a higher albumin level was associated with weaning success in a previous report [12]. The consciousness level was similar among all patients of our study at the initial hospital admission. The impaired consciousness in our patients, for the most part, was not due to primary neurologic disorders, but may have been related to hypoxemia, sepsis, and brain hypoperfusion during the clinical course before transferring to the RCC. An active pulmonary rehabilitation program was routinely conducted for patients in our RCC. In patients with a poor GCS score, the lack of active pulmonary rehabilitation may have contributed to the need of PMV. Moreover, patients with poor consciousness who could not protect their airways had a higher probability of aspiration after extubation. Therefore, diminished consciousness is associated with PMV, longer lengths of hospital stay, and high rates of tracheotomy [29].

Our study has the following limitations. First, this was a retrospective analysis conducted in a single, tertiary medical center. Because our patients were transferred from a wide range of critical units, including medical ICUs, the coronary care unit, general surgical ICUs, and neurological-neurosurgical ICUs, the results may differ from those obtained from other hospital systems. Second, HF was diagnosed prior to RCC admission, and serial data on cardiac echo or BNP level during or after SBT were unavailable. In the HF group, each patient received echocardiography, and 85% had a BNP test. Cardiac ultrasound and BNP were completed before transfer to the RCC, with a time interval of about 1~3 weeks, so the LVEF and BNP may not reflect immediate hemodynamic changes during the weaning process. Third, we did not assess long-term outcomes after discharge. The long-term effect of RRT and the benefit of drugs for patients with HF receiving PMV are yet to be determined.

Conclusion

Almost 60% of patients with HF failed weaning in the RCC, with up to 60% of those patients subsequently dying in hospital. The results affirmed that HF is a risk factor for weaning failure and death among patients requiring PMV. Having received a CABG is a risk factor for necessitating PMV in patients with HF, and cardiac dysfunction is related to requiring more RRT during admission. In our weaning regression model, high GCS scores and serum albumin were associated with successful weaning in patients with HF requiring PMV. Because patients with HF are a difficult-to-treat subgroup, we suggest that consideration of these factors could aid clinicians in formulating treatment

plans for weaning programs.

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長期使用呼吸器的心臟衰竭患者預後及預測因子分析

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前言：心臟衰竭是長期使用呼吸器的常見因素之一。我們針對心臟衰竭患者進行研究，統計脫離呼吸器的成功率以及分析脫離成功的相關因子。

方法：在此回顧觀察性研究，收入 2011 至 2013 年在呼吸照護中心長期用呼吸器的心臟衰竭患者。主要指標是呼吸器脫離成功率。

結果：研究期間共 117 例心臟衰竭患者與 634 例其他患者入住呼吸照護中心。心衰組有較低的呼吸器脫離成功率和較高的住院死亡率。在心衰組中，左心室收縮分率和 B 型鈉尿肽類在呼吸器脫離成功與失敗的人中數值相近，成功脫離呼吸器的心衰竭患者表現出較高的昏迷指數（GCS）評分、較少接受血液透析，具有較高的血清白蛋白值，以及較少接受冠狀動脈繞道手術。多變數分析顯示預測呼吸器脫離成功最關鍵的因子是較高的昏迷指數。其他臨床上重要的預測因子包括白蛋白值、減少血液透析。在心臟衰竭組中，成功脫離呼吸器的患者有較低的死亡率。

結論：心臟衰竭患者與其他長期使用呼吸器的患者比較起來表現出較低的呼吸器脫離成功率和較高的死亡率。在心臟衰竭患者中，意識分數較高、沒有血液透析，和沒有接受過冠狀動脈繞道手術史者更容易脫離機械通氣。*(胸腔醫學* ***2016; 31: 311-322)***

關鍵詞：心臟衰竭，長期呼吸器使用，呼吸器脫離成果

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Impact of Initial Appropriate Antibiotics on the Outcomes of Patients with Community-Acquired and Non-Community-Acquired Sepsis in Intensive Care Units

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Introduction: This retrospective study was conducted to investigate the impact of initial antimicrobial therapy on the survival of patients with culture-positive community-acquired and non-community-acquired (healthcare-associated and hospital-acquired) sepsis.

Methods: All patients admitted to the intensive care unit (ICU) of Taipei Tzu Chi Hospital throughout 2014 who had culture-positive sepsis were retrospectively identified. The administration of antibiotics to which the recovered pathogens were susceptible was considered appropriate. The impact of initial appropriate antimicrobial therapy and other risk factors on the survival of patients with sepsis was assessed in univariate and multivariate Cox regression analyses.

Results: Patients with non-community-acquired sepsis had more comorbidities, significantly longer length of stay in the ICU, and greater 28-day ICU mortality and 90-day mortality ($p \leq 0.002$). While a greater proportion of subjects with community-acquired sepsis received initial appropriate antibiotics before admission to the ICU ($p \leq 0.015$), initial appropriate antibiotic administration was significantly associated with improved survival only in patients with non-community-acquired sepsis ($p=0.010$), and not in those with community-acquired sepsis. Multivariate analysis showed that the risk of death increased with increasing Acute Physiology and Chronic Health Evaluation II (APACHE II) scores in both patients with community-acquired sepsis (HR=1.14, $p=0.008$) and those with non-community-acquired sepsis, (HR=1.18, $p=0.014$).

Conclusions: Thus, appropriate empirical antimicrobial therapy is particularly important for lowering the risk of mortality of patients with non-community-acquired sepsis. ***(Thorac Med 2016; 31: 323-334)***

Key words: community-acquired, healthcare-associated, hospital-acquired, sepsis, survival

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Introduction

Sepsis, defined as an infection with evidence of systemic inflammatory response syndrome (SIRS) [1], continues to be a source of considerable morbidity and mortality [2-3]; 19 million cases are seen worldwide each year [4]. Clinical practice guidelines have been developed by the Surviving Sepsis Campaign for Management of Severe Sepsis and Septic Shock to improve the processes of care used to treat sepsis patients [5-6]. An important element in these guidelines is the treatment of the infection within the first hour of diagnosis [7-11] using empiric antimicrobial therapy that takes into consideration the site of infection, medical history, and susceptibility [12].

Initial empiric antimicrobial treatments should ideally consist of broad-spectrum agents in concentrations that are likely to reach all impacted organs [13], with subsequent adjustment or de-escalation of the dosage once the pathogen has been identified and susceptibility testing performed [14]. In addition, combination empiric therapy can be administered in certain cases, including those with suspected multidrug-resistant bacterial infections. Previous studies have demonstrated the importance of appropriate antibiotic administration, before the pathogen has been identified and before antimicrobial susceptibility testing results become available, to the survival of critically ill patients, especially those with sepsis caused by multidrug-resistant organisms [7,15-17]. There is evidence that a high proportion of pathogens recovered from healthcare-associated and hospital-acquired sepsis patients are multidrug-resistant organisms. However, the impact of initial appropriate antibiotic treatment on patients with sepsis acquired in different clinical settings is not well known.

This retrospective, single-center, observational study was undertaken to investigate the relationships between the application of empirical therapy prior to identification of the pathogen and mortality in patients with community, healthcare-associated and hospital-acquired culture-positive sepsis. We hypothesized that the impact of appropriate antimicrobial treatment on patient survival may differ in different clinical settings of septic patients.

Materials and Methods

Study and patients

Medical data and outcomes of patients with sepsis treated at Taipei Tzu Chi Hospital from January 1, 2014 to December 31, 2014 were included in this retrospective study. Initial empiric antibiotics, sepsis severity score, source of infection and other clinical data were obtained from medical charts.

Patients who had sepsis and were admitted to the medical ICU were included in this study. Sepsis was defined according to the American College of Chest Physician-Society of Critical Care Medicine consensus criteria that included clinical signs of infection with at least 2 of the following: temperature >38°C or <36°C, heart rate >90 beats/min, respiratory rate >20 breaths/min or $PaCO_2$ <32 mmHg, and WBC >12,000 cells/mm^3, <4000 cells/mm^3, or >10% immature (band) forms [18-19].

Patients were excluded if they had SIRS not induced by a microbe (but due to acute pancreatitis, burns, trauma, etc.). Those with tuberculosis, and virus and fungus infections were also excluded. This study was approved by the Taipei Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation Institutional Review Board on

Jan., 7, 2015 (Protocol No.: 03-X29-100).

Based on the infection sources, septic patients were initially placed into 1 of 4 groups: 1) those with community-acquired sepsis, living at home; 2) those in chronic health care facilities or nursing homes; 3) health care-associated patients living at home who were receiving chemotherapy, intravenous injection at a hospital, large wound care, hemodialysis within the most recent 30 days, or hospitalization within the most recent 90 days; and 4) hospital-acquired (new infection identified more than 48 hours after emergency room admission). Groups 2, 3 and 4 were further collectively labeled "non-community acquired" because of the same demographics, rates of distribution of appropriate antibiotics and mortality outcomes, in contrast to the community-acquired setting. Septic shock was defined as sepsis-induced refractory hypotension despite adequate fluid resuscitation along with perfusion abnormalities that may include, but are not limited to lactic acidosis, oliguria, or an acute alteration in mental status [18-19]. Severe sepsis was defined as sepsis with ≥1 sign of organ failure [20-21].

Antibiotic administration and determination of appropriate treatment

Antibiotics were administered within the first hour after sepsis diagnosis, before admission to the ICU. The antibiotic selection was based on the guidelines of the Surviving Sepsis Campaign Guidelines Committee [5-6]. The antibiotics were designated as "appropriate" if the yielded etiologic organism was susceptible to the therapeutic agent, as determined by the available susceptibility testing culture results [22].

Following Clinical and Laboratory Standards Institute guidelines, all pathogens were tested to determine the minimum inhibitory concentration (MIC) of the antibiotic used with qualitative interpretation (susceptible, intermediate, or resistant) using VITEK®2 (bioMérieux, Lyon, France). α and β-streptococcus and *Haemophilus influenza* were tested using the BBL™ Sensi-Disc™ Susceptibility Test Discs, following the manufacturer's instructions (Becton Dickinson and Company, Franklin Lakes, NJ, USA). Multiple drug-resistant pathogens were confirmed using the Sensi-Disc™ Susceptibility Test Discs twice.

Statistical analysis

Continuous variables are presented as mean and standard deviation (SD), and independent t tests were performed to compare the differences between patients with community-acquired and non-community-acquired sepsis. Categorical variables were presented as counts and percentages, and chi-square tests were performed for group comparisons. Kaplan-Meier curves with log-rank tests were used to compare the differences between appropriate and inappropriate initial antibiotic use relative to survival, and 28-day and 90-day survival rates. Univariate and multivariate Cox proportional hazard models were used to investigate the factors affecting survival. Factors found to be significant in the univariate analysis were included in the multivariate analysis. All statistical analyses were performed with IBM SPSS statistical software version 22 for Windows (IBM Corp., Armonk, NY, USA); 2-tailed *P*-values <0.05 indicated statistical significance.

Results

Baseline characteristics of the subjects

Using ICD-9 codes 038.0 to 038.9, and

the key words "sepsis, severe sepsis and septic shock", 545 patient admissions were retrieved from medical records. Among these, 9 patients that had repeated admissions to the ICU, 26 that had confirmed negative culture results, and 4 patients that decided to transfer to the hospice ward were excluded. After these exclusions, a total of 506 patients were included in this study.

Of the 506 subjects, 231 were female and 275 were male. Based on the source of infection, 147 patients were placed in the community-acquired sepsis group and 359 in the non-community-acquired sepsis group. The length of stay in the ICU was significantly longer for patients with non-community-acquired sepsis than for those with community-acquired sepsis (14.88 vs. 11.23 days, p=0.002) (Table 1). The mean Acute Physiology and Chronic Health Evaluation II (APACHE II) score, and ABG_HCO_3, BUN, CRE, PLT, and neutrophil levels were significantly higher in patients with non-community-acquired sepsis (all $p \leq 0.02$). The mean RBC levels and Glasgow Coma Scale (GCS) were significantly lower in the non-community-acquired group than in the community-acquired group (p=0.03 and p=0.002, respectively). Significant differences between the groups were also found in the source of the infection and the need for oxygenation (mechanical ventilation) ($p \leq 0.023$). In addition, 28-day ICU mortality, 90-day hospital mortality, and comorbidities were higher in individuals with non-community-acquired sepsis ($p \leq 0.002$; Table 1). A greater proportion of subjects with community-acquired sepsis received initial appropriate antibiotics, compared to those with non-community-acquired sepsis ($p \leq 0.015$). Finally, 28-day ICU mortality and 90-day hospital mortality were significantly higher in patients with non-community-acquired sepsis (p=0.002 and p=0.001, respectively; Table 1).

Differences in survival between those given appropriate and inappropriate antibiotics before admission to the ICU

To determine the impact on patient survival of inappropriate antibiotic administration before admission to the ICU, Kaplan Meier survival analysis was undertaken. In patients with community-acquired sepsis, there was a beneficial trend but not a statistically significant difference in survival between those who received appropriate and inappropriate initial antibiotics, individually, before admission to the ICU (p=0.085, Figure 1A). Among patients with non-community-acquired sepsis, the survival rate was significantly higher for subjects treated with appropriate antibiotics before admission to the ICU (p=0.01, Figure 1B). Initial appropriate antibiotic administration in this group of patients was also associated with a survival benefit (p=0.013).

Univariate and multivariate analyses used to identify factors associated with survival

Univariate analysis identified the first APACHE II, ABG_pH, Na, K, and CK_MB as being significantly associated with the survival rate of patients with community-acquired sepsis (all $p \leq 0.05$; Table 2). When all those factors were included in multivariate analysis, we found that the risk of death increased with increasing APACHE II scores (HR=1.14, p=0.008). However, there were no significant associations between ABG_pH, Na, K and CK_MB and survival using multivariate analysis (all $p > 0.05$; Table 2).

