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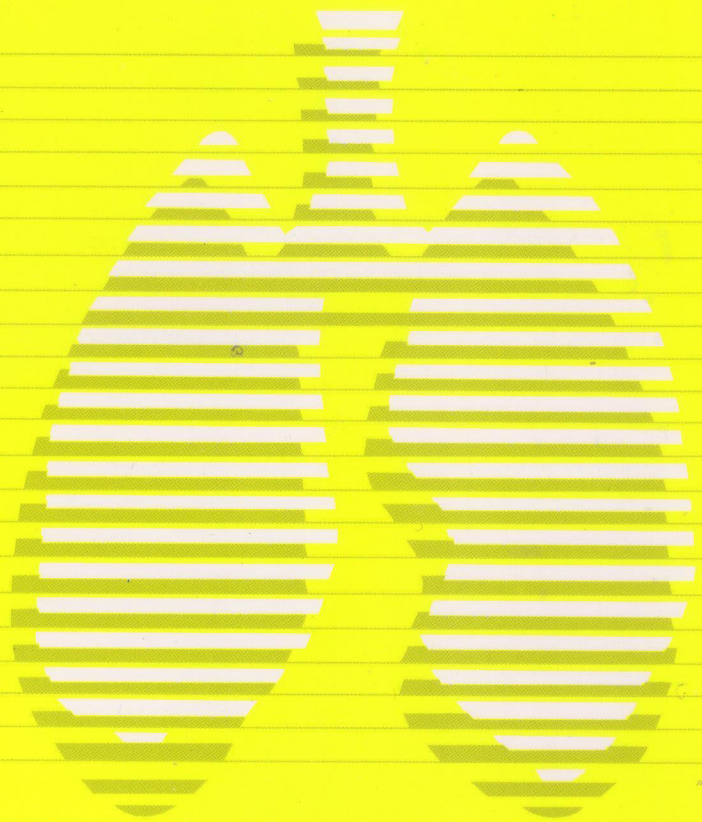

台灣胸腔暨重症加護醫學會

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Orginial Articles

Case Reports

Resistance of *Mycobacterium tuberculosis* to Four First-line Anti-tuberculosis Drugs in a Referral Hospital in Northern Taiwan, 2002-2006

Shian-Jiun Lin, Fang-Lan Yu*, Jau-Ching Lee*, Kuan-Jen Bai, Chun-Nin Lee, Han-Lin Hsu, Ming-Chih Yu

Introduction: The purpose of this retrospective study was to investigate the drug resistance of *Mycobacterium tuberculosis* to 4 first-line anti-tuberculosis (TB) drugs (isoniazid (INH), rifampin (RIF), ethambutol (EMB), streptomycin (SM)) at Taipei Medical University-Wan Fang Hospital from 2002 to 2006.

Methods: From 1 January 2002 through 31 December 2006, drug susceptibility testing for first-line anti-TB drugs, including INH, RIF, EMB, and SM, was performed using the indirect agar proportion method. A retrospective review of medical records to define the drug resistance of new, previously treated, and combined cases was conducted.

Results: Of the 436 *M. tuberculosis* isolates, 343 were recovered from new cases and 93 from previously treated cases. The combined drug resistance rate to at least 1 drug was 17.6%. The drug resistance rate to at least 1 drug among new cases was 11.7% and among previously treated cases was 39.8%. The combined drug resistance rate to individual drugs was 12.4% to INH, 7.1% to RIF, 3.2% to EMB, and 9.2% to SM. The rates of combined multidrug resistance (resistance to at least INH and RIF), among new cases, and previously treated cases were 5.7%, 1.5%, and 21.5%, respectively.

Conclusions: Drug resistance remains a serious problem in the treatment of TB in Taiwan. When treating a TB patient, drug resistance should be considered, especially in previously treated cases. ***(Thorac Med 2008; 23: 316-324)***

Key words: drug resistance, *Mycobacterium tuberculosis*

Introduction

Despite recent global control efforts, tuberculosis (TB) remains a major public health burden in most developing countries. The World Health Organization (WHO) estimated that 8.8 million new cases and 1.6 million deaths resulted from TB in 2005 [1] alone.

The emergence of drug-resistant strains occurs with the wide use and misuse of antimi-

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crobials [2]. The phenomenon of drug-resistant TB is a significant threat to TB control, because only a few effective drugs are available against *Mycobacterium tuberculosis* (*M. tuberculosis*). In particular, the spread of multidrug-resistant (MDR) strains that are resistant to at lest the 2 most important drugs, isoniazid (INH) and rifampin (RIF), could have serious repercussions on the epidemiology and control of TB [3]. While drug-resistant TB is generally treatable, it requires extensive chemotherapy with second-line anti-TB drugs, which are more costly than first-line drugs, and which produce adverse drug reactions that are more severe [4]. Therefore, besides the overall high incidence and mortality, the prevalence of drug-resistant TB is a concern in many parts of the world [5-14].

Taiwan's TB incidence of 67.38/100,000 and the mortality rate of 3.65/100,000 in 2006 are still high [15]. One of the major causes of this sustained high TB mortality is the emergence of drug-resistant TB [16]. Thus, the Taiwan Centers for Disease Control (CDC) initiated the Taiwan Surveillance of Drug Resistance in TB program in 2002 [17].

Causes of drug resistance and the appropriate intervention strategies may vary considerably among different hospitals. Therefore, although drug-resistant TB is a national problem, it is necessary to analyze actual resistance on a hospital basis in Taiwan [16, 18-24].

Taipei Medical University-Wan Fang Hospital (TMU-WFH) became a referral center in northern Taiwan in recent years, and an analysis of the drug resistance of *M. tuberculosis* at this hospital is needed. Therefore, this study aimed to investigate the drug resistance of *M. tuberculosis* to 4 first-line anti-TB drugs (INH, RIF, ethambutol (EMB), and streptomycin (SM)) at in TMU-WFH from 2002 to 2006.

Material and methods

Specimens

TMU-WFH is a 700-bed community hospital affiliated with a medical university in northern Taiwan. Since 2004, the TB Laboratory of TMU-WFH has been 1 of the 9 contract laboratories of the CDC, providing laboratory services for mycobacterial diseases at TMU-WFH and healthcare facilities in northern Taiwan.

All the positive *M. tuberculosis* cultures from patients at TMU-WFH who underwent drug susceptibility testing from 1 January 2002 through 31 December 2006 were included in this retrospective analysis.

Drug susceptibility test

Drug susceptibility testing to first-line anti-TB drugs, including INH, RIF, EMB, and SM, was performed using the indirect agar proportion method [25]. From 1 January 2002 through 31 August 2003, drug susceptibility testing was done in the TB Laboratory of Taipei Municipal Chronic Disease Hospital, which is also 1 of the 9 contract laboratories of the CDC. After that, the testing was performed in the TB Laboratory at TMU-WFH.

M. tuberculosis suspension was inoculated onto Middlebrook 7H10 agar that contained anti-TB drugs and agar without any drug as a control. The drug concentration in the medium was 0.2 μg/mL for INH, 1.0 μg/mL for RIF, 5 μg/mL for EMB, and 2.0 μg/mL for SM. These inoculated culture media were incubated at 37°C for 3 weeks. The number of colony-forming units (CFUs) growing on the drug-containing medium was compared with those growing on a drug-free medium. The drug-containing CFUs

were expressed as a percentage of the drug-free CFUs. Strains of *M. tuberculosis* for which growths on the drug-containing media presented more than 1% of the number of colonies that developed on the drug-free media were considered to be resistant to that agent.

Definitions

We retrospectively reviewed the medical records, with an emphasis on previous anti-TB history. Drug resistance among new cases was defined as the presence of resistant strains of *M. tuberculosis* in a newly diagnosed patient who has never received TB drugs or has received them for less than 1 month of treatment. Drug resistance among previously treated cases was defined as that found in a patient who has previously received at least 1 month of TB therapy. The combined prevalence of drug resistance was defined as that measured in all cases regardless of prior drug treatment [3].

Statistical analysis

To compare the drug resistance rates for different drugs between new and previously treated cases, a chi-squared test was performed. A p value less than 0.05 for differences between each group was considered to be statistically significant.

Results

A total of 1,988 mycobacterial isolates were recovered from 16,918 specimens from both inpatient and outpatient services during this period. After adjusting for duplicated isolates, deleting *Nontuberculous Mycobacteria* and contaminated isolates, 436 *M. tuberculosis* isolates remained and were analyzed.

The drug resistance patterns are summarized in Table 1. Combined resistance to any single drug was 8.5%, to any 2 drugs was 4.6%, to any 3 drugs was 4.4%, and to any 4 drugs was 0.2%.

The drug resistance rates among new, previously treated and combined cases are summarized in Table 2. The drug resistance rates against INH, RIF, EMB, SM, any drug, and MDR were all significantly different between new and previously treated TB cases (p<0.001).

The any-drug resistance rates for each year during this period are shown in Figure 1. We found that an abrupt increase in combined any-drug resistance rates, from 11.7% to 23.8%, occurred from 2003 to 2004. We further discovered that this increase was primarily due to an increase of resistance to any drug among previously treated cases (2003: 22.2%, 2004: 47.6%), and it resulted in an increased overall combined drug resistance rate at TMU-WFH. The main reason appears to be that since TMU-WFH became a major referral TB hospital in northern Taiwan in 2004, there has been an increase in the number of referred cases, with most of them exhibiting drug resistance, probably MDR.

Discussion

The drug resistance rates to at least 1 of the first-line anti-TB drugs (new cases: 11.9%, previously treated cases: 39.8% and combined cases: 17.6%) and MDR-TB (new cases: 1.5%, previously treated cases: 21.5% and combined cases: 5.7%) were high during this period. Thus, anti-TB drug resistance is a serious problem in our hospital.

It appears that primary drug resistance is the result of national TB control programs that were inefficient in the past [26]. The drug

Table 1. Drug resistance pattern among new, previously treated and combined cases at TMU-WFH, 2002-2006

	New cases (n=343)	Previously treated (n=93)	Combined cases (n=436)
One drug	26 (7.6%)	11 (11.8%)	37 (8.5%)
INH	11 (3.2%)	5 (5.4%)	16 (3.7%)
RIF	2 (0.6%)	2 (2.2%)	4 (0.9%)
EMB	2 (0.6%)	1 (1.1%)	3 (0.7%)
SM	11 (3.2%)	3 (3.2%)	14 (3.2%)
Two drugs	11 (3.2%)	9 (9.7%)	20 (4.6%)
INH+RIF	3 (0.9%)	4 (4.3%)	7 (1.6%)
INH+EMB	0 (0%)	0 (0%)	0 (0%)
INH+SM	7 (2.0%)	5 (5.4%)	12 (2.8%)
RIF+SM	0 (0%)	0 (0%)	0 (0%)
RIF+EMB	1 (0.3%)	0 (0%)	1 (0.2%)
EMB+SM	0 (0%)	0 (0%)	0 (0%)
Three drugs	3 (0.9%)	16 (17.2%)	19 (4.4%)
INH+RIF+EMB	0 (0%)	6 (6.5%)	6 (1.4%)
INH+RIF+SM	2 (0.6%)	9 (9.7)	11 (2.5%)
INH+EMB+SM	1 (0.3%)	0 (0%)	1 (0.2%)
RIF+EMB+SM	0 (0%)	1 (1.1%)	1 (0.2%)
Four drugs	0 (0%)	1 (1.1%)	1 (0.2%)
INH+RIF+EMB+SM	0 (0%)	1 (1.1%)	1 (0.2%)

Table 2. Drug resistance rate among new, previously treated and combined cases at TMU-WFH, 2002-2006

	New cases (n=343) n (%)	Previously treated (n=93) n (%)	Combined cases (n=436) n (%)	*p* value+
Any drug	40 (11.7%)	37 (39.8%)	77 (17.6%)	<0.001
INH	24 (7%)	30 (32.3%)	54 (12.4%)	<0.001
RIF	8 (2.3%)	23 (24.7%)	31 (7.1%)	<0.001
EMB	4 (1.2%)	10 (10.8%)	14 (3.2%)	<0.001
SM	21 (6.1%)	19 (20.4%)	40 (9.2%)	<0.001
MDR*	5 (1.5%)	20 (21.5%)	25 (5.7%)	<0.001

*MDR (multidrug resistance): resistance to at least isoniazid and rifampin

+*p* value: drug resistance rate between new cases and previously treated cases

resistance of previously treated cases reflects more recent case mismanagement. The combined prevalence of drug resistance represents an approximation to the proportion of drug-resistant strains circulating in the community [3]. Therefore, drug resistance must be clearly distinguished according to the treatment history of the patient in order to allow a correct interpretation of the data. In our analysis, drug resistance to first-line anti-TB drugs was higher in previously treated cases than in new cases. This result was consistent with previous stud-

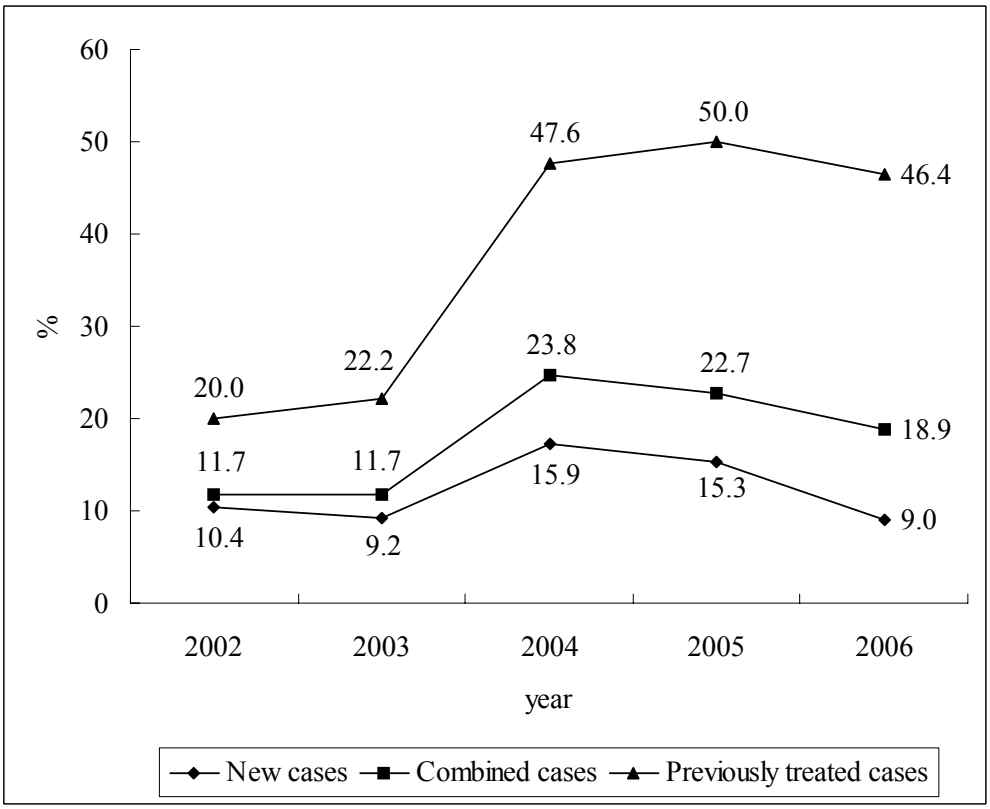

Fig. 1. Resistance rate for any drug among new, previously treated and combined cases at TMU-WFH, 2002-2006

ies [19-20]. Thus, when treating a patient with a previous anti-TB therapy history, drug resistance should be considered, especially in those patients demonstrating no clinical improvement after treatment.

In the third global drug resistance surveillance report, the median prevalence of combined drug resistance was 6.6% to INH, 1.3% to EMB, 2.2% to RIF, 6.1% to SM, 10.4% to any drug, and 1.7% to MDR [27]. The Taiwan Surveillance of Drug Resistance in Tuberculosis program showed the combined drug resistance rates were 9.5% to INH, 5.8% to EMB, 6.4% to RIF, 9.6% to SM, 20.0% to any drug, and 4.0% to MDR [17]. This clearly shows that drug resistance in Taiwan is still a significant problem when compared to the world data. Therefore, the Taiwan CDC recommends that drug susceptibility tests should be performed on initial isolates from all patients, and repeated if the patient continues to produce culture-positive sputum after 4 months of treatment or develops positive cultures after a period of negative cultures [28].

Taiwan susceptibility data from 1990 to 2002 reports showed primary resistance ranged from 4.7-14.9% for INH, 0.7-5.9% for EMB, 1-5.9% for RIF, and 4.8-11.4% for SM. Acquired resistance ranged from 25.6-63.0% for INH, 17.5-46.5% for RIF, 11.1-33.9% for EMB, and 17.1-21.5% for SM. The overall rates of MDR-TB among new cases and previously treated cases were 1.2-2.4% and 15.1-46%, respectively [29]. Our data were similar to previously

published results [29]. However, there was wide variability among these hospital-based data due to the different methods of drug susceptibility testing and cases selection, and the different locations and different characteristics (specialized TB hospitals or general hospitals) of the hospitals [29]. National surveillance of drug resistance should adhere to the following principles: (1) the survey sample must represent the population under study; (2) TB patients must be differentiated by previous history of treatment; and (3) laboratory results must be quality controlled, so it was difficult from our data to predict the trend of the resistance rates to individual anti-TB drugs in Taiwan [30]. However, analysis of anti-TB drug resistance on a hospital scale is needed for the management of TB patients in every hospital.

As seen in Figure 1, we found an abrupt increase in combined any-drug resistance rates in 2004, mainly because of an increase of resistance to any drug among previously treated cases at TMU-WFH. This was probably due to the following: First, a greater increase of new TB cases identified in general hospital settings than in specialized TB hospitals was seen after the initiation of a national health insurance program in 1995 in Taiwan. The formerly centralized TB control administrative and clinical infrastructure was reformed, and there was no specialized TB hospital in northern Taiwan. Thus, many drug-resistant TB patients were decentralized into general hospital settings [24]. Second, more respiratory isolation rooms that were originally prepared for severe acute respiratory syndrome (SARS) patients in 2003 were available at TMU-WFH. Thereafter, more TB cases with drug-resistant strains were referred to TMU-WFH for isolation and treatment.

Resistance of *M. tuberculosis* to antibiotics is a man-made amplification of spontaneous mutations in the genes of *M. tuberculosis*. Thus, there is a strong correlation between both the overall quality of TB control and the use of standardized short-course chemotherapy and low levels of drug resistance [3]. As a reponse, the Taiwan CDC has implemented a widespread Directly Observed Treatment, Short-course (DOTS) strategy since 2006, and a DOTS-Plus strategy for MDR-TB control since 2007.

There were several drawbacks in this study including the fact that drug susceptibility testing was not performed at TMU-WFH until Aug. 2003. It was previously performed in the TB Laboratory of Taipei Municipal Chronic Disease Hospital. Although these 2 TB laboratories were both contract TB laboratories of the CDC and followed the CDC recommendations for drug susceptibility testing, some inter-laboratory bias probably existed. In addition, quality assurance is necessary for the adequate performance of drug susceptibility testing in TB laboratories. However, external quality assessment for drug susceptibility testing was initiated in Taiwan only in 2006. In addition, the ability to accurately distinguish between primary and acquired resistance was not always possible in this retrospective study. Finally, some patients had several isolates with drug susceptibility testing results, but only 1 isolate result was included in this study, probably resulting in some selection bias.

Conclusions

In conclusion, drug resistance remains a serious problem in the treatment of TB in TMU-WFH. Regular surveillance of drug resistance is important in any hospital and interpretation of the data should be in accordance with the

standard definitions of drug resistance. In addition, when treating a TB patient, drug resistance should be considered, especially in previously treated cases.

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北臺灣某後送醫院之四種第一線抗結核藥物抗藥性研究，2002-2006

林賢君　余芳蘭*　李兆清*　白冠壬　李俊年　許翰琳　余明治

前言：探討2002至2006年，台北醫學大學˙萬芳醫院的結核菌對第一線抗結核菌藥物（isoniazid、rifampin、ethambutol及streptomycin）抗藥性情況。

方法：以回溯性方法來調查。從2002年1月至2006年12月，436株接受藥物敏感試驗之結核菌株被分析。藥物敏感試驗使用間接瓊脂比例法（indirect agar proportion method）。

結果：436株結核菌株中，343株來自於新病人，93株來自於曾經治療過的病人。全部菌株中，至少對一種抗結核菌藥物具抗藥性的比率為17.6%。新病人與曾經治療過病人中，至少對一種抗結核菌藥物具抗藥性的比率分別為11.7%與39.8%。全部菌株中，對個別抗結核菌藥物具抗藥性的比率分別為：isoniazid 12.4%、rifampin 7.1%、ethambutol 3.2%、streptomycin 9.2%。多重抗藥性（至少對isoniazid與rifampin具抗藥性）發生於全部病人、新病人、曾經治療過病人的比率分別為：5.7%、1.5%、21.5%。

結論：在臺灣，抗藥性的存在對治療結核病仍然是一嚴重問題。因此，在治療結核病時，特別對曾經使用過藥物的病人，應該要考慮到抗藥性問題。*(胸腔醫學* ***2008; 23: 316-324)***

關鍵詞：抗藥性，結核菌

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Respiratory Mechanics in a Mechanically-ventilated Patient with Developing Pneumothorax–A Case Report

Chu-Kuang Chen, Chang-Wen Chen, Meng-Yi Chou*

Pneumothorax that develops in intubated patients under volume-controlled ventilation (VCV) is usually associated with increased peak and plateau airway pressures [1-2]. We report the early evolutional changes in the respiratory mechanics of an intubated patient who developed pneumothorax immediately after a bronchoscopic examination while under volume-controlled ventilation. We found that the patient's airway plateau pressure did not increase in the early developing stage of pneumothorax, and that the decay of the plateau pressure was more pronounced. These findings may give us early warning signs of a developing pneumothorax in mechanically-ventilated patients. ***(Thorac Med 2008; 23: 325-329)***

Key words: pneumothorax, volume-controlled ventilation, airway pressure

Introduction

Pneumothorax that develops in intubated patients under volume-controlled ventilation (VCV) is usually associated with increased peak and plateau airway pressures [1-2]. But airway pressure profiles may be atypical when the pneumothorax is just beginning. Herein, we report a ventilated patient with newly-developing pneumothorax who showed interesting evolutional changes in respiratory mechanics.

