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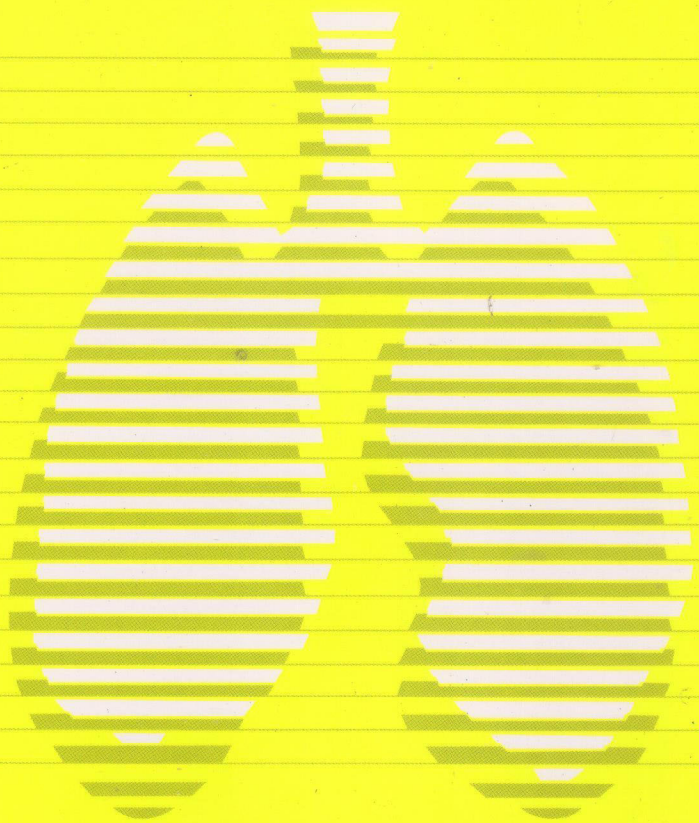

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Positional and Nonpositional Obstructive Sleep Apnea

Chun-Hsiung Huang, Ching-Hsiung Lin, Woei-Horng Chai, Cheng-Hsiung Chen, Chin-Shui Yah

Background: Many patients with obstructive sleep apnea have a significant worsening of apnea in the supine position. The aim of this study was to describe the impact of body position on the clinical and polysomnographic data of OSA patients.

Methods: A total of 765 consecutive OSA patients were diagnosed in our sleep center from March 2002 to December 2004. Among these, 512 patients who met the following criteria were recruited into this study: apnea hypopnea index (AHI) > 10, age > 20, and normally sleeping in either the supine, intermediate or lateral position for more than 30 minutes. We classified the subjects into a positional patients (PP) group (Supine AHI/Lateral AHI ≥ 2) and a nonpositional patients (NPP) group (Supine AHI/Lateral AHI< 2). Anthropomorphic data, overnight polysomnography, and Epworth Sleepiness Scale (ESS) scores were collected for analysis.

Results: Among the 512 subjects, 74% were positional patients and predominately male. Weight, body mass index (BMI), and neck circumference were significantly higher in the NPP group. Average weight in the NPP group was 8.8 kg heavier than in the PP group. ESS scores were also higher in the NPP group. The PP group tended to have a longer total sleep time and lower arousal index compared to the NPP group. The AHI and average apnea-hypopnea duration were significantly higher, and the average or minimal oxygen saturation was significantly lower in the NPP group. Using multiple logistic regression analysis, we found that the AHI, followed by the BMI and ESS scores, were strong predictive factors for the risk of developing positional OSA.

Conclusion: This study demonstrated that the majority of OSA patients were positional-dependent. These positional-dependent patients were thinner and had a lower severity of AHI and daytime sleepiness. The AHI is the most dominant variable predicting positional dependency. Body weight reduction and positional therapy are important strategies, in addition to nasal CPAP, in the treatment plan for OSA patients. ***(Thorac Med 2007; 22: 229-236)***

Key words: sleep position, obstructive sleep apnea

Introduction

Studies have shown that many obstructive sleep apnea (OSA) patients tend to experience significant worsening of apnea when they sleep in the supine position [1-5]. When OSA patients lie on their side, the apnea-hypopnea index (AHI) is about 40 to 50% lower than when they lie on

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their back [1, 6-13].

Cartwright and co-workers first defined Positional Patients (PP) as those OSA patients in whom the AHI was at least twice as high while sleeping in the supine position as in the lateral position [1, 8]. Those patients in whom the AHI in the supine position was less than twice that in the lateral position were called Non-Positional Patients (NPP). For positional OSA patients, the severity of the disease is mostly related to the sleep time spent in the supine position.

The percentage of PP among OSA patients in different reports varies from 9% to 60% [1, 8, 14-18]. This variation is probably due to the small patient numbers in the earlier study and the different types of OSA patients studied. Positional therapy, namely avoidance of the supine position during sleep, was estimated to be successful in treating about 50% of all OSA cases [8, 19]. However, there is no data, as yet, of positional OSA prevalence among Asians, and the factors influencing positional dependency.

The aim of this report was to compare the anthropomorphic and overnight PSG data between the PP and NPP groups formed by the 512 consecutive OSA patients diagnosed in our Sleep Medicine Center.

Materials and Methods

Study Subjects

From March 2002 to December 2004, 765 consecutive patients were diagnosed as having OSA at the Sleep Medicine Center, Changhua Christian Hospital. Among these, 512 patients, who were older than 20 years, had an AHI of more than 10, and slept for more than 30 minutes in either the supine or the lateral position, were included in the analysis. We classified the subjects into a positional patients (PP) group (Supine AHI/ Lateral AHI $\geq$ 2) and a non-positional patients (NPP) group (Supine AHI/ Lateral AHI $<$ 2).

Polysomnography

Polysomnography was recorded by a digital polygraph system (Alice 4, USA). The electroencephalogram (C3A2, C4A1, O1A2, and O2A1) was based on the 10-20 international electrode placement system. A right and left electrooculogram was used to record the sleep pattern. Thoraco-abdominal excursions were registered by strap gauges. Nasal airflow was measured by a pressure sensor. Pulse oximetry and electrocardiography were used to monitor oxygen saturation (SpO2) and heart rate. Daytime sleep function was assessed subjectively by means of the Epworth Sleepiness Scale (ESS) questionnaire [20]. A total amount of more than 10 points was assumed to be a sign of excessive daytime sleepiness. In addition, movements of the limbs and the intensity of snoring were recorded by electromyogram of the anterior tibialis muscle of both legs and a microphone affixed to the neck, respectively. Body position was determined by a position sensor (Alice 4, USA), which was attached to the midline of the abdominal wall. This sensor differentiated between the upright, left side, right side, prone and supine positions.

Abnormal respiratory events during sleep consist of apnea, defined as total absence of airflow for 10 seconds or longer, and hypopnea, defined as a decrease of more than 50% in the amplitude of breaths lasting for more than 10 seconds or a decrease of less than 50% in the amplitude of breaths associated with an arousal or a decrease in oxygen saturation of more than 3%. Obstructive apnea or hypopnea is defined by the absence or reduction of airflow in the presence of continuing respiratory efforts documented by paradoxical movement of the rib cage and

abdomen. Central apnea or hypopnea is defined as simultaneous cessation or reduction of airflow and thoraco-abdominal motion. The apnea-hypopnea index (AHI) is defined as the ratio of the number of episodes of apnea and hypopnea to total sleep time (hour). It is the most commonly used polysomnographic index for severity of sleep apnea (normal: less than 5.0; mild: 5.0~14.9; moderate: 15.0~29.9; and severe: 30.0 or more) [20]. History-taking and physical examination, including weight, height, blood pressure and neck circumference, were recorded before PSG examination.

Statistical Analysis

Statistical analysis was performed using SAS/PC 8.2 software. The chi-square test (or, when appropriate, Fisher's exact test) and Student's t test were used for testing differences in the characteristics of the 2 groups. Data are presented as mean ± standard deviation (SD) or numbers (percentage). Stepwise multivariate logistic regression analysis was performed to assess the factors contributing to positional OSA. A p value less than 0.05 was considered statistically significant.

Results

Among the 512 OSA patients, 380 (74%) were positional patients and 132 (26%) were non-positional patients (Table 1). The mean age was 50.3 and there was no significant difference between the 2 groups. The BMI was significantly higher in the NPP group ($p<0.001$), which was related to the higher weight in that group ($p<0.001$); the average weight in the NPP group was 8.8 kg higher than in the PP group. Neck circumference was smaller in the PP group than in the NPP group. Although ESS was slightly higher in the NPP group, both were less than 10.

Table 2 shows the sleep parameters of PSG data between the 2 groups of patients. The PP group had longer sleep time (411.6 ± 60.7 min vs. 366.3 ± 99.2 min, $p<0.001$), and total sleep time (358.0 ± 66.4 min vs. 313.5 ± 94.9 min, $p<0.001$). There was no difference in sleep efficiency (SE), sleep onset latency (SOL), and REM onset latency (ROL) between the 2 groups. The NPP group had a significantly higher percentage of lighter sleep stages (Stage 1, $p<0.001$), but not deeper sleep stages. The PP group had more sleep time in the REM stage. No significant difference was found between the 2 groups in the PLMD index. However, the arousal index was significantly higher in the NPP group.

Breathing parameters of PSG data between the 2 groups are summarized in Table 3. Mean AHI during total sleep time was significantly higher in the NPP group than in the PP group

Table 1. Study subjects characteristics

	Overall (n = 512)	PP (n = 380)	NPP (n = 132)	*p*-value
Age, yr	50.3 ± 13.3	50.8 ± 13.1	48.8 ± 13.7	0.131
Weight, kg	75.0 ± 14.5	72.7 ± 13.3	81.5 ± 15.9	<0.001
Height, cm	164.9 ± 9.3	164.6 ± 9.6	166.0 ± 8.3	0.106
BMI, kg/¢T	27.4 ± 4.4	26.6 ± 4.0	29.4 ± 5.0	<0.001
Neck gird, cm	38.8 ± 3.7	38.2 ± 3.4	40.4 ± 4.0	<0.001
ESS	8.5 ± 5.2	7.9 ± 4.7	9.9 ± 6.0	<0.001

BMI = Body mass index; ESS = Epworth sleepiness scale

Table 2. Comparison of sleep parameters between the PP and NPP groups

	PP (n = 380)	NPP (n = 132)	*p*-value
SPT, min	411.6 (60.7)	366.3 (99.2)	<0.001
TST, min	358.0 (66.4)	313.5 (94.9)	<0.001
WK, min	53.7 (42.2)	52.8 (45.2)	0.843
SE, %	82.9 (12.3)	81.6(13.1)	0.327
SOL, min	16.7 (28.2)	15.8 (25.4)	0.766
ROL, min	127.3 (76.2)	130.6 (75.4)	0.750
REM.SPT, min	57.1 (28.6)	46.3 (30.4)	<0.001
REM.SPT, %	13.7 (6.3)	12.2 (6.7)	0.017
S1.SPT, %	20.5 (9.7)	25.3 (13.7)	<0.001
S2.SPT, %	48.7 (13.8)	44.7 (17.2)	0.017
S3.SPT, %	3.1 (4.1)	2.5 (5.2)	0.232
S4.SPT, %	1.1 (5.8)	1.8 (7.2)	0.312
Arousal index	30.2 (14.8)	51.0 (25.4)	<0.001
PLMD index	10.4 (22.9)	10.5 (26.7)	0.973

SPT = sleep period time; TST = total sleep time; WK = wake time; SOL = sleep onset latency; ROL = REM onset latency; REM.SPT = REM sleep period time

Table 3. PSG Breathing Parameters

	PP (n = 380)	NPP (n = 132)	*p*-value
AHI TST	26.5 (16.5)	53.7 (28.4)	<0.001
AHI NREM	25.7 (18.1)	53.6 (30.8)	<0.001
AHI REM	30.8 (20.5)	48.8 (26.6)	<0.001
AHI Max, sec	57.0 (25.6)	67.0 (30.8)	0.001
AHI Mean, sec	22.2 (5.0)	23.4 (6.2)	0.038
Avg SpO2	83.7 (8.6)	79.1 (13.4)	0.001
Min SpO2	80.7 (7.3)	73.4 (12.7)	<0.001
Snoring	1358.4 (1057.4)	1441.8 (1083.7)	0.438

AHI = apnea-hypopnea index; AHI Max = maximal duration of apnea-hyponea, AHI Mean = mean duration of apnea-hyponea, Avg SpO2 = Average SpO2; Min SpO2 = minimum saturation level

(53.7 ± 28.4 vs. 26.5 ± 16.5, $p<0.001$). Average oxygen saturation level and maximal desaturation level were significantly lower in the NPP group than in the PP group. There was no difference in snoring frequency between the 2 groups.

Table 4 summarizes the results of stepwise multivariate logistic regression analysis, indicating the dominant variables that correlate with positional dependency. In the logistic regression model in which the NPP group is the dependent variable, 3 variables appeared to predict the risk of developing positional OSA. They were AHI (OR = 0.231, CI: 0.145-0.366), BMI (OR = 0.469, CI: 0.280-0.785), and ESS (OR = 0.444, CI: 0.236-0.835).

Table 4. Multivariate logistic regression analysis of positional dependency

	β	S.E.	OR	OR (95% CI)	*p*-value
AHI > 30	-1.467	0.236	0.231	(0.145, 0.366)	<0.001
BMI > 30	-0.757	0.263	0.469	(0.280, 0.785)	0.004
NC > 40	-0.277	0.246	0.758	(0.468, 1.227)	0.259
ESS > 15	-0.813	0.323	0.444	(0.236, 0.835)	0.012

NC = neck circumference

Discussion

This study has shown that the majority (74%) of OSA patients in our Sleep Medicine Center were in the PP group. This is consistent with other studies with much larger sample sizes. In Oksenberg's data, 55.9% of the patients in a large unselected OSA population were positional [22]. Therefore, for the diagnostic evaluation and suggested treatment, the PSG report should detail the amount of supine sleep and the AHI during supine and non-supine sleep.

The lateral position is commonly recommended for the improvement of obstructive apnea events in OSA patients. Surprisingly, little information is available regarding the improvement mechanism and upper airway site influenced by the lateral position. However, the gravity effect on the upper airway is the factor most likely responsible for this phenomenon. Using a slim endoscope under general anesthesia, Isono and co-workers found that the static pressure-area curve of the lateral position was above those of the supine position [23]. Both retropalatal and retroglossal airways were enlarged from the supine to the lateral position.

BMI had been showed to have an inverse relationship to positional dependency; the prevalence of PP patients will decrease as mean BMI increases [22]. In our study, the BMI was significantly higher in the NPP group and the average weight in this group was 8.8 kg higher than in the PP group. This suggests that the amount of weight probably would have to be reduced to convert NPP into PP. One study has shown that the collapsibility of the upper airway is decreased after weight loss [24]. Neck circumference was smaller in the PP group than in the NPP group in this study, indicating that nuchal obesity is also important for positional dependency.

Sleep quality was better in the PP group than in the NPP group, both in duration and continuity. The PP group had longer total sleep time and a significantly lower arousal index (30.2 ± 14.8 vs. 51.0 ± 25.4, $p<0.001$). Such differences in sleep architecture can be ascribed to the lower AHI and maximal arterial oxygen desaturation level (80.7 ± 7.3 vs. 73.4 ± 12.7, $p<0.001$) in the PP group, which leads to sleep fragmentation and daytime sleepiness. The fact that the ESS score was significantly higher in the NPP group supports these observations.

Most studies related to the effect of body position on sleep apnea suggest that sleep in the supine position will increase the severity of sleep apnea [1, 8, 14]. Our study confirmed that AHI during total sleep time was significantly higher in the NPP group than in the PP group. Average oxygen saturation level and maximal desaturation level were also significantly lower in the NPP group than in the PP group. However, Oksenberg proposed another means of evaluation, which included apnea length, delta oxygen desaturation, length and occurrence of arousals, snoring loud-

ness and delta brady/tachycardia [25]. Oksenberg's study showed that even for the NPP group, the supine position aggravates breathing abnormalities during sleep.

Using multiple logistic regression analysis, we found that the AHI, followed by the BMI and ESS scores, is a strong predictive factor for the risk of developing positional OSA. Therefore, mild to moderate OSA patients are mostly positional, and they are the optimal candidates for positional therapy. On the other hand, in severe OSA and obese patients, apnea occurred in all body positions and CPAP was required for upper airway patency.

In conclusion, this study demonstrated that the majority of OSA patients were positional-dependent. These positional-dependent patients were thinner and had a lower severity of AHI and daytime sleepiness. The AHI is the most dominant variable predicting positional dependency. The PSG report should detail the amount of supine sleep and the AHI during supine and non-supine sleep. Body weight reduction and positional therapy are important strategies, in addition to nasal CPAP, in the treatment plan for OSA patients.

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睡眠體位與非睡眠體位阻塞型睡眠呼吸中止症

黃俊雄　林慶雄　蔡偉宏　陳正雄　葉金水

背景：很多阻塞型睡眠呼吸中止症病患仰臥時，呼吸中止會惡化。本篇研究的目的，是描述睡眠體位對阻塞型睡眠症呼吸中止症病患，在臨床及睡眠多項生理檢查儀資料的影響。

方法：從 2002 年 3 月到 2004 年 12 月，在我們的睡眠中心，總共有 765 名病患，被診斷為阻塞型睡眠呼吸中止症。其中有 512 名符合納入研究的條件；呼吸停止 - 呼吸不足指數(AHI)大於 10 ，年齡大於 20 ，及某一睡眠體位如側睡或仰睡超過 30 分鐘。我們將病患分為：睡眠體位病患組(仰睡 AHI/ 側睡 AHI ≥ 2)、與非睡眠體位病患組(仰睡 AHI/ 側睡 AHI < 2)。收集病患資料、過夜睡眠多項生理檢查儀資料、及依波沃斯睡眠量表(Epworth Sleepiness Scale, ESS)並加以分析。

結果：在 512 位病患中， 74% 是睡眠體位阻塞型睡眠呼吸中止症的病患，以男性為主。非睡眠體位阻塞型睡眠呼吸中止症的病患，明顯比較重，質量指數(BMI)較高，頸圍大，比睡眠體位阻塞型睡眠呼吸中止症的病患重 8.8 公斤，且依波沃斯睡眠計量較高。同時，呼吸停止呼吸不足指數也較高，其發生時間也較長，明顯的較低氧飽合度。而睡眠體位阻塞型睡眠呼吸中止症的病患相較於非睡眠體位病患組，傾向於有較長睡眠時期及較高快速動眼期睡眠百分比。經多變項邏輯迴歸分析，我們發現呼吸停止呼吸不足指數、質量指數、及依波沃斯睡眠計量，可用以預測發現睡眠體位阻塞型睡眠呼吸中止症的危險性。

結論：此研究顯示阻塞型睡眠呼吸中止症患者中，有一大部份是起因睡眠體位。睡眠體位阻塞型睡眠呼吸中止症患者，體重較輕，呼吸停止呼吸不足指數較低，白天嗜睡度較低。呼吸停止呼吸不足指數，是預測睡眠體位阻塞型睡眠呼吸中止症的主要因子。對於睡眠體位阻塞型睡眠呼吸中止症患者的處置，除了經鼻陽壓呼吸器的使用外，減重和體位療法亦是治療阻塞型睡眠呼吸中止症病患的重要方法之一。*(胸腔醫學 **2007; 22: 229-236**)*

關鍵詞：體位，阻塞型睡眠呼吸中止症

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Acute Renal Failure and Hypercalcemia: Rare Initial Manifestations of Sarcoidosis — A Case Report

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Sarcoidosis is a multisystem, inflammatory disorder that can involve any organ, especially the lungs; however, significant renal involvement is rare [1].

We report a 58-year-old male who had nausea and vomiting for 3 months. Laboratory data showed elevated serum creatinine and calcium levels. Sarcoidosis with renal and endocrine gland involvement was confirmed by typical chest radiography findings, Gallium-67 citrate scanning, mediastinoscopic biopsy of the mediastinal lymphadenopathy, and kidney biopsy. Oral prednisolone, 0.5 mg/kg/day, resulted in laboratory improvement. ***(Thorac Med 2007; 22: 237-242)***

Key words: sarcoidosis, acute renal failure, hypercalcemia

Introduction

Sarcoidosis is a multisystem, inflammatory disorder that can involve any organ, especially the lungs. The cause of sarcoidosis remains unknown. Sarcoidosis often presents with hilar lymphadenopathy, pulmonary infiltration, and eye and skin lesions. Rarely, sarcoidosis may present with both acute renal failure and hypercalcemia [2]. Hypercalcemia occurs because of increased 1,25-dihydroxy-vitamin D production by activated macrophages in sarcoidal granulomas. If left untreated, hypercalcemia can result in renal calculi, nephrocalcinosis and renal failure.

The American Thoracic Society criteria for diagnosis of sarcoidosis include (1) the presence of a consistent clinical and radiographic picture; (2) the demonstration of noncaseating granuloma on biopsy; (3) exclusion of other conditions that can produce a similar pathology, including infections, autoimmune disorders, and inhalational diseases [3]. Oral corticosteroids remain the first-line therapy in most cases.

Herein, we report a 58-year-old male who had nausea and vomiting for 3 months. Acute renal failure and hypercalcemia were found initially by laboratory examination. Later, sarcoidosis with renal and endocrine gland involvement was diagnosed.

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Case Report

A 58-year-old male had had type 2 diabetes mellitus for 4 years. The blood glucose was being controlled by oral hypoglycemic agents with glibenclamide 5 mg po qd and metformin hydrochloride 250 mg po bid. In March, 2006, he was sent to a local hospital due to a sudden onset of comatose consciousness. Laboratory examinations revealed hypoglycemia, acute renal failure, and hyperkalemia. Renal replacement therapy with hemodialysis was suggested, but the patient hesitated. In April, 2006, he was admitted to our institute with presentations of nausea and vomiting. During hospitalization, laboratory data were as follows: blood urea nitrogen (BUN): 84 mg/dl (normal range: 5-25 mg/dl); serum creatinine (Cr): 7.1 mg/dl (normal range: 0.7-1.4 mg/dl); serum sodium (Na): 139 mEq/l (normal range: 137-153 mEq/l); serum potassium (K): 4.7 mEq/l (normal range: 3.5-5.3 mEq/l); serum calcium (Ca): 12.2 mg/dl (normal range: 8.4-10.2 mg/dl); serum intact parathyroid hormone (i-PTH): < 3.00 pg/ml (normal range: 12-72 pg/ml); serum phosphate (P): 4.5 mg/dl (normal range: 2.5-4.5 mg/dl). Sonography of the abdomen revealed enlargement of bilateral kidneys (right kidney: 108 mm. left kidney: 117 mm). Kidney biopsy was suggested after nephrologic consultation, but again, the patient hesitated. No definite diagnosis was made. The patient was discharged, but the symptoms of nausea and vomiting persisted.

