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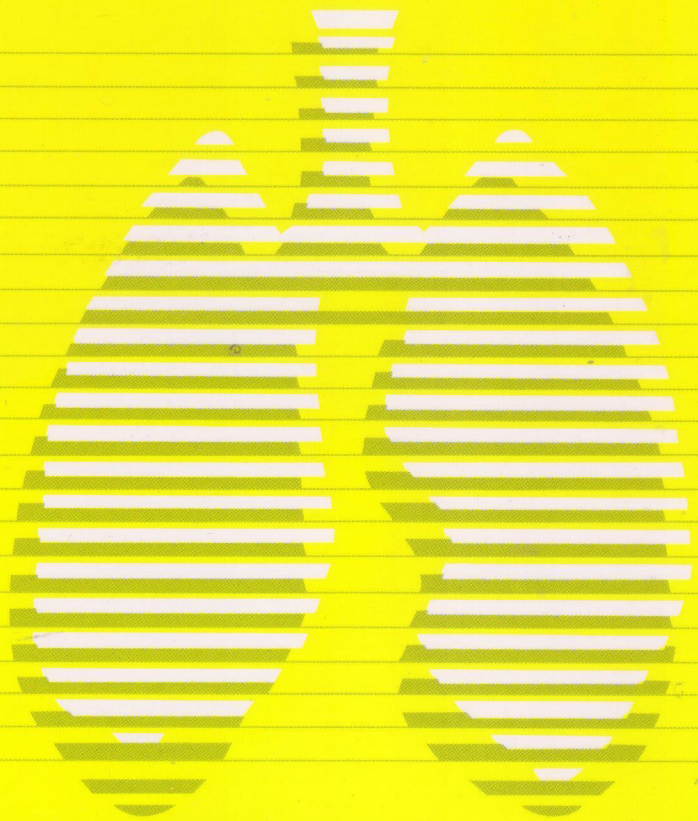

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原著

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Orginial Articles

Case Reports

Characteristics of Clinical and Radiological Manifestations in Empiric Antibiotic-Delayed Diagnosis of Pulmonary Tuberculosis

Guan-Yuan Chen, Meng-Hen Shieh, Yue-Fu Fang, Jie-Mo Lin, Jr-Hau Jang, Horng-Chyuan Lin

Background: Delays in the diagnosis of pulmonary tuberculosis (TB) may result in increased patient morbidity and further spread of the disease. Recent published reports suggest that antibiotic treatment might be associated with the delayed diagnosis of TB. The aim of this study was to evaluate the impact of clinical and radiological manifestations in the delayed diagnosis of TB among different antibiotic classes in an endemic TB area.

Methods: Patients with culture or tissue biopsy-confirmed TB diagnosed between January 2005 and December 2006 were included and their medical records reviewed and analyzed.

Results: Eighty-three of the 403 patients (20.6%) received a fluoroquinolone (FQ group) and 129 (32%) received non-FQ antibiotics (AB group) before the diagnosis of TB. The median duration from initial visit to ordering a TB study was longer in the FQ and AB groups than in the control group (2 and 2 vs. 0 days). More patients in the FQ and AB groups had underlying disease (65.1% and 79.8% vs. 37.2%, respectively), hypoalbuminemia (63.9% and 55.8% vs. 26.2%, respectively) and a positive acid-fast bacilli (AFB) sputum smear (69.9% and 52.7% vs. 49.7%). Specific radiologic patterns and distribution among patients receiving antibiotics, regardless of class, were significantly different from those among patients without antibiotics, and included alveolar consolidation (37.3% vs. 21.9%), multiple lobe infiltrations (50.9% vs. 39.8%) and lower lung involvement (55.2% vs. 31.9%).

Conclusion: Patients who received empiric antibiotics before the diagnosis of TB had a higher percentage of underlying diseases, hypoalbuminemia and positive AFB sputum smears. Antibiotic treatment irrespective of class for presumed CAP delayed the diagnosis of pulmonary TB, and the delay was similar regardless of which antibiotic class had been prescribed. The specific radiologic pattern of alveolar consolidation and atypical distribution with multiple lobes and lower lung involvement contributed to masking the underlying pulmonary TB. Clinicians should consider pulmonary TB in their differential diagnosis when prescribing antibiotics for the treatment of CAP, particularly when encountering the specific radiologic features and distribution reported in this study. ***(Thorac Med 2012; 27: 71-80)***

Key words: radiological manifestations, community acquired-pneumonia, fluoroquinolone, delayed diagnosis, pulmonary tuberculosis

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Introduction

The global incidence of tuberculosis (TB) continues to rise [1]. Early diagnosis and immediate initiation of treatment are essential for an effective TB control program. The potential risks of any delays in diagnosing TB are significant, including prolonged morbidity [2-3], increased mortality [4-7] and TB transmission [8-10].

Previous studies have indicated that antibiotic treatment for presumed community-acquired pneumonia (CAP), using fluoroquinolones (FQ) and other antibiotic classes, is associated with delays in the diagnosis and treatment of TB [11-13]. CAP and TB present similar clinical manifestations, making it difficult to distinguish between the 2 diseases. Radiographic examinations have been required traditionally to make a diagnosis of TB, and the characteristic chest x-ray (CXR) features can enhance an early suspicion of pulmonary TB [14-16]. However, patients with pulmonary TB may present with atypical CXR patterns, potentially leading to empiric antibiotics being prescribed for an initial misdiagnosis of CAP.

In this study, we performed a retrospective analysis of patients with confirmed pulmonary TB, to elucidate the association between different classes of antibiotic treatment for presumed CAP and delays in the diagnosis of TB, and also to compare the specific CXR patterns among patients using different classes of antibiotics and those without antibiotic treatment.

Materials and Methods

Subjects

A retrospective review of patients in Linkou Chang Gung Memorial Hospital from January 2005 to December 2006 was performed. Subjects with a diagnosis of pulmonary TB confirmed by culture or tissue biopsy found in the Linkou Chang Gung Memorial Hospital Department of Microbiology database were enrolled. The exclusion criteria were a clinical diagnosis of pulmonary TB and receiving therapeutic trials of pulmonary TB drugs.

Case notes were also reviewed and the patients were divided into those that took FQ antibiotics (FQ group), those that took non-FQ antibiotics (AB group), and those that did not receive antibiotics (control group). Variables, including demographics, age and gender, past medical history, sputum microbiology, and CXR were recorded and analyzed.

Microbiology

Sputum samples were stained directly for acid-fast bacilli (AFB) and decontaminated in 5% oxalic acid with neutralized sodium hydroxide (4% final concentration). They were cultured using an automated liquid method in the Mycobacteria Growth Indicator Tubes (MGIT) system (Becton Dickinson, Sparks, MD, USA) and on solid media (Lowenstein Jensen [LJ] slopes) [17]. MGIT tubes were incubated for 42 days and LJ slopes for 8 weeks. After 1 *Mycobacterium* sp. was identified from an individual patient, at least 2 repeat specimens were sent for both culture and identification.

Chest Radiology

Standard full-size posteroanterior CXR were performed at the time of the initial visit before TB diagnosis, and 6 categories of radiographic patterns of pulmonary TB were used: fibronodular infiltrates, alveolar consolidation, multiple nodules or mass, fibrotic change, miliary shadowing, and cavity.

The distribution of the patterns on CXR was defined as multiple lobes if more than 1 lobe area was seen in different lobes. Pulmonary TB confined below an imaginary line traced across the mid-point of the hilum and including the parahilar regions was defined as lower lung field TB [18].

To decrease inter-reader variations, the CXR were independently reviewed by 2 pulmonary specialists. If a discrepancy was noted between their interpretations, a 3rd pulmonologist joined the discussion and made the final decision.

Statistical analysis

Differences between groups were analyzed using unpaired t-tests for continuous variables and the chi-square test for categorical variables. A p value less than 0.05 was considered to be statistically significant.

Results

A total of 403 patients with TB confirmed by culture or tissue biopsy between January 2005 and December 2006 were enrolled in this study. Eighty-three of the 403 patients (20.6%) comprised the FQ group, and 129 (32.0%) formed the AB group; 191 (47.4%) did not receive any antibiotics before the diagnosis of TB, and were designated as the control group.

Table 1. Characteristics of the 403 patients with confirmed TB

Characteristic	Empiric antibiotic use (n=212)		No antibiotic Control group (n=191)
	FQ group (n=83)	AB group (n=129)	
Age >65 years	35 (42.2%)	47 (36.4%)	77 (40.3%)
Male sex	59 (71.1%)	96 (74.4%)	128 (67.0%)
Underlying disease	54 (65.1%)$^{+\text{Π}}$	103 (79.8%)$^{\text{II}}$	71 (37.2%)
Diabetes mellitus	24 (16.9%)$^{+}$	31 (24.1%)	32 (16.7%)
Malignancy	9 (10.8%)	20 (15.5%)	21 (10.9%)
Chronic renal insufficiency*	15 (18.1%)$^{+}$	17 (13.2%)$^{\text{II}}$	6 (3.1%)
Receiving steroids	7 (8.4%)$^{+}$	3 (2.3%)	4 (2.1%)
AIDS	1 (1.2%)	3 (2.3%)	2 (1.0%)
Liver cirrhosis	1 (1.2%)	6 (4.7%)	5 (2.6%)
Alcoholism	6 (7.2%)	19 (14.7%)	19 (9.9%)
Smoking			
Current smoker	33 (39.8%)	58 (44.9%)	65 (34.0%)
Ex-smoker	4 (4.8%)$^{+}$	2 (1.6%)	1 (0.5%)
Albumin (g/dl) <3.5 / ≥3.5	53 (63.9%)$^{+}$	72 (55.8%)$^{\text{II}}$	50 (26.2%)
Positive AFB sputum smear	58 (69.9%)$^{+\text{Π}}$	68 (52.7%)	95 (49.7%)

FQ group: receiving fluoroquinolones; AB group: receiving non-FQ antibiotics; Control group: receiving no antibiotics before the diagnosis of TB

AFB: acid-fast bacillus; AIDS: acquired immunodeficiency syndrome

***** Chronic renal insufficiency was defined as a serum creatinine level > 20 mg/l [25]

$^{+}$ p<0.05: FQ group vs. Control group

$^{\text{II}}$ p<0.05: AB group vs. Control group

$^{\text{Π}}$ p<0.05: FQ group vs. AB group

Table 2. Management of the 403 patients with confirmed TB

Characteristic	Empiric antibiotic use (n=212)		No antibiotic Control group (n=191)
	FQ group (n=83)	AB group (n=129)	
Initial visit to ordering TB study (days)*	2 (0-240)$^{+}$	2 (0-315)^{II}	0 (0-261)
TB study to anti-TB treatment (days)*	5 (0-128)	2 (-1-156)	7 (-7-244)
Initial visit to anti-TB treatment (days)*	10 (0-247)	3 (0-156)	7 (0-268)
Ordering TB study at initial visit	28 (33.7%)$^{+}$	46 (35.7%)^{II}	114 (59.7%)

FQ group: receiving FQ; AB group: receiving non-FQ antibiotics; Control group: receiving no antibiotics before the diagnosis of TB

***** Data presented as median (range)

$^{+}$ p<0.05: FQ group vs. Control group

^{II} p<0.05: AB group vs. Control group

Table 3. Radiological manifestations of the 403 patients with confirmed TB

CXR findings	FQ group (n=83)	AB group (n=129)	Antibiotic group (n=212)	No antibiotic group (n=191)
Patterns				
Fibronodular infiltrates	37 (44.6%)	58 (44.9%)	95 (44.8%)	104 (54.5%)
Alveolar consolidation	34 (40.9%)*	45 (34.9%)$^{+}$	79 (37.3%)$^{\pi}$	42 (21.9%)
Multiple nodules or masses	5 (6.0%)*	18 (13.9%)	23 (10.8%)$^{\pi}$	35 (18.3%)
Fibrotic change	22 (26.5%)	26 (20.2%)	48 (22.6%)	35 (18.3%)
Miliary shadowing	0 (0%)^{II}	11 (8.5%)$^{+}$	11 (5.2%)	5 (2.6%)
Cavitary lesion	6 (7.2%)	12 (9.3%)	18 (8.5%)	25 (13.1%)
Distribution				
Multiple lobe involvement	46 (55.4%)*	62 (48.1%)	108 (50.9%)$^{\pi}$	76 (39.8%)
Bilateral lobe involvement	39 (46.9%)	57 (44.2%)	96 (45.2%)	80 (41.9%)
Lower lung TB	46 (55.4%)*	71 (55.0%)$^{+}$	117 (55.2%)$^{\pi}$	61 (31.9%)

FQ group: receiving FQ; AB group: receiving non-FQ antibiotics; CXR: chest radiograph

* p<0.05: FQ group vs. No antibiotics control group

$^{+}$ p<0.05: AB group vs. No antibiotics control group

^{II} p<0.05: FQ group vs. AB group

$^{\pi}$ p<0.05: Antibiotic group (regardless of class) vs. No antibiotics control group

The baseline characteristics of the 403 patients are summarized in Table 1. The presence of underlying diseases, the serum albumin level, and the results of sputum AFB smears were significantly different in the 3 groups. The patients receiving empiric antibiotics before the diagnosis of TB had significantly more underlying diseases, such as chronic renal insufficiency and diabetes, than those without antibiotic treatment. There were also significantly more patients with lower levels of serum albumin (<3.5 g/dl) in the FQ and AB groups compared

with the control group. The patients in the FQ group had a higher percentage of steroids use (8.4%) and positive sputum smears for AFB (69.9%) than those in the control group (2.1% and 49.7%, $p<0.05$ respectively).

The median duration from initial visit to ordering a TB study in the control group was 0 days, while the median duration was significantly longer in the other 2 groups (2 days and 2 days, $p<0.05$, respectively) (Table 2); there was no significant difference between the FQ group and the AB group ($p=0.78$). The percentage of TB studies ordered in the control group (54.4%) was significantly higher than in the other 2 groups (FQ group: 33.7%, $p<0.05$; AB group: 35.0%, $p<0.05$).

The radiologic patterns and distribution of the 403 patients confirmed to have pulmonary TB are summarized in Table 3. Regardless of class of antibiotics, the percentage of patients presenting with alveolar consolidation on CXR was significantly higher in the antibiotic groups (combined: 37.3%, $p<0.05$; FQ group: 40.9%, $p<0.05$; AB group: 34.9%, $p<0.05$) than in the control group (21.9%). In contrast, the percentage of patients presenting with multiple nodules or masses on CXR was significantly lower in the antibiotic groups (combined: 10.8%, $p<0.05$), and especially in the FQ group (6.0%, $p<0.05$), than in the control group (18.3%). Considering the radiologic distribution, the percentage of patients presenting with lower lung and multiple lobe involvement on CXR was significantly higher in the antibiotic groups (combined: 55.2% and 50.9%, respectively, $p<0.05$), and especially in the FQ group (55.4% and 55.4%, respectively, $p<0.05$), than in the control group (31.9% and 39.8%, respectively, $p<0.05$).

Discussion

Depending on the prevalence of TB in a specific area, a percentage of patients with CAP who are empirically treated with a FQ or non-FQ antibiotic will actually have pulmonary TB with or without infection due to a co-pathogen. In our study, 212 (52.6%) of the 403 patients received empiric antibiotics for presumed bacterial pneumonia before TB was diagnosed and treated. Among them, 83 (20.6%) received FQs and 129 (32%) received non-FQ antibiotics. We found that a lower percentage of TB studies had been ordered initially for patients who received empiric antibiotics before TB was diagnosed, and that there was a longer median duration from initial visit to TB study. Moreover, those patients who received empiric antibiotics also had higher percentages of underlying diseases, hypoalbuminemia and positive AFB sputum smears. On CXR presentation, the patients who received empiric antibiotics had a higher percentage of alveolar consolidation and a lower percentage of multiple nodules or masses. Moreover, lower lung and multiple lobe involvement on CXR had specific distributions in those patients who received empiric antibiotics, especially those receiving FQs.

Our findings showed that empiric antibiotics therapy, ostensibly for CAP, and in particular with FQs, was associated with a more frequent co-existence of underlying diseases and hypoalbuminemia, in agreement with the report by Wang *et al*. [19]. Previous reports have shown that death from TB is significantly affected by the presence of conditions that would alter cell-mediated immunity, including underlying systemic diseases such as diabetes mellitus, chronic renal insufficiency, and a low serum albumin level [20-22]. It is supposed that

the TB infection in patients with these underlying conditions will have more severe clinical presentations that may mistakenly lead to a diagnosis of CAP and, pursuant to the recommendations for the treatment of CAP, may lead to the prescription of an FQ antibiotic [23].

There was no difference in the median time to the diagnosis of TB in patients receiving FQs compared to those who received non-FQ antibiotics, but it was longer than in patients who did not receive any antibiotics ($p<0.05$). These findings differ from those of previous studies conducted in TB-sporadic [12] and endemic areas [19]. These studies claimed that only initial empiric treatment of CAP with FQs was associated with a delay in the initiation of appropriate anti-TB treatment. Subsequent studies [24-25] also suggested that FQs should not be the first-line antibiotic to treat CAP in areas of endemic TB. The major reason for the delay in anti-TB treatment with FQ monotherapy is its good anti-mycobacterial activity, resulting in a clinical response in both TB and bacterial pneumonia [12, 19]. However, in the present study, the delay was similar regardless of which antibiotic class had been prescribed. This finding indicates that the delay was not due to the anti-TB activity of the antibiotics, but rather the time inherent in taking a course of antibiotics and waiting to see if there is a clinical response. This is consistent with a more recent analysis [11] in which patients receiving antibiotics (including FQs and non-FQs) prior to TB confirmation experienced a process-related, rather than a particular antibiotic class-related delay in starting treatment.

In our study, the patients in the FQ group had a higher percentage of positive AFB sputum smears than those in the control group, suggesting that the patients in the FQ group had a greater impairment of cell-mediated immunity against TB infection. Our analysis suggests that this may be due to an association with the co-existence of underlying diseases (diabetes and chronic renal insufficiency), steroids use and hypoalbuminemia. Therefore, our data suggest that routine TB examinations (sputum smears and cultures) for presumed CAP before the prescription of FQs will not only prompt the early diagnosis and treatment of TB, but also avoid the risk of developing FQ-resistant TB. The bacterial load would affect the time to positive in liquid culture and influence the time to initiation of treatment [26]. In our study, it was presumed that patients in the control group might represent a less severe clinical condition and that their sputum contained a lower detectible bacterial load than the antibiotic groups.

The importance of a CXR in diagnosing CAP is well known [23]. CXR can also provide timely indications and plays an important role in the clinical diagnosis of pulmonary TB [27-28]. A previous study by Golub *et al*. suggested that patients who receive antibiotics prior to TB diagnosis have a diagnostic delay compared to patients who do not receive antibiotics [13]. They claimed that this may be due to a low utilization of CXR when antibiotics are prescribed for an initial diagnosis of pneumonia. Therefore, the widespread use of CXR when diagnosing CAP should reduce delays in diagnosing TB. In our study, there was no significant difference in ordering CXR between the antibiotic groups (FQ and non-FQ) and the control group.

CXR features are crucial for distinguishing between bacterial pneumonia and pulmonary TB in most instances; however, these infections may sometimes mimic each another radiographically. As such, radiologic patterns favoring bacterial pneumonia may mask underlying pulmonary TB. A previous study demonstrated

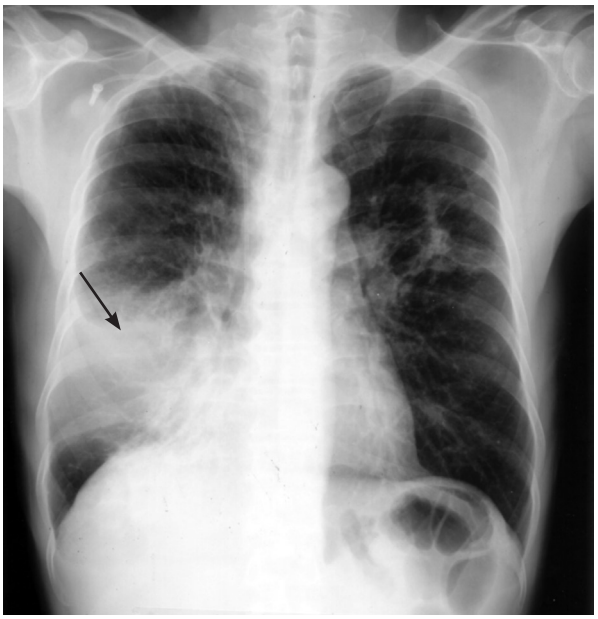

Fig. 1. Alveolar consolidation. A 67-year-old female presented with dry cough for 3 weeks. CXR showed air-space consolidation in the right lower lung (arrows).