Case Report

A 65-year-old female was intubated and admitted to our intensive care unit (ICU) due to idiopathic pulmonary fibrosis with acute respiratory failure. One week after admission, bronchoalveolar lavage (BAL) was performed to obtain a quantitative bacteriological culture, due to the suspicion of ventilator-associated pneumonia. Informed consent was obtained from the patient's next of kin for the measurement of respiratory mechanics before and after BAL. The patient was sedated, pain-controlled and paralyzed immediately before BAL, and was under VCV with a tidal volume of 400 ml, a constant flow of 0.8 liter/second, a positive end-expiratory pressure level of 8 cmH_2O, and a respiratory rate of 20 times/minute. BAL was done via bronchoscope with 125 ml of normal saline in the left basal segment; about 75 ml of fluid was

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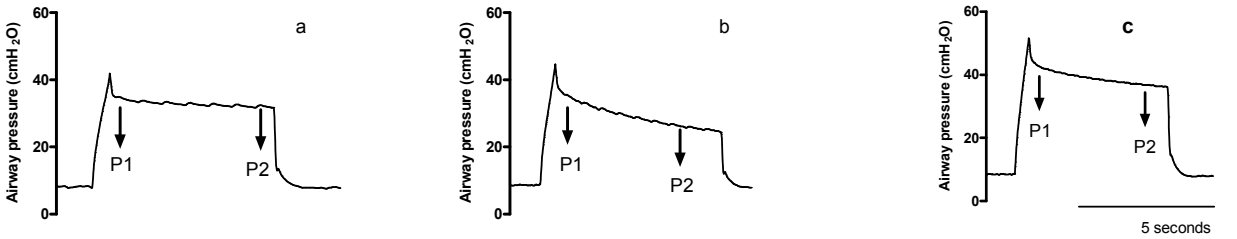

Fig. 1. Airway pressure tracings during measurement of respiratory mechanics using the rapid airway occlusion technique in this patient receiving BAL to obtain a quantitative bacteriological culture. (a) Before BAL (b) Immediately after BAL (c) 30 minutes after BAL

recovered. The procedure lasted approximately 5 minutes and no changes in oxygen saturation or hemodynamics were found. Measurement of respiratory mechanics was done using the rapid airway occlusion technique. This technique was performed before, after immediately, and 30 minutes after BAL. The evolutional changes in airway pressure under the same tidal volume and flow rate are shown in Figure 1. Prior to BAL, airway pressure tracing during an inspiratory hold showed a small drop from Pmax (peak airway pressure) to P1 (airway pressure at zero flow, Pmax-P1 = 6.69 cmH_2O) and a slow decay from P1 to P2 (plateau pressure 5 seconds after P1; and ΔP = P1-P2 =3.5 cmH_2O) (Figure 1a). The Rmin [minimal resistance = (Pmax-P1)/flow] was 8.64 cmH_2O/L/S. The ΔR [delta resistance = (P1-P2)/flow] was 4.53 cmH_2O/L/S. However, a measurement taken immediately after BAL revealed a remarkable change in the conformation of the plateau pressure tracing (no evident change in Pmax-P1, and the Rmin = 7.4 cmH_2O/L/S; with widened ΔP = 10.7 cmH2O, and increased ΔR = 13.91 cmH_2O/L/S) (Figure 1b). This finding was unusual, based on our past experience. Circuit leakage was considered at first, but was excluded after careful examination. The breathing sound in the bilateral lungs remained stationary at that time. Since there was no obvious deterioration in the clinical condition, the measurement was repeated 30 minutes later, and both Pmax and P1 had clearly increased, but the conformation of the plateau pressure tracing remained abnormal, with ΔP = 8.3 cmH_2O (Figure 1c). The Rmin only slightly increased (8.77 cmH_2O/L/S) and the ΔR became 11.89 cmH_2O/L/S. After the last measurement, we repeated auscultation and noted a decreased breathing sound in the left lung. Systemic hypotension occurred soon after that,

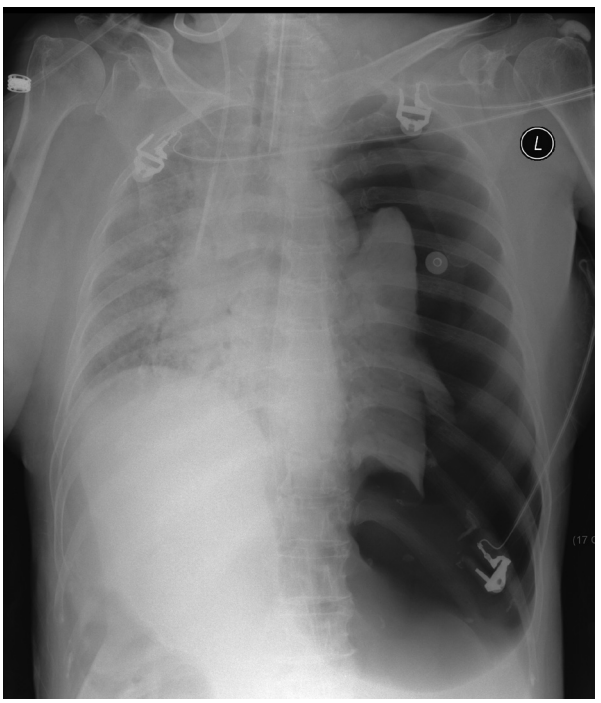

Fig. 2. Chest radiograph after BAL showed evident left pneumothorax.

and the diagnosis of tension pneumothorax was confirmed by chest radiography (Figure 2). We then performed an emergent tube thoracotomy for the left pneumothorax, and her vital signs stabilized thereafter.

Discussion

Pneumothorax developing in a mechanically-ventilated patient is an emergency event in the ICU, due to its great impact on hemodynamics and oxygenation. In addition to the clinical features indicating a deteriorated condition, elevated peak airway and plateau pressure were reported. Therefore, these 2 indicators can be used as supportive evidence of this catastrophe [1]. In our current case report, we noted an elevated peak airway pressure from the beginning of the pneumothorax. However, the plateau pressure decreased at first, and became elevated 30 minutes later. We believe this is the first live demonstration of evolutional changes in the respiratory mechanics of a mechanically-ventilated patient with developing pneumothorax.

The respiratory system is composed of a viscoelastic material. Following the application of constant flow ventilation, airway plateau pressure will not remain constant because stress relaxation of the respiratory system may occur. With this ventilator setting, the use of the interrupter method for the measurement of respiratory mechanics allows possible quantification of the viscoelastic properties of the respiratory system [3]. The difference between Pmax and P1 provides major information about airway resistance (Rmin), while the difference between P1 and P2 (ΔP) represents viscoelastic resistance or the Pendelluft effect of the respiratory system. It is obvious that the principle change after pneumothorax was the ΔP of this patient. Of more interest is the nature of the evolutional changes in her respiratory mechanics. The following is our speculation regarding this.

In the initial stage of the development of pneumothorax, the plateau pressure did not increase because the intrapleural pressure may have been much lower than the alveolar pressure. As a result, a fast pressure drop occurred during the inspiratory hold. Later, increases in peak airway and plateau pressure became evident after significant intrapleural air accumulation. Of note was the persistently widened ΔP as the pneumothorax continued, reflecting changes in the viscoelastic properties and/or the mechanical inhomogeneities of the walls of the lung and chest [4]. We also found decreased amplitude of airway pressure fluctuation caused by the cardiogenic oscillation (Figure 1). This could be explained by the cushion effect of air in the left pleural space with a possibly decreased stroke volume [5].

We had unexpectedly recorded the evolutional changes in respiratory mechanics in a mechanically-ventilated patient with developing pneumothorax after BAL for diagnostic purposes. We were puzzled when we could not find a reason to explain the widened P1-P2 initially. The subsequent proof of developing pneumothorax gave us the proper answer. Decreased plateau pressure or widened ΔP in a mechanically ventilated patient under VCV may be an early warning sign of developing pneumothorax, if there is no leakage in the ventilator circuit.

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一個接受機械通氣的病人發生進展中氣胸的呼吸力學—個案報告

陳主光　陳昌文　周孟誼*

一個接受容積控制通氣模式的插管病人發生氣胸，通常其呼吸道峰值壓力與平原壓力會上升。而我們報導一位接受容積控制通氣模式之插管病人，於接受完支氣管鏡檢查後，隨即發生氣胸的早期呼吸力學變化，我們發現於其氣胸發展的早期，呼吸道平原壓力並沒有立即升高，而其平原壓力的衰減是較一般的情形要來得顯著，這些發現或許可以當作是使用呼吸器的病人發生氣胸的早期徵兆。*(胸腔醫學* ***2008; 23: 325-329****)*

關鍵詞：氣胸，容積控制通氣模式，呼吸道壓力

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Primary Malignant Fibrous Histiocytoma of the Lung with an Initial Presentation of Extremities Pain: A Case Report

Chao-Yang Hung, Yung-Wei Tung*, Ya-Chiung Chu, Shien-Tung Pan**

Primary malignant fibrous histiocytoma (MFH) of the lung is a very rare pulmonary malignancy. It is often diagnosed only after other primary origin of the tumor have been excluded. Thus, the patient must be carefully evaluated for possible metastasis. There is so far no documented benefit from adjuvant chemotherapy and radiotherapy. For this reason, the favorable outcome of the patient will primarily depend on an optimal surgical resection. We report herein, for the first time, a patient presenting with a bilateral lower leg pain that turned out to be a case of MFH. We noted that the patient presented with hypereosinophilia and bilateral lower leg hypertrophic pulmonary osteoarthropathy. Subsequently, the patient underwent surgery in order to complete the removal of the tumor. After the surgical procedure, the patient recovered dramatically, and was thoroughly monitored and followed-up for 15-months, during which, the patient remained disease-free and in good condition. ***(Thorac Med 2008; 23: 330-336)***

Key words: malignant fibrous histiocytoma, leg pain, hypereosinophilia, hypertrophic pulmonary osteoarthropathy

Introduction

Malignant fibrous histiocytoma (MFH) is the most common soft tissue sarcoma of late adulthood, and especially involves the lower extremities [1, 3, 9], but it rarely occurs in the lung [1, 3, 5, 8]. Primary lung MFH often presents with respiratory tract symptoms, but never with muscular symptoms. Herein, we describe a patient whose chief complaint was bilateral lower leg pain and general weakness, which surprisingly turned out to be an intrathoracic malignancy.

Case Report

A 51-year-old man with a past history of rheumatic arthritis, suffered from severe soreness in the bilateral lower legs for 2 weeks, and right shoulder pain with limited external rota-

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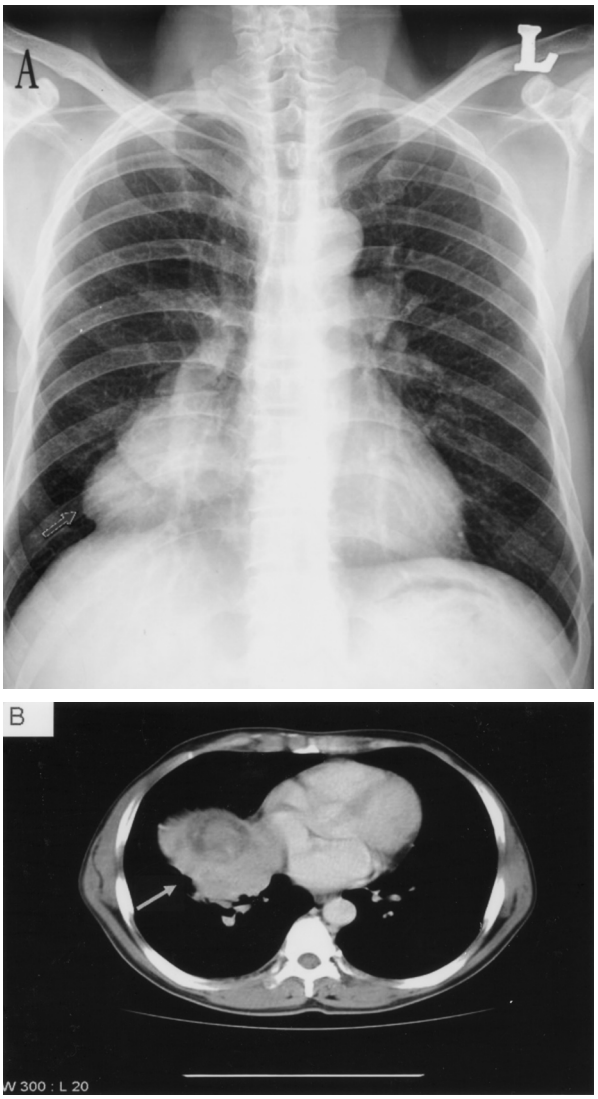


Fig. 1. (A) Chest X-ray PA view showing RML mass (arrow); (B) Mass compressing cardiac chamber (arrow)

tion for several months. No improvement was noted after taking pain relief medications. The discomfort was localized in the para-articular area of the lower legs, with pain and tenderness. Rheumatic arthritis was not the correct diagnosis, for no characteristic symmetrical arthritis in the proximal interphalangeal and metacarpophalangeal joints was noted. Routine chest roentgenography (Figure 1A) revealed a large mass in the right middle lobe (RML) and chest computed tomography (CT) (Figure 1B) disclosed a large lobulated heterogeneous mass (9×7 cm) compressing the cardiac chamber without any mediastinal lymphadenopathy. Distinct laboratory results included hypereosinophilia (WBC: 19500, eosinophil: 22.6%). A whole body tumor scan showed increased density in the right middle lung (Figure 2). Bone scans showed no bony metastasis, but bilateral forearms and lower legs presented hypertrophic pulmonary osteoarthropathy (Figure 3A).

Bronchoscopy revealed an external compression at the RML without visible tumor, and CT-guided biopsy showed only focal necrosis with inflammatory cells, but malignancy was highly suspected. We suspected first that the patient might have Wegener's granulomatosis, but the negative result for antineutrophilic cytoplasmic antibodies made this diagnosis unlikely. Thoracoscopy showed a mass measuring 10×9×8 cm located at the lateral segment of the RML, with an extension to the hilar region invading the right lower lobe (RLL), accompanied with little pleural effusion. The frozen section of the tumor showed inflammatory cells

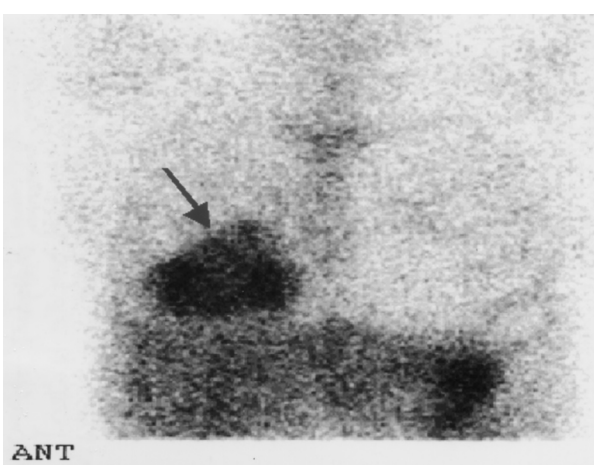


Fig. 2. Whole body tumor scan showed right middle lung increased density (arrow)

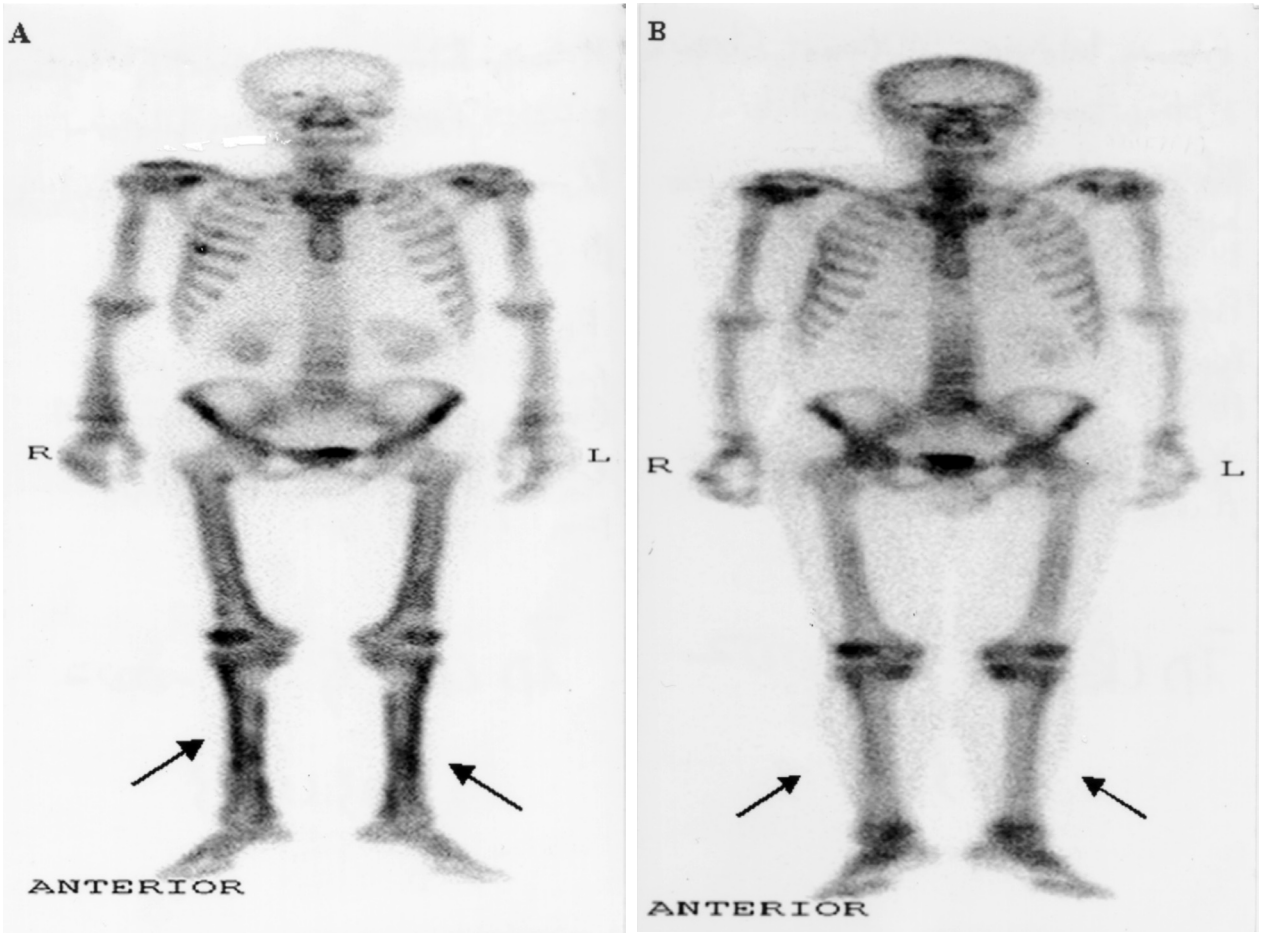


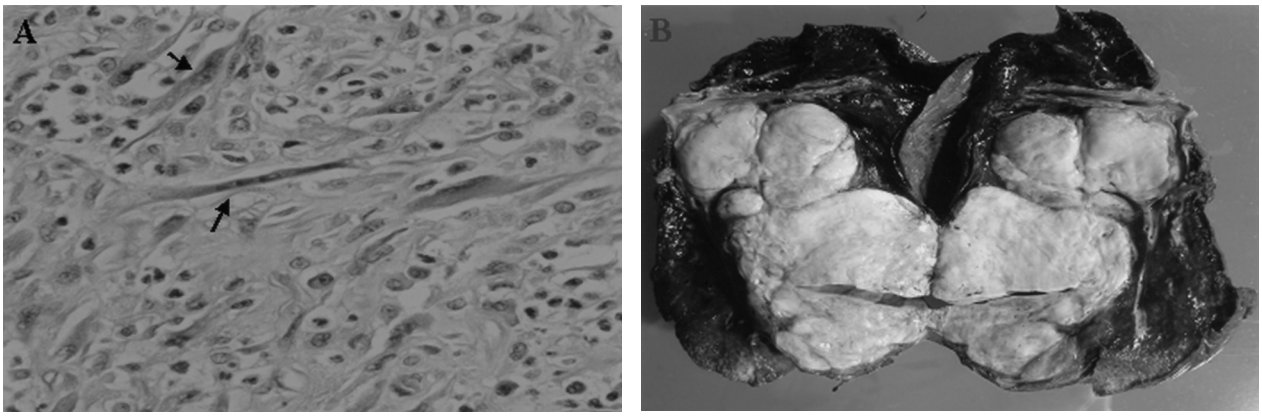
Fig. 3. (A) Bilateral lower legs hypertrophic pulmonary osteoarthropathy (arrow); (B) showed improvement 3 months after operation (arrow)

without malignant cells. So, only a part of the RML tumor was resected and sent for pathological study.

The immunohistochemical stains displayed a positive reaction to vimentin and CD68, but no reactivity to EMA, S-100 protein, CD30, and desmin. The tissues showed an inflammatory-type solid lesion with scattered and focal aggregates of atypical cells. The cells displayed large multinucleated giant nuclei with pleomorphism, and were accompanied with numerous inflammatory eosinophils, lymphocytes, plasma cells and neutrophils (Figure 4A). Based on the results of hematoxilin and eosin staining, plus immunohistochemical studies, the diagnosis of inflammatory malignant fibrous histiocytoma (undifferentiated pleomorphic sarcoma with prominent inflammation) was finally made.

The patient received a bilobectomy of the RML and RLL after the definite pathological diagnosis had been made. The operational findings yielded a gray-white and firm multinodular tumor measuring 17×16.5×11 cm (Figure 4B).

After that, the patient received regular clinical follow-up without adjuvant chemotherapy and radiotherapy. A bone scan 3 months later showed resolution of the hypertrophic pulmonary osteoarthropathy in the bilateral forearms



(A) (B)

Fig. 4. (A) (Hematoxilin & Eosin stain 200X) Microscopic finding of thoracoscopy: spindle cells with scattered bizarre giant nuclei (arrows), background with various inflammatory cells; (B) Gross picture of the tumor

and lower legs' (Figure 3B). The hypereosinophilia improved concomitantly (WBC: 6600, eosinophil: 2.0%). Fifteen months following the operation, the patient was doing well.

Discussion

MFH, originally described by O'Brien and Stout in 1964, is the most common malignant soft tissue tumor among elderly adults. The most common sites of occurrence are the extremities (lower extremities 49%, upper extremities 19%), retroperitoneum and trunks [1, 4, 6, 9, 11]. Patients with MFH range in age from 5-93 years, with a mean of 52 years, and with a peak incidence occurring at 61-70 years of age. There is a slight male prevalence [3-4, 7, 9], but some female occurrence has been observed [1, 15]. Five types of MFH have been identified: storiform-pleomorphic, myxoid, inflammatory, giant cell, and angiomatoid [1]; the majority is of the storiform variety [3, 7, 9, 14]. The local recurrence rate of the tumor is 44% and the metastatic rate is 42%. The most frequent metastatic sites are the lung (82%) and lymph nodes (32%) [5, 8-9]. Although the lung is the organ most frequently involved in metastatic MFH, metastases from MFH rarely occur before the primary tumor is found.

