Pulmonary *Mycobacterium avium* Complex (MAC)-Analysis of 124 Cases in a Medical Center in Taiwan

Chuang-Chou Tu, Gwan-Han Shen, Jeng-Yuan Hsu

One hundred twenty-four cases with positive sputum *Mycobacterium avium* complex (MAC) cultures at a medical center in Taiwan were reviewed retrospectively. Seventeen of the caases fulfilled the criteria of pulmonary MAC, according to the guidelines published in 1997 by the American Thoracic Society (ATS). These patients were analyzed on the basis of: (1) age and sex distribution; (2) underlying co-morbidity; (3) radiographic pattern and location of the lesions; (4) the hospital sections that the patients visited and the treatment rate in each section; and (5) treatment regimens, duration of therapy, and treatment results. The pulmonary MAC patients in this hospital were predominantly males.

Most of the patients in the male group were elderly and had underlying chronic lung disease or other systemic diseases, while those in the elderly female group denied any underlying lung or systemic disease. The cases of 2 elderly female patients reviewed for analysis revealed an atypical presentation of pulmonary MAC disease that fulfilled the criteria of "Lady Windermere's syndrome", which include: (1) middle or lingular lobes infiltrates; (2) no underlying lung disease or history of smoking; and (3) elderly women exclusively. The treatment rate of these patients was low, whether in the chest medicine or other sections, and the treatment outcome was poor. This result indicates that hospitals should pay much more attention to the education of doctors and patients regarding pulmonary MAC disease, in order to improve disease management and patient compliance. With a greater awareness of this disease, an earlier correct diagnosis can be achieved and proper therapy initiated. ***(Thorac Med 2006; 21: 133-140)***

Key words: *mycobacterium avium* complex

Introduction

Pulmonary *Mycobacterium avium* complex (MAC) disease is the most common non-tuberculous mycobacterial infection, and its incidence has been increasing. However, this disease is often ignored; pathogen is indistinguishable from traditional *M. tuberculosis* under microscopic examination, which increases the difficulty in diagnosis. In this report, we investigated the characteristics of pulmonary MAC disease in a hospital in Taiwan. The radiographic pictures of these patients were carefully reviewed, and the treatment rate in each section that the patients

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visited was analyzed and compared. We were also very interested in the treatment regimens used and the outcome.

Patients and Methods

Patients

The cases of 124 patients with a positive sputum culture for MAC were retrospectively reviewed between January 2001 and July 2003, at Taichung Veterans General Hospital. The symptoms, radiological changes, and sputum mycobacterium culture results of 17 patients (14 men, 3 women) fulfilled the criteria of pulmonary MAC disease that were proposed by the American Thoracic Society (ATS) in 1997 [1].

The following criteria apply to symptomatic patents with infiltrates, nodular or cavitary disease, or high resolution computed tomography scans showing multifocal bronchiectasis and/or multiple small nodules

A. If 3 sputum/bronchial wash results are available from the previous 12 months:

1. 3 positive cultures with negative AFB smear results or
2. 2 positive cultures and 1 positive AFB smear;

B. If only 1 bronchial wash is available:

1. a positive culture with a 2+, 3+, 4+ growth on solid media

C. If sputum/bronchial wash evaluations are non-diagnostic or another disease cannot be excluded:

1. transbronchial or lung biopsy yielding a MAC or
2. biopsy showing mycobacterial histopathologic features (granulomatous inflammation and/or AFB), and 1 or more sputum or bronchial washings that are positive for MAC, even in low numbers.

The 17 patients presented herein met the criteria symptomatically, and had typical chest radiographic changes and 3 positive sputum cultures for MAC.

Date analysis

We compared the differences in the chest radiography lesion locations between the male and female groups, and the differences in sputum conversion and chest radiography response between the treatment group and the non-treatment group. The chi-square method was used, and all analyses were performed with SPSS 10.0 for Windows software.

General data and co-morbidity

Age, sex, occupational exposure to dust, previous pulmonary diseases, and conditions that may have impaired immune defenses, e.g., diabetes mellitus, rheumatoid arthritis, lymphoma, leukemia, use of corticosteroids and/or immunosuppressive drugs, were recorded. In addition, chronic CNS disorders (old CVA, dementia, seizure, hypoxic encephalopathy), cardiovascular diseases (old MI, CAD s/p PTCA), and a post-gastrectomy history were all on the list of co-morbidities.

Radiography

The pre-treatment and subsequent radiographs and computed tomography were read by co-ordinating physicians, including 1 chest physician and 1 radiologist. The radiographic patterns were classified into 3 groups: fibrous/interstitial, cavitied, and nodular. The distributions of lesions were classified into the upper lung lobes, middle or lingular lobes, and diffused locations.

Treatment regimens, bacteriology and treatment results

The culture medium for Mycobacterium used in our hospital was the BACTEC MIGIT culture medium. We used the BD probeTEC system, following the manufacture's recommended procedures, to confirm the diagnosis of MAC infection. The treatment regimen data for each patient were collected from the medical records. Sputum conversion was defined as 3 consecutive negative sputum cultures within 6 months [2].

Results

Clinical demographic data

Of the 17 patients that fulfilled the diagnostic criteria, 14 (82.4%) were male, and 3 (17.6%) were female. Elderly patients (≥60 years-old) outnumbered younger patients, among both males and females. Ten (71%) males and 2 (67%) females were older than 60 years.

Of the total group, 14.2% of the males and 66.7% of the females were without underlying diseases (Table 1). The most common co-morbidity of the males was chronic lung disease, and the next most common was a past history of pulmonary tuberculosis. Only 1 woman had an underlying disease, which was a case of SLE with chronic steroid use.

Table 1. Age distribution and sex of patients with pulmonary MAC disease.

Age (years)	Male	Female	Total
30-39	1	1	2 (11.8%)
40-49	2	0	2 (11.8%)
50-59	1	0	1 (5.9%)
60-69	2	2	4 (23.5%)
70-79	6	0	6 (35.3%)
80-89	2	0	2 (11.8%)
Total	14 (82.4%)	3 (17.6%)	17

MAC, *Mycobacterium-avium complex*

Radiographic features

As for the radiographic evidence (Table 2), most male patients (50%) presented with fibrous interstitial patterns, and the remainder presented with cavitary (14.2%) and nodular (35.5%) patterns. Interestingly, the female patients showed pure (100%) nodular patterns. The most common distribution sites of lesions for the male patients were diffused locations (42.6%) and the upper lung fields (35.5%), and the least common sites were the middle or lingular lobes (21.3%).

The lesion location and distribution sites for the women, as revealed by chest radiography were all within the middle or lingular lobes (100%; p=0.01). The relationship between gender

Table 2. Co-morbidity of patients with pulmonary MAC disease.

Underlying disease	Male (n=14)	Female (n=3)
DM	1 (7.1%)	0 (0%)
Chronic lung disease	6 (42.6%)	0 (0%)
Malignancy	1 (7.1%)	0 (0%)
Chronic CNS disorder	2 (14.2%)	0 (0%)
Cardiac vascular disease	1 (7.1%)	0 (0%)
Immunocompromised or use of steroid	1 (7.1%)	1 (33.3%)
History of pulmonary TB with or without TX 6 months before admission	5 (35.5%)	0 (0%)
Post-gastrectomy	2 (14.2%)	0 (0%)
No underlying disease	2 (14.2%)	2 (66.6%)

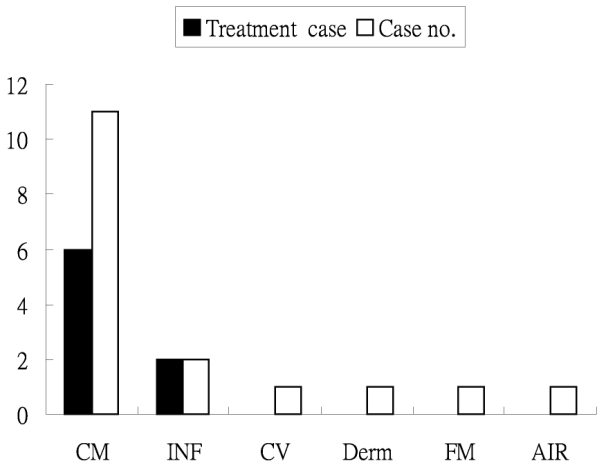

Fig. 1. The distribution of pulmonary MAC patients among the different sections and the treatment case number in each section.

and this disease will be discussed later in this report.

Treatment regimens and outcome

All the patients diagnosed with pulmonary MAC disease were classified according to the hospital sections that they visited (Figure 1). Eleven patients (65%) followed up at the chest medicine section, and 6 (54%) of them received treatment. Two patients (12%) visited the infection section initially, and all of them (100%) received anti-MAC therapy. There was only 1 patient each in the cardiovascular (6%), dermatology (6%), family medicine(6%), and rheumatology (6%) sections. None of the patients in these sections took anti-MAC medication. Eight patients (47%) received therapy (Table 3). The treatment regimen, as well as the treatment duration varied from patient to patient. One doctor (13%) treated the pulmonary MAC patients with traditional anti-tuberculosis regimens (INH, EMB, RIF, PZA) as soon as the initial sputum smear showed positive results for acid-fast stain, and continued the regimen even after the culture results revealed MAC infection. The other 7 doctors (87%) initiated therapy with traditional anti-mycobacterium medication plus klaricid or erythromycin. None of the 8 patients completed the whole course of therapy laid out in the ATS guidelines. Three of the the 8 patients (38%) showed bacteriologic conversion; the other 5 (62%) had persistent positive cultures for MAC.

As for the radiographic status, 2 patients (25%) showed a resolution of the lesion, 1 (12.5%) was in stable condition, and the other 5 (63%) revealed a progressive status in the radiographic pattern.

Nine patients (53%) received no treatment (Table 4). Of this group, only 1 patient (11%) showed bacteriologic conversion; the other 8 (89%) showed none. Radiologically, 1 patient (11%) showed improvement, 3 (3%) were in stable condition, and the other 5 (56%) showed progressive disease. There was no obvious difference in the bacteriological conversion (p= 0.081) and radiological response (p=0.132) between the treatment and no treatment groups.

Table 3. Radiographic findings of patients with pulmonary MAC disease.

		Male (n=14)	Female (n=3)
Pattern	Fibrous/interstitial	7 (50%)	0 (0%)
	Cavity	2 (14.2%)	0 (0%)
	Nodular	5 (35.5%)	3 (100%)
Distribution	Upper lung lobes	5 (35.5%)	0 (0%)
	Middle or lingular lobe	3 (21.3%)	3 (100%)
	Diffused	6 (42.6%)	0 (0%)

Table 4. Bacteriological results and radiographic status in 8 patients with several combinations of chemotherapy.

Patient	Regimens	TX duration	Results				
			Bacteriological conversion		Radiographic status		
			Yes	No	Improved	stable	Progression
1	RF+EM+Kla	1 year	V		V		
2	INH+EM++RF+Kla	4 months	V		V		
3	RF+EM+Ofl+Kla	10 months		V			V
4	RF+INH+PZA+EM	1 year	V			V	
5	RF+EM+Ery	1 month		V			V
6	RF+EM+PZA+Kla	4 month		V			V
7	Ofl+Kla	1 month		V			V
8	EM+Sin+Kla	1 month		V			V
Total: 8			3 (38%)	5 (62%)	2 (25%)	1(13%)	5(63%)

RF: Rifampin; EM: Embutamol; INH: Isonizid; Kla: Klaricid; Ofl: Ofloxacin; Sin: Sinflo

Discussion

Those patients that were diagnosed with pulmonary MAC disease in the hospital under study were predominately males. A review of the literature has revealed no definite evidence of sexual predominance for this disease, so this characteristic may be due to the fact that this hospital is a veterans' hospital. As for the distribution of age, most of the patients in the male and female groups were older than 60 years. In comparing the elderly male and female patients, it was interesting to find that almost all the male patients had underlying lung diseases, such as chronic obstructive lung disease, bronchiectasis, and pneumoconiosis, and a pulmonary tuberculosis history, while the elderly female patients did not . It seems reasonable that patients with chronic lung disease could suffer from poor sputum expectoration, to some extent, due to destroyed lung anatomy. This condition might lead to chronic inflammation and predispose the patients to MAC infection.

When reviewing the radiographic patterns of the patients, and classifying them according to the pattern and distribution of the lesions, most of the male patients showed a fibrous interstitial pattern with a diffused distribution. In contrast to the male patients, we found that the radiographic pattern and distribution of lesions in the female group were purely nodular; the involved fields were limited to the middle or lingular lobes. The symptoms of these elderly female patients fulfilled the criteria of "Lady Windermere's syndrome"[3].

The term "Lady Windermere's syndrome" was first used in 1992 to describe a symptom complex of elderly women without preexisting lung disease, who developed MAC pulmonary infection limited to the middle lobe or lingual [4-5]. The middle lobe and lingula have long, narrow, dependent bronchi and an absence of collateral ventilation that predisposes them to inflammation [6]. Since women are more likely to regard expectoration as socially unacceptable behavior, their voluntary cough suppression leads to an inability to clear secretions, which results in a chronic nidus for inflammation that favors subsequent infection by MAC. Two elderly female

pulmonary MAC patients in this study had the typical presentations of Lady Windermere's syndrome, and the chest CT scan proved the infiltrates in the middle or lingular lobe to be bronchiectasis. A greater awareness of the syndrome by clinicians should provide an earlier diagnosis and initiation of therapy.

As we classified all the patients according to the hospital they visited initially, it was surprising to find that only about 55% of patients in the chest medicine section had received therapy, and that none of the patients in sections other than the chest and infection sections received therapy. The reasons why most of the doctors in the chest medicine and other sections did not initiate therapy requires further investigation. The revelation of so many patients (53%) who did not receive correct treatment and who saw their disease eventually progress, reminded us how important it is to educate doctors regarding pulmonary MAC disease.

When we reviewed the treatment regimens and treatment duration, as shown in Table 3, we found there was great deviation in the choice of drugs and treatment duration from patient to patient. Historically, the medical treatment of MAC infectious disease in HIV-negative patients has been disappointing. Before the introduction of macrolides in the 1990s, multi-drug regimens, including isonized, rifampine, ethambutol, and streptomycin had been recommended. The long-term success rate was less than 50%, mainly due to treatment failure and relapse [7-9]. The newer macrolides, clarithromycin and azithromycin, have shown excellent in vitro and clinical results in recent studies. For the treatment of adults without HIV infection, the ATS recommends a regimen of clarithromycin or azithromycin, rifampin or rifabutin, and ethambutol, to be taken daily. This therapy must continue for at least 12 months after sputum conversion. Streptomycin should also be considered, especially for patients who have radiographically extensive or cavitary disease, and particularly when this is accompanied by strongly positive sputum smears [1]. However, it was surprising to find that none of the patients reviewed had undergone an adequate duration of treatment , as set forth by the ATS guidelines.

Thelower bacteriological conversion rate and high incidence of radiographic status progression in this hospital could be due to incorrect treatment and an inadequate treatment duration.

Table 5. Bacteriological results and radiographic status in 9 patients without treatment

Patient	Results				
	Bacteriological conversion		Radiographic status		
	Yes	No	Improved	stable	Progression
1		V			V
2		V		V	
3		V		V	
4		V			V
5		V			V
6	V		V		
7		V		V	
8		V			V
9		V			V
Total: 9	1 (11%)	8 (89%)	1 (11%)	3 (33%)	5 (56%)

There were 9 patients in the no-treatment group (Table 5). One patient was accidentally found to have shown sputum conversion and improvement in the chest lesions. This finding of sputum conversion could be due to a false negative result in the sputum microbiology or a laboratory error. And the initial chest film presentation could be the result of MAC infection with a bacterial co-infection. That the follow-up chest film showed improvement may be the result of a remission of the bacterial infection. However, the above are only hypotheses. If we had had a longer observation period for this patient, we might have found the answer.

In conclusion, most of the pulmonary MAC patients in this hospital were males. The elderly were predominant among both male and female patients. Most of the elderly male patients had underlying lung disease, while all the elderly female patients fulfilled the criteria of Lady Windermere's syndrome, with middle or lingular lobe involvement. The treatment rate was low, both in the chest medicine and other sections, and the treatment outcome was poor. A greater awareness of the diagnostic criteria and treatment of this disease may lead to a prompt diagnosis and better outcome.

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肺部鳥型分枝桿菌感染—台灣一醫學中心之病例分析

涂川洲　沈光漢　許正園

我們以回朔的方式，回顧124位痰液培養為鳥型分枝桿菌的病人，發現其中有17位病人符合1997年美國胸腔醫學會診斷肺部鳥型分枝桿菌感染之條件。我們將這17位病患依照年齡及性別之分佈、本身原來之疾病、肺部X光之型態及分佈、病患看診之科別及各科治療率、治療之藥物及治療療程和結果來做分析。結果發現本院之病患大部份為男性，且大部份為老年有肺部或全身性之疾病之病人，而老年女性病患則無其它疾病且符合“Lady Windermere”症候群之診斷要件。在本院不管是胸腔科或其他科別對於此疾病之治療律都偏低且預後都不佳。所以，我們要注意來教育醫師及病患有關肺部鳥型分枝桿菌感染之知識，以增加此病之治癒率及病患之治療耐受性。及早查覺此疾病，就可及早得到正確之診斷和治療。*(胸腔醫學* ***2006; 21: 133-140)***

關鍵詞：肺部鳥型分枝桿菌疾病

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Use of 18-Fluorodeoxyglucose-Positron Emission Tomography in Differentiating between Malignant and Benign Pulmonary Diseases in a Region with a High Incidence Rate of Tuberculosis

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Study objective: To evaluate the accuracy of 18-fluorodeoxyglucose- positron emission tomography/computed tomography (FDG-PET/CT) in the diagnosis of pulmonary diseases in a region with a high incidence rate of tuberculosis.

Materials and Methods: Data on patients with newly found intrathoracic lesions on FDG-PET examination were screened from our PET scan database. A total of 81 patients with a definitive diagnosis were included in this retrospective study.

Results: Seventy of 81 patients had histopathological and/or microbiological proof of the final diagnosis. Thirty-six patients proved to have malignancy, and 45 had other benign diseases. The mean maximal standardized uptake value (SUV) was significantly higher in the group with malignant disease compared with the group with benign disease ($p < 0.05$). However, there was no statistical difference between the mean maximal SUVs of benign granulomatous disease and those of malignant disease ($p > 0.05$). If a maximal SUV > 2.5 was used as the cut-off value for malignant disease, the sensitivity was 97%, the specificity was 27%, the positive predictive value was 51%, and the negative predictive value was 92%.

Conclusion: In geographic regions with a high incidence rate of granulomatous diseases, positive FDG PET results should be interpreted with caution in differentiating benign from malignant pulmonary abnormalities. ***(Thorac Med 2006; 21: 141-148)***

Key words: 18-fluorodeoxyglucose-positron emission tomography, lung cancer, granulomatous disease

Introduction

Several studies have addressed the diagnostic accuracy of F-18 fluorodeoxyglucose positron emission tomography (FDG-PET) for identifying malignant focal pulmonary lesions. Reports have shown a high sensitivity (88%-100%) and various specificity rates (40%-100%) for the evaluation of malignancy in patients presenting with new lung findings [1-16]. However, a significant degree of overlap is known to exist between the uptake values of benign and malignant lesions [17]. One study reported on 10 patients with histopathologically-proven tuberculoma, of

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whom 9 had increased FDG uptake on PET scans [18]. In tuberculosis-endemic areas, an increase of 18F-FDG uptake in pulmonary lesions may lead to misdiagnoses of malignancies in patients with benign diseases. The purpose of this study was to evaluate the accuracy of FDG-PET/CT in the diagnosis of pulmonary diseases in a region with a high incidence rate of tuberculosis.

Materials and Methods

From March 2001 to October 2004, data on a total of 10,826 patients were screened from our PET scan database. Patients with abnormal intrathoracic lesions on the PET scan were reviewed, and only those patients with definitive diagnoses were included in this study. If histopathology was not obtained, the diagnosis of a benign condition was established if follow-up imaging demonstrated lesion regression or lesion stability for a minimum of 12 months. Patients with known prior malignant diseases or with evidence of metastatic disease were not included in this study. A total of 81 patients (49 men, 31 women; mean age, 56 years; range, 29-79 years) were enrolled in this retrospective study.

The FDG-PET scans were performed with a Siemens ECAT EXACT HR+, model 962 (Knoxville, TN), or a GE discovery LS PET/CT hybrid scanner. Patients were required to fast for at least 8 h before the PET scan, and were instructed to be well hydrated and to avoid strenuous work or exercise for 24 h before the scan. They were scanned in as many sequential images as necessary to include the entire head, thorax, abdomen, and pelvis. After intravenous administration of 370 MBq (10 mCi) of FDG, emission images were acquired for 5 min per bed position. The uptake period between FDG injection and the beginning of the emission scan was 60 ± 10 min. The images were reconstructed and re-sliced into coronal, transaxial, and sagittal projections. The maximal standardized uptake values (SUVs) were measured in all patients. If the patient presented with multiple nodules, the SUV was measured from the dominant lesion identified on CT. We defined SUV > 2.5 as the cut-off value for a diagnosis of probable malignancy.

Statistical analysis was carried out for the patient group by computing the mean and standard deviation. Statistical differences were analyzed using the independent sample Student's *t*-test. The level of significance was set as $p < 0.05$.

Results

Of 81 patients, 70 had histopathological and/or microbiological proof for a definitive diagnosis. Eleven of 81 patients were diagnosed as having benign diseases by follow-up imaging demonstrating lesion regression or lesion stability for a minimum of 12 months. Of 81 enrolled patients, 36 were diagnosed with malignancy, and 45 had other benign diseases (Tables 1 and 2). The mean maximal SUVs of the benign and malignant diseases were significantly different ($p = 0.01$), and are presented in Figure 1. When we further divided the benign diseases into granulomatous and non-granulomatous disease groups, there was still a significant difference between the SUVs of the non-granulomatous diseases and malignant diseases ($p = 0.000$). However, the mean maximal SUVs between the granulomatous diseases and malignant diseases were not statistically different ($p = 0.20$). In addition, the range of the standard deviation of the mean maximal SUV in the granulomatous diseases was much wider than that of the non-granulomatous and malignant pulmonary

Table 1. Summary of Malignant Diseases (n=36)

Small cell lung cancer	2
Non-small cell lung cancer	33
Adenocarcinoma	21
Squamous cell carcinoma	8
Bronchioalveolar cell carcinoma	3
Poorly differential carcinoma	1
Lymphoma	1

Table 2. Summary of Benign Diseases (n=45)

Tuberculosis/tuberculoma	23
Mycobacterium avium complex	1
Mediastinal lymphadenopathy*	7
Bacterial pneumonia	3
Sarcoidosis	3
Organizing pneumonia	1
Pulmonary sequestration	1
Inflammatory pseudotumor	1
Anthrasilicosis	1
Benign pulmonary nodule*	4

* diagnosed by follow-up imaging

diseases.

There were 33 false positive results and 1 false negative result in our series. Of the 33 false positives, 22 were caused by granulomatous diseases (tuberculosis = 19, sarcoidosis = 3) (Table 3). The 1 false negative finding was seen in a patient with squamous cell carcinoma.

If a maximal SUV > 2.5 was used as the cut-off value for malignant disease, the sensitivity was 97%; the specificity was 27%; the positive predictive value was 51%; and the negative predictive value was 92%. The overall diagnostic accuracy was 58%.

Discussion

Several studies have addressed the diagnostic accuracy of F18 FDG-PET for identifying malignant focal pulmonary lesions. Reports have shown a high sensitivity (88%-100%) and various specificity levels (40%-100%) for the evaluation

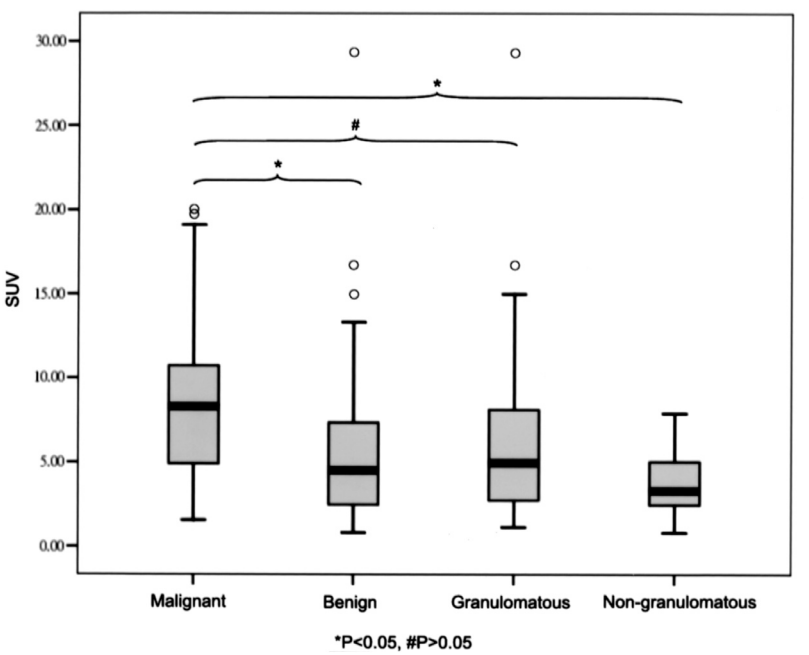

Fig. 1. Maximal SUV in benign and malignant diseases

Table 3. Benign Lung Lesions with Maximal SUV > 2.5

Patient No.	Sex	Age	Diagnosis	Maximal SUV
1	M	29	TB	7.6
2	M	65	TB	5
3	M	47	TB	2.62
4	F	39	TB	29.31
5	M	72	TB	19.1
6	M	18	TB	5.8
7	M	62	TB	8
8	M	71	TB	3.65
9	F	57	TB	10.28
10	M	47	TB	4.5
11	F	54	TB	13
12	M	45	TB	2.85
13	M	75	TB	7.49
14	M	75	TB	8.22
15	F	70	TB	4.69
16	M	68	TB	6.2
17	F	77	TB	4.9
18	F	26	TB	3.6
19	M	39	TB	3.47
20	M	39	Sarcoidosis	15
21	M	51	Sarcoidosis	13.3
22	F	49	Sarcoidosis	7.34
23	M	54	Benign LAP *	4.6
24	F	47	Benign LAP *	3.3
25	F	62	Benign LAP *	3.26
26	M	65	Benign LAP *	4.27
27	F	74	Benign LAP *	5.03
28	M	56	Benign LAP*	2.91
29	M	50	Organizing pneumonia	6
30	M	47	Pulmonary sequestration	4.1
31	M	73	Inflammatory pseudotumor	6.19
32	M	57	Anthrasilicosis	7.9
33	M	43	Pneumonia	5.95

LAP = lymphadenopathy, TB = tuberculosis

* diagnosed by follow-up imaging

of malignancy in patients presenting with new lung lesions [1-16]. In our series, the sensitivity (97%) of FDG-PET for identifying lung lesions as benign or malignant was similar to previously published reports. However, the specificity (24%) was distinctly lower than that found in previously published reports.