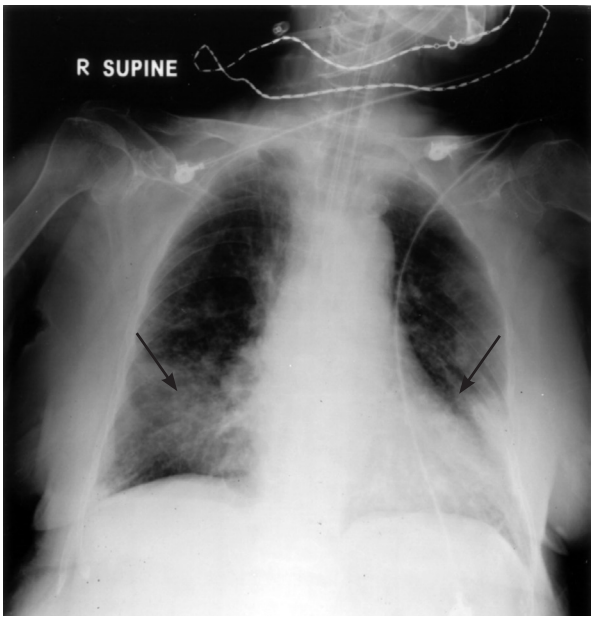

Fig. 2. Lower lung opacities. A 78-year-old male, a representative case with a complaint of intermittent blood-tinged sputum for 1 month. CXR revealed bilateral lower lung opacities (arrows).

that in patients with caseous pneumonia, specific changes were bilateral, with the involvement of 2 or more lobes with destruction and bronchogenic dissemination, but in those with CAP, the pulmonary processes were predominantly bilateral at the lower lobar site [29]. In contrast, a report from Malaysia [30] showed that upper lobe involvement and cavitary infiltrates were predictive of pulmonary TB. In our study, we found that specific radiologic patterns and distribution, including alveolar consolidation (Figure 1), multiple lobe infiltration (Figure 2), and lower lung involvement (Figure 3), would lead to a delay in ordering TB studies due to presumed bacterial infection and the use of empiric antibiotics, regardless of class. Another important implication was that the antibiotic groups showed more radiologic patterns of alveolar consolidation and multiple lobe distribution. This was consistent with the results of the study

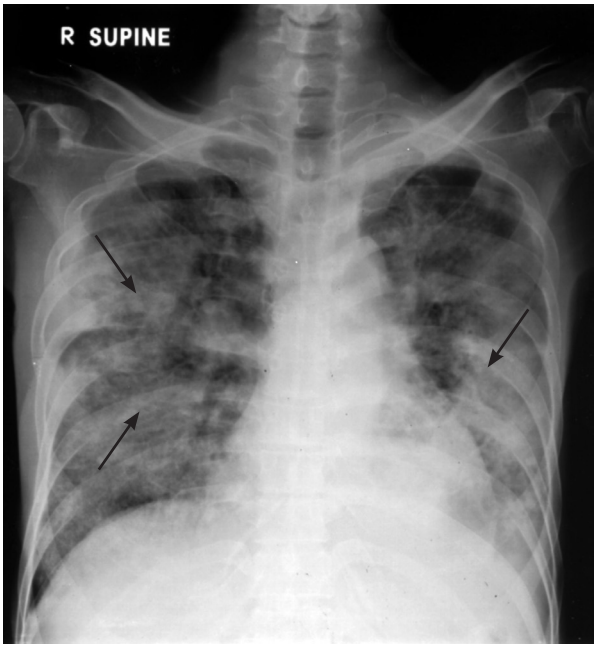

Fig. 3. Multiple lobe infiltration. A 55-year-old male had a history of progressive shortness of breath for 2 weeks. CXR showed bilateral and multiple-lobe lung infiltration (arrows) with alveolar confluence.

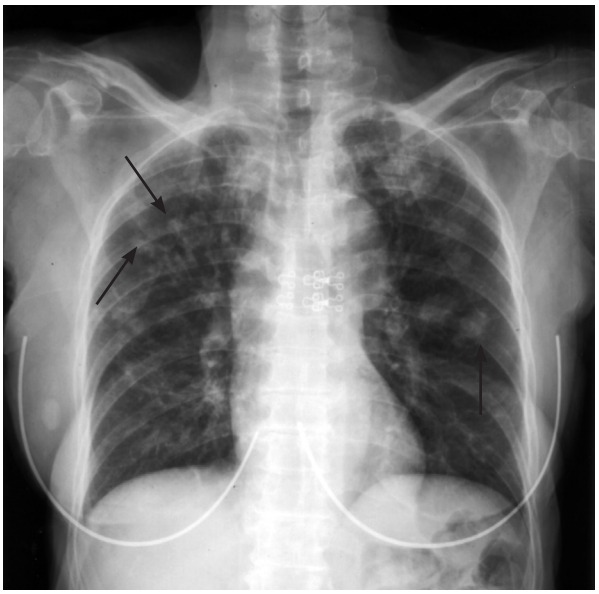

Fig. 4. Multiple lung nodules. A representative case of a 76-year-male patient who had complained of general malaise for 2 weeks. CXR revealed multiple nodular lesions (arrows).

by Anna *et al*. [31], which reported that alveolar consolidation and the proportion of the lung affected in adults with smear-positive pulmonary TB was correlated with baseline clinical and microbiological severity, as well as the response to treatment. In contrast, CXR patterns with multiple nodules or masses (Figure 4) prompted the consideration of pulmonary TB, thus avoiding the unnecessary use of antibiotics. In this study, there was no difference in the radiologic patterns of the FQ group and the non-FQ group, except in the pattern of "miliary shadowing" (0% vs. 8.5%, $p<0.05$). This may be due to the smaller population in the FQ group. A larger FQ population will be needed in the future to elucidate the difference in radiologic patterns between the FQ group and the non-FQ group. This study is limited by its inability to define the relationship between bacterial load and culture time. In addition, we did not discuss whether the delay would influence outcome.

In conclusion, patients who received empiric antibiotics before the diagnosis of TB had a higher percentage of underlying diseases, hypoalbuminemia and positive AFB in sputum smears. Antibiotic treatment irrespective of class for presumed CAP delayed the diagnosis of pulmonary TB. The specific radiologic pattern of alveolar consolidation, and distribution with multiple lobe and lower lung involvement, contributed to masking the underlying pulmonary TB. Thus, we suggest that clinicians should take pulmonary TB into account in the differential diagnosis of CAP by CXR, particularly when encountering the specific radiologic features and distribution reported in this study.

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造成肺結核延遲診斷之臨床及放射線影像特徵

陳冠元　謝孟亨　枋岳甫　林玠模　張志豪　林鴻銓

肺結核延遲診斷會增加發病率及疾病的散播。近年有文獻報告因社區型肺炎而使用經驗性抗生素治療，不論使用何種抗生素，會造成肺結核延遲診斷。本研究探討在肺結核病盛行地區是否有相同情況，並探討不同臨床表現與放射線影像的型態對肺結核病患一開始經驗性抗生素選擇使用所造成的影響。

我們回顧403位經由微生物學或組織切片確定診斷為肺結核的病人之病歷記錄，分析其包括臨床表徵，抗生素使用情況及放射線影像型態。另外，我們依照抗生素使用情況，將病人分成三組，分別為接受fluoroquinolone類抗生素（FQ group），接受非fluoroquinolone類抗生素（AB group），及沒有使用任何抗生素（No antibiotic group）。

結果403位病人中，在肺結核診斷之前，有83位（20.6%）接受fluoroquinolone類抗生素，有129位（32%）接受非fluoroquinolone類抗生素。而從病人初至門診到臨床醫師開立結核檢查的中位期間在FQ group, AB group 及 Control group三組分別為2天，2天，0天，有顯著的差異（p<0.05）。在使用FQ類及non-FQ類抗生素的病人中有較多病人存有原在性疾病（underlying disease）分別是（65.1% and 79.8% vs 37.2%）及低白蛋白血症（hypoalbuminemia）分別是（63.9% and 55.8% vs 26.2%）。另外,使用抗生組（FQ類及non-FQ類）相對於無使用抗生素組有較高比例抗酸性染色呈現陽性（69.9% and 52.7% vs 49.7%）。對於403位肺結核病人中，在放射線影像型態及病變分佈方面，有接受抗生素者（不論是使用FQ類或non-FQ類）與沒有使用抗生素者有顯著的不同。這些差異包括肺泡實質化型態（37.3% vs 21.9%），多發性肺葉浸潤（50.9% vs 39.8%）及肺下部侵犯（55.2% vs 31.9%）。

因此，特殊的影像型態及分布包括肺泡實質化型態，多發性肺葉浸潤及肺下部侵犯容易造成肺結核診斷的誤判。所以，臨床醫師在診斷社區型肺炎並給予經驗性抗生素治療的同時，必須將肺結核列入鑑別診斷；尤其是在遇到本研究論文中所提及的特殊放射線影像型態及病變分佈的情況時。*(胸腔醫學* ***2012; 27: 71-80)***

關鍵詞：特殊放射線影像型態，社區型肺炎，延遲性診斷，肺結核，Fluroquinolone

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Evaluation of a Portable Device for Diagnosing Sleep Apnea/Hypopnea Syndrome

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To limit time spent in the sleep-lab ward and avoid a delayed diagnosis of sleep apnea, adequate and accurate diagnosis/monitoring of sleep apnea/hypopnea using a portable device may be of benefit. This study was designed to evaluate the use of a portable sleep monitoring device in the diagnosis of sleep apnea/hypopnea syndrome. A high correlation in the apnea-hypopnia index (AHI) and the lowest oxygen saturation was noted between standard polysomnography and this portable device. The agreement between the 2 methods was also good (linear regression: R^2 0.799, *p* value <0.001). Extremely good sensitivity (97.3%) and specificity (88.6%) were noted at the diagnostic threshold of AHI ≥30, which means this portable device is a good screening and monitoring tool for severe sleep apnea/hypopnea disorders at home and may reduce waiting time and costs in medical resources. ***(Thorac Med 2012; 27: 81-87)***

Key words: sleep apnea/hypopnea disorders, portable polysomnography

Introduction

The prevalence rate of sleep apnea/hypopnea syndrome in the world is around 1~4%, and the disorder results in daytime sleepiness, impaired performance, traffic accidents and cardiovascular events [1-4]. The standard method of diagnosis of sleep apnea has been in-laboratory overnight sleep recording with polysomnography [5]. Because of limited medical resources, the waiting time for examination has become longer [6-7]. Multiple studies have suggested that the delayed diagnosis and treatment of sleep apnea/hypopnea syndrome would result in disease progression [6]. A home-based, portable device for clinical measurement may be both useful and efficacious, but the accuracy of the device needs to be documented [8]. This study was designed to test the accuracy of the portable device against standard polysomnography.

Material and Methods

Protocol

The patients received a standard polysom-

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nography examination and synchronized recordings using the portable device in the sleep lab on the same night. The outcomes of the validation trial were to determine the correlation between standard polysomnography and the portable device.

Nocturnal Measurements and Analysis

This portable device was designed as a watch and put on the upper arm. It records the limb movements, heart rate, oxygen saturation and API using a special program to analyze limb movement and heart rate variation. The initiation of sleep time was marked in the portable device as soon as respiration settled down to a rhythmic, stable pattern. The end was set either in accordance with the patient's information or a change in the quality of the tracings and the regularity of the breathing pattern.

Polysomnography was performed in the standard sleep lab of Chang-Gung Memorial Hospital, using a computerized recording system (Alice© 4 Respironics, Marietta, Georgia, U.S.A.) consisting of an overnight recording of more than 6 hours duration, electro-encephalography (EEG) channels, including C3,C4,O1,O2, F3 and F4, eye movements (EOG), chin and leg electromyography (sub-mental and leg EMG), airflow (nasal pressure and oral/nasal thermocouple), respiratory effort (chest and abdomen), oxygen saturation, and electrocardiogram.

Each patient's studies were scored by the same observer. Apnea was defined as complete cessation of airflow for ≥10 seconds. Hypopnea was defined as a reduction in the nasal pressure amplitude of ≥50% for ≥10 seconds with 3% oxygen desaturation or an arousal episode.

Statistical Analysis

The diagnostic accuracy and reproducibility of the portable device was tested against the AHI using the linear regression test, which evaluated the agreement between standard polysomnography and the portable device. Pearson's correlation analysis was used to evaluate the significance of agreement in saturation, and the paired samples t-test was performed to evaluate differences in the AHI and lowest saturation in the standard polysomnography and portable device. Tests were 2-tailed, and $p<0.05$ was accepted as statistically significant. Data are presented as mean ± SD (standard deviation) unless otherwise stated.

Results

Sixty patients were enrolled in the study and most of them completed standard polysomnography synchronized with the portable device in our sleep lab. The average AHI using standard polysomnography was 36.67/h ± 35.47/h, and 33.97/h ±18.49/h with the portable device (Table 1). The correlation between normal-to-mild disease (AHI ≤15) and moderate-to-severe disease (AHI >15) appeared to be more significant in the latter group (Table 1).

Sensitivity and specificity at different AHI cut-off levels are presented using receiver operating characteristic (ROC) analysis (Figure 1). Sensitivity and specificity with a cut-off level of AHI ≥30 was high, and an acceptable result was AHI ≥15. Detailed data on the diagnostic accuracy of using the diagnostic thresholds of AHI 15 and 30 are listed in Table 2.

The results of Pearson's correlation of AHI between standard polysomnography and the portable device appeared good in moderate-to-severe disease (Figure 2. AHI <15: n = 23, r = 0.29, p = 0.18; AHI ≥15: n = 37, r = 0.86, $p<0.0001$; AHI ≥30: n = 25, r = 0.78,

Table 1. Correlation of different degrees of sleep apnea/hypopnea disorder between standard PSG and the portable device

	Standard PSG (AHI, /h)		
	Total	Normal to Mild Disease (n=23)	Moderate to Severe Disease (n=37)
Pearson's Correlation			
p value	< 0.0001	0.18	< 0.0001
R	0.8893	0.29	0.86
PSG	36.67 ± 35.47	8.21 ± 4.84	54.36 ± 34.77
Portable device	33.97 ± 18.49	21.03 ± 5.87	42.01 ± 19.13

Data are presented as mean ± SD (standard deviation). PSG: polysomnography. AHI: apnea-hypopnea index.

Table 2. Comparison of results using the portable device and standard polysomnography with diagnostic thresholds of API of more than 15/h and 30/h

	AHI ≥15	AHI ≥30
Sensitivity	36/37 (97.3%)	22/25 (88.0%)
Specificity	2/23 (8.7%)	31/35 (88.6%)
Positive predictive value	36/57 (63.2%)	22/26 (84.6%)
Negative predictive value	2/3 (66.7%)	31/34 (91.2%)
Accuracy	38/60 (63.3%)	53/60 (88.3%)
Prevalence	37/60 (5.7%)	25/60 (41.7%)

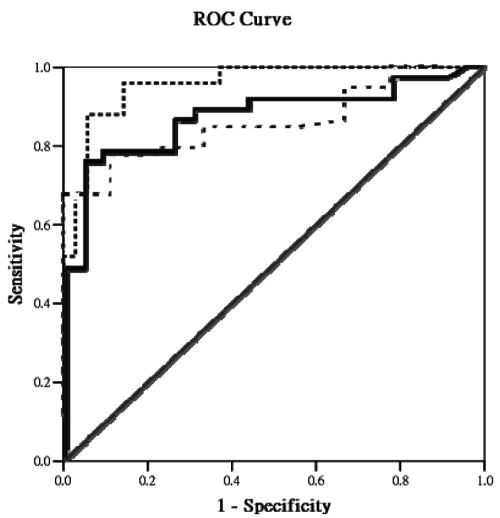

Fig. 1. ROC analysis of AHI sensitivity and specificity at different thresholds. High sensitivity and specificity were noted when using a diagnostic threshold of AHI ≥30 (Area under the curve, AUC = 0.958; Standard error, SE = 0.023); "・・・"AHI ≥5; "—" AHI ≥15; "•••" AHI ≥30.

p<0.0001). The correlation of oxygen saturation between the 2 methods appeared good, as well (Figure 3: r = 0.8732, *p*<0.0001). The residual plot and sample regression line for AHI are shown in Figure 3 and Figure 4 (linear regression: R^2 0.799, *p* value <0.001).

Discussion

Our data revealed good correlation of the AHI between standard polysomnography and the portable device we tested, especially in moderate-to-severe sleep apnea/hypopnea disease. ROC analysis tested the different diagnostic thresholds of AHI; good sensitivity and specificity were noted when using a diagnostic threshold of more than 30/h. Screening patients

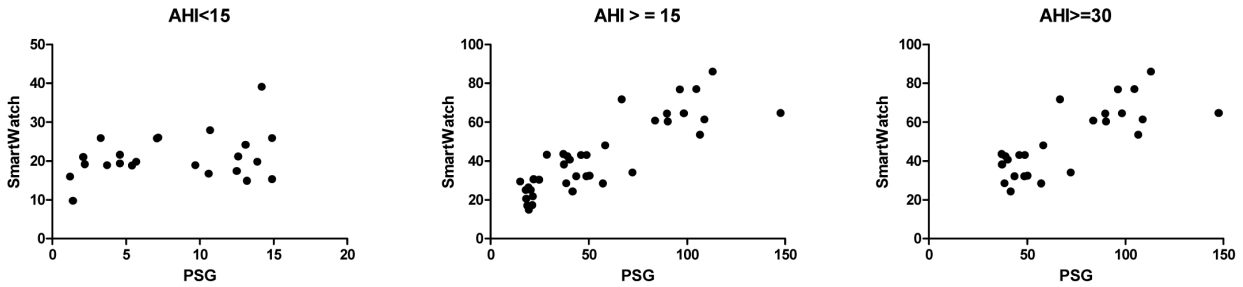

Fig. 2. Pearson's correlation plots for the AHI at different diagnostic thresholds. (AHI <15: n = 23, r = 0.29, $p = 0.18$; AHI ≥15: n = 37, r = 0.86, $p < 0.0001$; AHI ≥30: n = 25, r = 0.78, $p < 0.0001$).