For patients with non-community-acquired sepsis, univariate analysis revealed that initial antibiotic use, the presence of multi-organ

Table 1. Baseline Characteristics of Subjects (n=506)

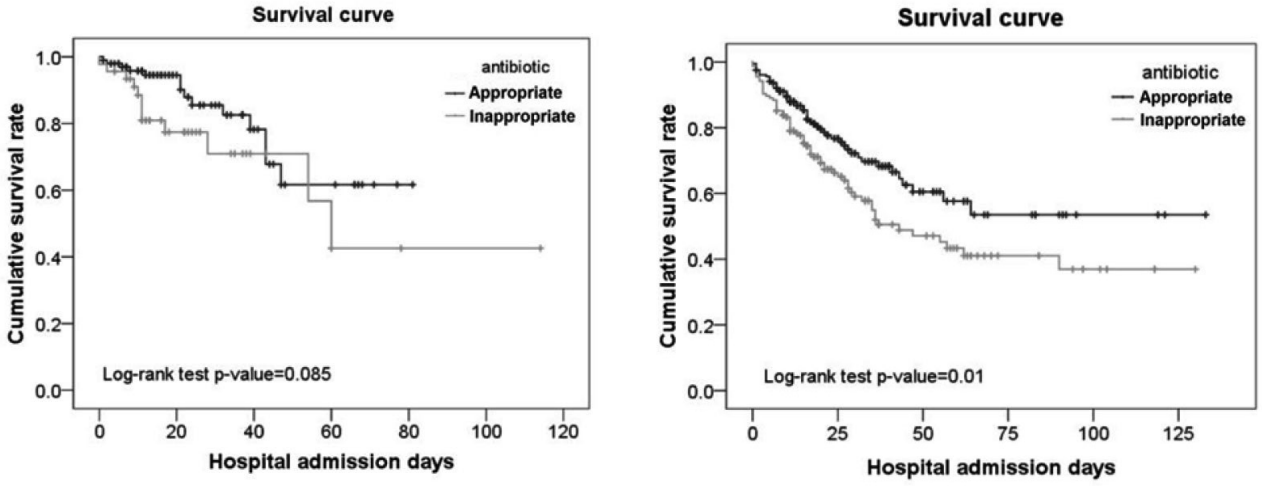
	Community (N=147)	Non-community (N=359)	*p*-value
28-day ICU mortality			0.002*
No	126 (85.7%)	261 (72.7%)	
Yes	21 (14.3%)	98 (27.3%)	
90-day hospital mortality			0.001*
No	121 (82.3%)	242 (67.4%)	
Yes	26 (17.7%)	117 (32.6%)	
Gender			0.111
Female	59 (40.1%)	172 (47.9%)	
Male	88 (59.9%)	187 (52.1%)	
Antibiotic			0.013*
Appropriate	101 (68.7%)	204 (56.8%)	
Inappropriate	46 (31.3%)	155 (43.2%)	
Source of infections			0.023*
Pneumonia/lung	73 (49.7%)	188 (52.4%)	
Abdomen other than urinary tract	13 (8.8%)	9 (2.5%)	
Urinary tract	15 (10.2%)	43 (12.0%)	
Blood	13 (8.8%)	24 (6.7%)	
Multiple sources (>1)	32 (21.8%)	85 (23.7%)	
Others	1 (0.7%)	10 (2.8%)	
Multi-organ dysfunction			0.745
No organ failure	13 (8.8%)	39 (10.9%)	
One organ failure	53 (36.1%)	120 (33.4%)	
Two organ failures	40 (27.2%)	109 (30.4%)	
≥3 organ failures	41 (27.9%)	91 (25.4%)	
Vasopressors			0.252
No	77 (52.4%)	208 (57.9%)	
Yes	70 (47.6%)	151 (42.1%)	
Oxygenation and ventilation			0.001*
Oxygen not needed	7 (4.8%)	25 (7.0%)	
Oxygen supplement	66 (44.9%)	97 (27.0%)	
Bi-PAP	15 (10.2%)	43 (12.0%)	
Ventilator	59 (40.1%)	194 (54.0%)	
Comorbidities			<0.001*
No	72 (49.0%)	78 (21.7%)	
Yes	75 (51.0%)	281 (78.3%)	
Length of stay in ICU (days)	11.2±11.0	14.9±13.4	0.002*
Hospital admission days	23.6±19.3	27.2±24.9	0.079

	Community (N=147)	Non-community (N=359)	*p*-value
APACHE II	23.9±6.8	26.9±6.4	<0.001*
ABG_pH	7.4±0.1	7.4±0.1	0.621
ABG_pCO_2 (mmHg)	40.4±20.5	42.4±21.1	0.334
ABG_pO_2 (mmHg)	106.2±72.6	117.8±83.4	0.141
ABG_HCO_3 (mEq/L)	21.3±6.7	23.0±7.4	0.018*
ABG_SaO_2 (%)	91.0±13.8	91.1±15.1	0.964
Na^+ (mEq/L)	134.3±8.4	133.9±8.6	0.695
K^+ (mEq/L)	4.1±1.0	4.1±0.9	0.767
GLU (mg/dL)	212.9±191.7	198.5±176.2	0.415
BUN (mg/dL)	37.7±27.8	46.4±37.8	0.004*
CRE (mg/dL)	2.1±1.6	2.5±2.3	0.02*
TBI (mg/dL)	2.3±3.9	2.3±4.6	0.947
AST (SGOT) (U/L)	207.8±757.5	93.5±400.5	0.229
ALT (SGPT) (U/L)	103.4±460.8	48.4±140.8	0.199
CK (mcg/L)	499.3±1555.7	230.0±843.7	0.201
CK_MB (mcg/L)	41.9±76.6	31.5±33.9	0.248
ALB (g/dL)	2.3±0.6	2.1±1.5	0.356
Tro_I (ng/mL)	0.2±0.6	0.2±0.6	0.336
CRP (mg/L)	11.0±11.1	10.6±9.5	0.753
NT_PROBNP (pg/mL)	6837.2±8280.7	8627.6±8265.5	0.308
PCT (μg/L)	14.4±34.4	10.7±29.6	0.529
Lactate (mmol/L)	4.1±4.1	3.6±3.5	0.33
PT (seconds)	12.3±2.4	12.4±3.9	0.809
APTT (seconds)	33.4±7.7	39.8±32.6	0.077
INR	1.2±0.3	1.2±0.4	0.671
WBC (10^3 cell/μL)	13.1±10.2	14.2±8.6	0.213
RBC (10^6 cell/μL)	3.9±1.0	3.7±0.9	0.03*
Hb (g/dL)	11.4±2.6	10.7±2.4	0.002*
Hct (%)	34.1±7.6	32.3±7.0	0.008*
MCV (fL)	89.1±9.1	88.4±9.5	0.480
PLT (10^3/μL)	178.1±89.8	205.2±109.0	0.004*
N_bandforms (%)	4.4±7.5	3.4±7.0	0.154
Neutrophils (%)	75.4±14.6	78.8±13.2	0.012*
Lymphocytes (%)	13.4±12.6	11.4±9.8	0.089
Monocytes (%)	4.9±3.7	4.9±3.5	0.983
Glascow coma scale (scales)	11.6±3.9	10.4±4.1	0.002*
Temperature (°C)	36.7±0.9	36.7±0.8	0.762

	Community (N=147)	Non-community (N=359)	*p*-value
Heart rate (bpm)	104.3±23.1	102.2±22.7	0.356
Respiratory rate (/min)	22.5±5.6	23.1±6.1	0.358
SBP (mmHg)	113.1±73.8	110.2±32.2	0.550

* $p<0.05$, representing a significant difference between the groups.

Abbreviations: ICU, intensive care unit; ER, emergency room; Bi-PAP, Bi-level positive airway pressure; APACHE II, Acute Physiology and Chronic Health Evaluation II; ABG_pH, arterial blood gas; GLU, glucose; BUN, blood urea nitrogen; CRE, creatinine; TBI, total bilirubin; SGOT, serum glutamic oxaloacetic transaminase; AST, aspartate transaminase; SGPT, serum glutamate-pyruvate transaminase; ALT, alanine transaminase; CK, creatine phosphokinase; MB, creatine phosphokinase-MB; ALB, albumin; Tro_I, troponin I; CRP, C reactive protein; NT_PROBNP, N-terminal prohormone of brain natriuretic peptide; PCT, procalcitonin; PT, prothrombin time; APTT, activated partial thromboplastin time; INR, international normalized ratio; WBC, white blood cell; RBC, red blood cell; Hb, hemoglobin; HCT, hematocrit; MCV: mean corpuscular volume; PLT, platelet; SBP, systolic blood pressure



(A) (B)

Fig. 1. Survival curves by appropriate and inappropriate antibiotic use in patients with sepsis. Kaplan Meier survival analysis was undertaken in patients with (A) community-acquired and (B) non-community acquired sepsis throughout their hospital stay.

dysfunction (≥3 organs), the need for drugs to raise blood pressure in the ICU, oxygenation, APACHE II, and BUN, CRE, ALB, CRP, lactate, neutrophil, monocyte, and heart rate levels significantly affected survival (all $p\leq0.05$; Table 2). After adjusting for all significant factors identified in univariate analysis, multivariate analysis showed that the risk of death increased with increasing APACHE II (HR=1.18, p=0.014) and CRP levels (HR=1.06, p=0.017), and decreased with increasing neutrophil levels (HR=0.91, p=0.002; Table 2).

Discussion

Our current study revealed that APACHE scores remained the most significant prognostic factor in both community-acquired and non-

Table 2. Univariate and Multivariate Analyses to Detect Factors Associated with Survival in Patients with Community-Acquired Sepsis (N=147) and Non-Community-Acquired Sepsis (N=359)

	Univariate		Multivariate	
	HR (95% CI)	*p*-value	HR (95% CI)	*p*-value
For patients with community-acquired sepsis (N=147)				
Antibiotic				
Appropriate	Ref		ref	
Inappropriate	1.9 (0.9-4.2)	0.092	1.8 (0.4-7.1)	0.43
APACHE II	1.15 (1.07-1.22)	<0.001*	1.1 (1.0-1.3)	0.008*
ABG_pH	0.06 (0.004-0.93)	0.044*	0.6 (0.1-58.6)	0.838
Na^+	0.96 (0.92-0.99)	0.020*	0.9 (0.8-1.0)	0.08
K^+	1.7 (1.1-2.6)	0.023*	1.4 (0.5-3.9)	0.539
CK_MB	1.004 (1.000-1.008)	0.036*	1.00 (0.99-1.01)	0.783
For patients with non-community-acquired sepsis (N=359)				
Antibiotic				
Appropriate	Ref		ref	
Inappropriate	1.6 (1.1-2.3)	0.011*	0.5 (0.1-1.5)	0.187
Multi-organ dysfunction numbers				
No organ failure	Ref		ref	
One organ failure	2.4 (0.8-6.7)	0.102	11.4 (0-62.7)	0.929
Two organ failures	2.3 (0.8-6.6)	0.111	49.4 (0-273.0)	0.935
≥3 organ failures	4.6 (1.7-12.8)	0.003*	54.4 (0-301.0)	0.95
Vasopressors				
No	Ref			
Yes	1.5 (1.0-2.1)	0.034*	1.3 (0.4-4.4)	0.675
Oxygenation and ventilation				
Oxygen not needed	Ref		ref	
Oxygen supplement	4.9 (0.7-36.2)	0.121	8.1 (0-25.8)	0.686
Bi-PAP	7.7 (1.0-57.8)	0.047*	8.55 (0-26.8)	0.685
Ventilator	6.7 (0.9-47.9)	0.06	28.5 (0-85.5)	0.696
APACHE II	1.1 (1.07-1.14)	<0.001*	1.2 (1.0-1.3)	0.014*
BUN	1.005 (1.001-1.009)	0.026*	1.00 (0.99-1.02)	0.642
CRE	1.08 (1.00-1.15)	0.039*	1.0 (0.8-1.2)	0.788
ALB	0.7 (0.5-1.0)	0.039*	2.8 (0.9-8.5)	0.064
CRP	1.04 (1.01-1.06)	0.001*	1.06 (1.01-1.12)	0.017*
Lactate (mmol/L)	1.11 (1.05-1.17)	<0.001*	1.1 (1.0-1.3)	0.102
Neutrophils	0.99 (0.98-1.00)	0.036*	0.91 (0.85-0.96)	0.002*
Monocytes	1.05 (1.01-1.09)	0.014*	0.9 (0.8-1.2)	0.543
Heart rate (bpm)	1.01 (1.00-1.02)	0.026*	1.00 (0.98-1.02)	0.774

* $p<0.05$, significantly associated with survival.

community-acquired sepsis. We also found that initial inappropriate antibiotic therapy was associated with final survival only in patients with non-community-acquired sepsis.

Significant differences in virulence factors and antibiotic-resistance of pathogens isolated from different clinical settings have been reported [23]. In this study, a greater proportion of subjects with community-acquired sepsis received appropriate initial antibiotics, but this was associated with a non-significant trend toward better survival. The possible reason for this finding may be the less severe condition of the patients in the community-acquired sepsis group at presentation, as evidenced by significantly less co-morbidity, less required mechanical ventilation, lower APACHE II scores, better renal function, higher levels of hemoglobin and higher GCS (see Table 1). It is likely that a less severe condition at presentation may prolong the decision to escalate treatment until the culture results are known 2 to 5 days later. In contrast, administration of appropriate initial antibiotics was associated with better survival in those with non-community-acquired sepsis. The patients with non-community acquired sepsis had more severe disease, as evidenced by the higher APACHE II scores and other parameters (Table 1). A higher proportion of these patients may have been admitted previously and/or received repeated rounds of antibiotic therapy, which may have increased their likelihood of obtaining an infection by a drug-resistant pathogen, and thereby increased their chances of being classified as having been treated with inappropriate antibiotics. In the present study, 68.7% of patients with community-acquired sepsis versus 56.8% of those with non-community-acquired sepsis received initial appropriate antibiotics; this is lower than the 82% reported by Capp *et al* [24]. It is possible that a greater proportion of those with non-community-acquired sepsis that received ineffective treatment had infections caused by highly virulent, drug-resistant organisms, as in other studies [23-24].

Previous studies have shown that sepsis severity (i.e., APACHE II score) is an important predictor of mortality in patients with Sensi-Disc™ Susceptibility Test Discs-confirmed bacteremia and sepsis, severe sepsis, or septic shock [25], as well as in those with bacteremia and severe sepsis or septic shock due to a Gram-negative organism [26]. Frakking *et al*. [27] reported that presentation with severe sepsis was associated with 30-day mortality in patients with sepsis caused by extended-spectrum β-lactamase (ESBL)-producing bacteria. In the present study, multivariate analysis showed that the risk of death increased as APACHE II scores increased in patients with community-acquired sepsis (HR=1.14) and in those with non-community-acquired sepsis (HR=1.18). In addition, mortality was found to be significantly associated with CRP and neutrophil levels in those with non-community-acquired sepsis in a Portuguese ICU-admitted community-acquired sepsis study [28]. Further studies should consider the particular pathogen involved, especially given the changing landscape of healthcare-associated pathogens, including methicillin-susceptible *Staphylococcus aureus* [29].