Primary lung sarcomas are rare, with an incidence of around 1 in every 500 carcinomas. The most frequent primary pulmonary sarcomas are fibrosarcoma and leimyosarcoma [1-5, 8, 11]. Among all lung cancers, MFH ranks third, comprising 0.02%-0.3% of cases [1, 4, 7, 12-13]. Bedrossian *et al*., reported the first pulmonary MFH case in 1979 and designated it a mesenchymal sarcoma [10]. The most common presenting symptoms are chest pain, cough, dyspnea and hemoptysis, but some patients may be asymptomatic. After a thorough search of the current literature, we found no other mention of a complaint of myalgia of primary lung MFH as in our case. [1, 5-6, 11-14] Most primary pulmonary MFH were located peripherally, without preference for the left or right, and with a slight preponderance to the middle and lower lobes [3-5, 7, 11-12, 14]. Most primary lung sarcomas presented as a mass-like lesion on chest roentography [1-2, 4, 6-7]. No charac-

teristic pulmonary MFH image findings have been put forth, but according to Halyard *et al*. [4], the tumor is usually large, solitary and non-cavitating.

Preoperative diagnosis of pulmonary MFH is difficult, even with a perioperative frozen section examination [6, 8], as in our case. Previous studies have shown that, the final diagnosis requires permanent resection [6, 8]. Since this tumor originates from mesenchymal cells and rarely invades the bronchial mucosa, the sputum cytological examination often yields negative results. Bronchoscopy rarely reveals a solid tumor [8, 13].

In a Medline search, we found no reports describing hematological abnormality in pulmonary MFH. Thus, we have tried to identify the cause of the hypereosinophilia in this patient. The so-called "hypereosinophilia syndromes" can be divided into 3 main categories: reactive eosinophilia, clonal eosinophilia and idiopathic eosinophilia [17-18]. Since the hypereosinophilia of this patient subsided after removal of the tumor, we believe that this hematological abnormality could be linked to pulmonary MFH. In addition, the possibility that our patient had an allergic response to a drug, parasitic infection, atopic disease or hematological malignancy can be ruled out.

Microscopic primary lung MFH can show malignant spindle cells and can be differentiated from other sarcoma by evidence of histiocytic cells, fibroblastic cells and multinucleated giant cells [3, 8, 11, 13]. An immunohistochemical study of MFH showed a positive reaction to vimentin, CD68, and alpha-1-antitrypsin, and a negative reaction to SMA, EMA, Desmin, S-100, cytokeratin, CD34, CD 117 and caldesmon [3, 5, 11, 13]. The histology findings and immunohistochemical staining substantially reconfirmed our diagnosis.

The treatment of choice for primary lung MFH is complete surgical resection [3, 6-8, 11-13, 15-16]. Incomplete resection of metastatic lung MFH is associated with decreased survival [16]. The role of chemotherapy and radiotherapy has not yet been determined [3, 11-12, 14-15]. Some authorities have emphasized the prognostic value of regional lymph node involvement [3, 6]. Maeda *et al*. observed an obviously better 5-year survival rate when no lymph node metastasis occurred (27% vs. 49%), suggesting the importance of regional lymph node systemic dissection [6].

Primary lung MFH is a malignancy with a high rate of local recurrence and metastasis. The contributing factors include tumor depth, size, and inflammatory components [9]. Metastasis is not rare and the brain is the most common site of occurrence [3]. Aoe *et al*. suggested that there is a 12-month median survival [15], but long-term survival of up to 5 years has been reported [3, 11, 15]. The survival rate is not related to histologic type, but is influenced by presenting symptoms, staging at diagnosis, surgical mode, and occurrence of metastasis [1, 4, 11]. Age, gender, tumor size and tumor location have no prognostic value [15].

Our patient was in good condition after the operation and no recurrent signs were noted in 15 months of follow-up. Based on a current literature search, this is the first reported case of malignant fibrous histiocytoma presenting with the paraneoplastic symptoms of hypertrophic pulmonary osteoarthropathy and hypereosinophilia.

Abbreviations: Malignant Fibrous Histiocytoma (MFH)

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原發性肺部惡性纖維組織瘤以雙下肢疼痛爲表現：病例報告

洪朝陽　童詠偉*　朱亞瓊　潘憲棠**

原發性肺部惡性纖維組織瘤為一類極罕見之肺癌。診斷為肺原發前必須先排除其他原發部位。必須檢查病人是否有轉移病灶。預後因素決定在手術切除範圍，目前沒有證據証明術後化學療法和放射療法之好處。本病例是首位以雙下肢疼痛表現之報告。病人一開始出現高嗜伊紅性血球症及雙下肢肥大性肺病骨關節病變，可是這些病徵在腫瘤切除後便消失。而且病人在術後十五個月持續表現良好。*(胸腔醫學* ***2008; 23: 330-336)***

關鍵詞：原發性肺部惡性纖維組織瘤，高嗜伊紅性血球症，肥大性肺病骨關節病變

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Thyroid Metastasis from Lung Adenocarcinoma: Report of a Case

Chung-Hsing Hsieh*, Chien-Da Huang*,***, Chih-Wei Wang **, Horng-Chyuan Lin*

Metastasis to the thyroid gland is rare, despite the rich vascular supply. Thyroid metastasis from lung carcinoma indicates a poor prognosis, and the average survival is 2 months. We report a 44-year-old woman with adenocarcinoma of the lung metastatic to the thyroid that responded poorly to tyrosine kinase inhibitor (TKI) target therapy. Ultimately, the patient succumbed to her disease. ***(Thorac Med 2008; 23: 337-343)***

Key words: lung cancer, thyroid gland, metastases

Introduction

Despite the high vascular perfusion of the thyroid gland, second only to the adrenal gland, it is rarely a site of clinically significant metastatic disease [1]. Previous studies have found that metastatic thyroid tumor is detected by surgical pathology in only 1.4% of clinically evident patients. It was also reported that the application of pre-operative fine-needle aspiration (FNA) cytology for thyroid masses showed incidences of metastatic thyroid involvement of 5.7% to 7.5% [2-4]. Therefore, metastatic thyroid tumor is rarely diagnosed clinically. The most frequent sites of primary tumor include the kidney and breast; metastatic thyroid tumor from lung cancer dysfunction is extremely rare. The prognosis is poor when the thyroid gland is involved [2].

Herein, we present the case of a 44-year-old female with a metastatic spread of lung adenocarcinoma to multiple areas, including lung-to-lung, the pericardium, spine, liver, and left ovary, right malignant pleural effusion, and the thyroid gland.

Case Report

This 44-year-old female patient, a non-smoker, had been diagnosed with thyroid nodular goiter in November 2002, without regular follow-up at an outpatient department. She had had dry cough since April 2005, and on September 2005, the cough became productive with whitish sputum. And, she had tachycardia and exertional shortness of breath, even

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when walking up 1 flight of steps in the most recent 2 months. She went to National Taiwan University Hospital (NTUH) for follow-up of the thyroid goiter. Two thyroid nodules were palpable. Thyroid echo was performed and revealed 2 nodules of mixed echogenecity. Fine-needle aspiration cytology (FNAC) of the thyroid showed adenocarcinoma. Chest radiography was taken for the dyspnea and prolonged cough, and revealed bilateral infiltrates with right pleural effusion. Because of the dyspnea and prolonged cough, she came to our chest outpatient clinic on March 28, 2006. Chest radiography revealed bilateral infiltrates with right pleural effusion (Figure 1A) and admission was arranged.

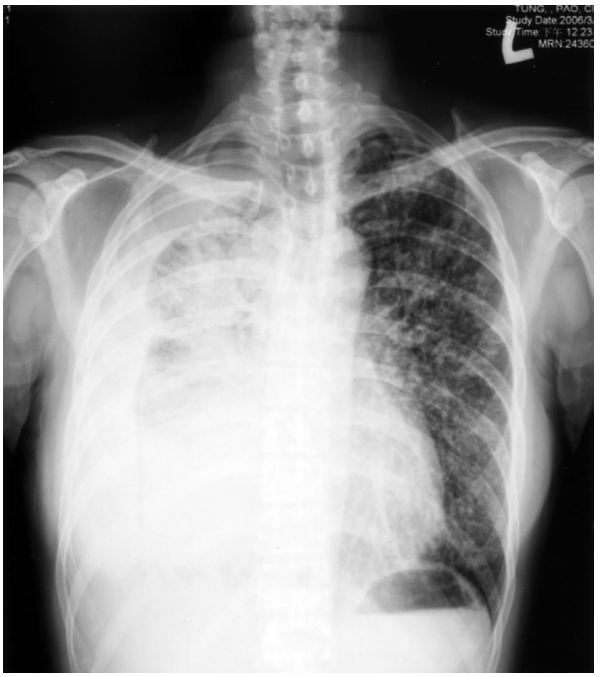

Fig. 1A. Chest radiograph shows bilateral lung field infiltrates with right pleural effusion.

After admission, a whole body CT (Figure 1B) with contrast enhancement was performed, and showed a left thyroid goiter of 28 mm in size, right lung infiltration forming consolidation around the hilum, right massive pleural effusion, and numerous miliary nodular lesions in the left lung field. Lung metastasis or lung cancer with lung-to-lung metastases was suspected. Abdominal CT revealed 2 liver nodules at S4 and S6, 12 mm and 1 cm in size, respectively, as well as a left ovarian neoplasm, 4 cm in size, which could have been a primary tumor or metastases.

The total serum triiodothyronine (T3), thy-

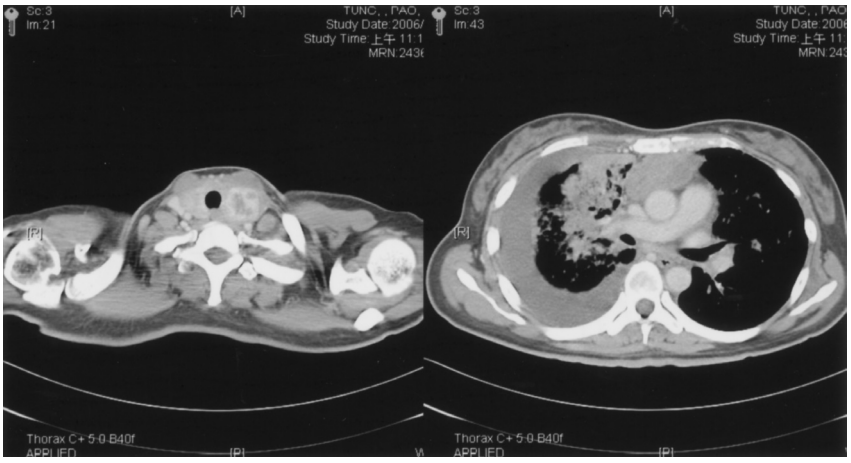

Fig. 1B. Computed tomography with contrast enhancement of the chest shows a left thyroid goiter of 28 mm in size, right lung infiltration forming consolidation around the hilum, right massive pleural effusion, and numerous miliary nodular lesions at the left lung field.

roxin (T4), and thyrotropin (TSH) were within normal ranges of 81.1 ng/dl (62~168 ng/dl), 8.20 ug/dl (5~12 ug/dl), and 1.33 uU/ml (0.25~4 uU/ml), respectively. However, tumor markers, including carcinoembryonic antigen (CEA) and CA-125, were elevated to 130 ng/ml (<5, <7 (smoker) ng/ml) and 185 U/ml (<35 U/ml), respectively.

We performed bronchoscopy, which showed polyp-like lesions in the lower trachea, and the right bronchial trees showed diffused erythematous and edematous change. Furthermore, we performed radial endobronchial ultrasound (EBUS), which revealed an ill-defined margin with linear air-bronchogram (Figure 2). Transbronchial biopsy, bronchial washing and brushing from RB4 and 5 were performed, and the pathology showed poorly differentiated adenocarcinoma. Immunohistochemical study was performed to determine whether the adenocarcinoma was from the lung, ovary or thyroid. The tumor cells showed positive for thyroid transcription factor-1 (TTF-1) and cytokeratin 7 (CK7), and negative for CK20. Therefore, it was shown to be a primary pulmonary adenocarcinoma. Furthermore, a chest echogram was performed, showing a massive amount of right-side pleural effusion, and thoracocentesis was performed, which revealed positive for metastatic adenocarcinoma.

Neck CT showed a soft tissue mass of 2.5× 2.7 cm in the left thyroid, in the avid heterogeneous contrast enhancement. CT-guided core biopsy of the thyroid tumor was performed to differentiate whether it was metastatic adenocarcinoma or primary thyroid cancer with synchronous lung metastases. The pathology of the thyroid biopsy showed a core of thyroid tissue with focal papillary adenocarcinoma, without the nuclear characteristics of thyroid papillary carcinoma (Figure 3). Immunohistochemical study showed the adenocarcinoma cells were negative for thyroglobulin, positive for CK7, and focally positive for CK19. The neoplastic thyroid follicles were positive for thyroglobulin and negative for CK-7 and CK-19. Therefore, the adenocarcinoma was determined to be a metastatic tumor, and lung origin was favored.

Intravenous chemotherapy was not considered because of the poor performance status.

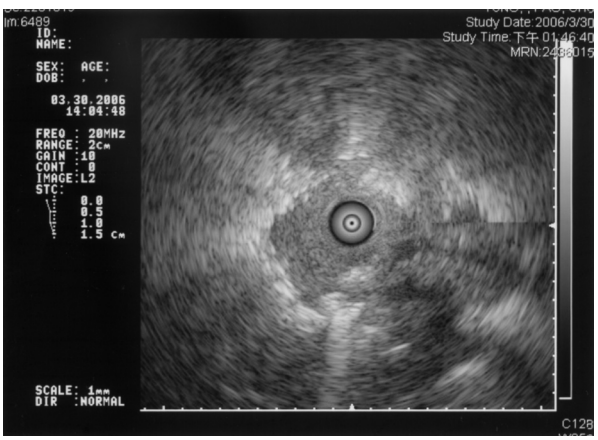

Fig. 2. EBUS with a small-caliber ultrasound probe reveals a lesion with heteroechogenecity of an ill-defined margin with linear air-bronchogram.

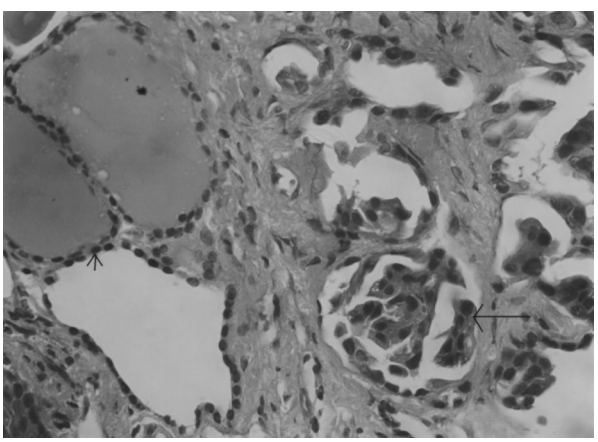

Fig. 3. The biopsy of the thyroid gland shows invasive nests of metastatic pulmonary adenocarcinoma (long arrow) within the thyroid tissue. The adjacent thyroid follicles (short arrow) are also seen (hematoxylin & eosin stain, 400X).

Gefitinib was started on April 6, 2006, and the CEA of 26.8 ng/ml (<5, <7 (smoker) ng/ml) showed improvement. The patient was discharged on April 25, 2006, with a relatively stable clinical condition.

Despite treatment with gefitinib, her condition rapidly deteriorated 2 months later and she died of septic shock. The family refused to give permission for a postmortem examination.

Discussion

Metastasis to the thyroid gland is rare, despite its rich vascular supply. At autopsy, the prevalence of metastatic thyroid gland involvement was found to range from 1.9~24% [1]. The most common primary source has varied among some series, and included lung cancer, breast cancer, and renal cell carcinoma [6-8]. Although the prevalence of metastatic thyroid lesion can reach 24% in autopsy, clinically overt metastasis in the thyroid gland is unusual and may be a diagnostic problem. Particularly, most metastatic lesions have no abnormal thyroid function, and are in a euthyroid status. Hyperthyroidism or hypothyroidism is rarely seen in metastatic lesions [8-10]. Secondly, the clinical presentation of the metastatic tumor may be confused with primary thyroid disease [3]. Finally, it is difficult to differentiate by cytology or histology whether it is a primary or metastatic lesion. In our case, the pathology of the thyroid biopsy showed a core of thyroid tissue with focal papillary adenocarcinoma, similar to the characteristics of thyroid cancer. In these cases, immunohistochemical studies are helpful in discriminating between primary and metastatic adenocarcinomas of the lung and also useful in suggesting the primary sites of some metastatic adenocarcinomas [11-12]. The series examinations in the present case revealed tumor lesions in the lung, ovary and thyroid. Radiographic features are not useful in making a determination. Therefore, immunohistochemical studies were performed in order to differentiate whether the adenocarcinoma was from the lung, ovary or thyroid. Pathological tissue from both the lung and thyroid gland showed similar histological findings. The lung tumor cells were positive for TTF-1 and CK7, and negative for CK20. The thyroid lesion was then determined to be a primary pulmonary adenocarcinoma. Furthermore, immunohistochemical studies showed the thyroid adenocarcinoma cells were negative for thyroglobulin, positive for CK7, and focally positive for CK19. The non-neoplastic thyroid follicles were positive for thyroglobulin and negative for CK-7 and CK-19. Therefore, the thyroid cancer was determined to be a metastatic tumor, and lung origin was favored.

The appearance of thyroid metastasis indicates a poor prognosis in lung carcinoma, where it represents a pre-terminal event, with an average survival from diagnosis to death of 2 months [8]. The effectiveness of conventional treatment has been questioned [13]. In one series, Vassilopoulou-Sellin demonstrated that occult thyroid cancer or metastatic thyroid cancer may present as an incidental finding; clinically relevant thyroid cancer did not develop in any of the patients during the duration of documented follow-up (1-15 years). Most of the mortality was due to the primary tumor or unrelated disease. (Three patients died of progressive tongue cancer, 1 patient of unrelated pulmonary disease, and 4 patients remained alive without evidence of disease throughout the 1 to 15 years of available follow-up) [14]. In our case, aside from the 2 palpable thyroid nodules, there was

no other symptom of thyroid disease. Instead, a symptomatic manifestation of pulmonary disease appeared to be the initial manifestation. Therefore, the thyroid metastasis might be neglected or misdiagnosed as thyroid goiter.

There is no standard of treatment for thyroid metastases. Although some series reported poor clinical outcomes with conventional treatment, 1 series suggested if isolated metastatic cancer to the thyroid is found, surgical resection should be performed, usually by lobectomy and isthmusectomy. Unfortunately, the prognosis is poor, but surgery often prolongs the disease-free interval and occasionally the disease will not recur [5]. Recently, another series suggested that resection of the metastatic tumor with thyroidectomy may achieve long-term survival, especially in renal cell carcinoma with an isolated thyroid lesion [6, 15]. Although detection of metastasis to the thyroid gland often indicates a poor prognosis, aggressive surgical and medical therapy may be effective in a small percentage of patients [16].

Survival in the present case was only 2 months, which was consistent with that recorded in previous studies of lung adenocarcinoma with clinically overt thyroid metastasis. However, 1 series showed that occult thyroid metastases led to a completely different clinical result. The kind of patient that is prone to having clinically occult lesion and the factors that tend to make the lesion evident seem to be related to the aggressiveness of the tumor and patient survival. Better understanding of the kind of patient that might develop occult lesion could be helpful in guiding us to discover new therapeutic options, and an understanding of factors that lead to destructive disease could be helpful in shedding light on the possibility of modifying such factors and the accompanying poor prognosis.

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肺腺癌轉移至甲狀腺：一病例報告

謝宗鑫* 黃建達*,*** 王志偉** 林鴻銓*

轉移至甲狀腺是非常罕見的，既使它具有豐富的血管。來自肺癌的甲狀腺轉移是惡劣的預後指數而它的平均存活的時間是二個月。我們提出一44歲女性因肺腺癌轉移至甲狀腺接受酪胺酸kinase抑制劑（TKI）標靶治療。最後病人對標靶治療無效而死亡。*(胸腔醫學* ***2008; 23: 337-343)***

關鍵詞：肺癌，甲狀腺，腫瘤轉移

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Diffuse Pulmonary Nodules with Bilateral Hilar Lymphadenopathy as a Clinical Presentation of Primary Amyloidosis with Pulmonary Involvement: A Case Report

Hsien-Chih Huang, Jung-Sen Liu*, Yi-Ying Wu**, Chih-Yu Hsu

Amyloidosis is a relatively rare disease in clinical practice. However, pulmonary involvement in patients with amyloidosis is common. We report a 46-year-old female who presented chronic cough with mild dyspnea on exertion for about 5 weeks. Chest radiography showed diffuse pulmonary nodules with bilateral hilar lymphadenopathy. Serum protein electrophoresis followed by immunofixation electrophoresis revealed a monoclonal band of IgG-λ specificity, and multifocal amyloid deposits were found in the lung biopsy via video-assisted thoracoscopic surgery. A diagnosis of primary amyloidosis with pulmonary involvement was confirmed. ***(Thorac Med 2008; 23: 344-348)***

Key words: lung, primary amyloidosis

Introduction

Systemic amyloidosis is caused by the deposition of mainly (92%) amyloid light chain (AL) proteins in multiple organs [1]. The 4 organs most commonly involved are the heart, kidneys, liver, and peripheral nerves [2]. Respiratory tract involvement is common [3-4], but rarely produces symptoms of clinical importance [5]. Five forms of pulmonary involvement are seen in systemic AL amyloidosis: (1) diffuse interstitial or alveolar-septal disease; (2) nodular disease; (3) intra- and extrathoracic adenopathy; (4) pleural disease; and, rarely, (5) diaphragm deposition [6]. Both mediastinal and hilar lymphadenopathy are common in AL-type systemic amyloidosis (75%) [7], and are usually associated with parenchymal disease (50%) [1].

Case Report

A 46-year-old woman was a non-smoker and had no past medical or surgical illnesses. She ordinarily assisted her husband in car repairs, and exhaust was inhaled inevitably. One particular thing was mentioned, and that was that the patient was accustomed to using detergents to clean almost all objects that she touched, and had had the habit for decades. In June 2007,

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she was admitted because of chronic cough with mild dyspnea on exertion for about 5 weeks, and denied fever, chills, loss of weight, hemoptysis, or leg edema. On physical examination, no palpable neck lymphadenopathy was noted and the breathing sound was clear.