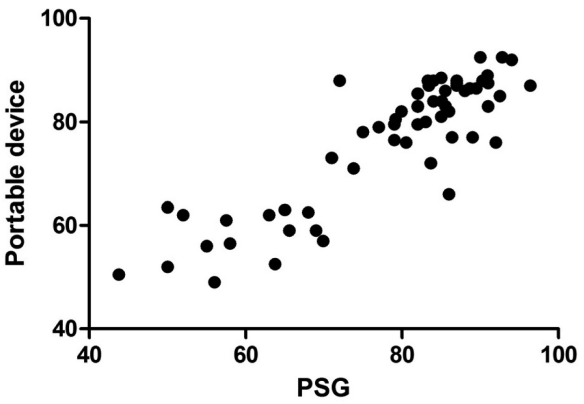

Fig. 3. Oxygen saturation correlation between the portable device and standard polysomnography (n = 60, r = 0.8732, $p < 0.0001$)

using a diagnostic threshold of more than 15/h also showed high sensitivity and could produce useful clinical results, which means the portable device could be used as a screening tool in clinical practice. If a patient came to the clinic with a suspicion of sleep apnea/hypopnea syndrome, that person would be diagnosed as having sleep apnea disorder when the typical clinical presentation was AHI ≥15 plus symptoms or AHI ≥30 alone using this portal device, due to the higher correlation in the higher severity group during this validation study [8]. If the portable device yielded controversial clinical symptoms and equivocal results, the patient may be consid-

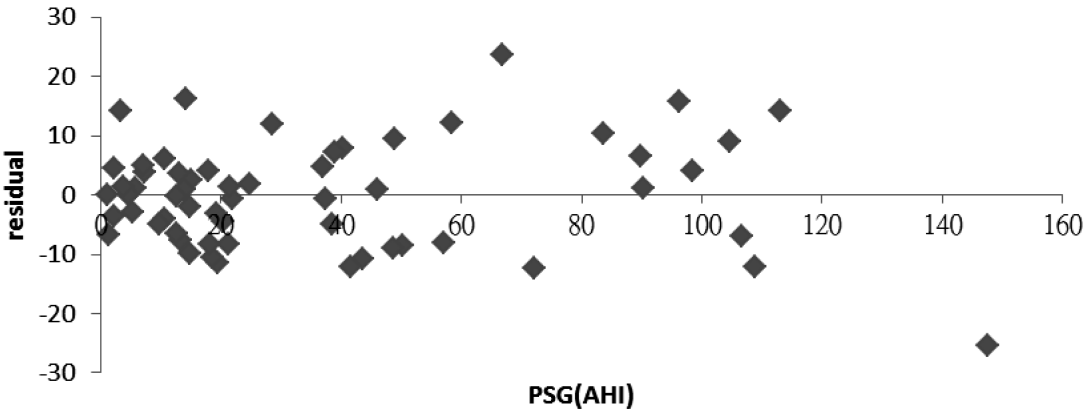

Fig. 4. Residual plot for the AHI (portable device)

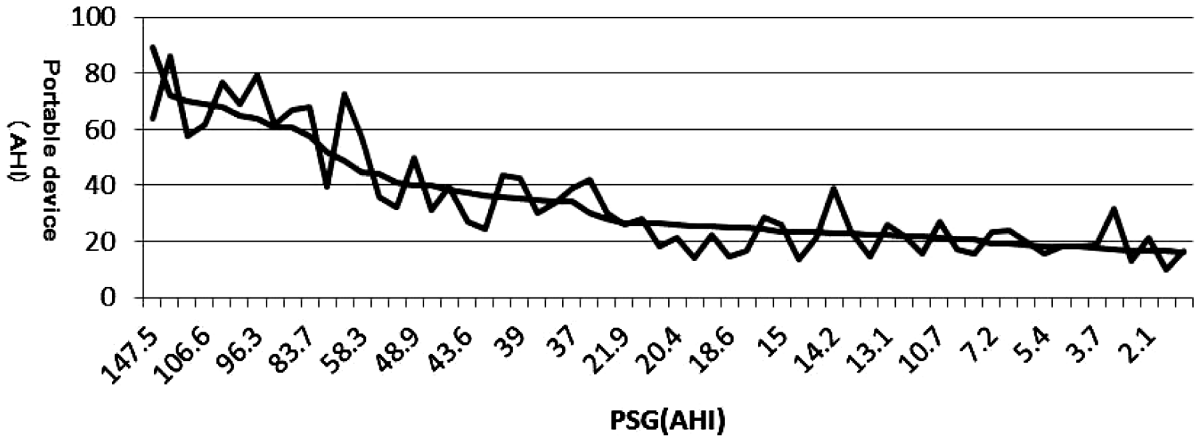

Fig. 5. Sample regression line for the AHI

* Blue line: Portable device result for the AHI level; Red line: predictive AHI level

ered for referral to the sleep lab for a standard polysomnography study. This procedure would lessen costs and waiting time for the sleep-lab, and avoid a delay in treatment for sleep apnea/hypopnea disorders [8-9].

The correlation of oxygen saturation between the portable device and standard polysomnography was good (Figure 3: r = 0.87, p<0.0001). This suggested that the portable device could not only be a screening tool but also monitor the effect of using continuous positive airway pressure (CPAP) at home [10].

The analysis in this study was dependent on the sleep apnea/hypopnea disorder diagnostic threshold used. Many studies, as well as our study, have suggested a conservative cut-off point for AHI of 15/h plus symptoms. This was due to evidence of the benefits of CPAP therapy for symptomatic patients with AHI >15/h [11-12].

Although there is high sensitivity for the sleep apnea/hypopnea diagnosis, it need to be kept in mind that low AHI result couldn't exclude the possibility of sleep apnea/hypopnea disorders completely in clinical applications. Besides, with frequent or repeated micro-arousals, actual sleep time is difficult to determinate with the portable device, since there are no EEG recordings [13]. This was also the reason for the discrepancy between standard polysomnography and the portable device. The portable device was designed for monitoring of sleep apnea/hypopnea, saturation and limb movement only. It was not intended to replace full polysomnography in a full-view evaluation of sleep disorders [13]. The absence of off-detector monitoring and the variance in operator skills were other limitations of using this portable device at home. The learning effect with regard to the portable device would also influence home studies. In the absence of EEG recordings, total recording time or self-reported sleep time could be used as conventional total sleep time for calculating the AHI. This would account for some discrepancy in results between the portable device and standard polysomnography when using the portable device at home.

The limitations of this study include the number of subjects and the venue of the studies [14]. We performed this synchronized study in a

sleep-lab using both standard polysomnography and the portable device to avoid night-to-night variance [15]. The sleep quality differences in the sleep-lab and at home were difficult to assess, especially in patients with sleep apnea/hypopnea disorder [14-17].

In conclusion, this portable device is a good tool for screening and monitoring sleep apnea/hypopnea disorders and may reduce the waiting time and costs in medical resources. But for an accurate diagnosis of sleep apnea/hypopnea disorders, a complete polysomnography is still the "gold standard".

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驗證攜帶式睡眠呼吸生理檢查機應用於睡眠呼吸障礙之診斷

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呼吸睡眠障礙近年來逐漸接受到大家的重視，但睡眠中心有限的資源常導致延遲診斷睡眠呼吸障礙，而未診斷的睡眠呼吸障礙常導致車禍、心血管疾病危險性增加等併發症；若能有攜帶式的睡眠呼吸生理檢查讓病患可於家中接受檢查，可減少等待的時間。但攜帶式的呼吸生理檢查機應用於睡眠呼吸障礙症候群之診斷準確度是需要驗證。本研究希望藉由調查驗證此攜帶式的睡眠呼吸生理檢查機與正規睡眠呼吸生理檢查機之間的差異。結果顯示兩種機型診斷在中重度以上之睡眠呼吸中止症有高度正相關（ROC：AHI ≥15：n = 37, r = 0.86, p<0.0001; AHI ≥30：n = 25, r = 0.78, p<0.0001）；且具高敏感性（97.3%）、高特異性（88.57%）於重度睡眠呼吸障礙病患，適合用於篩選於被高度懷疑為睡眠呼吸障礙臨床症狀之病人，可降低等待檢查的時間以及減少醫療資源的支出。*(胸腔醫學* ***2012; 27: 81-87)***

關鍵詞：睡眠呼吸障礙，驗證攜帶式簡易睡眠呼吸生理檢查機

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Pulmonary Arteriovenous Malformations Mimicking Solitary Pulmonary Nodule with No Symptoms: A Case Report

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Pulmonary arteriovenous malformations (PAVMs) consist of abnormal communications between pulmonary arteries and veins that cause pulmonary blood flow diversion. This splits the blood flow through the abnormal anastomosis, not through the alveolar capillaries, leading to gas exchange. PAVMs are mostly located at both sides of the lower lobes, and range from single to multiple occurrences. Most patients have symptoms indicative of PAVMs, or underlying hereditary hemorrhagic telangectasia (HHT). We reported a patient with an abnormal CXR showing a solitary pulmonary nodule (SPN) with no symptoms that was diagnosed as PAVM using video-assisted thoracoscopic (VATS) surgical wedge resection. In this case, we learned that a SPN could be a PAVM, and prior to the advent of good imaging studies, CT-guided fine-needle biopsy for pulmonary lesions was not totally safe and could cause lethal complications. ***(Thorac Med 2012; 27: 88-93)***

Key words: pulmonary arteriovenous malformations, solitary pulmonary nodule, CT-guided fine-needle biopsy, video-assisted thoracoscopic wedge resection, hereditary hemorrhagic telangectasia

Introduction

Pulmonary arteriovenous malformations (PAVMs) are rare and have a wide spectrum of symptoms ranging from none to life-threatening hemoptysis. Pulmonary symptoms include dyspnea on exertion, platypnea, orthodeoxia, and hemoptysis. Extrapulmonary symptoms encompass chest pain, epistaxis, headache, transient ischemic attacks, and cerebrovascular disease [1]. The patient presented herein revealed none of these symptoms and was diagnosed by video-assisted thoracoscopic surgery (VATS) wedge resection.

Case Report

A 60-year-old woman who was on regular oral hypoglycemic agents and had a 10-year history of type 2 diabetes mellitus came to our chest outpatient department with an abnormal CXR. She had no fever, productive cough, dyspnea, chest pain, or body weight loss to indicate respiratory tract infection or chronic lung

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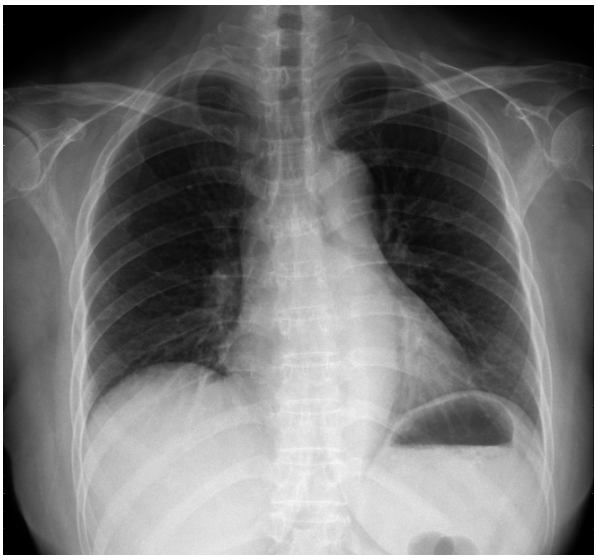
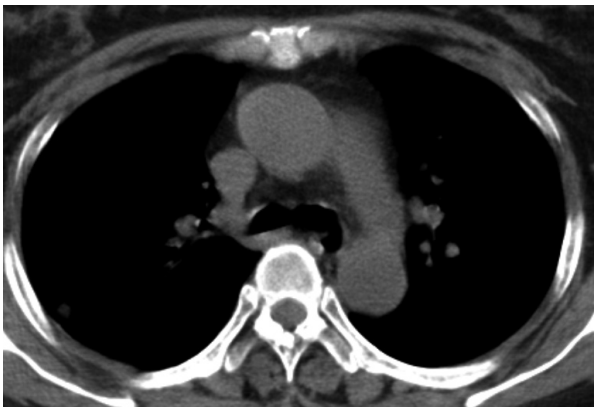


(A)



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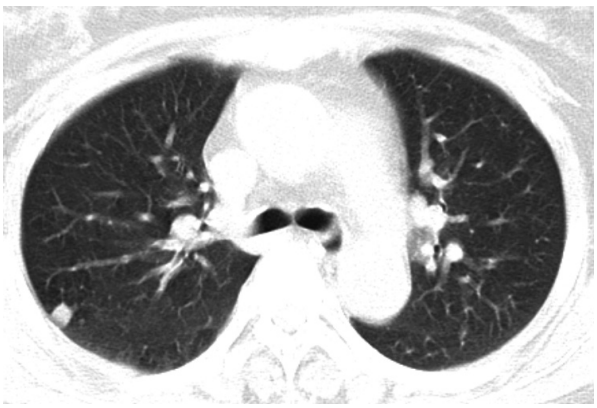


(C)

Fig. 1. (A) CXR showing a right upper lobe nodule <1 cm with ground-glass opacification and peribronchovascular thickening at the bilateral lower lobes. (B), (C) Chest CT demonstrated a well-defined, homogenous, non-calcified pulmonary nodule at the right upper lobe <1 cm.

disease. She had had no epistaxis, hemoptysis, seizure, migraine headache, transient ischemic attack, cerebrovascular accident, brain abscess, hypoxemia, or exercise intolerance.

She was admitted to the chest ward for further study but laboratory data showed neither anemia nor polycythemia. A physical examination indicated no superficial telangectasias on her lips, or hereditary hemorrhagic telangectasia (HHT) syndrome. Her lung function test showed moderate restrictive ventilatory impairment and chest computed tomography (CT) showed a ~1 cm right pleural-based nodule (Figure 1). The patient opted for surgical intervention rather than CT-guided percutaneous biopsy. Under VATS, the nodule located at the peripheral region of the right upper lobe was transected. It was about 1 cm in size, whitish in color, hardened, and with no pleural traction. Her frozen section showed benign lesions with a caseous necrosis pattern. A 24-Fr chest tube was then emplaced and fixed. The VATS wedge resection of the right upper lung nodule was smooth and without complication. With wound care, pain control, adequate IV nutrition, deep breathing and cough training, her general condition gradually improved. After observation for a few days her chest tube was removed without pneumothorax or hemothorax. Her pathology study reported arteriovenous malformation with multiple fibrinoid nodules (up to 1 cm). She was discharged and followed up as an outpa-

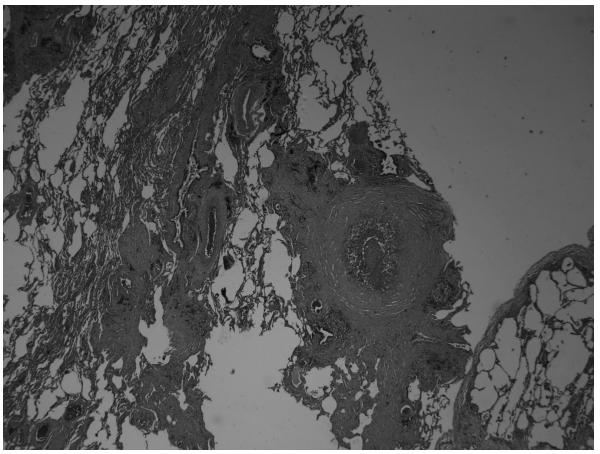
tient.

Discussion

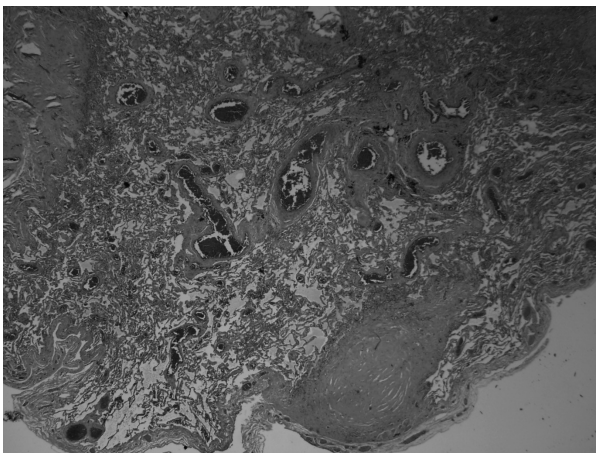
PAVMs were first described in 1897, when Churton reported the autopsy findings of a young boy with cyanosis [2]. The triad of cyanosis, polycythemia, and clubbing of the fingers and toes was identified in PAVMs in 1932 [3]. PAVMs have been described as pulmonary arteriovenous fistulae, pulmonary arteriovenous aneurysms, and cavernous angiomas of the pulmonary telangiectases. Although one study detected only 3 subjects with PAVMs in 15,000 consecutive autopsies [4], about 76% of patients had symptoms indicative of PAVMs, or underlying HHT. HHT symptoms often develop before 20 years of age, but PAVM symptoms develop at age 40 to 60.

Some studies have shown the occurrence of HHT, number and size of the PAVMs, and magnitude of the shunt fraction to correlate with symptom severity [5-8]. PAVMs and their vascular anatomy can be appraised with 3-dimensional helical CT [9]. A report comparing contrast-enhanced, ultrafast CT with selective pulmonary angiography found CT to be more sensitive than angiography in detecting PAVMs, while angiography was better for showing the angioarchitecture of individual PAVMs [10-12].

We diagnosed a nearly 1-cm solitary pulmonary nodule (SPN) using non-contrast enhanced CT because of the patient's previous allergic reactions to contrast material (Figure 1). If malignant, common causes of PAVMs include primary lung cancer, carcinoid tumors, and lung metastases. There is a 50% or greater chance of a malignant etiology at age 60 or above [13], thus surgical intervention was suggested for the patient. Nevertheless, she had no evidence of



(A)



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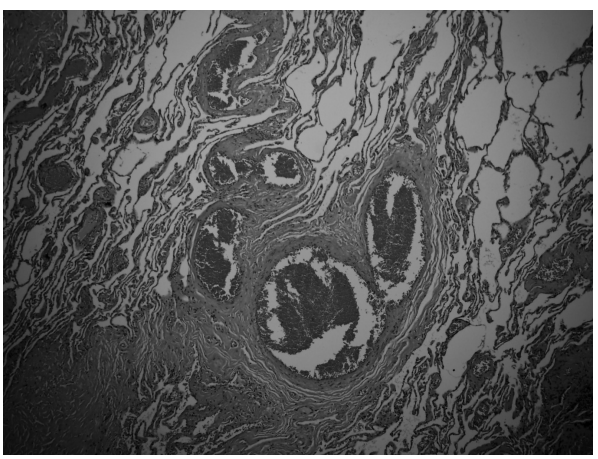

(C)

Fig. 2. Sections of the lung tissue: (A), (B) Multiple pulmonary arteriovenous malformations (PAVMs) associated with many foci of vascular fibrinoid necrosis with occasional calcification (HE, x40), (C) PAVMs embraced with ectatic blood vessels with variable wall thickness (HE, x100). There was no evidence of malignancy.

HHT; spontaneous and recurrent epistaxis, multiple characteristic telangiectasias, or visceral lesions, or a first-degree relative with HHT.

After discussion with the chest surgeon, the patient opted for VATS instead of CT-guided biopsy. The operation confirmed arteriovenous malformations associated with many foci of vascular fibrinoid necrosis with occasional calcification (Figure 2), and no evidence of malignancy. VATS wedge resection identified a PAVM in this case.

Embolization therapy (embolotherapy) is a form of treatment based on the angiographic occlusion of the feeding arteries to a PAVM and was first described in 1977. Embolotherapy would be an alternative treatment for the patient if her PAVM had been identified prior to surgery. Long-term outcome after embolotherapy is generally good. In 1 case series, 39 patients with bilateral PAVM were followed for a mean of 43 months, and prevention of complications and improvement of dyspnea, as well as improvement in PaO_2 could be achieved after successful embolization in most patients [14].

Conventional thoracotomy using vascular ligation, pulmonary wedge excision, and lobectomy or pneumonectomy had similar surgical morbidity and mortality, including a prolonged hospital stay and its associated cost. Thoracoscopy should be considered when pulmonary embolization therapy is difficult or unsuccessful in patients with PAVMs, for it is a less invasive surgical method that results in less postoperative pain, less respiratory dysfunction, and a shorter hospital stay compared with conventional thoracotomy. Several case series have reported thoracoscopic surgical resection provides a high degree of certainty of eliminating fistulae and was associated with lower morbidity, lower mortality, shorter hospital stays and lower associated expenses [15-16].

In summary, we reported a rare case with an abnormal CXR showing a solitary pulmonary nodule, but with no symptoms. The patient was diagnosed with PAVM using VATS surgical wedge resection. Untreated PAVMs remain significantly related to morbidity and mortality, mostly due to stroke and cerebral abscess [17-18]. If this patient had opted the CT-guided biopsy, she may have become complicated with deadly massive hemothorax; however, the most prevalent complication of CT-guided fine-needle biopsy for pulmonary lesions was pneumothorax, which did not lead to death [19]. In this case, we learned that SPN could be a PAVM, and before the availability of good imaging studies, CT-guided fine-needle biopsy for pulmonary lesions was not totally safe and could cause lethal complications.