In conclusion, appropriate empirical antimicrobial therapy is particularly important for lowering the mortality of patients with non-community-acquired sepsis. Early inquiry into the sepsis patient's previous admission history is easier than calculating APACHE II scores, and also helps the physician choose the appropriate antibiotic sooner.

Acknowledgements

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內科加護病房敗血症患者依臨床分類對適當抗生素的衝擊及病情預後的影響

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前言：回顧性研究調查來源不同的敗血症病人（社區型、非社區型），對初始抗生素治療適當性的衝擊以及對患者存活率的影響。

方法：回顧性世代研究 2014 年台北慈濟醫院的內科加護病房（ICU）敗血症病人，符合細菌培養陽性。細菌的藥物敏感性試驗結果作為初始抗生素適當性的判斷依據。適當的初始抗生素治療與其他風險因子共同分析對敗血症患者的生存影響，由單因素和多因素 Cox 回歸分析進行評估。

結果：非社區型敗血症患者有較多合併症，更長的 ICU 住院天數以及較高的 28 天 ICU 死亡率和 90 天住院死亡率（$p \leq 0.002$）。雖然社區型敗血症患者入住 ICU 前接受適當抗生素給藥比率較高但不影響存活率（$p \leq 0.015$），然而在非社區型敗血症在入住 ICU 前接受適當抗生素給藥存活率顯著較高（p 值 =0.010）。多因素分析顯示，死亡的危險性與急性生理和慢性健康評估 II（APACHE II）嚴重度有關，社區型敗血症（HR=1.14，p=0.008），非社區型敗血症（HR=1.18，p=0.014）。

結論：敗血症重症病患入住內科加護病房除了評估 APACHE II 分數，並且快速分辨病人來源，以慎選適當的抗生素治療，以降低非社區型敗血症的死亡率。***(胸腔醫學 2016; 31: 323-334)***

關鍵詞：社區型，敗血症，存活率

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An Unusual Case of Endotracheal Neurofibromatosis – A Case Report and Review

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Neurofibromatosis type 1 (NF-1) is an autosomal-dominant disorder with the major clinical features of cafe-au-lait spots, peripheral neurofibromas, and Lisch nodules. Tracheal involvement is an extremely rare manifestation in patients with NF-1. We present the case of a 26-year-old man with NF-1 who suffered from progressive dyspnea. He had a chronic cough for three months and thought it was related to his history of betel nut aspiration. After examination, chest CT revealed a foreign body located at the distal part of the trachea. Bronchoscopy confirmed a tumor-like lesion adherent to the right main bronchus wall with near-total occlusion of the airway. Due to impending respiratory failure, rigid bronchoscopy was arranged for excision and removal of the tumor. The final pathology was neurofibroma. The patient recovered well with smooth breathing after tumor removal. He was discharged 1 week after surgery. ***(Thorac Med 2016; 31: 335-340)***

Key words: neurofibromatosis, tracheal tumor

Introduction

Neurofibromatosis type 1 (NF-1) is an autosomal-dominant disorder caused by mutations in the NF1 gene [1]. The typical clinical manifestations are cafe-au-lait spots, freckling in the axillary or inguinal region, neurofibromas, and Lisch nodules (iris hamartomas) [2]. The diagnosis of NF-1 is based on the presence of characteristic clinical features; genetic testing is not required to make the diagnosis [2]. Patients with NF1 are at an increased risk of both benign and malignant tumors throughout life; neurofibromas are the most common type of benign tumor that develops in patients with NF1 [3]. Neurofibromas may involve the skin (cutaneous neurofibromas) or tissues deeper inside the body [4]; however, endotracheal neurofibroma is an extremely rare manifestation [5-8]. There are no therapeutic agents specifically approved for patients with NF1. The individual manifestations are treated as they arise.

In this report, we present the case of a 26-year-old man with NF-1 who suffered from impending respiratory failure due to airway obstruction by an intratracheal neurofibroma.

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The tumor location was confirmed by chest computed tomography (CT) and bronchoscopy. Rigid bronchoscopy was then used for tumor resection.

Case Report

A 26-year-old man was admitted to our hospital with progressive dyspnea during the most recent 3 days. He was known to have NF-1 since childhood, and had a positive family history of NF-1. He was not followed up regularly in the pediatric OPD. Besides progressive dyspnea, he also had chronic cough for 3 months and a history of choking on betel nut 1 month previous to this admission. He thought the dyspnea was caused by foreign body aspiration. He went to a local hospital, where chest plain film/roentgenogram showed an unclear nodular lesion above the carina (Figure 1), and CT revealed a 2.8 × 2.8 × 2-cm solid soft tissue lesion in the trachea (Figure 2).

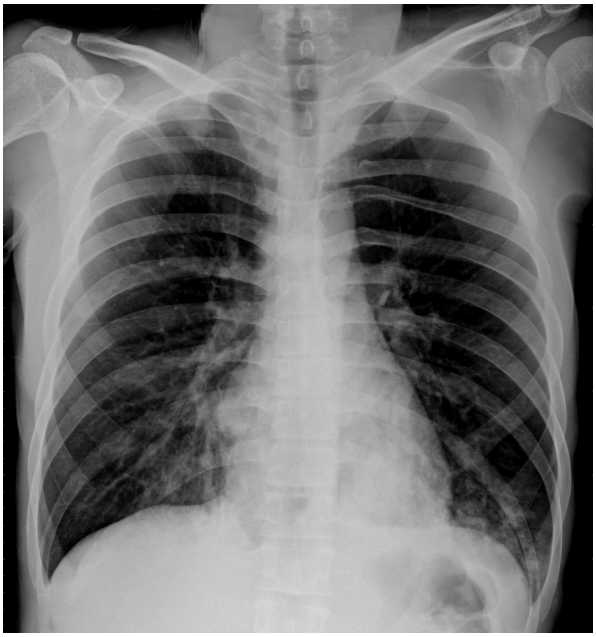

Fig. 1. Chest radiography showed a nodular-like lesion in the lower portion of the trachea.

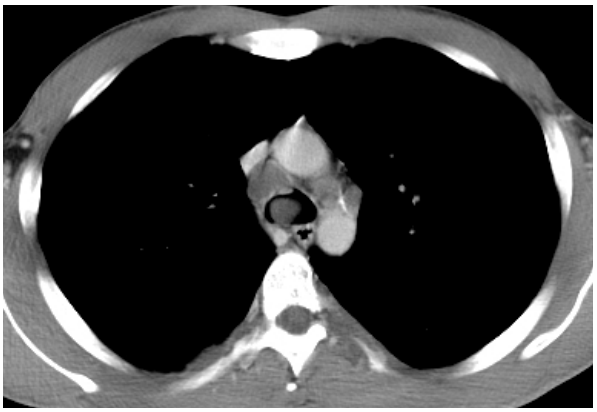

Fig. 2. Computed tomography revealed an exophytic nodule at the membranous portion of the lower trachea

He was then transferred to our emergency department due to an unknown lesion in the trachea. Physical examination revealed the typical clinical features of NF-1 with multiple cutaneous neurofibromas and cafe-au-lait spots all over his body. There were decreased breathing sounds but no inspiratory stridor. Flexible bronchoscopy was arranged for suspected foreign body obstruction. During the examination, a tumor-like lesion was found at the distal trachea arising from the right posterolateral wall with near-total occlusion of the trachea (Figure 3).

At admission, the dyspnea had worsened and oxygen saturation was 88% under a simple mask of flow 6 L/min. Because of hypoxemia with impending respiratory failure, the thoracic surgeon suggested an emergency rigid bronchoscopy excision and removal of the tumor (Figure 4). The tumor was resected smoothly without active bleeding and the pathology was a benign neurofibroma.

The patient recovered well after operation. He was able to walk around beginning on postoperative day 2. Spirometry revealed normal pulmonary functio (FEV1/FVC: 91%, FVC:

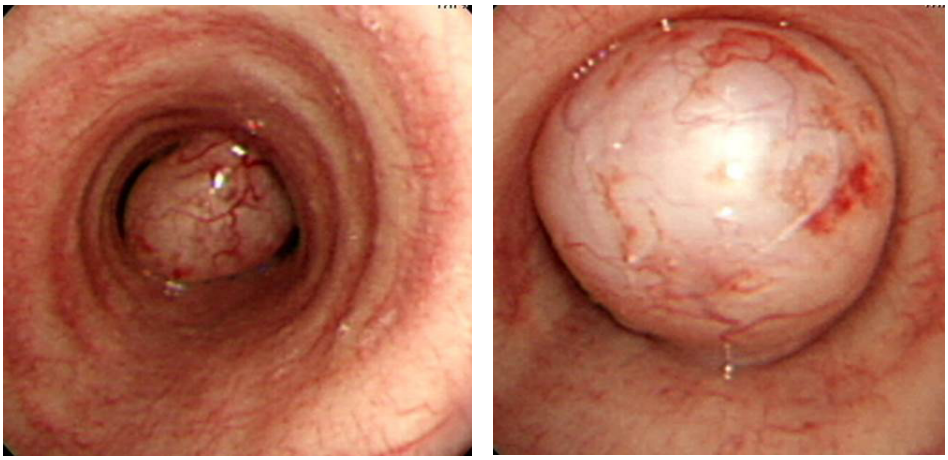

Fig. 3. Flexible bronchoscopy revealed a tracheal tumor with near-total obstruction of the airway.

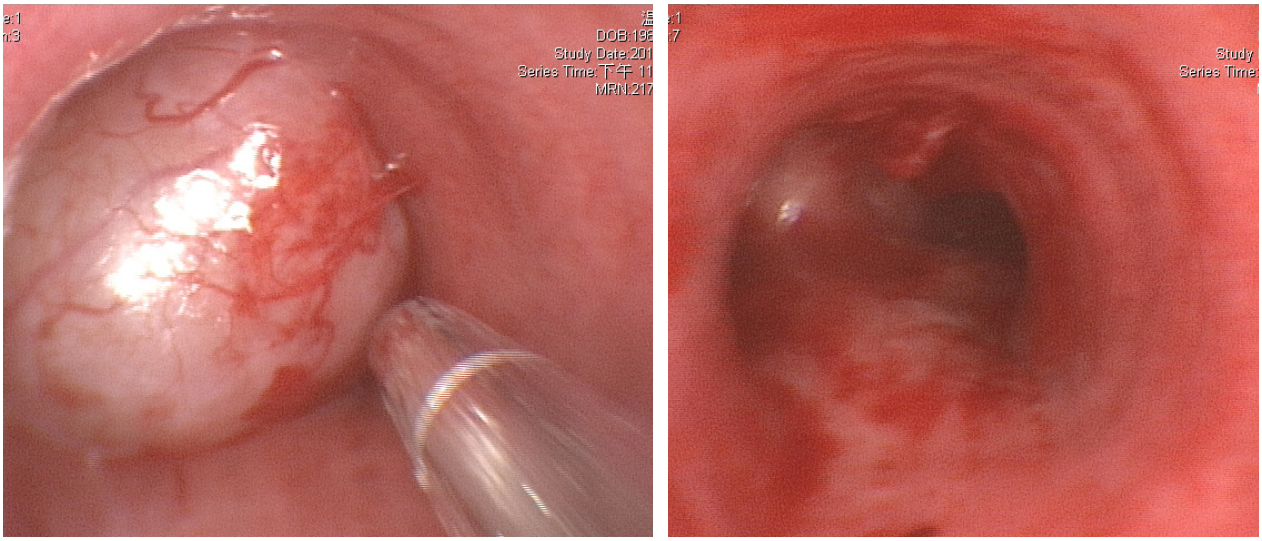

Fig. 4. Rigid bronchoscopy guided excision of the obstructing tumor.

3.52L, 84%, FEV1: 3.21L, 88%). No further treatment was needed for the benign neurofibroma and the patient was discharged 1 week after the operation.

Discussion

Tracheal tumor is rare and accounts for less than 1% of all tumors of the respiratory tract [9]. In adults, most primary tumors of the trachea are malignant, and the most common primary intratracheal tumors are squamous cell carcinoma and adenoid cystic carcinoma [10]. Metastases to the tracheal wall are very rare, and the primary origin may be the breast, colon, or skin (melanomas) [10].

Reports of benign intratracheal neoplasms are very rare and are often reported as single cases or small series. In a reported series, benign tracheal tumor occurred in less than 10%

of 357 patients during more than 40 years [10]. Mesenchymal benign tracheal tumors include fibroma, hemangioma, granular cell tumor, schwannoma, leiomyoma, neurofibroma, chondroma, and lipoma [10]. Intratracheal neurofibroma is an extremely rare manifestation in patients with NF-1. Thus far, reports of fewer than 10 patients with both NF-1 and intratracheal neurofibroma have been published in the literature [5-8].

In cases with tracheal abnormalities, CT is an excellent modality for evaluation of the airway distal to the obstruction and the extent of disease. However, it fails to accurately detect a tumor within the submucosa or mucosa. Hence, management of tracheal tumors with both CT and bronchoscopy is needed. CT images of neurofibromas are not uniform, and they have been reported to be hypo- to isodense on CT compared with adjacent muscle tissue. After contrast infusion, most neurofibromas show heterogeneous enhancement because of the variable lipid or water content within the mucinous matrix, the presence of cystic degeneration, or the entrapment of perineural adipose tissue [11].

Bronchoscopy with biopsy is the "gold standard" for histopathologic analysis of tracheal neoplasms. Before biopsy, we used bronchoscopy for direct visualization and localization of the tumor position. Evaluation of abnormal mucosal lesions in the lumen of the airway could then be done by laser immunofluorescence [12]. Endobronchial ultrasound may provide additional information about tracheal wall thickness, extent of the extrinsic tumor, and vessels surrounding the tumor [12]. Flexible bronchoscopy could be used in all of these procedures.