Increased FDG activity has been observed in a variety of benign pulmonary diseases [17]. These include infectious diseases such as lung

abscess, Mycobacterium avium intracellulare, bacterial pneumonia, tuberculosis, actinomycosis, histoplasmosis, blastomycosis, aspergillosis and cryptococcosis. Some inflammatory diseases, such as anthrasilicosis, sarcoidosis, Wegener's granulomatosis, rheumatoid nodule, inflammatory pseudotumor, and radiation pneumonitis, and benign neoplasms such as carcinoid tumor, harmatoma, schwannoma, neurofibroma, fibrous mesothelioma, chondrosarcoma, and chondroharmatoma can also exhibit increased FDG activity.

In 1 study, FDG-PET was used in differentiating non-small cell lung cancer from benign solitary pulmonary nodules in a region with a high endemic rate of histoplasmosis [9]. In detecting malignant solitary pulmonary nodules, FDG-PET imaging had a sensitivity of 93% and a specificity of 40%. They concluded that in a region with a high prevalence of pulmonary fungal infection, FDG-PET is sensitive, but has a low specificity for identifying NSCLC. In a report on 10 patients with histopathologicallyproven tuberculoma, 9 of which had increased FDG uptake on PET scans, the researchers concluded that in a tuberculosis-endemic area, an increase of 18F-FDG uptake in pulmonary lesions may lead to misdiagnoses of malignancies in patients with benign diseases. [18]

Thirty-three of the 45 patients with benign disease in our study had false positive findings. All of the false positives were the result of active inflammatory or infectious diseases, including 22 granulomatous diseases (19 tuberculosis and 3 sarcoidosis), and 11 other benign pulmonary diseases. The false positive rates of granulomatous and non-granulomatous diseases (including 6 patients with benign hilar or mediastinal lymphadenopathy) were 81.5% and 61%, respectively. In addition, the mean maximal SUVs between granulomatous and malignant diseases showed no statistical difference. The range of the standard deviation of the mean maximal SUV in granulomatous diseases was also much wider than in non-granulomatous and malignant pulmonary diseases. This result suggests that granulomatous diseases may have a very wide range of 18F-FDG uptake, which creates difficulty in their differentiation from malignant diseases.

Several factors may have decreased the specificity rate of this study. The first is the incidence rate of tuberculosis in Taiwan. In our study, 19 of 23 (82.6%) patients with active tuberculosis showed positive results on FDG-PET imaging. According to data published by the Center of Disease Control in Taiwan in 2004, the incident rate of tuberculosis in the Taiwanese population was 74.6 per 100,000 in 2002. Most of the published articles evaluating the use of the PET scan in differentiating benign and malignant pulmonary diseases were published from developed countries, such as Japan, the United States, Canada, and Europe. The incidence rates of tuberculosis in these countries are much lower than in Taiwan, and range from 5 to 36 per 100,000. In addition, 6 patients in our study were diagnosed as having benign mediastinal or hilar lymphadenopathy by follow-up imaging. Considering the higher incidence rate of tuberculosis infection in Taiwan, we surmise that some of these benign diseases may have been caused by latent TB infection. The second factor is bias in the selection of patients. First, most of the previously published articles focused on radiographically indeterminate pulmonary lesions. However, our study was a retrospective study. Some of the patients' definitive diagnoses could have been made by radiographic imaging and microbiological study, and might not have required FDG-PET imaging. Secondly, some of the patients with high SUV pulmonary lesions, which were suspec-

ted to be a malignant pulmonary disease, were not included in this study because they did not undergo histopathologic study.

Previous reports have documented that some primary lung tumors may have false-negative results on FDG-PET scanning. One study identified 20 false negative cases in 3,912 patients with a pulmonary abnormality suspicious for lung cancer [19]. Tumor histology included adenocarcinoma, bronchioalveolar cell carcinoma, carcinoid, squamous cell carcinoma, unspecified non-small cell lung cancer, and sarcomatoid neoplasm. All of the 3 histopathologicallyproven bronchioalveolar cell carcinomas in our study were correctly detected by FDG-PET. Their maximal SUVs were 5.50, 3.57 and 6.43, respectively. Only 1 false-negative case was found in our study, which was a small squamous cell carcinoma (size = 1.48 cm, SUV = 1.56), a stage Ia disease that was proved by subsequent surgical resection. The false negative result may be explained by grading and the small size of the tumor. Several studies have demonstrated that the intensity of FDG uptake of the primary tumor is highly correlated with survival [20-23]. Survival has been consistently found to be better among patients with less metabolically active tumors, when the patients are dichotomized using a threshold SUV value. Size was reported in some studies to be a factor responsible for false negative indications in tumors smaller than 1.2 cm [16]. However, another study showed that the sensitivity and specificity of PET were not statistically different when comparing nodules > 1.5 cm in size with nodules 0.7 to 1.5 cm in size [24]. In conclusion, FDG-PET imaging is a very sensitive modality for the detection of malignant pulmonary lesions. It is, however, limited by its low specificity. Our results suggest that in geographic regions with a high incidence rate of tuberculous infection, positive FDG PET results should be interpreted with caution in differentiating benign from malignant pulmonary abnormalities.

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於結核病盛行地區利用 18-FDG PET 分辨良性與惡性胸腔病變之應用

林鎮均　高尚志　林嘉謨

目的：評估於結核病盛行地區利用 FDG-PET/CT 診斷胸腔疾病之準確性。

方法：本篇為一回溯性研究，我們整理了 PET 資料庫中胸腔有異常顯影之病例，將有確定診斷之病例列入此研究，一共蒐集了 81 位。

結果：所有 81 例病例中，有 70 位病例是經由病理學或微生物學來確定其最後診斷，其中 36 例為惡性病變，34 例為良性病變。另有 11 例病例則是臨床追蹤至少一年顯示無明顯變化，最後被歸類為良性病變。分析結果發現惡性病變之 maximal SUV 值明顯高於良性病變 ($p < 0.05$)，但惡性病變與肉芽腫性良性病變之 maximal SUV 則沒有統計學上差異 ($p > 0.05$)。若以 maximal SUV > 2.5 當作認定惡性病變之臨界值時我們所得到之敏感度，特異度，陽性預估值及陰性預估值分別為 97% ， 27% ， 51% 以及 92% 。

結論：在結核病盛行地區，以 PET 異常顯影來分辨良性與惡性胸腔病變是一不可靠之方法。*(胸腔醫學* ***2006; 21: 141-148)***

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Analysis of Transbronchial Lung Biopsy in Localized Lung Lesion, Results in 141 Patients

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Background: This study was designed to analyze the diagnostic accuracy and complication rate of transbronchial lung biopsy (TBLB), and to study the factors (lesion size, location, age, sex, complications) influencing diagnostic results.

Methods: We prospectively studied 141 patients with a lung nodule or mass present on the chest roentgenogram, and no visible endobronchial lesions. To evaluate the safety and diagnostic yield of TBLB, we calculated the diagnostic accuracy and complication rate. Lesion size, biopsy location, age, sex, and complications were also analyzed for their influence on the diagnostic yield.

Results: We evaluated the complications associated with TBLB, the diagnostic yield of the procedure, and the correlation between age, sex, lesion size, biopsy site complication, and diagnosis. Complications associated with these procedures included the following: 10 (7.1%) patients with pneumothorax, with 2 patients requiring tubal thoracostomy in their management, and 40 (28.4%) patients with bronchial hemorrhage. The overall complication rate was 35.5%, but no patients expired from these complications. There was no statistical significance between age (p = 0.39), sex (p = 0.89), lesion size (p = 0.412), complications (p = 0.251 for pneumothorax, p = 0.146 for bleeding), and diagnosis. Biopsy from the left upper lobe had a greater diagnostic yield than biopsy from the other sites, with statistical significance (p = 0.041). Biopsy from the left lower lobe had a lower diagnostic yield. Of the 141 patients, 52 patients were diagnosed from TBLB. The overall diagnostic rate was 36.9%.

Conclusion: The results of this study suggest that TBLB is a safe procedure in every age group and with variable lesion patterns. However, the diagnostic rate is low. ***(Thorac Med 2006; 21: 149-156)***

Key words: bronchoscope, transbronchial lung biopsy, pneumothorax

Introduction

Open-lung biopsy is a well-established method for the direct sampling of lung tissue, with a relatively high sensitivity and specificity for the diagnosis of underlying lung disease [1, 4]. The

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procedure is usually performed in the operation room under general anesthesia, but incurs too much suffering to be accepted by patients. The development of bronchoscopy for the sampling of distal airway secretions (e.g., bronchoalveolar lavage, bronchial brushing) has greatly facilitated our ability to establish a specific diagnosis in many such patients, without the need for surgical intervention [5-6]. However, some patients will still require lung tissue examination to establish a specific diagnosis, usually after inconclusive results have been obtained from these less invasive methods.

As an initial diagnostic procedure for patients with diffuse parenchymal disease or localized densities beyond direct bronchoscopic vision, TBLB offers an attractive alternative to open lung biopsy. Unlike bronchoscopy, TBLB, guided by the chest roentgenogram, can easily obtain a lesion biopsy using forceps. This procedure must be performed by an experienced bronchoscopist, and has a better diagnostic yield and fewer complications. Some anatomical difficulties are encountered during transbronchial lung biopsy through a flexible bronchoscope: the branching angles of some subsegmental bronchi from their mother bronchi are large, and the differences in branching angles during respiration may also be large [7], making insertion of the forceps difficult.

Complications, such as pneumothorax and bleeding after transbronchial lung biopsy, may frequently occur, especially in those patients whose chest roentgenograms show diffuse interstitial infiltration. For this study, we hypothesized that the complication rate may be decreased in those patients whose chest roentgenograms show a lung mass or nodule.

Patients and Methods

This study reports on cases that developed at Chang Gung Memorial Hospital, a 2500-bed medical center in Kaohsiung, a large urban center located in southern Taiwan. One hundred and forty-one consecutive patients with peripheral pulmonary lesions, who underwent fiberoptic bronchoscopy with TBLB between November 1998 and June 2003, were prospectively evaluated. Chest roentgenograms and CT were performed with all patients to assist in guiding the TBLB to the target lesion. General exclusion criteria for the performance of TBLB included the following: the presence of an uncorrectable bleeding diathesis (e.g., platelet count of $< 50 \times 10^3$ thrombocytes/mm sup 3); inability to adequately oxygenate the patient during bronchoscopy (i.e., arterial oxygen saturation of < 90%); hemodynamic instability (mean arterial pressure [MAP] of < 60 mm Hg); and a clinical suspicion of the presence of severe pulmonary hypertension. Cases in which a visible endobronchial lesion could be seen in the broncoscopic image were also excluded from our study.

One bronchoscopist, with over 10 years of training and experience in bronchoscopy, performed all TBLB procedures. Each patient was premedicated using 0.5 mg atropine sulfates. Local anesthesia of the upper respiratory airway tract was achieved using 2% lidocaine via nasal spraying, without administration of parenteral general sedation. The flexible bronchoscope was inserted into the target bronchus as deep as possible under direct vision. The forceps were inserted through a bronchoscope as distally as possible, and then were withdrawn 1 cm and the biopsy was performed. Five pieces of tissue speci-men were biopsied from each patient. All biopsies were placed in formalin, with some placed in saline for culture, at the discretion of the operator. Biopsies for culture were transported to the

microbiology laboratory and were processed for bacterial, mycobacterial, fungal, and/or viral cultures. The locating of the target bronchus was guided by chest CT. If the pathologic findings were negative, other diagnostic methods, such as open-lung biopsy, CT-guided biopsy or repeated TBLB, were suggested to patients if their general condition could tolerate the procedures.

Data collection

The following was documented in every patient with a peripheral pulmonary lesion: lesion size, location of biopsy, age, sex, complications, pathologic diagnosis, and final diagnosis. Lesion size included 2 patterns: nodule and mass. A nodular lesion was a lesion with a long axis of less than 3 cm, assured by chest CT, and a mass lesion was a lesion with a long axis of more than 3 cm. The location for biopsy was confirmed and adjusted by chest CT scan; the patient's age and sex were also collected for analysis. Complications such as pneumothorax and bleeding were documented during and after the procedure. A chest roentgenogram was taken routinely, within 1 hour after the procedure. We calculated the diagnosis and complication rate, and evaluated the correlation between complication, age, sex, biopsy site, lesion size, and diagnostic yield.

Statistical Analysis

Univariate analysis by means of the Student's *t* test was used to evaluate demographic variables and complications between groups. Chi-square analysis was used to compare categorical variables. All p values were 2-tailed, and $p < 0.05$ was considered statistically significant.

Results

During this study period, a lung mass or nodule detected in each of 141 patients (83 males, 58 females) underwent TBLB by the same bronchoscopist. In terms of the lung lesion pattern, 93 cases were defined as a mass, and 48 were defined as a nodule. Twenty-four cases were biopsied from the right upper lobe (RUL), 34 from the left upper lobe (LUL), 19 from the right middle lobe (RML), 41 from the right lower lobe (RLL), and 23 from the left lower lobe (LLL).

There were no procedure-related deaths, episodes of sepsis, clinically important arrhythmias, or pneumonia. Specific complications attributed to TBLB were pneumothorax and bleeding; 10 patients developed pneumothorax, and 2 required thoracotomy tube emplacement. The others were managed with supportive treatment only, without tubal thoracostomy. All cases of pneumothorax were noted immediately after the TBLB procedure.

Bleeding complications were resolved with bronchoscopic tamponade or with the instillation of epinephrine. No patient developed hypotension (mean artery pressure < 60 mm Hg) or clinically important oxygen desaturation (arterial oxygen saturation of < 90%) in association with their bronchial hemorrhage. Four patients were complicated with pneumothorax and bleeding. The complication rate was 35.5%; 7% was pneumothorax and 28.2% was bleeding.

The major diagnoses in this study were lung cancer and pulmonary tuberculosis. Of the 34 lung cancer cases, 13 were diagnosed as adenocarcinoma, 3 as bronchoalveolar carcinoma, 6 as squamous cell carcinoma, and 1 as small cell lung cancer. There were 11 cases of non-small cell lung cancer, which could not be differentiated into adenocarcinoma or squamous cell carcinoma. Sixteen patients were diagnosed with pulmonary tuberculosis, 2 with interstitial fibrosis, 1 with cryptococosis, and 1 with metastatic

transitional cell carcinoma. In those with an inadequate tissue amount, but still an abnormal pathological finding, 37 cases were diagnosed as chronic inflammation and 4 as atypical cells; 46 cases had negative findings. The overall diagnostic rate was 36.9% (chronic inflammation, atypical cells, and interstitial fibrosis [do not be enrolled in true diagnoses—were not considered true diagnoses?]-this is not clear) (Table 1).

For initial diagnoses such as chronic inflammation, atypical cells, or negative findings, further diagnostic procedures, such as open lung biopsy, CT-guided biopsy or repeated TBLB, were encouraged, if the patient could tolerate the procedure. For the final diagnosis of chronic inflammation, 10 cases were found to be pulmonary tuberculosis, 14 were lung cancer, 2 were organizing pneumonia, and 1 case was lymphoma. Ten patients did not undergo further procedures due to patient hesitation. For those with an initial diagnosis of atypical cells, 3 patients were diagnosed as adenocarcinoma, and 1 patient died before further procedures could be initiated. In those cases diagnosed as negative findings initially, 13 turned out to be lung cancer, 8 were tuberculosis, 5 were organizing pneumonia, 2 were cryptococosis, 2 were diagnosed as actinomycosis, and 16 cases did not undergo further procedures due to patient hesitation and being lost to follow-up (Table 2).

Table 1. Overall diagnosis of transbronchial lung biopsy

Diagnosis	Number
Lung cancer	34
Adenocarcinoma	13
Bronchioalveolar carcinoma	3
Squamous cell carcinoma	6
Small cell carcinoma	1
Nonsmall cell carcinoma	11
Tuberculosis	16
Metastatic transitional cell carcinoma	1
Cryptococcosis	1
Chronic inflammation	37
Atypical cells	4
Interstitial fibrosis	2
Negative	46
Overall diagnostic rate = 36.9%	

Table 2. Final diagnosis of those with the initial pathological findings of chronic inflammation, atypical cells, and negative findings

Initial diagnosis	Final diagnosis	Number
Chronic inflammation	Lung cancer	14
	Tuberculosis	10
	Organizing pneumonia	2
	Malignant lymphoma	1
	Negative	10
Atypical cells	Lung cancer	3
	Negative	1
Negative findings	Lung cancer	13
	Tuberculosis	8
	Organizing pneumonia	5
	Cryptococosis	2
	Actinomycosis	2
	Negative	16

Statistical analysis revealed that the diagnosis was not correlated to age ($p = 0.39$), sex ($p = 0.89$), lesion size ($p = 0.412$), or complications ($p = 0.251$ in pneumothorax and $p = 0.146$ in bleeding). The rate of diagnosis from biopsies from the left upper lobe was statistically significant compared with biopsies from other sites ($p = 0.041$), and the left lower lobe was the site of least diagnosis (Table 3).

Discussion

This study evaluated the safety and diagnostic value of TBLB performed on patients of every age group and with variable patterns of lung lesion. There were no procedure-related deaths and life-threatening complications. Patients with

Table 3. Univariate analysis of transbronchial lung biopsy based on the diagnostic yield

Factor	Diagnostic rate		OR (95%C.I.)	P-value[1]
	Yes=52	No=89		
Age	58.1 ± 13.2	62.2 ± 13.6		0.136
Sex Female	21 (40.4%)	37 (41.6%)	0.95 (0.47 - 1.91)	0.890
Size mass	39 (75 %)	54 (60.7%)	1.39 (0.63 - 3.05)	0.412
nodule	13 (25%)	35 (39.3%)		
Site RUL[2]	8 (15.4%)	16 (17.9%)	1.80 (0.49 - 6.64)[3]	0.041
RML[2]	10 (19.2%)	9 (10.1%)	4.00 (1.05 -15.26)[3]	
RLL[2]	11(21.2%)	30 (33.7%)	1.32 (0.39 - 4.42)[3]	
LUL[2]	18 (34.6%)	16 (17.9%)	4.05 (1.22-13.42)[3]	
LLL[2]	5 (9.6%)	18 (20.2%)		
Pneumothorax	2 (3.69%)	8 (8.98%)	0.41 (0.08 - 1.98)	0.251
Bleeding	11 (21.2%)	29 (32.6%)	0.55 (0.25 - 1.23)	0.146

1: Continuous data were analyzed by *t*-test, and categorical data by chi-square test.

2: RUL: right upper lobe
RML: right middle lobe
RLL: right lower lobe
LUL: left upper lobe
LLL: left lower lobe

3: Relative to LLL.

pneumothoraces required less tubal thoracostomy and had less biopsy-related bleeding, and although this occurred in a significant portion of patients, no obvious morbidity or mortality resulted. This emphasizes the safety and low complication rate of TBLB, but patients with very poor pulmonary function and coagulative abnormalities or blood dyscrasias must be screened carefully [8-13].

The traditional means of obtaining lung tissue for the diagnosis of pulmonary infiltrates in patients has been open-lung biopsy [1, 4]. This procedure usually requires patient transport to the operating room, as well as tubal thoracostomy, which may significantly increase patient risk and morbidity, and is less accepted by the patient. Additionally, TBLB allows the repeated sampling of lung tissue to be more easily and less expensively performed than with open-lung biopsy. Despite these advantages of TBLB, inadequate tissue or sampling errors, yielding nonspecific diagnoses such as “chronic inflammation”, “atypical cells” or “fibrosis”, remain an important limitation of this technique [14-15]. Therefore, open-lung biopsy will continue to play a role in the evaluation of some patients, especially after a previous non-diagnostic transbronchial biopsy [16-17].

For anatomical reasons, all subsegmental bronchi have different branching angles, resulting in different degrees of difficulty in reaching the target lesion. In other words, TBLB with different subsegmental bronchi has a variable diagnostic success rate. Lesions localized at the left upper lobe are generally thought to be more difficult to approach through bronchoscopy [7, 18], however, our study showed that biopsy from the left upper lobe had a greater diagnostic yield than biopsy from other sites. It may be said that biopsy from the left upper lobe, especially the left 1+2a+b,

requires a more difficult technique, but if the tissue specimen can be obtained from the left upper lobe successfully, it may have more diagnostic yield than that of other sites. If the pulmonary lesion is larger, it will involve more area of the subsegmental bronchi, and the rate of successful biopsy of the target lesion is higher. We analyzed the correlation between pulmonary lesion size and diagnosis rate, and reached the conclusion is that there is no statistical significance. By definition, TBLB denotes biopsy of the lung or pathologic process occurring within the pulmonary parenchyma. Biopsy of peripheral nodules originating in the bronchial wall does not represent TBLB. Nevertheless, the term "TBLB" is loosely used in clinical practice well as in the literature to describe biopsy of any bronchoscopically invisible lesion. The diagnostic rates of TBLB can be considered separately for diffuse and localized lesions. In a review of several series of diffuse lung lesions, the overall diagnostic yield was 72%, and for localized lesions, biopsy of lesions larger than 3.0 cm provided a greater than 60% diagnostic yield, whereas lesions less than 3.0 cm in diameter yielded a diagnosis in less than 25% [19-20]. Our data for diagnostic yield are: 41.9% for mass and 34.2% for nodule. This is a relatively low diagnostic rate. A large portion of the diagnoses was nonspecific, such as "chronic inflammation", "atypical cells", or "fibrosis". This may be due to inadequate tissue specimens, or that the pathologists did not understand the clinical features. Therefore, clear communication between the bronchoscopist and the pathologist is important, especially before the biopsy specimen is obtained.

Based on our experience, we suggest that TBLB be considered as an alternative to open-lung biopsy in any patient with variable pulmonary lesions. Exclusion criteria for the performance of TBLB should include the presence of an uncorrectable bleeding diathesis, inability to adequately oxygenate the patient during bronchoscopy, hemodynamic instability, and the presence of severe impairment of lung function with pulmonary hypertension. Additionally, the time interval for proceeding to TBLB should depend on the severity of the patient's underlying medical condition and the likelihood that the results obtained will significantly influence medical management.

TBLB is a traditional procedure and has been well established. In recent years, endobronchial ultrasound has been developed for localizing and improving the diagnostic yield of TBLB in peripheral lung cancer [18, 21-22]. However, diagnostic accuracy has varied in recent published reports, and endobronchial ultrasound still has room for development. With more technique and experience, the diagnostic accuracy of TBLB will improve in the future.

TBLB is a safe procedure in patients whose chest roentgenograms showed localized lesions, such as lung mass or nodule, but a low diagnostic rate has been noted. TBLB can be the first choice in patients whose chest roentgenograms show a localized lesion, but no visible lesion when using the bronchoscope.

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侷限性肺病灶作經氣管肺切片的併發症

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背景：分析經氣管肺切片的診斷準確度及併發症機率。並且分析會影響報告結果的因素（病灶大小、切片位置、年紀、性別及併發症）。

方法：我們前瞻性的研究 141 位胸部 X 光上具有肺結節或肺腫塊且無可見的氣管內病灶的患者。為了評估經氣管肺切片的安全性及診斷率，我們計算了診斷準確度及併發症發生率。病灶大小、切片位置、年紀、性別及併發症也被用來分析是否會引響診斷準確度的因素。

結果：我們計算出了經氣管肺切片的併發率及診斷率及評估關於年紀、性別、病灶大小、切片位置、併發症與診斷率之間的相關性。切片檢查所造成的併發症包括：10 個氣胸的病患（7.1%），其中 2 個病患需要插胸管引流作治療，40 個病患（28.4%）造成出血。總併發率為 35.5%，但是沒有病患死於這一些併發症。關於年紀（p=0.39）、性別（p=0.89）、病灶大小（p=0.412）、併發症（氣胸：p=0.251；出血：p=0.146）與診斷準確度並無統計學上的意義。但是經由左上肺葉作切片比起其他肺葉作切片有更多的診斷率，並且具有統計學上的意義（p=0.041）。而從左下肺葉作切片診斷率最低。在 141 位病患當中有 52 個病患經由經氣管肺切片有做出診斷，總診斷率為 36.9%。

總結：這一個研究指出經氣管肺切片在各個年齡層及不同樣式的肺部病灶都是一個安全的檢查。然而在診斷率方面卻依然是低的。*(胸腔醫學* ***2006; 21: 149-156)***

關鍵詞：經氣管肺切片，支氣管鏡，氣胸

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The Diagnosis and Clinical Outcomes of Patients with Sepsis-induced Disseminated Intravascular Coagulation in a Medical Intensive Care Unit

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Background: Disseminated intravascular coagulation (DIC) has been reported to play an important role in the development of multi-organ failure and death. However, there is no single available laboratory test sufficiently sensitive or specific to enable a diagnosis of DIC. Objective: To compare the outcomes of septic patients with overt and non-overt DIC diagnosed by a score system in a medical intensive care unit, and to determine the relationship between the DIC score and the number of organ failures.

Method: The study population was recruited from a 37-bed medical intensive care unit (MICU) in a medical center. Patients who presented with sepsis while admitted to the MICU were included in this study. We divided these patients into 2 groups, the overt and non-overt DIC group, according to the DIC score. Baseline characteristics of the patients, ICU mortality rate, hospital mortality rate, 10-day mortality, 30-day mortality, duration of ICU stay, duration of hospital stay, and duration of mechanical ventilator support were compared between the 2 groups. The study also determined the correlation between the DIC score and the number of organ failures.

Results: A total of 43 male and 16 female patients (a total of 59 patients) were included. Patients with overt DIC had a higher APACHE II score (28.3 ± 11.4 vs. 22.9 ± 8.7, $p = 0.045$) and DIC score (6.1 ± 1.3 vs. 2.2 ± 1.2, $p < 0.001$) than those with non-overt DIC. The 30-day mortality rate (58.3% vs. 31.4%, $p = 0.040$), ICU mortality rate (54.2% vs. 25.7%, $p = 0.026$), and in-hospital mortality rate (62.5 % vs. 28.6 %, $p = 0.010$) were significantly higher in the overt DIC patients. The number of organ failures in patients with overt DIC was significantly higher (4.2 ± 1.3 vs. 2.3 ± 1.2, $p < 0.001$). The organ failure number was positively correlated with the DIC score ($r = 0.66$; $p < 0.001$).

Conclusion: The septic patients with overt DIC had worse outcomes than those with non-overt DIC. The diagnosis of overt DIC is a warning sign and should prompt more intensive therapeutic strategies focusing on the underlying disease and complications. ***(Thorac Med 2006; 21: 157-167)***

Key words: disseminated intravascular coagulation (DIC), sepsis, DIC score

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Introduction

Disseminated intravascular coagulation (DIC), characterized by a systemic activation of intravascular coagulation, has been reported to play an important role in the development of multi-organ failure and death [1]. DIC is always secondary to certain underlying disorders, and the outcomes of DIC are mainly related to the underlying etiology and associated complications. DIC may be induced by sepsis or major trauma through the activation of a systemic inflammatory response, leading to activation of the cytokine network and subsequent activation of coagulation [2]. In addition, the release or exposure of procoagulant material into the bloodstream by malignancy or obstetrical disorders may also be associated with the development of DIC.