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肺動靜脈畸形仿似孤立性肺結節，CT引導下細針穿刺切片可能引起致命的併發症：一病例報告

丘偉鴻　馮　瑤*　林靖南**　謝俊民

肺動靜脈畸形（PAVMs）為一由異常肺動脈和肺靜脈的交通，造成肺血分流。這導致血液流經此異常吻合，不經過肺泡毛細血管行氣體交換。肺動靜脈畸形多位於兩側下肺葉，數量上可以是單個或多個。大部分的病人都會有相關症狀來呈現肺動靜脈畸形或遺傳性出血性毛細血管擴張症。我們報告一位病人，沒有症狀，因為胸部X光異常來求診，其X光以孤立性肺結節（SPN）呈現，最終使用影像輔助胸腔鏡楔形切除術診斷出肺動靜脈畸形。在這種情況下，我們了解到，SPN可以是PAVMs，在未充分取得影像學診斷下，貿然以電腦斷層導引下細針穿刺切片，可能會帶來致命性的併發症。*(胸腔醫學* ***2012; 27: 88-93)***

關鍵詞：肺動靜脈畸形，孤立性肺結節，CT引導下細針穿刺切片，影像輔助胸腔鏡楔形切除術，遺傳性出血性毛細血管擴張症

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Herbal Medicine-Induced Lung Injury Presenting as Acute Respiratory Distress Syndrome

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Drug use may lead to serious adverse effects in the lungs, and pulmonary drug toxicity is increasingly being diagnosed as a cause of acute and chronic lung diseases. We reported a case of herbal medicine-induced lung injury presenting as acute respiratory distress syndrome (ARDS).

A 41-year-old male suffered from dry cough with intermittent fever and chills for 2 weeks prior to this admission; generalized muscle pain and mild diarrhea developed a few days later. The patient was treated for atypical pneumonia. Unfortunately, ARDS developed despite the use of moxifloxacin and Tamiflu. Diagnostic bronchoalveolar lavage (BAL) was performed, and the majority of alveolar macrophages in the BAL fluid had a foamy appearance and showed positive for Sudan black stain. Sudan black stain is used to detect pulmonary phospholipidosis. Drug-induced lung injury was highly suspected, and the patient then underwent pulse therapy with methylprednisolone. The lung lesions improved dramatically and the patient was discharged with maintenance oral steroid.

This case highlights the realization that herbal medicine, with its complex compositions, should be considered to be a cause of drug-induced lung injury. BAL may be of value in aiding the diagnosis of drug-induced lung injury as suggested by pulmonary phospholipidosis. ***(Thorac Med 2012; 27: 94-99)***

Key words: herbal medicines, drug-induced lung injury, acute respiratory distress syndrome, phospholipidosis

Introduction

The lungs receive blood from throughout the body, and are directly exposed to the outside environment, making them vulnerable to injury. Direct injuries from various microorganisms and inhaled irritants, and even indirect injuries from inflammatory cytokines of various diseases or conditions are well-known causes of acute respiratory distress syndrome (ARDS).

Drug use may lead to serious adverse effects in the lungs, and drug-induced lung injury is increasingly being diagnosed as a cause of acute and chronic lung diseases. However, the

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clinical, physiological and radiological findings of most drug-induced lung diseases are not specific, and present a challenge to physicians. Herbal medicine, with its complex compositions, may result in lung injury. Herein, we reported a case of herbal medicine-induced lung injury presenting as ARDS.

Case Report

A 41-year-old robust male was a heavy smoker, consuming 2 packs per day for 20 years. He worked in a grain store as a manager. He had suffered from dry cough with intermittent fever and chills for about 2 weeks prior to this admission. Generalized muscle pain and mild diarrhea developed a few days later. He visited a local hospital for help but the symptom of dyspnea worsened, despite medical treatment. He was then transferred to our emergency department and was admitted because of increased dyspnea. The patient was treated as having atypical pneumonia due to the predominantly extrapulmonary symptoms and pulmo-

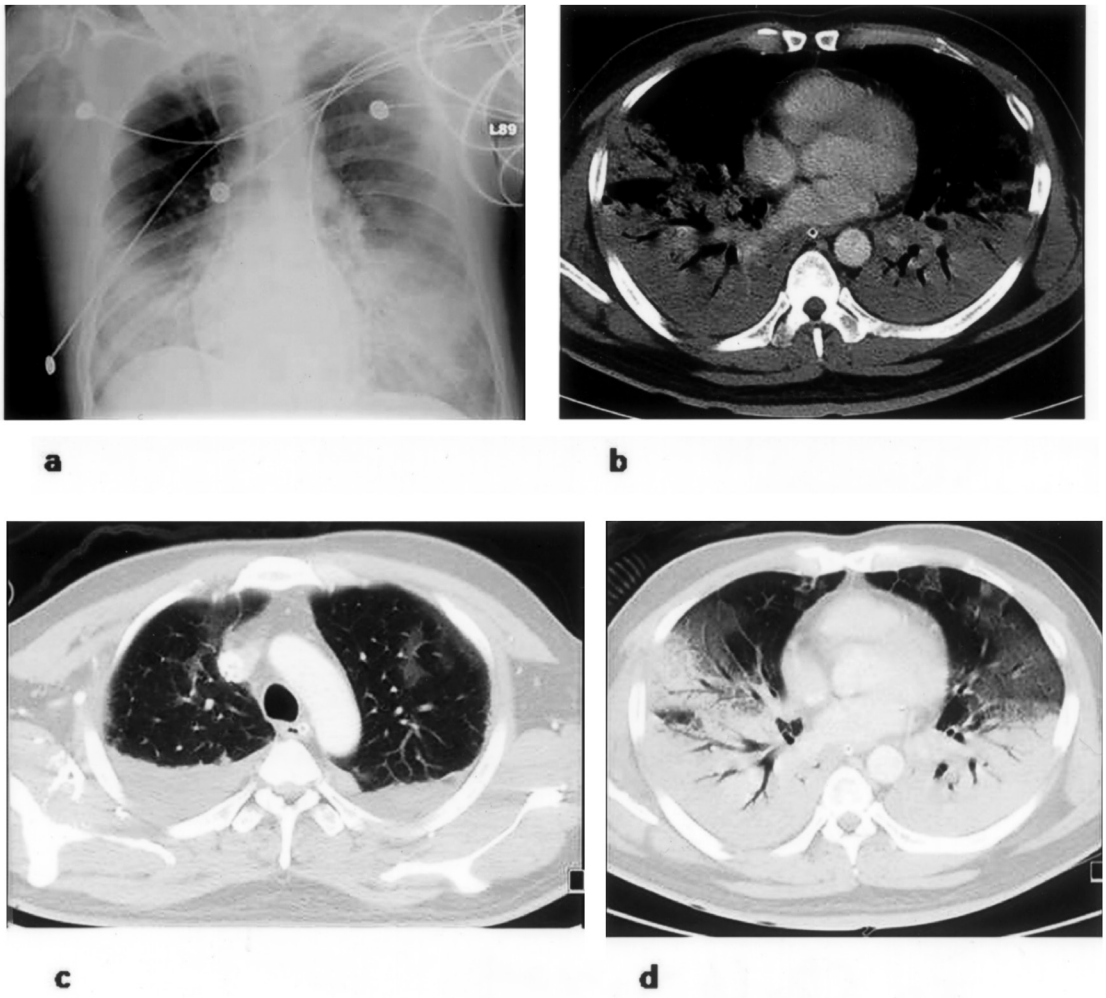

Fig. 1. Chest radiograph (a) shows consolidations in bilateral lower lung fields. Thoracic HRCT scans (b,c,d) reveal consolidations in the dependent lungs, particularly in the lower lung fields, and multiple ground-glass opacities.

nary infiltrates on chest radiographs (Figure 1), without obvious leukocytosis and no left shift in the blood neutrophils. ARDS developed despite the use of moxifloxacin and Tamiflu, and the patient then underwent endotracheal intubation and mechanical ventilation.

The results of laboratory examinations, including H1N1 antigen (Ag), *Aspergillus galatomannan* Ag, cytomegalovirus (CMV) IgM, *Chlamydophila pneumonia* IgM (immunoglobulin M), mycoplasma pneumonia Ab, *Legionella pneumophila* urine Ag, anti-HIV (human immunodeficiency virus) test, measles virus IgM, mumps virus IgM, herpes simplex virus IgM, hepatitis B and C markers, and thyroid function, showed no specific findings. Since there was stationary in the clinical condition, requirement of a high FiO_2 (fraction of inspiratory oxygen), and no obvious pathogenic etiology for ARDS noted, diagnostic bronchoalveolar lavage (BAL) was performed to help identify the nature of the pulmonary lesions. Cytological examination of the BAL fluid (BALF) showed no malignant cells, and no evidence of CMV inclusion body or *Pneumocystis jiroveci* pneumonia, and microbiological studies of the BALF, including viral, bacterial, fungal and mycobacterial cultures, yielded negative results. In addition, the cell profile of the BALF was non-specific. Nevertheless, a majority of the alveolar macrophages in the BALF had a foamy appearance and were positive for Sudan black stain, which was used to detect pulmonary phospholipidosis (Figure 2). Drug-induced lung injury was highly suspected, and the patient then underwent pulse therapy with methylprednisolone 1000 mg for 3 days. The lung lesions improved dramatically and the patient was weaned from mechanical ventilation a few days later. The patient was then discharged with oral low-dose prednisolone treatment. The drug exposure history of the patient was reviewed in detail, and only herbal medicines, including *Cordyceps sinensis* (Berk.) Sacc., deer velvet, and clam extract powder, had been used in recent months and appeared to be the most likely cause of his lung injury.

Discussion

Drug-induced lung disease is not uncommon nowadays. It may present as asthma, bronchiolitis obliterans organizing pneumonia, drug-induced systemic lupus erythematosis, hypersensivity pneumonitis, interstitial pneumonia or fibrosis, noncardiogenic pulmonary edema, pulmonary hemorrhage, pleural effusion, pulmonary eosinophilia, pulmonary vascular disease, etc. [1]. High-resolution computed tomography (HRCT) of the chest provides more information than chest radiography [2]. The radiological findings of drug-induced lung injury include ground-glass opacities, consolidation, bronchial dilatation, interlobular septal thickening, honeycombing and nodularity [3]. The imaging patterns may be classified into interstitial pneumonitis (IP) with or without fibrosis, diffuse alveolar damage (DAD), organizing pneumonia or hypersensivity reactions [3]. Previous studies have indicated that patients with DAD and IP with fibrosis were associated with a poor prognosis [4-5]. However, the imaging patterns of thoracic HRCT did not correlate well with the histological patterns in the patients with drug-induced lung injury [3].

The thoracic HRCT findings in our reported case resembled those of DAD, and the PaO_2/FiO_2 value was less than 200. The cell profile of BALF did not reveal lymphocytosis, neutrocytosis or eosinophilia, and microbiological cultures yielded no growth. However, the majority

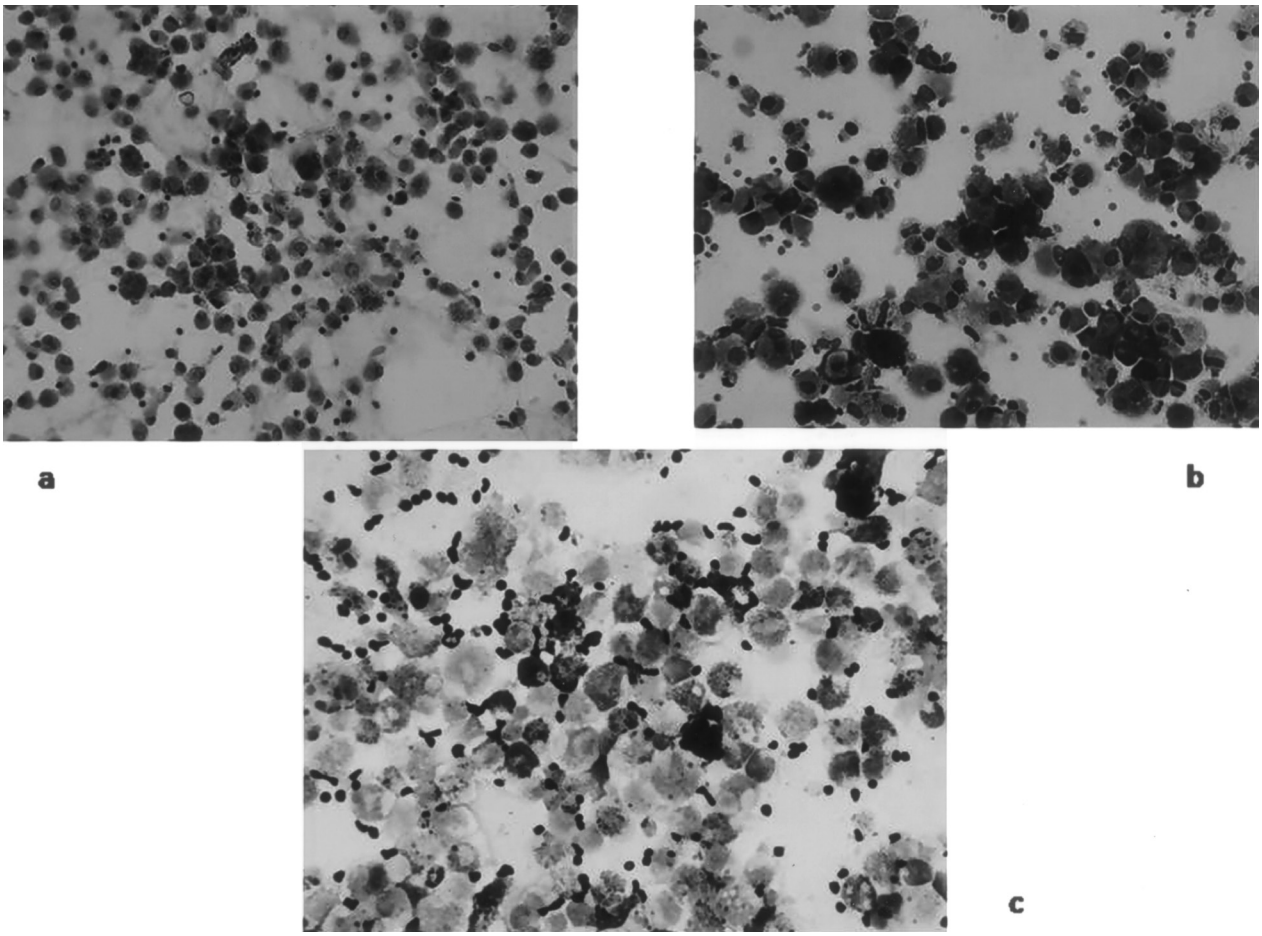

Fig. 2. Cytological smears of BALF reveal many foamy macrophages showing positive for Sudan-black stain, but no lymphocytosis, neutrocytosis or eosinophilia was found. (a) Papanicolaou stain X 400. (b) Liu's stain, X 400. (c) Sudan-black stain X 400.

of the alveolar macrophages had a foamy appearance and showed positive for Sudan black stain, which revealed pulmonary phospholipidosis. Pulmonary phospholipidosis is a condition in which cells develop lipid storage disorders. Metabolic dysfunction with genetic disorders may produce lysosomal storage of phospholipids, such as Niemann-Pick disease or Tay-Sachs disease [6]. And, many drugs, chemicals, and hormones may alter the metabolism of the cells, resulting in pulmonary phospholipidosis. Drugs may bind to phospholipids, making them an unsuitable substrate for phospholipases. The drugs or chemicals may inhibit phospholipase directly with resultant impairment of lipid metabolism in the cells. In addition, they may influence the synthesis of phospholipids [6]. Many cationic amphophilic drugs that induce generalized lipid storage disorders in the tissue of the body have been well studied [7]. Antipsychotic drugs, anorexic drugs and antiarrhythmic drugs, for example, amiodarone, are well-known cationic amphophilic drugs [8]. Immediate and timely withdrawal of the offending drug with or without steroid treatment may be of utmost importance in the management of drug-induced lung

injury.

For patients with acute lung lesions leading to respiratory failure, microorganisms are the most common culprits. Nevertheless, after diligent surveillance, no definite pathogens could be identified in our case. Other etiologies should be investigated aggressively to find out the probable causes of lung lesions. In the past, aggressive lung biopsy, either by transbronchial lung biopsy (TBLB) or open lung biopsy, was used. However, in certain critical conditions, TBLB or open lung biopsy may not be feasible. Accordingly, BAL may be indicated and performed even in patients with acute respiratory distress as shown by bilateral diffuse pulmonary infiltrates and a low PaO_2/FiO_2 value. BALF examinations may provide information other than the detection of microorganisms, and can be of value in aiding the diagnosis of a variety of benign conditions, including sarcoidosis, hypersensitivity pneumonitis, allergic lung disease, drug-induced lung injury, idiopathic pulmonary alveolar proteinosis, etc.

The cultures of blood and BALF from our patient yielded no growth; therefore, ARDS due to infection was not likely. The pulmonary symptoms and lesions that developed a few months after using herbal medicines, the pulmonary phospholipidosis as shown by the foamy appearance of the alveolar macrophages and the marked improvement of the lung lesions after discontinuation of herbal medicines and initiation of steroid treatment, met most of the criteria of drug-induced lung injury [9]. Herbal medicines were most likely the cause of the lung injury in this patient. Because of the severe lung injury that was possibly caused by herbal medicines, rechallenge of the drugs was not performed. It may be argued that pulmonary phospholipidosis is not diagnostic for drug-induced lung injury. However, pulmonary phospholipidosis may be of value in narrowing down the list of differential diagnoses and in aiding a diagnosis of drug-induced lung injury after extensive clinical exclusion.

In conclusion, the case presented may highlight the realization that herbal medicine, with its complex compositions, should be considered as a cause of drug-induced lung injury presenting as ARDS. BAL may be of value in aiding a diagnosis of drug-induced lung injury.

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中藥引起肺部損傷導致急性呼吸窘迫症候群

洪明輝* 黎俊義* 林芳綺*,** 張西川*,***

藥物會導致肺傷害，越來越多的報告顯示，藥物引致肺部不良反應是急慢性肺疾患的原因。我們報告一例中藥引致肺傷害而導致急性呼吸窘迫徵候群。

一位41歲男性在住院前兩週開始有乾咳及發燒的症狀，幾天之後發生全身肌肉酸痛及腹瀉的現象。根據臨床資料，病人被診斷為非典型肺炎而接受治療。未久，病人很快進展急性呼吸窘迫症候群。因為導致急性呼吸窘迫症候群的病因不明，病人接受支氣管肺泡灌洗術。支氣管肺泡灌洗液的細胞學檢查發現，許多肺泡吞噬細胞呈現泡沫狀細胞，且對蘇丹黑染色呈現陽性反應。在高度懷疑藥物引致性肺損傷，給予脈衝類固醇治療後，肺部病灶快速改善，病人順利出院。詳細詢問病人過去病史，病人所服用的中藥可能是造成此次生病的主要原因。

本案例警示中藥的成分複雜，可能會引致肺傷害或導致急性呼吸窘迫症候群，支氣管灌肺泡洗術對於藥物引致性肺傷害之診斷有其臨床效益。*(胸腔醫學* ***2012; 27: 94-99)***

關鍵詞：中藥，藥物引致肺部損傷，急性呼吸窘迫症候群

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Chronic Intractable Cough Caused by Cervical Spinal Cord Injury: A Case Report

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Cervical spinal cord injury (SCI) is a rare cause of chronic cough in adults. We report a 53-year-old man who fell from the 3rd to the 2nd floor, who later developed tetraparesis and an intractable chronic cough. These conditions were caused by C3-4 retrolisthesis and a central herniated intervertebral disc (HIVD) at C3/4-C4/5, with narrowing of the spinal canal and SCI. The cough improved after anterior spinal fusion with spinal instrumentation and C3/4-C4/5 discectomy. The patient was continually monitored in our outpatient department, and was maintained in a stable condition. ***(Thorac Med 2012; 27: 100-104)***

Key words: cervical spinal cord injury, chronic cough, discectomy, retrolisthesis

Introduction

Cervical spinal cord injury (SCI) is a rare cause of chronic cough in adults [1]. The evaluation and classification of cough are based on the duration. Acute cough is defined as a cough lasting less than 3 weeks. Chronic cough that lasts more than 8 weeks can be caused by many different conditions [2], ranging from postnasal drip syndrome (PND) 41%, asthma 24%, gastroesophageal reflux disease (GERD) 21%, chronic bronchitis 5%, bronchiectasis 4%, and miscellaneous conditions 5% [3]. This case report describes a patient with cervical SCI that caused chronic cough.