Laboratory tests showed that the hemoglobin level was 13.0 g/dl, and the hematocrit was 39.1%. The white blood cell count was 4660/cu mm, with a normal differential count (neutrophils 72.1%; lymphocytes 20.4%; monocytes 6.0%; eosinophils 1.1%; and basophils 0.4%). The serum level of total protein was 7.2 g/dl, with 4.2 g/dl of albumin. Serum biochemical studies of the hepatic and renal functions were normal. Chest radiography showed diffuse tiny nodules in both lung fields, with a prominent right hilar shadow (Figure 1). High resolution computed tomography of the chest revealed micronodular infiltrate, ranging from 0.1~0.3 cm in diameter in both lungs, with bilateral lymphadenopathy (Figure 2). The pulmonary function test disclosed normal spirometric data, including lung volumes and diffusing capacity of carbon monoxide.

Serum protein electrophoresis followed by immunofixation revealed a monoclonal band of IgG-λ specificity. The serum levels of immunoglobulins disclosed IgA 33.90 mg/dl (normal, 159.90 to 314.30 mg/dl); IgM 40.00 mg/dl (normal, 78.90 to 195.30 mg/dl); IgG 1350.0 mg/dl (normal, 939.6 to 1398.4 mg/dl). Urinalysis revealed traces of protein, identified as albumin by electrophoresis of a 10-fold concentrated specimen; however, Bence-Jones protein was not found.

Wedge resection of segment 1+2 of the left lung was done by video-assisted thoracoscopic surgery. The specimen measured 8.3×2.8×2.4 cm in size. Grossly, it was gray to brown and

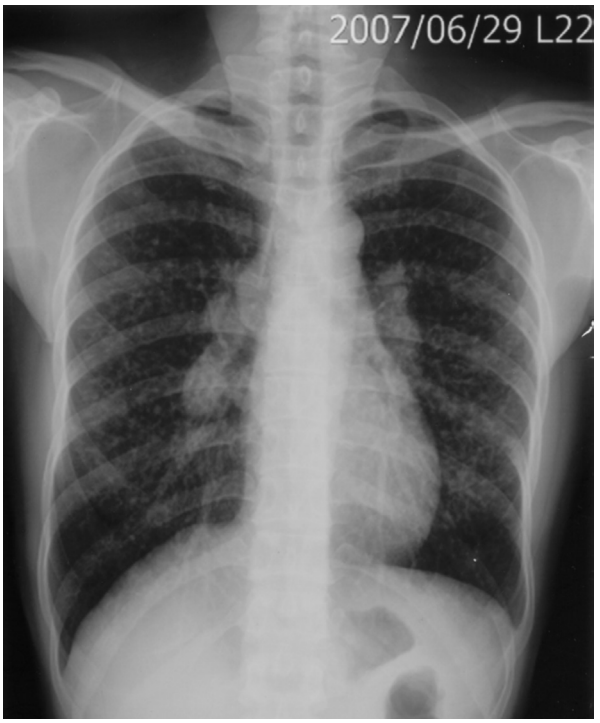


Fig. 1. Chest radiography showed diffuse tiny nodules in both lung fields with a prominent bilateral hilar shadow.

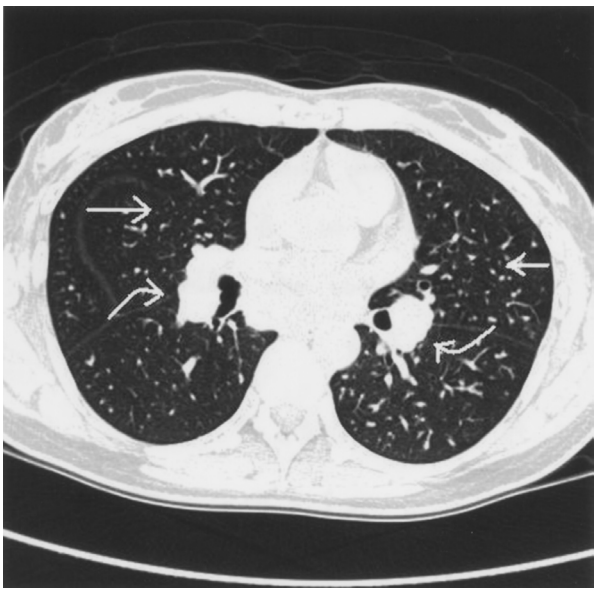
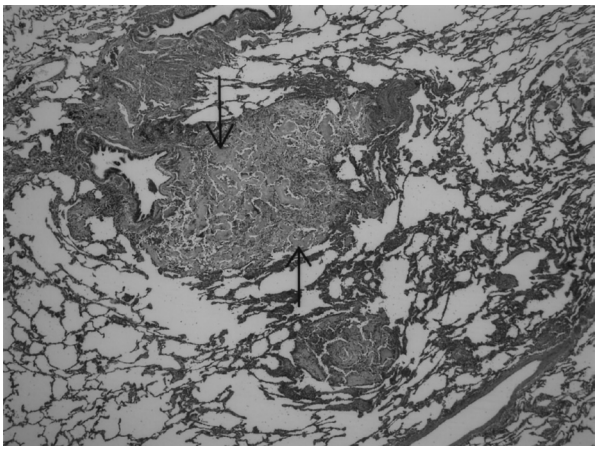
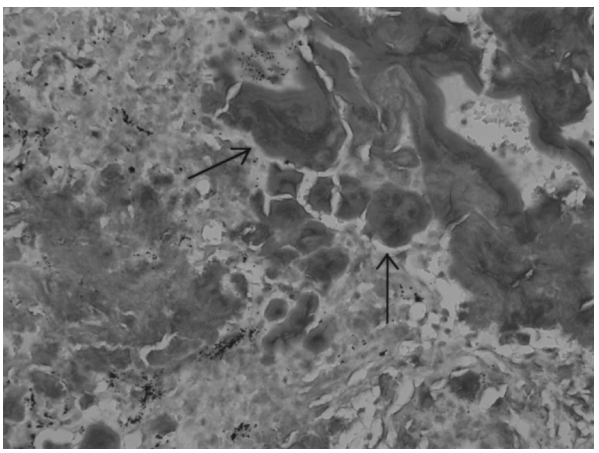


Fig. 2. High resolution computed tomography of the chest revealed micronodular infiltrates in both lungs (straight arrows) with bilateral hilar lymphadenopathy (curved arrows)



(A)



(B)

Fig. 3. (A) Multifoci of nodular depositions of granular or amorphous eosinophilic material could be seen (arrows) in the pulmonary parenchyma or around the bronchi. Associated multinucleated giant cells and some lymphoplasma cells were also seen (hematoxylin and eosin stain, 40X); (B) the deposits (arrows) were positive for Congo red (Congo red stain, 400X).

spongy with small ill-defined gray to black nodules, raging from 1 to 3 mm in diameter.

Microscopically, there were multifoci of nodular depositions of granular or amorphous eosinophilic material in the pulmonary parenchyma or around the bronchi. Associated multinucleated giant cells and some lymphoplasma cells were also seen. In special staining, the deposits were positive for Congo red (Figure 3). The overall histopathological picture was compatible with amyloidosis of the lung, and a diagnosis of primary amyloidosis with pulmonary involvement was confirmed.

The patient went to another hospital for a second opinion after surgery. The doctor suggested repeating the lung biopsy, but the patient was unwilling to undergo any further invasive procedure. An empiric trial of oral prednisolone 0.5 mg per kg was prescribed for about 1 month, but showed limited clinical improvement. The patient then decided to take herbal medicine and was lost to follow-up.

Discussion

Since the symptoms of amyloidosis are often vague (e.g., fatigue, edema, and weight loss), they are generally not useful in targeting a diagnosis. Moreover, the physical findings, such as enlargement of the tongue and periorbital purpura, although highly specific, are seen in fewer than one-fifth of the patients and are not sensitive [8]. Therefore, a diagnosis of amyloidosis remains a challenge in clinical practice. Although the chest radiography of the patient showed diffuse parenchymal infiltration, mild clinical illness might have been noted with normal results on the pulmonary function test. The disproportion between clinical severity and laboratory findings may be a feature of pulmonary amyloidosis.

In the majority of patients with respiratory tract amyloidosis, the chest radiograph is normal [9]. Otherwise, radiographic findings are generally non-specific, and consist of a reticular pattern, nodules, large airway thickening, or post-obstructive features such as atelectasis and consolidation. Diffuse pulmonary nodules with bilateral hilar lymphadenopathy are a rare presentation in pulmonary involvement

of amyloidosis [10]. The differential diagnoses include tuberculosis, metastatic malignancies, and sarcoidosis. In fact, the coincidence of sarcoidosis and amyloidosis has been described in the literature [11-12]. The possibility of an immunologic linkage between sarcoidosis and amyloidosis has also been discussed, but this conclusion is controversial.

We suspected a clinical association between detergents and amyloidosis. In 1999, Dobson et al. successfully converted a small α/β protein, acylphosphatase, from its soluble and native form into insoluble amyloid fibrils of the type observed in a range of pathological conditions, using trifluoroethanol, a common component in detergents [13]. Other detergents, including octyl-β-glucopyranoside and sodium dodecyl sulfate, or solvents, including hexafluoroisopropanol, also alter the secondary structure of soluble amyloid β-protein [14]. Environmental detergents may be a possible factor in the pathogenesis of amyloidosis, although this has not been confirmed by clinical experience.

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以瀰漫性肺節結合併兩側肺門及縱隔腔淋巴結腫大做爲臨床表現的肺部類澱粉沈積症：一病例報告

黃憲治　劉榮森*　吳毅穎**　徐志育

類澱粉沈積症在臨床上被視為一種相對罕見的疾病，然而它對肺部的影響卻是很常見的。我們報告一位46歲的女性病患，以慢性咳嗽和輕微的氣促持續5週為其臨床表現。影像學顯示瀰漫性肺節結合併兩側肺門淋巴結腫大。血清蛋白的免疫電泳分析法（immunoelectrophoresis）及免疫固定電泳分析法（immunofixation electrophoresis）呈現特異性單源球蛋白IgG-λ，而肺部切片則顯示多處的類澱粉質沉積。此病灶證實為原發性肺部類澱粉沈積症。*(胸腔醫學 **2008; 23: 344-348**)*

關鍵詞：肺部，原發性類澱粉沈積症

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Alpha-1-antitrypsin Deficiency in a Young Adult: The First Case Report in Taiwan and an Epidemiological Review of Asia

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The prevalence of Alpha-1-antitrypsin (α1AT) deficiency in Taiwan is not known as yet, since there are extremely rare case reports and the prevalence is normally lower among Asian countries than Western countries. We report an 18-year-old male non-smoker with the chief complaint of effort dyspnea. He was diagnosed as having α1AT deficiency-related emphysema, based on imaging studies, pulmonary function tests and the level of α1AT in the serum. This is the first case report of α1AT deficiency-related emphysema in a young adult in Taiwan. The incidence and contribution of α1AT deficiency to the development of chronic obstructive pulmonary disease among nonsmokers, and the prognosis, need further investigation in Asia. ***(Thorac Med 2008; 23: 349-354)***

Key words: alpha-1-antitrypsin, emphysema, chronic obstructive pulmonary disease, prevalence

Introduction

Chronic obstructive pulmonary disease (COPD) is a disease with chronic airway inflammation associated with airflow limitation. In addition to inflammation, a protease and anti-protease imbalance may lead to tissue destruction and an impaired defense mechanism [1]. These processes can arise from environmental exposure to noxious particles [2] or be attributed to genetic factors [3]. A deficiency of alpha-1-antitrypsin (α1AT), which can inhibit a number of serine proteases such as neutrophil elastase, increases the risk of developing pulmonary emphysema [4]. Although this genetic disorder is not uncommon in Caucasians [5-6], it is extremely rare in Asians [7-9]. We report the first case of α1AT deficiency in a young adult in Taiwan, who had severe panacinar emphysema of the lungs.

Case Report

An 18-year-old male nonsmoker presented to our outpatient clinic with the chief complaint of effort dyspnea for more than 1 year. He was robust and had been good at exercise in the past. Unfortunately, he felt exhausted and had

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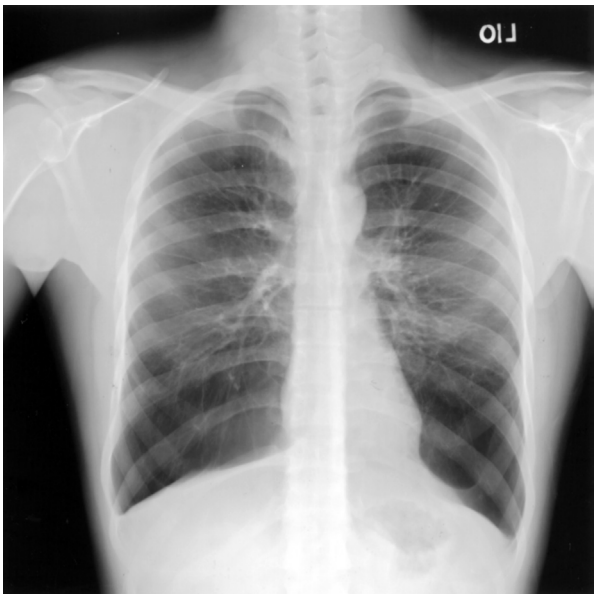

Fig. 1. Roentgenogram revealed emphysematous change and hyperlucency in the lower lobes bilaterally.

progressive dyspnea while doing exercise in the most recent 3 years. He was a university student and had no history of asthma, allergic rhinitis or other systemic diseases. Family history was not contributory. Physical examination at a clinic disclosed no signs of tachypnea, tachycardia, cyanosis or clubbing fingers, although there were diminished breathing sounds in the bilateral lower lung fields. A chest X-ray film revealed emphysematous change, with more radiolucence in the lower lobes bilaterally (Figure 1). High resolution computed tomography demonstrated panlobular emphysema with a lower lobe preponderance (Figure 2). The pulmonary function test revealed moderately obstructive ventilatory impairment with a negative bron-

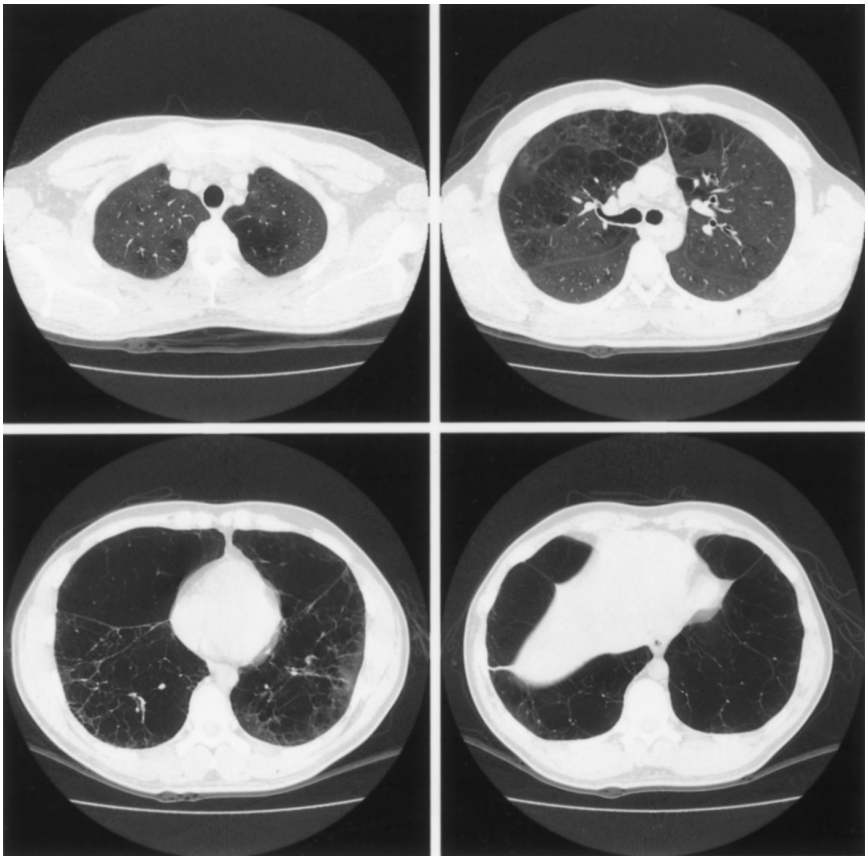

Fig. 2. High resolution computed tomography demonstrated panlobular emphysema with a lower lobe preponderance.

chodilator response. The pre-bronchodilator forced expiratory volume in 1 second (FEV1) was 2.03L (51% predicted), the forced vital capacity (FVC) was 3.71L (84%), and the ratio of FEV1 to FVC (FEV1/FVC) was 55%. The post-bronchodilator FEV1 was 2.09L (53%), which showed a 2% improvement of the pre-bronchodilator FEV1. The diffusing capacity of carbon monoxide was normal (94% predicted). The serum level of α1AT was 52 mg/dl (normal range: 80-230 mg/dl), as measured by radioimmunodiffusion assay. Genotyping was not performed. The liver function tests and sonography of the liver were normal. The patient was diagnosed with pulmonary emphysema resulting from α1AT deficiency. Augmentation therapy was not given at that time. Regular follow-up was recommended for this patient.

Discussion

α1AT deficiency is a hereditary disorder with an autosomal recessive inheritance [10]. In Western countries, epidemiological screening in newborns revealed that the prevalence of α1AT deficiency ranged from 1 in 1600 to 1 in 5097 [11]. α1AT deficiency-related emphysema is extremely rare in Asian countries. There were no case reports in Korea until the year 2001 [8]. In China, researchers could not identify either PiZ or PiS mutants in healthy subjects or patients with COPD, and α1AT deficiency was no longer mistaken as an important factor in the development of COPD in China [9]. Similarly, α1AT deficiency is a rare risk factor in Japan, as tobacco smoking was found to be the major factor contributing to COPD [12]. This is the first report in Taiwan regarding α1AT deficiency-related emphysema, especially occurred in a nonsmoking young adult.

Symptoms of α1AT deficiency usually develop between 32 and 41 years of age in individuals with a history of smoking [13-14]. The pulmonary function of individuals with an α1AT deficiency is usually preserved at the age of 26 years [15]. In later life, FEV1 decline rates in smokers range from 70 to 317 ml per year, in contrast to 41 to 80 ml per year in non-smokers [16-18]. A survey in North America of 1,129 patients with severe α1AT deficiency demonstrated that the mean FEV1 decline was 54 ml/year. The risk factors for FEV1 decline included males, those aged 30 to 44 years, current smokers, FEV1 35% to 79% predicted, and those who had ever had a bronchodilator response [19]. Concerning the prognosis, a Danish study with 347 patients enrolled indicated that FEV1 was the most important predictor of survival. Median survival for patients with FEV1 less than 25% predicted was 6.3 years. Increased survival to 14.2 years was observed for those patients with FEV1 above 50% predicted [18].

The most frequently manifested symptom was dyspnea on exertion. Wheezing independent of respiratory tract infection was not uncommon [20]. The characteristic feature in the lung is panacinar emphysema [10], which is similar to that of smoking-induced COPD [16]. The chest X-ray films in patients with α1AT deficiency usually show a pattern of “basilar hyperlucency”, as presented in this patient. The emphysema is more prominent in the lower lungs than in the apicals. A basal distribution was associated with a greater impairment of FEV1, but less impairment of gas exchange and the alveolar-arterial oxygen gradient, than an apical distribution [21].

The normal range of α1AT is 150-400 mg/dl, as measured by radioimmunodiffusion, and

83-220 mg/dl by nephelometry [22]. The protective threshold from damage by elastase is 80 and 50 mg/dl, respectively. The α1AT level in this patient was measured by radioimmunodiffusion (Binding Site, Birmingham, UK). The limitation of this test is that it tends to overestimate α1AT levels in serum [23]. In addition, α1AT is a kind of acute phase protein which is easily up-regulated in acute inflammation. Diagnostic testing for the candidate phenotype (e.g., PI*ZZ, PI*MZ, PI*Mmalton), especially for individuals with symptoms and/or signs consistent with α1AT deficiency-related emphysema, is required.

The major focus of therapy is to prevent the lung destruction attributed to α1AT deficiency. The clinical effect on survival of augmentation of α1AT levels by infusion or inhalation is unclear. However, several studies indicated that augmentation therapy may slow the annual decline in FEV1, compared to untreated groups [22]. On the other hand, patients with α1AT deficiency may present clinical symptoms similar to those in obstructive airway diseases. They may benefit from bronchodilator treatment, although bronchodilator reversibility may be lacking.

In summary, the prevalence of α1AT deficiency-related emphysema in Taiwan is unknown. Although this is the first case report in Taiwan, patients may be underdiagnosed or misdiagnosed as having asthma or COPD without identification of α1AT deficiency. We should keep this disease in mind for those patients with unusual presentations, such as dyspnea on exertion in young adults without an apparent asthma history, early-onset emphysema among smokers aged less than 45 years, a family history of emphysema in the presence or absence of a smoking habit, as well as chest film revealing panacinar emphysema with lower lung predominance. Spirometry and a roentgenogram are helpful, and serum levels of α1AT are essential for the diagnosis. Clinical awareness of this inherited disorder is required before we move to population-based screening and further investigation.

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年輕男性的甲1型抗胰蛋白腖缺乏症：台灣第一例病例報告及亞洲的流行病學的文獻回顧

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甲1型抗胰蛋白酶缺乏症在台灣的盛行率不明而病例報告極為罕見，亞洲國家相較於西方國家的盛行率較低。我們報告一位18歲非抽煙的男性主訴運動時呼吸困難。根據影像學檢查、肺功能及甲1型抗胰蛋白腖的濃度，他被診斷為甲1型抗胰蛋白腖缺乏症引起的肺氣腫。這是台灣第一例發生在年輕男性甲1型抗胰蛋白腖缺乏症引起肺氣腫的病例報告。在亞洲，甲1型抗胰蛋白腖缺乏症非吸煙者之間的發生率及對形成肺氣腫的貢獻及預後需要進一步的研究。*(胸腔醫學* ***2008; 23: 349-354)***

關鍵詞：甲1型抗胰蛋白腖，肺氣腫，慢性阻塞性肺病，盛行率

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Anterior Mediastinal Type B3 Invasive Thymoma with Multiple Intrapulmonary Metastases: A Case Report

Hsin-Kai Huang, Chih-Hsiung Chen, Shian-Chin Ko, Kuo-Chen Cheng, Jiunn-Min Shieh, Kuo-Hwa Chiang

Almost all metastatic lesions from thymomas invade adjacent organs or spread along the pleura or pericardium. Intrapulmonary metastases are rare, and extensive multiple intrapulmonary metastases are extremely rare. We report the case of an invasive thymoma with multiple lung metastases in an asymptomatic 45-year-old woman. Her chest computed tomographic (CT) scan showed an irregular-shaped calcified tumor in the anterior mediastinum and multiple well-defined variable-sized tumors in both lung parenchymas. She underwent a CT-guided biopsy of the retrocardial metastatic lesion. The morphology was spindle-shaped, which was once considered to be type A thymoma according to the World Health Organization classification. The anterior mediastinal tumor was resected and proved to be type B3. Differences in the histology between the main tumor and the deep-seated metastatic lesions are possible, depending on the choice of diagnostic tools. Thymoma with extensive multiple intrapulmonary metastases is extremely rare. It should be emphasized that thymectomy is necessary to achieve a correct diagnosis in this condition. The influence of the differences on invasiveness, best treatment, and long-term outcome remains unclear. ***(Thorac Med 2008; 23: 355-361)***

Key words: invasive thymoma, type B3, type A, multiple intrapulmonary metastases

Introduction

Type A thymomas are recognized as a benign tissue type by the World Health Organization (WHO) committee on histogenetic classification, based on the morphology of neoplastic thymic epithelial cells. They are encapsulated, and believed to have an excellent prognosis, although they may invade their capsule. Their metastases into the lung parenchyma are rare conditions. We report herein an extremely rare condition, a case in which an asymptomatic patient with anterior mediastinal type B3 thymoma had synchronized multiple intrapulmonary metastases that were type A.