In June, 2006, he was admitted to our institute again due to persistent nausea and vomiting. During hospitalization, laboratory data were as follows: BUN: 71 mg/dl; Cr: 7.4 mg/dl; Na: 146 mEq/l; K: 4.3 mEq/l; Ca: 13.2 mg/dl. Chest radiography was taken and revealed bilateral hilar lymphadenopathy enlargement (Figure 1). Computed tomography of the chest also revealed multiple lymphadenopathies in the mediastinum and bilateral hilar regions (Figure 2). Sarcoidosis with renal and endocrine gland involvement was highly suspected.

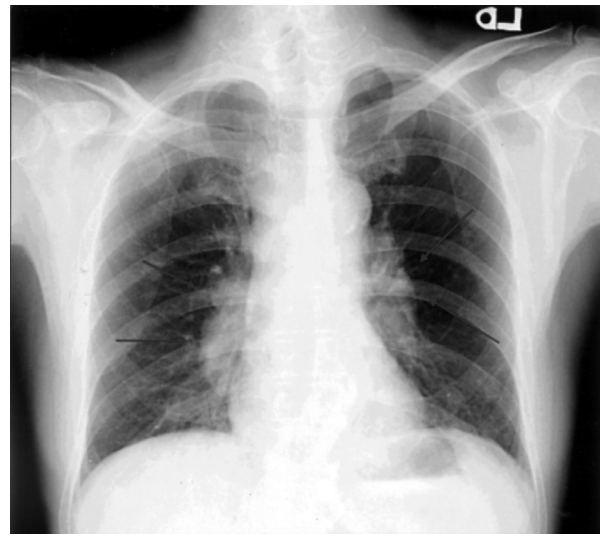

Fig. 1. Chest radiograph revealing bilateral hilar lymphadenopathy enlargement (red arrows)

Gallium-67 citrate scanning revealed increased gallium uptake in the mediastinum and bilateral pulmonary hili (lambda sign) (Figure 3). Finally, the patient underwent mediastinoscopic biopsy for mediastinal lymphadenopathy (Figure 4) and percutaneous renal biopsy (Figure 5). Both of them were consistent with sarcoidosis. In addition to fluid supplementation, we started oral prednisolone, 0.5 mg/kg/day on 23 June, 2006, which resulted in markedly laboratory improvement (Table 1).

Discussion

Sarcoidosis is an immunomediated disease of unknown cause, characterized by noncaseating epithelioid granulomas which affect multiple organs, and especially hilar lymphadenopathy, pulmonary infiltration, eye and skin lesions.

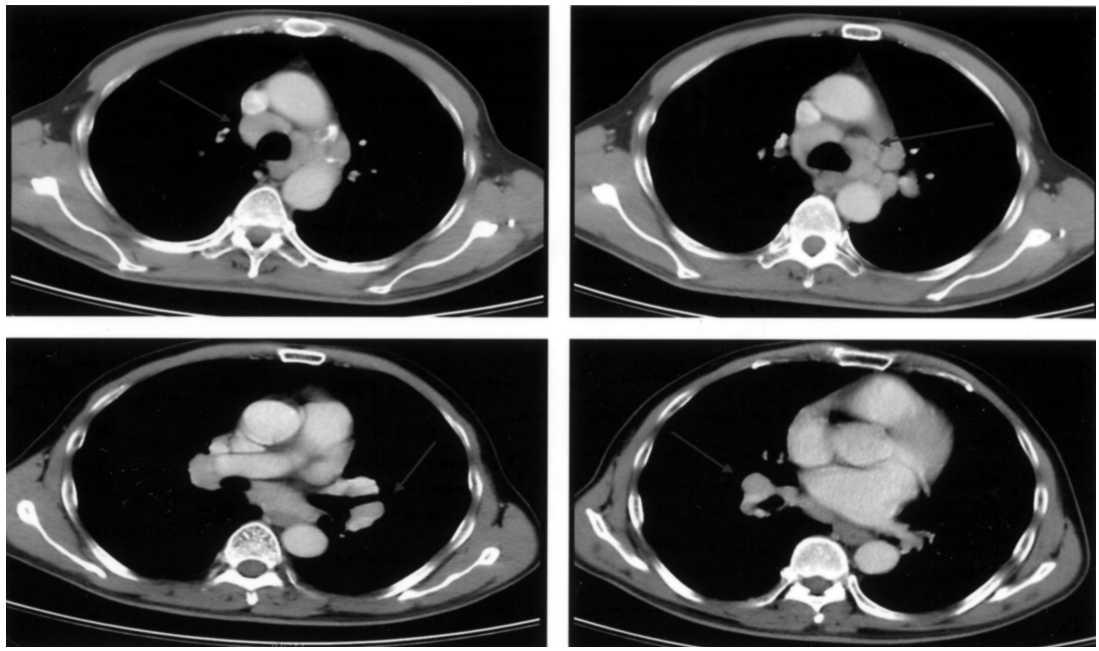

Fig. 2. Computed tomography of the chest revealing multiple lymphadenopathies in the mediastinum and bilateral hilar regions (red arrows)

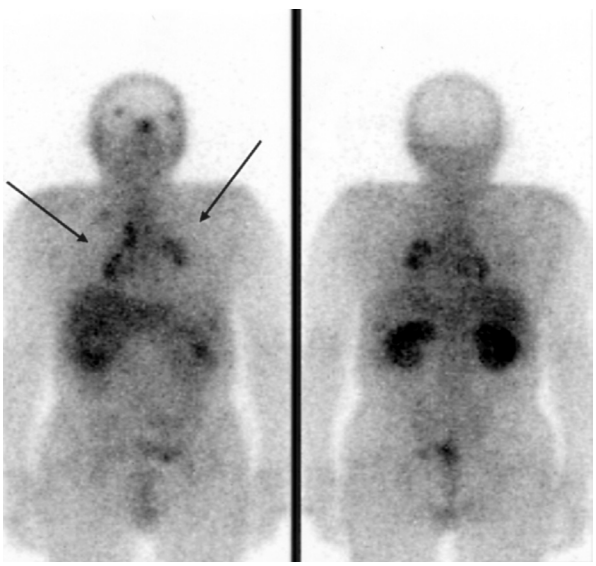

Fig. 3. Gallium-67 citrate scanning revealing increased gallium uptake in the mediastinum and bilateral pulmonary hili (lambda sign) (red arrows)

Clinically apparent renal involvement is rare and has been documented mostly as case reports. The incidence of renal involvement ranges from 3-23%, with a wide spectrum of abnormalities [4]. Sarcoidosis causes renal dysfunction mainly through altered calcium metabolism [5]. An endogenous overproduction of 1, 25-dihydroxyvitamin D [1, 25-$(OH)_2$-D_3] by granulomatous tissue and activated macrophages results in an increase in intestinal absorption of calcium. Hypercalcemia occurs in about 10-13% of sarcoidosis patients [6].

Oral corticosteroids remain the first-line therapy in most cases. The use of oral corticosteroids in sarcoidosis is aimed at the relief of symptoms and modulation of disease activity to prevent serious morbidity and mortality related to vital organ damage. The American Thoracic Society consensus statement suggests that patients with acute pulmonary sarcoidosis (stage I disease with isolated bilateral hilar adenopathy) not be treated because of the generally excellent outcome [7]. Corticosteroids should not be initiated until after a period of clinical observation of 3 to 6 months,

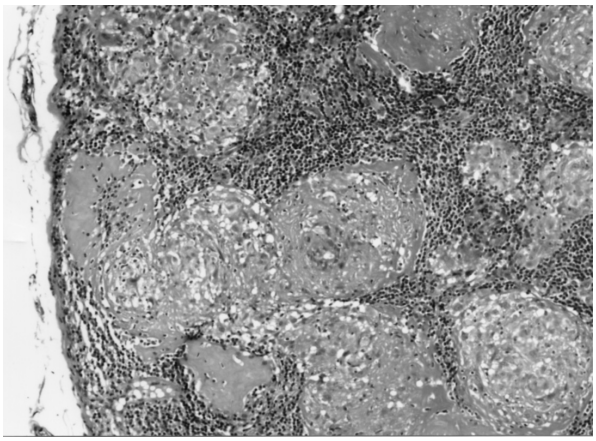

Fig. 4. Mediastinal lymphadenopathy biopsy revealing granulomatous infiltration (H&E stain, 100X)

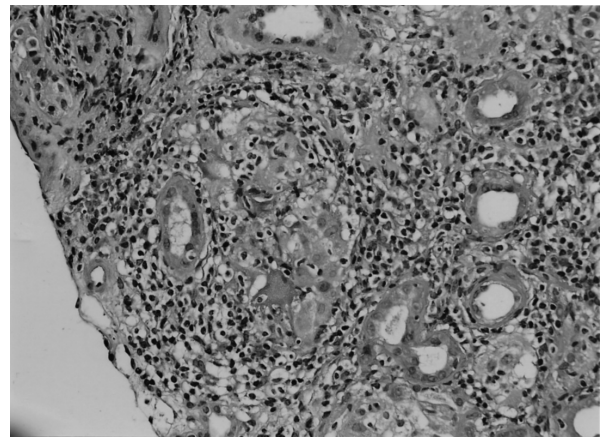

Fig. 5. Percutaneous renal biopsy revealing granulomatous infiltration (H&E stain, 400X)

Table 1. Laboratory data

Date	Na	K	Cl	Ca	BUN	Cr
2006.04.25	139	4.7	102	12.2	84	7.1
2006.06.19	143	4.2				7.3
2006.06.28	137	2.9		9.6		5.4
2006.11.08	137	4.1	101	9.6	53	4.1

Definition of abbreviations: Na=serum sodium (normal range: 137-153 mEq/l); K = serum potassium (normal range: 3.5-5.3 mEq/l); Cl = serum chloride (normal range: 95-105 mEq/l); Ca = serum calcium (normal range: 8.4-10.2 mg/dl); BUN = blood urea nitrogen (normal range: 5-25 mg/dl); Cr = serum creatinine (normal range: 0.7-1.4 mg/dl).

unless there is a life- or sight-threatening indication to treat immediately. Such urgent indications include eye disease, cardiac involvement, neurologic involvement, hypercalcemia, hypercalciuria with associated renal insufficiency or recurrent nephrolithiasis, severe disfiguring skin lesions, progressive hepatic failure, severe incapacitating osseous or muscle involvement, and severe pulmonary involvement that is significantly impairing gas exchange.

In acute renal failure, patients are frequently hypocalcemic. Usually, the presence of hypercalcemia associated with acute renal failure is indicative of the presence of comorbidity, including sarcoidosis, multiple myeloma, cancer, hyperparathyroidism, vitamin D intoxication, or leprosy [8].

Our patient suffered from acute renal failure and hypercalcemia, instead of hypocalcemia which is usually seen in patients with acute renal failure. Plasma i-PTH was suppressed. Our patient denied taking any possible offending drug that would contribute to hypercalcemia. His chest radiography disclosed bilateral hilar lymphadenopathy enlargement. Sarcoidosis with renal and endocrine gland involvement was highly suspected. Mediastinal lymphadenopathy biopsy and percutaneous renal biopsy confirmed our initial impression. In addition to fluid supplement for dehydration due to persistent nausea and vomiting, oral prednisolone, 0.5 mg/kg/day was prescribed. Both of them resulted in a gradual

recovery of renal function.

In conclusion, hemodialysis is a costly therapy in renal failure patients. The patient presented herein was an uncommon case of renal failure with reversible etiology and atypical initial manifestations.

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急性腎衰竭及高血鈣：以罕見的初始症狀表現之類肉瘤病—病例報告

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類肉瘤病乃一全身性發炎的疾病，可以侵犯任何器官，尤其是肺部。雖然所有器官都可能受侵犯，但侵犯到腎臟卻是相當罕見。

我們報告了一個 58 歲男性病人，因為持續噁心、嘔吐三個月而住院。實驗室檢查發現血液肌酸酐及血鈣升高。最後，我們經由胸部 X 光片，核醫鎵 67 發炎掃瞄(Gallium-67 citrate scanning)，縱膈腔淋巴結切片檢查，及腎臟切片檢查確定診斷病人罹患類肉瘤病併腎臟及內分泌系統侵犯。病人在接受類固醇治療後，腎功能及血鈣皆逐漸獲得改善。*(胸腔醫學* ***2007; 22: 237-242)***

關鍵詞：類肉瘤病，急性腎衰竭，高鈣血

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Acute Pulmonary Embolism and Occult Lung Adenocarcinoma: A Case Report of Trousseau's Syndrome

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In patients with underlying malignancy, systemic venous thromboembolism (VTE) is a common complication in the cancer-related hypercoagulable state. Under certain circumstances, systemic VTE may be the only presentation before cancer is diagnosed. Acute pulmonary embolism (PE) is a severe form of systemic VTE. Its symptoms manifest from asymptomatic state, dyspnea, chest pain, and syncope, to sudden circulatory collapse. Acute PE is a less common diagnostic entity in Asian countries than in Western countries. In addition, patients with acute PE seem to have a higher cancer occurrence than those with other mild VTE presentations. This population difference leads to an underestimation, and therefore, delays in the early detection of an occult cancer. Herein, we report a 54-year-old man who was admitted due to acute PE. He was finally diagnosed with lung adenocarcinoma with multiple liver and bony metastasis. However, he had symptoms related to acute PE only, and no cancer-related complaints were noted. Based on this unusual case experience, we suggest a detailed search for occult malignancy is crucial to prevent a delayed diagnosis in patients presenting with acute PE without a known etiology of thrombosis. ***(Thorac Med 2007; 22: 243-248)***

Key words: acute pulmonary embolism, lung adenocarcinoma, Trousseau's syndrome

Introduction

Systemic venous thromboembolism (VTE) includes deep vein thrombosis (DVT) and acute pulmonary embolism (PE). Some risk factors are inherited, such as a deficiency of antithrombin III, protein C, or protein S; and acquired, for example, old age, smoking, obesity, oral contraceptive pill use, astherosclerosis, or malignancy [1]. The events increase sharply after the age of 60, and acute PE accounts for the majority of the increase. If all inherited and acquired causes are excluded, VTE is classified as idiopathic. More and more studies have revealed that idiopathic VTE is the sign of occult malignancy, no matter the tumor size or the clinical manifestations of DVT or acute PE. Acute PE is the most severe form of systemic venous thrombosis. It is interesting that there is far less incidence of acute PE in Asian populations than in Western populations.

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This population difference leads to an underestimation, and therefore, delays in the early detection of an occult cancer if the patient was treated only with thrombolytic therapy.

In this report, we describe a patient who was finally diagnosed with lung adenocarcinoma with liver and bony metastasis. However, he had the manifestations of acute PE only. We also discuss the studies of low-molecular weight heparins (LMWHs) in cancer patients with systemic VTE. In relatively small populations of acute PE patients among idiopathic VTE patients, clinicians should keep in mind the possibility of an occult malignancy.

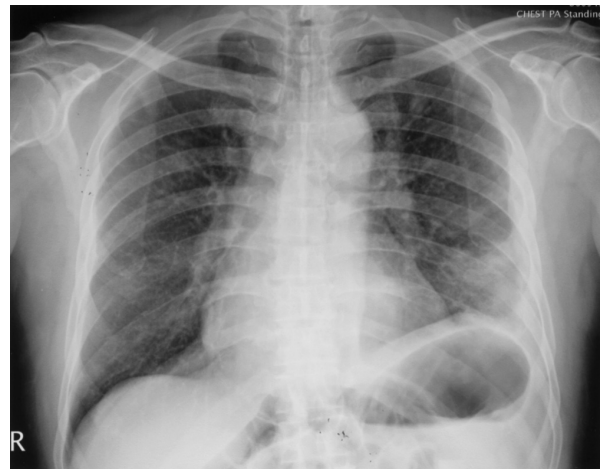

Fig. 1. A chest radiograph showing consolidation in the left lower lung field

Case Report

A 54-year-old man was admitted to this hospital because of fever, dyspnea, chest pain without radiation, and productive cough with blood-twisted sputum. The patient was a gardener in good health, without any underlying disease. He sometimes took Chinese herbal medications for his arthralgia. He had no previous smoking history, no drinking, and reported no allergies.

One month prior to this admission, he noticed that he had dyspnea on exertion and bilateral lower limbs edema, especially on the left side when walking. There was no improvement after he visited his family physician and received some medications. Because the fever, productive cough, and chest pain were aggravated, he visited the chest clinic in this hospital. A chest radiograph was taken and revealed consolidation in the left lower lung field (Figure 1); pneumonia was suspected. After a 1-week course of antibiotics therapy, he reported no improvement, but had cough with blood-twisted sputum in the following visit. Persistent dyspnea on exertion, bilateral lower limbs painful edema, and low oxygenation of about 90~95% in the pulse oxymeter, were noted in the clinic. The blood test for D-dimer revealed a 3561 ug/L level. With the impression of acute pulmonary embolism, the patient was admitted.

Blood levels of electrolytes and serum levels of urea nitrogen, creatinine, aspartate aminotransferase, alanine aminotransferase, and glucose were normal. His white-cell count was 15,800 per cubic meter with 3% band forms and 71% segment forms. Lung perfusion scan on the second hospital day revealed a multiple ventilation-perfusion mismatch (Figure 2). On the third day, his chest computed tomographic (CT) scan with contrast showed multiple filling defects, mainly within the segmental branches of the pulmonary arteries and more severe on the right side, compatible with the pulmonary embolism diagnosis (Figure 3). The lower limbs color duplex showed DVT of both femoral and popliteal veins. In addition, multiple subaortic tumor growth and liver nodules were also noted on the chest CT scan. Bone scan confirmed multiple bony metastasis. The cytology of left-side pleural effusion revealed adenocarcinoma. The lung and liver tumors were proved to be adenocarcinoma in the

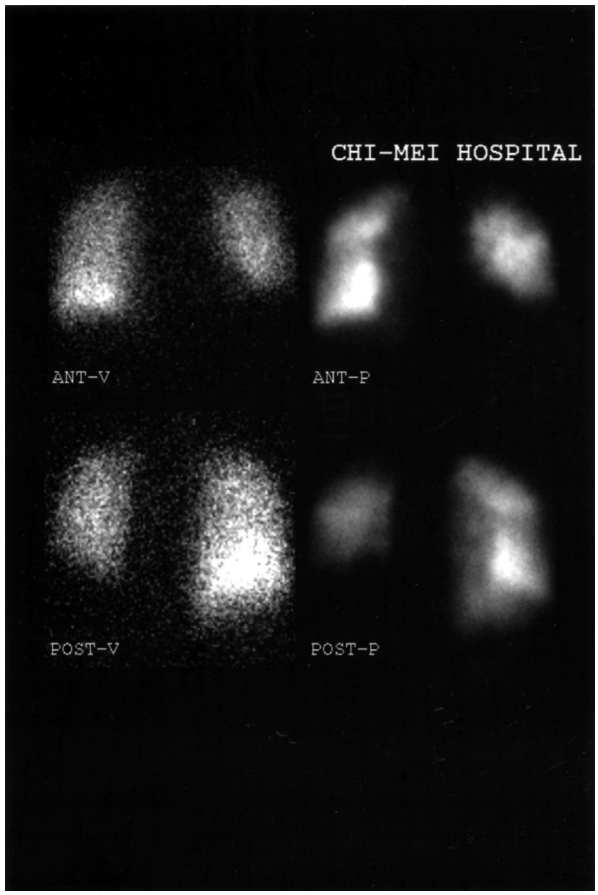

Fig. 2. Lung perfusion scan revealing a multiple ventilation-perfusion mismatch

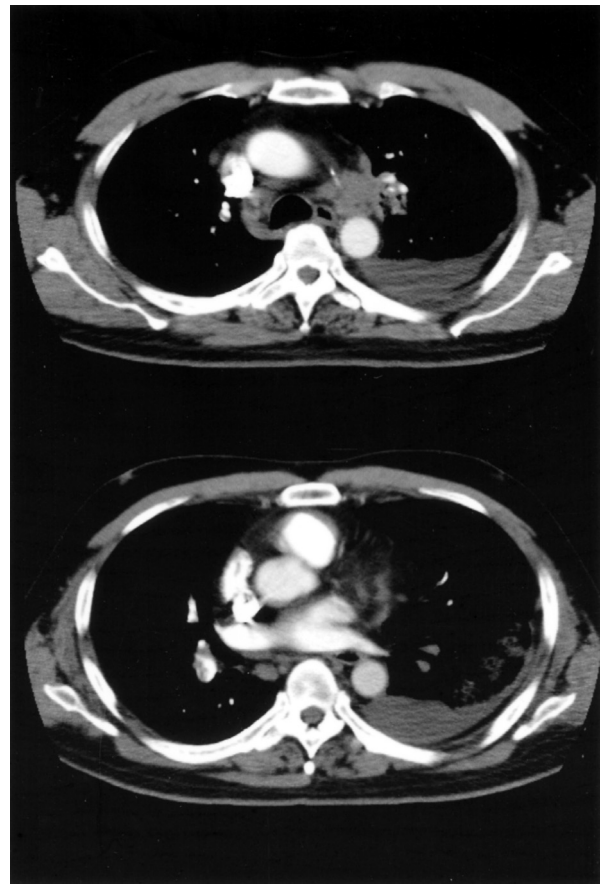

Fig. 3. Chest computed tomographic scan with contrast showing subaortic tumor growth and multiple filling defects within segmental branches of the right-side pulmonary arteries, compatible with the pulmonary embolism diagnosis.

ultrasonographic-guided lung and liver biopsy.

The final diagnosis was adenocarcinoma of the lung with malignant pleural effusion, and multiple bony and liver metastasis. He was treated with heparin and oral warfarin for acute PE and DVT. Chemotherapy with gemcitabine and cisplatin was prescribed. Local palliative radiotherapy was also administered for multiple bony metastases. The patient was discharged in a stable condition, and was followed up at the chest clinic.

Discussion

In 1861, Dr. Armand Trousseau reported a patient with cancer and cancer cachexia who developed migratory thrombophlebitis [2]. In patients with underlying malignancy, the cancer-associated hypercoagulable states may cause spontaneous blood clotting in the deep veins of the extremities, or in superficial veins anywhere in the body. These hypercoagulable states result in recurrent deep venous thrombosis that can migrate anywhere in the body, and chronic disseminated intravascular coagulopathy [3]. This paraneoplastic syndrome was called Trousseau's syndrome. Trousseau's syndrome associates migratory thrombophlebitis with an underlying malignancy, such as lung, colon, pancreatic, or

gastric cancer. Ironically, Dr. Armand Trousseau was finally found to have gastric cancer when he observed that he himself had this sign [2]. In some studies, about 60% of patients with cancer manifest at least 1 episode of thrombophlebitis and migratory thrombophlebitis [4]. It is very clear that systemic VTE may occur in the form of mild migratory thrombophlebitis, as well as DVT, acute PE, or both, in patients with preexisting cancer.