Sepsis is 1 of the most common causes of DIC [3]. Many microorganisms, including Gram-positive and -negative bacteria and viruses cause DIC [4-5]. Uncontrolled infection may induce both inflammation and procoagulant responses [1, 3, 6]. Sepsis-induced inflammatory cytokines, including interleukin-1β, interleukin-6, and tumor necrosis factor-*a*, stimulate the expression of tissue factor on monocytes and endothelium [5, 7]. The activated tissue factor pathway activates the diffusely extrinsic coagulation pathway with thrombin formation [5, 7-8]. In addition, dysfunction of the endogenous anticoagulation system was also noted in patients with DIC [5, 9-10]. The imbalance between the procoagulation and anticoagulation systems results in diffused microvascular thrombosis, which may lead to multi-organ failure and mortality.

To date, there is no single available laboratory test sufficiently sensitive or specific to enable a diagnosis of DIC. The subcommittee on DIC of the International Society on Thrombosis and Haemostasis (ISTH) presented a scoring system [10] that uses simple laboratory tests that are available in almost all hospital laboratories. Prospective studies have shown a high accuracy for this scoring system in the diagnosis of DIC (sensitivity 91%, and specificity 97%).

In the present study, we compared the clinical outcomes of septic patients with overt DIC and those with non-overt DIC in a medical intensive care unit, and determined the correlation between the DIC score and the number of organ failures among the patients with sepsis.

Materials and Methods

Patients

The study population was recruited from a 37-bed medical intensive care unit (MICU) in a medical center. Patients who presented with sepsis while admitted to the MICU were included in this study. The definition of sepsis was based on the presence of infection and at least 2 of the following criteria [11]: temperature > 38°C or < 36°C (please use correct degree symbol), heart rate > 90 beats/min, respiratory rate >20 breaths/min or $PaCO_2$ < 32 mmHg, and WBC > 12000/mm^3 or < 4000 k/mm^3 or >10% immature (band) forms. The study was conducted from Apr. 2004 to Dec. 2004. Forty-three male and 16 female patients (a total of 59 patients) were included.

Baseline assessment

Baseline characteristics of patients were recorded, and included age, vital signs, blood gas analysis, organ failure number, and hematologic and biochemistry tests. The definition of organ failure was based on the criteria of the Consensus Committee of the American College of Chest Physicians and the Society of Critical Care

Medicine [12], as follows: Respiratory failure: requiring mechanical ventilation, Cardiovascular failure: systolic BP ≤ 90 mmHg or mean arterial pressure ≤ 60 mmHg for 1 hour despite fluid bolus, Renal failure: low urine output (e.g., < 0.5 mL/kg/hr), increased creatinine (≥ 50% increase from baseline), or requiring acute dialysis, Hematologic failure: low platelet count (< 100,000 /mm^3) or PT/PTT > upper limit of normal, Metabolic failure: low pH with high lactate (e. g., pH < 7.30 and plasma lactate > upper limit of normal), Hepatic failure: liver enzymes > 2x upper limit of normal, CNS failure: altered consciousness or a reduced Glasgow Coma Score. We used the 5-step algorithm (Table 1) proposed by the SSC/ISTH subcommittee to calculate the DIC scores of these septic patients. A score of 5 or more was considered to be compatible with overt DIC, while a score less than 5 was considered to be non-overt DIC. The Acute Physiology and Chronic Health Evaluation II (APACHE II) score [13] was used for the assessment of illness severity. The DIC and APACHE II scores were rated within 24 hours of ICU admission. The underlying medical history, including diabetes mellitus, hypertension, neurologic disease, congestive heart failure, history of malignancy, and chronic airway diseases (asthma, chronic airway obstructive disease, and bronchiectasis), was also reviewed.

Outcome assessment

The end-points of the study in terms of clinical outcomes included 10-day, 30-day, ICU, and in-hospital mortality, length of ICU and hospital stay, and duration of mechanical ventilation. Furthermore, the occurrence of sepsis-associated complications, including upper gastrointestinal bleeding, nosocomial pneumonia, and adult respiratory distress syndrome (ARDS) were compared between both groups. In addition, the correlation between the DIC score and the number of organ failures was assessed.

Statistical Analysis

Descriptive statistics were employed to examine the demographic characteristics of the study population. Data were expressed as mean

Table1. Diagnostic algorithm for the diagnosis of overt DIC

1. Risk assessment: Does the patient have an underlying disorder known to be associated with overt DIC?
   If yes: proceed; If no: do not use this algorithm;
2. Order global coagulation tests (platelet count, prothrombin time (PT), fibrinogen, soluble fibrin monomers or fibrin degradation products)
3. Score global coagulation test results
   a. platelet count *(>100 = 0; <100 = 1; <50= 2)*
   b. elevated fibrin-related marker (e.g. soluble fibrin monomers/fibrin degradation products)
      (no increase: 0; moderate increase: 2; strong increase: 3)
   c. prolonged prothrombin time
      (< 3 sec.= 0; > 3 sec. but < 6 sec.= 1; > 6 sec. = 2)
   d. fibrinogen level
      (> 1.0 gram/l = 0; < 1.0 gram/l = 1)
4. Calculate score
5. If > 5: compatible with overt DIC; repeat scoring daily
   If < 5: suggestive (not affirmative) for non-overt DIC; repeat next 1-2 days

± SD (standard deviation). The quantitative variables between the patients with overt and non-overt DIC were compared using the two-tailed Student *t*-test and chi-square test for continuous and categorical variables, respectively. Ten-day and 30-day mortality were measured from the date of admission into the ICU to the date of death within 10 and 30 days, from all causes. Survival proportions, according to patients with overt and non-overt DIC, were traced with the Kaplan-Meier method, and comparisons of curves were based on the log rank test. The relationship between numbers of organ failures and the DIC score was analyzed with Pearson's coefficient of correlation. A *p*-value less than 0.05 was considered as statistically significant. All analyses were performed using SPSS software version 10.0 (Chicago, IL, USA).

Results

Baseline characteristics

A total of 43 (72%) male and 16 (28%) female patients were enrolled in this study. Twenty-four (41%) patients had overt DIC. There was no difference between the patients with overt and non-overt DIC in terms of age, gender, body temperature, respiratory rate, and heart rate. Patients with overt DIC had a higher illness severity, as indicated by the APACHE II score (28.3 ± 11.4 vs. 22.9 ± 8.7, $p = 0.045$). The DIC scores of patients with overt DIC differed from those with non-overt DIC (6.1 ± 1.3 vs. 2.2 ± 1.2, $p < 0.001$). The mean arterial pressure in subjects with overt DIC was significantly lower than in subjects with non-overt DIC (74.4 ± 15.2 mmHg vs. 85.7 ± 15.4 mmHg, $p = 0.007$) (Table 2). In addition, chronic coexisting conditions,

Table 2. Patient characteristics of mechanically ventilated patients

	overt DIC, N = 24	Non-overt DIC, N = 35	*P*- value
Age, mean ± SD yr	68.5 ± 15.2	68.8 ± 14.2	.924
Female sex, No. (%)	4 (16.7%)	12 (34.3%)	.135
APACHE II Score [a], mean ± SD	28.3 ± 11.4	22.9 ± 8.7	.045
DIC score, mean ± SD	6.1 ± 1.3	2.2 ± 1.2	<.001
Temperature, mean ± SD ºC	37.4 ± 1.3	37.0 ± 0.8	.106
Respiratory rate (f_R), mean ± SD breath/min	24.3 ± 6.1	23 ± 5.5	.387
Heart rate, mean ± SD beat/min	105.5 ± 26.6	104.6 ± 26.6	.910
Mean arterial pressure, mean ± SD mmHg	74.4 ± 15.2	85.7 ± 15.4	.007
Chronic coexisting conditions, No. (%)			
Diabetes Mellitus	9 (37.5%)	16 (45.7%)	.531
Hypertension	8 (33.3%)	16 (45.7%)	.341
Congestive heart failure	4 (16.7%)	5 (14.3%)	.803
Renal insufficiency	4 (16.7%)	7 (20%)	.747
Neurological disease	3 (12.5%)	11 (31.4%)	.093
Chronic obstructive pulmonary disease	5 (20.8%)	9 (25.7%)	.665
History of malignancy	6 (20.8%)	10 (25.7%)	.762

[a]APACHE II denotes Acute Physical and Chronic Health Evaluation II score, an assessment of severity of illness.

[b] V_T: tidal volume, liter

[*] *P* value for chi-square test in the case of categorical variables, and for 2-tailed independent *t* test in the case of quantitative variables.

SD: standard deviation

Table 3. Baseline blood laboratory data

Variable	overt DIC, N = 24	Non-overt DIC, N = 35	*P*- value
Arterial blood gas			
pH	7.310 ± 0.138	7.352 ± 0.151	.289
$PaCO_2$, mmHg	39.9 ± 17	42.6 ± 17.4	.558
PaO_2, mmHg	101.5 ± 82.5	104.6 ± 26.6	.910
PaO_2/FiO_2	224.9 ± 149.6	254 ± 139.2	.448
Hemotology			
White-cell count, per mm^3	13045 ± 7819	17065 ± 9295	.088
Hemoglobin, g/dL	10.2 ± 2.5	11 ± 2.4	.188
Platelet, 1000/μL	127.5 ± 108.9	276.5 ± 131.8	<.001
Prothrombin time, sec.	26.6 ± 20.4	14.6 ± 1.6	.001
Activated partial prothrombin time, sec.	33.6 ± 19.7	25 ± 4.3	.016
Blood biochemistry			
GOT[a], μ/L	643 ± 1476.4	42.1 ± 50.4	<.001
Total bilirubin, mg/dL	3.2 ± 3.8	0.7 ± 0.5	<.001
Albumin, g/dL	2.6 ± 0.6	2.5 ± 0.7	.818
Blood urea nitrogen, mg/dL	42 ± 29.1	48.7 ± 26.6	.364
Creatinine, mg/dL	2.2 ± 2.6	2.4 ± 1.9	.660
Sodium, meq/L	134.6 ± 9.3	140.2 ± 8.3	.018
Potassium, meq/L	4.5 ± 1.2	4.2 ± 1	.253

Plus-minus values are mean + standard deviation (SD)

a. GOT denotes glutamic oxaloacetic transaminase

*P value for chi-square test in the case of categorical variables, and for 2-tailed independent t test in the case of quantitative variables.

including diabetes mellitus, hypertension, congestive heart failure, chronic renal insufficiency, neurological disease, chronic airway disease, and malignancy, in patients with overt and non-overt DIC, were similar (Table 2).

Blood laboratory data

The arterial blood gas analyses, including pH, $PaCO_2$, PaO_2 and PaO_2/FiO_2, were similar between patients with overt and non-overt DIC (Table 3). There were no differences in the white-cell counts and hemoglobin levels between patients with overt and those with non-overt DIC. The patients with overt DIC had a significantly lower platelet count (127.5 ± 108.9 x 1000/μL vs. 276.5 ± 131.8 x 1000/μL, $p < 0.001$) and prolonged prothrombin time (26.6 ± 20.4 sec. vs. 14.6 ± 1.6 sec., $p = 0.01$), as well as activated partial prothrombin time (33.6 ± 19.7 sec. vs. 25 ± 4.3 sec., $p = 0.016$), than those without overt DIC. Serum levels of asparate aminotransferase (AST) (643 ± 1476.4 vs. 42.1 ± 50.4, $p < 0.001$) and total bilirubin (3.2 ± 3.8 vs. 0.7 ± 0.5, $p < 0.001$) were elevated among patients with overt DIC, while serum levels of albumin, blood urea nitrogen and creatinine were similar between both groups (Table 3). However, the sodium level was lower in the overt DIC group (134.6 ± 9.3 meq/L vs. 140.2 ± 8.3 meq/L, $p = 0.018$) when compared with the non-overt DIC group. The mean potassium level was not significantly different between the 2 groups (Table 3).

Outcome assessment

The patients with overt DIC had a worse survival outcome than patients with non-overt DIC. The 10-day mortality rate did not differ between the patients with overt and non-overt DIC (29 % vs. 14.3%, $p = 0.163$), however, the 30-day (58.3% vs. 31.4%, $p = 0.040$), ICU (54.2% vs. 25.7%, $p = 0.026$) and in-hospital (62.5 % vs. 28.6 %, $p = 0.010$) mortality rate were all significantly increased in patients with overt DIC when compared with patients with non-overt DIC. The length of ICU and hospital stay and duration of mechanical ventilation were similar between the 2 groups. The number of organ failures in patients with overt DIC was significantly higher (4.2 ± 1.3 vs. 2.3 ± 1.2, $p < 0.001$) than in those with non-overt DIC (Table 4). In addition, patients with overt DIC had a significantly higher incidence of renal (87.5 % vs. 40.0%, $p < 0.001$), hematologic (100% vs. 8.6%, $p < 0.001$) and hepatic (25 % vs. 5.7%, $p = 0.037$) failure than the non-overt DIC patients (Table 5). Kaplan-Meier analysis of the survival rate of patients illustrated a decreased survival rate for overt DIC patients (log rank test, $p = 0.043$; hazard ratio: 2.33; 95% confidence interval: 1.03-5.81) (Figure 1). Furthermore, the organ failure number was positively correlated with the DIC score ($r = 0.66$; $p < 0.001$) (Figure 2).

Clinical complications

The development of clinical complications, including ARDS, nosocomial pneumonia, and cardiopulmonary edema were similar between patients with overt and non-overt DIC. However, patients with overt DIC had a higher incidence of a development of upper gastrointestinal bleeding than patients with non-overt DIC (45.8% vs. 14.3%, $p = 0.07$) (Table 3).

Discussion

Table 4. Clinical outcomes of patients

	overt DIC, N = 24	Non-overt DIC, N = 35	*P*-value
Outcomes			
10-day mortality rate, No (%)	7 (29.2%)	5 (14.3%)	.163
30-day mortality rate, No (%)	14 (58.3%)	11 (31.4%)	.040
ICU [a] mortality, No (%)	13 (54.2%)	9 (25.7%)	.026
In-hospital mortality, No (%)	15 (62.5%)	10 (28.6%)	.010
Days of ICU [a] stay (mean ± SD)	14.6 ± 8.2	11.2 ± 9.2	.146
Days of hospital stay (mean ± SD)	31.7 ± 22.5	30.6 ± 22.9	.859
Duration of mechanical ventilation, days (mean ± SD)	15.4 ± 14.7	10.1 ± 12.2	.140
Number of organ failures (mean ± SD)	4.2 ± 1.3	2.3 ± 1.2	<.001
Complications, No (%)			
Adult respiratory distress syndrome (ARDS)	5 (20.8%)	7 (20%)	.939
Nosocomial pneumonia	13 (54.2%)	12 (34.3%)	.129
Cardiopulmonary edema	5 (20.8%)	3 (8.6%)	.177
Upper gastrointestinal bleeding	11 (45.8%)	5 (14.3%)	.007

[a] ICU: intensive care unit

[*] *P* value for chi-square test in the case of categorical variables, and for 2-tailed independent *t* test in the case of quantitative variables.

SD: standard deviation

Table 5. Organ failure of patients

Variable	overt DIC, N = 24	Non-overt DIC, N = 35	*P*- value
Respiratory failure	24 (100%)	33 (94.3%)	.233
Cardiovascular failure	9 (37.5%)	6 (17.1%)	.078
Renal failure	21 (87.5%)	14 (40.0%)	<.001
Hematologic failure	24 (100%)	3 (8.6%)	<.001
Metabolic failure	10 (41.7%)	9 (25.7%)	.198
Hepatic failure	6 (25%)	2 (5.7%)	.034
Neurologic failure	6 (25%)	9 (25.7%)	.951

*P value for chi-square test in the case of categorical variables

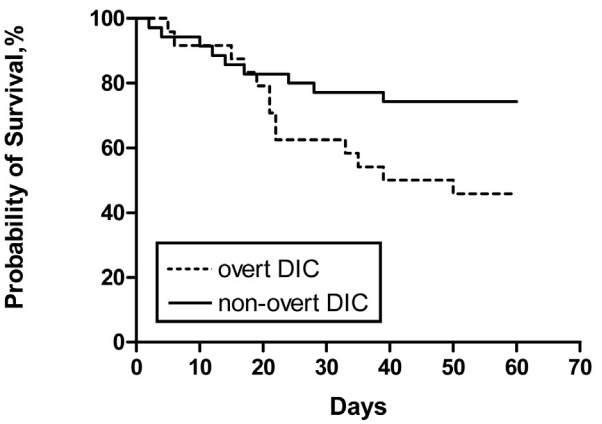

Fig. 1. Kaplan-Meier Analysis of Survival Proportions. Survival proportions according to patients with and without DIC were traced using the Kaplan-Meier method (log rank test, $p = 0.043$; hazard ratio: 2.33; 95% confidence interval: 1.03-5.81). The dashed line represents patients with overt DIC; the continuous line represents patients with non-overt DIC.

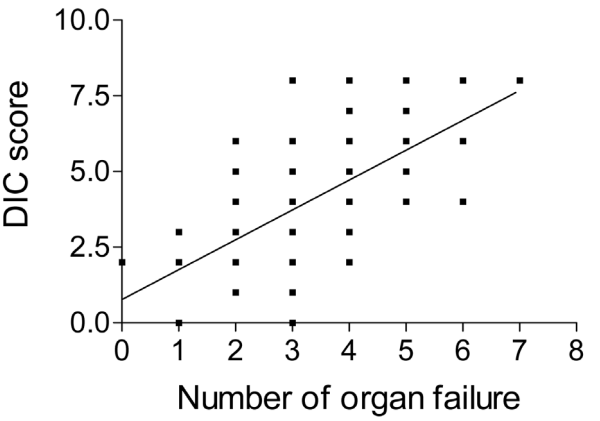

Fig. 2. The Relationship between Numbers of Organ Failures and DIC Score. Positive correlation between the numbers of organ failures and DIC score. Correlation was analyzed using Pearson's coefficient of correlation ($r = 0.66$; $p < 0.001$).

In this study, we assessed the DIC score, provided by the subcommittee on DIC of the ISTH, of each patient with sepsis, and divided them into overt and non-overt DIC groups. The patients with overt DIC had higher grades of illness severity, as indicated by the APACHE II score and the numbers of organ failures. Meanwhile, our study demonstrated that the overt DIC group had worse outcomes than the non-overt DIC group in the 30-day, ICU, and hospital mortality rate. In addition, we also found that the DIC score was positively correlated with the numbers of organ failures.

Despite major improvements in intensive care medicine and antibiotic therapy, the mortality and morbidity rates due to sepsis remain high. The presence of the systemic inflammatory response syndrome triggers the activation of blood coagulation [14]. DIC contributes to the adverse outcome [15]. Consistent with previous reports, our study demonstrated that the presence of overt DIC has a grave impact on septic patients' out-

comes. DIC is characterized by the widespread activation of coagulation, resulting in the intravascular formation of fibrin, and ultimately the thrombotic occlusion of vessels, followed by the derangement of the oxygen supply and demand to the cells and tissues [3]. Furthermore, the persistent thrombotic activity in patients with DIC is closely linked to multiple organ dysfunction syndrome (MODS) and higher mortality rates [16-17]. These factors suggest that important cross-talk exists between the procoagulation and inflammatory mechanisms in the pathogenesis of organ failure and mortality in septic patients with DIC. Our study demonstrated that the advanced illness severity indicated by the higher APACHE II score and the increased number of organ failures among the overt DIC group may have contributed to the increased mortality rate among these patients.

MODS is a clinical entity characterized by generalized microvascular thrombosis that may develop as part of the DIC syndrome, especially in Gram-negative sepsis. A study of 1,789 ICU patients showed that the mortality of patients with DIC was significantly correlated with the sepsis-related organ failure assessment (SOFA) score [18]. Our study revealed that DIC patients not only had an increased number of organ failures, but also had a higher chance of developing sepsis-associated organ failure. The patients with overt DIC experienced an increase in the incidence of renal and hepatic failure. The activated and deregulated endothelium has been reported to play a pivotal role in the cross-talk between inflammation and coagulation during sepsis [19]. Sepsis-induced endothelial damage with intravascular fluid re-distribution has been reported to be associated with the development of septic shock [20]. Impaired liver function may be induced by ischemia of the hepatocytes and endothelial damage in septic patients [21]. Meanwhile, the increased incidence of upper gastrointestinal bleeding in patients with overt DIC may result from a depletion of platelets and clotting factors, leading to concurrent thrombotic and bleeding complications [22]. In addition, the correlation between the DIC score and the number of organ failures suggests that DIC is engaged in MODS.

DIC is thought to contribute to multi-organ failure and death in a variety of underlying conditions. Experimental studies of DIC associated with sepsis or low-grade activation of coagulation have repeatedly demonstrated that the effective inhibition of DIC can indeed reduce mortality. Several studies have suggested a direct effect of fibrin on inflammatory activity: fibrinogen interacts with bacteria and modulates their activity, fibrin serves to encapsulate bacteria, or fibrin cleavage peptides may trigger the release of pro-inflammatory cytokines [23]. In contrast, many investigators currently believe that it is not DIC, and particularly not fibrin formation itself, that is harmful, but rather it is the generation of serine proteases and their potential interactions with pro-inflammatory mediators that contribute to organ failure and death [24]. Therefore, further study is needed to investigate the exact mechanisms by which DIC contributes to multi-organ failure in sepsis.

There is no single laboratory test that can establish or rule out the diagnosis of DIC. However, a combination of test results in a patient with a clinical condition known to be associated with DIC can be used to diagnose the disorder [3]. The DIC score presented by the subcommittee on DIC of ISTH employs simple laboratory tests that are available in almost all hospital laboratories. Prospective studies have shown the high accuracy of this scoring system for the diagnosis of DIC, with a sensitivity of 91% and a specificity of 97%

[25]. Since no specific effective treatment is available for DIC, therapies focus on the treatment of the underlying disorder. Because the development of DIC is associated with a markedly negative impact on survival outcomes, the diagnosis of DIC warrants immediate therapeutic strategies with special attention to the correctable underlying conditions. Implementation of the DIC score in the routine studies of an ICU offers a convenient and rapid diagnosis of the development of overt DIC. Thus, further study is necessary to clarify the effect of the implementation of a routine DIC scoring system in the ICU on the survival outcomes of patients with sepsis.

In conclusion, the DIC score provided by the subcommittee on DIC of the ISTH is a convenient and useful tool in the diagnosis of DIC among patients with sepsis. The development of overt DIC among patients with sepsis has a grave impact on their survival outcomes. In addition, the diagnosis of overt DIC is a warning sign and should prompt more intensive therapeutic strategies focused on the underlying disease.

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內科加護病房內敗血症引起的瀰漫性血管內血液凝結之病患的診斷及臨床預後的評估

王郁閔　林恕民　王志冉　林定佑　郭漢彬　林鴻銓

背景：目前已經有很多研究發現瀰漫性血管內血液凝結對於病患所發生之多重器官衰竭及死亡扮演著很重要的角色。然而，目前並沒有任何單一項實驗室檢查能有足夠的敏感度及特異度能用來診斷瀰漫性血管內血液凝結。

主題：依血栓及血液凝集國際協會 (International Society on Thrombosis and Haemostasis, ISTH) 所訂定之瀰漫性血管內血液凝結評分系統，我們將內科加護病房內患有敗血症之病患分為明顯及非明顯瀰漫性血管內血液凝結兩組，進而比較這兩組病患器官衰竭及預後的情形與瀰漫性血管內血液凝結評分結果的關係。

方法：我們的病患來源是收集自一個 37 床病床規模的醫學中心內科加護病房。所有患有敗血症的病患都將納入我們的研究。依此瀰漫性血管內血液凝結評分系統，我們將病患分為明顯及非明顯瀰漫性血管內血液凝結兩組，進而比較這兩組病患基本特性、加護病房死亡率、住院死亡率、住院 10 天內死亡率、住院 30 天內死亡率、加護病房住院天數、總住院天數、呼吸器使用天數 及器官衰竭數目。

結果：總共收集了 43 為男性病患及 16 位女性病患.。具明顯瀰漫性血管內血液凝結的病患比非明顯瀰漫性血管內血液凝結的病患有比較高的 APACHE II 分數 (28.3 ± 11.4 vs. 22.9 ± 8.7, $p = 0.045$) 及瀰漫性血管內血液凝結之分數。此外，具明顯瀰漫性血管內血液凝結的病患之 30 天死亡率 (58.3% vs. 31.4%, $p = 0.040$)、加護病房死亡率 (54.2% vs. 25.7%, $p = 0.026$) 及住院死亡率 (62.5 % vs. 28.6 %, $p = 0.010$) 都表現出有意義的增加。器官衰竭數目在明顯瀰漫性血管內血液凝結的病患也呈現有意義的增加 (4.2 ± 1.3 vs. 2.3 ± 1.2, $p < 0.001$)。此外，器官衰竭數目與瀰漫性血管內血液凝結之分數呈現有意義的正相關 (r = 0.66; $p < 0.001$)。

結論：具明顯瀰漫性血管內血液凝結之敗血病患比非明顯瀰漫性血管內血液凝結之病患有較差的臨床預後。因此，明顯瀰漫性血管內血液凝結的診斷提醒著我們必須積極處理其造成的因素及其併發症。*(胸腔醫學* ***2006; 21: 157-167****)*

關鍵詞：瀰漫性血管內血液凝結，敗血症，瀰漫性血管內血液凝結之評分

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Massive Hemoptysis Due to an Anomalous Origin of the Right Pulmonary Artery from the Ascending Aorta — A Case Report

Renin Chang, Chien-Wei Hsu, Chih-Hsun Lin, Pei-Loon Kang**, Shao-Lin Lin*, Hong-Yang Tao

Massive hemoptysis is 1 of the most dreaded of all respiratory emergencies, and can have a variety of underlying causes. The associated mortality rate depends mainly on the underlying etiology and the magnitude of bleeding. The unpredictable and potentially lethal course of massive hemoptysis requires prompt resuscitation, airway protection, and correction of the underlying causes. Many of the etiologies, such as chronic inflammatory conditions (including bronchiectasis, tuberculosis, and lung abscess) and lung malignancies, have been surveyed. Vascular disorders such as pulmonary emboli, arteriovenous malformations, and bronchial telangiectasis also play a role. A pulmonary artery originating from the ascending aorta is a rare (less than 1% of all congenital cardiopathies) and frequently fatal malformation, if early surgical repair is not performed. Herein, we report a 23-year-old female with an anomalous origin of the right pulmonary artery from the ascending aorta demonstrated by a computerized tomography scan of the chest, who presented massive hemoptysis, progressive dyspnea, and respiratory failure 3 days after Caesarean section. ***(Thorac Med 2006; 21: 168-174)***

Key words: anomalous origin of the right pulmonary artery, hemoptysis

Introduction

Hemoptysis may be the presenting symptom of a great many diseases, with mortality ranging from 7% to 30% [1]. Life-threatening hemoptysis is 1 of the most challenging conditions encountered in critical care, and requires a thorough and timely investigation.

The anomalous origin of a pulmonary artery from the ascending aorta is a rare, frequently fatal congenital cardiac malformation, if early surgical repair is not performed. The clinical manifestation usually occurs in infants or, more rarely, in the newborn as respiratory distress or congestive heart failure due to increased pulmonary resistance. It more commonly involves the right pulmonary artery than the left, and is more frequently associated with other cardiac anomalies such as patent ductus arteriosus and ventricular septal defect [2]. The clinical setting is characterized by increased pulmonary blood flow, congestive heart failure, and cyanosis when the pulmo-

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nary pressure and vascular resistance are too high. The present case is exceptional because the patient had been almost symptom-free for more than 20 years.