Case Report

A 45-year-old woman was admitted to Chi Mei Foundation Medical Center because of ab-

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normal findings in her chest radiograph on her health examination. She was a housewife in a good state of health, without underlying disease and free of any other symptoms such as chest pain, dyspnea, and muscle weakness before admission. She did not smoke or drink, and had no previous medical history of surgery or allergies. There were no abnormalities on physical examination, including neurological testing, after admission to our ward. Her complete cell counts, blood levels of electrolytes, and serum levels of urea nitrogen, creatinine, aspartate aminotransferase, alanine aminotransferase, and glucose were all normal.

Her chest roentgenogram showed multiple variable-sized tumors without calcification and necrosis in the bilateral lung areas (Figure 1). The chest computed tomographic (CT) scan revealed a retrosternal irregular-shaped soft tissue mass with calcification in the anterior mediastinum, measuring 2.5×2.8×3.0 cm in size (Figure 2) and bilateral multiple variable-sized tumors (Figure 3). The tumor markers of carcinoembryonic antigen, alpha-fetoprotein, and cancer antigen-125 were 2.18 ng/ml, 2.43 ng/ml, and 3.0 U/mL respectively, all within normal limits. Another tumor marker of cancer antigen-199 was below 2.0U/mL.

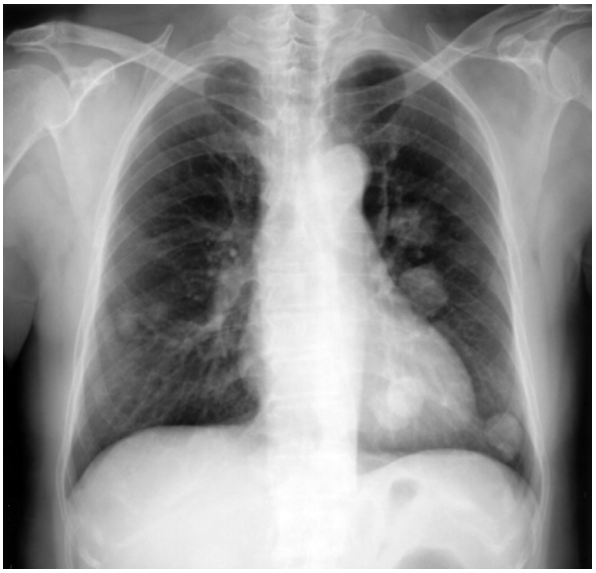

Fig. 1. Chest radiograph shows multiple lung tumors in bilateral lung fields.

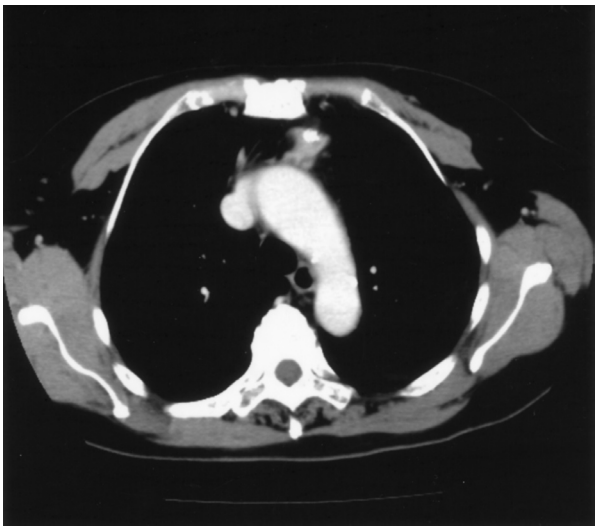

Fig. 2. Chest CT reveals an anterior mediastinal irregular-shaped soft tissue mass with calcification.

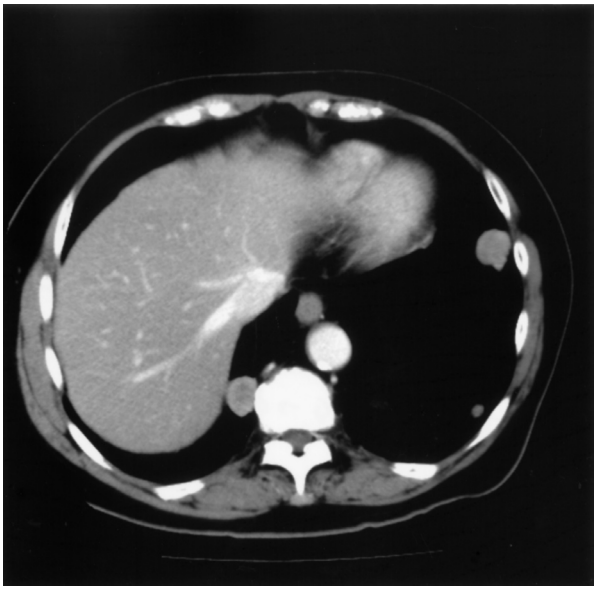

Fig. 3. Chest CT confirms multiple intrapulmonary variable-sized tumors.

She was suggested to undergo CT-guided biopsy of the metastatic tumors for further workup. The procedure was performed in the left lower lobe with 1 of the tumors at a retrocardiac site adjacent to the spinal process. The biopsy cores show a tumor composed of spindle to oval cells in sheets, without obvious lymphoid infiltration by hematoxylin and eosin stain sections. In addition, the mitotic activity was low (Figure 4). Immunohistochemically, the tumor cells were positive for cytokeratin AE1/AE3 (Figure 5), focally positive for vimentin, and negative for CD5 and thyroid transcription factor-1. Based on the above findings, the tumor would most likely be a type A thymoma. Two weeks later, she received a resection of the thymic tumor and wedge resection of the right middle lobe (RML) of the lung for a pulmonary nodule found at the RML. The thymic lesion revealed an infiltrating growth pattern penetrating the surrounding thymic tissue, using hematoxylin and eosin stain (Figure 6). At

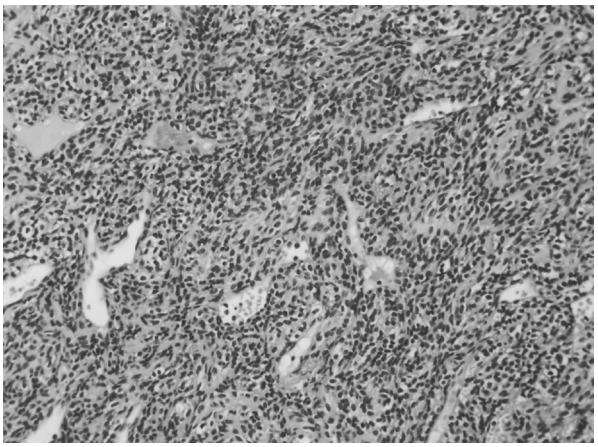

Fig. 4. The pathologic findings of the lung tumor reveal spindle to oval cells in sheets without obvious lymphoid infiltration (hematoxylin and eosin stain, 400X).

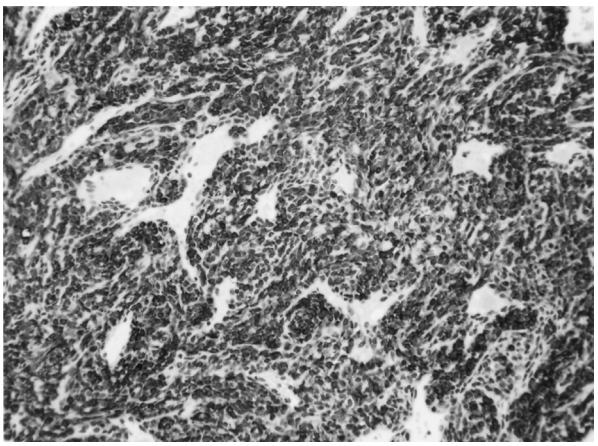

Fig. 5. The immunohistochemical staining of the lung tumor was positive for cytokeratin AE1/AE3 (400X).

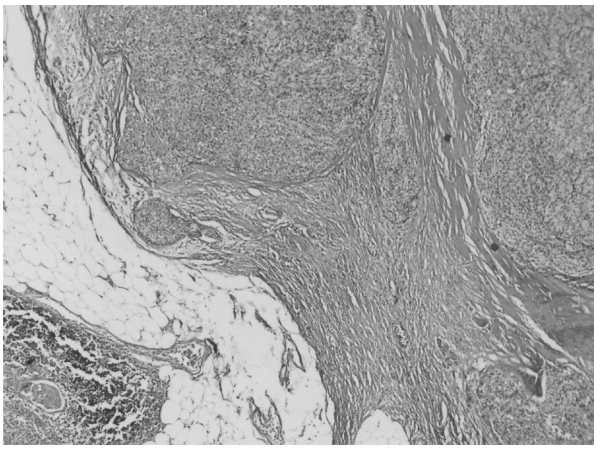

Fig. 6. The pathologic findings of the thymic lesion reveal an infiltrating growth pattern penetrating the surrounding thymic tissue (hematoxylin and eosin stain, 100X).

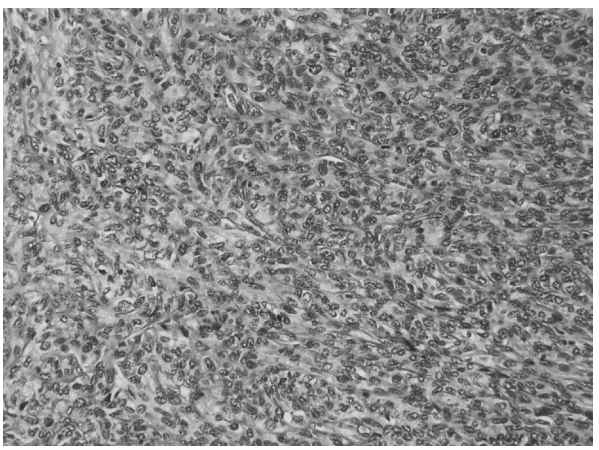

Fig. 7. The pathologic findings of the thymic lesion reveal plumper cells in sheets. Mitotic figures can easily be identified (hematoxylin and eosin stain, 400X).

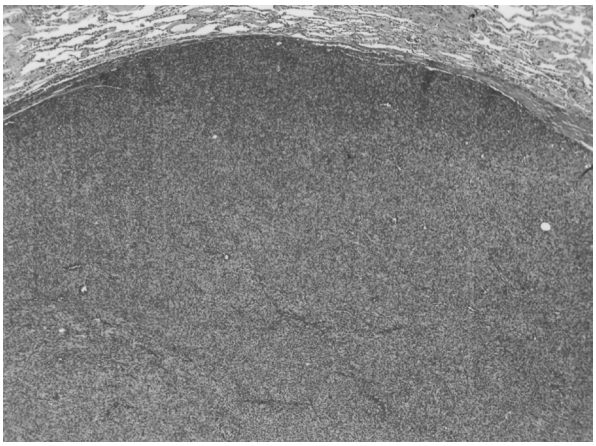

Fig. 8. The pathologic findings of the resected lung nodule also show plump spindle cells exhibiting prominent nuclei and occasional mitotic figures (hematoxylin and eosin stain, 100X).

a higher magnification, the lesion was seen to be composed of plumper cells in sheets. Mitotic figures could easily be identified (Figure 7). The resected lung nodule showed features identical to the thymic lesion, with plump spindle cells exhibiting prominent nuclei and occasional mitotic figures (Figure 8). Hence, invasive thymoma, type B3 with lung metastasis was the final pathological diagnosis. She received chemotherapy in the oncology section later but the response was poor.

Discussion

Many different kinds of neoplasms arising in the thymus have previously been classified as "thymoma", although they are histologically unrelated. It is very clear that some tumors, such as thymic carcinoid tumors, various malignant lymphomas, and germ cell tumors that originate in the thymus, differ from tumors originating in the epithelium, not only pathologically but also in their clinical behavior [1]. In 1978, the term "thymoma" was restricted to neoplasms of the thymus epithelial tissue, using Rosai and Levine's definition. Therefore, carcinoid tumor, malignant lymphoma, germinal tumor, and other anaplastic carcinomas were excluded [2]. In 1985, the Marino and Muller-Hermelink group proposed a histogenetic thymoma classification, based on the morphology of the neoplastic epithelial cells, of medullary, mixed, mainly cortical, and cortical thymomas, plus well-differentiated thymic carcinoma [3]. These different types of thymoma have significant differences in their invasiveness, prognosis, and association with thymoma-related paraneoplastic syndromes [4-5].

The current classification system has been proposed by the World Health Organization (WHO) committee. The WHO classification system is histologically-based, and was shown in recent studies to have prognostic significance [6]. It distinguished thymomas from thymic carcinomas and recognized 5 thymoma classes. Based on the appearance of the malignant epithelial cells, there are 3 major classes, spindle-shaped (type A), epitheloid (type B), and mixed (type AB) in the WHO system. Class A and AB thymoma have been associated with less invasive and aggressive clinical courses than class B thymoma.

Type A thymomas have also been designated medullary thymomas in the Marino and Muller-Hermelink system. They are composed predominantly of spindle-shaped epithelial cells without nuclear atypia and with rare lymphocytes throughout all the sections. They are called "medullary" because their cells resemble spindle- and oval-shaped normal thymic medullary epithelial cells at the ultra-fine structural level. Most type A thymomas are encapsulated, but some may invade the capsule, and a few have extended into the lung. These tumors are considered benign and have an excellent prog-

nosis in several histologically clinicopathological correlation studies [4, 7-8]. In contrast, type B3 thymoma is also known to be a well-differentiated thymic carcinoma (WDTC). It is a distinct typical carcinoma of the thymus with low-grade malignancy, characterized by a predominance of epithelial cells with usually low mitotic rates, and an epidermoid differentiation with slight to moderate cytological atypia. The tumor differs from lymphocyte-depleted cortical thymomas and benign epithelial-rich medullary thymomas. WDTC shares with type A thymoma a predominantly or almost exclusively epithelial composition, but differs from type A, in that the shape of the cells are polygonal or round, not spindle or oval. It has a higher rate of association with myasthenia gravis, more easily invades adjacent organs, and has more endothoracic metastasis than cortical thymomas, but less than other thymic carcinomas [9].

According to the Masaoka staging system for the invasiveness of thymoma, most thymomas are stage I or II at presentation. Stage IV invasion accounts for 6.5% to 10% [10-12] and the most frequent metastatic sites are pleural, followed by pericardial dissemination, which is denoted to be stage IVa. Distant metastases either by lymphatic or hematogenous spread, classified as Masaoka stage IVb, is found in a very small portion of patients [13]. Our reported patient was a case of stage IVb invasive thymoma with widespread metastases into the lung parenchyma. Interestingly, due to the initial impression of double cancers, the patient received CT-guided biopsy followed by thymectomy. The histology of synchronized multiple intrapulmonary metastases was type A thymoma, different from the main tumor, type B3 thymoma. This case implied extensive multiple intrapulmonary metastases with different clinical histologies for the main tumor and the metastatic lesions. The best treatment for stage IVb diseases is unknown. It is possible that different diagnoses could lead to different types of clinical management. Under this extremely rare condition, we suggest that needle biopsy for intrapulmonary metastasis was not enough and that the main tumor should be resected for a more detailed workup.

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前縱膈B3侵犯型胸腺瘤伴隨多處肺部轉移

黃信凱　陳志雄　柯獻欽　鄭高珍　謝俊民　江國華

幾乎從胸腺腫瘤轉移來的病灶都會侵入鄰近的器官或沿著肋膜或心包膜散佈。肺內轉移很少見而且大量多處的肺內轉移更是少見。我們將報告一位45歲沒有症狀的女性，她有侵襲性胸腺瘤伴隨多處肺部轉移。她的胸部電腦斷層掃描顯示前縱膈腔內有一個不規則形狀的鈣化腫瘤，而且在兩側肺實質內有多處的界線明顯而不同大小的腫瘤。她接受針對心臟後的轉移病灶做電腦斷層導向的切片檢查，細胞形態學上是紡錘型。根據世界衛生組織的分類一度被認為是A型胸腺腫瘤，前縱膈腔的腫瘤被切掉且被證實是B型。因為選擇不同的診斷工具，主要腫瘤和深部轉移的病灶其組織學上會不同是有可能的。胸腺腫瘤半隨大量多處的肺內轉移是相當少見的。要強調的是在這種情況下，胸腺切除來達成正確的診斷是必須要的。至於對侵襲性，最適宜的治療和長期的結果其不同處的影響仍然是未知的。*(胸腔醫學* ***2008; 23: 355-361)***

關鍵詞：侵襲性胸腺瘤，多處的肺內轉移

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Unilateral Choroid Metastasis as an Initial Presentation of Lung Cancer – Two Case Reports

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Lung cancer is 1 of the major health problems in the world and the leading cause of cancer death in Taiwan. Well-known metastatic sites of lung cancer include the lung, lymph nodes, brain, bone, liver, etc. Choroid metastasis is rare and the diagnosis is based primarily on clinical findings supplemented by imaging studies. However, clinicians do not routinely evaluate the possibility of intraocular metastasis, mainly because of the low incidence of asymptomatic choroid metastasis. The most commonly used treatment in patients with symptomatic intraocular metastasis is radiotherapy. Herein, we report the cases of 2 patients who had blurred vision as the initial presentation, and were diagnosed with adenocarcinoma of the lung with brain and choroid metastasis. They refused radiotherapy of the eye, and commenced systemic chemotherapy and brain radiation therapy. One received plaxitaxel and the other received vinorelbine. Throughout serial follow-ups, their visual acuity subjectively improved, along with a reduction in the size of the intraocular tumor, as seen by ophthalmoscopic examination in 1 case. ***(Thorac Med 2008; 23: 362-368)***

Key words: choroid metastasis, lung cancer

Introduction

Malignancy was the leading cause of death in Taiwan in 2004, and lung cancer led among the malignancies. The most common metastatic sites of lung cancer included the lung, lymph nodes, brain, bone, and liver. The choroid plexus is a rare metastatic site for lung cancer. Usually, lung cancers are asymptomatic or present with pulmonary symptoms, such as chronic cough, hemoptysis, or pleuritic chest pain. Sometimes, distant metastasis causes dominant symptoms before detection of the primary lung cancer. However, it is rare that blurred vision is the first manifestation of lung cancer, resulting from metastasis to the choroid plexus. In considering life quality, visual acuity is quite significant. So, the early recognition and treatment of ocular metastasis are undoubtedly important clinical oncologic issues. Herein, we would like to present 2 cases of lung cancer with choroid metastasis, with the initial chief complaints of blurred

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vision, rather than respiratory tract symptoms.

Case Reports

Case 1

This 42-year-old woman had been previously well. About 1 week prior to hospitalization, she suffered from blurred vision of the left eye and went to ophthalmic clinics. Ophthalmoscopic examination disclosed 2 choroid masses without pigmentation, 1 located superio-temporally to the macula and the other inferior to the disc with serous retinal detachment in the left eye (Figure 1A). The fluorescein angiography (FAG) showed hyperfluorescent dots in these areas in the early phase, and dye leakage with pooling in the subretinal space in the late phase. On B-scan ultrasound, there were 2 acoustically solid masses with retinal detachment. Magnetic resonance imaging (MRI) of the orbits disclosed a left-side eyeball choroid tumor with retinal detachment and brain metastasis at the right medial temporal region. The chest X-ray (CXR) revealed a solitary pulmonary mass in the left hilar region (Figure 2), so a chest physician was consulted. Bronchoscopic brushing was performed and the cytopathologic findings confirmed adenocarcinoma. External-beam radiotherapy for choroid metastasis was suggested initially, but the patient hesitated after a complete discussion with the radio-oncologist about the benefit and possible side effects of radiotherapy for an intraocular mass. Therefore, she decided to receive systemic chemotherapy with a regimen of plaxitaxel, and radiotherapy for brain metastasis. Two months later, the ophthalmoscopic exam revealed regression of the intra-ocular tumor size (Figure 1B). Her blurred vision also showed much improvement in the same period.