More and more studies have discovered that idiopathic VTE is the sign of occult cancer. Schulman *et al.* demonstrated the cancer incidence in patients with a first episode of systemic VTE without a preexisting malignancy diagnosis. In that study, a total of 111 patients were diagnosed with cancer during a mean follow-up of 8.1 years, accounting for 13.0 percent in 854 patients. There was a malignancy incidence of 3.4% in the first year of the VTE episode, and a 1.3~2.2% incidence in the following 5 years [5]. In elderly persons with idiopathic VTE, occult malignancy should be considered. In a large postmortem examination study, adenocarcinoma was the most common histopathologic type in thrombotic PE, followed by leukemia. The digestive and respiratory tracts were the top 2 involved systems [6].

In Taiwan, 2 studies were designed to study the incidence of cancer in patients with a clinical diagnosis of DVT and acute PE respectively. Lee HC *et al.* retrospectively reviewed 245 patients with the diagnosis of DVT between 1989 and 1995. Among these patients, 40 (16.3%) had cancer. Adenocarcinoma was the most common type of malignancy (25 patients, 62.5%), and the gastrointestinal tract (16 patients, 40%) was the most frequently involved system [7]. Chen LK *et al.* published their study on the association of occult malignancy with acute PE. Forty-five patients with acute PE, from July 1993 to June 1998, were included in this study. The cancer incidence after or concomitant with acute PE was 47.37%, significantly higher than in previous reports [8]. Adenocarcinoma was the most common histological type. The occult cancer origins were mainly in the gastrointestinal tract, similar to reports from Western countries and Lee HC's study. In these studies, there seemed to be a higher cancer incidence in the more severe form of systemic VTE, that is to say, higher in patients with acute PE.

These study results imply a practical clinical guideline in the search for unknown malignancy in patients with acute PE. In addition to the serum level of D-dimer and the lung perfusion scan, chest CT with intravenous contrast has become a principal diagnostic tool in an integrated approach to the evaluation of patients with suspected PE. The chest CT is at least as accurate as invasive pulmonary angiography, even in the detection of pulmonary subsegmental embolization. Because the majority of occult cancers hide in the gastrointestinal tract [5-8], the CT scan may extend its scanning area to the abdomen in patients with acute PE to search for possible sites of unknown cancer.

Recent studies have shown that the hemostatic system plays a key role at different stages in the process of tumorigenesis [9-10]. In their studies, Schulman *et al.* also found a lower cancer incidence risk among patients treated with oral anticoagulants for 6 months than among those treated for 6 weeks [5]. It was supposed that vitamin K antagonists express an antineoplastic effect by influencing the pathway involving tissue factor and factor VIIa, which inhibit tumor invasion [9]. It will be important to clarify what mechanisms of antithrombotic agents exert a possible antineoplastic effect, through large studies with long follow-up periods.

In conclusion, acute PE is uncommonly seen in Asian populations and should be considered as a pre-cancer sign. This condition requires a detailed workup for an underlying malignancy. CT scan is the diagnostic tool of choice, and should be performed in not only the chest, but also the abdomen, whenever possible.

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急性肺栓塞和潛藏的肺腺癌：Trousseau 症候群之一病例報告

陳志雄　翁子傑　許聯輝　林煒能　蔣士仁　謝俊民

因為癌症會造成高凝血狀態，所以全身靜脈血栓栓塞症在癌症病人身上是很常見的併發症。在特定情形下，全身靜脈血栓栓塞症可能是病人在最終被發現有癌症前唯一的臨床表現。急性肺栓塞是一種嚴重的全身靜脈血栓栓塞症，它臨床表現不一，從沒有症狀、呼吸喘、胸痛、昏厥、甚至到突然猝死都有。相較於西方，急性肺栓塞在東方是比較罕見的診斷。此外，對照於比較輕微的全身靜脈血栓栓塞症，在急性肺栓塞的病人似乎具有比較高的癌症發生率。這種東西方的人群差異讓本病比較少被診斷出來，因此可能會延後發現病人其實潛藏了未知癌症。在本篇文章中，我們報告一名 54 歲的男性病人因為急性肺栓塞住院，最後他被診斷出肺腺癌併多處轉移。然而，除了因為急性肺栓塞造成的臨床表現外，這個病人並沒有任何和癌症相關的不適症狀。基於這種罕見的病人經驗，我們建議在沒有明顯容易造成血栓症原因的病人，如果出現了急性肺栓塞，徹底地檢查體內是否藏有未知惡性腫瘤是相當重要的工作。*(胸腔醫學* ***2007; 22: 243-248)***

關鍵詞：急性肺栓塞，肺腺癌， Trousseau 症候群

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"Postural Maneuver" Promotes the Successful Removal of a Tracheobronchial Foreign Body by Ultra-Thin Flexible Video Bronchoscopy in an Adult: A Case Report

Kuo-Tung Huang*, Yu-Hsiu Chung*,**, Meng-Chih Lin*,**

Tracheobronchial foreign body (TFB) aspiration can be a life-threatening emergency requiring immediate intervention, even though it is less common in adults than in children. It also can be a chronic non-specific symptom mimicking other lung diseases, from bronchial asthma to severe obstructive pneumonia. Successful removal of the TFB in different circumstances should be performed to reduce morbidity and mortality.

A 78-year-old man aspirated a metallic dental implant, with the presenting symptoms of cough and mild fever. The implant was not visible by flexible video bronchoscopy in the supine position. It was subsequently removed successfully by flexible video bronchoscopy using the simple method of a "postural maneuver". ***(Thorac Med 2007; 22: 249-254)***

Key words: tracheobronchial foreign body, flexible video bronchoscopy, postural maneuver

Introduction

Tracheobronchial foreign body (TFB) aspiration may present as an acute upper airway obstruction with life threatening or chronic non-specific coughs, wheezing, and breathlessness. It sometimes mimics bronchial asthma or chronic obstructive pulmonary disease. High mortality and morbidity were noted to be due to serious subsequent complications of atelectasis, obstructive pneumonitis, pneumonia, and lung abscess.

Early detection and elimination of TFB may be life saving. Rigid bronchoscopic removal under general anesthesia used to be the choice of management [1-2]. Today, the usefulness of flexible bronchoscopy under local anesthesia for the removal of TFB has been documented in patients with no evidence of respiratory compromise or airway obstruction [3]. If flexible bronchoscopy fails to remove the TFB, or there is evidence of airway compromise, rigid bronchoscopy or surgery should be used promptly to extract the foreign body. The successful removal of the TFB by flexible bronchoscopy is essential to reduce mortality and morbidity, as well as to avoid the risks of rigid bronchocopy and surgery.

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Law, *et al*. performed the inhalation-postural drainage technique before using bronchoscopy as the initial management of TFB in children [4]. Some bronchologists have used traditional postural drainage to promote the removal of TFB located centrally. Neither the inhalation-postural drainage technique nor traditional postural drainage has been used to promote the removal of peripheral TFB by flexible bronchoscopy in an adult.

The patient we report herein had aspirated a metallic dental implant during a dental procedure. Initially, the implant was not visible by flexible video bronchoscopy. After using a "postural maneuver", which is a simple and safe maneuver that differs from both the inhalation-postural drainage and traditional postural drainage techniques, the TFB was successful removed.

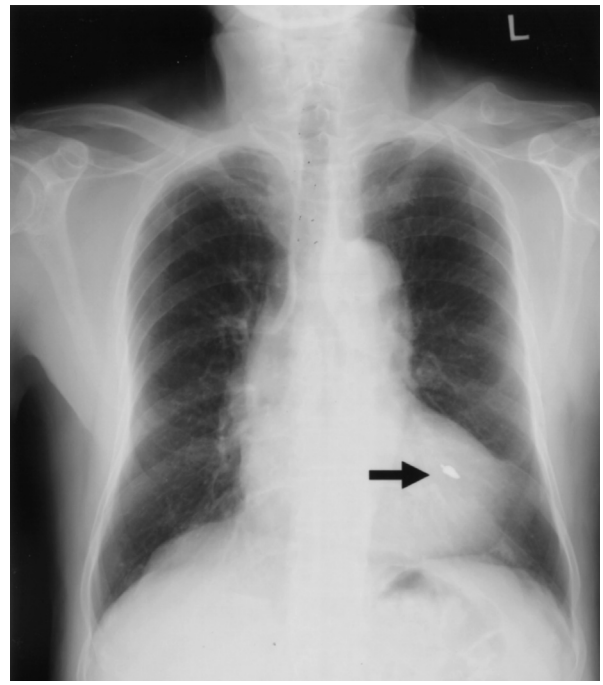
Case Report

A 78-year-old man suffered from metallic dental implant aspiration during a dental procedure at another medical center. Emergent flexible video bronchoscopy was performed under the guidance of chest radiography and computed tomography (CT) (Figure 1A-1B), but failed due to the invisibility of the foreign body.

The patient visited our hospital for a second opinion 6 days later, with symptoms of cough and mild fever. Repeated chest radiography and CT (Figure 2A-2B) showed that the foreign body had migrated from the left lower lobe to the posterior basal segment of the right lower lobe.

A flexible video bronchoscopy unit (P260F, Olympus, Tokyo, Japan) equipped with a high-definition monitor (OEV181H, Olympus, Tokyo, Japan) was used under local anesthesia with 2% lidocaine.

Initially, the dental implant was not visible when the patient was in the supine position. After a "postural maneuver" (changing the patient's position from a supine to a position facilitating



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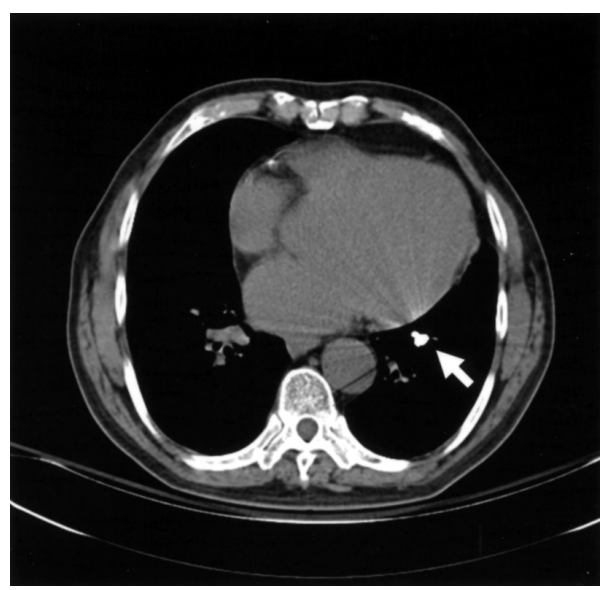

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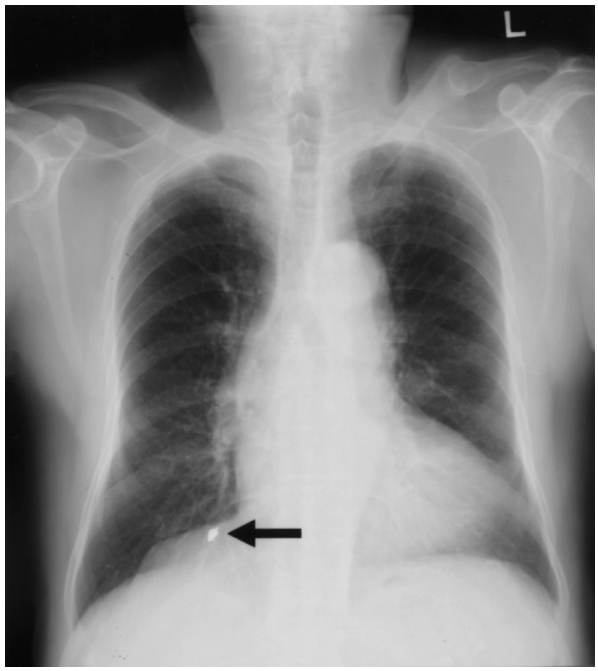
Fig. 1. The TFB (metallic dental implant) was noted in the left lower lobe, using chest radiography and CT at the original medical center



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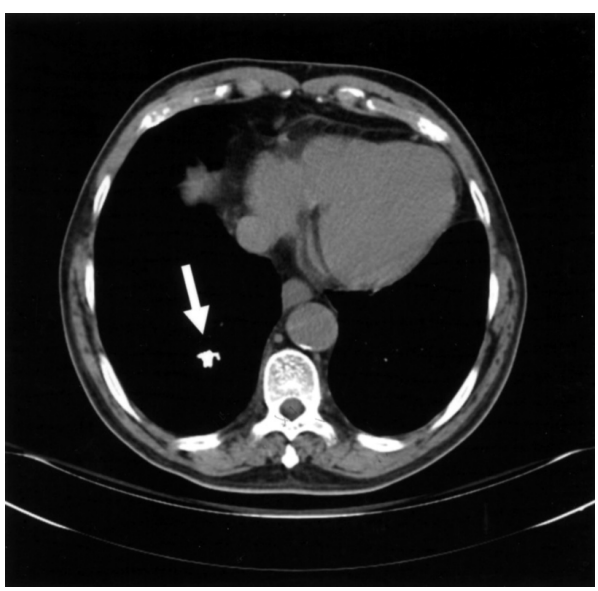

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Fig. 2. The TFB (metallic dental implant) migrated to the right posterior basal segment and was noted at our hospital using chest radiography and CT

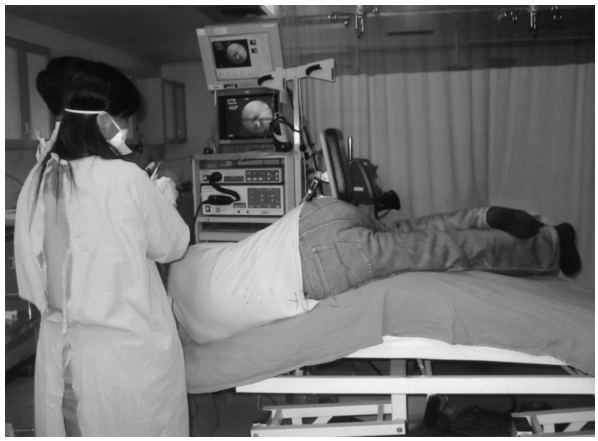
the postural drainage of the right lower lobe) (Figure 3A), as well as chest percussion for a few minutes at the right posterior chest wall, the dental implant was seen to be lodged at the right RB10a (Figure 3B), and was removed smoothly by biopsy forceps (FB-15C-1, Olympus) (Figure 3C) without complication.

Discussion

Tracheobronchial foreign body (TFB) aspiration is more common in children than in adults [5-6]. The presenting symptoms are "penetration syndrome," a syndrome with a sudden onset of choking and intractable cough with or without vomiting (49%), cough (37%), fever (31%), breathlessness (31%), and wheezing (26%); occasionally, there are no symptoms (2%) [7]. The incidence is lower adults, but significant mortality and morbidity are observed, since diagnosis in adults is more difficult than in children. Symptoms are usually obscured and unnoticed in adults, and the patients do not always volunteer or recall a history of choking [8-9].

A TFB may be seen unexpectedly during flexible bronchoscopic examination when the patient presents symptoms of endobronchial disease, such as chronic cough, hemoptysis, asthma not responding to therapy, or recurrent/non-resolving pneumonia. The radiographic findings in adults and children are atelectasis (50% and 14%), air trapping (17% and 64%), pneumonia (17% and 13%), visible foreign bodies (11% and 4%), and normal radiographs (11% and 12%) [7].

The most typical lodgment location for adults is the distal bronchus, especially the right lower lobe and bronchus intermedius (37% and 22%) [10]. Early diagnosis and removal of the TFB is critical to avoid subsequent complications, such as hemoptysis, airway obstruction, granulation tissue formation, and obstructive pneumonitis/pneumonia or lung abscess. The gold standard



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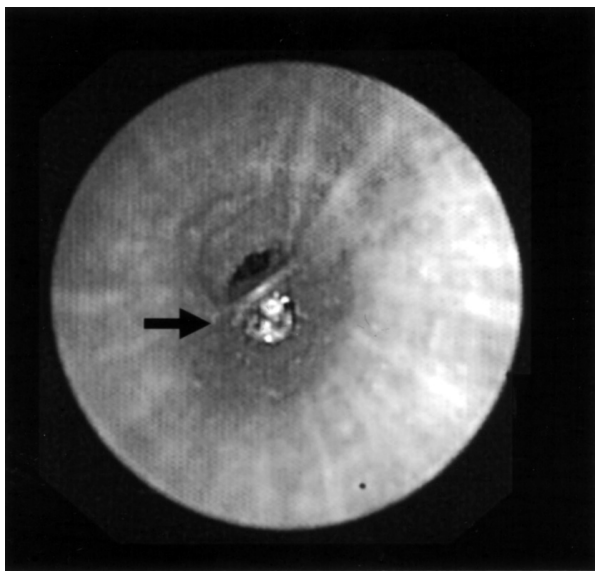

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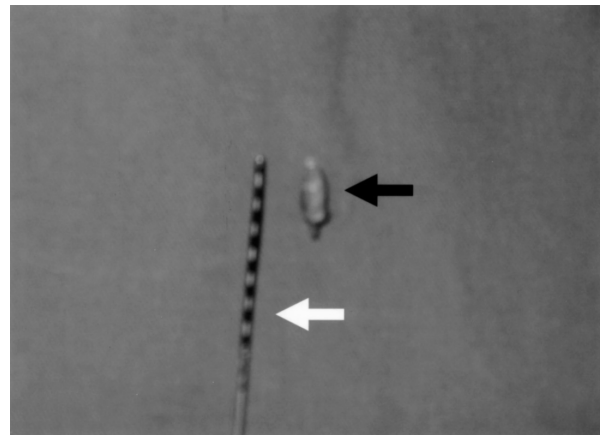

(C)

Fig. 3. A: The "postural maneuver": The patient's position was changed to facilitate the postural drainage of the right lower lobe. B: The TFB (metallic dental implant) was lodged at RB10a <The image of the flexible video bronchoscopy>. C: The TFB (metallic dental implant, 1 cm in length, <black arrow>) was removed successfully. White arrow: measuring device (M2-4k, Olympus, Tokyo, Japan)

of intervention was rigid bronchoscopy under general anesthesia.

Flexible bronchoscopy has several advantages over rigid bronchoscopy [11], including minimal risk and complications, the use of local anesthesia only, the easy approach to the distal airway, and the possibility of performing it in mechanically-ventilated patients, so this method has become more favored in the removal of TFB. Surka, *et al*. [3], reviewed the existing literature and evidence-based medicine, and suggested the use of flexible bronchoscopy for the removal of TFB in stable patients without evidence of respiratory compromise or airway obstruction (recommendation grade B). If flexible bronchoscopy fails to remove a TFB, or there is evidence of airway compromise, rigid bronchoscopy or surgery should be used to promptly extract the foreign body (recommendation grade B).

Traditionally, the patient is placed in the supine position for removal of a TFB by flexible bronchoscopy. A Fogarty balloon catheter, grasping forceps, or retrieval basket are used to extract the TFB, based on its location, size and the morphology. Removal of a peripherally located TFB, invisible to the flexible bronchoscopy, is extremely difficult. Kenneth, *et al*. have used the "fluoroscopic-snare technique" to remove a TFB located in a peripheral tracheobronchial tree [12]. Ultra-thin flexible bronchoscopy (BF-XP260F; Olympus, Tokyo, Japan) is another alternative technique in extracting a TFB lodged periphe-

rally, and may be performed without fluoroscopy [13].

In this case, flexible bronchoscopy was used initially in the first hospital. Surgical intervention was suggested because the metallic dental implant was invisible by flexible video bronchoscopy. The patient visited this hospital, and a second ultra-thin flexible video bronchoscopy (P260F, Olympus, Tokyo, Japan) was performed in the supine position, but failed to remove the TFB again. Then the "postural maneuver" (changing the patient's position to facilitate the postural drainage of the right lower lobe) was used because the metallic dental implant was migratory. Finally, the metallic dental implant became visible and was removed successfully by biopsy forceps without any complication.

Law, *et al*. performed the inhalation-postural drainage technique to remove TFBs in 49 children. Twelve of the 49 children successfully coughed out the foreign body (25%)[4]. This used to be done before bronchoscopy as the initial management of TFB in children. Traditional postural drainage has been used by some bronchologists to promote the removal of TFB located centrally. It is always performed before the bronchoscopy. Neither the inhalation-postural drainage technique nor traditional postural drainage has been used to promote the removal of peripheral TFB by flexible brochoscopy in adults before. The "postural maneuver" differs from the inhalation-postural drainage technique, and is also different from traditional postural drainage. Our case is the first to use this maneuver to retrieve a TFB located in the peripheral bronchial tree.

We conclude and suggest that the "postural maneuver" is a simple and safe procedure to perform during flexible video bronchsocopy. It can be used as a concomitant therapy for removal of a TFB which is located in a more distal airway and invisible to ultra-thin flexible video bronchoscopy in an adult in a traditional supine position.

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“姿勢輔助法”可促進使用軟式影像細支氣管鏡移除成人氣管內異物的成功率—病例報告

黃國棟* 鍾聿修*,** 林孟志*,**

異物吸入常發生於小孩，是一個須緊急處理的急症，成人雖較少發生，但臨床上診斷較小孩困難，故死亡率較高。臨床症狀可從慢性非特異性的呼吸道症狀、氣喘、阻塞性肺炎到呼吸衰竭甚至死亡。我們應嘗試任何可以幫助移除氣管內異物的方法來移除氣管內異物，降低病患的傷害及死亡率。

本例是一位 78 歲男性病患，於外院進行假牙植入時發生金屬假牙吸入氣管的意外。我們無法在使用傳統躺臥姿勢下進行的軟式影像細支氣管鏡檢查中找到金屬假牙，因此我們使用了“姿勢輔助法”來協助並進行軟式影像細支氣管鏡檢查，順利的找到了金屬假牙並將其成功地移除。*(胸腔醫學* ***2007; 22: 249-254)***

關鍵詞：氣管內異物，軟式影像細支氣管鏡，姿勢輔助法

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Esophagoscopy-Guided Surgical Enucleation of a Small Esophageal Lipoma — A Case Report

Chin-Chih Chang*, Yih-Leong Chang**, Pei-Ming Huang*,***, Yung-Chie Lee*,***

Lipomas of the esophagus are rare benign tumors. Patients with esophageal lipomas are usually asymptomatic until tumors become large enough to cause symptoms. We report a rare case of a small esophageal tumor, only 1.0 cm in diameter, which caused indolent symptoms; surgical enucleation was successfully performed with a right lateral mini-thoracotomy with simultaneous esophagoscopic guidance. A 70-year-old woman complained of a foreign body sensation in her chest for 4 months. Body weight loss was also noted. Both barium esophagography and endoscopic ultrasonography revealed a submucosal tumor in the middle esophagus. Biopsy failed to demonstrate the submucosal tissue. Intraoperative esophagoscopic-guided tumor enucleation via a right lateral mini-thoracotomy was performed. A lipoma, 1.0 cm at the largest diameter, in the submucosa of the middle esophagus, was confirmed by pathology. The postoperative course was uneventful. ***(Thorac Med 2007; 22: 255-258)***

Key words: esophageal lipoma, endoscopy

Introduction

Lipomas of the esophagus are rarely encountered. Most patients are asymptomatic and the lipoma is found incidentally. Symptoms are usually related to the tumor size, and dysphagia is the most common complaint. Tumor removal is advisable to remedy or avoid symptoms. Endoscopic excision is indicated in small intraluminal tumors, or pedunculated or mobile sessile submucosal tumors [1]. In large or immobile tumors, surgical excision is necessary. We herein present a rare case of small esophageal lipoma, which was surgically enucleated with intraoperative esophagoscopic guidance.