Case Report

This 23-year-old primigravida presented at 38 weeks of gestation with hemoptysis and dyspnea 3 days after delivery. She had been admitted to our obstetric ward for Caesarean section. She had been well previously, except for exercise intolerance. Mild hemoptysis without associated symptoms had occurred in the most recent 2 years. There was no motion-limitation due to cardiopulmonary distress in her daily activity. She denied tobacco use or drug addiction. She had been to our cardiology out-patient clinic before marriage on October, 2001, when physical examination showed no leg edema, but a soft systolic murmur in the pulmonary area, and echocardiography showed a normal left ventricular systolic function without chamber dilatation, but mild mitral and tricuspid regurgitation; transesophageal echocardiography subsequently revealed a small leakage at the lower edge of the foramen ovale, with a left-to-right shunt and mild pulmonary hypertension. She had visited our emergency department due to mild hemoptysis on March 9, 2002, with spontaneous resolution, and, since June 2004, she had been regularly followed up at our obstetric outpatient clinic after becoming pregnant.

She underwent Caesarean section smoothly on December 1, 2004, with the assistance of spinal anesthesia. A small amount of fresh bloody hemoptysis occurred at night following childbirth. The initial clinical examination showed a young woman in slight respiratory distress, but without cyanosis. She was 155 cm in height and weighed 67 kg; her blood pressure was 130/70 mm Hg, pulse rate 80 beats/min, body temperature 36.6°C, and respiratory rate 22/min. Chest auscultation revealed rales on the left side without wheezing or stridor. Cardiac auscultation revealed a faint systolic murmur around the pulmonary area, with normal S1. Another episode of hemoptysis was noted on the next day. She began suffering from progressive dyspnea on December 4, 2004, when oxygen saturation was only 74% in room air; her condition did not improve despite the use of a non-rebreathing mask. General cyanosis and respiratory failure ensued. She was intubated with the support of a mechanical ventilator set in the assist/control mode and at 100% FiO_2. Arterial blood analysis gas showed a pH value of 7.24, $PaCO_2$ of 46.4 mm Hg, PaO_2 of 76.4 mm Hg, and HCO_3^- of 18 mmol/L. Chest radiography demonstrated diffuse infiltrates in the left lung field (Figure 1). Extracorporeal membrane oxygenation (ECMO) was utilized due to progressive hypoxemia, but massive hemoptysis was still noted after intubation. High peak airway pressure developed and subcutaneous emphysema occurred. The tidal volume which could be delivered was less than 50 mini-liters due to frank

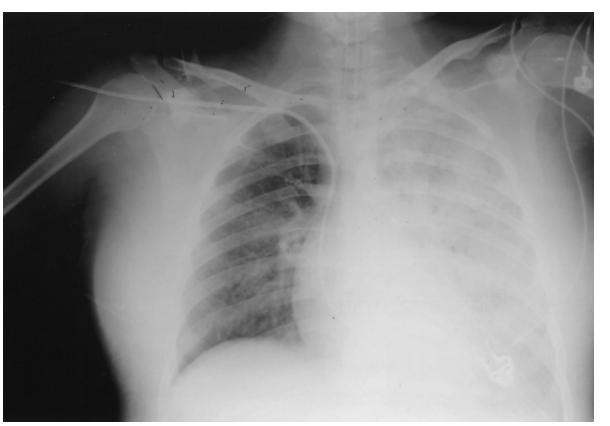

Fig. 1. Anterior-posterior chest radiograph reveals diffuse infiltrates in the left lung field when hemoptysis and dyspnea progressed to respiratory failure.

obstruction of the trachea by a huge blood clot. A flexible fiberoptic bronchoscopy was undertaken, which demonstrated a huge blood clot in the trachea just below the vocal cords, and the carina was not visible. The blood clots appeared soft, and could not be pulled out by forceps. Biopsy was done, and the results showed inflammatory exudates composed of fibrins and polymorphonuclear leukocytes without lung parenchyma; there were no mycobacteria, fungi, bacteria, or malignancy present. A second bronchoscopy was arranged 10 days later, after the huge blood clot was expectorated, and the result revealed a great many blood clots retained in the left main bronchus, with the right side clear and without active bleeders. After her condition had stabilized, the ECMO was removed. A chest CT scan was done and showed the right main pulmonary artery arising from the ascending aorta, forming an extra-cardiac left-to-right shunt (Figure 2). After aggressive medical treatment, including mechanical ventilation, double lumen endotracheal tube intubation, and extracorporeal circulation, her condition improved gradually. Finally, she was extubated successfully and discharged.

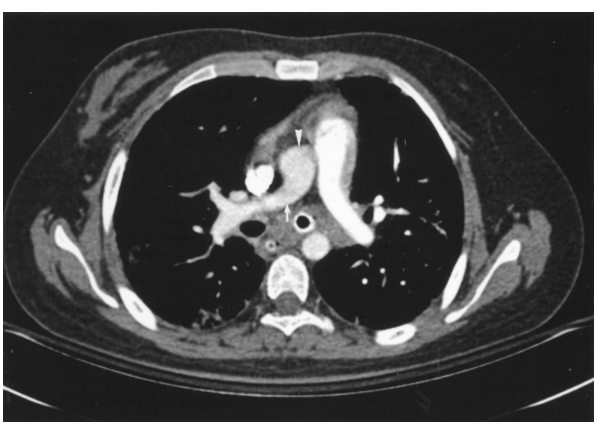

Fig. 2. Computed tomography scan of the chest shows the right main pulmonary artery arising from the ascending aorta, forming an extra-cardiac left-to-right shunt with normal pulmonary trunk and aortic root.

Discussion

Hemoptysis is 1 of the most alarming symptoms frequently heralding the recognition of serious disease. According to recently published data, 28% of chest clinicians had experienced a patient's death from massive hemoptysis during a previous 1-year period [3]. Although there is no generally accepted definition of the volume of blood that constitutes massive hemoptysis, a more relevant definition of massive hemoptysis is the volume that is life threatening by virtue of airway obstruction or blood loss [4]. Hemoptysis originates from the bronchial and pulmonary circulation in 90% and 5% of cases, respectively [5]. In a minority of cases (5%), massive hemoptysis may originate from the aorta or the systemic arterial supply to the lungs [6]. Bleeding from the bronchial arteries has the propensity to cause massive hemoptysis, as it is a circulation at systemic pressure. Alveolar hemorrhage is a recognized cause of hemoptysis, but rarely causes massive bleeding, as the alveoli have the capacity to accommodate a large volume of blood. A more common presentation is mild hemoptysis, pulmonary infiltrates, and anemia. Massive hemoptysis may result from various causes, and the frequency differs greatly between the Western and the non-Western world. Pulmonary tuberculosis is the most common underlying cause in the latter. Bronchogenic carcinoma and chronic inflammatory lung diseases due to bronchiectasis, cystic fibrosis, or aspergillosis are the more prevalent causes in Western countries [7]. Other causes include lung abscess, pneumonia, chronic bronchitis, pneumoconiosis, aortobronchial fistula, ruptured aortic aneurysm, pulmonary artery aneurysm, and congenital cardiac or pulmonary vascular anomalies [8]. The physical examination may provide valuable clues leading to the diagnosis.

The presence of stridor or localized wheezing should raise the suspicion of tracheolaryngeal tumors or a foreign body. Oral or genital aphthous ulcerations, uveitis, and cutaneous nodules may be clinical presentations in patients with Behcet's disease. A saddle nose with rhinitis and septal perforation are signs of Wegner's granulomatosis. The diagnosis of Goodpasture's syndrome should be considered if blood is also detected in the urine, although the absence of hematuria does not exclude the diagnosis. Clubbing may be a sign of lung carcinoma or bronchiectasis.

Chest radiography is readily available and is a very important diagnostic tool in finding the cause of the bleeding. Although 20% to 30% of patients with hemoptysis have a normal chest X-ray, it helps to identify many lung parenchymal pathologies, such as cavitary lesions, tumors, infiltrates, and atelectasis. Intra-alveolar bleeding may produce a fine reticulonodular pattern in the involved lobes that can be taken for pneumonia. As in this case (Figure 1), the asymmetric distribution of the diffuse coalescent opacities with air-bronchogram signs denote lesions within the lung parenchyma. The absence of cardiac arrhythmias and acute myocardial infarction with a normal-sized heart might suggest a noncardiac etiology. Another cause of the uneven distribution of pulmonary opacity is a concomitant infection. However, this patient did not suffer from fever, leukocytosis, or purulent sputum. Hemorrhage is an important cause of diffuse coalescent opacities, because it may lead to extensive air-space consolidation. Making a specific diagnosis of pulmonary hemorrhage based on radiographic findings is difficult. We usually arrange a computed tomography scan of the chest to differentiate diffuse pulmonary hemorrhaging from focal pulmonary hemorrhaging occurring as a result of abnormalities such as bronchiectasis, chronic bronchitis, active infection, neoplasm, pulmonary embolism, or other vascular abnormalities, such as arteriovenous fistula. Using a CT scan, we incidentally discovered an anomalous origin of the right pulmonary artery in this patient.

An anomalous pulmonary artery originating from the ascending aorta is a rare, frequently fatal malformation if early surgical repair is not performed. Fraentzel first described the anomaly in 1868. The anomalous origin of a pulmonary artery from the aorta is frequently associated with other cardiac malformations, and rarely presents as an isolated anomaly [9]. Although either 1 or both of the pulmonary arteries can originate directly from the aorta, either from the ascending portion or the transverse arch portion, in almost 80% of cases it is the right pulmonary artery that originates from the ascending aorta, and in approximately 75% of cases a patent ductus arteriosus is present. In such conditions, a pulmonary artery from the aorta occurs in the presence of separated aortic and pulmonary valves, and should be differentiated from the truncus arteriosus, in which the pulmonary arteries originate from the ascending aorta, but in the presence of a common semilunar valve [10].

The clinical presentation is accentuated pulmonary vasculature and severe early pulmonary hypertension that leads to congestive heart failure. There are few reports of successful interventions, even in adolescent and adult patients [11-12]. In this case, the patient had had mild exertional dyspnea since childhood. Several episodes of mild hemoptysis had occurred in recent years, but these did not affect her daily activity. Ultrasound examination can strongly suggest the condition, but can easily be misinterpreted [13]. Such is the case described herein, which initially was not detected in the clinical and echocardiographic examination.

The origin of the pulmonary artery from the ascending aorta is responsible for a great left-to-right shunt at the systemic-pulmonary level. The contralateral lung receives all the cardiac output of the right ventricle. From the right ventricle, only 1 pulmonary artery can be entered, and pressure is usually significantly elevated [14]. The exact cause of pulmonary hypertension in the left pulmonary artery remains unknown. However, reflex vasoconstriction and neurogenic crossover have been postulated [15].

It is interesting that this tragedy occurred just after delivery. The onset of dyspnea in the peripartum period requires consideration for a differential diagnosis that includes amniotic fluid or venous air embolism, aspiration of gastric contents, sepsis, preeclampsia with pulmonary edema, and peripartum cardiomyopathy. Amniotic fluid embolism is a rare yet often lethal complication resulting from rapid cardiovascular collapse. It has been reported to occur under a variety of conditions, including Caesarean section, first and second trimester abortions, abdominal trauma, and up to 48 hours postpartum [16].

Classically, amniotic fluid embolism presents as sudden dyspnea and hypotension during labor or shortly postpartum. In 10% to 15% of cases, a bleeding diathesis is the initial manifestation. Seizure activity may be the initial sign in 10% to 20% of cases. Half of all patients die within the first hour. From reviewing this patient's clinical presentation, the diagnosis was unlikely. There was no evidence of aspiration episodes before dyspnea occurred. She did not experience fever, chills, local tenderness, productive cough, or other signs of infection, so a suspected sepsis-related dyspnea was unlikely. Abrupt hemodynamic change during peripartum may have played a role in this tragedy. Under normal circumstances, increases in cardiac output (30%-50%), blood volume (40%-50%), and oxygen consumption (20%), and reductions in systemic vascular resistance, are observed during pregnancy [17]. These changes begin early in pregnancy, reach a peak during the second trimester, and then remain relatively constant until delivery. Hemodynamic adaptations to pregnancy persist after delivery and gradually return to pre-pregnancy levels within 12 to 24 weeks after delivery. The physiologic events place a great demand on the cardiovascular system, and the greatest incidence of mortality occurs during the first several days after delivery because of right ventricular failure [18]. It is noted that a temporary increase in venous return may occur immediately after delivery because of the relief of caval pressure, which results in a substantial increase in ventricular filling pressures, stroke volume, and cardiac output, and may lead to clinical deterioration.

In this case, the increase in venous return after delivery may have contributed to acute aggravated pulmonary hypertension, even leading to pulmonary hemorrhage from the capillaries. Furthermore, the patient had expectorated a huge blood clot in a "trachea-bifurcation" shape via the endotracheal tube. Before it was removed, we struggled with her low tidal volume (below 50 ml) and high airway pressure in managing the mechanical ventilator. Our assumption above is supported by the bronchoscopy and transthoracic echocardiography findings (the D-shape of the inter-ventricular septum during both the systolic and diastolic phase). In addition, the presence of cyanosis can be explained by a right-to-left shunt through the persistence of the foramen ovale in the presence of high pulmonary resistance.

In conclusion, the clinical approach for the management of massive hemoptysis should be guided by the underlying etiology. Although the clinical history or physical examination may

provide important leads toward the diagnosis, a presumptive or premature diagnosis should be avoided. Confirmation of the diagnosis by chest radiograph, CT scan, or bronchoscopy is mandatory.

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右肺動脈起源異常引起之大量咳血—病例報告

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大量咳血是所有肺部急症中最可怕的一項且可以源自於多種原因。死亡率主要和潛在病因及咳血的程度有關。大量咳血具有生命危險，所以我們需要立即對病人施予搶救，保護呼吸道及嘗試治療潛在病因。很多因素可以引發大量咳血如支氣管擴張症、肺結核、肺膿瘍等慢性發炎及肺癌。血管方面的疾病如肺栓塞、肺部靜脈瘺管及肺部微血管擴張症等亦會引發大量咳血。左側或右側肺動脈異常起源自上升主動脈，是少見的先天性異常；如果沒有早期接受手術通常會致命。這種先天性異常在今日已可在產前檢查發現。我們報告一位 23 歲女性，其右肺動脈異常起源自上升主動脈，以產後大量咳血合併呼吸衰竭做為表現。為了確立大量咳血的原因，吾人必須進行仔細的病始詢問，身體檢查，同時合併考量胸部素片，甚至電腦斷層掃瞄，支氣管鏡及血管攝影的結果，以避免誤診的情形。*(胸腔醫學* ***2006; 21: 168-174)***

關鍵詞：右肺動脈起源異常，咳血

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Primary Teratoma of the Pons Presenting as Lentil Aspiration Pneumonia — A Case Report

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A 22-year-old female patient was brought to our emergency room presenting with an intermittent fever, chillness, and shortness of breath. She had been treated for an upper respiratory tract infection about 2 weeks prior to her visit to our hospital. Her fever did not remit and the dyspnea became significant with heavy yellowish sputum. She was admitted to our chest ward under the impression of pneumonia and suspected miliary tuberculosis (TB). Anti-TB drugs and antibiotics failed to improve her symptoms. She was transferred to the intensive care unit (ICU) twice due to acute respiratory failure. During the second stay at the ICU, open lung biopsy was performed, and the specimen showed diffuse granulation with vegetable content around the small airways and the alveoli, which strongly suggested food aspiration. An esophagogram revealed spillage of the contrast dye into the major airway, with only a scant amount of contrast dye seen in the esophagus. The pertinent evidence suggested that she had both a swallowing disturbance and an impaired cough reflex, leading to food aspiration. The possibility of a central neurological defect, which not only interfered with her swallowing function, but also her cough reflex, was considered. The brain magnetic resonance image (MRI), indeed, showed a solid tumor with a cystic component situated at the pons. The pathologic diagnosis of the partially removed tumor was immature teratoma. We report herein this rare case of brain tumor presenting primarily as respiratory symptoms without obvious neurological deficit. ***(Thorac Med 2006; 21: 175-181)***

Key words: teratoma, lentil aspiration pneumonia

Introduction

Food aspiration is a frequent consequence of dysphagia, posing a strong risk of developing pneumonia. There are many medical conditions that cause aspiration pneumonia, including neurological, gastrointestinal, and respiratory disorders [1-2]. Herein, we report a rare case of primary pontine teratoma presenting chiefly as pneumonia, rather than an obvious neurological deficit. The cause of the pneumonia, although suspected initially to be miliary tuberculosis, as seen on the chest X-ray films, was later confirmed to be lentil aspiration pneumonia, based on open lung biopsy.

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Case Report

A 22-year-old female student had been rather well before she started experiencing respiratory tract symptoms. She visited our hospital presenting with a fever, chills, and shortness of breath for about 2 weeks. The initial vital signs were as follows: body temperature 37°C, pulse rate 126/min, respiratory rate 18/min, and blood pressure 103/62 mmHg. The physical findings on chest auscultation were diffuse wheezing and crackles. There was no obvious neurological deficit when she was first seen in the emergency room. Laboratory data were mostly within normal limits, except for leukocytosis (white blood cell count: 20650 × 10^3/μl). The chest radiograph showed that there were multiple small nodules in both lungs, especially in the lower lung fields, and a mottled opacity in the left upper lung field (Figure 1). She was admitted under the impression of pneumonia and suspected miliary tuberculosis. A combination of antibiotics and anti-tuberculosis therapy was ineffective, and she developed acute respiratory failure on the third day of admission. Her arterial blood gas at room air was pH: 7.449, PCO_2: 27.1 mmHg, PO_2: 48.5 mmHg, and HCO_3: 18.9 meq/L. During her stay at the ICU, serology studies, including cryptococcal antigen, legionella, human immunodeficiency virus, and mycoplasma, all yielded negative results. The sputum smears for acid-fast stain (AFB) and cytology were also negative. She returned to the ordinary ward after being successfully weaned from the ventilator.

The anti-microbial treatment was shifted to those drugs that might cover legionellosis, *Pneumocystis carinii*, and tuberculosis. However, she developed a spiking fever again, followed by recurrent respiratory failure the day after her nasogastric tube was removed. She was then transferred back to the ICU. High-resolution computed tomography (HRCT) of the chest revealed irregular consolidated patches and micronodules in both lungs (Figure 2). The follow-up open lung biopsy showed the pattern of aspiration pneumonia, presenting with multiple discrete ill-defined foci of mixed acute and chronic inflammation involving variously-sized bronchioles and their surrounding alveoli (Figure 3A). Disintegrated components of vegetable tissue eliciting a foreign body-type tissue reaction were noted in the bronchiolar lumens and in the adjacent pulmonary parenchyma. In addition to the fragments of a non-specific cellulose-comprised wall, characteristic particles of lentil pulses were seen in

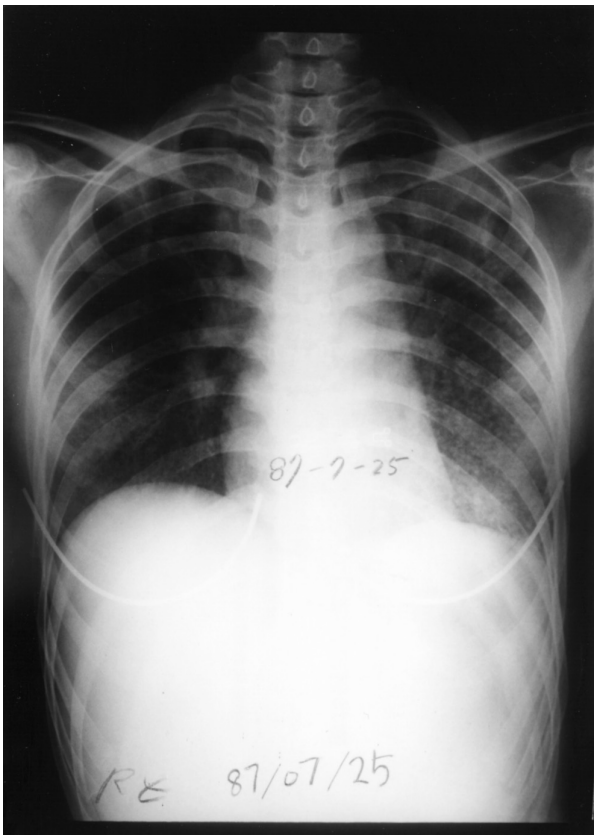

Fig. 1. Chest radiograph shows that there were multiple small nodules in both lungs, especially in the lower lung fields, and a mottled opacity in the left upper lung field.

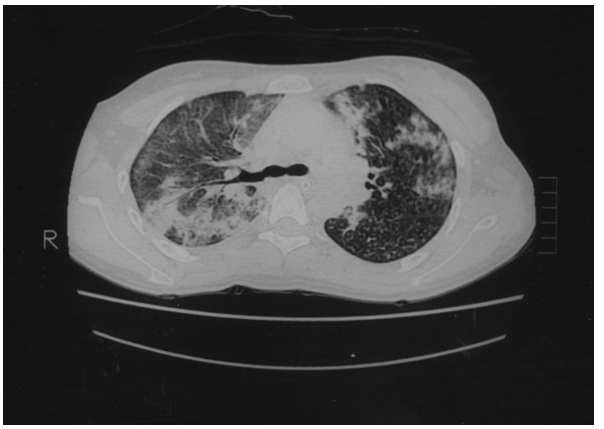

Fig. 2. CT scan of the chest reveals irregular consolidated patches and micronodules in both lungs.

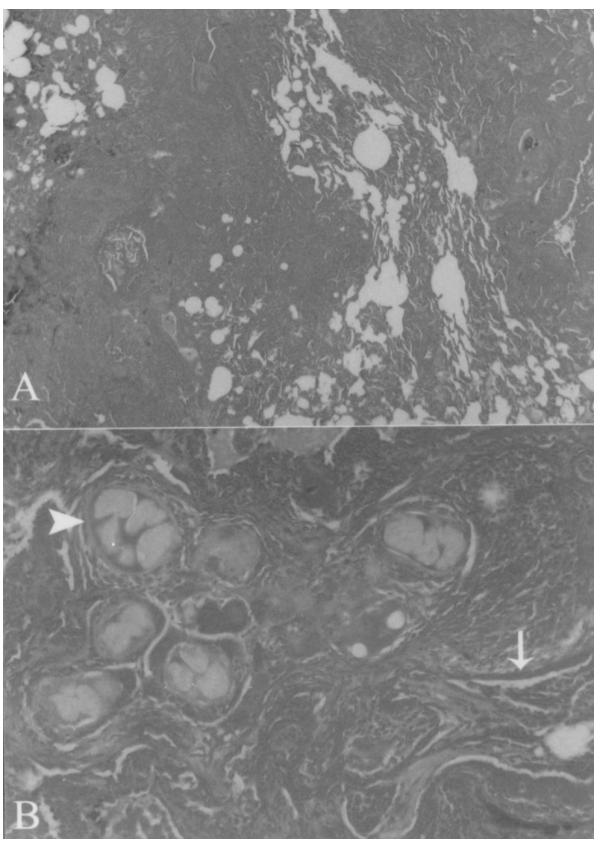

Fig. 3. A: The sections reveal the pattern of aspiration pneumonia, presenting with multiple discrete ill-defined foci of mixed acute and chronic inflammation involving variously-sized bronchioles and their surrounding alveoli. (H&E 40X) B: Lentil pulses (arrowhead) engulfed by multinucleated giant cells were found in a partially destroyed small bronchiole (arrow). (H&E 200X)

places (Figure 3B). Therefore, a swallowing disturbance was suspected to have resulted in the lung lesions. After weaning from the ventilator, she was scheduled for an esophagographic examination when her consciousness was clear. Throughout the examination, the patient had no cough reflex, although the contrast dye spilled into her tracheo-bronchial tree (Figure 4). This suggested that the patient had both a swallowing and a cough disturbance. She was immediately restricted to nasogastric feeding. A brain MRI disclosed a solid tumor with a cystic component situated at the dorsal aspect of the pons (Figure 5). The patient underwent craniotomy with a partial removal of the brain tumor and decompression surgery. The surgical pathology revealed an immature teratoma (Figure 6). She received both chemotherapy and radiotherapy, and was discharged for follow-up at the outpatient clinic with complete

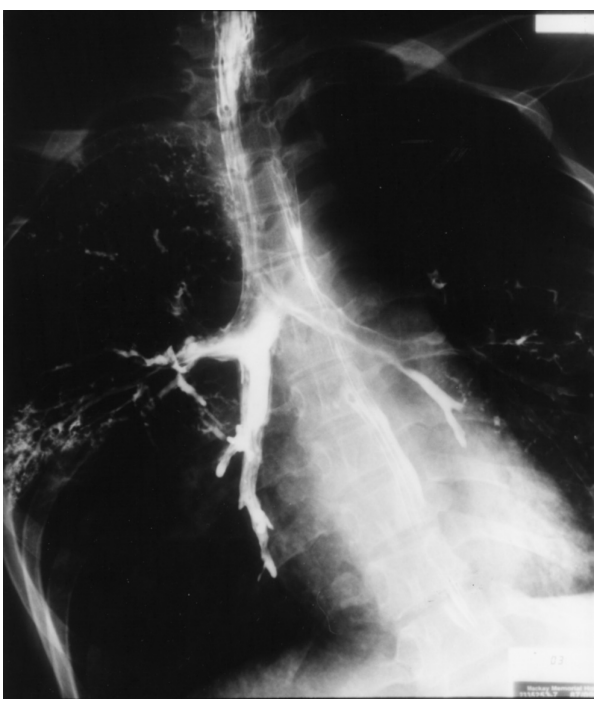

Fig. 4. The esophagogram shows spillage of the contrast dye into the tracheo-bronchial tree.

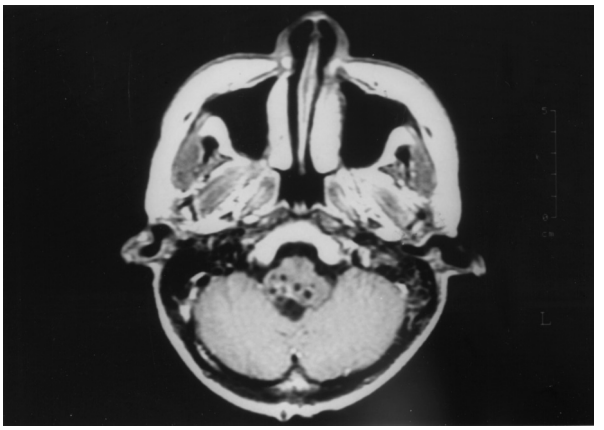

Fig. 5. Axial T1-weighted image shows a solid tumor with a cystic component at the pons.