Case Report

A 53-year-old man fell from the 3rd to the 2nd floor 3 months prior to admission. He was sent to our emergency department (ED), where he was alert, but had a facial laceration wound, weakness in all 4 limbs, numbness, neck pain, and limited range of motion of the neck. C-spine x-ray revealed C-4 spinal process fracture, and C-spine computed tomography (CT) (Figure 1A, 1B) revealed C-4 spinal process fracture and a central herniated intervertebral disc at C3/4-C4/5, with slight compression to the spinal cord. Cervical spine MR of the sagittal T2-weighted (upper) and T1-weighted (lower) images (Figure 1C, 1D) revealed C3-4

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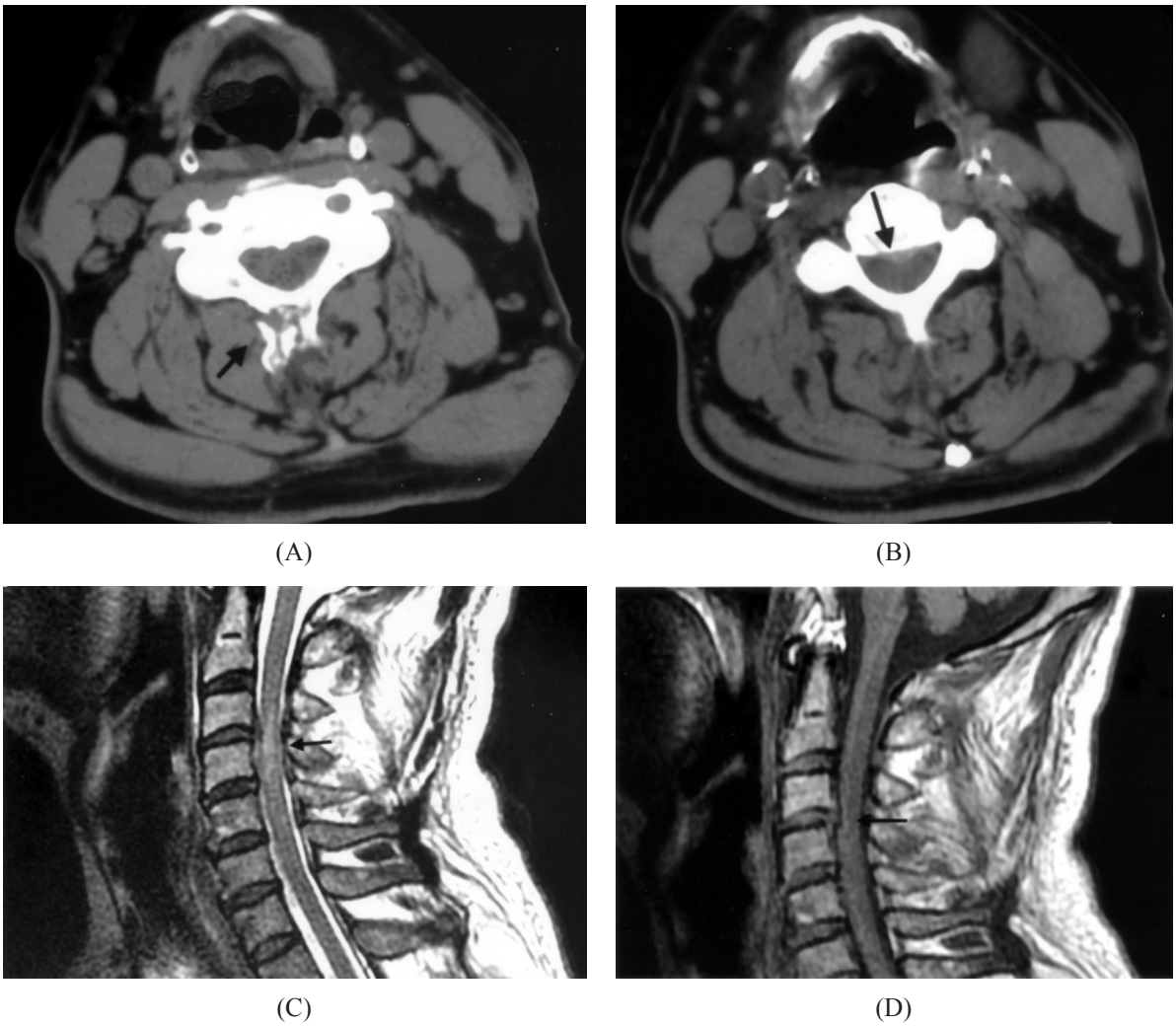

Fig. 1. CT scans of the C-spine without IV contrast shows (A) C4 spinal process fracture and (B) Central herniated intervertebral disc at C3/4-C4/5 with slight compression to the spinal cord. (C) Sagittal T2- and (D) T1-weighted MR images of the cervical spine without IV contrast medium enhancement revealed C3-4 retrolisthesis with displacement of the posterior longitudinal ligament, resulting in the narrowing of the spinal canal and spinal cord myelopathy.

retrolisthesis with displacement of the posterior longitudinal ligament, with spinal canal narrowing and cord compression. We consulted a neurosurgeon and neurological examination revealed tetraparesis with bilateral upper muscle power right/left: 4/2-3, and bilateral lower muscle power right/left: 4/4. We suggested that the patient consider having an operation, but he refused. The patient received conservative pharmacotherapy and wore a soft collar.

After that episode, he experienced chronic cough with dyspnea. The cough also induced seizures, wheezing and cyanosis. He had gone to our ED many times in the most recent 3 months, where his SaO_2 was found to be about 96-98%, but failed to show any improvement. Because of the intractable cough, he visited our chest outpatient department (OPD) for a 2nd opinion. Chest auscultation revealed bilateral mild wheezing and crackles. Chest x-ray (CXR)

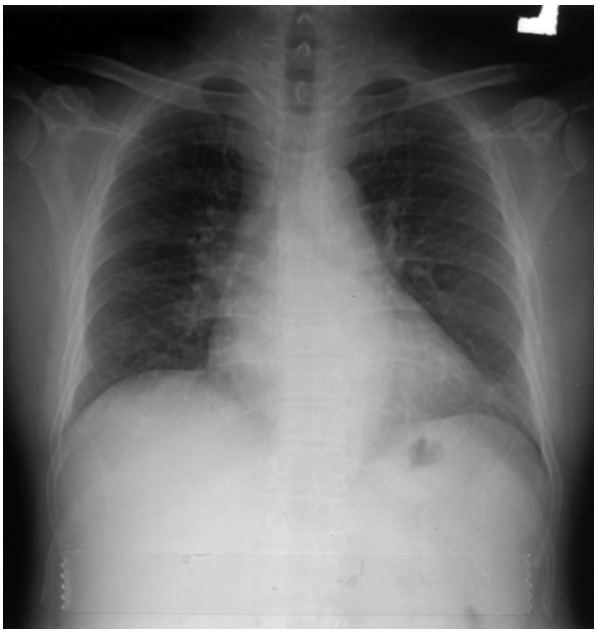

Fig. 2. CSR shows mild infiltrations in bilateral lower lung fields and mild cardiomegaly.

revealed mild infiltrations in the bilateral lower lung fields and mild cardiomegaly (Figure 2). We also arranged for a pulmonary function test which revealed FVC 2.48L (79%), FEV1 1.85L (72%), FEV1/FVC 74%, FEF 25-75% 1.31L (46%), TLC 4.00L (79%), RV 1.52 (85%), RV/TLC 38%, VC 2.48L (79%) and mild restrictive ventilation impairment. He had no history of asthma, smoking, or heart-burn sensation. Under suspicion of chronic cough, he was admitted for further evaluation and treatment.

During hospitalization, we consulted a neurologist, and the neurological examination revealed tetraparesis with bilateral upper muscle power of 4/4 and bilateral lower muscle power of 4/4. Body temperature was 37.4ºC, pulse rate was 82/minute, respiratory rate was 20/minute, blood pressure was 142/62 mmHg, and SaO_2 was 98%. All the patient's blood tests were within the normal range. He was given antibiotics, amoxicillin/lavulanate and clarithromycin, but no improvement of symptoms was noted. Bronchoscopic examination revealed no endobronchial lesion. We suspected the intractable cough was associated with the previous cervical SCI, and consulted the neurosurgeon again. The doctor reviewed the patient's history, performed a thorough physical examination, and suggested that the patient undergo an operation.

After surgical intervention for decompression by anterior spinal fusion with spinal instrumentation and C3/4-C4/5 discectomy, the symptoms of intractable cough, neck pain, limited range of motion of the neck, and weakness were relieved immediately. The patient achieved a stable condition and was discharged 10 days later. Improvement of symptoms continued after discharge, and was confirmed by OPD follow-up 1 month later.

Discussion

Chronic cough caused by cervical SCI is extremely rare in adults [1]. Cough is 1 of the most common symptoms of outpatients [4]. Chronic cough is defined as cough of more than 8 weeks in duration. In our case, the patient's cough lasted more than 12 weeks and was classified as chronic cough. Chronic cough can be caused by many different conditions, including PND, asthma, GERD, chronic obstructive pulmonary disease (COPD), chronic bronchitis, lung cancer, an inhaled foreign body, pulmonary tuberculosis, bronchiectasis, sarcoidosis, idiopathic pulmonary fibrosis, and heart failure [2-3].

Cough reflex is initiated by activation of mechanically and chemically sensitive vagal afferent nerves terminating in the airways [4]. The afferent fibers converge via the vagus or laryngeal nerves on brainstem sites in the nucleus tractus solitarius. The nucleus tractus solitarius

is connected to respiratory-related neurons in the central respiratory generator, which coordinates the efferent cough response. The efferent pathway descends through the spinal cord to the diaphragm, and the abdominal and intercostal muscles [5-6].

The loss of innervation of the respiratory muscles due to cervical SCI results in an ineffective cough, but the sensitivity of the cough reflex is preserved [7-8]. Patients with cervical and thoracic SCI also have bronchial hyperresponsiveness and increased cough sensitivity [2, 8]. Patients with tetraplegia caused by cervical SCI, as compared to paraplegia or other neuromuscular disease, have a unique pattern of respiratory impairment characterized by lung volume restriction, and a greater compromise of expiratory compared to inspiratory muscle function that contributes to ineffective cough [9]. Patients with cervical SCI and lung function volume restriction have limitations with regard to cough, but most patients will adapt to the condition [10]. Patients with cervical SCI also have 1 or more respiratory symptoms, including breathlessness, chronic cough, chronic sputum production, and chronic wheeze [11].

We have described a rare clinical condition associated with cough reflex in a 53-year-old man who fell from the 3rd to the 2nd floor, developing C3-4 SCI and an intractable chronic cough and chronic wheeze. The cough persisted for more than 12 weeks, and he came to our chest OPD for help. CXR revealed mild infiltrations in the bilateral lower lung fields and mild cardiomegaly. The pulmonary function test revealed mild restrictive ventilation impairment. All of the conditions were compatible with chronic intractable cough caused by cervical SCI. The cough and related symptoms were effectively managed after decompression surgery. Awareness of this difficult-to-diagnose chronic intractable cough and the history of cervical and thoracic SCI will alert clinicians to the diagnostic possibility of cases such as this. Further investigation and interventions are necessary to confirm this type of diagnosis and the treatment, as it was in this patient's case.

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頸脊髓損傷造成慢性難治療的咳嗽

張孟祥　江俊士　洪良一*　張正一**　黃建文

頸脊髓損傷是成人慢性咳嗽的少見病因之一。我們提出一位53歲的男性因為從樓梯三樓跌倒到二樓，導致第三第四節頸椎向後移位以及中央突出型椎間盤突出併發脊髓腔狹窄以及頸脊髓損傷，後來發生了四肢輕癱以及難治療的咳嗽。之後咳嗽藉由前頸椎融合手術加上脊椎內固定器以及第三第四和第四第五椎間盤切除術獲得改善，並於門診追蹤，保持穩定狀態。*(胸腔醫學* ***2012; 27: 100-104)***

關鍵詞：頸脊髓損傷，慢性咳嗽，椎間盤切除術，頸椎向後移位

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High-Frequency Chest Wall Oscillation May Facilitate Extubation in Patients with Hypoxic Encephalopathy: A Case Report

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Impaired airway clearance leads to pulmonary complications, such as pneumonia, atelectasis, asphyxia, respiratory failure, and death. High-frequency chest wall oscillation (HFCWO) provides a safe, effective and well-tolerated therapy for removal of excessive airway secretions. We describe a 68-year-old man with hypoxic encephalopathy who was extubated successfully with the assistance of HFCWO which improved airway secretion clearance and prevented atelectasis. HFCWO therapy was stopped 5 days after extubation. Unfortunately, the patient died of hypoxemia as a result of suspected retention of airway secretions 2 weeks after extubation. HFCWO may be of use in the short term for facilitating extubation in patients with hypoxic encephalopathy complicated with ineffective cough. However, the long-term effect and safety of HFCWO with these patients should be further investigated. ***(Thorac Med 2012; 27: 105-111)***

Key words: high-frequency chest wall oscillation, hypoxic encephalopathy, extubation

Introduction

Impaired airway clearance can lead to pulmonary complications, such as pneumonia, atelectasis, asphyxia, respiratory failure, and death. Over the past half century, manual chest physiotherapy has been used to facilitate the clearance of postoperative pulmonary secretions. Several clinical trials have demonstrated that manual chest physiotherapy can be beneficial [1-2]. However, conventional chest physiotherapy is highly technique-dependent, labor-intensive and sometimes not well tolerated by acutely ill patients [3]. Moreover, it may carry the risk of iatrogenic complications, such as bony fractures, hemoptysis, hypoxemia, heart irregularities and vomiting [4-7].

High-frequency chest-wall oscillation (HFCWO) utilizes rapid but gentle external compressions to the thorax to generate air flow

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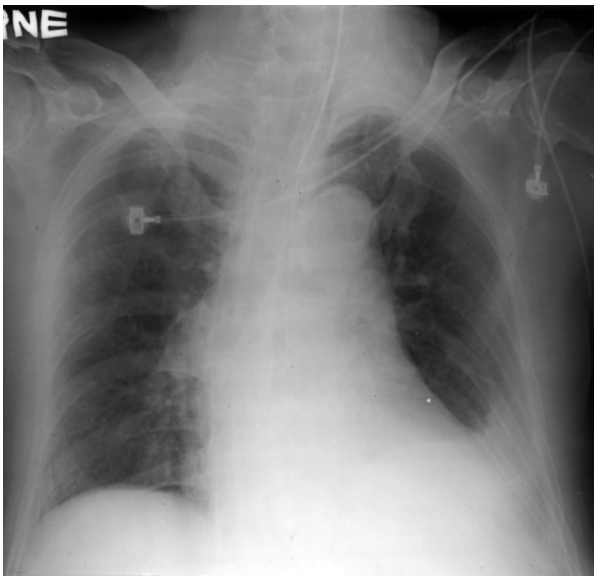
velocities that facilitate bronchopulmonary secretion clearance [8]. The air-pulse generator attaches to a flexible hose which is connected to an inflatable vest worn by the patient. During the past 20 years, HFCWO has been established as a safe and effective therapy in the management of non-surgical and surgical patients who have impaired bronchial secretion clearance, including individuals with neuromuscular disorders [9-11], chronic obstructive pulmonary disease [12], cystic fibrosis [13-15], and blunt thoracic trauma [16], and those who have been hospitalized for cardiac/abdominal/thoracic surgery [17]. However, the application of HFCWO to facilitate extubation of patients with hypoxic encephalopathy has not been established.

This case report describes a patient with prolonged mechanical ventilation (PMV) due to hypoxic encephalopathy who was extubated successfully with the assistance of HFCWO.

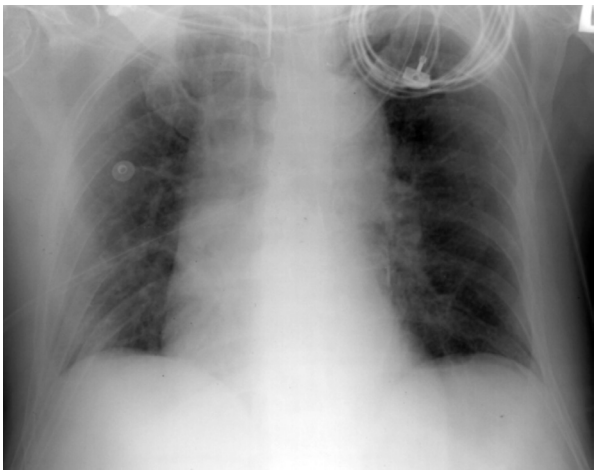
Case Report

A 68-year-old man with a history of hypertension, coronary artery disease and adenocarcinoma of the rectum came to our emergency room (ER) with a sudden onset of loss of consciousness and cardiac arrest. Initially, the patient complained of a sensation of episodic breathlessness and chest tightness followed by an episode of syncope lasting for a few minutes at home prior to cardiopulmonary collapse. On physical examination, the patient was found to be comatose with dilatation of the bilateral pupils without light reflex. There were no detectable vital signs on arrival. Laboratory tests revealed leukocytosis (white blood cell 14000/cumm), elevated serum creatinine (1.6 mg/dl), hypoxemia (PO_2 40.7 mmHg), and elevated arterial PCO_2 (66.7 mmHg); the other parameters, including hemoglobin, platelet, glutamate oxaloacetate transaminase, sodium, potassium, calcium, blood glucose, and cardiac enzymes, were within normal limits. Return of spontaneous circulation was noted after cardiopulmonary resuscitation and airway intubation. However, the patient remained comatose after the return of spontaneous circulation. Computed tomography imaging of the brain revealed neither intracranial hemorrhage nor ischemic stroke. Mechanical ventilation was initiated and the patient was admitted to the intensive care unit (ICU). Magnetic resonance imaging of the brain was performed due to the persistent comatose state (Glasgow Coma Scale: E3VtM4), and the diagnosis of hypoxic encephalopathy was confirmed.