Case Report

A 70-year-old woman complained of chest discomfort with a foreign body sensation beginning 4 months before coming to our hospital. Body weight loss was also noted, although she had no obvious dysphagia. The physical and lab examinations were unremarkable. Barium esophagography showed a wide-based 1.5-cm lesion with a smooth surface in the middle esophagus,

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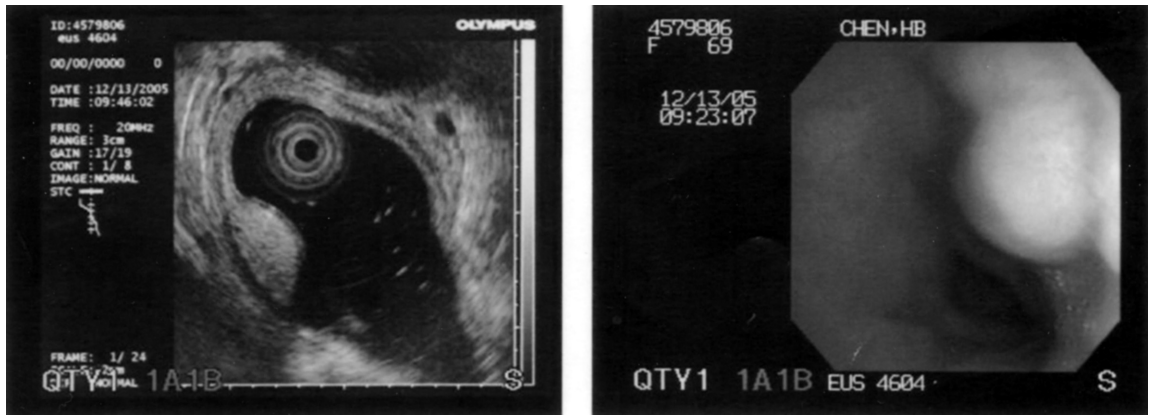

Fig. 1. Endoscopic ultrasonography revealing a 1.0 cm polypoid hyperechoic tumor arising from the third layer of the esophageal wall, with intact mucosa at 27 cm below the incisors in the middle esophagus.

slightly below the level of the left main bronchus. Endoscopic ultrasonography revealed a 1.0-cm polypoid hyperechoic tumor arising from the third layer of the esophageal wall with intact mucosa at 27 cm below the incisors in the middle esophagus (Figure 1). Biopsy showed squamous hyperplasia of the squamous epithelium, with no submucosal component included. Right-sided video-assisted thoracoscopic surgery (VATS) was performed initially, but the procedure was shifted to a right lateral mini-thoracotomy because the tumor was too small and soft to identify. Therefore, we performed a simultaneous esophagoscopy intraoperatively for localization of the tumor. With the transluminal effect of the esophagoscopy, the tumor was identified and was enucleated with a local esophagotomy. A yellowish, soft tumor, 1.0 x 0.6 x 0.4 cm in size, was found in the submucosal layer of the middle esophagus. Pathology demonstrated a submucosal esophageal lipoma, composed of S-100 protein immunoreactive mature adipocytes. The postoperative course was uneventful. Follow-up contrast esophagography on the 12th postoperative day showed no esophageal leakage. She resumed oral intake without incident.

Discussion

Lipomas of the esophagus are rare benign tumors, and amount to 2% of all benign esophageal tumors [2]. They originate from undifferentiated mesenchymal cells in the submucosal layer. Esophageal lipomas may exceed 10 cm in length and can be intraluminal or intramural. Intraluminal tumors can be pedunculated or sessile. Symptoms of esophageal lipomas are usually of mechanical origin, with dysphagia, pain, regurgitation, or hemorrhage.

Tumor removal is the treatment of choice for esophageal lipomas to remedy or avoid symptoms because of their potential of slow growth. Variable means of management are available, depending on tumor size, location, and the operator's experience. Endoscopic excision is indicated in small intraluminal tumors, or pedunculated or mobile sessile submucosal tumors [1]. In large or immobile tumors, surgical excision is necessary. Open thoracotomy or laparotomy is the standard procedure. In our case, surgical intervention was indicated for the following reasons: The tumor was immobile and submucosal in the middle third of the esophagus. It was symp-

tomatic, with chest discomfort and body weight loss, and its histopathological behavior was unclear.

We successfully carried out a surgical enucleation of a small esophageal submucosal lipoma with a lateral mini-thoracotomy and simultaneous esophagoscopic guidance in a 70-year-old patient. A VATS was performed, but the procedure was then shifted to a minithoracotomy because the tumor was too small and soft to identify. To our knowledge, this is the smallest esophageal lipoma with symptoms reported in the English literature [2-4]. We used an esophagoscopy to localize the tumor and enucleated it. Intraoperative endoscopy is helpful for localizing small tumors and identifying the dissecting plane using a translumination effect (diaphanoscopy) [5].

In conclusion, we report a rare case of small esophageal lipoma, which was surgically enucleated with intraoperative esophagoscopic guidance. For the surgical excision of small esophageal lipomas, intraoperative endoscopy helps in the accurate localization of tumors, and minimizes esophagotomy and surgical wounds.

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以食道鏡引導手術切除微小食道脂肪瘤—病例報告

張金池 * 張逸良 ** 黃培銘 *,*** 李元麒 *,***

食道脂肪瘤是罕見的良性腫瘤。食道脂肪瘤的病患通常沒有症狀直到腫瘤變得夠大時才引起症狀。此報告為一罕見微小食道脂肪瘤的病例，大小只有 1 公分，卻引起輕微的症狀，並且成功地在食道鏡引導下以右側迷你開胸手術切除腫瘤。一位 70 歲女性主訴胸部異物感已四個月，並有體重減少。鋇劑食道攝影及內視鏡超音波皆顯示在中段食道有一個黏膜下腫瘤。切片無法夾到腫瘤部分。我們進行右側迷你開胸術，並在手術中以食道鏡引導下施行了腫瘤切除手術。病理檢查確定其為一個食道黏膜下脂肪瘤。手術後過程恢復順利。*(胸腔醫學* ***2007; 22: 255-258)***

關鍵詞：食道脂肪瘤，內視鏡

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Acute Pulmonary Edema Following Transjugular Intrahepatic Portosystemic Stent Shunt Creation in a Cirrhotic Patient: A Case Report

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Through lowering portal hypertension, transjugular intrahepatic portosystemic stent shunt (TIPSS) can control life-threatening esophageal or gastric variceal bleeding and refractory ascites more effectively, and thereby provide a better chance of survival. Post-TIPSS complications, even in many patients with successfully functioning shunts, were reported to be mainly severe hepatic encephalopathy, acute or subacute hepatic failure, severe sepsis, and immediate technical complications such as acute occlusion, hepatobiliary perforation, and procedure-related intraabdominal bleeding. Herein, we report a 54-year-old man who was admitted to the medical intensive care unit due to life-threatening variceal hemorrhage. After he had undergone TIPSS, acute shortness of breath developed. He was found to have acute pulmonary edema possibly due to acute systemic and pulmonary hemodynamic change post-TIPSS. His dyspnea and lung condition in the chest radiograph improved after diuretics therapy. This is an uncommon complication post-TIPSS. The efficacy of diuretic therapy in in-stent stenosis and the long-term outcome remain unclear. ***(Thorac Med 2007; 22: 259-264)***

Key words: acute pulmonary edema, liver cirrhosis, transjugular intrahepatic portosystemic stent shunt

Introduction

Life-threatening hemorrhagic shock is often encountered in the medical intensive care unit (ICU). In cirrhotic variceal hemorrhagic conditions, it can be managed by transjugular intrahepatic portosystemic stent shunt (TIPSS). The procedure was developed to decrease portal hypertension, and thereby reduce acute massive esophageal and/or gastric variceal bleeding more effectively [1]. In addition, TIPSS also exerts a much more effective control over refractory ascites than large volume paracentesis, and has the advantage of providing a better chance of survival [2].

Post- TIPSS adverse effects are reported to be mainly severe hepatic encephalopathy, acute or subacute hepatic failure, severe sepsis, and mechanical complications such as acute occlusion, perforation, and procedure-related bleeding. There is far less discussion and fewer reports on systemic and pulmonary hemodynamic change

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post-TIPSS, although liver cirrhosis is well documented with hyperdynamic circulation, due to the increase in cardiac output and a decrease in peripheral vascular resistance [3]. We report an uncommon complication resulting from acute hemodynamic change after TIPSS implantation in a 54-year-old man. He developed acute shortness of breath after he had received TIPSS for his life-threatening variceal hemorrhage.

Case Report

A 54-year-old man was admitted to Chi Mei Foundation Medical Center because of a large amount of bloody vomiting. The patient was a heavy alcoholic and drank either beer or wine almost everyday. He sometimes smoked, but seldom chewed betel nut. He reported no allergy to food or medications. There was no previous history of heart disease. He was diagnosed with liver cirrhosis about 5 years ago owing to general jaundice. He had several episodes of esophageal variceal bleeding and had received esophageal variceal ligation therapies.

About 1 month before this admission, the patient was discharged from this hospital after an episode of esophageal variceal bleeding. However, he drank again after he went home. On the morning of the day of admission, the patient vomited about 200 to 300 ml fresh blood after his morning drinking. Tachycardia, dizziness, and general malaise were mentioned. He was brought to the emergency department for help. His systolic blood pressure was 94 mmHg, diastolic blood pressure was 37 mmHg, and vital signs were as follows: temperature 36.8 degrees, respiratory rate 25 per minute, and heart rate 125 per minute. His complete blood cell count revealed a low hemoglobin level of 6.8 g/dL and platelet count of 101,000/uL. He was treated with intravenous terlipressin 2 mg bolus and then 1 mg every 4 hours. Endoscopic esophageal variceal ligation was also performed shortly after he was admitted.

Four days later, the patient noticed he had bloody emesis of about 200~300 ml and fresh bloody diarrhea. Dizziness, palpitation, and dyspnea were also mentioned. His blood pressure was systolic 83 mmHg and diastolic 45 mmHg, and the heart rate was 120~130 beats per minute. Under the impression of another episode of esophageal variceal bleeding with hypovolemic shock, a Sengstaken-Blakemore tube balloon tamponade was performed after he was transferred to the medical ICU (Figure 1).

There was no more fluid overload and no further blood product transfusion after the successful Sengstaken-Blakemore tube balloon tamponade. The patient was suggested to undergo a TIPSS for portal hypertension-related esophageal bleeding. This procedure was performed via the right internal jugular vein. A shunt was created from

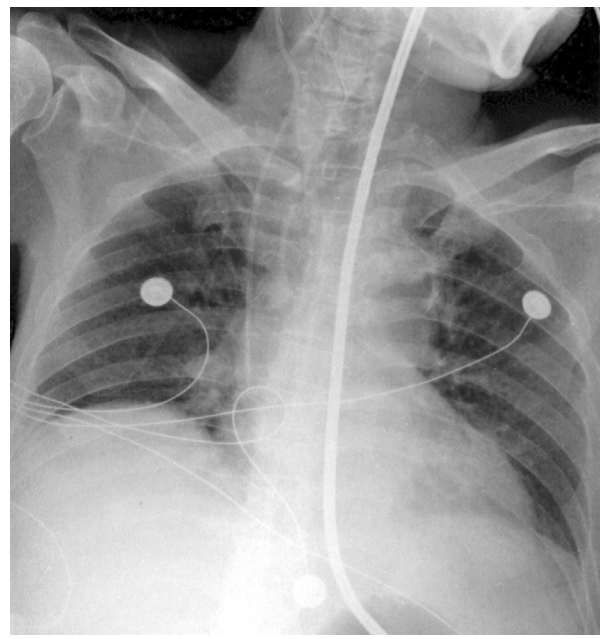

Fig. 1. The supine chest radiograph after Sengstaken-Blakemore tube balloon tamponade, demonstrating bilateral clear lung fields

the right hepatic vein to the right portal vein, and sequentially dilated with multiple 8 mm balloon catheters and followed with a metallic stent. The post-stenting portography revealed complete disappearance of the esophageal varices. Pre-stenting portal pressure was 35 mmHg and central venous pressure was -1 mmHg. Post-stenting portal pressure was 18 mmHg and central venous pressure was 8 mmHg (Figure 2). No immediate complication was noted. However, progressive dyspnea developed later. A supine chest radiograph was taken and revealed an alveolar pattern, and acute pulmonary edema was suspected clinically (Figure 3).

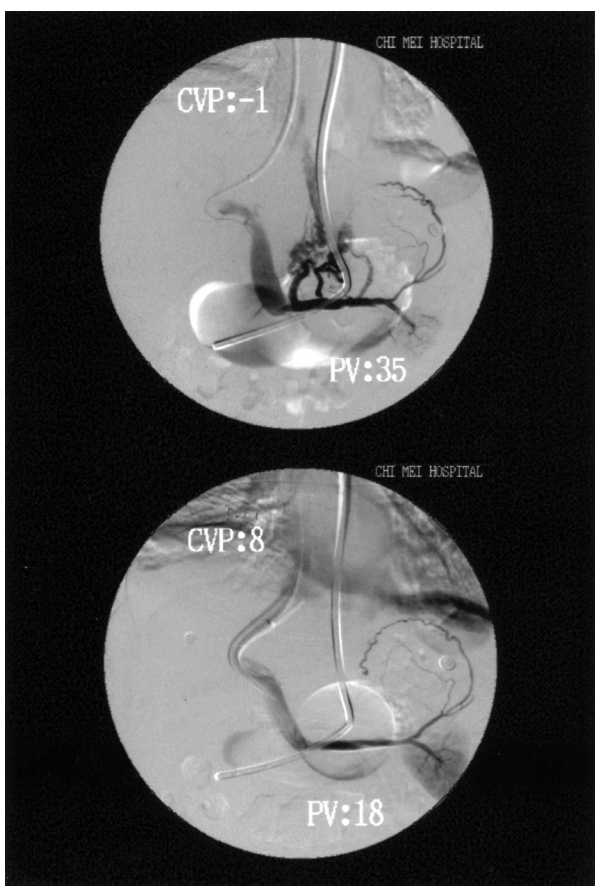

Fig. 2. The post-stenting portography showing complete resolution of the esophageal varices, with pre-stenting portal pressure 35 mmHg and central venous pressure -1 mmHg compared with post-stenting 18 mmHg and 8 mmHg, respectively

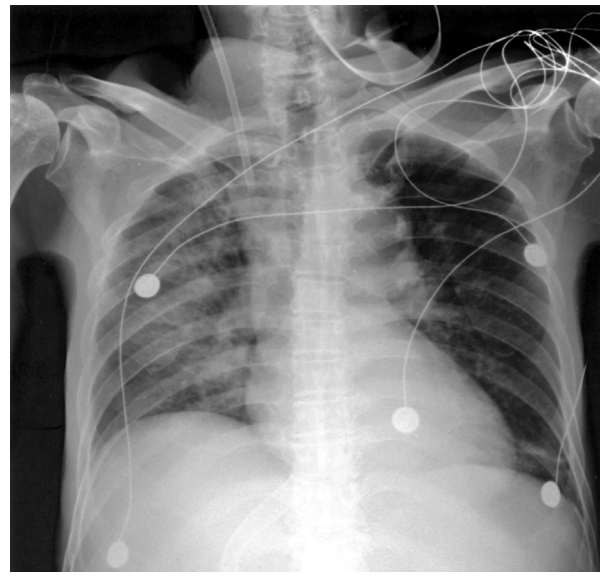

Fig. 3. Chest radiograph showing a stent at the portal area and acute lung edema

The patient was treated with intravenous furosemide 20 mg every 6 hours. The dyspnea improved after the negative fluid status was created. The follow-up chest radiograph showed improvement (not shown here) after furosemide therapy and he was transferred to the general ward. Till he was discharged with home care, there was no consciousness change and no further respiratory distress.

Discussion

This concept of transjugular placement of an intrahepatic stent to create a portosystemic shunt to relieve portal hypertension may be traced back to the 1960s. The first clinically successful experience was in 1988 [4], nearly 30 years later. A puncture needle was introduced in a catheter through the inferior vena cava into a hepatic vein; then an intrahepatic branch of the portal vein was punctured and an expandable stent of metallic mesh was implanted to establish the shunt. This procedure was called transjugular intrahepatic

portosystemic stent shunt. It is well established and evidence-based, and an effective and safe treatment for cirrhotic variceal bleeding and refractory ascites in patients with portal hypertension [1-2, 5]. The long-term outcomes in some patients are excellent; however, in other patients with more severe end-stage liver disease, it also serves as a bridge to liver transplantation [6]. Because the procedure-related mortality rate is far lower than surgical porto-systemic shunt intervention, it has become the most popular procedure since 1990 in the critical care of life-threatening cirrhotic variceal hemorrhage [7]. In the early developmental stage of the procedure, most post-procedure complications were reported as severe hepatic encephalopathy [8], nosocomial sepsis [9], and early complications related to the technique itself, such as massive extrahepatic bleeding, hemobilias, and intra-abdominal bleeding [10].

Liver cirrhosis is associated with hyperdynamic circulation by the increase in cardiac output and decrease in peripheral vascular resistance. The anastomosis of systemic and portal circulation causes the rapid pressure change in the pulmonary circulation [11] and deteriorates pulmonary hypertension [12]. There is little discussion of post-TIPSS circulation and hemodynamic profile change in past reports. Acute respiratory failure may develop, which in turn results in patient death. The first mortality was reported in 1989, although no definite etiology was identified [13].

Azoulay *et al*. reported TIPSS might worsen the hyperdynamic circulatory state in cirrhotic patients. He made an assessment of the immediate and short-term sequelae of TIPSS on the circulatory hyperdynamic state in 12 cirrhotic patients. This study demonstrated a continuous portoatrial pressure gradient decrease, systemic vascular resistance decrease, and cardiac index increase at 30 minutes and 30 days after the procedure. Although apparently noninvasive, this procedure should be considered with caution in cirrhotic patients with limited cardiac reserve. A similar hyperdynamic phenomenon was observed in Wagatsuma's study [14].

Despite the obvious evidence of the effects on the pulmonary hemodynamic profile, there are few case reports in the literature. In some large serial studies, pulmonary hemodynamic complications represent a very small portion and have rarely been paid serious attention [15-16]. This may be because most TIPSS candidates are relatively too young to develop heart disease, and strong enough to bear the rapid pulmonary hemodynamic change and the underlying hypovolemic state in acute the bleeding stage.

In a small series report by Naritaka *et al*., postoperative cardiac output increased markedly on the 2nd and 3rd day, and declined on the 5th postoperative day, while there were no particular variations in mean blood pressure or heart rate. Right atrial pressure, pulmonary arterial pressure and pulmonary capillary wedge pressure also increased transiently during this time [3]. This study suggested that the 2nd and 3rd postoperative days had the highest risk to develop acute heart failure. However, the reason why these hemodynamic profile changes vary in different postoperative day remains unclear.

The liver can metabolize some vasoactive agents. In severe hepatic dysfunction, renal artery dilatation causes hepatorenal syndrome, and pulmonary artery dilatation causes hepatopulmonary syndrome. These metabolites also have the potential effects of creating capillary permeability. Pulmonary capillary permeability change due to these vasoactive agents, escaping the hepatic metabolism after TIPSS, seems to be another

factor that may predispose the acute pulmonary edema.

In our patient, the pulmonary and systemic hemodynamic changes after TIPSS complicated the underlying cirrhotic hyperdynamic state by the abrupt increase in pulmonary circulation, which in turn caused a preload increase and heart failure. The direct release of vasoactive agents escaping from the hepatic catabolism also predisposed and deteriorated the condition. We report this uncommon complication not only because of its rarity but also that life-threatening congestive heart failure might occur in patients receiving TIPSS implantation. Any patient receiving TIPSS for variceal hemorrhage should be closely monitored, to see if acute shortness of breath develops.

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經頸靜脈肝內肝門靜脈造流術術後的急性肺水腫：一病例報告

林煒能　柯獻欽　陳志雄 *　楊煦星 *　鄭高珍 *　謝俊民

經頸靜脈肝內肝門靜脈造流術可以藉由降低門脈高壓，非常有效地控制危及生命的食道或是胃靜脈瘤出血和頑治性腹水，因此提高病人存活的機會。然而，就算造流術成功，術後分流功能正常，術後併發症卻很常見。這些不良作用主要是肝性腦病變、急性或是亞急性肝衰竭、嚴重敗血症，和技術上的併發症如急性阻塞、肝膽道穿孔、術式造成的腹內出血等。此外，因為肝硬化會出現心輸出量增加和週邊血管阻力下降，造成高血行動力學循環狀態，但造流術術後的肺部血行動力學改變卻很少受到注意。在本篇文章中，我們報導一名因為危急生命的靜脈瘤出血而住進加護病房的 54 歲男性病人，在病人接受經頸靜脈肝內肝門靜脈造流術之後，併發呼吸急促的問題，後來他被發現因為造流術術後產生的全身和肺部血行動力學改變後的急性肺水腫，在給予利尿劑治療後，呼吸喘的程度和胸部 X 光都有改善。然而，利尿劑治療對於造成支架內狹窄和病人長期預後的角色仍然不清楚。*(胸腔醫學* ***2007; 22: 259-264)***

關鍵詞：急性肺水腫，肝硬化，經頸靜脈肝內肝門靜脈造流術

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Iatrogenic Pseudoaneurysm Caused by Central Venous Cannulation — 3 Case Reports

Hsu-Chung Liu, Ki-Ming Chang, Jeng-Yuan Hsu

Pseudoaneurysm of great vessels is 1 of the severe mechanical complications that can occur during central venous cannulation. Our first case developed a pseudoaneurysm after cannulation via the left subclavian route; the second and third cases developed a pseudoaneurysm after cannulation via the right internal jugular route. Different diagnostic examinations, including conventional angiography and Multi-Detector Computed Tomography (MDCT) angiography were used in these cases, respectively. Successful transcatheter embolization of the pseudoaneurysm was performed in case 1. Case 2 and case 3 received conventional surgical repair due to the different anatomical location. In conclusion, MDCT angiography is adequate for the initial evaluation of neck vessel injury, and has the advantage of less invasiveness compared with conventional angiography. The treatment options include ultrasound-guided compression, transcatheter interventions, percutaneous thrombin injection, and open surgical repair. The choice should always be based on the clinician's judgment and applicability to the clinical condition. ***(Thorac Med 2007; 22: 265-272)***

Key words: pseudoaneurysm, central venous cannulation, conventional angiography, multi-detector computed tomography angiography, transcatheter embolization

Introduction

Percutaneous central venous catheters are widely used in critical care medicine. Fluid supply, hemodyamic monitoring, vascular access and hyperalimentation are the major applications. Because of the invasiveness and blind approach of this procedure, complications including mechanical trauma, infection and thrombosis are not uncommon. The most common mechanical events include arterial puncture, pneumothorax, and hematoma. Severe complications such as pseudoaneurysms form when an arterial puncture site does not seal after compression, allowing blood leakage into perivascular tissues and forming a pulsatile hematoma. Herein we report 3 cases of iatrogenic pseudoaneurysm after failed central venous cannulation. We will discuss the clinical course, diagnosis and management.