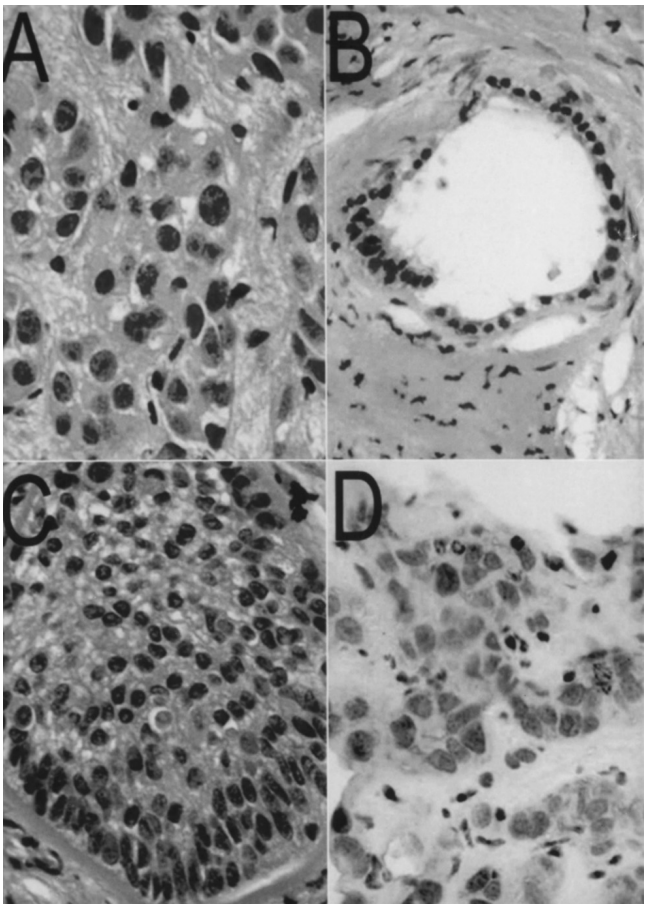

Fig. 6. A: The brain tumor reveals small nests of polygonal neoplastic cells set in a fibrous stroma. (H&E 200X) B: A gland-like structure lined with low-to-modest columnar tumor cells is occasionally seen in the brain tumor. (H&E 200X) C: Squamous epithelial differentiation is present in the brain tumor. (H&E 200X) D: The tumor cells show immunoreactivity for placental alkaline phosphatase (PLAP). (Immunostain 200X)

recovery of her swallowing function.

Discussion

Conditions that predispose to aspiration include: 1) consciousness impairment, resulting in a compromise of the cough reflex and glottic closure, 2) dysphagia from neurological deficits, 3) disorders of the upper gastrointestinal tract, 4) mechanical disruption of the glottic closure or cardiac sphincter, 5) pharyngeal anesthesia, and 6) miscellaneous conditions such as protracted vomiting, large volume tube feeding, feeding gastrostomy, and the recumbent position [2]. Dysphagia can occur in all age groups and its incidence reaches 2 peaks in infants and the elderly [3]. There are many medical conditions that may cause dysphagia, including neurological disorders, myasthenia gravis, myopathies, oropharyngeal or esophageal tumors, Zenker's diverticulum, achalasia, pharyngeal web, mediastinal masses, or even cervical spur, [1].

Cough is a particularly important defense mechanism for preventing aspiration. In fact, a markedly decreased cough reflex was observed in elderly patients with aspiration pneumonia [4]. Evidence to date suggests that the cough center is diffusely located in the brain stem, which is also the center for controlling swallowing. The reason why patients with neurogenic dysphagia are prone to aspiration is that they usually cannot cough or cough ineffectively. In some neurological diseases, dysphagia may persist for a long period of time without being complained of by the patients [5], as shown in our case. This so-called "silent aspiration" means that the entry of material into the airway does not always trigger

a cough [6]. By contrast, it has been reported that patients with neurogenic dysphagia do not have a reduced sensitivity to triggering cough [7]. In our patient, contrast medium spilled over into the trachea without causing any cough during the esophagographic examination. This suggested an existing central nervous system (CNS) lesion causing neurogenic dysphagia that abolished the cough reflex. Indeed, she was later proved to have a pontine teratoma. Primary intracranial germ-cell tumors are rare (approximately 3.1% of all primary brain tumors in Japan [8]) and they usually involve children and young adults. The tumors are pathologically divided into germinoma and non-germinoma, which include teratoma, embryonal carcinoma, endodermal sinus tumor, and choriocarcinoma [9]. Intracranial germ-cell tumors display specificity at the site of origin. Ninety-one percent arise along the midline from the suprasellar cistern (37%) to the pineal gland (48%), and an additional 6% involve both sites [10].

In addition, aspirated food or gastric contents may lead to chemical or bacterial pneumonia. Occasionally, the aspiration of more specific types of food, such as beans in our case, will produce a distinct type of pneumonia that differs from ordinary aspiration pneumonia by its nodular and granulomatous character [11]. When patients survive the acute stage of lentil pneumonia, a progression of the lesion from the acute stage to the granulomatous stage takes place. Pathologically, the granulomatous lesions, consisting of epithelioid and giant cells surrounding a solid or caseating center, resemble those seen in sarcoidosis or tuberculosis. At this stage, the radiographic picture becomes suggestive of miliary tuberculosis [12-13]. The lesions are mostly attributed to inhalation or aspiration of leguminous seeds. The structure of a leguminous seed is that of a shell or spermoderm surrounding the cytoledon. The shell is made up of cellulose. In 1 study, it was concluded that the granuloma-inducing substance was the cellulose component of the lentil particles [12]. Our patient had multiple patches or nodular lesions. The centrally located small bronchi or bronchioles are surrounded by foreign body granulomas with acute and chronic inflammatory cells and an infiltration of fibrosis. Numerous food particles can be seen. Portions of legume seeds that are better markers of food aspiration are prominent.

Lentil aspiration pneumonia usually manifests on chest radiographs with small (1-3 mm) nodular opacities [14-15]. Larger nodules (up to 1.0 cm in diameter), as seen in 1 case report, are less common [16]. The radiological findings in our patient showed a pattern of diffuse miliary nodules measuring less than 0.5 mm in diameter and mimicking miliary tuberculosis. The differential diagnosis should include fungal disease, histiocytosis X, hypersensitivity pneumonitis, interstitial fibrosis, some primary and metastatic malignant conditions, pneumoconiosis, and granulomatous disease, such as sarcoidosis or tuberculosis [17]. Lentil aspiration pneumonia manifesting on high-resolution CT may show centrilobular nodular and branching opacities (a tree-in-bud pattern [18]).

Although as a rare case of pulmonary infiltrates, lentil pneumonia should be suspected in specific patients, such as infants, chronic alcoholics, the mentally retarded, senile and debilitated patients, or those with seizures, i.e., those patients most likely to be susceptible to a dysfunction in swallowing [19]. In addition, obstetric and emergency surgical procedures, tracheoesophageal fistula, congenital esophageal stenosis, or achalasia should be taken into consideration [12].

Although lentil pneumonia is an infrequently

occurring entity, it may need to be included in the gamut of diffuse miliary nodules in patients with the clinical picture of recurrent pneumonia, a history of chronic hospitalization, and/or swallowing dysfunction, as shown in this case of primary pontine teratoma. In this patient, the brain tumor presented primarily as respiratory symptoms rather than an obvious neurological deficit.

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原發性橋腦畸胎瘤併吸入性豆肺炎：病例報告

黃呈誼　呂衍達*　陳碧芳**

原發性橋腦畸胎瘤併吸入性豆肺炎於臨床上非常罕見，我們報告一位二十三歲女性主訴發燒及呼吸困難達兩週之久。胸部 X 片顯示雙側網狀小節結病變併實質化病灶。一開始的臨床診斷是肺炎暨疑似肺結核，經廣效性抗生素暨抗結核菌藥物治療後，病況未見改善，患者因呼吸衰竭反覆進入加護病房兩次。因病因不明，我們實施左下肺葉切片手術，病理報告顯示為吸入性豆肺炎。食道攝影發現有吞嚥障礙併缺乏咳嗽反應，至此認為患者有中樞神經病變。經核磁共振檢查及腦切片檢查確定為原發性橋腦畸胎瘤。我們報告此一罕見腦幹腫瘤病例，一開始並沒有明顯神經學症狀，而以吸入性豆肺炎來表現，並做文獻回顧與討論。*(胸腔醫學 **2006; 21: 175-181**)*

關鍵詞：畸胎瘤，吸入性豆肺炎

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Pulmonary Metastatic Malignant Melanoma with Endobronchial Involvement: A Case Report and Literature Review

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Endobronchial metastasis is found in 2-5% of patients at autopsy who die from extrathoracic cancer. Malignant melanoma has a tendency to metastasize to the lung during the course of tumor growth, but endobronchial metastasis is rare. We report a case of pulmonary metastatic malignant melanoma with endobronchial involvement presenting with cough and hemoptysis, which was diagnosed by fiberoptic bronchoscopy with bronchial biopsy. The specific bronchoscopic picture highlights the value of bronchoscopy in the differential diagnosis of endobronchial tumor. The relevant literature is reviewed, including clinical manifestations, image presentations, diagnosis, and treatment options. ***(Thorac Med 2006; 21: 182-189)***

Key words: endobronchial metastasis, malignant melanoma, fiberoptic bronchoscopy

Introduction

Endobronchial metastasis from nonpulmonary tumors occurs in 2-5% of the autopsy cases of patients who have died from extrathoracic cancer [1]. Common primary sites included the kidney, colorectum, and breast [1-3]. Malignant melanoma has a tendency to metastasize to the lung during the course of tumor growth, but endobronchial involvement is rare [4]. We report a case of pulmonary metastatic malignant melanoma with endobronchial involvement presenting with cough and hemoptysis. The specific bronchoscopic picture, which provided a valuable clue for the final diagnosis, is presented. We also reviewed the English literature on Medline from 1966 to 2005 for relevant reports, letters and articles regarding malignant melanoma with endobronchial metastasis.

Case Report

A 53-year-old man was admitted to a university hospital because of cough with hemoptysis occurring episodically for 1 month. He was a heavy smoker, smoking 1 pack per day for more than 30 years. He had been well until 6 months before admission, when he had a sudden onset of cough and blood-tinged sputum. He visited a local hospital where chest radiography (CXR) showed an ill-defined lesion near the right hilum. His symptoms subsided a few days later without

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any specific treatment. One month before admission, he suffered from an episode of hemoptysis. He was in Mainland China at that time, where he received a CXR which showed a right hilar nodule. He visited the outpatient clinic at a university hospital after coming back to Taiwan, and was admitted for further management. He had no history of fever, chills, night sweats or weight loss.

On admission, his temperature was 36.4°C, pulse was 76 beats per minute, and respiratory rate was 20 breaths per minute. The patient's blood pressure was 118/70 mmHg, and the oxygen saturation was 98% while breathing ambient air. On physical examination, the breathing sounds were clear, and the heart sounds were normal. There was no lymphadenopathy, no hepatosplenomegaly, and no abnormal skin lesions. Laboratory data showed that the white blood cell count was 5240 per mm^3, with 45.4% polymorphonuclear leukocytes, and 44.5% lymphocytes. The hemoglobin was 15.8 mg per 100 ml, and the platelet count was 188,000 per mm^3. Biochemistry was all within normal limits. Sputum cytology was negative for malignant cells in 3 consecutive samples. The CXR showed a lobulated mass near the right hilum and a round nodule adjacent to the left hilum (Figure 1). Computed tomography (CT) of the chest showed a 4.7 cm lobulated mass at the anterior segment of the right upper lobe with some satellite nodules, and a 2.4 cm large nodule at the superior segment of the left lower lobe adjacent to the left hilum (Figure 2). Lymphadenopathy was noted at the right paratracheal area. The CT scan also showed multiple ill-defined low-density lesions at the hepatic dome. Fiberoptic bronchoscopy showed an irregular, dark brownish endobronchial tumor completely obliterating the right B3b bronchus, with easy touch bleeding; no mucosa infiltration was seen (Figure 3). The pathology of the bronchial biopsy demonstrated uniform tumor cells with hyperchromatic nuclei, prominent nucleoli,

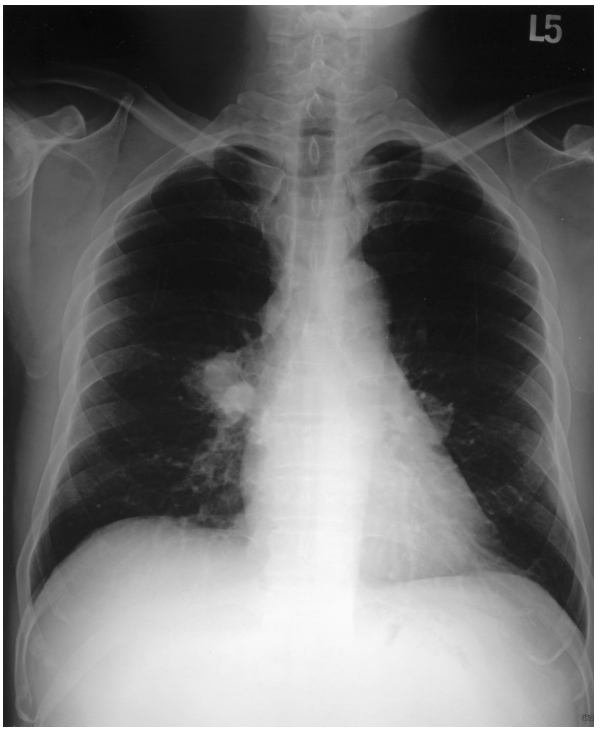

Fig. 1. Chest radiograph, posterior-anterior view, showed a lobulated mass near the right hilum and a round nodule adjacent to the left hilum.

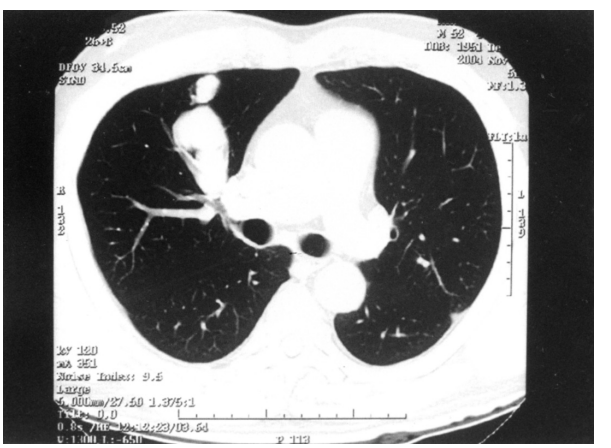

Fig. 2. Computed tomography (CT) of the chest showed a 4.7-cm lobulated mass at the anterior segment of the right upper lobe, with some satellite nodules.

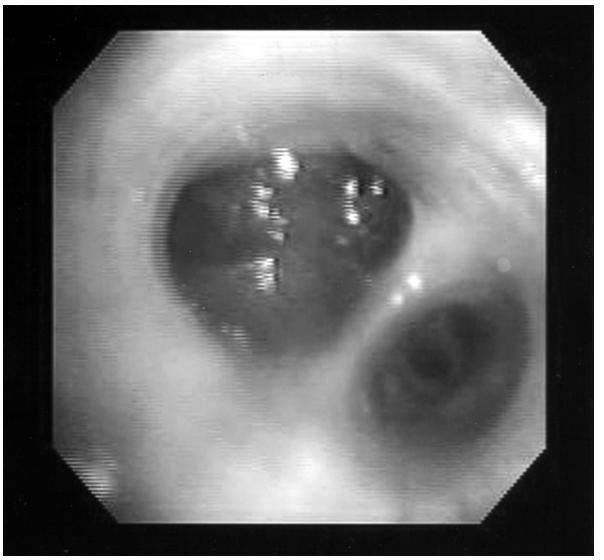

Fig. 3. A bronchoscopic examination showed a dark brownish endobronchial tumor completely obliterating the right B3b bronchus.

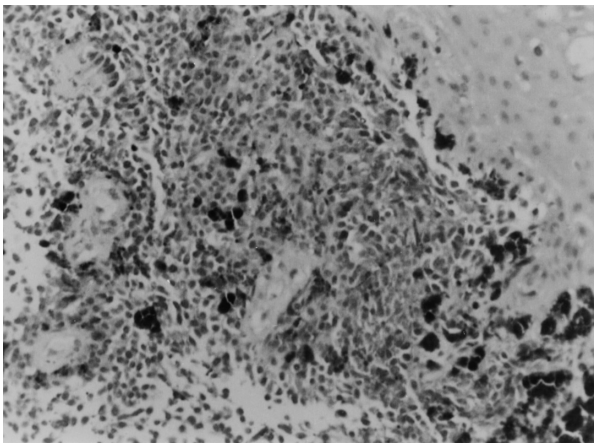

Fig. 4. The pathology of the bronchial biopsy demonstrated uniform tumor cells with hyperchromatic nuclei, prominent nucleoli, and melanin-laden cytoplasm (H&E stain, 100X).

melanin-laden cytoplasm in a sheet-like pattern and surface squamous metaplasia. The immunohistochemical stain revealed positive for HMB-45 (Figure 4), and negative for thyroid transcription factor-1, leukocyte common antigen, and cytokeratin. Metastatic malignant melanoma was diagnosed. The pathology of the CT-guided biopsy revealed the same results. The whole body bone scan was negative. Magnetic resonance imaging (MRI) of the brain revealed no definite lesion. The dermatologist performed a thorough check-up of the body surface area, and only a giant congenital melanocytic nevus at the buttocks was noted, with no evidence of cutaneous melanoma macroscopically. He received 2 courses of immunotherapy with interleukin (IL)-2 (Proleukin). During the course of IL-2 therapy, side effects such as flu-like symptoms, fever, myalgia, and skin rash developed. The symptoms and signs gradually subsided after symptomatic treatment and dosage adjustment. After completing 2 courses of immunotherapy, he was discharged and regularly followed up at an oncology clinic.

Discussion

Endobronchial metastasis is defined as a metastatic lesion in a major bronchus, which is both clinically and radiologically similar in appearance to primary bronchogenic carcinoma [5]. As previously reported in cases of pulmonary metastasis from malignant melanoma, endobronchial involvement is very uncommon, [6-7]. Salud *et al.* reviewed 2,389 bronchoscopic procedures with bronchial biopsy over a 9-year-period, and reported that the overall incidence of endobronchial metastasis from nonpulmonary tumors was 2.3%, and only 2 of them were from malignant melanoma [6]. Metastatic melanoma was occasionally found clinically preceding the detection of the primary lesion [8].

The clinical and roentgenographic features of malignant melanoma with endobronchial metastasis were indistinguishable from those of primary bronchogenic carcinoma [9]. The com-

mon clinical manifestations included cough, hemoptysis, and dyspnea; however, some patients had no symptoms [6, 10]. In cases without any clinical manifestations of pulmonary metastasis, it is often difficult to diagnose endobronchial involvement if there has been no bronchoscopic examination. A thorough literature review was conducted that disclosed a total of 16 cases of malignant melanoma with endobronchial metastasis, including the present case [1, 2, 6, 9-14]. The clinical characteristics of these cases are summarized in Table 1.

There are 5 possible routes for carcinoma to spread to the bronchus: 1) parenchymal lung metastasis with bronchial invasion, 2) a mediastinal tumor with direct extension, 3) direct lymphatic spread to the bronchial wall, 4) a transbronchial aspiration of cancer cells, and 5) hematogeneous spread to the bronchial wall [5, 9]. Because the chest CT scan of our patient showed 2 pulmonary lesions and multiple hepatic metastatic tumors, we inferred that the route of metastasis in this case was probably hematogeneous. The diagnosis of endobronchial metastasis to a major airway is readily feasible by bronchoscopic examination. In the Shepherd series, 25 out of 90 surgical patients with pulmonary metastasis had endobronchial tumors, and all of the lesions were readily visible bronchoscopically [2]. Thus, bronchoscopy is valuable in establishing the diagnosis of metastatic endobronchial tumor. The bronchoscopic picture of metastatic malignant melanoma with endobronchial involvement may be a dark pigmented endobronchial tumor, which is the most commonly seen, diffuse melanosis of the airways, and sometimes a grossly amelanotic lesion [1, 10, 12-14]. When lacking pigmentation, metastatic melanoma in the airway may be confused with other endobronchial lesions, including primary bronchogenic carcinoma [10].

The treatment results for metastatic malignant melanoma remain disappointing. Both the clinical outcomes and management of metastatic malignant melanoma with and without endobronchial involvement, and of the classic forms, are the same [6, 15]. The search for the primary site must be clinically oriented, and consist of a thorough examination of the skin and mucosa (nasopharygeal, ophthalmologic and genitourinary), and the area of past surgical excision of skin lesions [15]. Malignant melanoma presenting as metastatic disease without an apparent primary site occurs in about 4% of cases, and is referred to as occult primary melanoma. One study revealed that survival was longer in this group of patients, which may reflect an intrinsically superior host-tumor interaction [16]. Some investigators have reported that the resection of isolated pulmonary metastases should be performed unless other extrapulmonary lesions are present [15, 17-20]. Harpole *et al.* analyzed 945 cases with pulmonary metastatic melanoma and suggested that the complete resection of isolated pulmonary metastases, in addition to chemotherapy in selected cases, can increase 5-year survival from 4% to 20% [17]. Gorenstein et al. reviewed the clinical pictures of 56 patients with a known history of malignant melanoma with a suspicion of pulmonary metastases and concluded that resecting pulmonary metastases can preferentially influence their long-term outcome [19]. Tafra *et al*. reviewed the database of 984 patients with metastatic malignant melanoma involving the lung or thorax. The multivariate analysis showed that the surgical resection of the pulmonary metastases and immunotherapy were both independent predictors of survival. They concluded that surgical resection plus adjuvant immunotherapy is the treatment of choice for selected patients with pulmonary metastatic malignant

Table 1. Summary of Reported Cases of Metastatic Malignant Melanoma with Endobronchial Involvement

Reference	Year	No. of patients	Primary tumor site (n)	Symptoms (n)	Pattern in CXR (n)	Location (n)	Bronchoscopy Finding (n)	Therapy (n)	Survival (mo)
Schoenbaum [11]	1971	1	Skin	Hemoptysis	Infiltrate	LLL*	Negative	Surgery	N/A
Sutton [10]	1974	3	Skin(3)	Cough (2) Wheeze (1) Hemoptysis(1) Dyspnea (1) None (1)	Mass (1) Atelectasis (2) Multiple nodules (1)	LLL (1) Right main (1) Bilateral bronchial trees (1)	An amelanotic mass (1) A large melanotic mass(1) Diffuse melanosis, no visible mass (1)	C/T (3)	N/A
Braman [1]	1975	1	Skin	Dysphagia	Normal	Trachea#	N/A	Supportive	N/A
Fitzgerald [9]	1977	1	Skin	Cough	Nodule	N/A	N/A	C/T	10
Shepherd [2]	1982	4	skin	N/A	N/A	N/A	N/A	Surgery (2)	4-11
Harada [14]	1983	1	Intraocular, choroid	None	Solitary nodule	RML Br.	A glossy black tumor	Surgery Immunotherapy	16
Kim [13]	1988	1	skin	Cough Hemoptysis Wheeze	Atelectasis	LLL Br.	A fungating dark grayish mass	C/T	N/A
Salud [6]	1996	2	Skin	N/A	N/A	Bronchial trees	N/A	N/A	12-24
Ondo [12]	2000	1	gum	None	Solitary nodule	Right B6	A polypoid black tumor	Surgery	9
Present case	2005	1	unknown	Cough Hemoptysis	Mass Nodule	Right B3	An irregular dark brownish tumor	Immunotherapy	> 6

n: numbers of patients; N/A: non-applicable; Br.: bronchus; RML: right middle lobe; LLL: left lower lobe; B6: superior segment bronchus; B3: anterior segment bronchus; C/T: chemotherapy.

*Bronchogram showed a mass protruding a contour defect in the LLL bronchus, distal to the origin of the superior segment.

#Postmortem examination showed a large tumor in the mediastinum, with trachea and both main bronchi involvement.

Reference: [1, 2, 6, 9-14]

melanoma [20]. However, the patients in the above studies were highly selected, and it is unlikely that there will ever be randomized clinical trial data available to prove the effectiveness of such interventions [21].

If surgical resection is not feasible in patients with multiple metastases, chemotherapy alone should be considered. Single agents, such as dacarbazine, temozolomide, and fotemustine continue to be widely used in the systemic chemotherapy of metastatic melanoma, because of their fairly low toxicity and simplicity of administration, and, furthermore, there is no survival benefit with combination chemotherapy [22]. Immunotherapy, particularly high-dose IL-2, has shown a response rate of approximately 15%, and it is often long-lasting. A small but finite cure rate of 5% has been reported with high-dose IL-2 [23].

In summary, we report a case of pulmonary metastatic melanoma with endobronchial involvement with an unknown primary site. The specific bronchoscopic picture highlights bronchoscopy as a valuable and expeditious method of establishing a diagnosis. Our experience from this case suggests that pulmonary metastatic malignant melanoma with endobronchial involvement should be highly suspected when a dark-colored endobronchial tumor is seen bronchoscopically, even though no primary lesion was found.

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肺部轉移性惡性黑色素細胞瘤合併支氣管內侵犯—一病例報告與文獻回顧

劉偉倫　古世基　楊泮池

罹患肺外惡性腫瘤而造成死亡的病人，約有2~5%在屍體解剖時會發現有支氣管內轉移。惡性黑色素細胞瘤在生長的過程中常有轉移至肺部的現象，但是支氣管內轉移則是非常罕見。我們報告一個肺部轉移性惡性黑色素細胞瘤合併支氣管內侵犯的病例，病人以咳嗽及咳血為主要表現，並經由支氣管鏡檢查及支氣管切片確立診斷。藉由這位病人其腫瘤在支氣管鏡下的特殊表現，彰顯了支氣管鏡對於支氣管內腫瘤的鑑別診斷之重要性。此外，我們並就肺部轉移性惡性黑色素細胞瘤合併支氣管侵犯之臨床表徵，影像學表現，診斷方式，以及治療的方向等方面，回顧相關的文獻報告。*(胸腔醫學* ***2006; 21: 182-189****)*

關鍵詞：支氣管內轉移，肺部轉移性惡性黑色素細胞瘤，支氣管鏡

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Scimitar Syndrome Variant Causing Massive Hematemesis — A Case Report

Renin Chang, Ruay-Sheng Lai, Chien-Wei Hsu, Pei-Loon Kang*

Patients with symptomatic scimitar syndrome usually suffer from either respiratory insufficiency and/or heart failure due to pulmonary hypertension, or recurrent pulmonary infections, especially in the right lower lobe, most likely due to an abnormal arterial supply and venous drainage, and hypogenesis of the right lung. But aberrant pulmonary venous drainage to the esopheal venous plexus, leading to variceal bleeding, is rarely a presentation of scimitar syndrome. Herein, we report a 17-year-old man presenting with several episodes of variceal bleeding due to such a partial anomalous pulmonary venous drainage. Successful surgical repair was performed by a reimplantation of the anomalous vein to the left atrium. After the repair, the patient no longer suffered from hematemesis episodes. ***(Thorac Med 2006; 21: 190-195)***

Key words: esophageal variceal bleeding, hematemesis, partial anomalous pulmonary venous return, scimitar syndrome, scimitar syndrome variant

Introduction

The scimitar syndrome is a rare congenital anomaly that is defined as total or partial anomalous venous drainage to the inferior vena cava (IVC). It has been a recognized entity for over a century, especially due to its felicitous nomenclature. Halasz and colleagues [1] described a peculiar "scimitar-shaped" vein found on X-ray films. This picture is most familiar to radiologists nowadays. In addition, the term "scimitar syndrome variant" has also been employed to represent a similar anomalous venous drainage to an atypical end-point, especially the left atrium [2]. In the classic form, associated common findings include partial agenesis or hypoplasia of the right lung and right pulmonary artery, and an abnormal systemic blood supply to at least part of the right lung, most frequently from branches of the abdominal aorta to the posterior basal segment of the lower lobe. We report a 17-year-old healthy male with a serpentine right inferior pulmonary vein draining into the right atrium via the esophageal venous plexus, leading to varices and a dreadful massive hematemesis. Angiography documented this unusual route of venous return. This case is presented to highlight the fact that one has to keep an open mind when dealing with esophageal varices bleeding, and that a detailed survey should be performed before initiating

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treatment.