The options for management of a tracheal tumor include therapeutic bronchoscopy, radiotherapy and surgical resection [13-14]. Biopsy is not obligatory before resection. Small obstructive lesions can be resected without biopsy, but histologic diagnosis may be needed in more extensive tumors to determine if they are primary or metastatic. In our case, we did not perform biopsy during the first bronchoscopy exam due to near total occlusion and impending respiratory failure. The tumor in our case was not large, so relief of acute obstructive symptoms was our first goal. For a patient in respiratory distress, rapid relief is provided by endotracheal resection or debulking [12].

Rigid bronchoscopy is usually recommended for the management of tracheal tumors [12]. The advantages of rigid bronchoscopy are the large field, direct airway control and the ability to use larger instruments for mechanical debulking; however, the possible complications of rigid bronchoscopy include severe desaturation, tracheal wall penetration, laryngeal edema, or bronchospasm [12]. In addition to mechanical debulking, a flexible bronchoscope could be passed through the lumen of the rigid scope to deploy a Cryoprobe or electrocautery snare to remove pedunculated lesions from the airway [13].

In conclusion, we reported a patient with NF-1 who had the rare manifestation of intratracheal neurofibroma. Our experience with this case indicates that bronchoscopy could accurately localize the tumor and effectively remove the exophytic mass from the trachea.

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氣管內神經纖維瘤：病例報告

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神經纖維瘤是自體顯性遺傳疾病，主要的表現有咖啡牛奶斑、皮膚神經纖維瘤及虹膜色素缺陷瘤。此疾病極少以侵犯至氣管作為臨床表現，本篇報告的是一位 26 歲神經纖維瘤的男性，主訴為漸發性呼吸困難，並在最近三個月有慢性咳嗽，因病患自訴曾有吞入檳榔的病史，所以在外院時當作異物吞入進行檢查。電腦斷層報告顯示在氣管中有明顯的異物但不確定是吞入外物或是內生性的組織，經支氣管鏡檢查後證實在氣管遠端有一個疑似腫瘤的病灶，此病灶與右側氣管壁相連而且幾乎把氣管塞住，並非是外來的吞入物。因為病患瀕臨呼吸衰竭，因此外科醫師安排硬式支氣管鏡手術將病灶切除，術後病理報告顯示為良性的神經纖維瘤，病患術後恢復良好，在術後一星期順利出院。*(胸腔醫學* ***2016; 31: 335-340)***

關鍵詞：神經纖維瘤，氣管腫瘤

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Reverse-Triggered Breaths in Mechanical Ventilation – A Case Report

Tien-Ching Lin, Chang-Wen Chen

Patient-ventilator asynchrony (PVA) is associated with prolonged mechanical ventilator use and related complications. "Reverse triggering" is a recently recognized pattern of PVA, in which the patient's breathing is triggered by a mandatory breath from the ventilator. This denotes a neuro-mechanical coupling in a repetitive and consistent manner. In reverse triggering, the deferred activation of the patient's inspiratory muscles may induce double triggering, impairment of expiration, and increasing alveolar pressure with lung injury. Reduction of the sedation level is recommended for this type of PVA. We report a case with this specific PVA with esophageal pressure recording. ***(Thorac Med 2016; 31: 341-345)***

Key words: reverse triggering, asynchrony, ventilator

Introduction

With the widespread use of graphic displays of airway pressure, flow and volume in modern ventilators, patient-ventilator asynchrony is now more commonly recognized by both respiratory therapists and critical care physicians [1]. Patient-ventilator asynchrony (PVA) can occur during either the triggering or the cycling phase [2]. Ineffective triggering (during either the inspiratory or the expiratory phase), auto-triggering, and double triggering are major types of PVA related to triggering [1-4]. Premature cycling and delayed cycling are PVAs caused by cycling asynchrony [1-2,4]. These types of PVAs are characterized by the discordance between the patient and the ventilator. There is no direct principal and subordinate relationship.

However, a new type of PVA, called "reverse triggering", has been described recently. This is a condition in which the patient's breathing is triggered by a ventilator-delivered breath [5]. "Entrainment" with resetting of respiratory rhythm is an advocated explanation for this type of PVA [5]. Here, we report the case of a mechanically ventilated patient with reverse triggering through esophageal pressure monitoring.

Case Report

A 90-year-old man, a heavy smoker (1 pack per day for 60 years), was brought to our emergency room (ER) due to a sudden loss of consciousness. In the ER, hypoglycemia (finger

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blood sugar: 46 mg/dL) was detected immediately, and profound hypoxemia was found by arterial blood gas analysis. The patient's consciousness improved after dextrose fluid infusion, but he was soon intubated for profound hypoxemia and hypotension. His chest radiograph revealed bilateral lung infiltrates, and pneumonia with acute respiratory failure was suspected. He was then admitted to our intensive care unit (ICU).

After admission, he was given broad-spectrum antibiotics (cefepime 1g IVD Q12H, and levofloxacin 250 mg IVD QD) and routine hemodynamic support. Echocardiograph examination revealed global left ventricular hypokinesis (left ventricular ejection fraction: 26%), accompanied with mild aortic valve regurgitation, mitral valve regurgitation, and tricuspid valve regurgitation. Therefore, dobutamine was given. The patient improved during the following week, and we had planned to start weaning. But then, patient-ventilator asynchrony under pressure-controlled ventilation was suspected from the ventilator's display screen, so we placed an esophageal pressure monitoring device in the patient. We noted the patient's breathing regularly lagged behind the mandatory ventilator breathing from time to time (Figure 1). This pattern of PVA was consistent with the definition of reverse triggering. The patient had an unsuccessful weaning trial, however, and underwent tracheostomy the next day. His hospital course was further complicated with hollow organ perforation and septic shock, and he passed away 1 month later.

Discussion

PVAs are common and the severity of asynchrony is related to the length of mechanical ventilation and longer ICU stays, and possibly hospital mortality [6-7]. Reverse triggering, a new type of PVA, is characterized by ventilator-triggered patient breathing. With reverse triggering, we can confirm the respiratory effort through esophageal pressure measurement. We believe this is the first case report of reverse triggering in Taiwan.

It is known that mammal respiration is controlled by a central pattern generator in the brainstem that is subjected to chemical, cortical or mechanical afferent inputs [8]. Fixed, temporal entrainment between the onset of neural inspiratory activity and a mechanical breath may be a reasonable explanation for reverse triggering [9]. During noninvasive ventilation, entrainment between ventilator-delivered breaths and spontaneous breaths has been demonstrated in the normal human during non-rapid eye movement sleep [9]. Similar entrainment was documented recently in intubated patients, and that is when the term "reverse triggering" was coined [5].

There are 2 factors that support the likelihood of our case being a case of reverse triggering. First, there were repetitive and consistent patterns of ventilator-induced breathing. The set breathing rate was 16 breaths per minute, and the time interval between each inspiration was around 3.75 seconds, based on our graphic analysis. This phenomenon would illustrate that the breathing was not triggered by the patient himself. Second, in reverse triggering, each patient's breathing closely follows the ventilator airflow without loss. This may support the argument for ventilator induction.

The proper management of reverse triggering is not yet fully clear. When reverse triggering is observed in the clinical setting, we should be cautious of concomitant induced double trig-

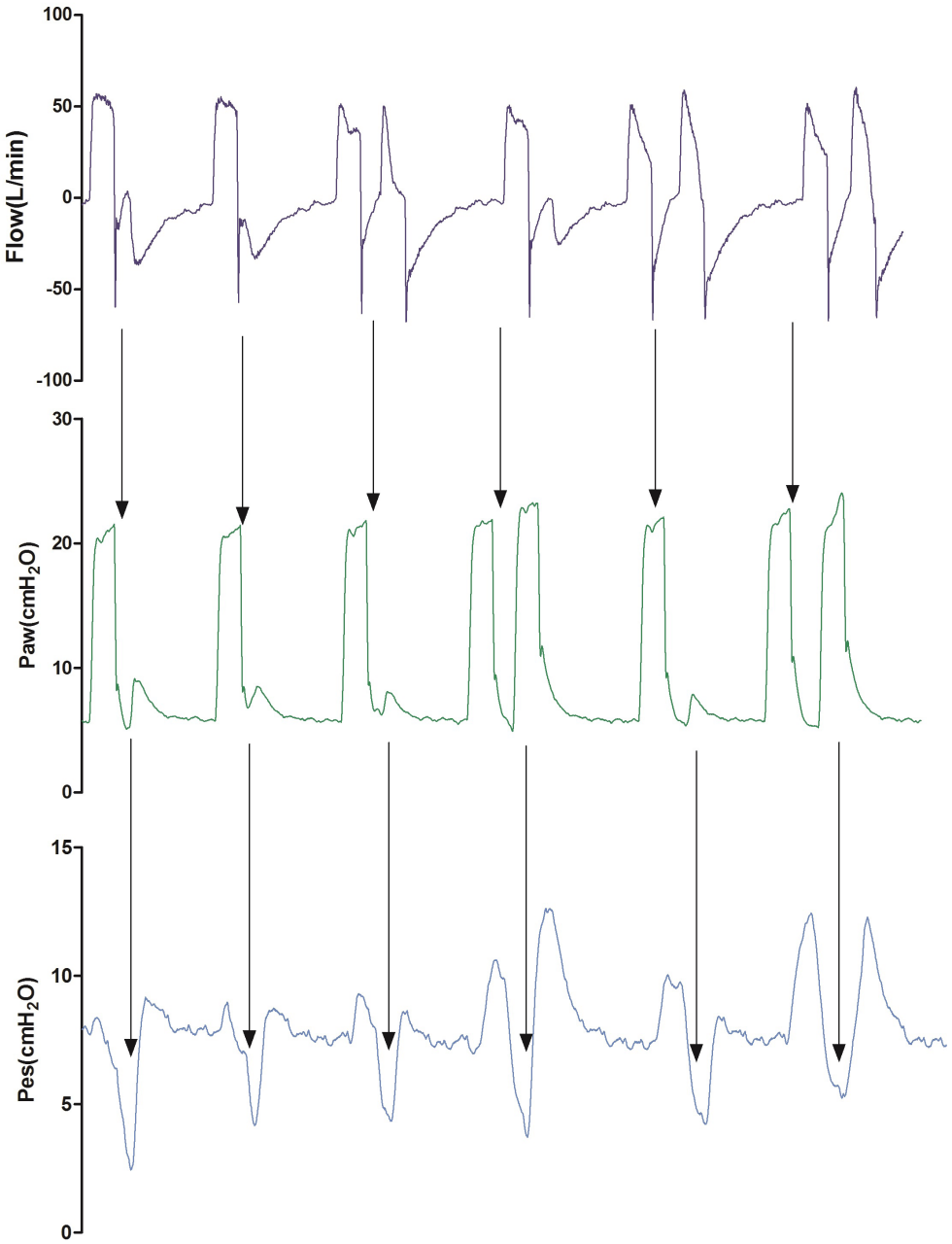

Fig. 1. From top to bottom, recording of flow, airway pressure (Paw), and esophageal pressure (Pes) over time during mechanical ventilation in a pressure-assisted controlled mode with the following settings: pressure-controlled level: 16 cm H_2O, PEEP: 5 cm H_2O, and FiO_2: 0.35. Respiratory rates are 16 breaths per minute, and flow trigger is 1 L/s. During a period of 25 seconds, all mechanical breaths are followed by downward deflection of esophageal pressure (indicated by an arrow). Three double-triggered breaths are noted (the first breath occurred at the ventilator set cycle). "Reverse triggering" can be confirmed from the graphic analysis, with a repetitive and consistent ventilator-induced pattern.

gering, which may lead to dynamic hyperinflation and lung injury. Since reverse triggering is associated with deep sedation, decreasing the level of sedation may reduce the phenomenon. Avoidance of hypocapnia or a decrease in the ventilator mandatory rate is also recommended [3,10]. More evidence is needed to determine the exact relationship between "reverse triggering" and clinical implications, such as ICU length of stay and mortality rates.

Conclusion

We presented here the first published case report of reverse triggering in a mechanically ventilated patient in Taiwan. This kind of PVA should be suspected when the flow and airway pressure on the ventilator display screen show either distortion in the early phase of expiration, or a double-triggered breath with the first mandatory breath. Adjustment of the level of anesthesia/sedation is recommended.

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呼吸器通氣中的反向驅動呼吸－病例報告

林典慶　陳昌文

病患 - 呼吸器不協調（patient-ventilator asynchrony）與呼吸器的延長使用及其併發症有關。「反向驅動（reverse triggering）」是其中一種最近才被確認的「病患 - 呼吸器不協調」模式，在此模式中患者的呼吸運動會被呼吸器強制誘發。它展現出一種反覆且固定的神經 - 機械偶合（neuro-mechanical coupling）模式。在「反向驅動」產生時，患者吸氣肌的延遲活化可能導致雙重驅動（double triggering）、吐氣期障礙、以及增加肺泡壓並伴隨肺損傷。在處理此種病患 - 呼吸器不協調上，建議減少鎮靜的深度。我們藉由食道球壓力監測，展示該模式下的一例個案。*(胸腔醫學 **2016; 31: 341-345**)*

關鍵詞：反向驅動，不協調，呼吸器

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Rapid Resolution of Acute Hypoxemic Respiratory Failure in a Perioperative Patient

Kwok-On Ng, Ming-Shan Chen

We reported the case of a 12-year-old girl who was scheduled for elective tonsillectomy under general anesthesia. An aspiration episode occurred during the induction of anesthesia prior to tracheal intubation. Respiratory distress with hypoxemia developed rapidly. Emergency interventions including respiratory tract suctioning, tracheal intubation and bronchoscopy were performed in the operating room. Three hours after presentation, the radiological abnormalities resolved, and the clinical features improved as well. She was weaned from the ventilator during the following 1 hour. Six days after the episode, she was discharged from the hospital without detectable sequelae. The brief course of her respiratory distress differed from that reported previously. We describe this uncommon event and discuss the role of bronchoscopy in a gastric acid aspiration episode such as this. ***(Thorac Med 2016; 31: 346-350)***

Key words: fiberoptic bronchoscopy, gastric acid aspiration

Introduction

Respiratory dysfunction may occur after aspiration of gastric contents. The stomach contains a variety of substances that will have different effects (chemical injury, obstruction of the airway). In 1946, Mendelson described a syndrome of pulmonary aspiration in 66 obstetrical patients during general anesthesia for surgery in a New York hospital [1]. The aspiration resulted in pneumonitis caused by a chemical injury due to gastric acid. Most cases of aspiration pneumonitis occur in patients who are hospitalized after a drug overdose [2], or in anesthetized patients [3]. Clinical manifestations include dyspnea, coughing, tachycardia, cyanosis and rales on chest auscultation. Approximately one-third of patients with aspiration pneumonitis progressed to acute respiratory distress syndrome (ARDS) [4]. In a literature review, the mortality rate of patients with ARDS resulting from aspiration pneumonitis was as high as 40% [5].