Case Presentations

Case 1

A 77-year-old female had a history of bron-

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chiectasis. She was admitted to our medical ICU for treatment of severe community-acquired pneumonia with respiratory failure. We inserted a central venous catheter via her left subclavian vein for fluid therapy. However, the procedure failed after numerous attempts. A pulsatile mass with bruit in her left neck was found 2 days later. The chest film showed an opaque area in the left supraclavicular region (Figure 1). The Color Doppler revealed a hypoechoic lesion abutting the left common carotid artery with obvious ejection flow. The conventional angiography showed a large pseudoaneurysm formation arising from the proximal portion of the left internal mammary artery (Figure 2). Transcatheter embolization was tried initially. After several manipulations, the follow-up angiogram revealed a disappearance of contrast extravasation. The patient was weaned from the ventilator several days later.

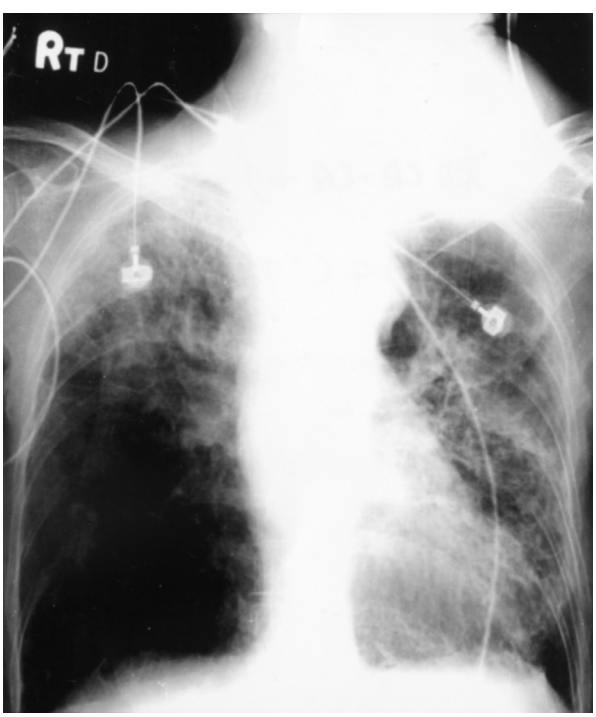

Fig. 1. Chest X-film showing a soft tissue density lesion in the left neck.

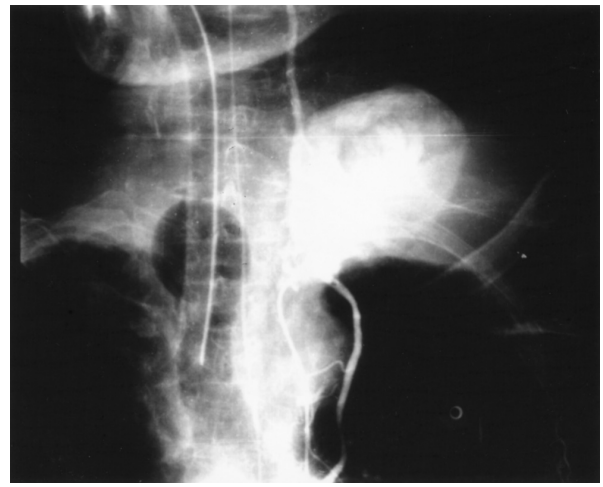

Fig. 2. Conventional angiography showing a pseudoaneurysm (10 cm in diameter) with sustained extravasation from the proximal portion of the left internal mammary artery.

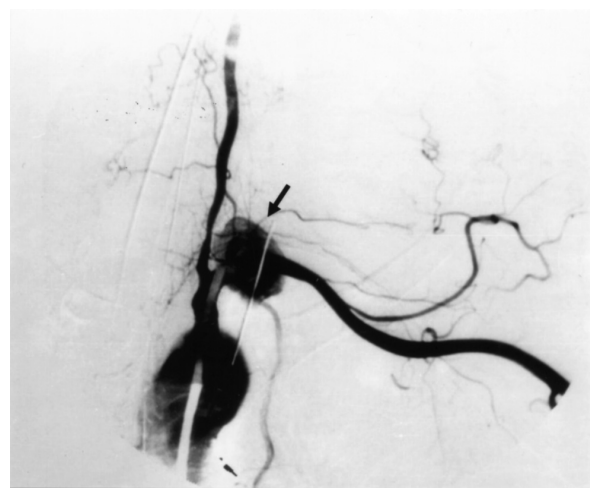

Fig. 3. The repeated angiography showing a smaller pseudoaneurysm (arrow) in the same site (compared with the previous angiography).

Unfortunately, dyspnea, hypotension and cyanosis struck on the day after weaning. A more enlarged mass was found in her left neck. Stridor was heard and she received intubation again for airway control. Under the impression of recurrent blood leakage via the left internal mammary artery, our radiologist performed rescue embolization. A 9F guiding catheter was put into the proximal portion of the left subclavian artery. A

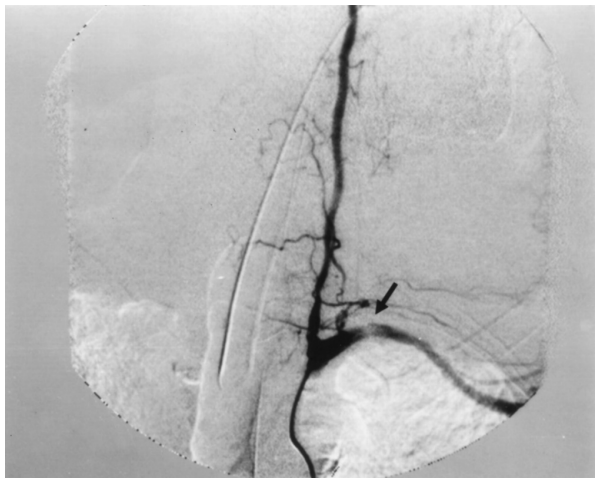

Fig. 4. The follow-up angiography showing a disappearance of the pseudoaneurysm (arrow) after embolization.

microcatheter was inserted into the lumen of the left internal mammary artery, just distal to the orifice of the pseudoaneurysm (Figure 3). Another occlusive balloon was put over the orifice of the left internal mammary artery for prevention of distal embolism. The catheter tip approached the neck of the aneurysm, and tissue glue (N-isobulyl cyanoacrylate, NBCA) was injected into it. After embolization, the angiogram showed no residual pseudoaneurysm, and patency of the left subclavian artery (Figure 4). Three days later, the cardiovascular surgeon removed the residual hematoma. There were no neurological sequelae and the patient was later weaned successfully from the mechanical ventilator.

Case 2

An 83-year-old female had had chronic renal failure for years. Several days before admission, she visited a local clinic owing to confused consciousness and severe bilateral leg edema. After serial examinations, uremia with encephalopathy was diagnosed. In preparation for emergency hemodialysis, a central venous cannulation was implemented via her right internal jugular vein. After several attempts, a pulsatile mass was found in her right neck. The mass enlarged progressively, resulting in tracheal compression. She developed stridor with impending respiratory failure several minutes later, and endotracheal intubation was performed immediately for airway protection. Then, she was sent to our hospital for further management. The Color Doppler revealed a pseudoaneurysm (4.7x2.7 cm) with active bleeding from the right common carotid artery. Since external compression was difficult, we arranged a Multi-Detector Computed Tomography (MDCT) angiography to localize the bleeding site. The CT angiography and 3D volume-rendered reconstruction image showed a pseudoaneurysm (5.2 cm in diameter) with leakage of contrast media from a tract in the right common carotid artery (Figure 5). Since transcatheter embolization via the common carotid artery has a high risk of embolic infarction of the brain, surgical repair of the pseudoaneurysm was

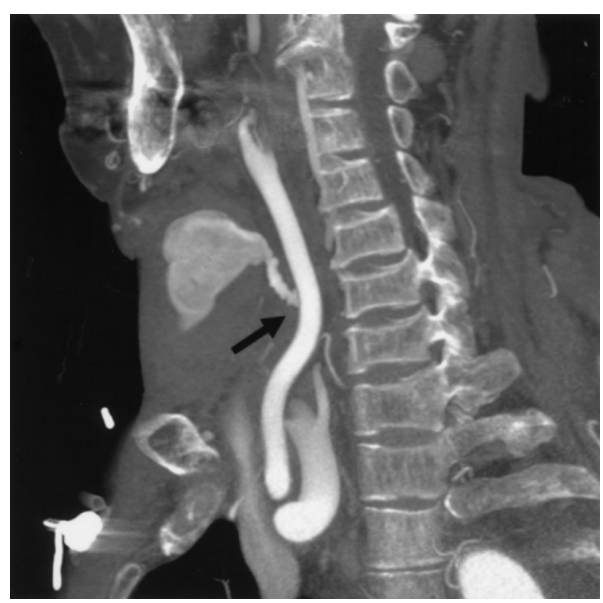

Fig. 5. The sagittal source MDCT angiography image showing a pseudoaneurysm (arrow) emanating from the right common carotid artery.

performed successfully by our cardiovascular surgeon. The patient's consciousness improved after hemodialysis several days later. Then, the endotracheal tube was removed and she was weaned successfully from ventilator support.

Case 3

An 88-year-old male had had a history of type 2 diabetes with chronic renal insufficiency for years. He was admitted due to symptoms of uremia. Several attempts were made at central venous cannulation from the right internal jugular route for temporary hemodialysis. Unfortunately, the common carotid artery was punctured during the procedure. Direct compression was applied to the right neck for several hours to prevent hematoma expansion. Hemodialysis was performed after a successful attempt at central cannulation via the right femoral route. Two days later, the patient's neck hematoma expanded with pain. A MDCT angiography was then arranged for further evaluation of neck vessel injury, and revealed injury in the right common carotid artery with a pseudoaneurysm formation (10x6cm) at the level of the C7-T1 vertebrae. The right internal jugular vein was compressed by the pseudoaneurysm, with lumen obliteration (Figure 6). Our cardiovascular surgeon performed surgical repair of the pseudoaneurysm, and an A-V shunt for regular hemodialysis was created at the same time. After the operation, the wound healed well and the patient was discharged 1 week later.

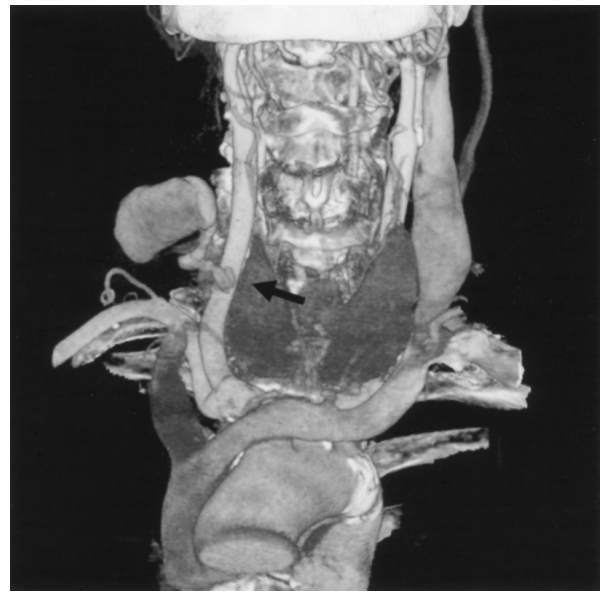

Fig. 6. The 3D reconstruction of the MDCT angiography shows that the right internal jugular vein was totally compressed by the pseudoaneurysm (arrow) arising from the right common carotid artery.

Discussion

The incidence of arterial puncture during central venous cannulation was about 6.3-9.4% via the internal jugular route, 3.1-4.9% via the subclavian route and 9.0-15.0% via the femoral route, respectively [1]. Pseudoaneurysm with sustained extravasation is rare, and often occurs in patients with a bleeding tendency, such as thrombocytopenia or coagulopathy. We know that abnormal platelet function in patients with chronic renal failure is common. Our case 2 and case 3 were in uremic status and both had prolonged bleeding time. This may explain why pseudoaneurysm formed easily after arterial puncture in our cases.

The suspicion of pseudoaneurysm during attempts at central venous cannulation should always be kept in mind by clinical physicians. This complication may cause massive blood loss, and the mass may compress the adjacent vital organs, which could be life-threatening. Our case 1 and case 2 both developed respiratory failure due to upper airway obstruction by the mass effect of the pseudoaneurysm. The most common physical finding is a hematoma located in the puncture area. The hematoma is often pulsatile, and the clinician may hear a bruit around the lesion.

The chest X-ray films may show an opaque lesion on the neck or upper intrathoracic field. The films provide less information about the lesion's character. In this situation, duplex ultrasound is a highly sensitive and specific test for arterial injuries [2-4]. It can provide rapid bedside assessment, but less information about the anatomical relationship of pseudoaneurysm. The definite diagnosis of pseudoaneurysm has been reached through conventional angiography in the past. Though this procedure is invasive, the angiography can demonstrate exactly the site of extravasation and the anatomic relationship of adjacent vessels, as in our case 1. However, case 2 and case 3 underwent MDCT scan, a new imaging technique. MDCT angiography is less invasive than conventional angiography, and can be performed quickly. The CT angiography and 3D volume-rendered reconstruction image can reveal precisely the location of the vessel injury and the 3-dimentional anatomical relationship of the pseudoaneurysm, feeding vessel and adjacent structure. Furthermore, it can guide the surgeon and radiologist in the treatment of pseudoaneurysm. Stuhlfaut *et al*. suggested MDCT angiography rather than conventional angiography as the study of choice for the initial evaluation of neck vessel trauma [5].

Treatment options for pseudoaneurysm include ultrasound-guided compression, transcatheter coil embolization, stent-graft deployment, percutaneous thrombin injection, and open surgical repair. In our cases, ultrasound-guided compression was not considered because of the low success rate in large-size pseudoaneurysms and the difficulty of approach. In case 1, initial surgical repair was not considered due to the patient's high-risk septic condition. Therefore, transcatheter embolization was performed after discussion with our radiologist. Though this case developed recurrent extravasation after the first embolization, the pseudoaneurysm was successfully sealed by repeat embolization. However, surgical removal of the huge hematoma was still needed for this case, due to her upper airway compression. Some case reports have shown that a coil could be a successful embolic agent in pseudoaneurysm [6-7]. In case 1, our radiologist used a new tissue glue agent (N-isobulyl – cyanoacrylate, NBCA) to occlude the pseudoaneurysm. This proved that tissue glue could be an alternative choice of embolic agent. In case 2 and case 3, transcatheter intervention via the common carotid artery was not chosen due to the high risk of embolic stroke. In addition, removal of the mass effect of pseudoaneurysm was considered, and a surgical approach from the neck would be relatively easy from the cervical area. Therefore, we selected traditional surgical repair for these 2 patients. Though there have been case reports of cervical arterial pseudoaneurysms which were successfully treated with percutaneous thrombin injection [8-9], this new technique was not available at our hospital. In recent studies, percutaneous injection of human thrombin by ultrasound guidance has become the treatment of choice for femoral arterial pseudoaneurysm [10-11].

Ultrasound guidance during attempted central venous cannulation has been proved to be useful to reduce the incidence of mechanical complications, catheter-placement failures, and the time required for insertion [12-13]. The ultrasound assistance could be performed in 2 ways: dynamic sonography and static sonography. In dynamic sonography, the operator performs the needle insertion under real-time sonographic guidance. This technique requires a sterile sonography probe and an experienced physician. In static sonography, the operator identifies the skin insertion site and marks the X spot

Table 1. Comparison of current treatments for pseudoaneurysm

Treatment	Advantages	Disadvantages
US-guided compression	Less invasive*	Discomfort and time- consumption
	Applied easily at bedside	Low success rate in large pseudoaneurysms and anticoagulation status
		Unsuitable in some anatomical sites
Endovascular interventions+	Less invasive*	Contrast nephrotoxicity
	Less anatomical limitation‡	Distal embolization
		Technique dependence
Percutaneous thrombin injection	Less invasive*	Distal embolization
		Allergy
		Unsuitable in some anatomical sites
Surgical repair	Removal of hematoma and relieving mass effect	Risk of anesthesia
		Invasiveness of operation
	The final option with failure of other treatments	
	Low recurrence rate	

* In comparison with surgical repair

\+ Includes transcatheter embolization and stent-graft deployment of feeding vessels

‡ In comparison with US-guided compression and percutaneous thrombin injection

under sonography. Then the needle advancement is performed without real-time sonography. Hence, we suggest that the use of dynamic sonographic guidance should be considered in hospitals with real-time sonography equipment and physicians with adequate training. If dynamic sonography guidance is not available, static sonographic assistance may be another choice.

In summary, the complication of pseudoaneurysm can be serious and life- threatening. The clinician should keep this in mind when using arterial puncture during attempts at central venous cannulation. If this complication is suspected, further diagnostic examinations and management should be implemented as soon as possible. In recent years, MDCT angiography has replaced conventional angiography as the initial evaluation tool for vessel trauma. Treatment for pseudoaneurysm used to rely on surgery, but today, more and more radiological interventions have been developed with encouraging results. We have listed the advantages and disadvantages of current therapeutic methods for pseudoaneurysm (Table 1). The choice of treatment depends on the size and the location of the lesion, the ease of approach, the underlying condition of the patients, and the applicability of new technique. To prevent the mechanical complication of central venous cannulation, ultrasound assistance should be considered routinely.

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中心靜脈導管插入所引發的僞動脈瘤—病例報告三例

劉旭崇　張開明　許正園

偽動脈瘤是中心靜脈導管插入過程所引發的嚴重併發症之一。案例一是經由左側鎖骨下靜脈插管不慎所造成，案例二及案例三則是經由右側內頸靜脈插管所引發。在這些案例中我們分別採用不同的診斷檢查，包括傳統血管攝影及多層次電腦斷層血管攝影。治療部分，案例一乃是接受動脈導管栓塞術且成功，另外兩例則是接受傳統外科修復手術。總結來說，多層次電腦斷層血管攝影術有較非侵入性的優點，且已經漸漸取代傳統血管攝影術成為評估頸部血管損傷的首選檢查。另一方面，目前對於偽動脈瘤的治療已經有越來越多新的方式，在臨床應用上包括超音波引導下壓迫、動脈導管栓塞術、超音波引導凝血酶注射、以及外科修復手術等等，對於選擇那一種治療還是取決於臨床醫師對病人病情的考量以及各種治療的適用性。*(胸腔醫學* ***2007; 22: 265-272)***

關鍵詞：偽動脈瘤，中心靜脈導管，血管攝影，多層次電腦斷層血管攝影，動脈導管栓塞術

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High-Grade Rib Osteosarcoma in a 57-Year-Old Man — A Case Report

Tzu-Tao Chen, Chieh-Jen Wang, Chien-Liang Wu, Hung-Chang Liu*

Osteosarcoma, usually seen in children and adolescents, is rarely found in adults. When it occurs, it is frequently found in the long bones, seldom in the flat bones. We report a 57-year-old man with a tender chest wall mass and massive pleural effusion. He was initially treated for presumptive tuberculosis, but did not respond to treatment. Further evaluation revealed a high-grade osteosarcoma of a rib. It was resected, followed by radiotherapy. When a lung metastasis was subsequently detected, chemotherapy was added. ***(Thorac Med 2007; 22: 273-278)***

Key words: osteosarcoma, rib, chest wall tumor, pleural effusion

Introduction

Osteosarcoma is the most common primary malignant tumor developing in the metaphysis of long tubular bones, especially the lower extremities [1]. It most commonly occurs in children and adolescents, seldom being found in adults. Chest wall tumors in adults, especially sarcomas, are most often related to radiation therapy, with a reported incidence between 0.03% and 0.8% [2]. Primary osteosarcoma in the chest wall is quite rare. In a study of 228 patients with non-Ewing sarcomas at St. Jude's Cancer Hospital, only 2 had primary osteosarcoma of the ribs. Akyuz *et al* reported 1 case of rib osteosarcoma among a total of 129 osteosarcoma cases [3]. The overall prognosis of osteosarcoma in flat bones is poor because of the difficulty of completely excising the tumor from sites such as the skull and pelvis. Wide local excision is possible with rib lesions, but the outcome is still frequently disappointing [3].

We report a rare case of rib osteosarcoma in a 57-year-old man.

Case Report

A 57-year-old man complained of intermittent left lower chest wall tenderness and a bulging mass beginning 4 months prior to admission. He was otherwise well, except for an 8-year history of type 2 diabetes. The chest pain worsened with arm movement and occasionally radiated to his lower back. It was slightly relieved by rest and massage. At another hospital, fine needle aspiration of the mass yielded only chronic inflammatory cells on cytology exam, and bacterial cultures were negative. A moderate left

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pleural effusion was seen on ultrasonography, so a thoracentesis was performed. However, a definitive diagnosis was still not apparent on cytology and culture. A presumptive diagnosis of tuberculous pleurisy was made and anti-tuberculosis medications were empirically prescribed. His symptoms did not improve over 1 month of treatment, and the pain became worse, with more frequent radiation to the back. He requested discharge from the original hospital and sought acupuncture, which yielded partial pain relief. However, exertional dyspnea developed about 2 months later and he came to our hospital seeking further treatment.

On initial physical examination, his temperature was 36ºC, pulse 135 beats per minute, respiratory rate 20 breaths per minute, and blood pressure 110/63 mmHg. There was a 6 x 6-cm focally tender mass on the left chest wall with overlying erythema. His breathing sounds were diminished on the left, without crackles or wheezes. There was no lymphadenopathy in the cervical or supraclavicular areas. Mild leukocytosis with a left shift (13000 cells/ul, neutrophils 91%) was found.

A chest radiograph (Figure 1) showed a hazy left hemithorax consistent with pleural effusion, and the mediastinum was slightly shifted to the right. There was a moderate amount of pleural effusion on chest ultrasound. A thoracentesis yielded bloody fluid which was an exudate (glucose 268 mg/dl, protein 4.7 g/dl, LDH 383 IU/L) with a white cell count of 715/cu mm (lymphocytes 93%, neutrophils 2%). Cytology, acid fast stains, culture, and PCR for *Mycobacterium tuberculosis* were all negative.