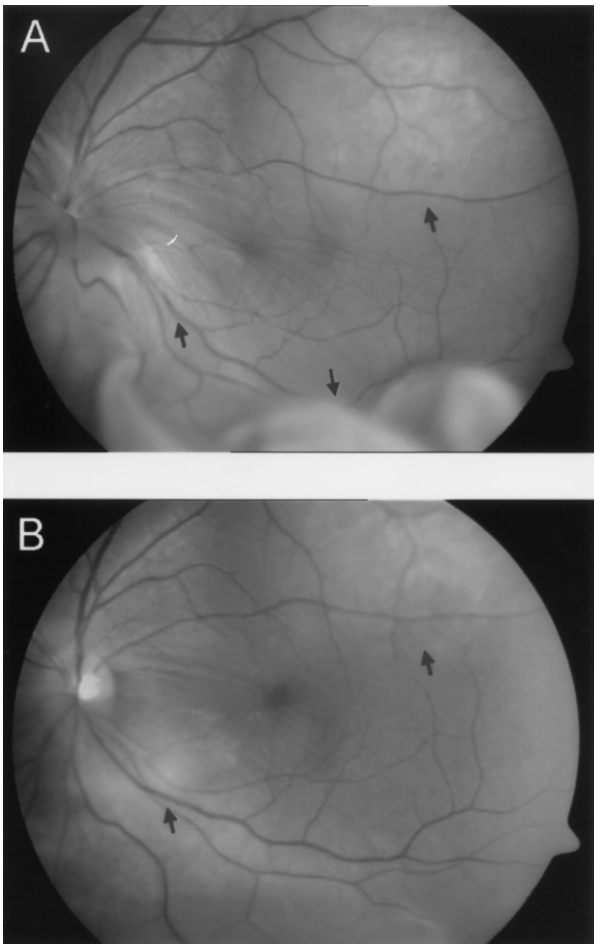

Fig. 1. Ophthalmoscopic examination of the left eye showed 2 choroid masses, 1 located superio-temporal to the macula and the other inferior to the disc (arrow pointing upward) with retinal detachment (arrow pointing downward). A: Before chemotherapy. B: After chemotherapy, showing regression of the tumor mass and remission of the subretinal fluid. (Case 1)

Case 2

This 60-year-old man denied any previous systemic disease. He began suffering from progressively blurred vision in the left eye around 1 month prior to admission. He called on ophthalmic clinics and the ophthalmoscopic examination showed a choroid mass in the left eye (Figure 3A). The FAG showed an irregular hyperfluorescent lesion in the early stage with increased intralesional dye accumulation in the

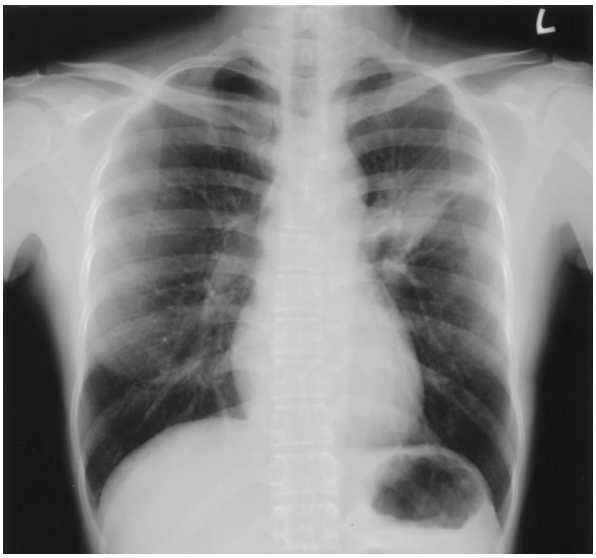

Fig. 2. Chest X-ray revealing a mass lesion about 3×3 cm in the left upper lung field. (Case 1)

late phase. The orbital MRI disclosed a choroid mass near the left upper nasal region. The CXR disclosed a 3.5-cm mass lesion in the right lower lobe (Figure 4). Bronchoscopy was done, and the brushing cytology revealed non-small cell carcinoma, most likely adenocarcinoma. Serial examinations for cancer staging were also arranged, and brain and bony metastasis were found. The patient received chemotherapy with a regimen of navelbine and cisplatin, and palliative brain radiotherapy. His visual acuity improved subjectively and the tumor mass revealed a stable state on ophthalmoscopic examination (Figure 3B). He has continued systemic chemotherapy and maintained a stable state of lung cancer, as seen in the chest images, up to this writing.

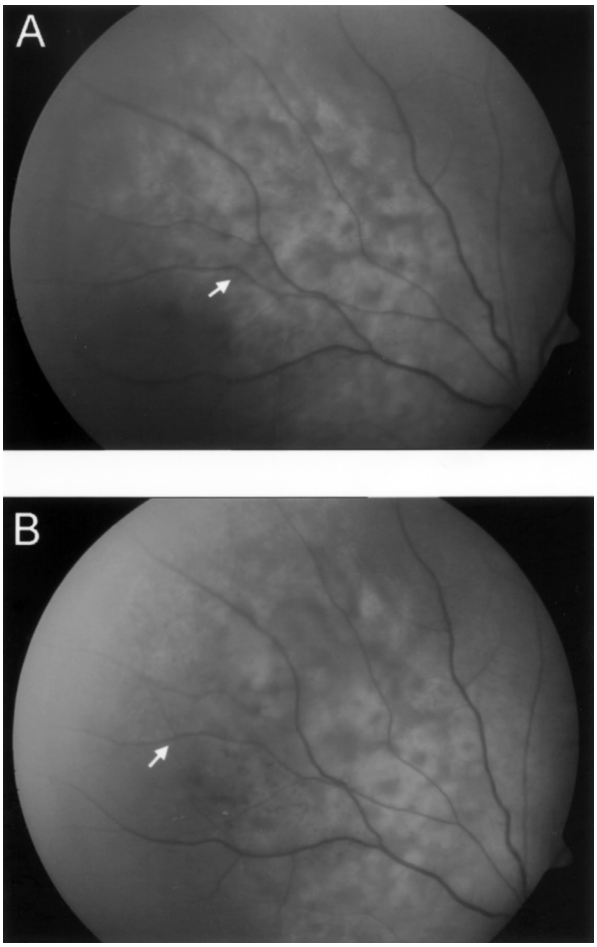

Fig. 3. Ophthalmoscopic examination of the left eye showing a choroid mass (white arrow) with pigmentation. A: Before chemotherapy. B: After chemotherapy, the tumor mass was in a stable state. (Case 2)

Discussion

Historically, metastatic carcinoma to the eye, particularly to the choroid, has been considered a very rare event. The frequency of microscopic metastases in postmortem examinations was 12.6%. But the frequency of gross metastases was only 1% [1]. Breast cancer is the most commonly detected malignancy with eye metastasis, accounting for up to 70% of patients with choroid metastasis [2]. Lung cancer is the second most frequent malignancy with metastasis to the eye. Choroid metastasis was present only in disseminated disease in which at least 2 other organ systems were affected by metastasis [3]. Among disseminated lung cancer patients with no eye symptoms, only

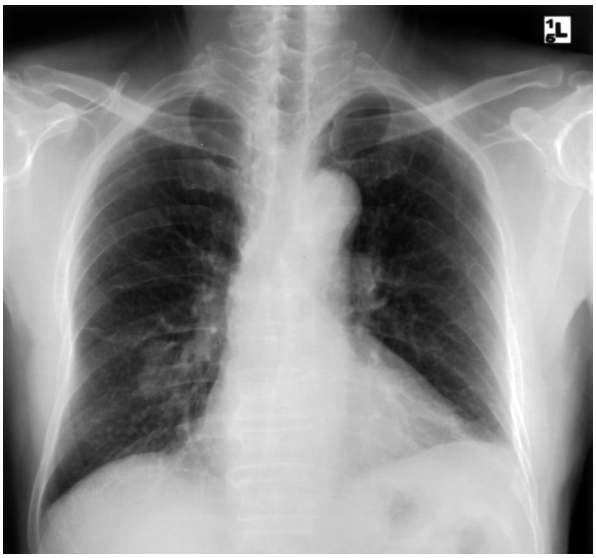

Fig. 4. Chest X-ray showing a mass lesion about 3.5 cm in the right lower lung field. (Case 2)

2.17% had asymptomatic choroid metastasis [4]. Hence, systemic screening for early detection of choroid metastasis in patients with lung cancer seems to be of very limited clinical benefit, even though it would lead to early therapeutic management, which is often vision-saving.

Choroid melanoma is the most common primary intraocular malignancy in adults. It occurs most commonly in Caucasians or other lightly pigmented individuals aged between 50 and 70 years old. Metastases almost invariably result from the hematogenous spread of melanoma to the liver. However, intraocular metastasis is now considered the most common malignancy of the eye. It can precede the diagnosis of the primary malignancy, ranging from 34~46% in different studies [5-6]. Lung cancer was the most common primary tumor detected in patients with no neoplasm at the time of ocular diagnosis. The majority of symptomatic patients note a decreased visual acuity at the time of presentation. Other signs or symptoms include diplopia, photophobia, ptosis, blepharitis, metamorphopsia, pain, flashes and floaters, mass lesion, uveitis, exophthalmos, secondary glaucoma, and detached retina.

The diagnosis of ocular metastases is based primarily on clinical findings supplemented by imaging studies. There are some differences between primary choroid melanomas and metastatic tumors. The choroid metastases usually appear as solid, flat, plaque-like, mottled, yellow-brown lesions. The choroid melanomas are typically brown, elevated, dome-shaped subretinal masses. A number of ophthalmologic procedures can assist in the diagnosis of metastatic tumors. These procedures include ultrasonography, FAG, computed tomography, MRI, fine-needle aspiration, or wedge biopsy. The most common angiographic finding in metastatic choroid tumors was fluorescence that appeared in the early arteriolar or arteriovenous phase, with progressive and more intense staining in the late phase [7]. In contrast, the double circulation pattern and prominent early choroid filling often seen in choroid melanomas are rarely found in metastatic tumors. Computed tomography and MRI have a limited role in the diagnosis of ocular metastasis. Nevertheless, brain imaging is useful before initiation of radiotherapy to assist in treatment planning.

A number of options are available for the treatment of ocular metastasis, including observation, chemotherapy, conventional external-beam radiotherapy, plaque brachytherapy, proton beam irradiation, laser photocoagulation, photodynamic therapy, and transpupillary thermotherapy. The therapy should be individualized for each patient, considering the needs of the patient and the patient's overall health. The 3 most favorable factors for predicting visual improvement are: excellent initial vision, age less than 55 years, and a choroid tumor with a

dimension base of less than 15 mm [8].

External-beam radiotherapy is the most commonly applied treatment. The most acceptable indications were (1) secondary retinal detachment, (2) decrease in visual acuity, (3) threat of decreased visual acuity, and (4) rapidly enlarging tumor [9]. The response rates varied in different studies. In a prospective study from 2002, visual acuity increased by 2 or more lines in 36% of symptomatic eyes, was stabilized in 50%, and decreased in 14% [10]. The usual dosage of radiotherapy was 30 to 40 Gy in 2 to 3 Gy fractions over a 3-5-week period, depending on the location and size of the tumor [11]. With current techniques and dosages, complications of radiotherapy, both acute and long-term, are uncommon. Possible complications include cataracts, radiation retinopathy, neovascularization of the iris, optic neuropathy, exposure keratopathy, and narrow-angle glaucoma. Caucasian race, increased intraocular pressure at diagnosis, and diagnosis by biopsy all predisposed toward the development of complications. On the other hand, factors not correlated with complications included biologically effective dose, energy type, lens-sparing technique, and concurrent systemic treatment [12].

In the past, most doctors thought that chemotherapy could not penetrate into the eyes and was not suitable for the treatment of intraocular metastasis, so its use in treating choroidal metastasis is not widely reported in the medical literature. Two reports described patients with choroidal metastasis who received chemotherapy and had tumor regression [13-14], suggesting that the choroid may not always be considered a chemotherapy "sanctuary site". In very select patients with asymptomatic tumors not fitting the indications for external-beam radiation, chemotherapy can be cautiously used as management for choroidal metastasis. But close ophthalmologic follow-up is obviously extremely important if radiotherapy is not used in the initial management. Combined sequential chemoradiotherapy may be another more effective treatment modality [2], but further studies are needed to confirm the effectiveness and side effects.

The efficacy of photodynamic therapy for choroid metastasis was reported by Martine in 2006 [15]. The mechanism of photodynamic therapy is probably the damage caused to new vessels within the choroid metastasis, but it does not target the tumor cells, and some of these cells may survive after treatment and later cause local recurrence. Photodynamic therapy can be used as a palliative procedure to ensure rapid vision improvement in the short term, especially for patients whose survival is already compromised.

In our cases, the patients had blurred vision due to ocular metastasis as the initial rare presentation of lung cancer. They chose chemotherapy as the initial treatment, and showed clinical improvement. Although tumor regression with improved visual acuity was observed after the initial chemotherapy, close follow-up is still necessary and external-beam radiotherapy should be considered if ocular symptoms progress.

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肺癌合併脈絡膜轉移—兩病例報告

沈協益* 賴瑞生*, ** 朱國安*, ** 洪美情***

癌症是台灣2004年十大死因之首，而肺癌則佔癌症死亡原因的第一位，故肺癌已成為國人重大健康問題之一。而肺癌常見的遠處轉移包括了腦部、骨頭、肝臟以及腎上腺，眼球脈絡膜則是較罕見的轉移位置，而其診斷主要是根據症狀及影像學之表現。然而，臨床上我們並不常規篩選病人是否有脈絡膜轉移，主要是因為無症狀之脈絡膜轉移病人比例甚低。對於已經有眼睛症狀的病人，考慮到其生活品質，正確診斷及積極治療是必須的，而放射線治療是目前最常選用的治療方式。在此我們報告兩位病人，他們皆以視力模糊作為最初之表現，最後診斷為肺癌合併腦部及脈絡膜轉移。在這兩個案例中，病人皆拒絕眼部之放射治療而選擇全身性化學治療及頭部之放射線治療，並且得到主觀之視力改善，且其中一病例於眼底鏡檢查下顯示腫瘤縮小。*(胸腔醫學* ***2008; 23: 362-368)***

關鍵詞：脈絡膜轉移，肺癌

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Synchronous Lung Squamous Cell Carcinoma and Carcinoid Tumor

Shang-Gin Wu, Chong-Jen Yu, Pan-Chyr Yang

We report the synchronous presence of lung squamous cell carcinoma and a carcinoid tumor in a 55-year-old male smoker. The patient presented with hemoptysis. The chest images and bronchoscopic washing cytology showed bilateral lung involvement, so chemotherapy was prescribed, as stage IV non-small cell lung cancer (NSCLC) with lung-to-lung metastasis was suspected. After 3 cycles of chemotherapy with docetaxol and carboplatin, the bilateral lung tumors responded discordantly. An aggressive surgical intervention was performed, and the pathology showed synchronous squamous cell carcinoma and a carcinoid tumor. We concluded that multiple lung lesions should be carefully interpreted, and different diseases occurring synchronously should be kept in mind. Aggressive intervention for diagnosis or treatment may be indicated, especially for the those with multiple lesions with different characteristics. ***(Thorac Med 2008; 23: 369-374)***

Key words: lung cancer, carcinoid, neoadjuvant chemotherapy

Introduction

Annually, around 1.2 million new cases of lung cancer are diagnosed globally [1]. The presence of a second tumor is frequently considered to be of a similar histologic type, and is classified as a T4 disease if located within the same lobe, or as an M1 disease if present in a different lobe [2]. However, some studies have considered that all multiple lung lesions may be primary tumors, and that aggressive surgical interventions could prolong survival [3-4].

We report a patient with lung squamous cell carcinoma who was classified as stage IV disease due to bilateral lung involvement. After chemotherapy and reevaluation, he received an aggressive surgical intervention bilaterally. The pathology showed synchronous squamous cell carcinoma and a carcinoid tumor. The presence of coexisting lung cancer and carcinoid tumors is rare. The aim of this study was to highlight the fact that different etiologies should be kept in mind for a patient with multiple lung lesions. Surgical intervention for diagnosis or treatment may be indicated for synchronous lung lesions.

Case Report

A 55-year-old man who had been a heavy smoker (1.5 packs per day for more than 35

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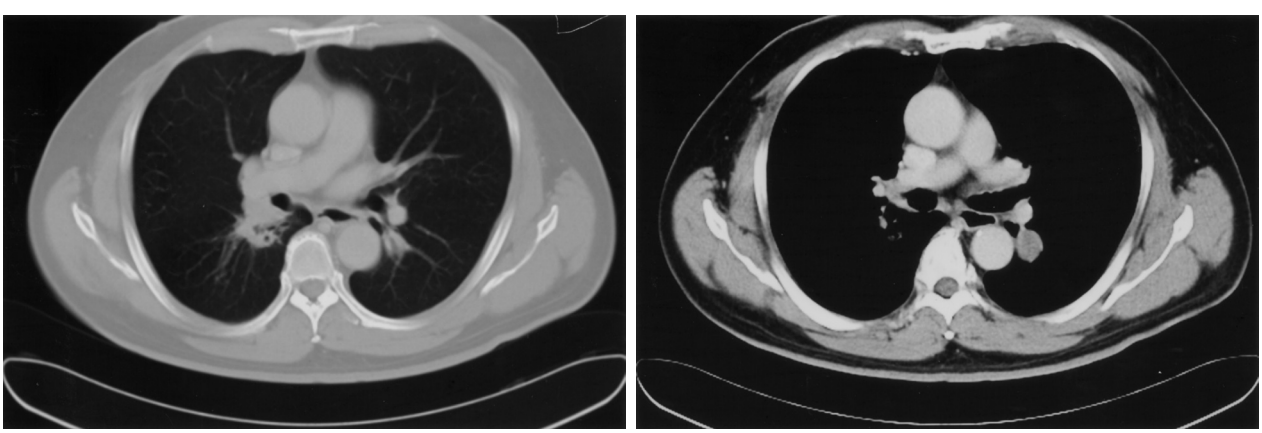
years), had been relatively well except for a duodenal ulcer more than 20 years previously. He had suffered from cough for a long time, especially in the morning, and complained of hemoptysis 3 times within 1 month. He also complained of discomfort in the anterior chest, and had lost 2.5 kg in weight within 1 month. He denied bone pain, hoarseness, dyspnea, poor appetite, nausea, vomiting, abdominal pain, or tarry stool.

He visited a local hospital initially. Although the chest X-ray was unremarkable, a chest computed tomography (CT) showed a mass about 2.9 cm at the right hilum and right lower lobe (RLL), with narrowing of the right common basal bronchus. In addition, a nodule, around 2.6 cm in size, located at the peripheral area of the superior segment of the left lower lobe (LLL), was noted with some nonspecific lymph nodes at the pretracheal and bilateral paratracheal regions. (Figures 1A and 1B) The pathology of the bronchoscopic biopsy of the RLL showed non-small cell lung cancer (NSCLC), and squamous cell carcinoma was favored. The patient then visited our institution for a second opinion. A repeat bronchoscopy showed a bulging submucosal lesion in the right main bronchus and a mucosal irregularity in the left main bronchus. Head CT showed neither intracranial, skull metastasis nor cervical lymphoadenopathy. Whole body bone scan findings revealed no hot spot.

Another bronchoscopy was arranged to diagnose the LLL lesion, which did not have the typical picture of malignancy (a round, well-enhanced nodule) in the chest CT. The bronchoscopic washing cytology in the left B6 still showed squamous cell carcinoma. In addition, whole body FDG positron emission tomography (FDG-PET) revealed a focal hot area with a standard uptake value (SUV) of 12.4 at the right hilar region encroaching the right main bronchus. Another hypermetabolic area was noted at the LLL, and its SUV was 5.1. The PET result was compatible with viable malignancies involving the right hilar region and the LLL. As stage IV disease was suspected, chemotherapy with docetaxol (35 mg/m^2) and carboplatin was prescribed, beginning in July 2007. After 3 cycles of chemotherapy, a chest CT showed cystic



(A) (B)

Fig. 1. At the initial diagnosis of lung cancer. A) a mass of about 2.9 cm at the right hilum and right lower lobe (RLL) with narrowing of the right common basal bronchus. B) a 2.6 cm nodule at the superior segment of the left lower lobe (LLL).

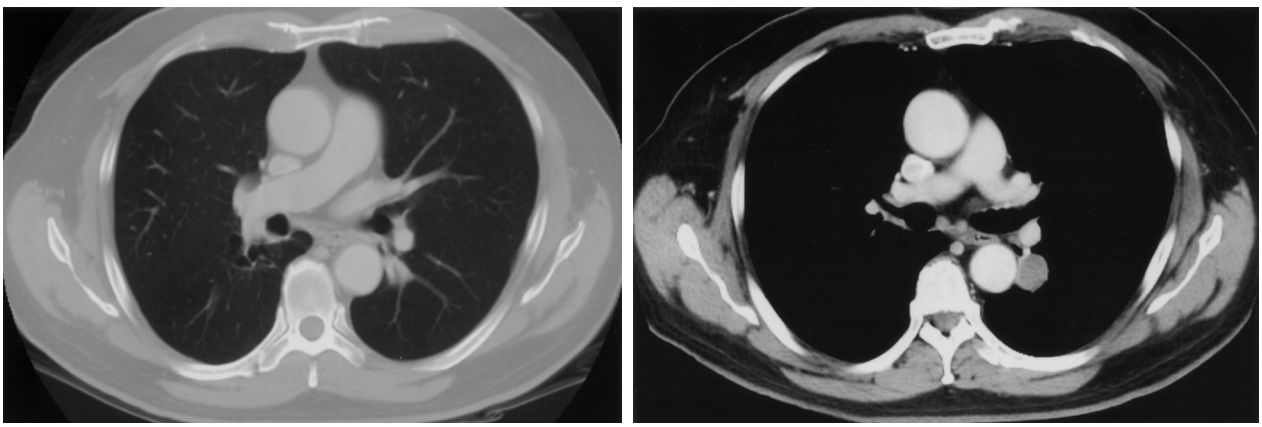
change at the superior segment of the RLL with mild peribronchial infiltration of the RLL bronchus and adjacent ground-glass opacity. (Figures 2A and 2B) However, the nodule at the left lung remained stationary, without any change. There was neither mediastinal lymph node enlargement nor a definite focal lesion of the visible pancreas, spleen, and bilateral adrenal glands.

After discussion with the chest surgeon, an aggressive surgical intervention was considered for suspected multiple primary lung cancers or different etiologies. He received a left B6 segmentectomy by video-assisted thoracoscopic surgery (VATS), and a 3×3-cm well-defined tumor was noted at the left lower lung adjacent to the aorta. In addition, right middle and lower lobes bilobectomy and group 3, 4, 7, 9 and 11 lymph node dissection was performed via thoracotomy. The pathology of the surgical specimens showed a residual squamous cell carcinoma in the right lung, and a carcinoid tumor in the LLL. All of the lymph nodes, including the right interlobar and group 3, 4, 7, 9 and 11, showed anthracosis. The pathological staging of lung cancer was revised to stage I (T1N0M0). After operation, the patient was regularly followed up at outpatient clinics, and no evidence of tumor recurrence had been detected up to the time of this writing (March, 2008, 5 months after operation).

Discussion

We report the synchronous growth of squamous cell carcinoma and a carcinoid tumor of the lung in a patient who received aggressive surgical intervention after chemotherapy. Although the treatment course was not compatible with the current treatment guidelines for NSCLC, the definite diagnosis of synchronous lung cancer and a carcinoid tumor was made. The patient had a good prognosis.

There are few reports of synchronous lung cancer and carcinoid tumors. Synchronous lung adenocarcinoma and carcinoid tumors were reported by Yano *et al*. in Japanese [5]; however, the carcinoid tumor diagnosis was made before surgical intervention. Jung-Legg *et al*. demonstrated a case with a bronchial carcinoid tumor, small cell carcinoma and adenocarcinoma of



(A) (B)

Fig. 2. After neoadjuvant chemotherapy. A) the RLL tumor showed cystic change with mild peribronchial infiltration. B) a stationary nodule at the superior segment of the LLL.

the right lung [6]. Seo *et al*. showed a patient with simultaneously occurring squamous cell and neuroendocrine carcinomas in association with cryptogenic fibrosing alveolitis [7]. The synchronous lung lesions of the above reports were all located in the same side of the lung in which patients had received resection. However, our patient had synchronous squamous cell carcinoma and a carcinoid tumor which were located in different sides of the lung. Surgical intervention for bilateral lung lesions is more difficult and risky.