In the ICU, the patient was found to be difficult-to-wean, and an ineffective cough was noted. The patient's family refused tracheostomy. Due to PMV, the patient was transferred to the respiratory care center (RCC). At the RCC, the weaning index measurements revealed the rapid shallow index was 78/L and the scale of cough strength was 2 (from 0 to 5, 2=weakly audible cough) [18]. Chest X-ray (CXR) showed atelectasis at the left lower lung field when he was ventilated with a pressure support mode of 8 cmH2O or underwent a 2-hour T-piece trial (Figure 1A). To facilitate airway secretion clearance, HFCWO with a duration of 15 minutes at 12 Hz twice daily was prescribed. The family discussed the issue of end-of-life with the specialist in hospice care before extubation and decided to sign the do-not-resuscitate consent form. Extubation was done 3 days after HFCWO had been initiated. On the day of extubation, follow-up CXR revealed no atelectasis in the bilateral lung fields (Figure 1B). HFCWO therapy was continued until 5



(A)



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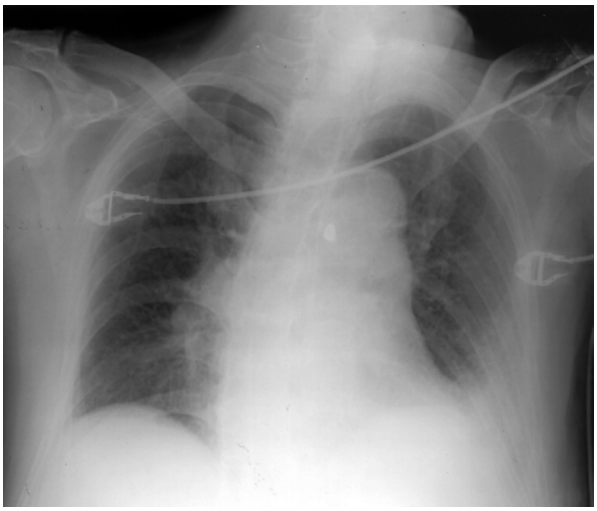

(C)

Fig. 1. (A) The chest roentgenogram on the 40th day of hospitalization showing atelectasis at the left lower lung field and obscure left hemidiaphragm before the utilization of HFCWO. (B) The chest roentgenogram on the day of extubation (the 50th day of hospitalization) showing no atelectasis after 3 days of HFCWO therapy. (C) The chest roentgenogram on the 57th day of hospitalization showing atelectasis in the left lower lung field and obscure left hemidiaphragm 2 days after HFCWO had been discontinued. The patient passed away on the 63th day of hospitalization.

days after extubation and stopped due to the financial burden. During the 8 days the patient received HFCWO therapy, data on the respiratory rate and heart rate were collected about 10 minutes prior to HFCWO and 10 minutes after HFCWO. The patient tolerated spontaneous breathing well. Under mechanical ventilation, before and after HFCWO therapy, there were no obvious variations in respiratory rate (17.33 ± 3.88/min vs. 20 ± 3.10/min) and heart rate (77 ± 4.05/min vs. 80 ± 4.69/min). After extubation, before and after HFCWO therapy, there were also no obvious variations in respiratory rate (24.78 ± 3.49/min vs. 25.89 ± 2.98/min) and heart rate (107.78 ± 5.85/min vs. 113.22 ± 7.05/min) (Figure 2).

The extubation was successful and the patient was transferred to a general ward. After discontinuation of HFCWO, manual chest physiotherapy was continued. However, progressive dyspnea with intermittent desaturation occurred 1 week after extubation. The follow-up CXR revealed recurrent atelectasis at the left lower lung field and obscure left hemidiaphragm 2

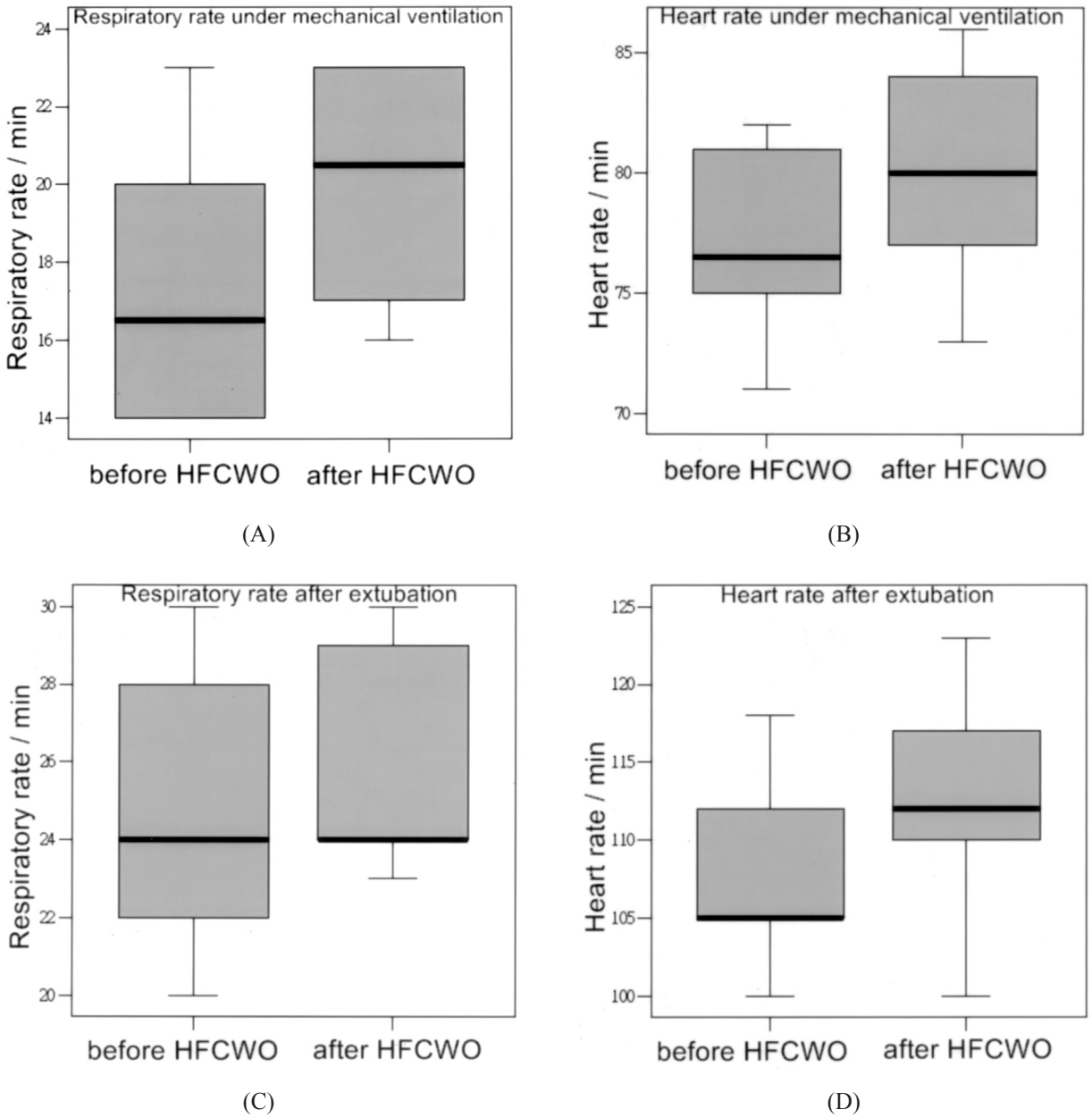

Fig. 2. The respiratory rate (A) and heart rate (B) under mechanical ventilation before and after each HFCWO therapy are depicted. The respiratory rate (C) and heart rate (D) before and after each HFCWO therapy after extubation are also depicted. The respiratory rates and heart rates showed no obvious variations during HFCWO therapy either under mechanical ventilation or after extubation.

days after HFCWO had been discontinued (Figure 1C). His family preferred palliative care and refused phlebotomy and CXR examination during the last 6 days before death. Finally, the patient died of hypoxemia as a result of suspected retention of airway secretions 2 weeks after extubation.

Discussion

Patients who can be considered for a spontaneous breathing trial must fulfill respiratory and cardiovascular criteria, and have an adequate mental status and an absence of correctable co-morbid conditions [18]. For patients completing a spontaneous breathing trial, the ability to protect the airway and clear secretions is a critical concern when deciding whether to remove the endotracheal tube. Glasgow coma scale, cough strength scale, white card test, the amount of endotracheal secretions and the frequency of endotracheal suctions are important predictors of extubation outcomes [19-20]. Hypoxic encephalopathy is usually associated with a limited ability to clear secretions and protect the airway due to muscle weakness and inability to cough. In addition, an increased duration of mechanical ventilation is associated with decreased diaphragmatic force [21]. Therefore, patients with hypoxic encephalopathy are usually not candidates for removal of the artificial airway as in our case. Tracheostomy is the standard and safer approach for patients with PMV resulting from hypoxic encephalopathy. However, for cultural reasons, patients and their families in Taiwan tend to show a far greater reluctance to permit tracheostomy than people in Western countries. As a result, the long-term use of an indwelling endotracheal tube in patients with hypoxic encephalopathy and PMV is increasing in Taiwan.

Because of advances in intensive care and the use of the Integrated Delivery System (IDS) for patients with PMV since 1998 in Taiwan, the number of patients with PMV has increased dramatically during the past 20 years with an accompanying rise in healthcare costs. Therefore, it is imperative to develop more effective therapeutic modalities that can facilitate extubation and weaning from mechanical ventilation in patients with PMV in the RCCs.

There is evidence that HFCWO is better than conventional chest physiotherapy in clearing excessive airway secretions [22-23]. Serial CXRs revealed atelectasis of the left lower lung field was resolved in our patient after HFCWO therapy, but recurred after HFCWO was discontinued. However, HFCWO seemed to be beneficial in clearing retained airway secretions and extubating this patient. Furthermore, the results of physiologic parameters measured before and after HFCWO revealed no significant differences before and after extubation (Figure 2). These results were consistent with previous findings that HFCWO is a safe and well-tolerated airway clearance therapy [16]. Although patients with hypoxic encephalopathy are not good candidates for extubation, this patient was successfully extubated with the assistance of HFCWO, which improved secretion clearance and prevented atelectasis. However, deteriorating retention of airway secretions with intermittent dyspnea developed after HFCWO had been discontinued.

In conclusion, HFCWO appears to be safe and have a short-term benefit in facilitating extubation in patients with PMV due to hypoxic encephalopathy. However, the long-term effects and safety of HFCWO in such patients should be further investigated.

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使用高頻胸廓震動系統可幫助缺氧性腦病變患者拔管—病例報告

陳俊榮* 吳碧珠** 陳昭瑢** 鄭雅華*** 許正園* 吳杰亮***,****

清除呼吸道分泌物能力不佳時可導致多種肺部併發症，如肺炎，肺膨脹不全，窒息，呼吸衰竭，甚至死亡。高頻胸廓震動系統（high-frequency chest wall oscillation）提供了安全，有效，且耐受性良好的治療，以除去過多的呼吸道分泌物。我們描述了一個患有缺氧性腦病變的68歲男子，藉由高頻胸廓震動系統促進呼吸道分泌物排除並避免肺塌陷的發生，幫助病人成功拔管。高頻胸廓震動系統在拔管5天後停用。不幸地，在拔管二個星期後，他因為疑似呼吸道分泌物增加造成低血氧而死亡。對於缺氧性腦病變患者合併咳嗽能力不佳，高頻胸廓震動系統對拔管可能有短期的效果。然而，對這類病人使用高頻胸廓震動系統的長期效益及安全性仍需進一步研究。*(胸腔醫學* ***2012; 27: 105-111)***

關鍵詞：高頻胸廓震動系統，缺氧性腦病變，拔管

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Negative Pressure Pulmonary Edema (NPPE) Following Extubation from Laryngeal Mask Airway—Case Report

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Acute negative pressure pulmonary edema (NPPE) has been reported as an unpredictable but dangerous clinical event. Its occurrence is typically due to an upper airway obstruction related to laryngospasm. We herein present a case of acute NPPE related to laryngospasm in a healthy young male patient ventilated via laryngeal mask airway (LMA). The laryngospasm that the patient developed was most likely an outcome of stimulation associated with LMA extubation. A history of recent upper respiratory tract infection (URI) also may predispose to laryngospasm. The patient was successfully managed with diuretics and continuous positive airway pressure (CPAP).Clinicians should be aware of these complications when utilizing LMA. ***(Thorac Med 2012; 27: 112-116)***

Key words: pulmonary edema, laryngospasm, laryngeal mask airway (LMA), young healthy male

Introduction

Acute negative pressure pulmonary edema (NPPE) typically is the result of an upper airway obstruction and usually develops from the generation of high negative intra-thoracic pressure. Oswalt *et al*. first described the symptoms of pulmonary edema following upper airway obstruction [1]. Young, healthy, and athletic patients appear to be at risk [2], with a prevalence of approximately 1 in 1,000 patients receiving anesthesia [2-4]. Among these, upper airway obstruction associated with post-extubation laryngospasm is most commonly reported. The other causes of pulmonary edema include initial airway problems, such as head and neck tumors, deep neck infection, croup, epiglottitis, enlarged tonsils, and foreign body aspiration [3]. However, acute NPPE following extubation from laryngeal mask airway (LMA) is an uncommon and unpredictable complication of general anesthesia. Herein, we report a case of NPPE in a healthy, strong young male patient following removal of LMA after arthroscopic operation.

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Case Report

A 16-year-old healthy adolescent (height, 165 cm; weight 75 kg) was initially admitted to the orthopedic ward for arthroscopy due to posterior cruciate ligament (PCL) tear and hemarthrosis of the right knee. The patient was categorized as American Society of Anesthesiologist (ASA) physical status I, without a history of allergy or cardiac disease. He was given anesthesia with fentanyl, xylocaine and propofol, and placed in a supine position. After achieving an acceptable depth of anesthesia, an LMA size 4 was placed *in situ* together with intravenous rocuronium. Anesthesia was maintained with a sevoflurane and nitrous oxide in oxygen mixture with mechanical ventilation. The procedure lasted approximately 100 minutes with minimal blood loss, 550 ml of urine output, and 800 ml of crystalloid fluid replacement. The patient's intra-operative course was unremarkable and the patient did not bite the tube during the procedure. After surgery, the patient was extubated and found to have developed stridor when breathing spontaneously, and was able to respond to verbal commands. However, the patient started to cough with pink, frothy sputum after transfer to the recovery room. He had oxygen desaturation (SpO_2: 88%) about 5 minutes after extubation and his respiratory rate was 26 breaths per minute. He was immediately given 10 L/min of oxygen via continuous positive airway pressure (CPAP), and 10 mg furosemide and 100 mg hydrocortisone intravenously. After the treatment, the SpO_2 returned to 98%. His electrocardiogram (ECG) was normal.

A chest specialist was consulted after the patient was transferred to the general ward. Physical examination revealed crackles at the bilateral lung bases and 92-93% SpO_2 in room air. Chest radiograph showed bilateral peri-hilar infiltrates, with the right lung affected more than the left (Figure 1). These findings were suggestive of pulmonary edema and a diagnosis of NPPE was made. Careful history-taking revealed that the patient had had some upper respiratory tract infection (URI) symptoms, like sore throat and cough, 2 weeks prior to surgery.

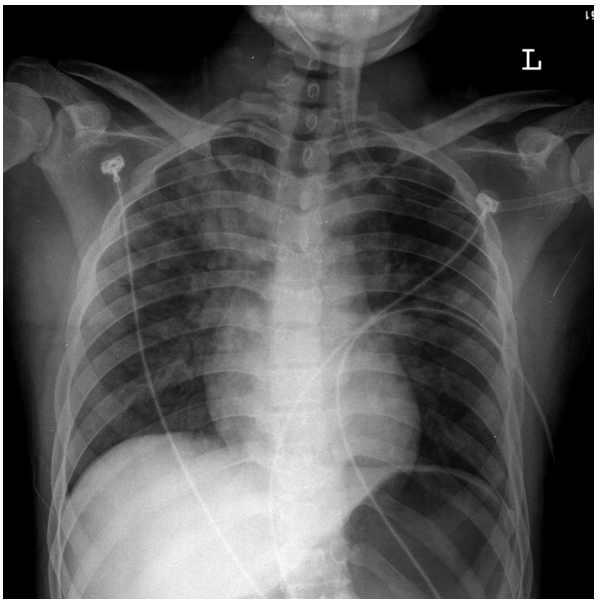

Fig. 1. Portable chest radiography showed bilateral peri-hilar infiltrates with right-sided predominance (2 hours post-operation).

Within a few hours of treatment, the patient's clinical symptoms improved and the SpO_2 level was 96%. After 2 days, the chest radiograph was clear (Figure 2), and the patient was discharged without cough or desaturation. Five days after discharge, he was free of respiratory symptoms and had resumed regular exercise without difficulty.

Discussion

We have reported a case of post-operative NPPE following LMA extubation. The diagnosis was based on the limited intravenous fluid

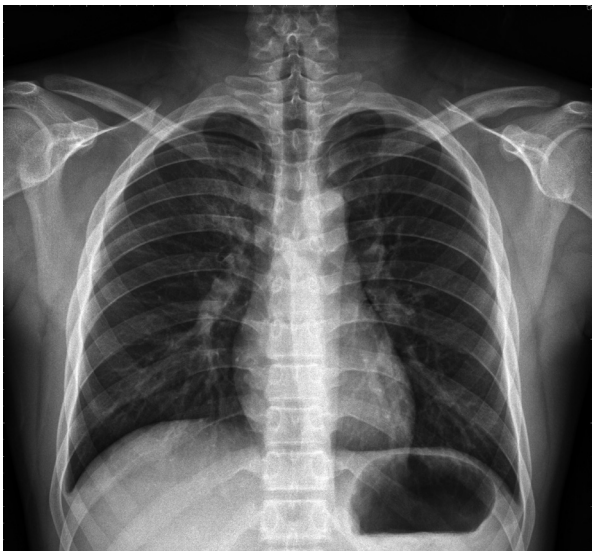

Fig. 2. Chest radiography showed improved pulmonary edema with clear lung fields (48 hours post-operation).

given during the procedure, lack of neurologic signs, fever, hives or wheezing during the operative course, and no co-morbid heart disease. The rapid clinical improvement was also compatible with NPPE.

The pathogenesis of NPPE related to upper airway obstruction is multifactorial [5-6]. Two different mechanisms may explain the development of pulmonary edema during airway obstruction (Figure 3). One of the possible mechanisms is that a large inspiratory force generated against a closed glottis (known as the Muller maneuver) [6], together with high negative intrathoracic pressure significantly shift fluid from the microvessels to the peri-microvascular interstitium. The second proposed mechanism is the increasing pulmonary capillary permeability from the damage that has occurred between the alveolar epithelium and pulmonary microvascular membranes due to severe mechanical stress, prolonged hypoxia, or hypotension [3, 6]. The development of NPPE in our patient was most likely due to strenuous inspiratory effort against an obstructed airway caused by laryngospasm. One possible predisposing factor for the development of laryngospasm in our patient was the history of recent URI, which might have caused airway hyper-irritability [7]. There was no tube bite during the procedure.

The initial clinical management of NPPE is relief from the obstructive event. Treatment may consist of using oxygenation, diuretics, morphine, glucocorticoids, and aminophylline. If there is prolonged laryngospasm or if hypoxia persists, re-intubation with mechanical ventilation and positive end-expiratory pressure may be required. Prophylactic CPAP is also advocated in at-risk patients to avoid intubation [6, 8]. Fortunately, NPPE is a generally benign condition, with full recovery within 12-48 hours if diagnosed early, and if the necessary supportive treatment is given [3].

LMA is a popular and easy-to-use tool for maintaining airway patency during general anesthesia. Although LMA is associated with a lower incidence of airway complications compared to endotracheal intubation [9], the occurrence laryngospasm and NPPE in our patient following LMA extubation suggests that these complications should always be considered in a patient that has used LMA.