A chest CT scan (Figure 2) revealed massive left pleural effusion with adjacent lateral chest wall thickening. Video-assisted thoracoscopy revealed a solitary tumor in the left pleural cavity

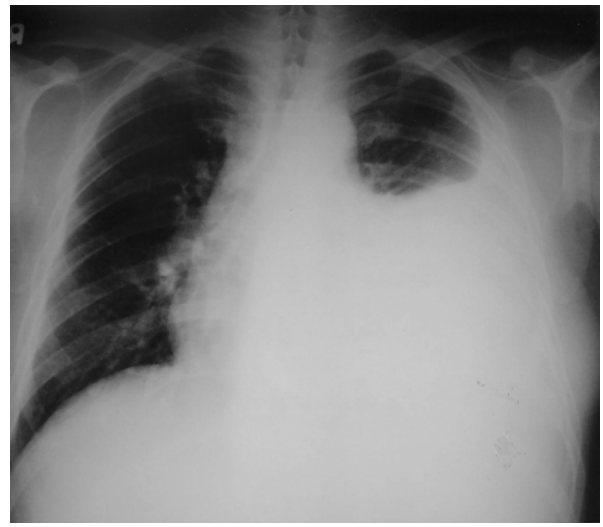

Fig. 1. Chest radiograph on admission showing a massive left pleural effusion with the heart shifted to the right.

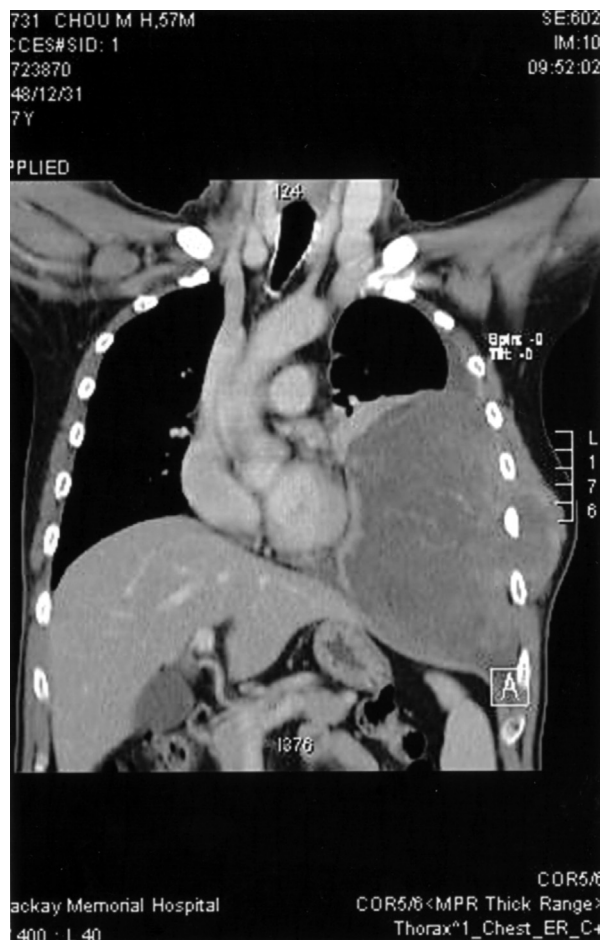

Fig. 2. Chest CT scan with enhancement revealing a massive left pleural effusion with adjacent atelectic lung and soft tissue thickening of the left lateral chest wall

with a well-defined margin and surrounded by 1000 ml of bloody pleural effusion. A biopsy specimen examined by frozen section was consistent with malignancy, most likely sarcoma. A subsequent Tc-99m bone scan demonstrated increased uptake in the left sixth rib, with mild, diffuse radiotracer accumulation in the left lower lung. These findings were suggestive of malignancy. Complete resection of the tumor with chest wall reconstruction (Figure 3) was performed. Both the resected rib and the attached chest wall soft tissue mass were found on pathology examination to contain invasive sclerotic osteosarcoma with diffuse tumor osteoid and mitoses (Figure 4). Immunostaining was positive for vimentin, and negative for cytokeratin, calretinin, smooth muscle actin, CD34, and CD68. The final pathology diagnosis was grade 4 osteosarcoma.

The patient was given 60 Gy of radiotherapy by electron beam in 30 fractions over the next 3 months for intractable bone pain. Once his condition improved, 6 courses of adjuvant chemotherapy with cisplatin and epirubicin were begun. However, chest CT 2 months after surgery revealed a well-defined round l.5-cm nodule in the left lower lobe of the lung. This was presumed to be a metastatic lesion from the sarcoma, but it did not appear to progress over the next 8 months.

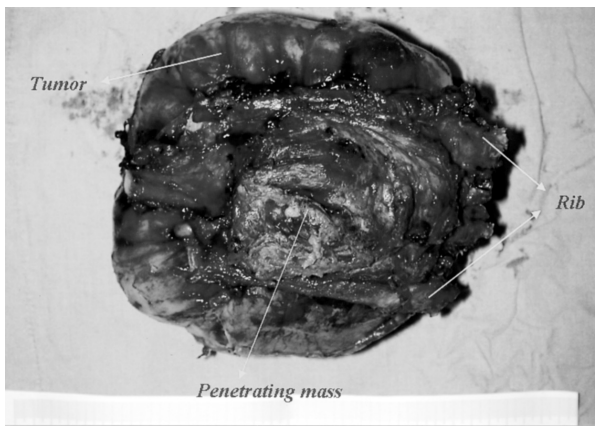

Fig. 3. Gross hypervascularized 25-cm tumor weighing 1872 gm found at surgery in the left thoracic cavity partially involving the diaphragm and lung.

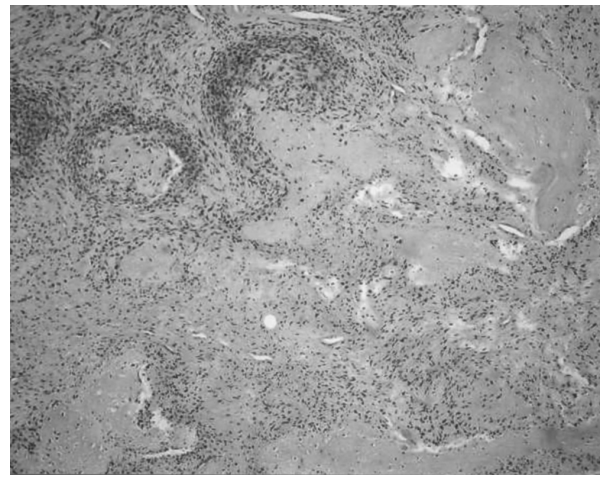

Fig. 4. Extra-osseous tumor composed mainly of spindle cells with osteoid and mitoses (H&E stain, 40x).

Discussion

Osteosarcoma is the most common primary sarcoma of the bone, occurring primarily in the metaphyses of adolescents. Most are found in individuals younger than 30 years old, with no specific risk factors [4]. While osteosarcomas are most commonly found at sites where the bone length and diameter are greatest (e.g., distal femur, proximal tibia, proximal humerus), they have also been found in flat bones, usually of the pelvis. They rarely occur in the scapula, spine, skull, or ribs [5].

There is a bimodal age distribution curve, with the first peak in the second and third decades and a second, smaller peak over the age of 60 (only 10% of patients with osteosarcomas). Osteosarcoma in older patients has a different anatomic distribution. For instance, more than 50% of young patients with classic osteosarcoma have lesions near the knee, whereas only 15% of

older patients have lesions in that location. Secondary osteosarcoma is also more prevalent in older patients, arising in regions of previous radiotherapy, Paget's disease of bone, fibrous dysplasia, or other pathologic abnormalities [6]. Our patient, slightly younger than 60, was near the second age peak, but he had no known risk factors for secondary osteosarcoma.

Morphologically, osteosarcoma is described as classic (45% of cases), fibroblastic (9%), chondroblastic (27%), anaplastic (17%), telangiectatic, low-grade-central, and other types (2%) [4]. Histologic grading systems for osteosarcoma are of little value, with considerable heterogeneity within any particular tumor depending on the site sampled. The number of mitoses and, degree of cellularity, anaplasia, or pleomorphism may differ from site to site within the tumor [7], therefore we chose not to place any weight on the histologic grading of this patient's tumor. According to the American Joint Committee on Cancer staging system for primary malignant bone tumors (2003) [8], the patient had stage IVa disease.

Most osteosarcomas present as a large, tender soft tissue mass with localized pain. Patients frequently report symptoms beginning after an injury that wax and wane over several months. Systemic symptoms such as malaise, weight loss, or fever are generally absent. About 10% to 20% of patients with osteosarcoma have macrometastases at presentation, most commonly in the lungs and other bones [9].

CT is generally less useful than MRI to assess primary bone tumors, but it is the best method for evaluating metastatic disease in the thorax [10]. Bone scans are also limited by a lack of specificity, especially in patients with trauma. A positive bone scan requires radiological confirmation to diagnose metastatic bone disease, especially if only a few lesions (<4) are present or the tumors are limited to the ribs [11]. In our case, the tumor was initially masked on the plain chest film by a massive pleural effusion. The presence of a chest wall mass was confirmed by the combination of chest CT and bone scan. This helped localize the lesion for biopsy, and the follow-up CT was of key importance in demonstrating pulmonary metastasis.

The results of fine needle aspiration of the mass in this case were not helpful, yielding only chronic inflammatory cells on cytology exam. Transthoracic needle aspiration reportedly results in a correct diagnosis of malignancy in 85% to 94.7% of cases; however, that leaves a substantial number of false-negatives. It is therefore recommended that nonspecific results be further evaluated by other diagnostic methods [12].

Given the rarity of adult osteosarcoma arising in a rib, it is not surprising that this diagnosis was not initially suspected in our patient, particularly as the large pleural effusion masked the tumor on radiography. While tuberculosis with a chest wall tuberculoma might have explained this patient's presentation, a more aggressive approach to diagnosis might have yielded an earlier diagnosis. It is certainly true that proving tuberculosis as the cause of a pleural effusion is not always easy, even with thoracoscopy, but attempts must be made to do so, with further imaging and biopsies as necessary. This man's sarcoma was likely already relatively advanced when he first sought treatment, but an earlier definitive diagnosis might have saved him and his family several months of uncertainty.

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源發於肋骨的高度惡性骨肉瘤—病例報告

陳資濤　王玠仁　吳健樑　劉洪彰 *

骨肉瘤(osteosarcoma)在成人的表現相較於兒童為少，且大多數為次發性(secondary)，而好發的部位以四肢骨與長骨為主，較罕見於扁平骨。我們報告一位57歲男性病患以觸痛的胸廓腫瘤合併大量肋膜積水表現，以抗結核病藥物治療無效後，至本院經過外科病理切片發現為源發於肋骨的高度骨肉瘤合併肺轉移，其後接受腫瘤切除與放射化學治療的病例。*(胸腔醫學* ***2007; 22: 273-278)***

關鍵詞：骨肉瘤，肋骨，胸廓腫瘤，肋膜積水

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Bilateral Malignant Pleural Effusion in Multiple Myeloma — A Case Report and Literature Review

Pei-Ming Huang, Chau-Chyun Sheu, Hui-Jen Tsai*, Wan-Ting Huang**, Jhi-Jhu Hwang, Ming-Shyan Huang

Pleural effusion is an uncommon manifestation of multiple myeloma. Several mechanisms have been proposed for the development of pleural effusion in multiple myeloma, and most of them are benign. We report a patient with IgG-λ multiple myeloma with bilateral malignant pleural effusions and cutaneous involvement. She initially presented with massive left-sided malignant pleural effusion, and shortly thereafter, she developed right-sided malignant pleural effusion. Even though aggressive chemotherapy was administered, she died 10 weeks after diagnosis. Our observation in this case was consistent with that of other reports, in that the presentation of malignant pleural effusion indicates an advanced stage and a very poor prognosis for patients with multiple myeloma. Further investigations on malignant plasma cell biology and the explicit mechanisms of malignant pleural effusion in multiple myeloma are needed in order to improve the management and outcome of this malignancy. ***(Thorac Med 2007; 22: 279-285)***

Key words: multiple myeloma, malignant pleural effusion

Introduction

Multiple myeloma represents the malignant proliferation of plasma cells which predominately invade bone marrow. It may also involve other organ-systems as well. Thoracic skeletal lesions, plasmacytomas (both intramedullary and extramedullary), pulmonary infiltrates, and pleural effusion (myelomatous and nonmyelomatous) may be seen when it involves the thorax [1-2]. Extraosseous involvement in multiple myeloma is uncommon and pleural involvement is rare [1]. According to a previous analysis, nearly 6% of patients with multiple myeloma develop pleural effusion during the course of their disease [1]. The etiology of the development of pleural effusion in patients with multiple myeloma is mutifactorial, and usually benign. The common causes include congestive heart failure secondary to amyloidosis, nephrotic syndrome, pulmonary infarctions or infections, and malignant pleural effusion due to myeloma cell infiltration [1-3]. Herein, we report a case of IgG-λ multiple myeloma with the unusual presentation of bilateral malignant pleural effusion and cutaneous involvement. The patient's malignancy responded

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poorly to chemotherapy, and she died 10 weeks after diagnosis.

Case Report

A 72-year-old woman presented to our hospital complaining of shortness of breath for 2 weeks. She had been generally quite well and did not have a history of chronic illness. She denied fever, cough, chest pain, hemoptysis, wheezing, and sweating. On physical examination, she looked unwell and breathless. Her blood pressure was 98/54 mmHg, the pulse 106 beats per minute, the respiratory rate 24 breaths per minute, and the temperature 37.3°C. Oxygen saturation was 98% under oxygen 2 L/min by nasal cannula. Auscultation of the lungs revealed decreased breathing sounds in the left lower lung area. Chest radiograph showed a remarkable amount of pleural effusion in the left lung (Figure 1). The complete blood count showed leukocytes 6,900 cell/μL, hemoglobin 6.2 g/dL, and platelets 115,000/μL. The patient's serum C-reactive protein (CRP) level was 14.4 mg/L (reference < 5 mg/L). Other serum values were as follows: albumin 1.8 g/dL, total protein 6.8 g/dL, uric acid 16.6 mg/dL, ionic calcium 5.89 mg/dL, creatinine 2.6 mg/dL, urea nitrogen 51.5 mg/dL, AST 17 U/L and ALT 8 U/L. Other abnormal laboratory data included a high serum lactate dehydrogenase (LDH) level of 287 U/L (normal range 91-180 U/L). Thoracentesis of the left pleural effusion revealed a hemorrhagic appearance, LDH 357 U/L, total protein 3.5 g/dL, and a cell count of 2,900 cell/μL with 100% mononuclear cells. Bacterial cultures of pleural effusion were negative. Cytological examination of the pleural effusion revealed neoplastic plasma cells with large pleomorphic nuclei, coarse chromatin, prominent nucleoli, and basophilic cytoplasm (Figure 2). Malignant pleural effusion from multiple myeloma was suspected. The discrepancy between serum total protein and albumin levels, the impaired renal function, and hypercalcemia also implied the probability of multiple myeloma. Therefore, serum immunoglobulins were quanti-

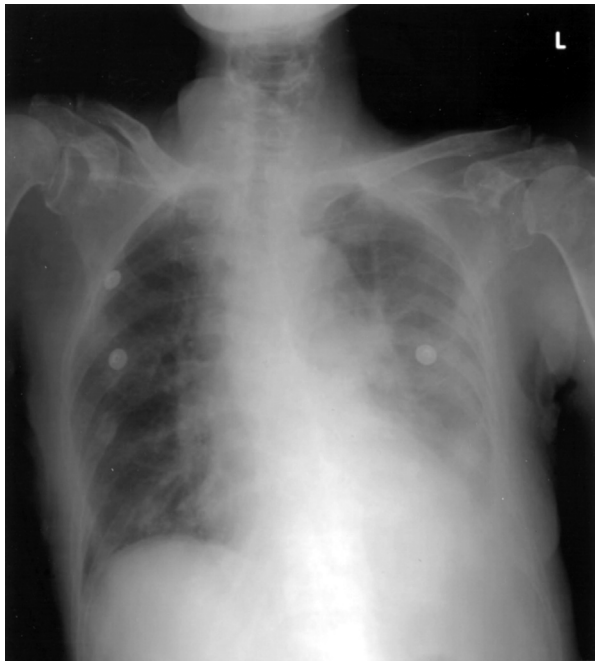

Fig. 1. Chest radiograph showing massive pleural effusion in the left lung

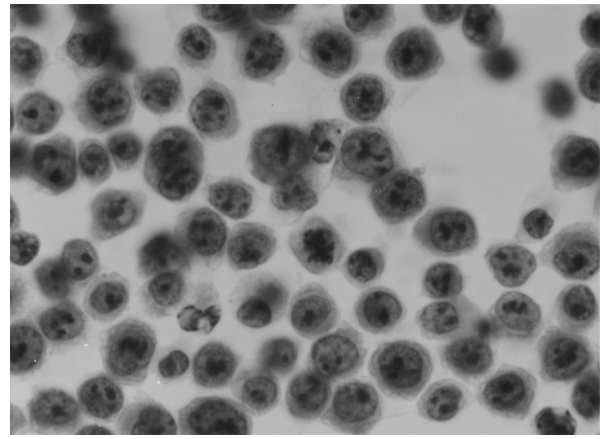

Fig. 2. The Papanicolaou-stain revealed neoplastic plasma cells with pleomorphic nuclei, prominent nucleoli and basophilic-stained cytoplasm. (conventional smear; Papanicolaou stain, X400)

fied and revealed IgG 3990 mg/dL, IgA 28.3 mg/dL, and IgM 11.0 mg/dL. A serum protein electrophoresis was also obtained, and revealed a discrete abnormal band measuring 3.8 g/dL in the gamma region. Serum and urine immunofixation electrophoresis identified a monoclonal spike comprised of IgG-λ. The patient's serum β-2 microglobulin level was 14 mg/L. A skeletal survey revealed multiple punched out lytic lesions on the skull (Figure 3) and compression fractures of the 6th, 9th and 12th thoracic vertebrae. A bone marrow aspiration disclosed diffuse infiltrates of plasma cells that comprised 88% of the cellular elements. Accordingly, the diagnosis of multiple myeloma was confirmed.

Her breathlessness resolved after tubal drainage of the left pleural effusion. However, on the 8th hospital day, she developed shortness of breath again. Chest sonography showed a large amount of pleural effusion on the right side. Thoracentesis of the right pleural effusion revealed a hemorrhagic appearance, LDH 171 U/L, total protein 3.29 g/dL, and a cell count of 3,800/μL with 100% mononuclear cells. Surprisingly, the cytological examination again proved malignant pleural effusion.

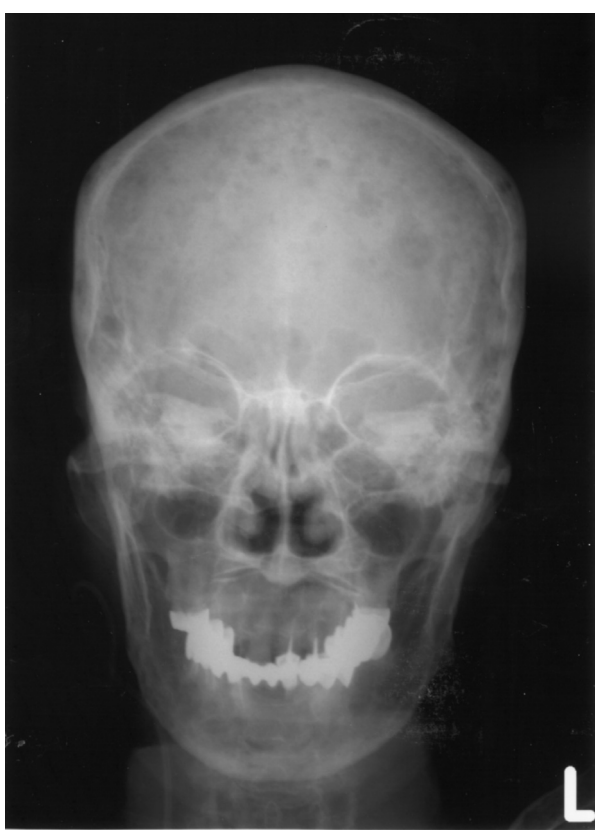

Fig. 3. Skull radiograph showing multiple punched out lytic lesions

Chemotherapy with combined melphalan (12 mg per day) and prednisolone (60 mg per day) for 4 days was administered for the multiple myeloma. After chemotherapy, the IgG level was reduced to 1850 mg/dL and the patient experienced a relief of symptoms and resolution of acute renal failure (serum creatinine from 2.6 to 0.8 mg/dL) and hypercalcemia (ionic calcium from 5.89 to 4.09 mg/dL). A chest radiograph demonstrated a decrease in the amount of bilateral pleural effusion and repeated thoracenteses revealed a decrease in the cell count (right: 180 cell/μL, left: 150 cell/μL). The patient was then discharged.

One week later, she was admitted to our hospital again because of fever (temperature of 38°C), shortness of breath and non-productive cough. Laboratory examinations revealed neutropenia (900 /μL) and thrombocytopenia (39,000 / μL). Pyuria was found on urine analysis. The chest radiograph demonstrated an increased amount of left pleural effusion. Thoracentesis was performed for relief of dyspnea and the effusion was sterile. Broad spectrum antibiotic (ampicillin/sulbactum) and antifungal agents (fluconazole) were administered. In addition, multiple erythematous cutaneous nodules involving the anterior chest and lower extremities were found on physical examination. Excisional biopsy from 1 of these lesions on the left anterior chest was pathologically consistent with the cutaneous involvement of myeloma (Figure 4). On the 27th hospital day, the patient died of severe sepsis and

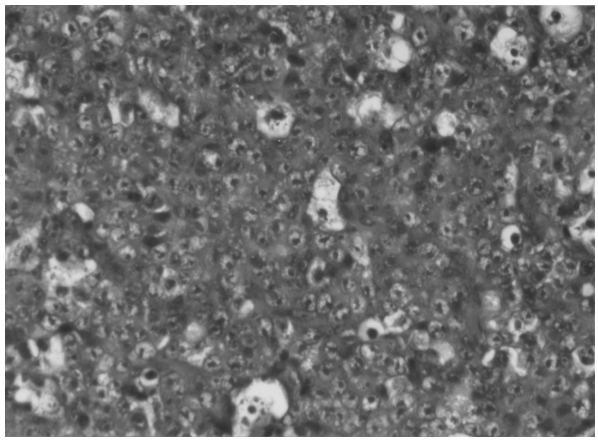

Fig. 4. The nodule consisted of neoplastic plasma cells with large nuclei, distinct nucleoli and numerous macrophage-ingested apoptotic tumor cells. (hematoxylin and eosin stain, X400)

acute respiratory failure.