Case Report

A 17-year-old man was referred to our hospital for evaluation of an abnormal shadow on a chest radiograph (Figure 1) and repeated bouts of massive hematemesis. He had been diagnosed with scimitar syndrome by chest X-ray and computed tomography of the chest 3 years ago, along with the presentation of chronic, mild hemoptysis. Only symptomatic treatment was applied. He was used to this condition, because hemoptysis can resolve spontaneously. There was mild exertional shortness of breath in daily activities. He did not drink alcoholic beverages, smoke cigarettes, or use drugs. He had no history of surgery, medication or allergy. In the most recent 3 days, he had had several bouts of massive hematemesis without aura or an associated trigger such as chest pain, intense retching or coughing. There was an estimated 300 ml of fresh blood in every episode. Melena was also noted. Physical examination revealed a well-developed, healthy man with normal findings, except decreased breathing sounds in the right chest. The vital signs were normal, despite a heart rate of 110 beats per minute. Esophagoscopy disclosed 4 blue varices, in forms of 2 to 3, with many red color signs in the lower third to upper third of the esophagus (Figure 2). Abdominal sonography showed a normal appearance of the liver, spleen and pancreas. Computed tomography of the chest revealed hypogenesis of the right lung, including both the pulmonary arteries and bronchial trees. In addition, there was partial aberrant right pulmonary venous drainage of the right lower lobe to the collateral veins in the esophagus, causing severe esophageal varices. Angiography confirmed the diagnosis of scimitar syndrome with 1 anomalous pulmonary vein draining into the esophageal venous plexus, leading to varices (Figure 3). Angiography also noted a normal

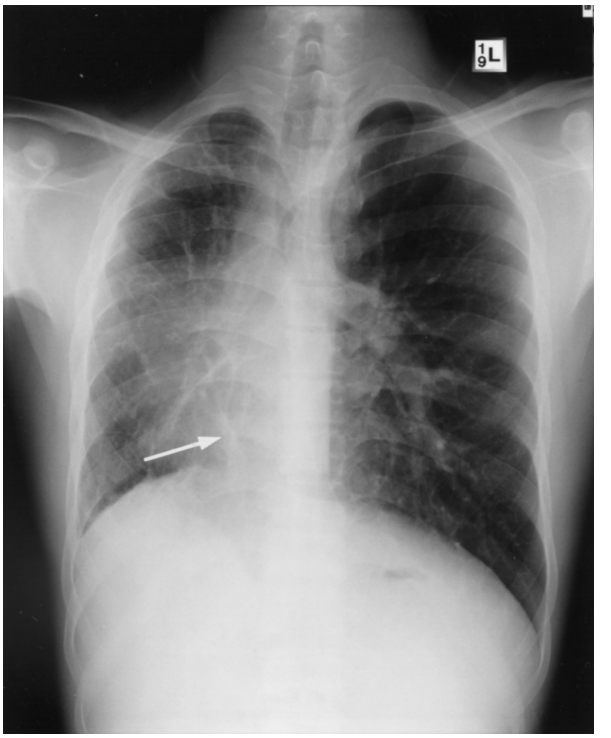

Fig. 1. Frontal X-ray film at this admission, showing a volume reduction of the right thorax, dextroposition of the cardiomediastinal structure and a scimitar vein along the right-side heart border (arrow), which indicates an anomalous pulmonary venous return.

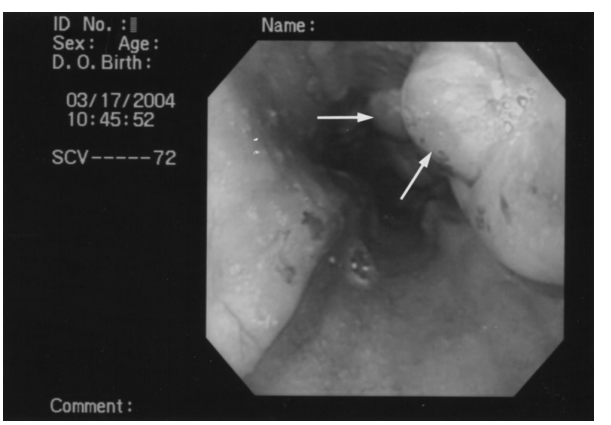

Fig. 2. Esophagoscopy, showing twisted esophageal varices (arrow) in the upper third to lower third portion of the esophagus, with many red color signs. The gastric content was relatively clear.

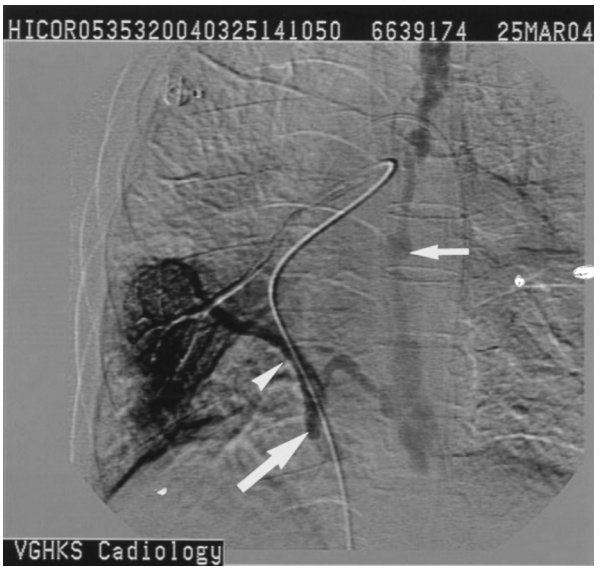

Fig. 3. Super-selective angiogram with injection from the right hypoplasticpulmonary artery at the venous phase. The partial anomalous pulmonary venous return, the so-called scimitar vein (arrowhead), drains into the esophageal varices (arrows) as a collateral route of return. Note the blind end (large arrow), which may indicate stenosis to the IVC.

arterial supply to the right lung in this case. No associated cardiovascular anomalies could be found in either the echocardiography or cardiac angiography. In combining the esophagoscopy and angiography results, a diagnosis of scimitar syndrome variant-related esophageal variceal bleeding was documented. Subsequent bronchoscopy revealed smaller orifices in the right lung without evidence of endobronchial lesions. After surgical correction of the extra-cardiac left-to-right shunt by a re-implantation of the right anomalous pulmonary vein into the left atrium, this patient became symptom-free from hematemesis.

Discussion

In this patient, there were findings consistent with some features of scimitar syndrome, which was first reported by Cooper in 1836 with a description of a case of an "imperfect development of the right lung with malposition of the heart". Halasz and colleagues first used the word "scimitar" in 1956 to depict the anomalous pulmonary vein draining into the inferior vena cava on the plain chest radiograph [1]. Dr. Catherine A. Neil was the first to utilize the term "scimitar syndrome" in a manuscript in 1960 [3]. Scimitar syndrome is a rare, complex congenital entity comprising anomalies in both cardiovascular and pulmonary aspects. The incidence is probably 1 to 3 of 100,000 live births [4]. Scimitar syndrome comprised only 3% to 5% of all cases of partial anomalous pulmonary venous drainage in one study [5]. Because many patients are asymptomatic and physicians may not be familiar with this syndrome, many cases are probably overlooked. Scimitar syndrome is characterized mainly by an anomalous pulmonary venous drainage of part or entire the right lung into the IVC. Other common associations included hypoplasia of the right lung (both airway and vasculature), dextroposition of the cardiomediastinal structures, and an anomalous systemic arterial supply to the lower lobe of the right lung from the aorta [3, 6]. Our case showed an anomalous right lower pulmonary venous drainage into the IVC and esophageal venous plexus with a normal arterial supply from the right pulmonary artery. The etiology of these malformations is unknown, but is believed to be an abnormal development of the entire right lung bud early in embryogenesis. The reason for the preference for the right lung is not understood, but "left-side scimitar" is extremely rare [7]. Approximately 25% of patients with scimitar syndrome have cardiac anomalies, most commonly atrial septal defects, but sometimes-ventricular septal defects, tetralogy of Fallot, and coarctation of the aorta [8-9]. In our case, there was no other associated cardiovascular anomaly. Dupuis *et al*. [4, 10]

reported that there is a distinction between the "infantile" and "adult" forms of scimitar syndrome in morbidity and mortality. The former refers to patients diagnosed in infancy and usually complicated with potentially fatal congenital anomalies, while the latter, diagnosed after 1 year of age, is usually asymptomatic and does not require invasive therapy. About a quarter of patients are symptomatic in the newborn period, presenting with cardiopulmonary distress. The pathophysiologic feature has been demonstrated to be pulmonary hypertension. The intra-cardiac left-to-right shunt (if associated with congenital heart defects, such as atrial septal defect), extra-cardiac left-to-right shunt (the systemic arterial supply to the right lung, the anomalous pulmonary venous return to the right atrium), and sometimes, the partial obstruction of the anomalous pulmonary venous drainage, may contribute to pulmonary hypertension [11-12]. The other presentation is associated with recurrent pulmonary infections during young adulthood [6, 13]. Repeated bronchitis or pneumonia occurs most often in the right lower lobe, which is the region most likely to have abnormal arterial and venous supplies in scimitar syndrome.

On frontal chest X-ray films, an anomalous pulmonary vein descends downward and medially along the right heart border to the diaphragm, resembling a Turkish sword, and is referred to as a scimitar sign. Although this is an important and familiar diagnostic finding for scimitar syndrome, it is not absolutely specific [14]. Some alternative conditions had been described, such as a scimitar vein returning to both the IVC and the left atrium [15-16]. Morgan and Forker [17] and Goodman *et al*. reported cases illustrated by a scimitar sign with a normal venous return to the left atrium. However, it is important to note that a dextroposition of the heart, particularly in association with hypoplasia of the right lung, is a common observation with this syndrome, and may be the first clue to the diagnosis. This case may be the first, so far as we know, demonstrating an anomalous venous return to the left atrium via the esophageal venous plexus, causing variceal bleeding.

Esophageal variceal bleeding is 1 of the most dreadful clinical entities in upper gastrointestinal hemorrhage. It has been long recognized. Traditionally, vascular resistance increases in cirrhosis, non-cirrhotic portal fibrosis, idiopathic portal hypertension, extra-hepatic portal vein obstruction, Budd-Chiari syndrome, and other portal hypertensive disorders, inducing blood congested in the splenic and mesenteric veins that lie upstream of the portal trunk. The stagnated blood must "find its way out", i.e., it has to escape from the native route, creating collateral vessels that involve veins of the esophagus, stomach, pelvis, retroperitoneum, liver, abdominal wall, and other areas. Our case demonstrated a rare cause of esophageal varices due to partial anomalous pulmonary drainage to the IVC and esophageal venous plexus. In a review of this patient's previous CT scan of the chest, the scimitar vein drained into the IVC only. The slow progression of stenosis (Figure 3) may have led to a "new" anomalous venous drainage to the esophageal venous plexus as a collateral route.

This case is presented to emphasize the fact that one has to keep an open- mind when dealing with massive esophageal varices bleeding in young men without underlying hepatobiliary disorders, and to conduct a detailed survey before initiating treatment.

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以食道靜脈瘤出血爲表現的土耳其彎刀症候群—病例報告

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一般而言，患有“土耳其彎刀症候群”的病人，臨床上可以沒有症狀。但在 1 歲以前被診斷出來的病人，多會以肺動脈高壓造成的呼吸窘迫或心臟衰竭；或者長大之後以重複發作的肺部感染做為表現。甚少文獻提及此症候群以食道靜脈瘤破裂並引發大量吐血作為臨床表現。我們報告一位 17 歲男性，因部分右肺靜脈異常迴流注入下腔靜脈，但在血管相接處呈現狹窄，轉而匯入食道靜脈叢，造成食道靜脈瘤，並且因為靜脈瘤破裂而導致數次大量而無預警的吐血。此少見的變異情形在我們配合臨床影像學（胸部Ｘ光片及胸部電腦斷層）、胃鏡檢查及心導管檢查而得到證實。病患在同一住院期間接受手術，將該迴流異常的肺靜脈接回左心房。手術之後，情況得到改善；病人於門診追蹤兩年都不再主訴有吐血的情形。*(胸腔醫學 **2006; 21: 190-195**)*

關鍵詞：食道靜脈瘤出血，吐血，部分肺靜脈回流異常，阿拉伯彎刀症候群

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Invasive Pulmonary Aspergillosis in Immunocompetent Patients — Two Case Reports

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Invasive aspergillosis in immunocompetent hosts rarely occurs. Herein, we report 2 cases of invasive pulmonary aspergillosis: 1 was a 72-year-old female with a history of hepatitis C, and the other, a 61-year-old male with a history of hepatitis B; both presented with fever, productive cough, dyspnea and subsequent respiratory failure. The pathology of their lung biopsies revealed invasive aspergillosis. Both patients died despite amphotericin B therapy that was began soon after the pathology was known. Invasive aspergillosis is generally opportunistic and occurs in patients with cell-mediated immunity dysfunction, but it is rarely seen in the immunocompetent host. Appropriate antifungal therapy may lead to a favorable outcome. An early identification of the etiology using an invasive procedure and earlier therapy is mandatory. ***(Thorac Med 2006; 21: 196-201)***

Key words: invasive pulmonary aspergillosis, immunocompetent hosts

Introduction

Aspergillosis is an illness caused by any member of the genus *Aspergillus*. The spectrum of human illness is extensive, ranging from allergic reactions to the colonization of preexisting pulmonary cavities to the invasion and destruction of the lung tissue with hematogenous spread to the brain, skin, and other organs, resulting in mortality. Invasive aspergillosis is regarded as an opportunistic disease, and is a severe and commonly fatal disease in immunocompromised patients [1-6]. However, there are few reports involving non-immunocompromised patients [7-9]. The clinical features usually present with respiratory symptoms that are consistent with bronchopneumonia. The symptoms and signs include fever, cough with sputum, and dyspnea, and no response to antibiotic treatment. Early diagnosis allows for early treatment, which may improve the prognosis [10]. Herein, we describe 2 cases of invasive pulmonary aspergillosis in seemingly immunocompetent hosts with chronic hepatitis. Both of them received surgical intervention for tissue proof, but died despite amphotericin B treatment.

Case Reports

Case 1

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A 72-year-old housewife suffered from fever, cough with a little tenacious yellowish sputum, and dyspnea 15 days prior to admission. She had been admitted into a local hospital for 10 days under the impression of pneumonia. Because the intermittent fever did not improve after medication, she was referred to our hospital for further management.

This patient had hypertensive cardiovascular disease and chronic hepatitis C, but she denied smoking or alcohol consumption. On admission, the vital signs were: blood pressure of 132/64 mmHg, pulse rate of 94/minute, respiration rate of 22/minute, and body temperature of 38°C. Crackles were heard throughout the bilateral lower lung fields. Other physical findings were unremarkable. The chest X-ray showed an asymmetric bilateral alveolar pattern, involving mainly the left lobes, and multiple patchy lesions in the right lung field (Figure 1). The complete blood cell count revealed a white cell count of 33,900/ul with 93% polymorphonuclear leukocytes; the platelet count was 252,000/ul. Blood chemistry showed blood urea nitrogen of 43 mg/dL, creatinine of 1.1 mg/dL, bilirubin (direct/total) of 3.20/4.79 mg/dL, AST of 50 IU/L, ALT of 20 IU/L, glucose of 140 mg/dL, and C-reactive protein of 32.24 mg/dL. Serum HBsAg was negative, but HCV Ab was positive. The abdominal ultrasonography revealed mild, coarse echogenicity of the liver parenchyma. Initially, we treated the condition as community-acquired pneumonia and prescribed intravenous ampicillin/sulbactam.

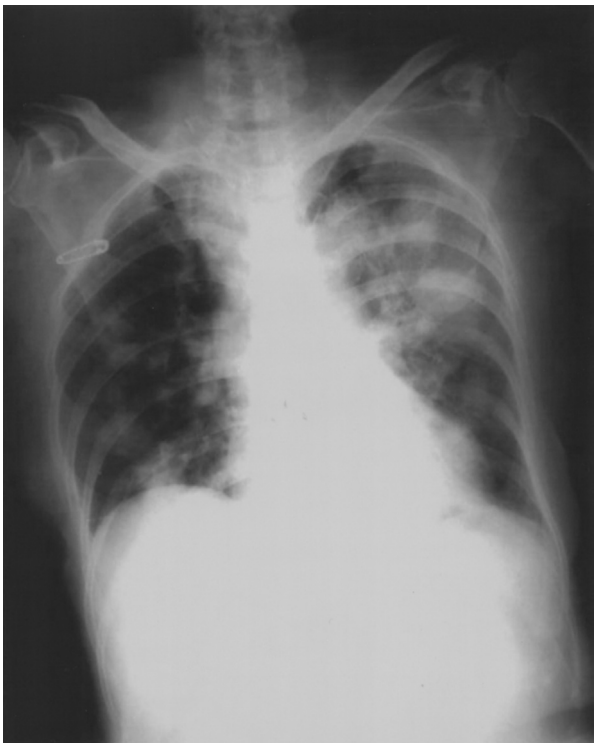


Fig. 1. The chest X-ray shows an asymmetric bilateral alveolar pattern, involving mainly the left lobes, and multiple patchy lesions in the right lobes.

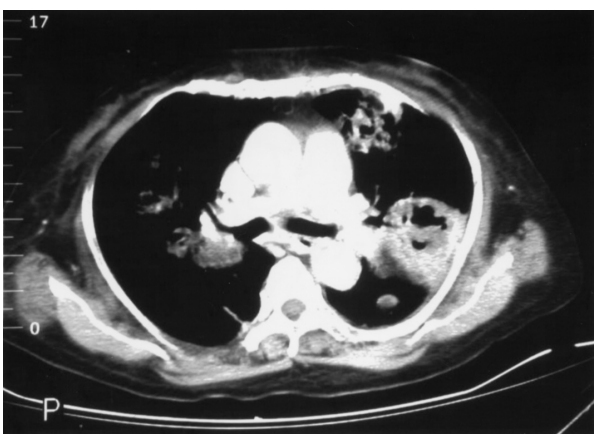


Fig. 2. HRCT of the chest shows multiple lesions in both lungs, some with a cavitary appearance.

On hospital day 9, the patient developed progressively strenuous dyspnea. The empiric antibiotics were switched to intravenous cefepime, because the sputum culture yielded *Pseudomonas aeruginosa.* On hospital day 10, the patient underwent intubation because of respiratory failure. Owing to the unusual clinical evolution and the delayed resolution of the lung lesions, we arranged high-resolution computed

tomographic (HRCT) scanning for further evaluation. The image showed multiple lesions in the bilateral lungs, some with a cavitary-like appearance (Figure 2). On hospital day 18, the patient received a wedge resection of the right middle lobe by video-assisted thoracoscopic surgery. The pathology showed multifocal invasive aspergillosis with focal vascular invasion and destruction of the vessel wall, and adjacent acute necrotizing bronchopneumonia. Therefore, we started amphotericin B therapy for this patient on hospital day 21, with an accumulated dose before discharge of 440 mg. However, the general condition of the patient went progressively downhill, so the family asked that the patient be discharged, against advice, on hospital day 31.

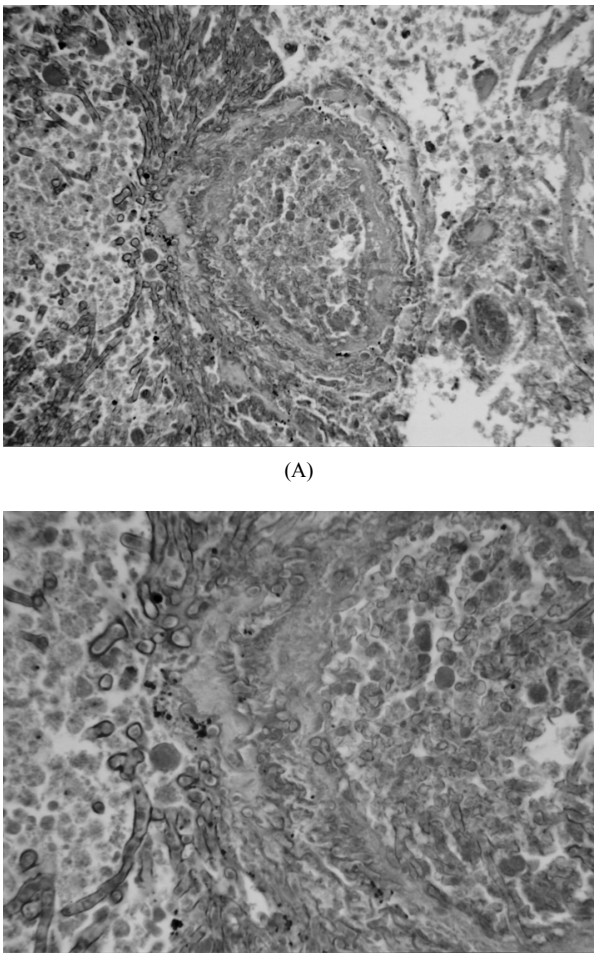
Case 2

A 61-year-old male was admitted to our ward because of chronic cough and exertional dyspnea for 6 months, and body weight loss of 5 kilograms. Prior to this admission, fever, chills and cough with tenacious yellowish sputum had been noted for 3 days. There was no hemoptysis, wheezing, orthopnea, paroxysmal nocturnal dyspnea or leg edema.

He had been a hepatitis B carrier with no episode of acute exacerbation or chronic activation. He had smoked 1 pack of cigarettes every day for 30 years and consumed a little alcohol occasionally.

On admission, the vital signs revealed blood pressure of 120/80 mmHg, a pulse rate of 88/minute, respiration rate of 24/minute, and body temperature of 38°C. An intermittently deep and rapid respiratory pattern was noted. Crackles and wheezing were heard in the right middle lung field. Other physical findings were unremarkable. The chest X-ray showed ill-defined radiopaque patches with a cavity in the right lung field. The chest CT showed a focal lesion, about 5 cm in diameter, with a cavitary appearance and internal gas-fluid content in the superior segment of the right lower lobe. The initial complete blood cell count revealed a leukocyte count of 8,330/ul with 69% polymorphonuclear leukocytes, and a platelet count of 215,000/ul. The blood chemistry showed blood urea nitrogen of 11 mg/dL, creatinine of 1.2 mg/dL, total bilirubin of 0.44 mg/dL, AST of 28 IU/L, ALT of 18 IU/L, glucose of 135 mg/dL, albumin of 2.7 g/dL, and C-reactive protein of 0.87 mg/dl. The serum cryptococcus antigen test was negative. The sputum acid-fast stain was also negative. Bronchoscopy was arranged for further evaluation, and revealed a narrow lumen and injected mucosa in RB6. The biopsy specimen showed acute and chronic inflammatory infiltration.

On hospital day 8, we prescribed empiric antibiotics with ampicillin/sulbactam under the impression of lung abscess. On day 21, antibiotics were shifted to imipenem because of persistent fever and *P. aeruginosa* yielded from the sputum culture. However, the leukocytosis, hypoalbumenia and lung infiltration were worsening. On day 57, the patient underwent a wedge resection of RB2 and RB6 by video-assisted thoracoscopic surgery. The pathology showed necrotizing aspergillosis with angio-invasion, massive coagulative necrosis, aspergilloma and abscess formation (Figure 3). An antifungal agent, amphotericin B, was prescribed on hospital day 63, with an accumulated dose before discharge of 290 mg. However, the patient's condition deteriorated with nosocomial infection complicated with septic shock and multiple organ failure. On day 72, the patient's family asked for the patient to be discharged, against medical advice.



(A)

(B)

Fig. 3. The pathology manifestation of case 2: showing necrotizing aspergillosis with angio-invasion. A) Hematoxylin and eosin x 400. B) Hematoxylin and eosin x 1000.

Discussion

Aspergillosis is the major cause of mortality and morbidity in the immunocompromised host [1]. The mortality of invasive aspergillosis is from 50% to 100% in collected series [13]. The major risk factors for invasive aspergillosis are profound neutropenia (<100 x 10^6/L), prolonged neutropenia, neutrophil function deficits, supraphysiologic corticosteroid therapy [2], graft-versus-host disease [3-4] and/or rejection in transplantation [5]. Early symptoms are often nonproductive cough, high fever, dyspnea, and pleuritic pain. High-resolution computed tomography (HRCT) of the chest plays a major role in the early diagnosis. Both the "halo" signs and "air-crescent" signs are highly suggestive of invasive fungal disease of the lung [13], although there is no good specific serological test for it [11, 14]. Amphotericin B is the drug of choice for invasive *Aspergillus* pneumonia.

The 2 patients reported herein presented with acute pulmonary infection that did not respond to empiric antibiotics. The diagnosis of aspergillosis was delayed. The chest CT did not show the typical "halo" and "air-crescent" signs. The percutaneous lung aspiration failed to identify the pathogen.

There have been reports of invasive aspergillosis occurring in non-immunocompromised patients [7-10]. A review of the literature revealed that 5 of the 14 previously reported cases of invasive aspergillosis in seemingly immunocompetent hosts were associated with alcoholic hepatitis, or ethanol-induced impairment in the function of the pulmonary alveolar macrophages [16-18]. In Taiwan, viral infection is the main cause of chronic hepatitis. One study from abroad found that plasma from patients with chronic active hepatitis reduced phagocytosis of both *Candida albicans* and brewer's yeast, but that the patients' cells had normal phagocytic and killing activity in the presence of normal plasma [18]. Thus, no intrinsic abnormality in neutrophil function was found in these patients, but plasma defects, which differed in cases of cirrhosis with different underlying etiologies, led to impaired neutrophil locomotion or phagocytosis [17-21].

The 2 patients in this report took no corticosteroid and had no underling problems, except chronic viral hepatitis. No significant cirrhotic

change was noted in the computed tomography and abdominal ultrasonography. To verify whether being a viral hepatitis carrier is a risk factor for invasive pulmonary aspergillosis requires more clinical evidence and further investigation.

The early clinical manifestation of invasive pulmonary aspergillosis may mimic bacterial pneumonia. When empiric therapy has failed, early recognition of the pathogen via invasive diagnostic procedures is suggested. This would allow an earlier initiation of appropriate antimicrobial therapy, which could lead to a favorable prognosis.