We describe a young, physically healthy girl who had regurgitation with extensive aspiration into the lungs during the induction of anesthesia. Aspiration pneumonitis with hypoxemia developed rapidly, but this clinical distress symptom subsided within 4 hours. She was transferred to a general ward the next day.

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Case Report

A 12-year-old girl was scheduled for tonsillectomy because of chronic tonsillitis. She weighed 52 kg and was 146 cm in height. She had no medical disease history, and no gastroesophageal disorders. Her vital signs were normal and physical examination revealed no significant findings. Preoperative electrocardiography and laboratory data, including complete blood count (hemoglobin, hematocrit, white blood cell count, and platelet count), liver function (glutamic oxaloacetic transaminase, glutamic pyruvic transaminase, and bilirubin), kidney function (blood urine nitrogen, creatinine) and coagulation (prothrombin time, partial thromboplastin time) were normal as well. General anesthesia was the choice of technique for this operation. No premedication was administered.

As was common practice in our hospital, we verified her identity, fasting status, and the type and site of operation upon arrival in the operating room. Once she was in the supine position, an electrocardiograph (ECG) monitor was put in place. Oxygen (4 l/min) was administered by mask. Blood pressure (106/40 mmHg), pulse rate (105 beats/min) and pulse oximetry (SpO_2: 99%) were measured. Noninvasive blood pressure was automatically recorded every 3 minutes. Lactated Ringer's solution (500 ml) was infused intravenously during the induction of anesthesia. General anesthesia was induced with fentanyl (0.7 ml) and propofol (100 mg) intravenously, and then inhaled sevoflurane (6%) was delivered by mask to facilitate a more stable hemodynamic profile at induction. After 3three minutes of inhalation, cisatracurium (7 mg) was administered to facilitate intubation. However, coughing and choking were observed soon after the administration of cisatracurium, followed by difficulty in mask ventilation. The oral cavity and the pharynx were inspected immediately with the use of a laryngoscope. Pooling of clear fluids was noted in the hypopharynx. A suction catheter was inserted into the pharynx and larynx to aspirate the fluid. Afterward, a Mallinckrodt tube with an internal diameter of 6.0 mm was inserted. A suction tube was passed through the endotracheal tube for repeated clearing of the trachea. Hypoxemia (SpO_2: 87%) supervened despite manual ventilation with 100% oxygen. A crackling sound while breathing was heard in both lungs on auscultation. A fiberoptic bronchoscope was inserted via the endotracheal tube to inspect the tracheobronchial tree. Clear fluids were also identified in the respiratory tract, especially in the left bronchus. Bronchoscopy revealed erythema of the trachea and left bronchus, indicating acid injury. A frothy discharge came out intermittently from the endotracheal tube. Hypoxemia persisted despite the aggressive interventions. The surgeon was notified that regurgitation and refractory hypoxemia had occurred. He terminated the surgery, and a portable chest radiograph was performed immediately in the operating room. Patchy consolidation of the left upper lobe was seen on chest imaging (Figure 1). Under sedation with 5 mg of midazolam and treated with 5 mg of dexamethasone, respectively, the patient was transferred to the intensive care unit (ICU) where she remained intubated. In the ICU, mechanical ventilation was administered at the pressure support mode with a 1.0 fraction of inspired oxygen (FiO_2), while pressure support was 15 cmH_2O and positive end-expiratory pressure was 5 cmH_2O. SpO_2 was 92% at this moment. Augmentin was prescribed for prophylaxis. Her

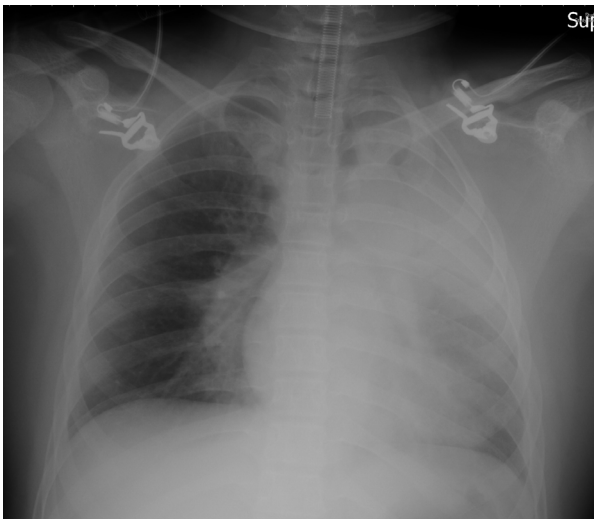

Fig. 1. Chest radiograph revealed patchy consolidation in the left upper lobe.

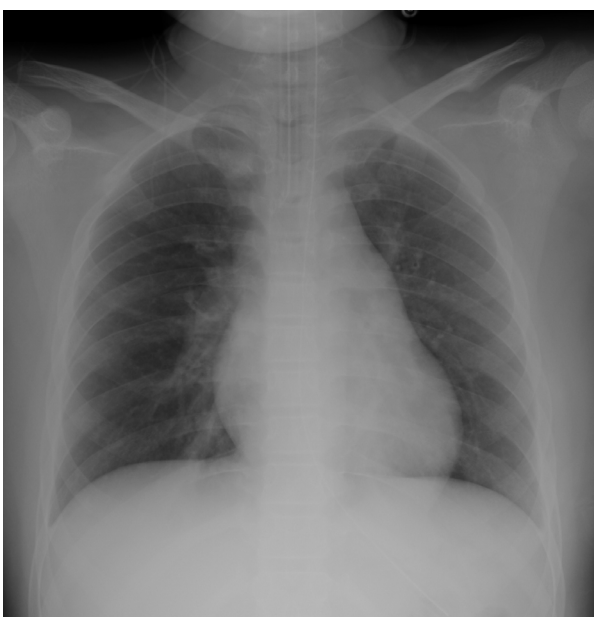

Fig. 2. Consolidation in the left upper lobe resolved 4 hours after the aspiration episode

respiratory complication was monitored every hour by both the pediatrician and our physicians every hour. Her clinical status did not deteriorate. Three hours after presentation, a follow-up chest radiograph revealed mild segmental atelectasis in both lungs (Figure 2). Meanwhile, her SpO_2 was 98% at 0.3 of FiO_2. Regaining consciousness in the next hour, she was weaned off the ventilator and extubated. On the day following the episode, she was transferred to a general ward for 4 days, and subsequently was discharged without detectable sequelae.

Discussion

A case of aspiration pneumonitis in a 7-year-old girl at induction of anesthesia was reported by Choi *et al* in 2005 [6]. Arterial blood gas analysis showed the partial pressure of oxygen was reduced to 73.6 mmHg. The chest radiograph that was obtained in the operating room after the episode showed left lung and right upper lobe atelectasis with mediastinal shifting. The physicians performed fiberoptic bronchoscopy for tracheal suction. The radiograph taken on arrival at the ICU revealed improved aeration in the collapsed lungs. The clinical features showed improvement, as well. Choi *et al*. concluded that bronchoscopy minimized the effects of the aspiration episode. However, they did not mention whether the respiratory tract was injured from the acidic aspirate. It seemed that the gastric contents resulted in obstruction of the airway rather than chemical injury. This was in contrast to our patient, who suffered from chemical injury as seen on bronchoscopy.

The occurrence of pulmonary sequelae depend upon the volume and acidity of the aspirated material, its characteristics (solid or liquid), and the immune response of the host [7]. In an earlier investigation of a monkey, aspiration pneumonitis occurred when the volume of aspirate was greater than 0.3 mL/kg and the pH was less than 2.5 [8-9]. Most authors concur with this statement, although there was an absence of clear evidence regarding humans in

a literature review [7]. An experimental study using intratracheal installation of acid into rats demonstrated a biphasic inflammatory pattern with the initial phase occurring within 1 hour and the second phase during the next 2-3 hours. The initial phase was caused by immediate direct chemical damage, and the second phase was caused by the subsequent inflammatory response of the epithelial cell lining [10]. The clinical recovery of the inflammatory response often occurs within 24 to 36 hours, with radiographic improvement within 48 to 72 hours [11]. Whang *et al*. reported a case of aspiration pneumonitis that was caused by deep sedation resulting from intrathecal morphine administration [12]. The patient developed hypoxemia (SpO_2: 69-71%) with bilateral patchy consolidation seen on chest imaging. Mechanical ventilation and antibiotic therapy were used, but not bronchoscopy. The radiological abnormalities regressed and the blood gas was within a normal range on the third day after the event. This report differed from ours, in that we used bronchoscopy on the scene for respiratory tract suctioning. The respiratory status of our patient improved dramatically. We found that acidic gastric contents led to varying degrees of inflammatory response that depended on the volume of acidic aspirate in the respiratory tract. Engelhardt and Webster mentioned that all of the gastric acid in the respiratory tract could be effectively neutralized within 15 seconds [11]. Immediate tracheal suction by bronchoscopy reduced the volume of acidic aspirate in the respiratory tract. This intervention probably resulted in a less fulminant form of lung injury.

In conclusion, when regurgitation and aspiration occur, immediate airway suctioning by bronchoscopy not only prevents airflow obstruction, but also reduces the amount of acidic damage to the epithelial cell lining on the bronchial and alveolar surfaces. This appears to be beneficial to the likelihood of an early recovery.

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手術期間急性缺氧的呼吸衰竭得到快速消除－病例報告

吳國安　陳明山

我們報告一位 12 歲的女孩在接受由全身麻醉進行的扁桃腺切例行手術。這吸入事件發生在麻醉誘導時，氣管內管插入前。呼吸窘迫及低血氧濃度立即發生。緊急處理包括在手術室內進行抽吸呼吸道，氣管內管置入，及支氣管鏡檢查。事件發生三小時後，胸部 X 光片上不正常處消失，臨床情況也改善。再過一小時後，病人脫離呼吸器並拔氣管內管。事件發生六日後，病人出院，沒有任何可察覺到的後遺症。這與文獻論述及一般認知不同。我們在此報告這不尋常的情況，及支氣管鏡在治療胃酸吸入肺事件的角色。
*(胸腔醫學 **2016; 31: 346-350**)*

關鍵詞：纖光支氣管鏡檢法，胃酸吸入

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Pulmonary Talcosis in an Intravenous Drug Abuser: A Case Report and Literature Review

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Talc is a mineral composed of hydrated magnesium silicate, and is used as a lubricant and excipient in some medications. Intravenous injection of heroin mixed with talc particles or crushed tablets is a major cause of pulmonary talcosis, which can lead to complications such as pulmonary artery hypertension, cor pulmonale, emphysema, and progressive massive fibrosis. A 42-year-old man, a former drug addict receiving methadone treatment, presented with progressive dyspnea on exertion and malaise for 3 months, and low-grade fever for 3 weeks. A chest radiograph and high resolution computed tomography revealed diffuse bilateral micronodular lesions. The initial differential diagnosis included miliary tuberculosis, silicosis, and rare pulmonary talcosis. The patient underwent video-assisted thoracoscopic wedge resection of the right middle lobe of the lung. The pathologic report revealed numerous foreign bodies (crystals) with granuloma formations along the lymphovascular bundles, as well as fibrosis and diffuse crystals deposited in the perivascular space and interstitium. These crystals exhibited birefringence under polarized light. Pulmonary talcosis was confirmed. At present, there is no established treatment for pulmonary talcosis. Lung transplantation is an option for advanced disease. ***(Thorac Med 2016; 31: 351-357)***

Key words: talcosis, intravenous drug abuse, micronodule

Introduction

Talc is a mineral composed of hydrated magnesium silicate. It is widely used in industry, and is also used as a lubricant and excipient in some medications. Talc can cause pulmonary problems, such as pneumoconiosis, pulmonary massive fibrosis, pulmonary hypertension, emphysema, and chronic respiratory failure through inhaled occupational exposure or intravenous injection [1-2]. Pulmonary talcosis is difficult to diagnose because of its rarity. Imaging studies are typically used to differentiate among pulmonary diseases, and high resolution

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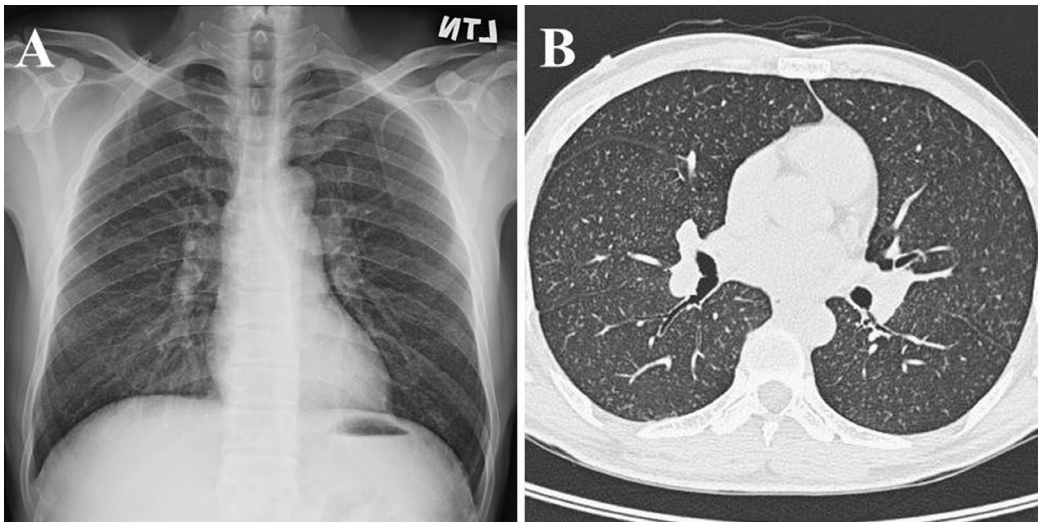

Fig. 1. (A).Chest radiography revealed diffuse micronodular lesions. (B). High resolution computed tomography showed diffuse randomized tiny 1-3 mm nodules.

computed tomography (HRCT) is capable of revealing the characteristics of talcosis, which include fine micronodular pattern, ground-glass attenuation, and emphysema [3]. Thus, pulmonary talcosis may occasionally be misdiagnosed as miliary tuberculosis [4]. We describe a patient with pulmonary talcosis mimicking miliary tuberculosis.