Discussion

Multiple myeloma, a malignant disorder of plasma cells, accounts for approximately 10% of hematologic malignancies. The most common presenting symptoms are bone pain (58%) and fatigue (32%) [4]. At diagnosis of this type of tumor, the usual clinical findings consist of bony destruction, hypercalcemia, renal failure, anemia, infection and neurological symptoms. Pleural effusion is a rare manifestation of multiple myeloma, and malignant pleural effusion due to myeloma occurs in less than 1% of cases [1]. Previous studies of malignant pleural effusion in multiple myeloma [2, 5-16] reveal that it more frequently involves the left thoracic cavity. For the remainder, the frequency of right-sided and bilateral involvement is essentially identical. Some investigators considered that IgA type myeloma may cause the majority of myelomatous pleural effusion because of its tendency toward extraosseous structural invasion [3, 13, 17]. However, Meoli *et al*. [16] and Kamble *et al*. [14] found that IgG type myeloma (40%) comprised the majority of this category, followed by IgA type (30%), light chain (12%) and unknown type (18%). The explanation is that IgG type myeloma contributes to more than half of myeloma. Furthermore, almost all cases had some abnormalities on chest radiograph and computed tomography, including lytic lesions in the thoracic skeleton, mediastinal mass, pulmonary infiltrates, and pleural thickening. Therefore, some authors proposed that the possible mechanisms causing myelomatous pleural effusion were infiltration by myeloma cells from adjacent skeletal or parenchymal tumors, direct implantation of plasma cells on the pleura, and mediastinal lymph node infiltration with lymphatic obstruction [1]. Our patient with IgG-λ myeloma presented with a rare manifestation - bilateral malignant pleural effusion which was confirmed by cytological examination. Though there was no lytic lesion in the ribs, compression fractures of thoracic vertebrae were seen on radiograph. According to the new International Staging System (ISS) [18], which utilizes the combination of serum β-2 microglobulin and albumin to categorize stages for multiple myeloma, our patient was classified as the most advanced stage - stage III with a median survival of 29 months. Kamble *et al*. analyzed 11 patients with multiple myeloma with malignant pleural effusion, and found a marked increase in plasma β-2 microglobulin and LDH and CRP levels at the time of occurrence of pleural effusion, compared to the initial presentation of myeloma [14]. The malignant pleural effusion of most cases was managed with systemic chemotherapy combined with chest tube drainage and/or pleurodesis. However, recurrences of pleural effusion were common. These patients had 4 months median survival from the onset of malignant pleural effusion, even with high-dose chemotherapy and

peripheral blood stem cell transplantation.

Our case had advanced age, anemia, and increased serum creatinine, CRP, and LDH levels, which were all poor prognostic factors for this cancer. Malignant pleural effusion may also be a predictor of a poor prognosis, as observed in previous reports [2, 5-14]. Our patient received 1 conventional dose of chemotherapy for multiple myeloma and tubal drainage of the effusion for this complication. Even so, rapid accumulation of pleural effusion and severe infection occurred, leaving the patient with less than 3 months of survival from the diagnosis of multiple myeloma. In addition to the presence of bilateral malignant pleural effusion and the strikingly high serum β-2 microglobulin level, the uncommon manifestation of cutaneous involvement of multiple myeloma in our patient also suggested an advanced disease stage and a very poor prognosis [19].

The observations with our patient, as well as in other reports, suggest that the occurrence of malignant pleural effusion in multiple myeloma represents an advanced, disseminated stage and the quite aggressive behavior of this tumor. However, there is not enough evidence from large-scale studies to demonstrate a poorer prognosis in cases of multiple myeloma with malignant pleural effusion compared to those without malignant pleural effusion. Further investigations on malignant plasma cell biology and the explicit mechanisms of malignant pleural effusion in multiple myeloma are also needed in order to improve the management and outcome of this malignancy.

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合併兩側惡性胸水的多發性骨髓瘤—病例報告與文獻探討

黃培銘　許超群　蔡慧珍*　黃琬婷**　黃吉志　黃明賢

胸水在多發性骨髓瘤的病人身上並不常見。有很多原因會產生這個情況，而大部份是良性的。我們報告一個IgG-λ多發性骨髓瘤的病人合併兩側惡性胸水以及皮膚的侵犯。病人最初以左側大量惡性胸水表現，並在很短的時間內發展出右側惡性胸水。雖然她接受了積極的化學治療，但其病情仍快速惡化，並在被診斷出多發性骨髓瘤十週後死亡。我們的觀察與其他的報告一致：當多發性骨髓瘤病患出現惡性胸水時，代表這個腫瘤已經到了末期，且預後極差。因此，我們必須更瞭解惡性漿細胞的生物學以及其產生惡性胸水的致病機轉，以期能改善我們對這個併發症的處理方式以及這個疾病的預後。*(胸腔醫學* ***2007; 22: 279-285)***

關鍵詞：多發性骨髓瘤，惡性胸水

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索取抽印本請聯絡：黃明賢醫師，高雄醫學大學附設中和紀念醫院　胸腔內科，高雄市自由一路 100 號

Solitary Pulmonary Fibrous Tumor with Initial Presentation of Hypoglycemia — A Case Report and Literature Review

Jiun-Long Wang*, Gee-Chen Chang*,**, Jeng-Yuan Hsu*, Jiun-Yi Hsia***, Po-Cheung Kwan****

Solitary fibrous tumor (SFT) is an uncommon slow-growing mesenchymal neoplasm. It usually involves the visceral pleural and rarely has an intrapulmonary distribution. It is very sharp and round in shape when appearing intrapulmonarily. About 4% of SFT has hypoglycemia as a part of the paraneoplastic syndrome. We report a case of solitary pulmonary fibrous tumor with the presentation of hypoglycemia. After complete resection of the tumor, the blood sugar returned to normal range. Imaging pictures of the solitary pulmonary fibrous tumor and the mechanism of hypoglycemia caused by SFT are discussed. ***(Thorac Med 2007; 22: 286-292)***

Key words: hypoglycemia, pulmonary tumor, solitary fibrous tumor

Introduction

Solitary fibrous tumor (SFT) is a rarely encountered mesenchymal neoplasm. Mostly, it is confined to the visceral pleural, but can also be found in the peritoneal, orbital, and thyroid areas, and others. An intrapulmonary manifestation is rare. About 4% of SFT has a hypoglycemic symptom as a part of the paraneoplastic syndrome. We report the case of a 55-year-old man diagnosed with solitary pulmonary fibrous tumor with an initial presentation of hypoglycemia, in terms of consciousness change. The blood sugar level returned to normal after complete resection of the tumor. One year after the surgery, the patient was well clinically and radiologically. We will describe the solitary pulmonary fibrous tumor radiographically and discuss the mechanism of the hypoglycemia caused by SFT.

Case Report

A 55-year-old male had been relatively robust before. In March 1999, he had an episode of palpitation and visited the local medical clinic. The initial investigation showed no specific finding but a solitary pulmonary nodule, 3 cm in diameter, was found accidentally on the left upper lobe (LUL), using chest radiography (CXR) (Figure 1). The patient was then lost to follow-

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up for 7 years.

In January 2006, the patient experienced diplopia and a dizziness sensation. He denied symptoms of cold sweats or vertigo. Then, he lost consciousness in the factory where he worked and was found by neighbors. He was sent to a local hospital for first aid. On arriving at the emergency room, the blood sugar level was 29 mg/dl. After a glucose water supplement, his consciousness recovered, about 2 hours after the syncope. Later, he was referred to our chest medicine division for further evaluation.

After admission to the ward, a general survey was performed. CXR showed a sharp and round solitary pulmonary mass, 10 cm in diameter, on the LUL (Figure 2). Chest CT showed a heterogenous tumor pattern after intravenous contrast medium infusion (Figure 3). Tumor work-up, including a whole body bone scan, abdominal sonography and brain CT revealed negative findings. Series studies for hypoglycemia were arranged. The renal and liver functions were within normal limits. There was no evidence of hypothyroidism or adrenal insufficiency. The serum level of insulin, at < 2.0 μU/ml (2.6-24.4 μU/ml), C-peptide < 0.5 ng/ml (0.9-4.0 ng/ml), growth

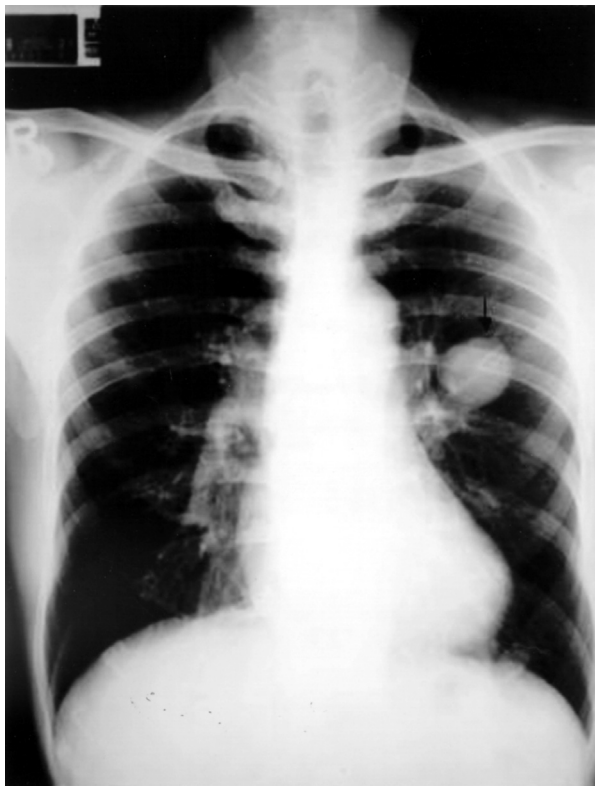

Fig. 1. CXR in May 1999, tumor size: 3 cm in diameter.

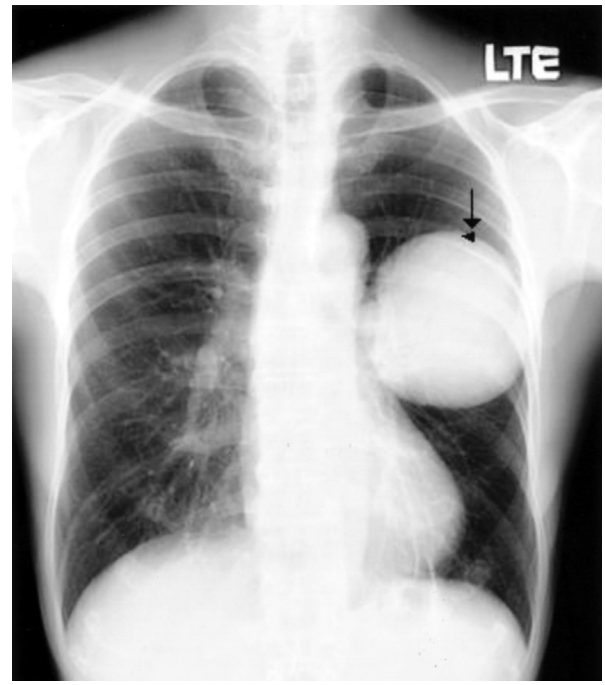

Fig. 2. CXR in February 2006, tumor size: 10 cm in diameter.

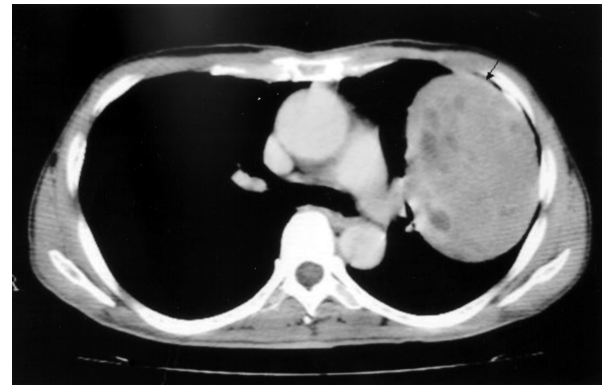

Fig.3. Heterogenous pattern of the tumor after contrast medium infusion on chest CT image.

hormone < 0.05 (ND-8.6 ng/ml), and insulin-like growth factor-I (IGF-I): 68.7 ng/ml (87-238 ng/ml) were all below the normal limit. Radical lobectomy of the LUL of the lung with lymph node dissection was performed. Grossly, the tumor measured 12x12x9 cm in size and weighed 570 grams. It was yellow and tan in color, on a cut surface (Figure 4). Ultrastructurally, it originated from the lung (Figure 5). It showed hypercellularity change and an abundance of spindle cells (Figure 6). It also revealed increased cellularity and a nuclear cytoplasmic (N/C) ratio (in H&E stain at a high power field) (Figure 7). The mitotic count was 36/100 HPF. The immunohistochemical stain was positive for neuron-specific enolase (NSE), CD34, CD99, and BCL2. The tumor was negative for S-100 protein, AE1/AE3, actin M851, CD10, EMA, and calretinin stains. Thus, solitary fibrous tumor was diagnosed by CD34 reaction. The blood sugar rose to 125 mg/dl after surgery. The follow-up values of serum insulin and C-peptide levels returned to normal ranges, 5.03 μU/ml and 2.0 ng/ml, respectively. There were no more episodes of hypoglycemia and no evidence of recurrence in the 1-year follow-up period.

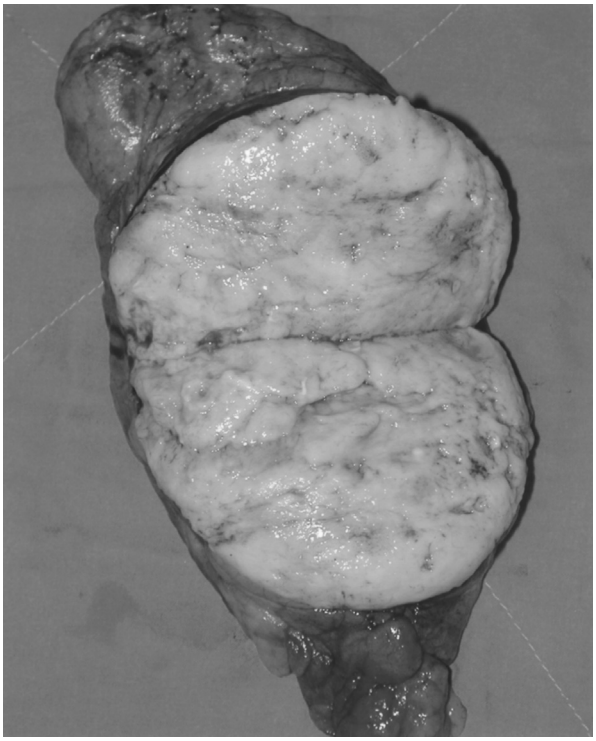

Fig. 4. Gross structure of the tumor.

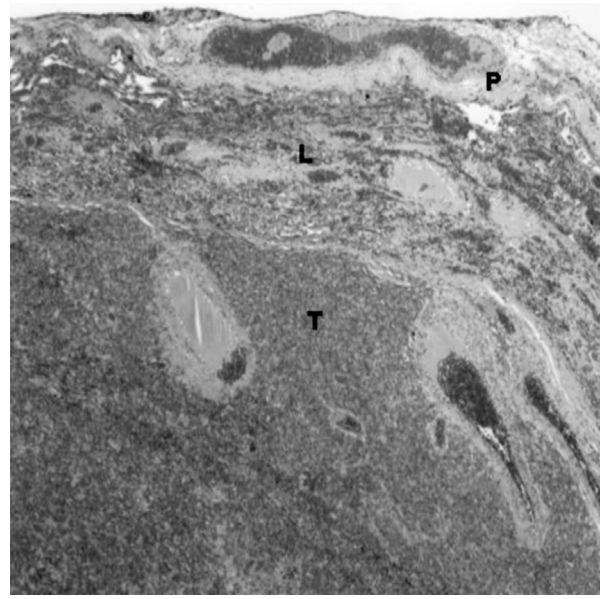

Fig. 5. Histopathology showed intrapulmonary tumor on H&E stain (x40). (P: pleural, L: lung, T: tumor)

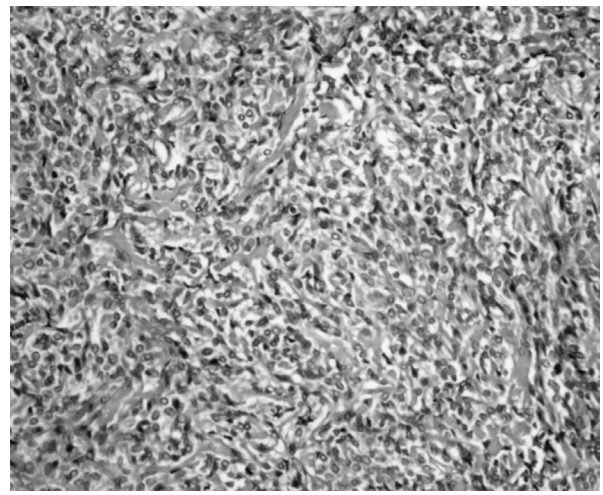

Fig. 6. Hypercellularity and an abundance of spindle cells on H&E stain (x200)

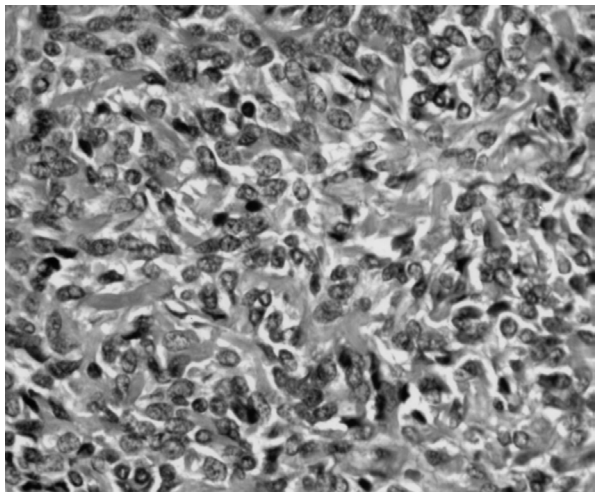

Fig. 7. Hypercellularity and increased N/C ratio on H&E stain (x400)

Discussion

Solitary fibrous tumor (SFT) is a less common spindle cell neoplasm [1]. It usually involves the pleura, especially the visceral pleura. It is also reported in other non-serosal sites, such as the orbit, thyroid, thymus, and parotid gland. [2]. Lung parenchyma involvement was rarely mentioned in a literature review. It usually appears in adult life (in the sixth to seventh decades) and there is no difference in distribution between the sexes [3]. Radiographically, we can see the well-defined ovoid or round pulmonary nodule (or mass) on the CXR (Figure 1, 2). Enhancement of SFT with a heterogenous pattern after intravenous contrast medium infusion in chest CT scans has been reported (Figure 3). The enhancement is usually avid in the periphery of the tumor [1, 4]. Other researchers have reported heterogeneous attenuation in chest CT images [4].

It is curious that the SFT presents as an intrapulmonary distribution. There are 2 main hypotheses for this [1, 5]. The first is that the subpleural mesenchyma has continuity with the connective tissues of the interlobular septum. Then, intrapulmonary fibrosis develops from the septal mesenchyma. The other hypothesis focuses on the tumor found in the submesothelial area of normal pulmonary parenchyma, in terms of facultative fibroblastic change [1, 5].

The SFT is a slow-growing tumor and is often asymptomatic at first. As it grows, it may present symptoms of fever, cough, and chest pain. As the tumor becomes larger, it may cause paraneoplastic syndromes including body weight loss, clubbing fingers, osteoarthropathy, and hypoglycemia [3, 6-11]. Briselli *et al.* [12] reported that 4% of solitary fibrous tumors present hypoglycemia, especially large and slow-growing tumors. We know that hypoglycemia is encountered as an emergency event in daily practice. The common causes of hypoglycemia are diabetes mellitus, impairment of renal or liver function, or medication with oral hypoglycemia agents, or it is tumor-related [13]. Those tumors which cause hypoglycemia are divided into 2 major groups. The first is pancreatic tumors which secrete insulin to cause hypoglycemia [14]. The other is non-islet-cell tumors via insulin-like growth factor (IGF) which reduces glucose [15]. In non-islet-cell tumor-related hypoglycemia (NICTH), the tumors may originate from mesenchymal, epithelial or hematopoeitic sites. In the mesenchymal neoplasma group, mesothelioma, leiomyosarcoma, fibrosarcoma and hemangiopericytoma may be encountered [13]. The insulin-like substance of the tumors is associated with hypoglycemia. Insulin-like growth factors I and II are contenders for this key role [16]. The circulating level of IGF-I in our case was low (68.7 ng/ml)(normal range 87-238 ng/ml), so IGF-I may not mediate the hypoglycemia mechanism [16]. It is reported that non-islet cell tumors which cause hypoglycemia often secrete incompletely processed insulin-like growth factor II (IGF-II)

[17-18]. The incompletely processed IGF-II can interact with insulin receptors in the liver, muscle, and adipose tissue to inhibit gluconeogenesis [13, 19]. IGF-II can also bind with IGF-I receptors in the pituitary gland and pancreas. Then growth hormone is suppressed and a reduction of the serum level of IGF-I occurs [13]. It has been reported that some SFT of the pleura possess IGF-I receptors which cause recurrent hypoglycemia, even though the circulating IGF-I level is low [16]. NICTH is often diagnosed by detecting low level of serum growth hormone, IGF-I, IGF-binding protein 3, and insulin along with low blood glucose and normal (or high) serum IGF-II level [13]. In this patient, the biochemical data were compatible except there was no available serum IGF-II level. We believe that identifying the insulin-like growth factor (IGF-I, IGF-II) of the SFT in our case was crucial. Once further techniques are developed, we can apply them and attain more understanding of the hypoglycemic mechanism of SFT in our daily practice.

Histologically, the SFT usually presents intense hypercellularity and an abundance of spindle cells (Figure 6). The nucleus is separated with bands of collagen fibers. Immunohistochemically, the CD 34 becomes the key point in SFT [20]. In addition, the strong expression of CD 99 and BCL2 support the diagnosis of SFT [2]. When the diagnosis is confirmed, we can distinguish benign from malignant tumors via one or more of the following histological features [6]: high cellularity, mitotic activity (more than 4 mitotic figures per 10 high power fields), pleomorphism, hemorrhage, and necrosis. Our patient had a borderline malignancy (mitotic count of 36/100 high power field).

Treatment of SFT is based on surgical resection [5]. It has been mentioned that the tumor has a high potential for malignant change once it grows to a large size [7]. The achieving of tumor-free margins during surgery to prevent local recurrence or distant metastasis has been emphasized [21-22]. One report found that intrathoracic SFT shows a local recurrence and distant metastasis rate up to 15%, and that extra-thoracic tumors may have malignant behavior in about 6% of cases [19].

Conclusion

SFT is slow-growing and usually confined to the pleural area. When it presents as an intrapulmonary nodule (or mass), it is very sharp and round in shape. About 4% of SFT has hypoglycemia as a symptom of paraneoplastic syndrome.