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侵襲性麴菌肺炎發生於免疫正常患者—病案報告兩例

梁信杰　陳鴻仁　涂智彥　杭良文

黴菌致病是一種伺機性感染，其中麴菌是常見之致病原之一。但絕大多數患者都是免疫功能不全者(immunocompromised)，諸如：使用類固醇者、接受器官移植者、使用免疫抑制劑者、患有惡性血液腫瘤疾病者以及愛滋病患者等等。而免疫功能正常的人 (Immunocompetent)，得到麴菌感染機會很少，要感染侵襲性麴菌肺炎 (invasive pulmonary aspergillosis, IPA) 更是稀少。這裡我們發表兩例侵襲性麴菌肺炎，一位是 72 歲女性，另一位是 61 歲男性；二者入院前，並沒有好發麴菌感染之危險因子存在。一開始，兩人都是以類似一般肺炎的症狀表現，但在經驗性抗生素使用下，病情未見好轉，且都引發呼吸衰竭。影像學上之進展，亦與一般肺炎不同。後來，兩人都經胸腔鏡手術取得檢體，病理證實是侵襲性麴菌肺炎；並且開始使用抗黴菌藥 amphotericin B 治療，但最後病人還是死亡。回顧臨床病程，病人被診斷侵襲性麴菌肺病仍顯太慢。雖然病人無明顯免疫功能缺損，當對經驗性抗生素無效時，如果須要施行侵入性診斷，仍宜及早進行，以利正確抗生素之使用，改善預後。*(胸腔醫學* ***2006; 21: 196-201)***

關鍵詞：侵襲性麴菌肺炎，免疫功能正常

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Polymyositis with Lung Involvement Presenting as Bronchiolitis Obliterans Organizing Pneumonia — A Case Report

Pang-Kai Chen, Tzu-Chin Wu

The incidence of interstitial lung disease (ILD) in polymyositis (PM) is low, and the histological pattern of ILD as bronchiolitis obliterans with organizing pneumonia (BOOP) is even less. ILD in PM usually indicates a poor prognosis, unless the histological presentation is BOOP.

We report a 61-year-old male without a history of cigarette smoking or systemic disease, who presented with fever, cough and dyspnea for 4 days before admission. Leukocytosis and elevated C-reactive protein were observed. Chest X-ray (CXR) revealed left lower lobe infiltrates. He was initially treated for pneumonia, but with a clinically poor response to antibiotics. Respiratory failure occurred and the CXR showed disease progression. Muscle weakness, tenderness, and elevated creatinine kinase developed after a few days. Upon completion of a series of studies, the diagnosis of PM with lung involvement presenting as BOOP was confirmed. Antibiotic was discontinued and steroid prescribed. The disease had a dramatic response to steroid therapy. The patient was then successfully weaned from the ventilator and later discharged. ***(Thorac Med 2006; 21: 202-209)***

Key words: polymyositis, interstitial lung disease, bronchiolitis obliterans organizing pneumonia

Introduction

Polymyositis (PM) is a systemic inflammatory disease of unknown etiology that affects the skeletal muscles and internal organs. The thorax may be affected, generally in 1 or more of 3 forms: (*a*) hypoventilation and respiratory failure as a result of involvement of the respiratory muscles; (*b*) interstitial lung disease or interstitial pneumonia, usually with a histological pattern of usual interstitial pneumonia (UIP), nonspecific interstitial pneumonia (NSIP) or diffuse alveolar damage (DAD), and (*c*) aspiration pneumonia, secondary to pharyngeal muscle weakness [1]. The prevalence of ILD in PM is around 10% [1-7]. The onset of ILD can precede the diagnosis of myositis, appear simultaneously, or occur after the muscle disease [8]. Patients with ILD usually present with dyspnea and nonproductive cough. The chest examination typically reveals dry bilateral basilar rales. The course of ILD is also variable. It may be fulminant, with fever and rapid

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progression of radiographic changes and respiratory failure, or, it may be slowly progressive, both radiographically and clinically, over a period of years. In other patients, the lung disease is asymptomatic, being detectable only by CXR or pulmonary function tests. The diagnosis of ILD in PM can be established by combined clinical presentations, CXR, a high resolution CT scan (HRCT), pulmonary function tests, and histopathological examination. The CXR provides the first indication whenever pulmonary involvement is suspected. HRCT has a pivotal role in distinguishing patients with UIP from other ILD. HRCT is helpful in guiding to the optimal locations for surgical biopsies and evaluating the response to therapy [9]. Surgical lung biopsy can establish a definitive diagnosis of ILD and provide a conclusive histological pattern. It also confirms or excludes an alternative diagnosis such as sarcoidosis, hypersensitivity pneumonitis, lymphangitic carcinoma, or the presence of an occupational disease such as hard metal disease. Furthermore, a histopathological examination is useful to identify or exclude an infectious origin in a complicated lung disease. [10].

Treatment of ILD in patients with myositis always involves corticosteroids. Myositis patients with ILD have a significantly shortened survival time, compared to those without lung involvement. Causes of death in those with ILD were pulmonary complications: progressive ILD, pulmonary hypertension, respiratory failure, or bacterial pneumonia.

Case Report

A 61-year-old male without a history of cigarette smoking or systemic disease was admitted to Chung Shan Medical University hospital because of fever and productive cough for 4 days. There was no travel, animal contact, or insect bite history. On admission, the patient's consciousness was clear and he was cooperative. His blood pressure was 124/66 mmHg, heart rate 89 beats per minute, respiratory rate 25 per minute, and body temperature 38.7 degree Celsius. The physical examination results were grossly normal, except for crackles in both lower lung fields. No skin rash, palpable lymph node, or muscle soreness was observed. Abnormal laboratory findings were WBC of 17960/mm^3 (neutrophils: 81%, lympocytes: 17%, monocytes: 2%) and C-reactive protein of 6.01 mg/dl. No anemia or thrombocytopenia was detected. Urine analysis was normal. CXR taken on admission revealed bilateral basilar infiltrates more prominently in the left lower lung field. (Figure 1A) Community-acquired pneumonia was initially considered. Clavulanic acid/amoxicillin 1.2 g IVD Q8h and azithromycin dihydrate 500 mg PO QD were prescribed. Blood and sputum cultures yielded no positive result.

Respiratory failure developed on day 10 and the CXR showed disease progression. (Figure 1B) Muscle weakness and tenderness in the right arm and thigh occurred on day 14, and elevated creatinine kinase (CK: 4109 IU/L) was observed. We then started to work out the cause of the rhabdomyolysis or myositis. Several viral titers, the autoimmune profile, possibility of underlying malignancies, and atypical infections were all studied. Lung HRCT was also performed, and interstitial lung disease was suspected. (Figure 2) Muscle biopsy from tender sites of the arm and thigh were also performed. The antibiotics were still maintained because the fever and leukocytosis persisted. The blood WBC increased to 37410 /mm^3. The muscle biopsy pathology revealed a compatible finding of PM (Figure 3). Other important positive laboratory findings

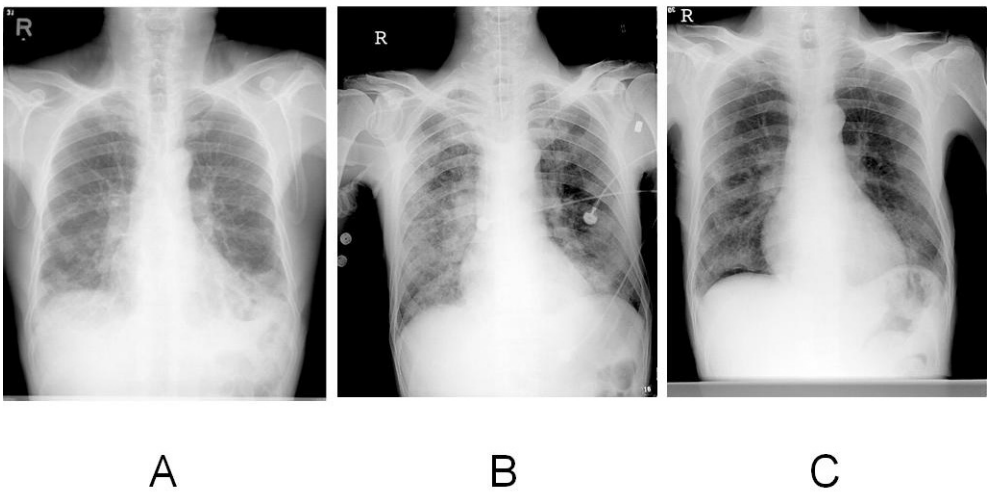


Fig. 1. CXR on admission (A); CXR on day 10, respiratory failure (B); CXR before discharge (C)

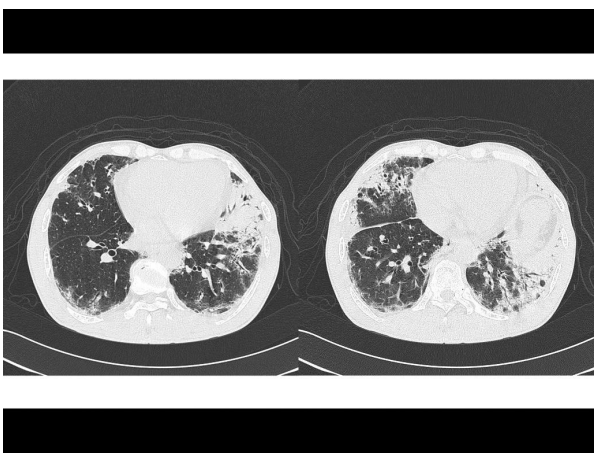


Fig. 2. Asymmetric ground glass opacities with a predominantly peripheral distribution.

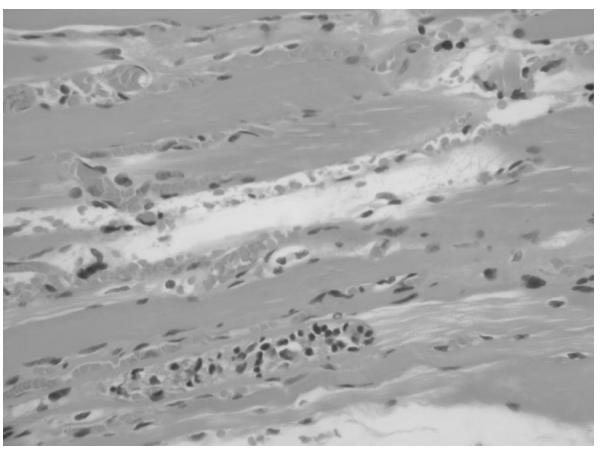
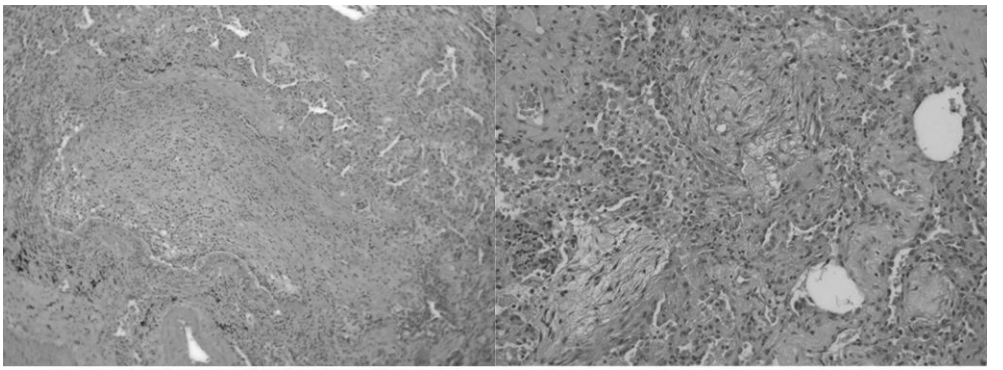


Fig. 3. Some muscle fibers are damaged and are infiltrated with lymphocytes, and some are regenerative. Haematoxylin & Eosin stain, X 400.

included positive ANA (160X) and anti-SCL-70 tests. No malignancy or infectious pathogen was detected. To confirm the lung involvement and the histological type of ILD, a surgical biopsy by video-assisted thoracopy was done at the left lower lobe and lingular lobe. Pathological findings of organizing pneumonia involving alveoli and alveolar ducts with intraluminal inflammatory polyps projecting into the terminal bronchioles were evident. A small amount of airspace fibrin in the well-preserved lung architecture was noted. Some connective tissue extended from the terminal bronchioles into the distal airways. No hemorrhage, neutrophil infiltration, or bacterial pneumonia could be detected (Figure 4A, B) PM with pulmonary involvement was confirmed.

Steroid therapy was prescribed with prednisone at a dose of 1.5 mg/kg per day (30 mg TID), and antibiotics were discontinued immediately.



A B

Fig. 4. (A) There is a presence of fibroblast plugs in the bronchiocentric and intraluminal area (Haematoxylin & Eosin stain, X 100). (B) Clusters of basophilic collagen intermixed with inflammatory cells is observed in the lung parenchyma (Haematoxylin & Eosin stain, X 200).

The fever dramatically subsided. The blood WBC level decreased to 15220/mm^3 and the CK level decreased to 624 IU/L 10 days later. His respiratory functions in terms of gas exchange and inspiratory muscle power improved, and he was successfully weaned from the ventilator and extubated 13 days after steroid therapy. A follow-up CXR demonstrated significant resolution of the lung infiltrates. (Figure 1C) The patient was discharged with oral prednisolone 15 mg BID.

Discussion

To make an early and accurate diagnosis of ILD, with the onset preceding myositis in a patient with an apparent ground-glass picture on the chest radiographic study, is difficult. The treatments for ILD and infection are completely different: the careful exclusion of an infectious disease and the searching for evidence for a differential diagnosis between ILD and pneumonia are mandatory and time-consuming. In this patient, the pathological confirmation of BOOP rather than pneumonia, hemorrhage, or DAD led to an adequate treatment.

In PM patients with ILD, the occurrence of ILD does not appear to be related to the severity of muscle disease as measured by weakness or CK elevation [2]. The major CXR finding is diffuse reticulonodular interstitial changes found predominantly in the lung bases. Patients with fulminant disease may have patchy “ground glass” infiltrates. Pleural effusion usually is not seen [8]. HRCT is a superior technique to CXR for characterizing nonspecific interstitial changes, and has a better diagnostic accuracy than CXR in detecting ILD [11]. Typical HRCT features of UIP are sufficiently characteristic to make a confident diagnosis, even without a surgical lung biopsy. HRCT may also provide clues to non-ILD disorders, such as sarcoidosis, hypersensitivity pneumonitis (HP), lymphangioleiomyomatosis, Langerhans’ cell histiocytosis, and pulmonary alveolar proteinosis [9]. However, HRCT presentations are not specific for ILD, other than UIP. Equivocal findings in HRCT

between UIP and another ILD, such as NSIP, BOOP or DAD, require further assessment of the patient, usually with transbronchial biopsy and bronchial lavage. If these should prove inconclusive, then a surgical lung biopsy may be required. Some patients may proceed directly from HRCT to a surgical biopsy, particularly if the radiological abnormality is subpleurally predominant or rapidly worsening [10]. In this patient, CXR and HRCT findings are not characteristic for a specific ILD. The areas of consolidation with ground-glass attenuation correspond histopathologically to HP or DAD. The irregular peribronchovascular thickening, subpleural lines, and prominent interlobular septa can be attributed to NSIP, BOOP or UIP [9]. No traction bronchiectasis or cystic change suggesting UIP was noted.

The relationship between some serologic markers and ILD has been reported. There is an association between ILD and the myositis-specific antibody anti-histidyl-tRNA synthetase (anti-Jo-1) [5, 12-13]. It is present in about 20% of cases and is strongly associated with interstitial lung disease, Raynaud phenomenon, arthritis, and mechanic's hands. Anti-alanyl-tRNA synthetase (anti-PL-12) antibody is present in only 3% to 4% of all dermatomyositis (DM) and PM patients; this defines a group of patients more likely to have ILD without clinical muscle disease than those with anti-Jo-1 [14]. KL-6, a glycoprotein expressed on alveolar and bronchiolar lining cells, is both a marker for ILD in a variety of rheumatic diseases including myositis and a measure of ILD disease activity [15].

Four-year survival is best in patients with a predominantly ground-glass appearance, and worse in those with a reticular pattern on radiographic films [16]. Myositis patients with ILD have a significantly shortened survival time, compared to those without lung disease [17-18]. Thus, it is the type of pulmonary involvement rather than the myositis itself that influences the prognosis. There was about a 40% mortality rate after 31 months in patients with ILD; this was significantly higher than in historical controls with myositis but no lung disease [17]. Furthermore, almost 60% of deaths in the ILD patients were due to progressive pulmonary disease. Most deaths in those with ILD were due to lung disease: progressive ILD, pulmonary hypertension, or bacterial pneumonia [7].

Several histological patterns of ILD have been observed in biopsy and autopsy studies [10, 19], including nonspecific interstitial pneumonitis, usual interstitial pneumonia, bronchiolitis obliterans with organizing pneumonia (BOOP), diffuse alveolar damage, and acute interstitial pneumonia (AIP). In a series of patients with either DM or PM and ILD who underwent surgical lung biopsy, NSIP by far was the most common finding (18 of 22 patients, 81 percent), followed by DAD (2 patients), UIP (1 patient), and BOOP (1 patient) [20]. Patients with DM or PM-associated NSIP appear to have a similar prognosis to those with idiopathic NSIP; the 5-year survival in this cohort was 60%. Patients with BOOP tend to have the best prognosis and response to treatment, while those with DAD have the worst. This patient presented with rapid worsening of pulmonary infiltrates which eventually resulted in respiratory failure. The differential diagnosis included aspiration pneumonia, congestive heart failure, pulmonary hemorrhage and rapid progressive changes of diffuse interstitial lung diseases such as AIP or DAD. The pathological finding indicated a diagnosis of BOOP and excluded hemorrhage, edema or bacterial infections.

Treatment of ILD in patients with myositis always involves corticosteroids. About 50% of

myositis patients with ILD respond favorably to corticosteroids. Patients most likely to respond include [21]: those with organizing pneumonia, those with a predominantly active cellular infiltration rather than fibrosis on HRCT or lung biopsy, younger patients, and those with an elevated CK at the onset of ILD. Corticosteroid therapy is initiated with prednisone at a dose of 0.5 to 1.5 mg/kg per day [22]. Normalization of muscle enzymes in responders occurs about 4 to 6 weeks after treatment. Improvement in muscle strength lags behind the enzyme response, occurring 2 to 3 months after the initiation of treatment. Once a full response has occurred, prednisone is tapered gradually, while the patient's muscle strength and plasma enzymes are monitored for signs of relapse. There is no standard tapering schedule, but a reasonable approach is to decrease by 5 mg/week down to 20 mg/day, then by 2.5 mg every 2 weeks down to 10 mg/day, and then by 1 mg/month until steroids are discontinued. Alternate-day treatment with steroids (50 to 60 mg every other day) can be used from the onset in mild cases [23] or after the disease is well controlled in more severe cases [24]. Immunosuppressive drugs, including cyclophosphamide and azathioprine, have been used in patients with evidence of predominant cellular infiltration who had a fulminant onset, a rapid progression of pulmonary disease, or who failed to respond to an initial course of prednisone. Published experience with these agents is limited, although the use of daily oral or monthly intravenous cyclophosphamide has been evaluated in a few reports, with favorable outcomes [25-26]. It has also been suggested that cyclophosphamide plus steroids may be more effective than steroids alone in idiopathic pulmonary fibrosis [27]. In addition, cyclosporine A has been reported to be effective in some cases of steroid-resistant ILD [21].

In this patient, BOOP preceded PM by 1 week. The clinical symptoms of fever, cough and dyspnea misled us to the diagnosis of pneumonia. The antibiotic therapy results were disappointing. The BOOP resulted in restrictive ventilatory defects, and worsening lung mechanics and gas exchange. The PM further compromised the respiratory muscle, impairing ventilatory capacity. Both BOOP and PM, occurring jointly and simultaneously, resulted in respiratory failure. The development of muscular symptoms and elevated CK directed us to the correct diagnosis. PM with lung involvement presenting as BOOP was confirmed after a series of studies. In response to steroid therapy, either BOOP or PM will improve immediately and dramatically within 2 weeks. Based on the concurrent onset of disease and similar response to treatment, together with positive ANA and anti-scl-70, it is assumed that the disease was caused by an unknown immunological inflammatory process involving both lung and proximal muscles.

In conclusion, to make an early and accurate diagnosis in a patient with ILD, careful searching for evidence for the differential diagnosis is mandatory. An HRCT is always helpful. However, if the disease appears to be fulminant with progressive deterioration, a surgical biopsy should be arranged. PM with BOOP is rare, yet the response to treatment is good.

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多發性肌炎導致阻塞性細支氣管炎合併器質化肺炎—病例報告

陳邦凱　吳子卿

多發性肌炎的病患中產生間質性肺炎的比例並不高，而其中組織型態以阻塞性細支氣管炎合併器質化肺炎表現者則更為稀少。患者若產生間質性肺炎通常代表較差的預後，但其中以阻塞性細支氣管炎合併器質化肺炎表現者除外。

本病例為一位六十一歲健康男性，無特殊病史。入院主訴為四天前開始發燒、咳嗽及呼吸困難。胸部X光浸潤、白血球及C反應蛋白升高符合肺炎診斷。但抗生素治療無效且病情進展至呼吸衰竭需使用呼吸器。幾天後，病患產生肌肉疼痛及無力的症狀且血清肌酐酸上升。經過一系列的追蹤檢查確定患者為多發性肌炎導致阻塞性細支氣管炎合併器質化肺炎。經施予類固醇治療後，病患病情迅速改善並成功脫離呼吸器，治癒出院。*(胸腔醫學**2006; 21: 202-209**)*

關鍵詞：多發性肌炎，間質性肺炎，阻塞性細支氣管炎合併器質化肺炎

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Intra-thoracic Extra-medullary Hematopoiesis — A Case Report

Lin-Keng Ng, Jhi-Jhu Hwang, Tung-Heng Wang, Wan-Yi Kang*, Ming-Shyan Huang

Intra-thoracic extra-medullary hematopoiesis (EMH) is a rare disease in the differential diagnosis of mediastinal masses. It is usually asymptomatic, and since masses tend to be slow-growing, patients should not be subjected to unnecessary surgical interventions. We present a case of spherocytosis with long-term anemia without blood transfusion. Multiple intra-thoracic tumors were noted and echo-guided biopsy revealed tri-lineage hematopoiesis, which was compatible with EMH. This case report serves to remind us of an unusual diagnosis for posterior mediastinal masses. Hence, EMH should be considered in the differential diagnosis of patients who have chronic anemia with asymptomatic intra-thoracic tumors, and care should be taken to prevent further aggressive diagnostic and therapeutic measures. Low-dose radiation can be considered for the palliative treatment of pleural and pulmonary EMH. ***(Thorac Med 2006; 21: 210-217)***

Key words: extra-medullary hematopoiesis, intra-thoracic tumor

Introduction

Intra-thoracic extra-medullary hematopoiesis (EMH) is a rare condition accompanying chronic hematologic diseases. It often occurs in hemoglobinopathies, hemolytic anemias, leukemias, lymphomas, and myeloproliferative disorders [1]. EMH is a compensatory mechanism for insufficient bone marrow blood cell production, in response to insufficient erythrogenesis. The liver, spleen, and lymph nodes are frequently involved [2-3]. However, EMH may also develop in other sites, such as the thymus, kidneys, retroperitoneum, and paravertebral areas of the thorax [1]. Herein, we report a case of spherocytosis with intra-thoracic EMH. The related medical literature is also reviewed.

Case Report

A 69-year-old female was admitted to our hospital for progressive dyspnea, cough and fatigue. The patient had had a history of anemia since childhood, with no definite diagnosis, but no systemic diseases. An abnormal shadow and bilateral pleural effusion was noted on a chest

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X-ray. Physical examination revealed the following: blood pressure of 120/60 mmHg; pulse, 80 beats per minute; and respiratory rate, 24 breaths per minute. Her skin and sclera were jaundiced. Decreased breathing sounds were noted in both lung fields, with basal inspiratory crackles and dullness by percussion. Heart findings were unremarkable, but the abdomen was soft and distended, with the liver and spleen mildly enlarged but not tender.

Biochemistry results revealed aspartate aminotransferase of 13 IU/L, alanine aminotransferase 10 IU/L, total bilirubin 5.9 mg/dl, and direct bilirubin 0.2 mg/dl. The initial hematological study revealed hemoglobin (Hb) of 7.6 g/dL, red blood cell count 2.42 x 10^6/μl, mean corpuscular hemoglobin 83.5 fl, white blood cell count 9230/μl, platelet count 26.9 k/μl, iron 36 μg/dl, ferritin 1110 ng/dl, and unsaturated iron-binding capacity 131 μg/dl. The HbA2 level was 2.4%, and HbA1 was 97.6%.

Due to the elevation of indirect bilirubin, diagnostic tests for hemolytic anemia were performed, and revealed a reticulocyte count of 9.63%, haptoglobin 8.77 mg/dl, lactate dehydrogenase 97 IU/L, and negative findings for the sugar water test, Ham's test, and Coomb's test (direct/indirect). A peripheral blood smear showed spherocytosis, while osmotic fragility was abnormally high. These findings were consistent with hereditary spherocytosis.

Thoracocentesis was performed, and obtained exudative pleural effusion with a cell count of 237/μl (Polymorphic neutrophil/monocyte: 12/88%). No malignant cells were noted via cytology. However, scanty mesothelial cells and histiocytes were measured. No microorganisms were isolated. Radiographic studies revealed bilateral lobulated para-spinal masses and pleural effusion (Figure 1). A computed tomography scan showed well-circumscribed, homogeneous, lobulated para-spinal soft tissue masses without associated bony changes. Magnetic resonance imaging revealed well-demarcated, heterogeneous, enhanced soft tissue masses at the mediastinum and bilateral pleural spaces, which showed heterogeneous iso to low signal intensity on T1W1 and hyper-intensity on T2W1 (Figure 2).

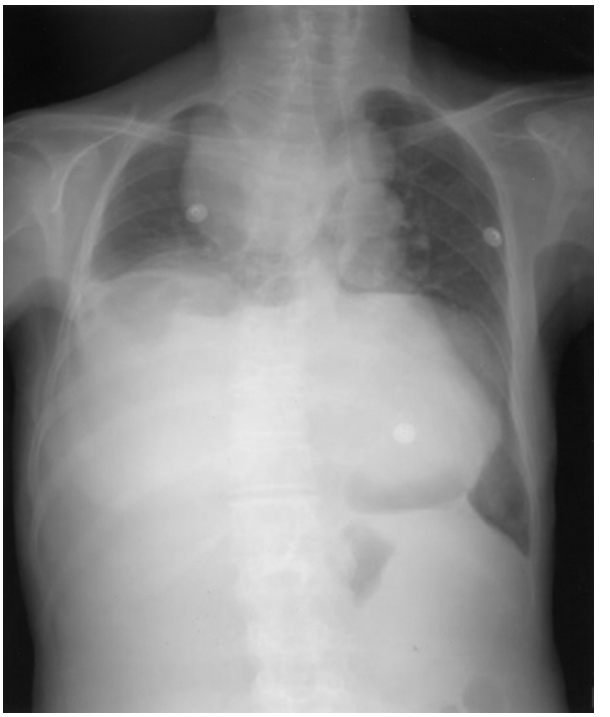

Fig. 1. Chest X-ray film reveals bilateral lobulated para-spinal masses and pleural effusion.