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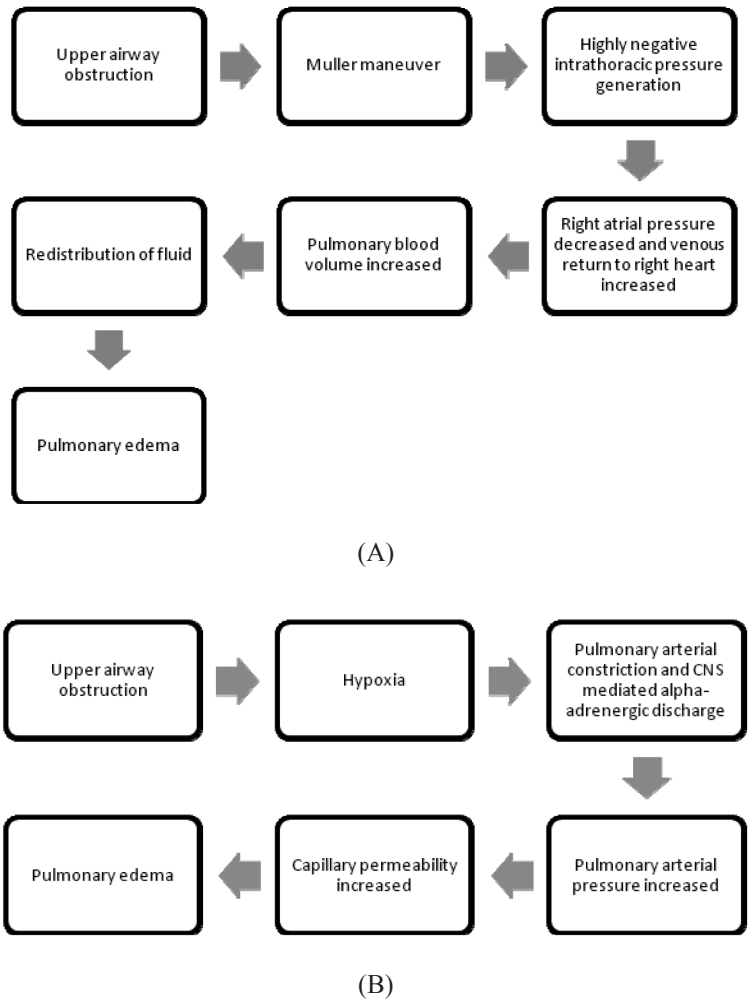

Fig. 3. The pathogenesis of NPPE-related upper airway obstruction.

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脫離喉罩式呼吸道（LMA）後之急性負壓肺水腫

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術後急性肺水腫是一種無法預測卻是危險的併發症，在第一時間做出正確診斷和治療是十分重要的。因為喉部痙攣引起上呼吸道阻塞是造成急性負壓肺水腫最常被廣泛討論的，而又以“年輕健壯男性”被認為是此併發症的好發族群。我們報告一位年輕健壯男性術後脫離喉罩式呼吸道（LMA）之急性負壓肺水腫，推測起因於使用喉罩式呼吸道所導致喉部痙攣，而最近的上呼吸道感染也是引發因子，病患成功地以利尿劑和連續正壓呼吸器（CPAP）治療出院。臨床醫師對於此併發症應審慎評估。***(胸腔醫學 2012; 27: 112-116)***

關鍵詞：急性肺水腫，喉部痙攣，喉罩式呼吸道（LMA），年輕健壯男性

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Pneumocystis jirovecii Pneumonia in a Patient with Smoldering Adult T Cell Leukemia/Lymphoma

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Jih-Shuin Jerng, Kwen-Tay Luh**

Pneumocystis jirovecii is 1 of the most common opportunistic infections in immunocompromised hosts, but rarely causes symptoms in immunocompetent adults. We report the case of a healthy 58-year-old male who was diagnosed with Pneumocystis pneumonia about 2 years ago. He presented with progressive dyspnea on exertion, dry cough and mild body weight loss for 2 months. *Pneumocystis jirovecii* pneumonia was proven by transbronchial lung biopsy. A survey for possible causes of the immunosuppressed status, including anti-HIV and venereal disease research laboratory tests, and hemograms, showed negative results, and no history of Chinese herb or steroid use was traced. After treatment for Pneumocystis pneumonia, serial chest radiographs showed gradual resolution of the lung lesions. After 20 months of follow-up, he developed the symptoms of upper airway infection, tongue base tumor, oral candidiasis, and bilateral neck lymphoadenopathies; adult T cell leukemia-lymphoma (ATLL) was then diagnosed. The patient died 2 months later due to disease progression, despite chemotherapy and treatment for complicated infections. In conclusion, a healthy patient with Pneumocystis infection should be considered as a healthy human T-cell lymphotropic virus type 1 (HTLV-1) carrier or smoldering ATLL patient. ***(Thorac Med 2012; 27: 117-123)***

Key words: *Pneumocystis jirovecii* pneumonia, smoldering adult T cell leukemia-lymphoma

Introduction

Pneumocystis jirovecii is well-known as a common cause of opportunistic infection in immunocompromised hosts and is often encountered in situations involving patients with acquired immunodeficiency syndrome (AIDS), those with allogeneic organ transplantations and under immunosuppressive therapy, or those with malignant diseases after chemotherapy treatment [1-2]. *Pneumocystis jirovecii* may also colonize in healthy individuals, as noted in a previous report, but infection has been rarely reported in immunocompetent or healthy hosts [3].

Adult T-cell leukemia/lymphoma (ATLL), which is caused by human T-cell lymphotropic virus type I (HTLV-1), is a heterogeneous dis-

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ease that can be divided broadly into 4 stages: smoldering, chronic, lymphoma, and acute-type. Both HTLV-1 carriers and smoldering ATLL patients are asymptomatic, relatively healthy individuals with normal or mildly increased white cell counts. Smoldering ATLL may progress to a chronic phase or have acute clinical manifestations, and the carrier may have impaired immunity due to CD4+ cells infected with HTLV-1 [4]. Nevertheless, most cases presented with Pneumocystis pneumonia after a definite diagnosis of acute ATLL; rarely have cases presented with Pneumocystis pneumonia preceding overt leukemia/lymphoma.

Herein, we report a healthy 56-year-old male in whom Pneumocystis pneumonia was proven by pathologic study. He remained well during follow-up until adult T cell lymphoma was diagnosed 20 months later.

Case Report

A 56-year-old male, a cement worker, had been reasonably healthy until September 2008, when he began to experience dyspnea on exertion and dry cough. He was referred to our hospital in November 2008 because pneumoconiosis or metastatic lung cancer was suspected at a chest clinic, and he complained of a gradual loss of weight, about 2 kilogram in 2 months. On arrival, the physical examinations showed no neck lymphoadenopathy or evidence of hepatosplenomegaly, but the chest radiograph (Figure 1A) revealed significant interstitial infiltrates with numerous nodular lesions in bilateral lungs. The subsequent computed tomography (CT) of the chest (Figures 1B and C) showed enlarged mediastinal lymph nodes, multiple nodules, and thickening of the interlobular septa of both lungs. His leukocyte count was 9.32 × 10^9 /L, with 80% neutrophils, 4% monocytes and 16% lymphocytes. There were no other laboratory abnormalities such as hypercalcemia or an increased level of lactate dehydrogenase (LDH). Microbiologic and cytologic studies of the sputum all showed negative results. How-

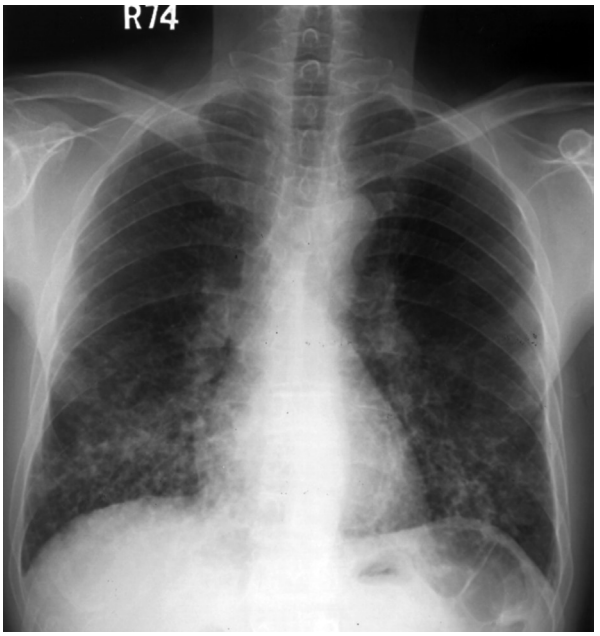

Fig. 1A. Chest radiograph shows reticulo-nodular lesions in bilateral lungs, more prominent at the bilateral hila and basal lungs, but no enlarged hilum.

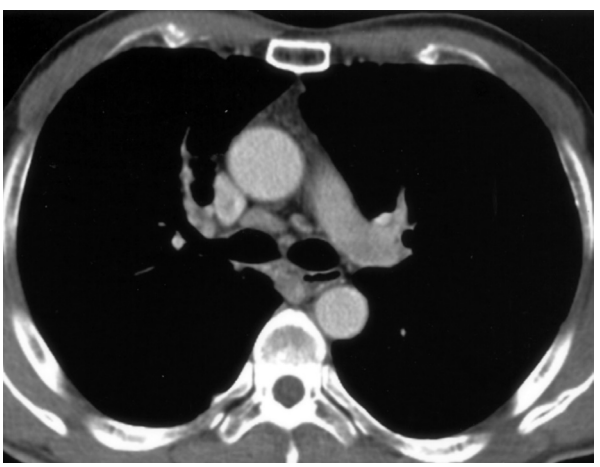

Fig. 1B. Chest CT with a mediastinal window view shows enlarged lymph nodes in the mediastium.

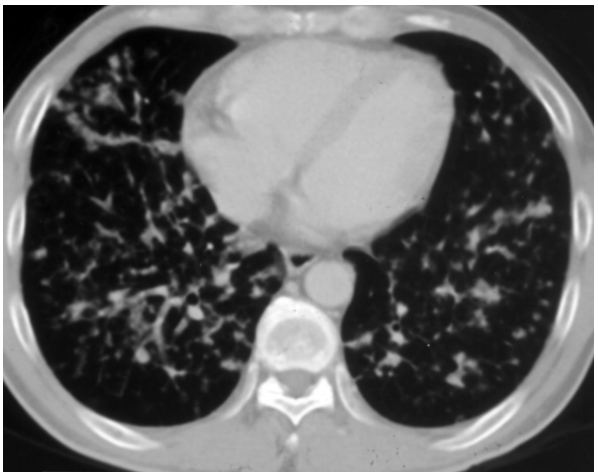

Fig. 1C. Chest CT with a lung window view, shows multiple nodules and thickening of the interlobular septa of both lungs.

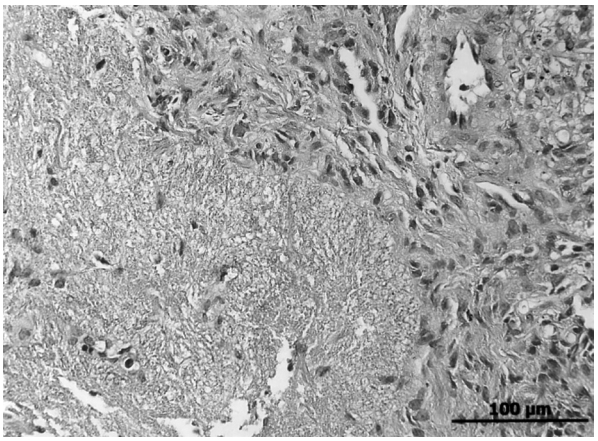

Fig. 2A. Microscopic examination of the transbronchial lung biopsy specimen of the lung showing alveolar spaces filled with eosinophilic frothy-appearing exudates and minute dot-like structures. (hematoxylin-eosin stain x 400)

ever, the pathologic study of the transbronchial lung biopsy specimen (Figures 2A and B) obtained by bronchoscopy was striking in that it showed numerous round or helmet-shaped organisms with Grocott's methenamine silver (GMS) stain (Figure 2B). The diagnosis of *Pneumocystis jirovecii* infection was confirmed, but no evidence of malignancy was found. He then began treatment with oral co-trimethoxazole, which improved his clinical symptoms. Further investigations, including anti-HIV and venereal disease research laboratory tests, and other laboratory findings all showed negative results. After completing the treatment course for Pneumocystis infection, follow-up chest radiography revealed resolution of the infiltrates in the bilateral lung fields (Figure 3A) and chest CT showed stationary mediastinal lymph nodes and marked resolution of the lung lesions (Figures 3B and C); the patient remained generally well during the following 20 months.

In late August 2010, the patient had fever and sore throat for 3 days. A left tongue base tumor and bilateral cervical lymphadenopathies

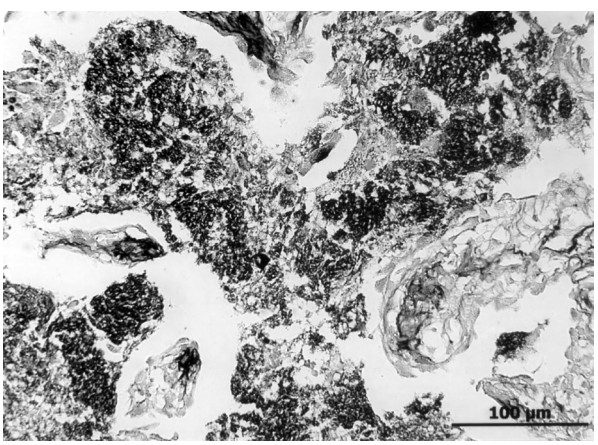

Fig. 2B. Highlighted round and sometimes helmet-shaped organisms (dark-stained) within the exudates. (Grocott's methenamine silver stain x 400)

were noted by an otolaryngologist, and laryngoscopy showed candidiasis at the glottic and supraglottic larynx. His leukocyte count was 5.60×10^9/L, with 53.0% neutrophils, 15.0% lymphocytes, and 22% abnormal lymphocytes. Peripheral blood smear showed lobulated nuclei lymphocytes, and a bone marrow study revealed surface markers positive for CD7, CD2, CD5, CD3, CD4, CD8, and CD25, which was compatible with adult T cell lymphoma. Biopsy of

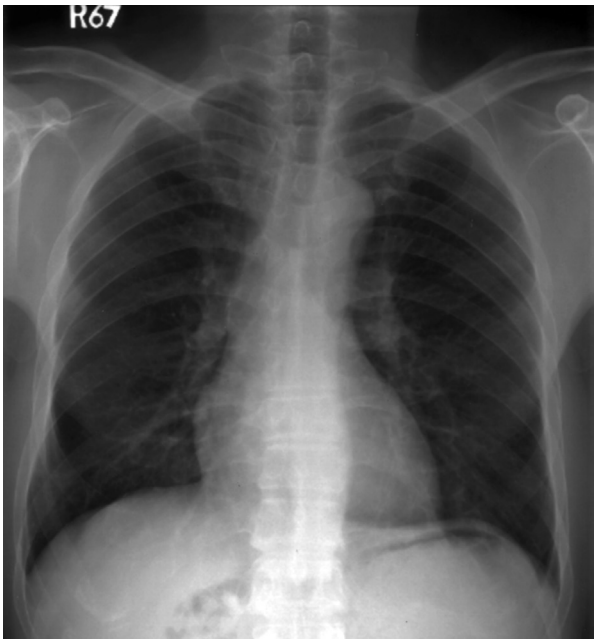

Fig. 3A. Chest radiograph shows mildly residual reticulo-nodular lesions in bilateral lungs, and still no enlarged hilum.

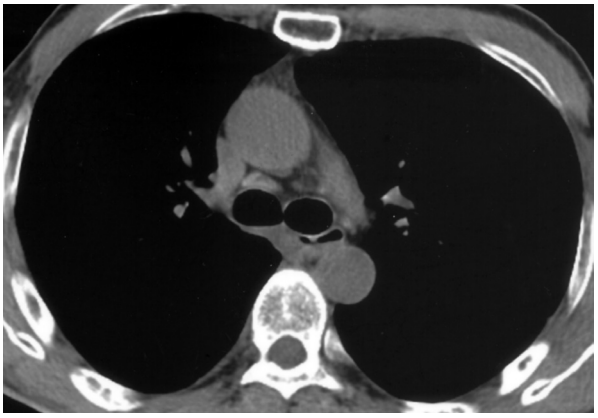

Fig. 3B. Chest CT without contrast enhancement in a mediastinal window view shows a stationary mediastinal lymph node, compared with the pre-treatment chest CT.

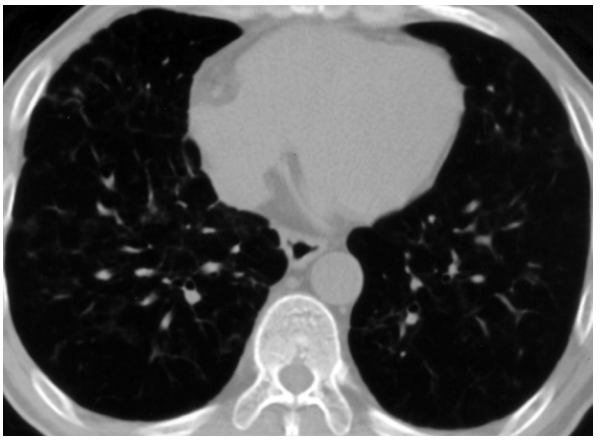

Fig. 3C. Chest CT with a lung window view shows near resolution of the pulmonary nodules, some ground-glass opacity, and mild thickening of the interlobular septa of both lungs.

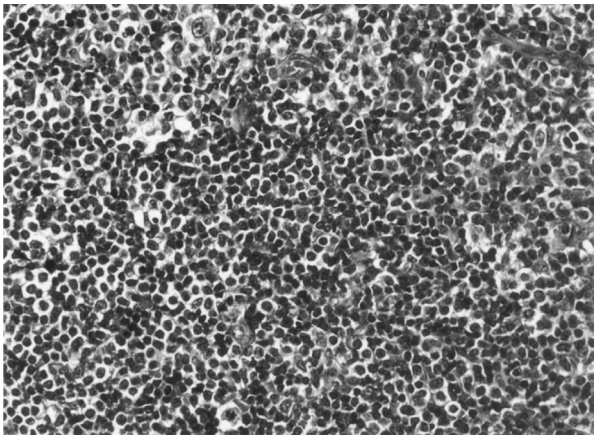

Fig. 4. Microscopic examination of a biopsy specimen of the neck lymph node showing tumor cells with pleomorphic hyperchromatic nuclei and focally clear cytoplasm. (Haematoxylin-Eosin stain x 400)

the neck lymph node (Figure 4) also confirmed the evidence of malignant lymphoma.

He was then hospitalized, and a whole body CT showed multiple lymphadenopathies at the bilateral lower neck, axilla, mediastinum and upper abdomen, hepatosplenomegaly, massive ascites, and bilateral pleural effusion. Cytologic study of the pleural effusion proved the presence of atypical lymphoid cells. Serology study also documented the HTLV-1 infection. Chemotherapy was started in November 2010. Despite the markedly decreased size of the neck nodes, the patient's treatment course was complicated with febrile neutropenia and opportunistic infections. Allogeneic peripheral blood stem cell transplantation was planned, but the infections

could not be well controlled, and lymphoma progressed thereafter, despite aggressive management. He finally died in December 2010 due to severe sepsis and hypoxemia.

Discussion

Pneumocystis jirovecii can cause a microbial colonization in both the oropharyngeal cavity and lower respiratory tract in healthy adults or infants [5-7]. Most of the patients identified with *Pneumocystis jirovecii* pneumonia had an immunodeficiency, such as AIDS, suffered from immunosuppressive disorders or had been receiving steroid therapy. Defending against Pneumocystis infection depends on the immune response, as mediated by complex interactions between CD4+ T lymphocytes, alveolar macrophages, neutrophils, and so on [1], of which CD4+ T cells play a pivotal role.

The retrovirus HTLV-1 also infects CD4+ T cells, and transmits via various routes, such as breast-feeding, sexual contact, and contaminated blood products [8-10]. Infected CD4+ cells with HTLV-I may induce neoplastic proliferation, yielding a high ratio of CD4+/CD8+. This differs from cases of AIDS, which have a lower ratio of CD4+/CD8+ [11]. The development of ATLL has been clearly associated with the early acquisition of HTLV-1 infection, with the latency between the initial infection and onset of the disease ranging from 40 to 70 years. Hosts with HTLV-1 infection, smoldering ATLL, which is less than 5% of all ATLL cases, or chronic ATLL types all share an indolent clinical course. ATLL cases are also accompanied by manifestations of limited skin and/or lung lesions, but no peripheral lymphocytosis, lymphadenopathy, or hypercalcemia [4]. In Japan, several cases of HTLV-1 or smoldering ATLL preceded with *Pneumocystis jirovecii* pneumonia were reported in the 1990s [11, 13]. Opportunistic infections, such as Pneumocystis pneumonia, cryptococcosis, and strongyloidosis, could be predictive of the development of overt leukemia/lymphoma in smoldering ATLL patients [14].