Case Report

This patient was a 42-year-old male who was employed as a plumber. He presented with progressive dyspnea on exertion, malaise, and weight loss (17 kg) for about 3 months. He also had low-grade fever in the afternoon, which lasted for 3 weeks. He had been an intravenous heroin addict, and began drug rehabilitation with regular methadone treatment 1 year prior to this presentation. He was also a hepatitis C virus carrier. He denied a history of chills, productive cough, chest pain, palpitation, night sweating, hemoptysis, leg swelling or orthopnea. He initially visited a local hospital, but was referred to our hospital when the chest radiograph disclosed diffuse lung nodules. Physical examinations were unremarkable, except for multiple injection marks along the veins in his forearm and antecubital area. Oxygen saturation using pulse oximetry was 93-98% under room air. Laboratory test results were within normal ranges, except for mildly elevated aspartate aminotransferase 89 U/L (normal range 8-38 U/L), alanine aminotransferase 89 U/L (normal range 10-50 U/L), and gamma-glutamyl transferase 109 U/L (normal range 4-63 U/L). Enzyme-linked immunosorbent assay for human immunodeficiency virus was negative. An electrocardiogram presented normal sinus rhythm. A chest radiograph revealed diffuse bilateral micronodular lesions (Figure 1A). HRCT was arranged and showed diffuse randomly distributed nodules measuring 1-3 mm in bilateral lung fields (Figure 1B). Miliary tuberculosis was suspected; however, 3 sets of acid-fast staining and tuberculosis culture of the sputum

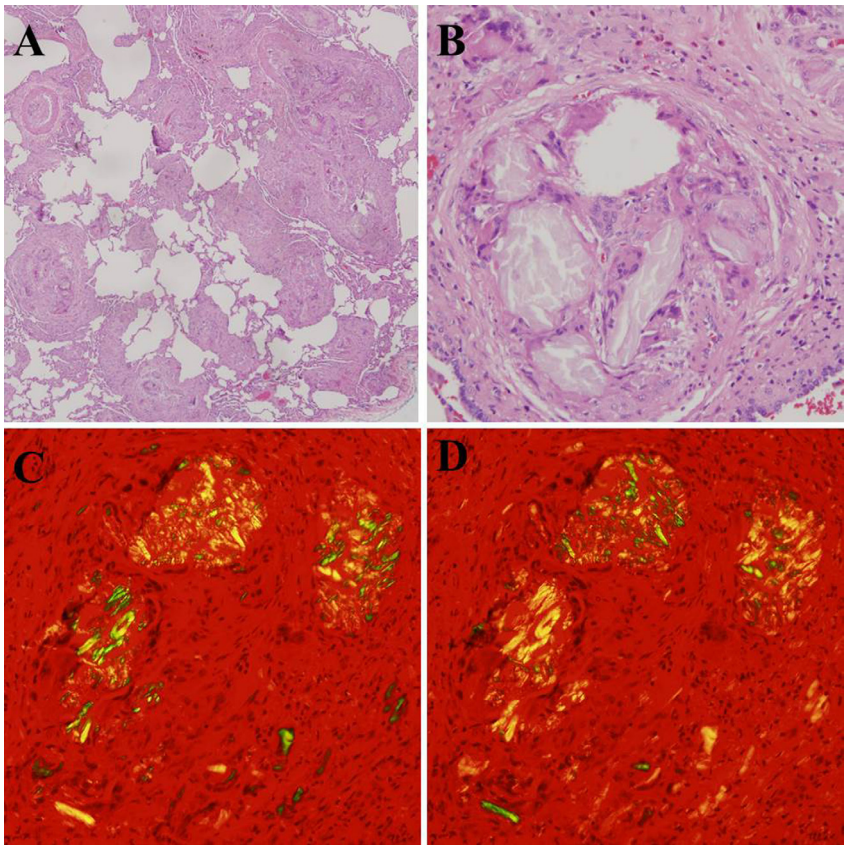

Fig. 2. (A) and (B). Diffuse crystals deposited in the perivascular space and interstitium, and numerous foreign bodies with granuloma formation along the lymphovascular bundles and fibrosis (hematoxylin and eosin stain, (A) 40X and (B) 200X. (C) and (D). Birefringent crystals under polarized light (hematoxylin and eosin stain, (C) 200X and (D) 200X).

revealed negative results. A bone marrow biopsy was then done, but the pathology disclosed neither caseous necrosis nor acid-fast bacilli. Therefore, video-assisted thoracoscopic surgery (VATS) wedge resection of the right middle lobe of the lung was performed. The pathologic report revealed diffuse crystals deposited in the perivascular space and interstitium. Numerous foreign body granuloma formations along the lymphovascular bundles were found, as well as fibrosis (Figure 2A and 2B). These crystals were birefringent under polarized light (Figure 2C and 2D). The pathologic findings were consistent with the diagnosis of talc granulomatosis.

Discussion

Talc is a mineral widely used in many industries. It is also used as a food additive and as a lubricant and filler in medications, including acetaminophen, cocaine, diazepam, heroin, methadone, methylphenidate, meperidine, oxymorphone, pentazocine, and promethazine [3,5-7]. Intravenous injection of heroin mixed with talc particles or crushed tablets is a major cause of pulmonary talcosis. Talc particles reach the pulmonary vasculature via the bloodstream,

leading to a talc embolism that initially results in arteritis. Then, talc particles are phagocytized by giant cells and macrophages after moving into the surrounding perivascular and pulmonary interstitium [8]. Unlike injected talc, inhaled talc is deposited predominantly around respiratory bronchioles and alveolar ducts [9]. The serial reactions finally result in the formation of foreign body granuloma with needle-shaped, birefringent talc crystals under polarized light [10-12].

Over time, diffuse micronodules replace the interstitial space, and pneumoconiosis, progressive massive fibrosis, and diffuse interstitial fibrosis emphysema develop because of the granulomatous inflammation [13-15]. Talc particles affect not only pulmonary tissue, but also other organs. Kringsholm B and Christoffersen P found birefringent material mainly within lung tissue (94%), followed by the spleen (76%), liver (55%), portal lymph nodes (39%), and bone marrow (24%) in a postmortem study of 33 intravenous drug addicts [10,16].

Patients with pulmonary talcosis can be asymptomatic or symptomatic. Most of the clinical presentations of symptomatic patients were nonspecific, and included progressive dyspnea on exertion, cough, increased sputum production, night sweats, weight loss, and hemoptysis [12]. More severe presentations include pulmonary artery hypertension, cor pulmonale, emphysema, spontaneous secondary pneumothorax, progressive massive fibrosis, acute respiratory distress syndrome, and chronic respiratory failure [12-14,17-20]. Pulmonary function tests usually reveal a mixed obstructive and restrictive physiology with a reduction in the diffusing capacity for carbon monoxide (DLCO) [7].

Imaging studies can play an important role in the diagnosis of pulmonary talcosis. Paré *et al*. [21] described the chest radiographic manifestations of 17 intravenous methadone addicts. Seven of them (41.2%) showed diffuse pinpoint micronodularity on the chest radiograph, similar to the presentation of our patient. In another study by Paré *et al*. [13], patients who injected talc-containing drugs and showed micronodularity on the chest radiograph also developed profounder lung injuries, including conglomerate masses, lower lobe emphysema, lower lobe bullae, and progressive massive fibrosis. Other manifestations in HRCT imaging studies include small centrilobular nodules, widespread ground-glass attenuation, confluent perihilar masses with areas of high attenuation, and panlobular emphysema in the lower lobes [12,22-23]. Although imaging studies supported our tentative diagnosis, the definitive diagnosis could only be obtained by histopathologic examination via transbronchial biopsy, fine-needle aspiration of pulmonary masses, VATS, or open lung biopsy.

Paré *et al*. [13] presented a long-term follow-up of 6 drug abusers with intravenous talcosis for more than 10 years. Even with the discontinuation of intravenous injection of oral drugs, the symptoms and complications related to pulmonary talcosis, including progressive dyspnea, pulmonary arterial hypertension, emphysema, hypoxia, and progressive interstitial lung disease, became more severe over time. Pulmonary function also declined. To date, there is no specific treatment for pulmonary talcosis besides best supportive care. Although treatment with systemic or inhaled glucocorticoids has been reported, there are currently few data supporting glucocorticoid therapy. Some patients have received successful lung transplantation [24-25]. Weinkauf JG *et al*. reported that there were no obvious differences in the rates

of survival and rates of being free from bronchiolitis obliterans syndrome after 1 and 5 years of follow-up between patients who received a lung transplant for talc lung granulomatosis and those who received a lung transplant for other indications [25]. Lung transplantation can be considered in patients with advanced pulmonary talcosis.

Conclusion

Although pulmonary talcosis is rare, detailed history-taking, especially drug abuse history and occupational exposure history, and cautious image interpretation can offer clues that may be useful in reaching the final diagnosis. Lung biopsy can confirm the diagnosis of pulmonary talcosis.

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滑石肺症在靜脈注射藥物濫用者：病例報告及文獻回顧

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滑石是由水合矽酸鎂所組成的礦物，可作為潤滑和稀釋藥物的物質。靜脈注射含有滑石成分的海洛因或搗碎的藥錠可能引起滑石肺症，進而造成肺高壓、肺心症、肺氣腫和進行性大塊型纖維化等併發症。一位 42 歲男性為藥物濫用者，從一年前開始戒毒並接受美沙酮治療。病人從三個月前開始有活動性喘及倦怠的症狀，近三周也有輕微發燒的情形產生。他接受了一系列的檢查，胸部 X 光以及高解析度電腦斷層掃描可見廣泛性微小結節。根據病史及影像學檢查，可能的鑑別診斷有粟粒性結核、矽肺症及滑石肺症。為求診斷，病人接受胸腔鏡輔助右中肺葉楔狀切除手術。病理報告顯示在血管周圍及間質中有晶體廣泛性的沉積，並且有許多肉芽腫沿著淋巴血管束分布；而這些沉積的晶體在偏極光下呈現雙折射的變化。綜合以上結果，病人確診為滑石肺症。然而針對滑石肺症，至今仍無藥物被證實可有效治療此疾病。若是病情較嚴重的患者，可考慮採取肺移植的治療方式。*(胸腔醫學 **2016; 31: 351-357**)*

關鍵詞：滑石症，靜脈注射藥物濫用，微小結節

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Primary Bronchial Leiomyoma Presenting as Lobar Atelectasis: A Case Report

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Bronchial leiomyoma is the rarest type of benign pulmonary neoplasm, comprising <2% of benign tumors of the lower respiratory tract. We report the case of a 50-year-old woman with an unremarkable medical history who presented at the emergency department due to right chest wall pain after trauma from a traffic accident. In addition to fracture of the right 5th to 7th ribs, chest radiograph revealed a collapsed left upper lobe. A tumor obstructing the left upper lobe bronchus, causing lobar atelectasis, was seen on chest computed tomography. Fiber-optic bronchoscopic biopsy of the tumor revealed benign leiomyoma. The patient recovered uneventfully after tumor resection via rigid bronchoscopy. This case highlights the possibility of complete tumor resection via rigid bronchoscopy to preserve the distal lung after thorough evaluation and confirmation of the exclusively endoluminal and benign nature of the tumor. ***(Thorac Med 2016; 31: 358-364)***

Key words: leiomyoma, bronchial tumor, atelectasis

Introduction

Bronchogenic tumors are mostly malignant; benign bronchial tumors account for only 5-10% of resected cases [1-2]. The most common type of benign bronchial tumor is benign pleomorphic adenoma, and the rarest form is bronchial leiomyoma, which comprises <2% of benign tumors of the lower respiratory tract [3]. Because of its rarity, the incidence and prevalence of bronchial leiomyoma are not fully understood. Bronchial leiomyoma is found in patients mainly between their third and fifth decades of life [4]. Although many risk factors for bronchogenic carcinoma, such as smoking, and exposure to chromium, arsenic, cadmium, silica, asbestos, nickel, welding fumes, diesel exhaust, polycyclic aromatic hydrocarbons, and ionizing radiation have been reported, no special risk factor for benign bronchial tumors has been identified [5]. The clinical presentations vary, from no symptoms to chronic cough,

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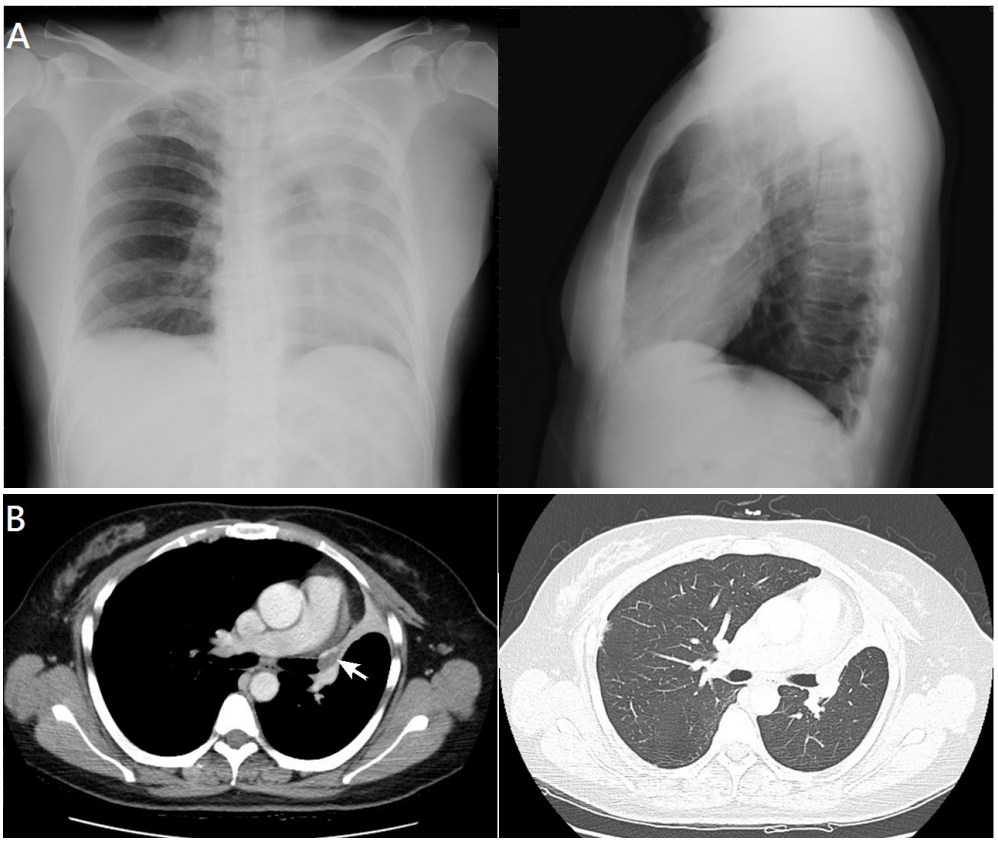

Fig. 1. (A) Chest radiograph showed fracture of the right 5th, 6th, and 7th ribs and collapse of the left upper lobe. (B) Chest computed tomography revealed a soft tissue (arrow) obstructing the left upper lobe bronchus and atelectasis of the left upper lobe.

and from dyspnea to hemoptysis and airway obstructive symptoms, depending on the tumor size and location. We herein report a case of primary bronchial leiomyoma presenting as lobar atelectasis.