Tc99m sulfur colloid scintigraphy revealed significant particle uptake in the mediastinum, lower thorax, and lower abdomen. Moreover, reactive bone marrow uptake in the distal femur and tibia was also demonstrated (Figure 3). Biopsy of the posterior mediastinal mass was done with an ultrasound-guided needle, obtaining hyperplastic, erythroid hemopoietic tissues with tri-lineage hematopoiesis (Figure 4). This finding led to the diagnosis of extra-medullary hematopoeisis.

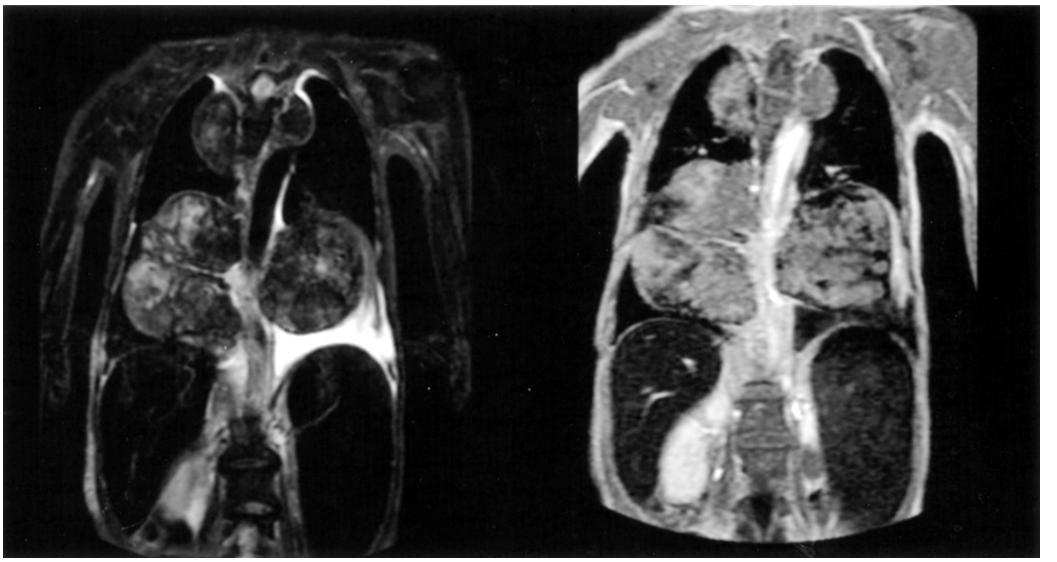

Fig. 2. Magnetic resonance imaging reveals well-demarcated heterogenous enhanced soft tissue masses at the mediastinum and bilateral pleural spaces, which showed heterogenous iso to low signal intensity on T1W1 and hyper-intensity on T2W1.

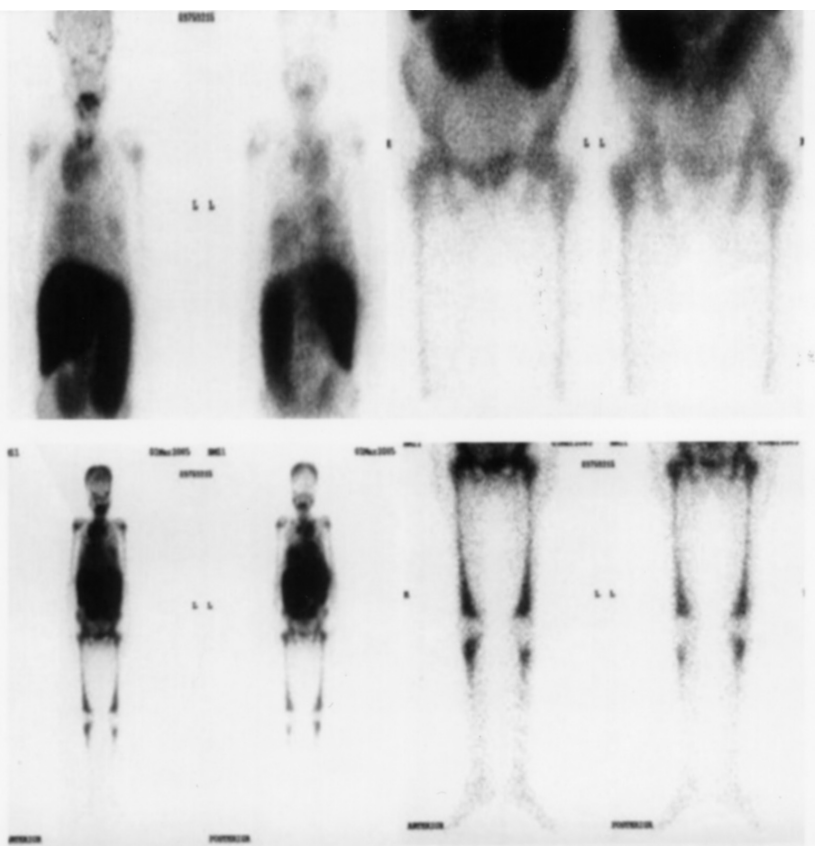

Fig. 3. Tc99m sulfur colloid scintigraphy shows significant particle uptake in the mediastinum, lower thorax, and lower abdomen. Reactive bone marrow uptake in the distal femur and tibia is also demonstrated.

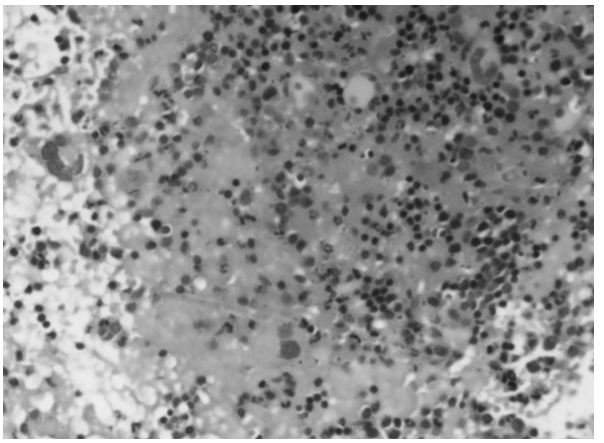

Fig. 4. Pathology of a posterior mediastinal mass reveals erythroid hemopoietic tissue with tri-lineage hematopoiesis.

For symptomatic relief, the pleural effusion was drained via a pigtail. However, the pleural effusion rapidly recurred, necessitating repeated aspiration for symptomatic relief. A total of 7.0 L of pleural fluid was removed within 2 months. Blood transfusion and splenectomy was suggested to the patient, but she refused. Supportive care with folic acid 5 mg/day was prescribed. Splenic irradiation, using a total of 500cGy, was performed for a radio-therapeutic splenectomy, which was meant to decrease the severity of hemolysis and the further progression of EMH. Due to the recurrence of pleural effusion, irradiation therapy (750cGy) to the bilateral pleural EMH was performed. Since then, the pleural effusion has been well-controlled, requiring no further thoracocentesis.

Discussion

Extra-medullary hematopoiesis (EMH) occurs normally in the fetus during gestation, since fetal blood is produced in the liver, spleen, lymph nodes, and other organs [4]. However, EMH is a compensatory response to chronic hematologic disorders [1]. Rarely is it a cause of thoracic masses usually involving the posterior mediastinum.

Intra-thoracic EMH is usually asymptomatic and slow-growing, and patients should not be subjected to aggressive diagnostic and therapeutic measures [5]. Fine needle aspiration cytology and echo-guided biopsy are useful methods of diagnosing EMH, and can aid in the planning of treatment [6]. The histo-pathologic examination demonstrates the presence of tri-lineage hematopoiesis. The histology of EMH depends upon its duration and the erythropoietic demands of the particular patient. Early in its evolution, immature and mature cells, mainly of the erythroid and myeloid series, and dilated sinusoids containing precursors of red cells, are revealed. Later, the lesion becomes inactive and reveals some fatty tissue and fibrosis, or massive iron deposits [4-5, 7].

The radiographic manifestations of intra-thoracic EMH are unilateral or bilateral, smooth, sharply delineated, often lobulated, para-spinal masses without erosion of the vertebral bodies or ribs, sometimes associated with sub-pleural and para-costal masses and an expansion of the ribs [8-9]. Two types of ultrasound appearance are possible: “para-osseous”, in which the normal medullary tissue of the bone marrow ruptures through the bone to present as a para-osseous soft tissue mass, and “extra-osseous”, in which the EMH occurs within the soft tissue [10].

The CT scan often shows well-circumscribed, smooth, soft tissue attenuation masses, usually at multiple levels in a para-spinal location without erosion or pressure changes on the adjacent ribs or vertebral bodies [11]. However, CT images that mimic malignancy have also been reported [12]. Magnetic resonance imaging is the radiological method of choice for diagnosing

EMH masses and for delineating the extent of spinal cord involvement [13]. Active recent extramedullary para-spinal hematopoietic masses show soft tissue behavior in both CT and MRI. Older, inactive masses may reveal iron deposition or fatty replacement. Combined imaging findings of para-spinal EMH can reveal the phase of its evolution and the correct diagnosis [4].

Radionuclide scanning, using 99mTc-labeled monoclonal antibody tracers, is a useful and non-invasive procedure to detect occult EMH [11, 14-15]. Bilateral pelvic involvement was an incidental finding in our case. Spontaneous rupture of a pelvic EMH or compression of the associated nerve should be prevented early on.

Most patients with intra-thoracic EMH are asymptomatic and should not be treated [16]. However, morbid clinical expressions of osseous changes with spontaneous fractures and osteoarthropathy have been reported. EMH presenting as tumor-like masses may cause pressure symptoms on adjacent organs. Spinal cord compressions by EMH are uncommon, but can lead to severe sequelae if not rapidly diagnosed [17]. Symptomatic pleural effusion and spontaneously ruptured EMH that produces a fatal hemothorax have been reported, but rarely [18-19].

Although most patients with EMH are asymptomatic and require no therapy, EMH tumors that cause symptoms, such as spinal cord compression and acute neurological deterioration, do require emergency surgery or radiotherapy. Total surgical excision is not usually feasible because of the diffuse nature of EMH tissue and the possibility of recurrence. However, EMH is radiosensitive and displays a rapid response to low dosages, so radiation therapy is recommended for residual tumors [20-21]. For patients with chronic hematologic diseases, hypertransfusion seems to be a promising treatment that should be recommended as a first-line approach or as an adjuvant therapy to other methods [13]. Hydroxyurea, stimulating fetal hemoglobin synthesis that increases the efficacy of erythropoiesis, may represent an alternative therapeutic approach [22].

Intra-thoracic EMH rarely involves the pleura [23]. However, symptomatic pleural effusion has been reported [18, 24]. These effusions are due to lymphatic drainage occlusion or an inflammatory process from pleural seeding. Moreover, trapped lung may occur when an intra-thoracic EMH covers all or a portion of the visceral pleura. This results in increased intra-pleural negative pressure and promotes the filling of the space. In our case, a total of 750cGY of radiation therapy effectively controlled the refractory pleural effusion.

Chemical pleurodesis has been reported for the control of symptomatic pleural effusion. A complete lung re-expansion following drainage of the pleural fluid is needed, but this is not a choice in cases of multi-loculated effusion, trapped lung, or airway compression. Repeat chemical pleurodesis and the systemic side effects of the chemical agent must be considered. The utilization of lower doses in our case revealed no myelotoxicity. Thus, radiation can be considered for the palliative treatment of pleural and pulmonary EMH, even though there is still no consensus on the dosage. Fatal hemothorax requires thoracotomy for the initial control of bleeding. Post-operatively, low-dosage radiation therapy to the mass may prevent a recurrence of the hemothorax [19, 25].

In conclusion, EMH should be considered in the differential diagnosis of patients who have chronic anemia with an intra-thoracic tumor. Most patients with intra-thoracic EMH are asymptomatic. However, morbid clinical expressions

have been reported. Combined imaging findings can provide the correct diagnosis, while fine needle aspiration cytology or echo-guided biopsy are useful methods of diagnosing EMH and preventing further aggressive diagnostic and therapeutic measures. Low-dose radiation can be considered for the palliative treatment of pleural and pulmonary EMH.

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胸腔內的髓外造血—病例報告

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胸腔內的髓外造血是一種罕見的縱隔腔腫瘤疾病。它通常無明顯症狀且生長非常緩慢，因此一般不需外科治療。在此我們提出一名以長期貧血而沒有接受輸血治療的球狀紅血球症的病例，在其胸腔內發現多個腫瘤,經由超音波引導的切片檢查顯示三線的造血生成，符合髓外造血的診斷。此病例報告顯示一罕見的後縱膈腔腫瘤的診斷。因此，對於慢性貧血的患者，若發現無症狀的胸腔內腫瘤，髓外造血為必要的鑑別診斷之一以避免不必要的侵犯性檢查及治療。對於肋膜或肺部的髓外造血所引起的症狀，放射治療為一可考慮的治療方式。*(胸腔醫學* ***2006; 21: 210-217****)*

關鍵詞：髓外造血，胸腔內腫瘤

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Thoracoscopic Resection of Paraesophageal Bronchogenic Cyst: Report of 4 Cases

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Bronchogenic cysts are benign congenital lesions caused by developmental anomalies of the tracheobronchial trees. Paraesophgeal bronchogenic cysts are even more intriguing due to the variable anatomical involvement and presentations of the upper digestive tract. The preoperative diagnosis is not difficult, yet evaluation of esophageal involvement is crucial to surgical intervention. Surgical resection using video-assisted thoracoscopic surgery (VATS) has been well-developed in recent years. Herein, we present our experience with the successful management of 4 patients with paraesophageal bronchogenic cysts with variable degrees of esophageal involvement, via the utilization of thoracoscopic surgery. ***(Thorac Med 2006; 21: 218-224)***

Key words: bronchogenic cyst, esophagus, thoracoscopic surgery

Introduction

Bronchogenic cysts are rare congenital lesions due to the abnormal embryological development of the tracheobronchial trees. Their locations are extremely varied [1-3]. Paraesophageal bronchogenic cysts are even rarer and draw extraordinary attention due to their close relationship to the esophagus, thus affecting operative concerns. Surgery remains the treatment of choice. The current trend of using video-assisted thoracoscopic surgery (VATS) as the approach of choice has been widely adopted in managing these lesions during the last 10 years, and its benefits over traditional thoracotomy are well-appreciated. Many authors regard VATS to be a less invasive entry and of better visualization for dissection, thus contributing to better postoperative outcomes. However, some have considered it to be unsuitable in the settings of major adhesions to vital structures [4-5]. We share our own experience in treating 4 patients with paraesophageal bronchogenic cysts and focus on the unique characteristics of these cysts that differentiate them from other bronchogenic cysts.

Patients and Methods

Patients

From May 1989 to January 2005, a total of

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21 patients underwent surgery for bronchogenic cysts in National Cheng-Kung University Hospital. Among them, 4 patients (19%), without a history of underlying diseases, were diagnosed to have a paraesophageal bronchogenic cyst. The cysts of all the patients were found incidentally from chest radiography of the lower mediastinum. The clinical data of these 4 patients are listed in Table 1. The image studies of a representative patient are demonstrated in Figure 1. The contrasted chest computed tomography (CT) scan of all the patients revealed homogenous hypodensed tumors at the posterior mediastinum, with variable degrees of adjacent esophageal involvement. Slightly loose contact was discovered in patients 1 and 3, while a notable indentation of the esophagus caused by tumor compression (between 1/3 and 1/2 of the circumference) was revealed in patient 4. Extreme conditions existed in patient 2, in whom marked compression and deviation of the esophagus were documented. Preoperative esophagography demonstrated no communication between the cyst and the esophagus.

Methods

All patients underwent surgical resection using a video-assisted thoracoscopic surgery (VATS) approach. A 1.5 to 2.0 cm incision for thoracoscopy, with an additional 5 to 10 cm minithoracotomy for dissection between the 7th and 9th intercostal space, were routinely used. Careful dissection of the cyst from the mediastinal pleura and the inferior pulmonary ligament was then carried out. The plane between the tumor and the esophagus was easily entered in patients 1 and 3, because of the loose adherence, therefore the cysts

Table 1. Patients with paraesophageal bronchogenic cysts who underwent surgical resections

Patients	1	2	3	4
Age	33	44	28	37
Sex	F	M	M	M
Symptoms	No	No	No	No
Initial diagnosis	X-ray	X-ray	X-ray	X-ray
Cyst size (cm)	5.0	6.3	5.3	6.0
Location (Posterior medisatinum)	Left lower	Right lower	Left lower	Right lower
Image-documented esophageal compression	No	Yes	No	Yes
Surgical procedures/approach	Excision/VATS	Excision with esophageal muscle layer repair/VATS	Excision/VATS	Excision with esophageal muscle layer repair/VATS
Depth of esophageal invasion	Adventitia	Submucosa	Adventitia	Submucosa
Complications/management	No	Residual pleural space/prolonged chest tube placement	No	Wound infection/ Wound care
Postoperative hospital stay (days)	5	15	5	5

* VATS, video-assisted thoracoscopic surgery.

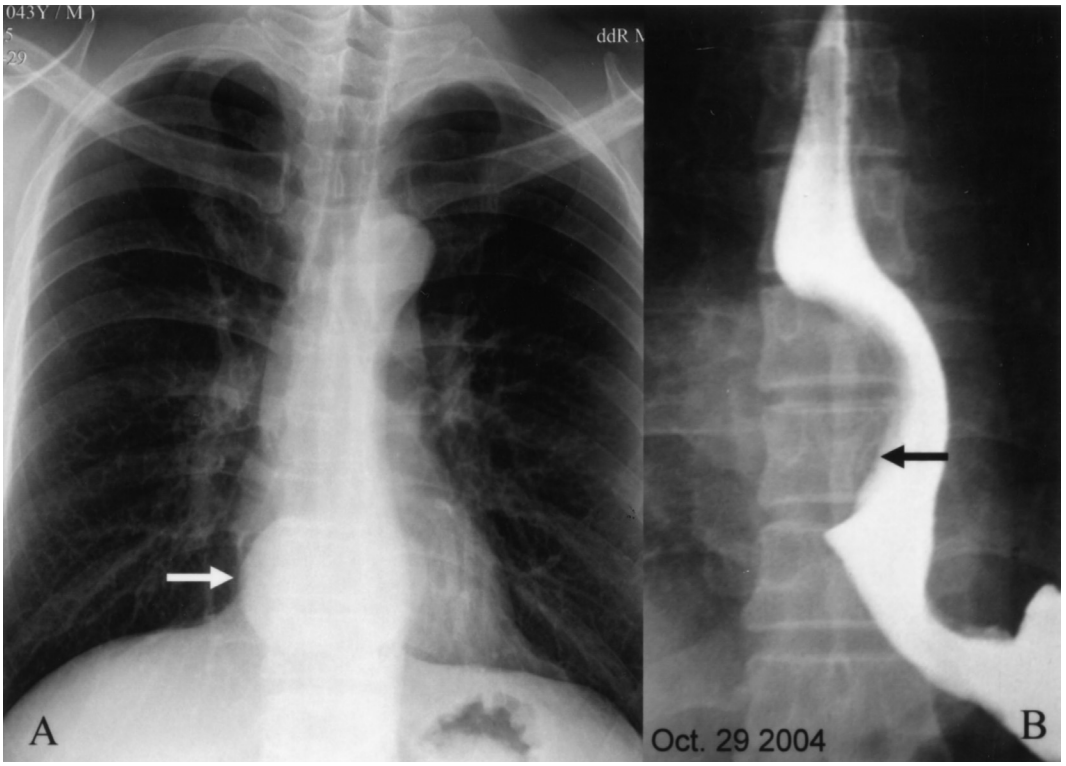

Fig. 1. Preoperative image study of patient 2. A. Chest radiography shows a round-shaped tumor (arrow) at the retrocardiac region. B. Esophagography reveals marked esophageal indentation due to external compression (arrow).

were smoothly detached and removed. In patient 2, the cystic component was decompressed first, for the ease of further removal, due to its bulky volume. Extensive esophageal invasion down to the submucosal layer of the cysts were encountered in patients 2 and 4. The dissection between the muscle and submucosal layers of the esophagus and the cystic wall was then performed with great caution, so as not to injure the mucosal layer. After enucleation of the lesion, esophageal mucosal integrity was checked with an esophagoscopy and insufflation under water. The defect in the esophageal muscle layer was closed in an interrupted fashion with non-absorbable sutures. Oral intake was resumed on the 1st postoperative day in patients 1 and 3, the 3rd day in patient 4, and the 7th day in patient 2. The postoperative courses went smoothly for patients 1 and 3, and they were discharged uneventfully on the 5th postoperative day. Minor complications were encountered in the residual pleural space in patient 2, which subsided after prolonged chest tube drainage, and wound infection in patient 4, which resolved after wound care. The patients showed no signs of ingestion problems or other sequelae during the course of follow-up (from 6 to 39 months, mean 14.8 months). Pathological review of the specimens revealed ciliated pseudostratified columnar epithelial linings admixed with bronchial glands and brownish to greenish mucus content; a hyaline cartilage component was also found in the specimen of patient 3.

Discussion

In embryogenesis, the laryngotracheal groove

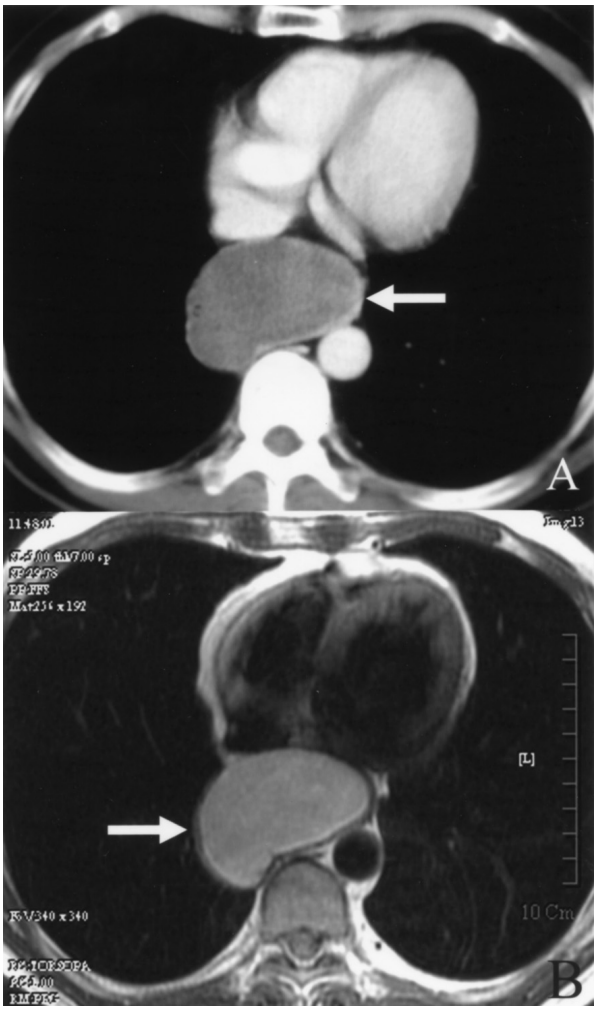

Fig. 2. CT (A) and MRI scan (B) of patient 2 reveals a hypodensed, homogenous lesion with mild ring enhancement (arrows). The esophageal structure was deformed at this level due to severe external compression.

appears at the end of the 3rd gestational foregut. The dorsal portion of the foregut later elongates to form the esophagus, and the ventral part further differentiates to become the respiratory tract. Both the respiratory and the digestive tracts are covered with ciliated epithelium at that time [6]. Disorders in the embryological event are proposed to be the common origin of congenital malformations of bronchogenic cysts and esophageal duplication cysts [7-8]. The etiology also explains why cysts lined with a respiratory-type mucosa are apt to develop not only in the lung, along the tracheobronchial trees, but also along the esophagus [7]. Paraesophageal bronchogenic cysts usually lie below the carina, and can be intramural or completely separate from the esophageal wall, as in the 4 cases presented herein [9], thus making preoperative evaluation important regarding the relationship of the cyst to the surrounding structures, especially the esophagus.

Bronchogenic cysts are generally asymptomatic and usually discovered as incidental radiological findings. As the lesions grow, clinical presentations, including cough, wheezing, fever, dyspnea, and stridor, mostly due to compression and irritation of the adjacent structures or recurrent infection caused by communication to the tracheobronchial trees, may develop and directly relate to the sites and size of the lesions [3, 8, 10]. Compared to intrapulmonary and subcarinal bronchogenic cysts, paraesophageal cysts cause fewer symptoms [11]. Our cumulative experience is consistent with that of previous publications [7].

Concerning the preoperative diagnosis, current advances in non-invasive modalities have greatly improved the preoperative differential diagnosis. Using CT and MRI, information regarding the morphology, location, and detailed relationship to surrounding tissues of the cysts can contribute to clinical judgment, in terms of the approach and procedures of surgical intervention [12]. Esophagoscopy or esophagography could be required to exclude endoluminal lesions or even rarer esophageal communication in the case of paraesophageal bronchogenic cyst [5]. Nevertheless, the definite pathological entity mandates a final histological review of the resected specimen because there exists no preoperative diagnostic tests that can make a

definite exclusion of other mediastinal cysts or malignancy. Therefore, some authors advocate routine excision for pathological confirmation and avoidance of subsequent complications.

To date, VATS is regarded as a beneficial option for the surgical approach in benign mediastinal tumors, except in cases of severe adhesion or tumor invasion, with no difference in mortality, morbidity, or long-term follow-up compared to standard thoracotomy [8, 13-15]. The advantages of VATS over conventional thoracotomy include less invasiveness, due to the smaller incisions that might contribute to fewer morbidities, and excellent visualization that facilitates accurate dissection. Resection of intrapulmonary bronchogenic cysts is frequently more complex than the simple excision of mediastinal cysts, which often requires concomitant anatomical or non-anatomical pulmonary resection. However, the excision of paraesophageal bronchogenic cysts demands meticulous surgical techniques, and more precise anatomical dissection of the cystic wall from the mucosal and submucosal layers of the esophagus without injury of them [16]. If giant, bulky cysts are encountered that jeopardize the subsequent removal of the cysts from mini-thoracotomy wounds, a preceding decompression of the cystic content could facilitate later manipulation, dissection, and removal of the cyst. However, caution should be taken not to contaminate the pleural space to avoid the risk of subsequent empyema. Later, mucosal integrity should be surveyed routinely during the operation, and a muscular defect closure with primary sutures or reinforcement with the pleura or cystic wall is highly recommended [17-18].

In conclusion, paraesophageal bronchogenic cysts are often asymptomatic and usually found incidentally. Surgical resection can be completely and safely preformed by VATS with excellent results.

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行胸腔鏡手術切除之食道旁支氣管性囊腫—四案例報告

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支氣管性囊腫乃氣管支氣管於胚胎發育過程中不正常的變異引發之良性先天性病灶，食道旁支氣管性囊腫相較於其他支氣管性囊腫更為特別，因為常合併有不同程度的食道侵犯及表徵。術前的診斷困難，可是術前的評估對於手術是極為重要的。近十年來胸腔鏡手術以漸成為支氣管性囊腫切除的首選手術切除方式。我們在此報告四例食道旁支氣管性囊腫的案例，分別有不同程度的食道侵犯，並討論在診斷及治療方面的策略。*(胸腔醫學* ***2006; 21: 218-224)***

關鍵詞：支氣管性囊腫，食道，胸腔鏡手術

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