Our patient, with no definite medical history, was deemed a healthy adult when he was diagnosed as having *Pneumocystis jirovecii* pneumonia. Follow-up hemograms did not reveal evidence of abnormal lymphocytes, lymphocytosis or other abnormalities, but the anti-HTLV-1 antibody test and measurement of CD4+ cell counts were not performed initially at our hospital. Currently, there is no consensus about workups for healthy hosts with Pneumocystis pneumonia, but detailed history-taking and laboratory studies, such as hemograms or anti-HIV antibody, are routinely done. Detection of anti-HTLV-1 antibody is controversial in this situation, because no treatment exists for infection with the HTLV virus. As previously stated, the CD4+ lymphocyte counts could be normal or increased in patients infected with HTLV-1. Therefore, ongoing monitoring should be instituted for detection of associated conditions such as ATLL and myelopathy/tropical spastic paraparesis.

After 20 months, the patient presented with acute illness due to overt ATLL, and the serology study also confirmed HTLV-1 infection. Therefore, in a retrospective analysis of the clinical course, the immune status of this patient might have been impaired at the diagnosis of Pneumocystis pneumonia, despite the fact that there was no traditional evidence. It is therefore reasonable to consider the presence of immune suppression in HTLV-I carriers and in patients with smoldering ATLL.

In conclusion, *Pneumocystis jirovecii* rarely causes clinically significant infection in healthy adults, and a patient deemed immunocompetent who is identified with Pneumocystis pneumonia should receive close follow-up and further detailed examination for possible underlying potential causes of the immunocompromised status, including HIV infection, immunosuppressive therapy, and malignancies. HTLV-1 in healthy carriers and smoldering ATLL are rare but possible causes of the impaired immunity underlying Pneumocystis infection.

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在鬱積型成人T細胞白血病/淋巴瘤病人罹患肺囊蟲肺炎：病例報告

梁勝鎧　姚　明　張逸良*　林中梧*　鄭之勛　陸坤泰**

肺囊蟲是在免疫不全的宿主最常見的伺機感染之一，但卻很少在免疫健全的成年人身上造成症狀。我們報告一個58歲健康男性於2年多前被診斷罹患肺囊蟲肺炎之病例。他表現出漸進氣促，咳嗽和輕度體重減輕持續了2個月的時間。支氣管鏡肺部活檢證實感染肺囊蟲肺炎。調查所有可能造成免疫抑制狀態原因的檢查都顯示陰性結果。經過肺囊蟲肺炎治療，一系列的胸部影像檢查均顯示肺部病變逐步改善。 經過20個月的後續追蹤，病人發生了上呼吸道感染症狀，舌根部腫瘤，口腔念珠菌病，和兩側頸部淋巴結腫大，因而診斷成人T細胞白血病/淋巴瘤。最後，儘管在積極的化學治療和準備異體周邊血液幹細胞移植，他仍在2個月後因病情惡化與併發傳染性疾病而去世。因此我們更要全面去檢查且密切追蹤這些病人是否有免疫功能低下疾病的臨床表現。*(胸腔醫學* ***2012; 27: 117-123)***

關鍵詞：肺囊蟲，鬱積型成人T細胞白血病/淋巴瘤

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Endobronchial Ultrasound-Guided Transbronchial Needle Aspiration as a Complementary Tool for Diagnosis of Esophageal Cancer—A Case Report

Yueh-Feng Wen, Chao-Chi Ho

Endoscopic ultrasound with fine needle aspiration (EUS-FNA) and endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) have emerged as valuable tools in the mediastinal nodal staging of lung cancer. Each modality alone has its limitations. The combination of both approaches therefore arises as a new idea for mediastinal nodal staging of lung cancer, and it has yielded promising results. Yet, the clinical impact of this strategy in the diagnosis of other mediastinal disease is still not well known. Herein, we report a case in which the diagnosis of esophageal cancer was established via EBUS-TBNA after endoscopic biopsy and EUS-FNA failed to obtain tissue confirmation. We concluded that in carefully selected patients, EBUS-TBNA may be an alternative diagnostic method before more invasive modalities are adopted. ***(Thorac Med 2012; 27: 124-130)***

Key words: endoscopic ultrasound with fine needle aspiration, endobronchial ultrasound-guided transbronchial needle aspiration, esophageal cancer

Introduction

Mediastinal sampling is undoubtedly important for decision making in the staging of lung cancer, metastatic lung tumors, and various benign mediastinal diseases [1-3]. Although there have been different techniques available for mediastinal sampling, tissue confirmation of mediastinal masses has been a great challenge for pulmonologists in past decades [4]. Standard tools for the diagnosis of mediastinal lesions include computed tomography (CT)-guided fine needle aspiration, mediastinoscopy, and video-assisted thoracoscopy [5]. Since many vital structures are found in this area, there is always the possibility that the patients may be subjected to minor or major complications when these standard procedures are used to obtain tissue samples from mediastinal masses [4-5]. In addition to the complication risks, patients who undergo mediastinoscopy and thoracoscopy require hospitalization and general anesthesia [4]. When performed under local anesthesia, endoscopic ultrasound with fine needle aspiration (EUS-FNA) generates a high yield in the diagnosis of mediastinal tumors, with only minor

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complications reported [6-7]. EUS-FNA has excellent access to the posterior mediastinum and subcarinal lesions; nonetheless, it fails to visualize some parts of the anterior mediastinum [4]. Visualization of and access to some parts of the anterior mediastinum that EUS-FNA fails to reach was made possible with the introduction of endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) in 2004 [8].

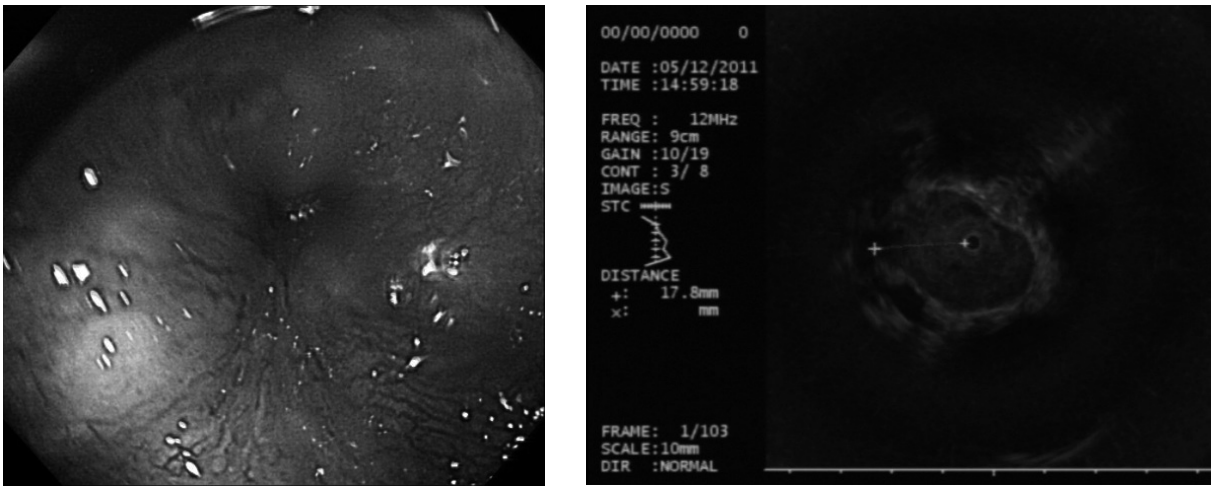
As a real-time, minimally invasive method requiring only consciousness sedation, EBUS-TBNA provides a relatively safe method for pathologic diagnosis of mediastinal lymphadenopathies [8-10]. Furthermore, numerous studies have proven the accuracy of EBUS-TBNA in the evaluation of hilar and mediastinal nodes in lung cancer [9-10]. Similar to EUS-FNA, EBUS-TBNA has its particular anatomical limitations. The posterior mediastinum along the esophagus cannot be assessed by EBUS-TBNA, as it can with EUS-FNA [4]. An accumulating amount of evidence has revealed that a strategy combining EUS-FNA and EBUS-TBNA for mediastinal nodal staging of lung cancer produces even better results [11-13]. However, little is known about the clinical significance of this strategy in the assessment of non-lung cancer-related mediastinal lesions.

Case Report

A 72-year-old man presented to our gastroenterology clinic with progressive dysphagia for months. Initially, there was difficulty in swallowing solid food, so the patient eventually progressed to a liquid diet. By the time he sought medical aid, he could hardly take any solid or liquid foods. Meanwhile, he had lost 8 kilograms. He did not report skin induration, headache, muscle ache and weakness, or dyspnea. Ten years prior to this visit, he had taken Chinese herbs for gouty arthritis. Otherwise, he denied any other medical or surgical history. He did not chew betel nuts but he drank alcohol socially. He had smoked 10 cigarettes every day for 30 years until 5 years ago.

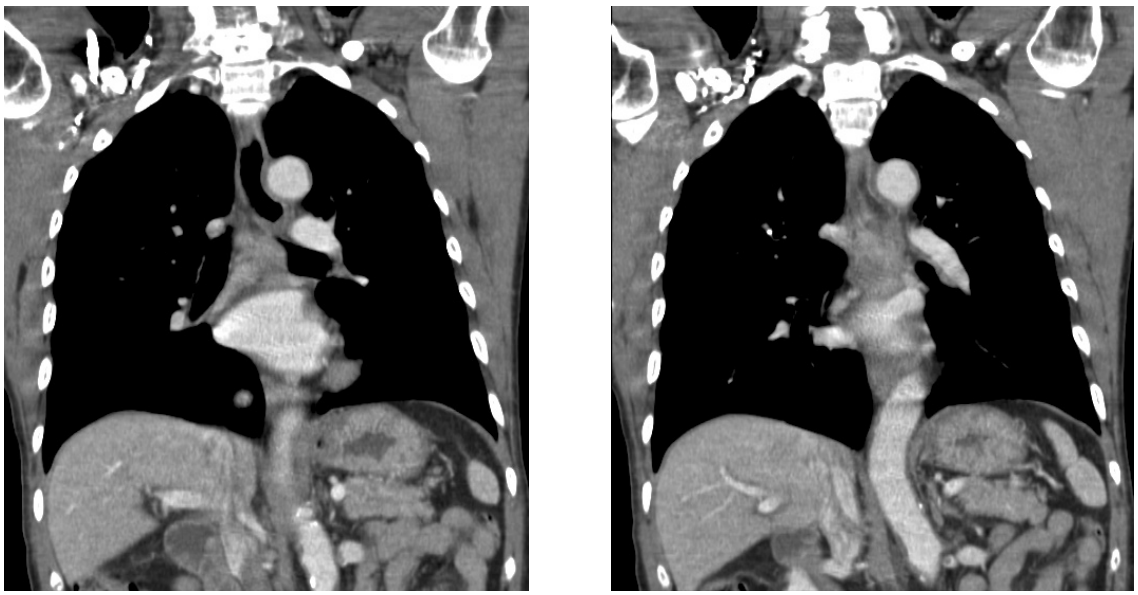
On examination, the patient was awake and appeared to be chronically ill. He had neither strange facial expressions nor involuntary movements of the body. His body temperature was 36.2^{o}C, pulse rate 68 beats per minute, respiratory rate 17 breaths per minute, and blood pressure was 118/70 mm Hg. His head, eye, ear, nose and throat examination disclosed normal findings. He had neither thyroid goiter nor palpable lymphadenopathies. His breathing sounds were symmetrical and clear to auscultation in all lung fields. His bowel sounds were normoactive to auscultation, and his abdomen was soft and non-tender to palpation in all 4 quadrants. He had no skin thickening on the fingers and hands, and had full muscle strength and normal deep tendon reflexes.

Esophagogastroduodenoscopy showed a pinhole esophageal stricture at 29 cm from the incisors, and the scope could not pass further (Figure 1A). The endoscopist therefore performed biopsy at the stricture site. The pathology study reported only squamous hyperplasia and focal capillary proliferation with stromal fibrosis. Chest CT scan disclosed marked wall thickening and a mass at the middle third of the esophagus, and enlarged lymph nodes at the anterior mediastinum, subcarina, and right pulmonary hilum (Figures 2A & 2B). The whole picture favored malignancy. The patient underwent EUS-FNA, but the study failed to obtain an adequate specimen (Figure 1B). As the chest CT scan showed enlarged subcarinal lymph nodes,



(A) (B)

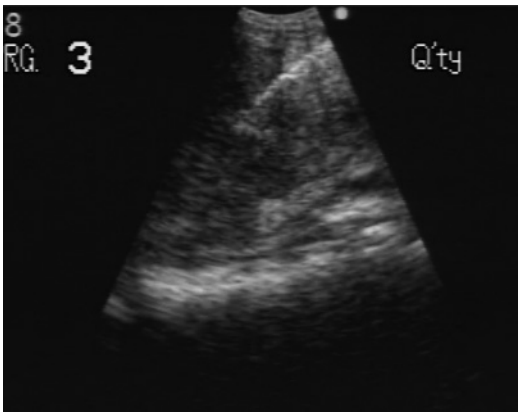
Fig. 1. Esophagogastroduodenoscopy (EGD) and endoscopic ultrasonography (EUS) images. (A) EGD showed a pinhole esophageal stricture at 29 cm from the incisors. Direct endoscopic biopsy at the stricture yielded no definite result. (B) EUS revealed a circumferential hypoechoic tumor with total-layer destruction; the maximal thickness of the tumor was 1.8 cm. Fine needle aspiration through the stricture into the tumor yielded an inadequate specimen.



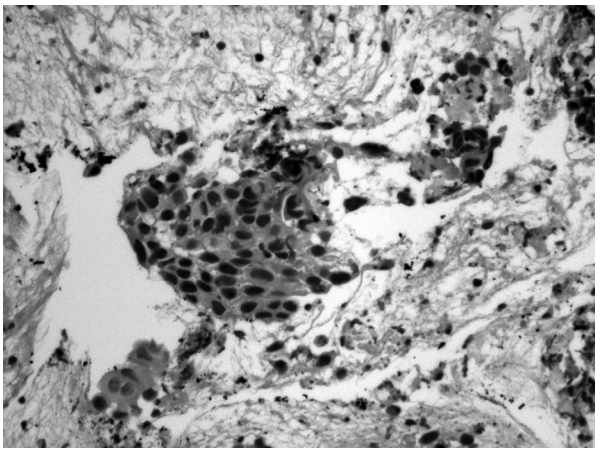
(A) (B)

Fig. 2. Chest computed tomography scan with contrast enhancement. (A) The coronal section through the carina showed enlarged subcarinal lymph nodes; (B) the coronal section through the posterior mediastinum disclosed a mass at the middle third of the esophagus.

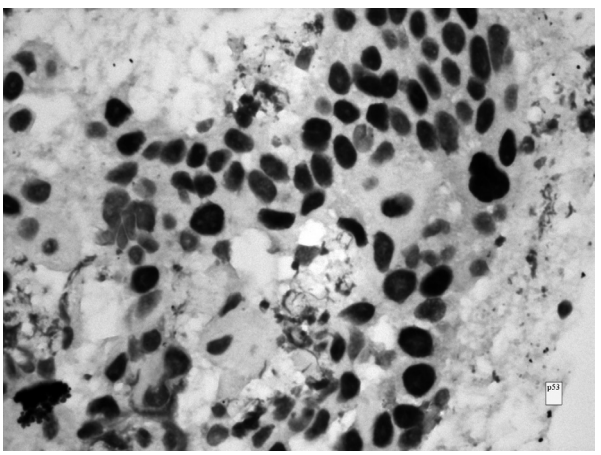
EBUS-TBNA was considered for tissue acquisition. The pulmonologist successfully sampled the subcarinal node with EBUS-TBNA (Figure 3A) and the pathology revealed squamous car-



(A)



(B)



(C)

Fig. 3. The pulmonologist successfully sampled the subcarinal node with endobronchial ultrasound-guided transbronchial needle aspiration (A) and the pathology revealed squamous carcinoma cells (B) with positive p53 staining (C). The diagnosis of esophageal cancer was established.

cinoma cells with positive p53 staining (Figures 3B & 3C). The diagnosis of esophageal cancer was established.

Discussion

The incidence of esophageal cancer is increasing [14]. Tissue diagnosis has been established traditionally by direct endoscopic biopsy [14]. Endoscopic ultrasonography helps with the management of esophageal cancer through its roles in diagnosis and staging [14-15]. It can accurately measure the extent of local and regional tumor growth [14], as seen in this case (Figure 1B). EUS-FNA can be used with mediastinal lesions undiagnosed by a previous conventional technique [15]. The subaortic, inferior mediastinal, and subcarinal spaces are acknowledged to be accessible with EUS-FNA [16-17]. In the present case, the tumor extended from below the middle third of the esophagus and encroached into the subcarinal space with enlarged lymph nodes, so it was surely a good candidate for tissue diagnosis by EUS-FNA after an unsuccessful endoscopic biopsy. Although EUS-FNA failed to yield an adequate tissue specimen in the end, this was not surprising because even in studies limited to lung cancer patients with abnormal mediastinal lymph nodes seen on CT scan, the sensitivity of EUS-

FNA reached only 90% [7].

The introduction of EBUS-TBNA allowed entry into the superior mediastinal, subcarinal, and hilar regions [16-17]. A prospective, crossover trial reached the conclusion that EBUS-TBNA surpasses mediastinoscopy in the sampling of paratracheal and subcarinal mediastinal adenopathy in patients with suspected non-small cell lung cancer [18]. Therefore, it has recently been incorporated into the algorithm for invasive staging in lung cancer [1]. A recent retrospective study also showed that EBUS-TBNA is a safe and minimally invasive approach for sampling mediastinal tissues of unknown etiology [4]. EBUS-TBNA was diagnostic (93.6%) for all disease categories (malignant 87.5%, benign 96.0%) and it altered the subsequent work-up or treatment plan in 80.0% of the study population (malignant 72.5%, benign 83.0%) [4]. It is noteworthy that esophageal cancer was not demonstrated in this study, and the authors commented that access to the posterior mediastinum along the esophagus was not feasible with EBUS-TBNA [4]. However, we believe that in selected patients, especially those whose tumors occur in the middle third of the esophagus with either direct invasion or bulky lymphadenopathies in the subcarinal area, EBUS-TBNA can be a complementary tool for tissue diagnosis of esophageal cancer. This area is not difficult to visualize since the subcarinal space can be reached by both techniques, as illustrated by our case. The successful use of EBUS-TBNA can spare the use of more invasive diagnostic procedures.

Conclusion

In the past 20 years, the development of EUS-FNA and EBUS-TBNA has offered accurate, safe alternatives for more invasive procedures in mediastinal sampling, and the list of applications is growing. The complementary role of each procedure in mediastinal nodal staging for lung cancer has been well documented. We believe that the value of this combined strategy in the diagnosis of other mediastinal abnormalities in carefully selected patients will be established in the near future.

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以支氣管內超音波導引經支氣管細針抽吸作爲診斷食道癌的輔助工具：案例報告

溫岳峯　何肇基

以食道內超音波導引細針抽吸和以支氣管內超音波導引經支氣管細針抽吸的技術在診斷攸關肺癌分期的縱隔腔淋巴結病變方面已經成為極有價值的工具。不過兩者都有其個別解剖位置的限制。同時結合這兩項技術於是成為診斷肺癌縱隔腔淋巴結病變的一個新的想法並且已經得到可靠的結果。然而這個策略對於診斷其他縱隔腔疾病的臨床影響目前仍不清楚。此處我們要提出一個案例報告，此案例的病人在嘗試過以直接內視鏡切片和食道內超音波導引細針抽吸的技術仍無法確診之後最終以支氣管內超音波導引經支氣管細針抽吸的技術建立食道癌的診斷。我們認為對於謹慎挑選的病人而言這可能提供了在採用更侵入性的診斷工具之前的一項替代選擇。*(胸腔醫學* ***2012; 27: 124-130)***

關鍵詞：食道內超音波導引細針抽吸，支氣管內超音波導引經支氣管細針抽吸，食道癌

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