Case Report

A 50-year-old woman with an unremarkable medical history presented at the emergency department due to chest wall pain after trauma from a traffic accident. Her vital signs were within normal limits and she denied having dizziness, dyspnea, or hemoptysis. Initial physical examination was unremarkable except for right chest wall tenderness. Chest radiograph showed fracture of the right 5th, 6th, and 7th ribs, as well as collapse of the left upper lobe (LUL) (Figure 1A). Laboratory examination showed normal blood cell counts, liver function, and renal function.

After admission, the LUL collapse persisted despite mucolytic therapy, adequate pain control, and chest physiotherapy. Chest computed tomography (CT) revealed a soft tissue obstructing the LUL bronchus, and LUL atelectasis (Figure 1B). The tumor markers were within normal limits (squamous cell carcinoma antigen: 1.2 ng/mL; carcinoembryonic antigen: 0.79 ng/mL; and tissue polypeptide antigen: <50 U/

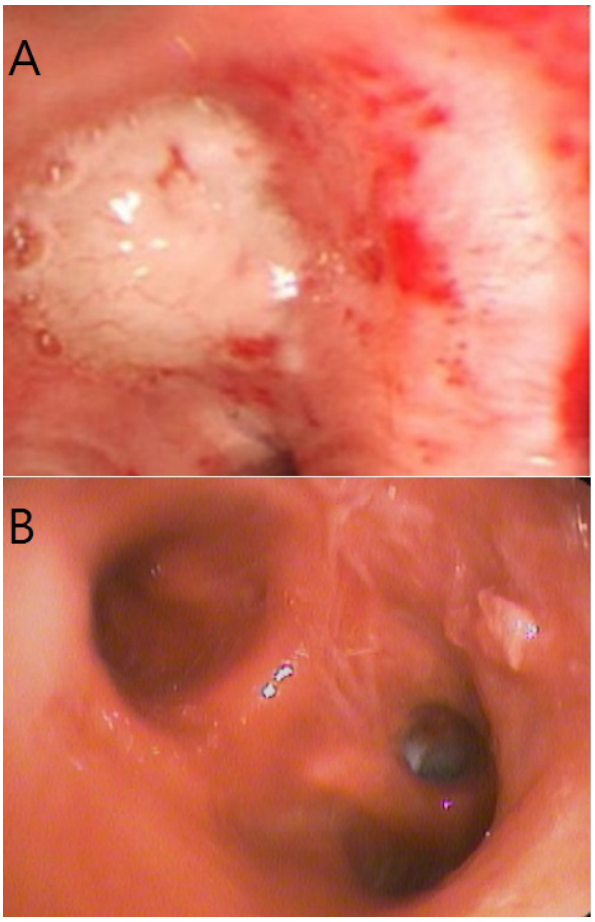

Fig. 2. (A) Bronchoscopy revealed a whitish hypo-vascular endobronchial tumor bulging from the left upper lobe bronchus, with nearly total obstruction. (B) After complete tumor resection via rigid bronchoscopy, a patent airway was restored.

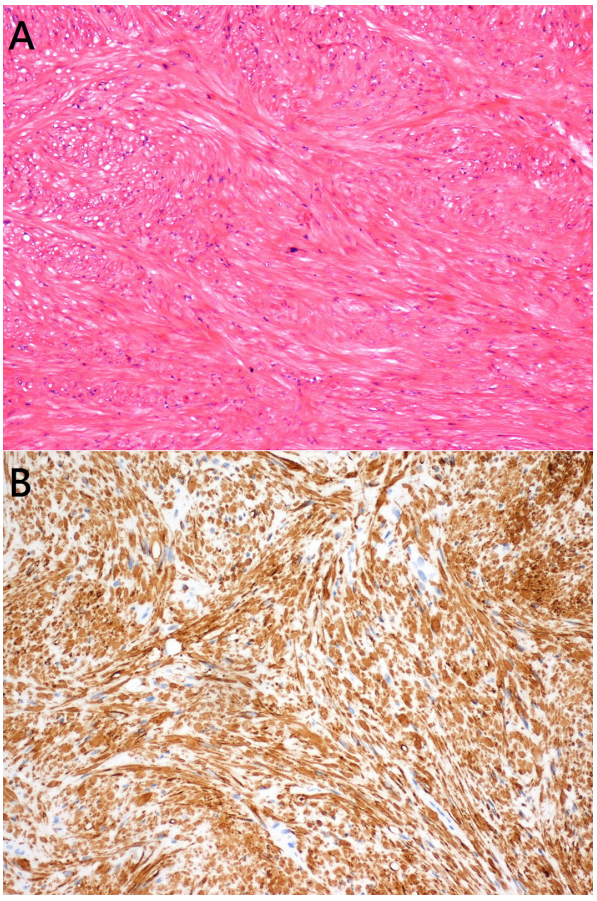

Fig. 3. Histopathologic examination of the endobronchial biopsy specimen showed (A) smooth muscle bundles in the submucosal layer (hematoxylin-eosin stain, original magnification: 200×) that were immuno-reactive to desmin (not shown) and (B) smooth muscle actin (immuno-histochemical stain, original magnification: 200×). These were suggestive of leiomyoma.

L), and 3 sets of sputum were negative for acid-fast bacilli.

Bronchoscopy revealed a whitish hypo-vascular endobronchial tumor bulging from the LUL bronchus, with nearly total obstruction (Figure 2A). Histopathologic examination of the endobronchial biopsy specimen showed smooth muscle bundles in the submucosal layer (Figure 3A) that were immuno-reactive to desmin and smooth muscle actin (Figure 3B). These findings were suggestive of leiomyoma.

The patient underwent complete tumor resection via rigid bronchoscopy and achieved patent airways (Figure 2B). The postoperative chest radiograph showed total resolution of the LUL atelectasis. Her recovery was uneventful, and on follow-up a few months later, she was asymptomatic; chest imaging showed no evidence of recurrence.

Discussion

Leiomyomas of the lower respiratory tract arise from the smooth muscles of the airways,

including the trachea, bronchi, and bronchioles. Tracheal leiomyomas account for approximately 1% of all tracheal tumors [6]. Pulmonary leiomyomas from the bronchi or bronchioles may present either as parenchymal or endobronchial lesions [7]. Lower respiratory tract leiomyomas may give rise to a variety of symptoms, depending mainly on their location. A parenchymal tumor usually causes no significant symptom, whereas a tracheal leiomyoma can lead to asphyxia due to airway compromise [4]. Common symptoms related to leiomyomas of the lower respiratory tract include chronic cough, dyspnea, and hemoptysis, and asthma-like symptoms [8]. Bronchial leiomyomas large enough to obstruct the airway may present as obstructive pneumonitis, pneumonia, or atelectasis. These conditions are the main reasons for the resection of these benign tumors.

Imaging studies and histopathologic examination of biopsy specimens play important roles in the pre-operative assessment, especially when planning for minimally invasive surgery with limited resection. Atelectasis is the most frequent finding of bronchial leiomyomas in chest radiographs [7]. Other findings include a normal image, a solitary mass, airspace infiltration mimicking pneumonitis, unilateral emphysema, and focal hyper-lucency due to air trapping [9]. CT imaging is an excellent tool for detecting bronchial lesions and delineating leiomyomas in the bronchial tree. The sensitivity of CT for detecting obstructive lesions in the respiratory tract is as high as 60-100% [10]. Leiomyomas usually have an attenuation of 25-46 Hounsfield units on unenhanced CT and 46-85 Hounsfield units on contrast enhanced CT [2].

Under bronchoscopy, leiomyomas often appear round, with a smooth surface, pinkish color, and a few visible vessels on the tumor surface that rarely bleed spontaneously [11]. Although fiber-optic bronchoscopy remains the interventional procedure of choice for examining endoluminal and mucosal lesions of the respiratory tract and for obtaining specimens, it provides limited information regarding the extent of extra-luminal involvement [12]. Virtual bronchoscopy and 3-D reconstruction of high-resolution CT, with visualization from multiple angles, are both non-invasive complementary examinations that can identify endoluminal lesions in the respiratory tract and provide significant information for planning surgical resection [13].

Most benign bronchial tumors present as non-specific soft-tissue masses in the airway wall, but lipoma and cartilaginous tumors have fat and calcium contents, respectively. Pathological examination of biopsy specimens is required for the diagnosis of leiomyoma because imaging findings are generally non-specific. Due to the difficulty in differentiating leiomyomas from other spindle tumors, such as fibromas, neurofibromas, and neurilemomas, immuno-histochemical staining is generally used to confirm the diagnosis of leiomyomas, which are often diffusely strongly positive for smooth muscle actin and desmin [14].

Various interventional techniques have been used to treat endotracheal and endobronchial lesions. The decision on which treatment modality to use depends on the location, size, and width of the tumor base and also on the reversibility of distal pulmonary changes resulting from the procedure. For a tracheal lesion or a main bronchial tumor requiring carinal reconstruction, surgical intervention via median sternotomy in the supine position is generally preferred. However, parenchymal resection

such as segmentectomy or lobectomy for a solitary parenchymal nodule or a tumor at the lobar bronchus or a more distal location, especially those with infection distal to the obstruction, is usually performed in the lateral decubitus position [7-8]. Minimally invasive procedures like bronchoplasty or bronchotomy that utilize sleeve resection of the involved bronchus without resection of the distal lung have been used as safe alternatives, especially for lesions involving only the main airway stem [15].

Total removal via rigid bronchoscopy is often possible for many benign tumors that are exclusively endoluminal and polypoid. The procedure provides many benefits, including minimal lung tissue loss, immediate symptom relief, rapid postoperative recovery, fewer perioperative complications, and shorter hospital stay [8,16]. However, surgery must still be considered for complete resection if the tumor has a wide base or is located in the distal airway and lung parenchyma, because bronchoscopic intervention for complete resection is nearly impossible [17]. The prognosis of leiomyoma is favorable after complete resection. Since the tumor in this patient was only endoluminal, complete tumor removal via rigid bronchoscopy was performed and she had an uneventful recovery.

In summary, bronchial leiomyoma with lobar atelectasis may be asymptomatic. After confirming the tumor's exclusively endoluminal and benign nature, rigid bronchoscopy may be performed for complete tumor resection and to preserve the distal lung.

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原發性支氣管肌瘤以肺葉塌陷表現－病例報告

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鍾飲文 *,*******

支氣管平滑肌瘤是一種極為罕見的良性肺腫瘤，在下呼吸道的良性腫瘤中佔不到 2%。在此，我們報告一位 50 歲無明顯過去病史的女性個案，因交通事故撞傷胸部導致右胸壁疼痛而來急診就診。胸部 X 光檢查除了顯示右邊第五、六、七肋骨骨折外，還發現左上肺葉塌陷。胸部電腦斷層顯示左上肺之氣管內有個腫瘤塞住管腔而導致左上肺葉塌陷。經支氣管鏡切片檢查顯示此腫瘤為平滑肌瘤。病人在接受經硬式支氣管鏡腫瘤切除術後，恢復狀況良好，且左上肺葉塌陷完全改善。此個案報告顯示在經過詳細評估明白該腫瘤是良性且侷限氣管內之後，可以使用經硬式支氣管鏡切除腫瘤，以保存遠端的肺部組織。*(胸腔醫學* ***2016; 31: 358-364)***

關鍵詞：平滑肌瘤，支氣管內腫瘤，肺塌陷

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Desquamative Interstitial Pneumonia Presenting with Consolidation and Hemoptysis

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Desquamative interstitial pneumonia (DIP) is a smoking-related interstitial lung disease. It usually develops in males, and presents with insidious exertional dyspnea and persistent nonproductive cough. Chest computed tomography usually shows diffuse ground-glass opacities in bilateral lungs. Here, we report a case of massive hemoptysis with right middle lobe (RML) consolidation and diffuse centrilobular ground glass opacities. The hemoptysis resolved after RML wedge resection, steroid therapy and smoking cessation. Hemoptysis and lung consolidation are rare presentations in patients with DIP. This case serves to remind us that tissue proof via surgical biopsy is of value in diagnosing interstitial lung disease, if less invasive examinations fail to obtain a definite diagnosis. ***(Thorac Med 2016; 31: 365-370)***

Key words: desquamative interstitial pneumonia, hemoptysis, lung consolidation

Introduction

Interstitial lung disease (ILD) is a group of pulmonary diseases with inflammatory-fibrotic infiltration of the alveolar septum, which may result in gas-exchange unit injury. This injury may increase alveolar permeability and enable serum contents to enter the alveolar space, thereby resulting in airspace abnormalities in addition to interstitial changes. ILD can be roughly divided into disorders of known cause and disorders of unknown cause. The group of ILDs with unknown cause (i.e., idiopathic ILD) can be further classified according to clinical, histopathologic, or radiologic parameters. Desquamative interstitial pneumonia (DIP) and respiratory bronchiolitis–associated ILD (RB-ILD) are both common forms of idiopathic ILD, and account for 15% to 20% of cases of idiopathic interstitial pneumonia in patients who have received lung biopsy [1-2]. These 2 diseases usually are associated with cigarette smoking and present with insidious exertional dyspnea and persistent nonproductive cough. Chest computed tomography (CT) findings of DIP usually show bilateral, moderately symmetrical, peripheral, and predominantly basal ground-glass opacity. Here, we report a case of DIP with the rare presentations of right middle lobe (RML) consolidation and hemoptysis.