Although multiple lung nodules are often considered as lung-to-lung metastasis, different etiologies should always be kept in mind. An invasive histological diagnosis may be necessary with clinical suspicion, especially when curative resection can be performed in the early stage. Therefore, even if both tumors are highly suspected of being malignant, as in the PET scan, histological diagnosis of both sides should be performed [8]. In addition, carcinoid tumors do not have specific radiological signs, and therefore can be mistaken as benign lesions or multiple metastasis [8]. Our patient received a third bronchoscopy to exclude the possibility of different etiologies of the left lung lesion. Finally, resection of the bilateral lung lesions proved the suspicion of different etiologies due to the differing responses to chemotherapy.

The diagnostic method of pulmonary cytopathology has been developed for several decades, and the overall sensitivity and specificity of techniques are excellent, ranging from 60% to 96% [9]. However, Thivolet-Bejui et al. reported a false-positive rate of 1% for respiratory cytology specimens, which was difficult to avoid even by highly-experienced cytopathologists [10]. Many conditions may cause false positive diagnoses of squamous cell carcinoma, including reactive metaplasia in chronic airway disease, fungus or mycobacterial infection, and post-tracheostomy atypia [11]. Therefore, in our case, the cause of the discrepancy in the washing cytology results from those of the second bronchoscopy and the final surgical pathology most likely resulted from misinterpretation by the cytologist. In order to reduce the false positivity of cytology, the physician should always pay attention to clinical correlation, radiographic analysis, sample processing and preservation [12].

With the increasing availability of early detection tools, such as multislice spiral CT and PET scanning, the incidence of multiple undetermined lung lesions has increased. The issue is becoming more and more important, especially for asymptomatic subjects who have had nodules detected in regular health examinations. For the staging workup of lung cancer, this condition is classified as “non-resectable” stages (IIIb and IV) for lung cancer patients who have bilateral lung lesions detected by images, according to the International Union Against Cancer TNM classification [2]. In 1975, Martini and Melamed outlined the criteria for differentiation between synchronous or metachronous lung cancers as physically being distinct and separate, and lymphatics common to both should not be involved [13]. However, it is difficult to decide preoperatively whether a synchronous lesion represents a metastatic tumorlet from the index tumor or a separate primary tumor.

Multiple primary lung cancers is an uncommon but important issue, and its incidence ranges from 0.2% to 20% [14]. There are no guidelines detailing recommendations for the selection and treatment of patients with synchronous multiple primary lung cancers. Ag-

gressive surgical intervention is mandatory. Chang *et al*. reported that an aggressive surgical approach is safe and justified in patients with synchronous multiple primary lung cancers and node-negative diseases [15]. The status of this particular form of NSCLC might be considered in the conventional TNM staging system for a more accurate prediction of patient prognosis.

In conclusion, multiple lung lesions in lung cancer patients should be carefully interpreted and managed because of the possibility of synchronous tumors of different pathologies or multiple primary lung cancers. Aggressive intervention, including invasive diagnosis or surgical excision, may be indicated for definite diagnosis and treatment.

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合併肺部鱗狀上皮癌及類癌之病歷報告

吳尚俊　余忠仁　楊泮池

我們報告一位55歲抽菸的男性，同時合併有肺部鱗狀上皮癌及類癌。病人一開始以咳血表現，因為胸部影像學檢查及支氣管鏡抽洗液細胞學檢查顯示兩側肺部皆有癌侵犯，所以在第四期非小細胞肺癌合併有肺部轉移的情形下開始接受化學治療，經過三個療程的剋癌易及卡鉑之化學治療，兩側肺腫瘤的反應不一致，因此採取積極的手術處理，而病理報告顯示兩側肺部腫瘤分別為鱗狀上皮癌及類癌。結論是對於多發性肺部病灶應謹慎判讀，考慮不同疾病並存的可能性，必要時採取積極的處理介入以便診斷或治療，尤其是具有不同影像或生物學特徵的多發性病灶。*(胸腔醫學* ***2008; 23: 369-374****)*

關鍵詞：肺部鱗狀上皮癌，類癌，前導性化學治療

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Mediastinal Parathyroid Adenoma: Report of a Case Treated Successfully by Video-Assisted Thoracoscopic Surgery

Chen-Chi Liu, Chien-Ying Wang, Wen-Hu Hsu

Herein, we report a rare case of mediastinal ectopic parathyroid adenoma successfully treated by video-assisted thoracoscopic surgery (VATS). A 71-year-old female initially presented with general weakness and consciousness change. Biochemical examination revealed hypercalcemia and an elevated intact parathyroid hormone (i-PTH) level. 99mTc-sestamibi (MIBI) scintigraphy revealed an ectopic parathyroid gland in the anterior mediastinum. Chest computed tomography (CT) scan revealed a relatively well-defined soft tissue mass at the right anterior mediastinum, that was successfully treated with a video-assisted thoracoscopic surgerical approach. The postoperative course was uneventful, and her serum calcium and i-PTH levels returned to a normal range after operation. The pathologic report confirmed ectopic parathyroid adenoma. We report this case with a review of the literature. ***(Thorac Med 2008; 23: 375-380)***

Key words: mediastinal parathyroid adenoma, video-assisted thoracoscopic surgery (VATS)

Introduction

Primary hyperparathyroidism is characterized by excessive secretion of parathyroid hormone (PTH), and is a leading cause of hyper-calcemia. Ectopic mediastinal parathyroid adenomas account for up to 25% of cases of patients with primary hyperparathyroidism [1]. The treatment comprises surgical excision via a cervical incision. However, 2% of ectopic parathyroid adenomas are not accessible using a standard cervical approach, as the gland is deeply embedded in the superior aspect of the anterior or posterior mediastinum, and is in close contact with the thymus [2]. In the past, these lesions were treated with a trans-sternal or transthoracic approach, using either sternotomy or thoracotomy. Until recently, some authors recommended the use of video-assisted thoracoscopic surgery (VATS) or video-assisted mediastinoscopic surgery (VAMS) as a gentler, minimally invasive procedure. We report the case of a patient with ectopic mediastinal parathyroid adenomas and primary hyperparathyroidism that was treated successfully by VATS.

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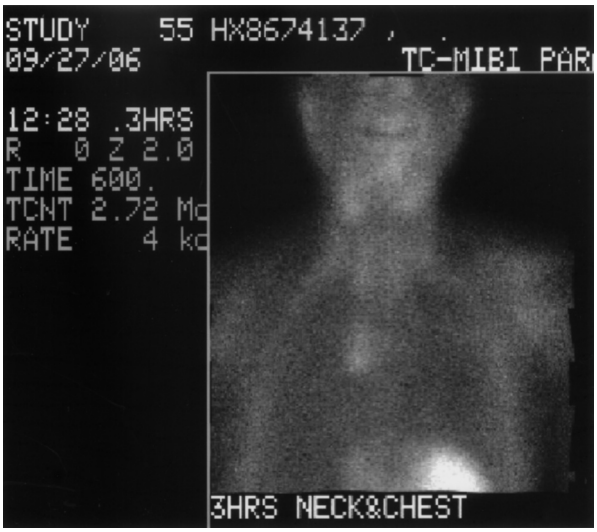

Fig. 1. Tc99m-sestamibi parathyroid scintigraphy demonstrated a focal area of increased uptake involving the right side of the anterior mediastinum

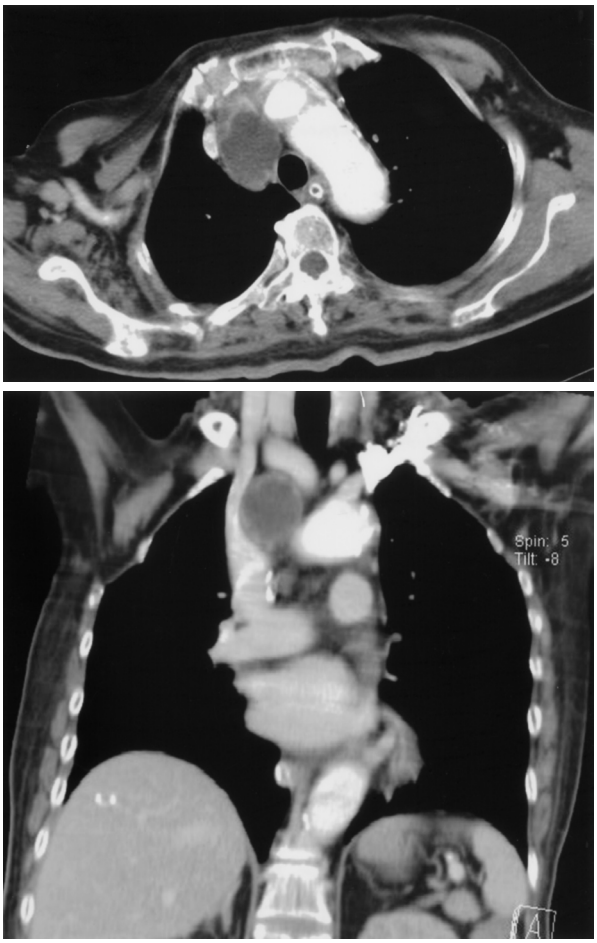

Fig. 2. Chest computed tomography scan revealed a 3.2×2.7×3.5-cm soft tissue mass with central low density in the right superior anterior mediastinum and abutting the superior vena cava.

Case Report

A 71-year-old woman had hypertension and type II diabetes mellitus with regular medical control. Her family history was unremarkable. Six months before, she noted a moderate resting tremor in both hands which brought her to a local clinic. She took some medication under the impression of Parkinsonism, but her symptoms persisted. She was sent to our emergency department due to general weakness and drowsy consciousness. Hypercalcemia (serum calcium: 19.3 mg/dl, free calcium: 2.97 mmol/l) and elevated intact PTH (1493 pg/ml) were noted. Her renal function had also deteriorated sharply (BUN: 63 mg/dl, creatinine: 3.1 mg/dl). After fluid hydration and the use of calcitonin, her condition gradually stabilized, but her serum calcium level remained at 12.6 mg/dl. Workup for multiple myeloma included a skull X-ray, brain MRI, and serum and urine immunoglobulin, which were all negative. Multiple endocrine neoplasia syndromes were also excluded due to normal urine VMA, and the abdominal ultrasonography results were negative. Neck ultrasonography located the nodular goiter, and there was no focal lesion in the bilateral retrothyroid regions. The Tc99m-sestamibi parathyroid scintigraphy demonstrated a focal area of increased uptake involving the right side of the anterior mediastinum (Figure 1), which suggested an ectopic parathyroid adenoma in the mediastinum. The chest computed tomography (CT) scan visualized a 3.2×2.7×3.5-cm soft tissue mass with central low density in the right superior anterior mediastinum, deeper than the brachiocephalic

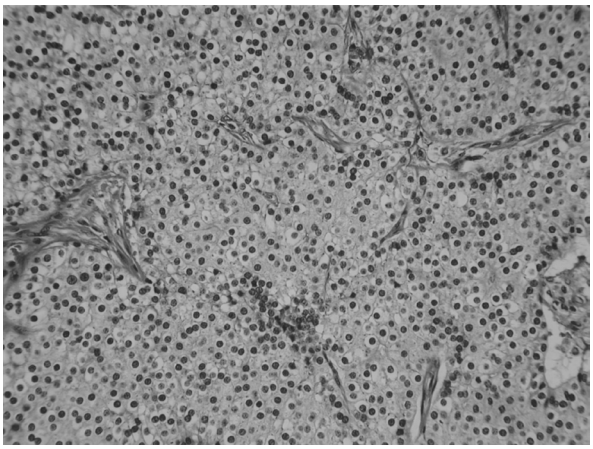

Fig. 3. Hematoxylin and eosin stain, 400X, showing the nodule composed mainly of chief cells. Nests of oxyphilic cells were also seen. The pathologic findings were compatible with parathyroid adenoma.

vein and abutting the superior vena cava (Figure 2). Tumor markers including CEA, beta-HCG, AFP, and CA-125 were all normal, and CA-199 was 49.58 U/ml. Under the impression of ectopic parathyroid adenoma in the mediastinum, a chest surgeon was consulted for operation. The tumor was removed successfully by VATS. The intact PTH and serum calcium level dropped to a normal range 24 hours following operation. The pathologic report pro-ved ectopic parathyroid adenoma (Figure 3). The postoperative course was uneventful. The patient was followed 1 and 6 months after operation and her calcium and intact PTH were within normal limits.

Discussion

The most frequent cause of hypercalcaemia is primary hyperparathyroidism. About 80% of primary hyperparathyroidism cases are caused by parathyroid adenomas and nearly 15% by parathyroid hyperplasia; parathyroid adenocarcinoma is an extremely rare etiology. The ectopic parathyroid glands account for 1-3% of these cases, and the possible sites of ectopic parathyroid tissue are parapharyngeal at the level of the mandible, intrathyroidal, and mediastinal. The occurrence of these lesions is explainable on an embryologic basis. The majority of mediastinal ectopic parathyroid adenomas are located in the anterior mediastinum; the less frequent locations are in the visceral compartment of the mediastinum, in a paraesophageal area, in the aortopulmonary window, or close to the right pulmonary artery near the tracheal bifurcation [4]. Since most ectopic parathyroid adenomas are proximate to the thymus gland [3], these can be excised using a collar incision. Nevertheless, in about 2% of the cases, the ectopic mediastinal parathyroid tissue is not accessible with this incision, rendering the procedure inadequate.

Precise localization of the ectopic parathyroid adenomas before operation is important for the surgical approach and successful resection. Improvements in the sensitivity and specificity of high-resolution ultrasonography and the advent of new imaging techniques, such as Tc99m-sestamibi parathyroid scintigraphy, have led to a more accurate localization of the lesions. A combination of thoracic CT and Tc99m-sestamibi parathyroid scintigraphy is the most commonly used and able to offer precise mapping.

The best approach to mediastinal parathyroid adenomas is still controversial. For parathyroid adenomas located deeper in the chest, median sternotomy or lateral thoracotomy were the traditional surgical approaches. Prinz *et al*. reported a 19-21% rate of complications after median sternotomy for removal of ectopic parathyroid tissue, including pulmonary complications (pneumothorax, pneumonitis, pleural effusion), wound complications, deep vein thrombosis, and atrial fibrillation [5]. Recently,

a number of less invasive modalities have been introduced, such as angiographic ablation and video-assisted mediastinal or thoracoscopic surgery (VAMS/VATS) [3]. Angiographic ablation is the least invasive by far. Since the failure rate of angiographic ablation is about 40% [6], it is usually used for patients who are poor surgical candidates. Peter *et al*. [8] reported 4 cases using VAMS for resection of ectopic parathyroid adenoma. Although several advantages of VAMS, such as the short operative time and hospital stay, less complex anesthesia and no violation of the pleural space, were described, 2 cases required a partial sternal split to facilitate exploration. The major limitation of VAMS might be the limited operative field of exploration.

VATS was developed by Landreneau and coworkers [7], and provides all the advantages of minimally invasive surgery, such as improved cosmesis, less pain, and shorter hospital stay. In cases of re-operation for primary hyperpara-thyroidism, especially, VATS is performed through an area not involved in the previous operation(s), and does not interfere with other surgical approaches. Thus, the risks of re-operation in relation to recurrent laryngeal nerve paralysis, hypoparathyroidism, and injury to other structures are low. There are several reports of successful resections of ectopic mediastinal parathyroid adenomas using VATS, with rare complications [1, 3]. Cupisti *et al*. [1] recommended VATS as the first-line procedure if the parathyroid adenoma is located clearly in the mediastinum, deeper than the brachiocephalic vein. Three of 4 patients they reported were treated successfully by VATS. The remainder underwent VATS followed by open sternotomy, due to false-negative frozen sections. We agree with the conclusions of Cupisti and understand that the lesions might be too small to identify. In our center, the intraoperative PTH-quick assay is not available. We check the serum calcium level to gauge the effect of resection of the small parathyroid adenoma.

After confirmation of primary hyperparathyroidism in our case, cervical ultrasonography and Tc99m-sestamibi parathyroid scintigraphy were systematically performed. Workups for exclusion of multiple myeloma and multiple endocrine neoplasia were also arranged. Furthermore, chest CT scan disclosed the tumor located at the right anterior mediastinum. We performed VATS and removed the tumor smoothly. Her intact PTH and serum calcium returned to a normal range after operation. In conclusion, we believe that the choice of a best surgical approach is strictly related to the position of the parathyroid adenoma, and that VATS is the first-line treatment for these lesions that have settled in the mediastinum.

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縱膈腔副甲狀腺腺瘤—成功以胸腔鏡手術治療之病例報告

劉鎮旗　王鑑瀛　許文虎

縱膈腔異位性副甲狀腺腺瘤是一種罕見的縱膈腔腫瘤，臨床上通常以高血鈣症及副甲狀腺素過高來表現，治療以手術切除為主。在此一病例報告中，我們呈現一位71歲女性病患因全身無力及意識昏迷至醫院就診，實驗室檢查發現有原發性副甲狀腺機能亢進的現象，副甲狀腺核醫掃瞄及胸腔電腦斷層顯現前縱膈腔有一功能亢進之病灶。病患接受胸腔鏡手術摘除此一病灶，病理檢查報告為一副甲狀腺腺瘤。病患術後恢復良好，在術後1個月及6個月追蹤並無發現高血鈣之情形。除了報告此一罕見病例外，我們也回顧縱膈腔副甲狀腺腺瘤的治療方式。*(胸腔醫學* ***2008; 23: 375-380****)*

關鍵詞：縱膈腔副甲狀腺腺瘤，胸腔鏡手術

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Primary Synovial Sarcoma of the Mediastinum: A Case Report

Yu-Sen Lin, Wen-Hu Hsu

Synovial sarcoma is a malignant neoplasm predominantly affecting the soft tissues of the extremities of adolescents and young adults. Primary mediastinal synovial sarcomas are rare and have been recognized only recently. We report a case of this rare disease with the initial presentation of back pain. Chest plain film and computerized tomography revealed a huge right-side tumor mass with pleural effusion. Computerized tomography-guided biopsy disclosed synovial sarcoma. A general survey showed no evidence of distal metastasis. The patient received palliative debulking surgery, had a poor response to adjuvant radiotherapy and chemotherapy, and expired 6 months after operation. Due to the rarity of primary mediastinal synovial sarcoma, there is no standardized therapy. Broad surgical resection is the cornerstone of therapy. We report a patient with this rare disease and review the literature. ***(Thorac Med 2008; 23: 381-385)***

Key words: mediastinal tumor, synovial sarcoma

Introduction

Synovial sarcoma is a malignant neoplasm predominantly affecting the soft tissues of the extremities of adolescents and young adults [1]. Although initially thought to arise from the synovium, more and more studies have shown that it is not related to normal synovium, but rather demonstrates evidence of epithelial differentiation. It has been proposed by some that this tumor be renamed carcinosarcoma or spindle cell carcinoma of the soft tissue [2-3]. Primary mediastinal synovial sarcoma is rare, and was first reported in the literature in 1989 [4]. Herein, we report a case of this rare disease.

Case Report

A 24-year-old man presented to our emergency department with right back pain and dyspnea. The patient had experienced right back pain for 6 months. He went to a local clinic and took some medicine under the impression of muscle sprain. The symptom persisted and dry cough, dyspnea, poor appetite, and night fever with sweating developed. He was sent to our emergency department due to progressive dyspnea. His past medical history was unremark-

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able, and he had had no previous surgeries. The physical examination was remarkable only for the absence of breathing sounds in the right lung field. Chest plain film showed total opacification of the right hemithorax (Figure 1). Chest computerized tomography (CT) demonstrated a 13×11 cm heterogenous soft tissue mass with a necrotic area at the right posterior mediastinum. The tumor invaded the pleura with compression to the right heart, esophagus and inferior vena cava. Collapse of the right lung, massive pleural effusion, and right 10th rib erosion were also noted (Figure 2). Laboratory tests, including blood cell count, electrolytes, carcino-embryonic antigen, alpha-fetoprotein, and beta-human chorionic gonadotropin, were within normal limits. Thoracocentesis disclosed transudation, and was negative for malignant cells. CT-guided biopsy showed synovial sarcoma. Whole body bone scan (WBBS) was negative. The patient was then referred to our department for surgical intervention. Right lower lobe lobectomy and palliative debulking

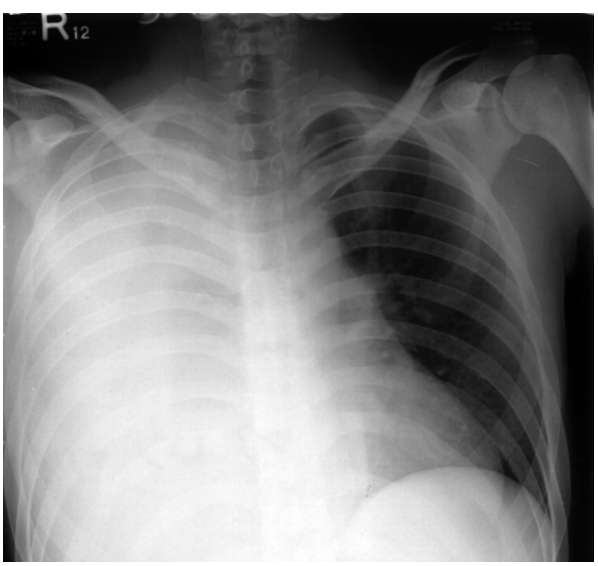

Fig. 1. Chest plain film showing total opacification in the right-side lung field.

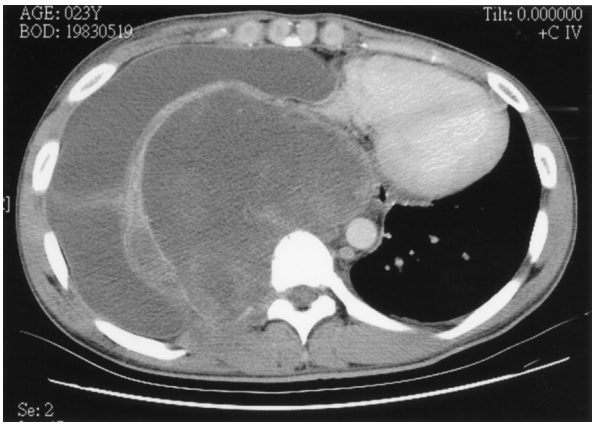

Fig. 2. Chest computerized tomography (CT) demonstrating a huge soft tissue mass with heterogenous density and a necrotic area at the right posterior mediastinum. Massive pleural effusion in the right pleural cavity was also noted.