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Case Report

In January 2016, a 35-year-old man was referred to our hospital due to cough, and hemoptysis for 1 week. The cough and hemoptysis developed suddenly with no other preceding respiratory symptoms. There was no fever. He was a heavy smoker (22.5 pack-years) and had a history of old pulmonary tuberculosis status post-complete treatment for more than 10 years. Otherwise, he denied any systemic underlying diseases or long-term medication use, including Chinese herbs. An initial chest X-ray revealed consolidation at the RML (Figure 1). The CT scan of the chest showed patchy consolidation at the RML and bilateral diffuse centrilobular ground glass opacity (Figure 2). Results of laboratory investigations at the emergency department included leukocytes, 8670/μL (segments, 63.3%; eosinophils, 1.0%; and lymphocytes, 29.5%); platelets (PLT), 259 k/μL; creatinine (Cre), 0.6 mg/dL; prothrombin time (PT), 9.8 sec (INR: 0.92) and partial thromboplastin time (PTT), 29.3 sec.

Combined with the clinical course and image findings, an infectious or inflammatory process was highly suspected. Empirical antibiotics with ampicillin and sulbactam were prescribed. Tranexamic acid was also used to treat the massive hemoptysis. An atypical pathogen survey including Chlamydia, Legionella, Mycoplasma, Aspergillus and Cryptococcus was also performed. All of the above examinations revealed negative findings. Three sets of sputum acid-fast bacillus (AFB) smears also showed negative findings. Sputum culture finally yielded normal mixed flora. Autoimmune profiles such as C3, C4 and anti-nuclear antibody (ANA) were all within normal limits. Antibodies associated with pulmonary vasculitis (i.e., c-ANCA [antineutrophil cytoplasmic antibody], p-ANCA and anti-GBM [glomerular basement membrane] antibody) all revealed negative findings.

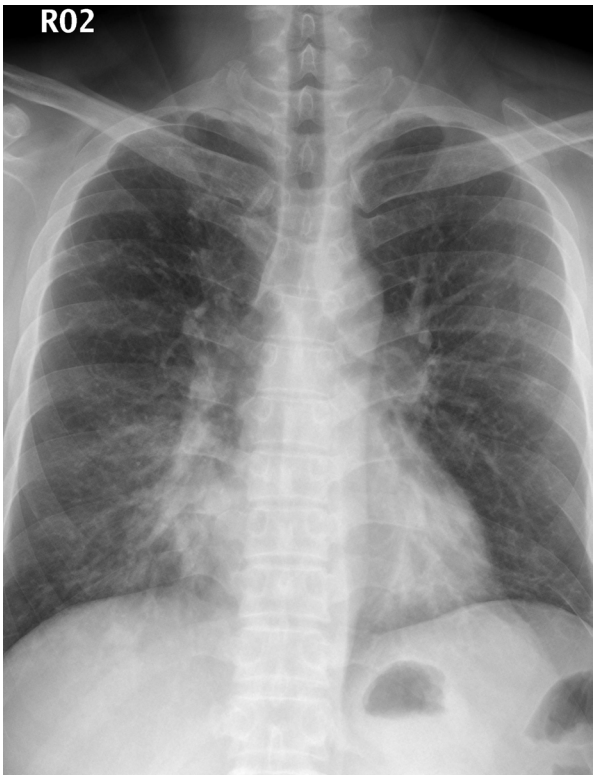
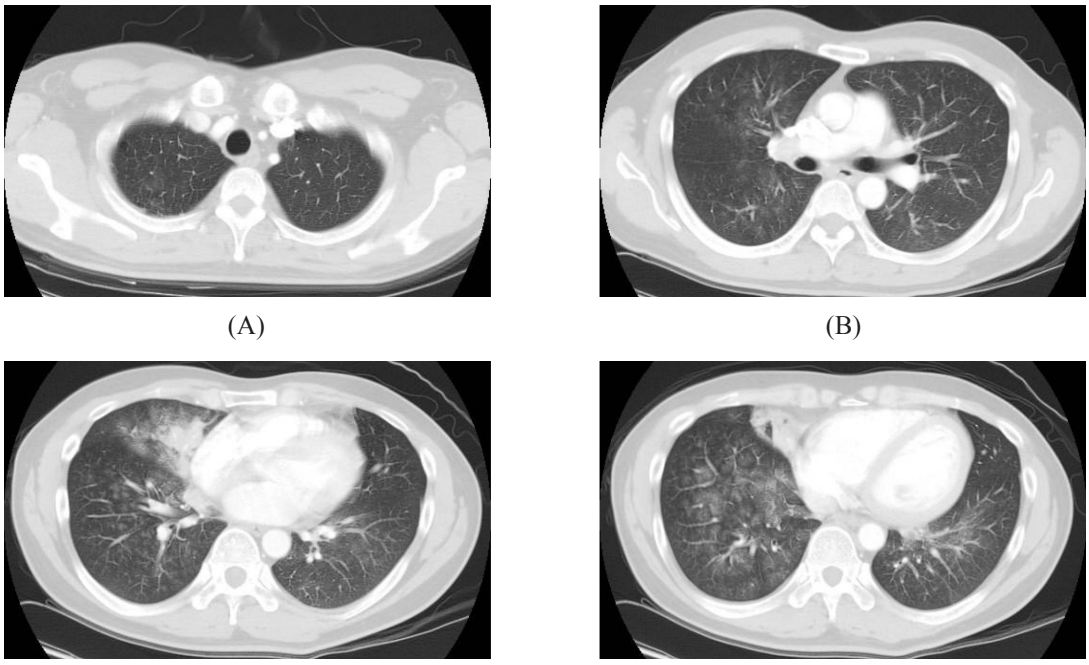


Fig. 1. Ill-defined opacity at the RML on chest X-ray.

Even with antibiotic and tranexamic acid treatment, his cough with much bloody sputum persisted. Bronchoscopy was then arranged because malignancy could not be excluded. During bronchoscopic examination, no endobronchial lesion was found, but obvious hemosputum, especially at the RML bronchus, was noted. Cytology of bronchial washing of the RML bronchus showed no evidence of malignancy. In addition, there was no elevation of tumor markers, including CEA, CA-199, SCC, and CA125.

Since his hemoptysis did not improve and seemed to aggravate, the patient finally agreed to undergo surgical intervention including bi-



(A) (B)

(C) (D)

Fig. 2. Chest CT showed patchy consolidation at the RML and bilateral diffuse centrilobular ground glass opacity, more prominent at the dependent part and lower lung.

opsy for tissue proof, RML wedge resection and right group 11 lymph node dissection via video-assisted thoracic surgery (VATS). During the operation, no obvious abnormal structure, except pleural adhesion, was noted. The patient's pathologic findings from the RML wedge resection showed pigmented macrophage accumulation and scattering in the alveolar spaces with focal hemorrhage (Figure 3). There was mild lymphocytic infiltration and no prominent interstitial fibrosis. Based on the morphology findings and history of heavy smoking, DIP with focal hemorrhage was diagnosed. Prednisolone 20 mg daily was prescribed, and we also provided help with smoking cessation. The hemoptysis then subsided and the patient was discharged. Follow-up chest CT at the outpatient clinic 2 months later showed dramatic im-

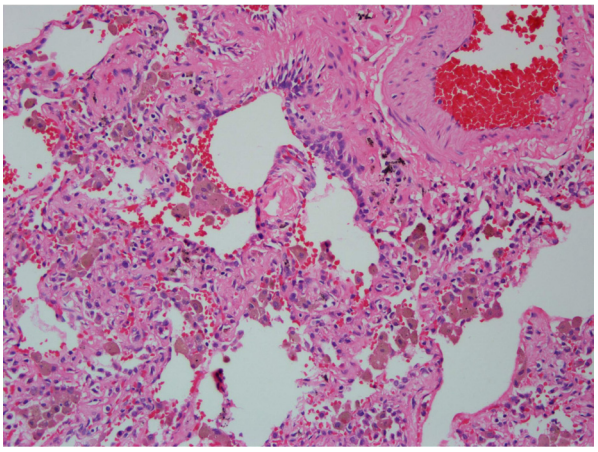


Fig. 3. Pathology of the RML wedge resection revealed pigmented macrophage accumulation and scattering in the alveolar spaces with focal hemorrhage.

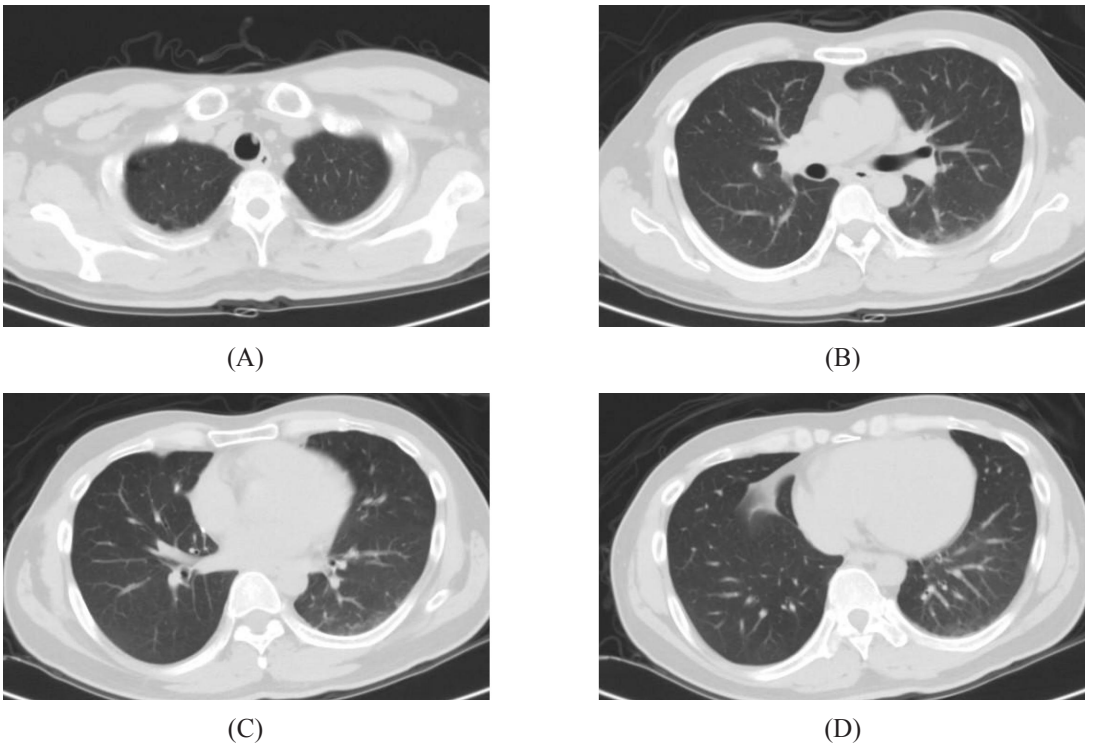


Fig. 4. Follow-up chest CT 2 months later showed resolution of the diffuse ground glass opacity.

provement (Figure 4).

Discussion

Both RB-ILD and DIP are smoking-related ILDs. The term "respiratory bronchiolitis–associated interstitial lung disease" (RB-ILD) is more anatomically accurate because it conveys important pathogenic implications. The term "desquamative interstitial pneumonia" (DIP) was introduced by Liebow, who believed that intra-alveolar cells, typical of this disease, were reactive alveolar pneumocytes "desquamated" from the alveolar surface [3]. These desquamated intra-alveolar cells were finally proved to be alveolar macrophages using electron microscopy; the pigmented macrophages typically were accumulated within respiratory bronchioles in RB-ILD. Therefore, RB-ILD and DIP could be considered as different degrees of severity of a reaction by small airways and lung parenchyma to cigarette smoke [4], although not all experts are in agreement with this point [5]. In clinical practice, there is no need to differentiate these 2 diseases due to their similar treatment strategy; DIP could be regarded as an advanced RB-ILD (i.e., a disease that extended from the respiratory bronchioles to the lung parenchyma).

DIP affects patients mostly between their third and sixth decades of life, and has a male predominance [6]. The most common presentation is insidious exertional dyspnea and persistent nonproductive cough. Some patients may experience weight loss or fatigue. Chest radiograph is insensitive when used to detect DIP and usually shows non-specific findings.

The major finding in chest CT is bilateral, moderately symmetrical, peripheral, and predominantly basal ground-glass opacity, which correlates with the homogeneous intra-alveolar accumulation of macrophages and thickening of the alveolar septa [7-8]. Lung function test may reveal a normal or mild-to-moderate restrictive ventilatory defect with a mildly decreased diffusion capacity. In a systematic review, smoke cessation and systemic steroid use resulted in improvement in approximately 50% of patients [9].

Our reported patient denied dyspnea or persistent cough before the episode of hemoptysis. Cough with hemosputum developed suddenly. This is a rare presentation of DIP. We searched Pubmed using the keywords "desquamative interstitial pneumonia" and "hemoptysis" or "hemosputum", focusing on case reports, and found no matching published literature. Also, there was no case report of DIP presenting with lung consolidation.

In conclusion, clinical manifestations of ILD might vary widely, even in cases with the same disease. This case serves as a reminder of the value of surgical biopsy, especially in an ILD with an undetermined diagnosis and persistent airway symptoms.

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脫屑性間質性肺炎（desquamative interstitial pneumonia）－以肺實質化及咳血表現

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脫屑性間質性肺炎是一種與吸菸高度相關的間質性肺病。常見的臨床表現是以運動性呼吸困難以及持續性乾咳為主。在胸部電腦斷層則主要呈現瀰漫性毛玻璃狀變化。我們提出討論的個案一開始以咳血表現，胸部電腦斷層顯示右中肺葉實質化加上瀰漫性毛玻璃狀的病變。藉由胸腔內視鏡輔助手術進行右中肺葉楔狀切除證實為脫屑性間質性肺炎，病人在接受類固醇治療以及戒菸之後咳血就改善了。咳血以及肺實質化都是脫屑性間質性肺炎罕見之表現，此個案提醒我們外科手術切片對於一些無法得到明確診斷的肺部間質疾病是非常有價值的。*(胸腔醫學 **2016; 31: 365-370**)*

關鍵詞：脫屑性間質性肺炎，咳血，肺實質化

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