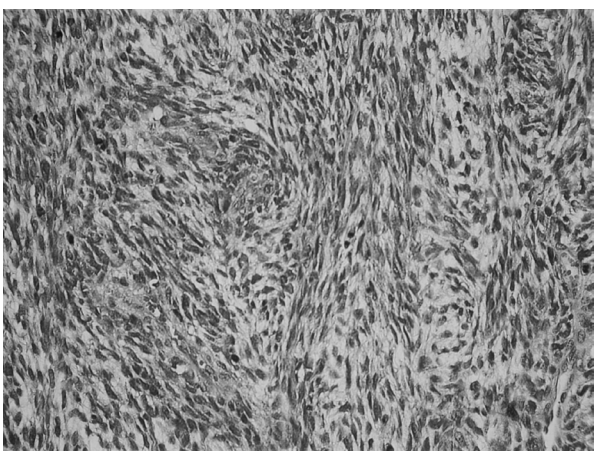

Fig. 3. Microscopically, the tumor demonstrated a spindle cell carcinomatous component (H&E stain, 200X).

of the involved ribs and vertebrae were done on 13 April 2007. The post-operative course was uneventful. The pathology examination showed infiltrating synovial sarcoma with extensive necrosis (Figure 3). Adjuvant radiotherapy was performed on 8 May. 2007, but the follow-up chest CT on 15 May. 2007 showed progressive change. Radiotherapy was discontinued due to the poor effect (total 1800 cGy in 9 fractions). The patient received chemotherapy with epi-

rubicin (90 mg/m^2) and ifosfamide (2.4 gm/m^2) on 24 May. 2007. WBBS on 20 July 2007 showed multiple bone metastases, so high-dose ifosfamide (5 gm/m^2) was given. The regimen was then shifted to gemcitabine (675 mg/m^2) and paclitaxel (100 mg/m^2) on 29 August 2007. Due to disease progression, the patient expired on 24 October 2007.

Discussion

The mediastinum is host to a vast array of both primary and metastatic neoplasms. The differential diagnosis is extensive and depends on the location involved, age of the patient, presentation and clinical history. Synovial sarcoma is a rare mesenchymal neoplasm that mainly affects soft tissues of the extremities. It is composed of 2 types of cells that form a characteristic biphasic pattern: epithelial cells resembling those of carcinoma, and fibrosarcoma-like spindle cells. Burt M, *et al*. reported that mediastinal sarcomas accounted for 1.4% of soft tissue sarcomas of all sites [5]. In Burt's study, there was only 1 case of primary mediastinal synovial sarcoma (46 cases of other primary mediastinal sarcomas). Primary synovial sarcoma in the mediastinum is extremely rare and has been recognized only recently [4]. Because of its rarity in this location, it may be mistaken for other neoplasms, particularly malignant mesothelioma. Detection of the chromosomal abnormalities t (x; 18) and SYT-SSX is considered useful for the differential diagnosis [6]. The possibility of metastasis to the mediastinum from a synovial sarcoma of the soft tissue should always be ruled out first, before making a diagnosis of primary synovial sarcoma at this site. The physical examination and image studies (abdominal, chest CT) of this patient showed no other lesion, so the diagnosis of primary mediastinal synovial sarcoma was made.

It has been recognized that only 10% of malignant mediastinal neoplasms are symptomatic; 90% of lesions that occur in asymptomatic patients are benign [7]. The symptoms can be nonspecific (chest pain, fever, weight loss), or caused by compression of the surrounding structures (dyspnea, cough, etc.). Our patient complained of both of these symptoms. The most common radiologic finding of primary synovial sarcoma of the chest is a heterogeneously enhancing soft tissue mass with well-defined margins and without calcification, best appreciated on CT [8]. These features are compatible with those of our patient.

The treatment of synovial sarcoma is primarily surgical with wide excision to avoid recurrences. Due to the rarity of this tumor, there is no standardized therapy for primary mediastinal synovial sarcoma. Most patients receive surgery or surgery and adjuvant radiation. Tumors are chemosensitive to ifosfamide and doxorubicin with an overall response rate of approximately 24% [9]. In a meta-analysis, adjuvant chemotherapy for sarcomas improved the time to local recurrence and the recurrence-free survival rate, with a trend toward a better overall survival rate [10]. The 5-year survival rate of patients with synovial sarcoma of the extremities ranges from 36% to 64% [1]. All of the reported synovial sarcomas of the mediastinum were large and tended to recur. The prognosis of this disease to the mediastinum is even poorer than that to the extremities [4, 11]. Factors predicting a worse prognosis of patients with synovial sarcoma include tumor size (>5 cm), male gender, older age (>20 years), extensive tumor necrosis, high grade, neurovascular invasion, and the SYT-SSX1 variant [12]. The

main prognostic factor is the ability to achieve a complete resection. Even so, the local recurrence rate in patients having a complete resection was high (64%) and surpassed the incidence of distant metastasis (43%) [5]. McLean TR *et al*. agreed that location may be the most important factor related to the local recurrence rate in mediastinal sarcoma. This was probably because a wide margin is difficult to obtain in this location [13].

The tumor in our patient was huge and compressed to the surrounding organs. The symptoms due to the tumor's mass effect progressed with time. Immediate reduction of the volume of the tumor was necessary. Furthermore, pre-operative survey disclosed no evidence of distant metastasis. Surgical intervention was indicated for the possibility of achieving complete resection. However, tumor invasion to the vertebral body was noted during operation, so debulking surgery was performed. After surgical intervention, this patient received adjuvant radiation. Unfortunately, the disease progressed and adjuvant chemotherapy was given. The patient had a poor response to each regimen of adjuvant chemotherapy and expired 6 months after operation.

In conclusion, mediastinal synovial sarcoma is a rare, aggressive disease. Broad surgical resection is the cornerstone of therapy. Multimodal therapy may be indicated because of the high recurrence rate. Further studies will be required to obtain the optimal therapy.

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原發性縱膈腔滑膜肉瘤—病例報告

林昱森　許文虎

滑膜肉瘤是一種影響四肢軟組織的惡性腫瘤，通常發生在青少年或年紀輕的成人。原發性縱膈腔滑膜肉瘤甚為罕見且最近才被報告。我們報告一個一開始是以背痛來表現的病例。胸部X光片和電腦斷層均顯示右側巨大腫瘤併肋膜積液。電腦斷層導引切片診斷為原發性縱膈腔滑膜肉瘤，全身性檢查顯示無遠端轉移跡象。病人接受姑息性切除性手術，但對於術後之放射線治療和化學藥物治療反應不佳。病人於術後六個月死亡。原發性縱膈腔滑膜肉瘤相當罕見，目前並無標準的治療方法。廣泛性的切除是最重要的治療方式。我們報告此一罕見疾病並回顧相關文獻。*(胸腔醫學 **2008; 23: 381-385**)*

關鍵詞：縱膈腔腫瘤，滑膜肉瘤

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Hyperbaric Oxygen Therapy as an Adjunct Treatment for Patients with Sternal Infection, Osteomyelitis and Mediastinitis – A Case Report

Wen-Kuang Yu, Jia-Horng Wang

Sternal infection and mediastinitis are uncommon but serious complications after cardiothoracic surgery via median sternotomy. They increase postoperative mortality, morbidity and overall cost. Early aggressive debridement and empiric antibiotic use are the primary treatment. The postulated mechanism of ischemia and hypoxia resulting in the development of sternal infection and mediastinitis provides a theoretical basis for the use of hyperbaric oxygen therapy (HBO). A review of case reports and some nonrandomized studies found that they all supported the use of HBO for sternal infection after cardiothoracic surgery. We report a case of sternal wound infection and osteomyelitis after median sternotomy. The patient received wound debridement and antibiotic treatment but without effect. After adjunct hyperbaric oxygen therapy, the sternal infection and mediastinitis improved dramatically and the patient was discharged without co-morbidity. We concluded that HBO therapy may be a variable adjunct treatment for sternal infection and mediastinitis after sternotomy. ***(Thorac Med 2008; 23: 386-392)***

Key words: hyperbaric oxygen therapy, sternal osteomyelitis, mediastinitis, sternotomy

Introduction

Sternal wound infection and dehiscence are major problems for patients who receive sternotomies. Patients who develop sternal wound infection have increased mortality and long-term morbidity. Many risk factors predispose to sternal infection. Ischemia after sternotomy may play an important role in wound infection. Current treatment includes wound debridement, irrigation, tissue flap reconstruction and antibiotic use based on culture sensitivity. Hyperbaric oxygen therapy (HBO) - the administration of 100% O2 at 2 to 3 times the absolute atmosphere pressure (ATA) -- is widely used in the treatment of various problem wounds and refractory osteomyelitis. Many mechanisms account for the effects of HBO therapy. We report a case of sternal wound infection and osteomyelitis after median sternotomy for thymectomy. The patient received wound debridement and antibiotic treatment, but without effect. After

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HBO therapy, the anterior mediastinitis improved dramatically and the patient was discharged without co-morbidity.

Case Report

A 54-year-old male was admitted with the chief complaint of a drop of the left upper eyelid for 2 months. He was an ex-smoker, 1 pack/day for 40 years, and had quit for 3 years. He had a history of hypertension and chronic obstructive pulmonary disease (COPD), and myasthenia gravis that was under medical treatment. He was admitted to our hospital with the aforementioned chief complaint. Chest X-ray revealed mediastinal widening (Figure 1). Computed tomography (CT) scan of chest showed a lobulated soft tissue about 25×27×43 mm in size at the right anterior mediastinum and in close contact with the ascending aorta and pericardium. Thymoma was impressed (Figure 2). He underwent a median sternotomy, thymectomy, wedge resection of the right upper lobe and pericardiectomy. The pathologic report revealed encapsulated thymoma, WHO type AB, and thymic cyst. However, wound dehiscence and turbid discharge from the lower part of the sternotomy wound occurred on the 10th day after operation

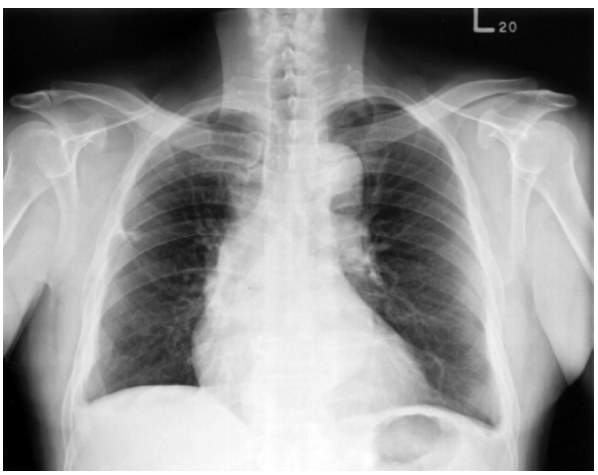

Fig. 1. Chest X-ray showing mediastinal widening and a lobulated lesion in the right anterior mediastinum.

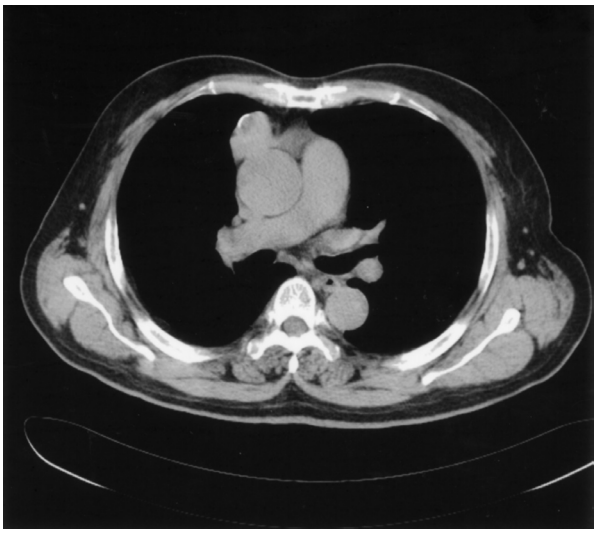

Fig. 2. Chest CT scan showing a soft tissue density in the right anterior mediastinum with calcification.

Fig. 3. Median sternotomy wound dehiscence and discharge

(Figure 3). In addition, fever was noted off and on. CT scan of the chest revealed an anterior mediastinal soft tissue infection with gas formation, abscess, and pleural involvement (Figure 4). Acute osteomyelitis along the incision wound in the sternum was also impressed via osteomyelitis scan. The culture from the turbid discharge showed *Staphylococcus aureus*. The patient underwent surgical debridement for 5 times (Figure 5), and antibiotics treatment based on the drug susceptibility of the microorganism. Due to poor control of the mediastinitis, sternal osteomyelitis and the problem wound, he received 17 treatments with hyperbaric oxygen therapy (2.5 ATA for 90 minutes). The infection condition and wound improved dramatically (Figure 6). He then received flap reconstruction. He was discharged without morbidity after 137 days of hospitalization.

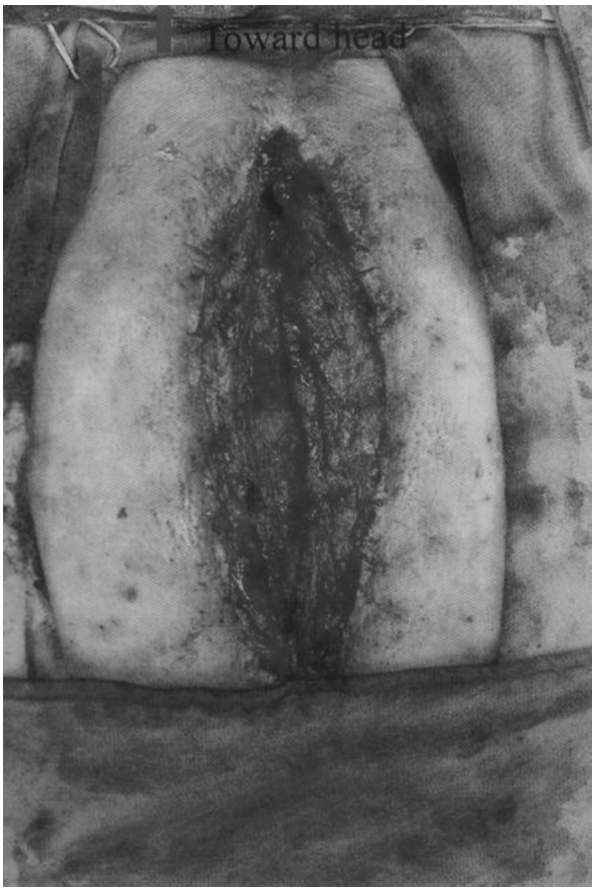

Fig. 5. After debridement, the wound healed poorly.

Discussion

Although the incidence of mediastinal wound infection in patients undergoing median sternotomy for cardiothoracic surgery is relatively low - less than 1% in recent reports [1-3], it is a serious complication and requires antibiotic treatment and further surgery, including repeated debridement and major surgical reconstruction. Patients who develop mediastinal wound infection have a significantly higher short-term and long-term mortality rate [4]. The average cost of hospitalization for patients with wound infection is 3 times than that of a patient with an uncomplicated postoperative course [5].

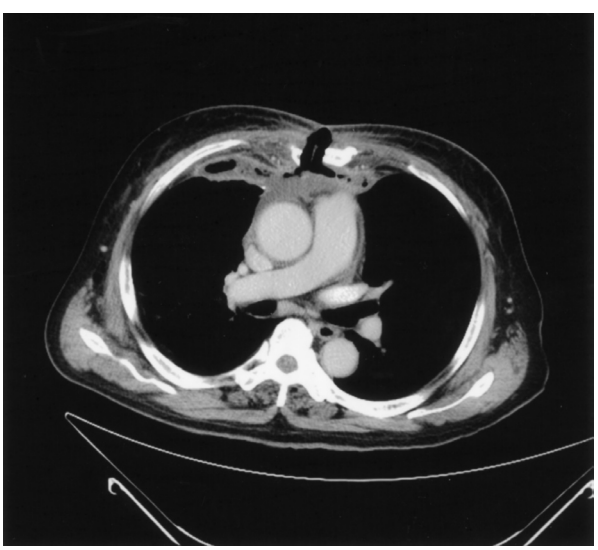

Fig. 4. Chest CT scan showing anterior chest wall and mediastinal soft tissue infection with gas formation, abscess formation and pleural involvement.

Risk factors for the development of poststernotomy mediastinitis include *preoperative factors*: a history of COPD, a history of prior

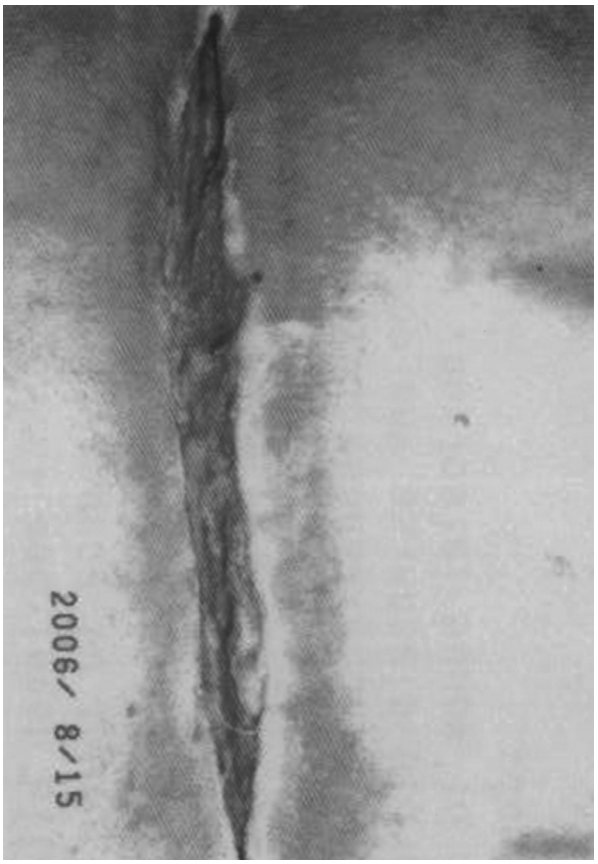

Fig. 6. After hyperbaric oxygen therapy, the wound showed improvement and granulation tissue growth and epithelialization.

sternotomy, pyuria, low ejection fraction and a high left ventricular end-diastolic pressure; *intraoperative factors*: valvular or aortic aneurysm surgery, prolonged bypass pump time, repeat placement of bypass, duration of surgery; and *postoperative factors*: surgical re-exploration due to postoperative hemorrhage, cardiopulmonary resuscitation in the immediate postoperative period, and prolonged time (>48 hours) on mechanical ventilation [6].

There are several mechanisms for the development sternal wound dehiscence, infection, osteomyelitis and even mediastinitis. Local ischemia of the sternum results in wire loosening and instability, followed by subsequent dehiscence of the overlying skin incision. The osteomyelitic bone and open wound are ideal culture media for bacterial growth. Inadequate sternal fixation and the resulting instability leading to skin dehiscence as a primary event is another theory. Alternatively, inadequate drainage of the mediastinum after operation results in a collection of blood and fluid that form an excellent culture media for bacteria [7].

The optimal treatment for sternal infection and osteomyelitis includes early debridement, collection of specimens for bacterial culture, use of broad-spectrum antibiotics and a change in antibiotics based on the results of the sensitivity test. When the infectious condition is under control, reconstruction of the wound should be instituted, including rewiring, and pectoralis or rectus muscle and omental flap rotation.

The definition of HBO therapy is an intermittent administration of 100% oxygen for a patient breathing inside a treatment chamber at a pressure higher than sea level pressure. Currently, the pressure should be 1.4 ATA or higher. There are many beneficial biochemical and cellular effects with this therapy. Refractory osteomyelitis is 1 of the indications for the HBO therapy. With the administration of HBO therapy, the partial oxygen pressure in the wound increases and promotes collagen matrix formation and angiogenesis [8]. Increased oxygen tension improves the ability of free radicals to kill bacteria through neutrophil-mediation [9]. Besides, HBO is bactericidal for certain anaerobes, including *Clostridium perfringens* [10], and bacteriostatic for certain species [11]. It also suppresses the clostridial production of alpha toxin [12]. The sternal wound, by nature, is ischemia and hypoxic. Therefore, the administration of HBO therapy can reverse hypoxia, reduce local edema, salvage marginally perfused

tissue and improve host defenses [13].

However, there are only a few case reports of patients with sternal infection after sternotomy who receive HBO therapy [14-15]. These authors suggested HBO therapy is a good and effective adjunct therapy for deep sternal wound infection or sternal osteomyelitis, and that is relatively safe. Siondaski *et al*. presented 55 cases of patients with sternal wound infection and/or mediastinitis during a 5-year period (between August 1997 and May 2002) who received aggressive surgical management and HBO therapy [16]. They concluded that the combination of surgical treatment and HBO therapy may improve clinical outcomes in patients with sterno-mediastinitis and post-sternotomy wound infection after cardiothoracic surgery. Another prospective nonrandomized study at a single institution, reported by Fabio *et al*. was designed to evaluate the effect of HBO therapy on organ/space sternal surgical site infection following cardiothoracic surgery [18]. A total of 32 patients were enrolled in the study from 1999 through 2005. They were divided into 2 groups according to whether HBO therapy was offered or not. The relapse, infection rate, the duration of intravenous antibiotic use and total hospital stay were significantly lower in the group that received HBO therapy.

In reviewing case reports and some nonrandomized studies, all support the use of HBO therapy for sternal infection after cardiothoracic surgery. Although there are no large randomized double-blinded control studies to support or refute the early use of HBO therapy in the management of sternal infection/osteomyelitis after cardiothoracic surgery, there are many case reports and nonrandomized studies that provide evidence supporting the use of HBO therapy. In this case, we administered HBO therapy as an adjunct treatment for post-sternotomy osteomyelitis/mediastinitis and achieved a good result. We suggested a combination of aggressive surgical debridement, antibiotic treatment and early adjunct HBO therapy for patients who develop sternal osteomyelitis/mediastinitis.

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高壓氧治療做爲胸骨切開手術術後併發骨髓炎與縱膈腔發炎之輔助治療病例報告與文獻回顧

余文光　王家弘

因心臟胸腔手術而併發胸骨骨髓炎與縱膈腔炎在臨床上並不常見，然而此併發症會提高死亡率、住院天數與醫療費用。積極地清瘡手術與使用廣效性抗生素為目前主要治療方法。手術部位局部缺氧與缺血的致病機轉理論提供了使用高壓氧治療作為輔助治療之根據。我們在此提出一位因胸腺瘤開刀切除病灶而引發胸骨骨髓炎，縱膈腔炎傷口裂開之病例報告，經過清瘡手術與抗生素治療後仍無法有效控制傷口與感染情況，在使用高壓氧作為輔助治療後，整體情況進步迅速。之後病人接受皮瓣重建手術並且順利出院。我們提出此病例報告並做相關文獻回顧。*(胸腔醫學* ***2008; 23: 386-392)***

關鍵詞：高壓氧治療，胸骨骨髓炎，縱膈腔炎，胸骨切開術

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