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以低血糖爲起始表現的肺內單獨纖維瘤 —病例報告及文獻回顧

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單獨纖維瘤是一種罕見且生長緩慢的實質腫瘤，通常以影響臟層的肋膜為主，很少會出現在肺內。當出現於肺內時，影像上可以看到圓型的腫瘤。大約百分之四的單獨纖維瘤會引起低血糖作為其副腫瘤症候群(paraneoplastic syndrome)的臨床表現。在文章裡，我們描述一位五十五歲的肺內單獨纖維瘤男性患者以低血糖合併意識不清作為起始的臨床表現。經由手術切除肺內腫瘤後，血糖即回昇到正常範圍內。經過一年的追蹤，臨床及影像上都無復發的跡象。文章中將就肺內單獨纖維瘤在影像上的表現及其引起低血糖的機轉做進一步的探討並回顧相關的文獻。*(胸腔醫學 **2007; 22: 286-292**)*

關鍵詞：低血糖，肺內腫瘤，單獨纖維瘤

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Pancreatic Pseudocyst Presenting as a Posterior Mediastinal Mass

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Pancreatic pseudocyst presenting as a mediastinal mass is very rare. Approximately 40 to 50 cases have been reported in the English literature over the last 2 decades. Usually, mediastinal tumors are asymptomatic or present with thoracic symptoms. By contrast, the most common presenting symptoms of mediastinal pancreatic pseudocysts are abdominal pain and weight loss.

We report a 48-year-old man with epigastric dull pain for 4 days and weight loss of 3 kilograms in the most recent months. He had a medical history of alcoholic pancreatitis and gall bladder stone. Chest radiography showed a posterior mediastinal mass. Reformatted oblique coronary computed tomography scan of the abdomen revealed a thick-wall pseudocyst extending from the pancreas to the lower mediastinum. After mediastinotomy, the pathology of the mass was found to be compatible with the diagnosis of pseudocyst. The patient was then managed surgically by external drainage. In the follow-up visit within 1 month after discharge, no recurrent symptom was found. ***(Thorac Med 2007; 22: 293-298)***

Key words: pancreatic pseudocyst, posterior mediastinal mass

Introduction

Causes of posterior mediastinal mass include esophageal lesions, congenital or acquired vascular lesion, foregut cysts, intrathoracic goiter, mediastinal pseudocysts, neurogenic tumors, infectious spondylitis [1-2], and others. Neurogenic tumor is the leading cause of posterior mediastinal masses, and accounts for about 20% of all cases [3]. Mediastinal pancreatic pseudocyst is a very rare cause of a posterior mediastinal mass. The symptoms most commonly associated with mediastinal tumors are chest pain, cough and shortness of breath. However, mediastinal pancreatic pseudocysts usually present with chest or abdominal pain and weight loss. We report a case of pancreatic pseudocyst presenting as a posterior mediastinal mass.

Case Report

A 48-year-old alcoholic Taiwanese was refer-

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red from a primary care physician to the gastrointestinal department of our hospital. The patient's chief complaint was persistent epigastric dull pain for 4 days. The pain was not associated with fever, nausea, vomiting or diarrhea. He did not experience postprandial fullness; nor did he have recent tarry stool. During the preceding month, he suffered a 3-kg weight loss. During the 5 years prior to hospital admission, he had been diagnosed with recurrent pancreatitis with intermittent upper abdominal pain, accompanied by amylase elevation.

On physical examination, his temperature was 36.9°C, pulse rate was 108/minute, respiratory rate was 24/minute, and blood pressure was 133/81 mmHg. Abdominal examination revealed a normal bowel sound and no tenderness or rebound pain. No hepatosplenomegaly was noted. Hematologic study showed red blood count, 3.81×10^6/μL; hemoglobin, 12.1 g/dL; white cell count, 8900/μL; neutrophils, 74.8%; lymphocytes, 19.3%; and platelets, 448,000/μL. Serum biochemistries, including amylase and lipase, were all within normal limits. Remarkable in his medical history were the presence of chronic alcoholic pancreatitis and gall bladder stone.

An ultrasound exanimation of the abdomen revealed a cystic lesion (about 7.3 cm in diameter) extending from the pancreas adjacent to the diaphragm. Endoscopic retrograde cholangiopancreatography (ERCP) was performed and revealed a normal common biliary duct without filing defect, no juxtapapillar diverticulum, and no focal stenosis of the biliary tract. Chest radiography revealed a well-defined soft tissue density mass in the lower mediastinum around the left paravertebral body area (Figure 1). The lateral chest radiograph view showed a mediastinal mass behind the heart shadow abutting the diaphragm (Figure 2). The differential diagnosis from the

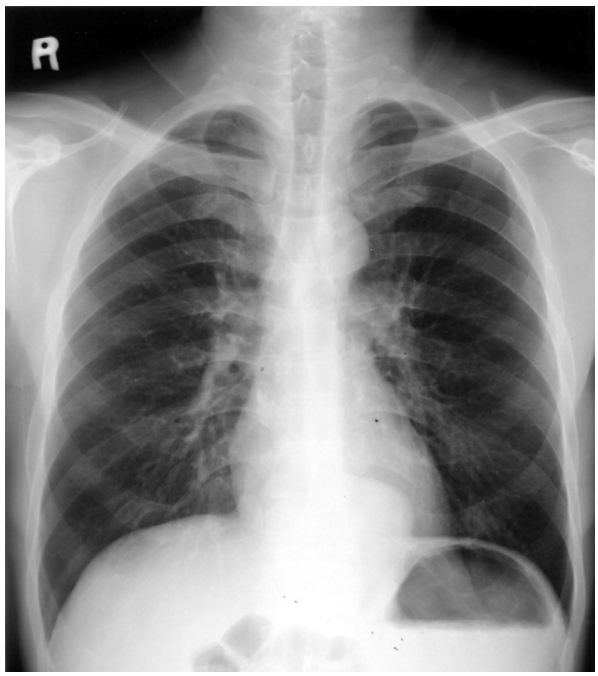

Fig. 1. Chest posteroanterior view showing a well-defined soft tissue mass in the lower mediastinum by the left paravertebral body area.

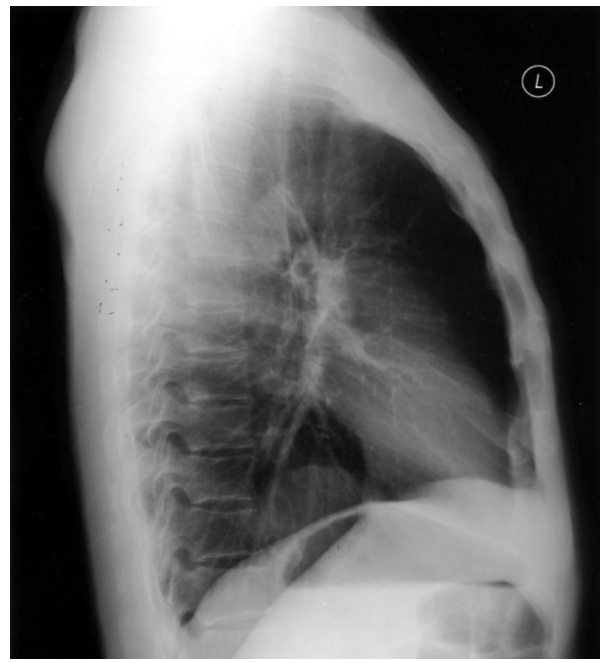

Fig. 2. Chest lateral view showing a lower mediastinal mass behind the heart shadow abutting the diaphragm.

chest radiographic image included posterior mediastinal tumor, esophageal duplication cyst, bronchogenic cyst, esophageal varices, hematoma, Bochdalek's hernia and intrathoracic aortic aneurysm. Abdominal computed tomography (CT) scan revealed pancreatic parenchymal atrophy, duct dilation (up to 1.0 cm) and calcification due to chronic pancreatitis. A large low-attenuation cystic mass was found in the lower mediastinum (Figure 3). The differential diagnosis included abscess, esophageal duplication cyst, bronchogenic cyst, and pancreatic cyst. Reformatted oblique coronary CT scan revealed that the pseudocyst extended from the pancreas to the lower mediastinum with a thick wall (Figure 4).

Mediastinotomy disclosed a protruding mass in the posterior mediastinum, near the diaphragm, heart and spine. Pathologic examination of the biopsy specimen revealed proliferative granulation tissue with foamy histiocytic and leukocytic infiltrates, fibrosis, and congestion, which were compatible with a pseudocyst (Figure 5-6). Based on the ultrasound exanimation, CT and pathology, pancreatic pseudocyst was diagnosed. He received external drainage and was discharged in 4 days. At the follow-up outpatient clinic within 1 month after discharge, no recurrent symptom was found.

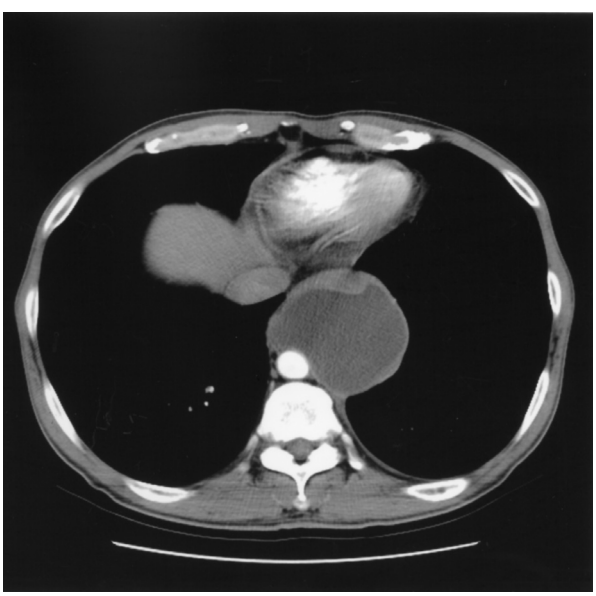

Fig. 3. CT scan showing a thick-walled, cystic, low-attenuation mass in the posterior mediastinum.

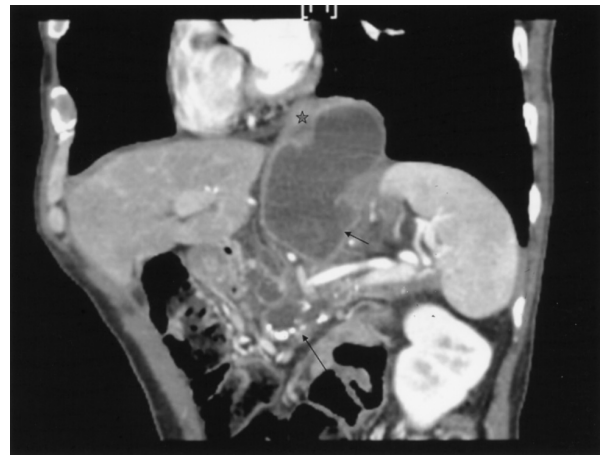

Fig. 4. Reformatted oblique coronary CT scan reveals atrophy of the pancreas, dilated pancreatic duct, and some calcification of the pancreatic parenchyma indicating chronic pancreatitis (long arrow). Pseudocyst extending from the pancreas to the lower mediastinum with a thick wall (short arrow); the pseudocyst compressed the esophagus (star).

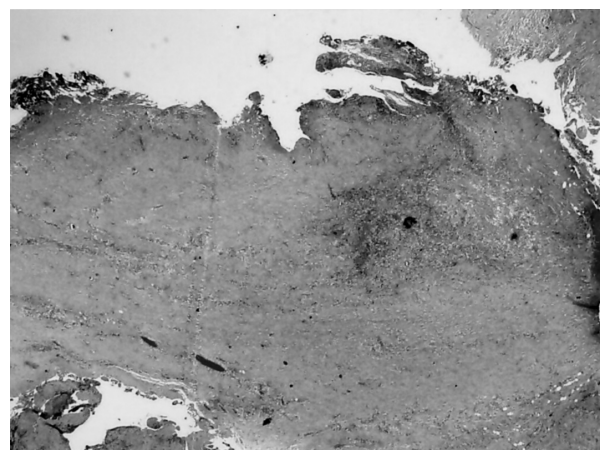

Fig. 5. Aggregates of foamy histiocytes and leukocytic aggregates are seen within the cystic wall.

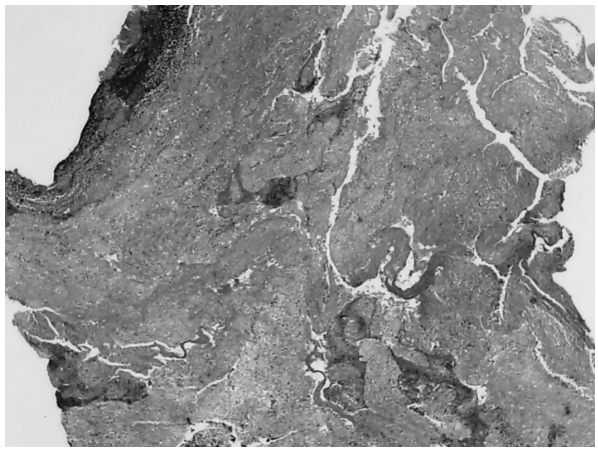

Fig. 6. The necrotic debris is recognized as eosinophilic amorphous material with fibrinous exudate.

Discussion

The approach to the diagnosis of a mediastinal mass is generally guided by its location. Neural tumors are the most common masses in the posterior mediastinum. In this patient, CT presented a cystic mass formation, for which the potential diagnosis can include bronchogenic cysts (50~60%), duplication esophageal cyst (12%), neurenteric cysts, abscess, pericardial cyst, thoracic meningocele and pancreatic pseudocyst [3]. Based on the ultrasound exanimation, CT and pathology reports, mediastinal pseudocyst was diagnosed.

Mediastinal pancreatic pseudocysts are a rare, with only about 40 to 50 cases reported in the English literature of the last 2 decades [4-10]. Approximately 85% of cases of pancreatic pseudocyst are located in the body or tail of the pancreas, and 15% in the head [11]. Mediastinal extension results from migration of pancreatic secretions and inflammatory products through the esophageal or aortic hiatus, or a defect of the diaphragm, appearing in the lower posterior mediastinum [12]. Since a pancreatic pseudocyst tends to extend through the esophageal or aortic hiatus, in most cases it is located in the posterior mediastinum. However, anterior (due to extension through the foramen of Morgagni) and middle mediastinal pseudocysts due to diaphragmatic erosion have been reported [7].

Usually, patients suffering from pancreatic pseudocyst have a history of alcohol abuse, recurrent pancreatitis, or abdominal trauma or surgery; our patient presented the characteristics of alcohol abuse, which contributed to the recurrent pancreatitis [12]. Symptoms may be present for weeks or months and vary greatly in severity. Pleural effusions may be present and can be distinguished by their high amylase content [7]. The serum amylase level is elevated in 75% of patients at some point during their illness and may fluctuate markedly [11]. The diagnosis is proved by X-ray examinations: chest radiography, computed tomography of the chest or upper abdominal component; magnetic resonance imaging (MRI); ERCP; esophago-gastroduodenum scanning of the liver; and transthoracic puncture of the cyst with laboratory examination (analysis of the cyst liquid) [13]. CT scan and ultrasonography are the best diagnostic examinations for pseudocysts.

Spontaneous resolution of mediastinal pseudocysts has been reported [9], but most cases were treated by surgical procedures. A pseudocyst that does not resolve spontaneously may lead to serious complications, such as (1) pain caused by expansion of the lesion and pressure on the viscera, (2) rupture, (3) hemorrhage, and (4) abscess. Rupture of a pancreatic pseudocyst is a particularly serious complication. Mortality rates range from 14%, if the rupture is not associated with hemorrhage, to over 60%, if hemorrhage has occurred [11]. In a literature review, the number of reports of experience in treating mediastinal pancreatic pseudocyst was limited. It would seem

logical to apply the established treatment principle for an abdominal pancreatic pseudocyst. Traditionally, pancreatic pseudocysts have been managed surgically by resection or by external or internal drainage. Most cases have been treated by internal drainage of the abdominal component [10]. In this patient, the mediastinal pseudocyst was isolated and the patient underwent external drainage. Nowadays, radiographic and endoscopic techniques have been developed whereby pseudocysts can be drained nonoperatively [7, 14].

In summary, the radiographic appearance of mediastinal pancreatic pseudocysts, especially on posteroanterior (PA) or lateral chest radiographs, is non-specific, and usually presents as a posterior mediastinal mass. Although the most common posterior mediastinal masses are neurogenic tumors, mediastinal pancreatic pseudocyst should be included in the differential diagnosis, especially in patients who present abdominal pain, a medical history of recurrent pancreatitis, or alcohol abuse.

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胰臟僞囊腫以後縱膈腫瘤表現：病例報告

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縱膈腫瘤的診斷通常可藉由其所在位置來考慮，在後縱膈最常見的腫瘤為神經細胞腫瘤，胰臟偽囊腫以後縱膈腫瘤表現非常少見，最近二十年來英文文獻大約只有 40 到 50 個案被報告。通常縱膈腫瘤大多沒有症狀或以胸腔方面的症候表現，相對於此縱膈胰臟偽囊腫則常以腹痛和體重減輕來表現。

我們將報告一個 48 歲男性表現上腹持續悶痛四天合併最近一個月體重減輕三公斤的病例，其胸腔影像呈現後縱膈腫瘤，經重組電腦斷層影像發現一個厚壁的偽囊腫自胰臟沿伸到下縱膈腔。且縱膈切開術與病理的發現符合縱膈胰臟偽囊腫的診斷。後來這個病患接受胸外引流的手術後，經一個月門診的追蹤並沒有發現任何復發的症狀。*(胸腔醫學* ***2007; 22: 293-298)***

關鍵詞：胰臟偽囊腫，後縱膈腫瘤

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Pneumoconiosis in a Dental Technician Presenting with Interstitial Pneumonitis: A Case Report

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Pneumoconiosis is rarely seen among dental technicians, although they are exposed to various inorganic substances consisting mainly of the dust of heavy metals and chemicals in their occupational environment. It has been suggested that these substances are potential causes of pulmonary injury among these workers. Reports in the past have proposed a causal relationship among disease progression and the type of particles inhaled, duration of exposure, and the dose-response reactions. This phenomenon can be seen in the declining lung function, progression of respiratory symptoms, and even cancer formation in patients. We report a young man who was a dental technician with pneumoconiosis, manifesting initially with interstitial pneumonitis of unknown origin. This case highlights the likelihood that frequent exacerbations of occupational lung disease due to interstitial pneumonitis might be attributed to the rapid deterioration of lung function in this patient group. ***(Thorac Med 2007; 22: 299-304)***

Key words: dental technician, pneumoconiosis, occupational exposure, interstitial pneumonitis

Introduction

Pneumoconiosis is rarely seen among dental technicians, who are exposed to potentially hazardous occupational elements such as dust, metal alloys and chemical substances. Prolonged exposure to these elements will cause lung damage and progress to fibrosis. We report a dental technician presenting with interstitial pneumonitis and pneumoconiosis that was diagnosed by tissue sample.

Case Report

A 34-year-old man had been well until 6 months before admission, when he began to experience exertional dyspnea. Symptoms subsided upon resting for 5~10 minutes and he remained fine for the rest of the day. Two months later, the patient visited a primary care physician because of progressive exertional dyspnea. However, these symptoms were not relieved with medication. During the past months prior to this admission, his breathlessness became worse and he was not able to climb up 3 flights of stairs. In addition, he complained of productive cough with whitish sputum. The patient did not have fever, rhinorrhea, arthralgia, or skin rash.

About 2 months before admission, the patient developed poor appetite, weight loss of 10 kilo-

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grams, and worsened dyspnea. He visited a pulmonologist at an outpatient clinic, where chest radiology (Figure 1) showed decreased lung volume with diffuse interstitial infiltration in the bilateral lung fields. The patient was referred to a tertiary medical center for further work-up. He had worked as a dental technician at a dental laboratory for 7 years, beginning when he was a 17-year-old. He would work in shifts of more than 8 hours a day, on average, without respiratory protection. The work area was described by the patient as a closed environment without either adequate ventilation or a local exhaust system. In addition, he smoked a pack of cigarettes per day for 22 years, and had quit smoking 1 year previously. He denied any travel history or close contact with animals.

On admission, the cough and dyspnea persisted. The vital signs were: body temperature, 37.2ºC; pulse rate, 92 beats/min; respiratory rate, 24 breaths per minute; and blood pressure, 104/80 mmHg. Physical examination showed bilateral diffuse coarse crackles. The hemogram revealed a red blood cell count of 5.64 M/μL, hemoglobin of 16.3 g/dl, platelet count of 297 K/μL and white blood cell count of 8.34 K/μL. The results of blood biochemistry were as follows: albumin, 4.8 g/dl; blood urea nitrogen, 9.6 mg/dl; serum creatinine, 1.0 mg/dl; sodium, 136 mmol/L; potassium, 4.3 mmol/L; asparate aminotransferase (AST), 24 U/L; alanine aminotransferase (ALT), 18 U/L; total bilirubin, 1.52 mg/dl; lactate dehydrogenase, 464 U/L, and C-reactive protein, 0.25 mg/dl. The immunological profile for antinuclear antibody (ANA) and rheumatoid factor (RF) were both negative.

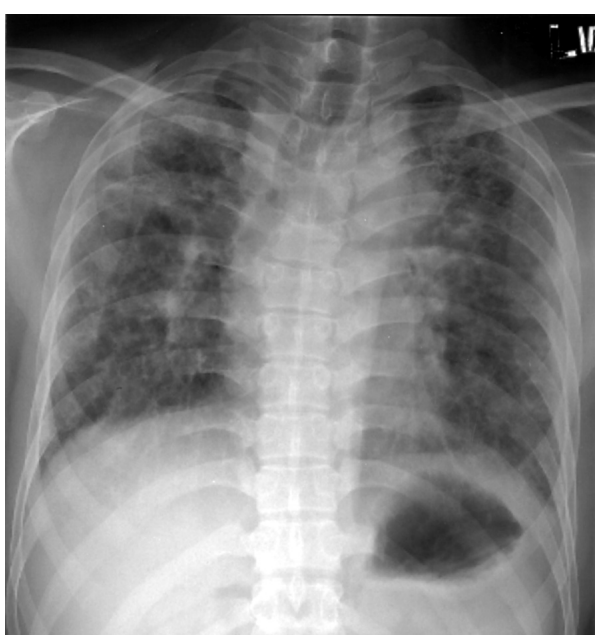
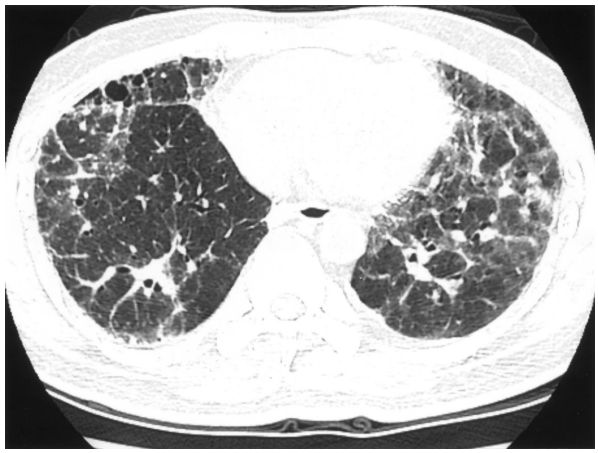
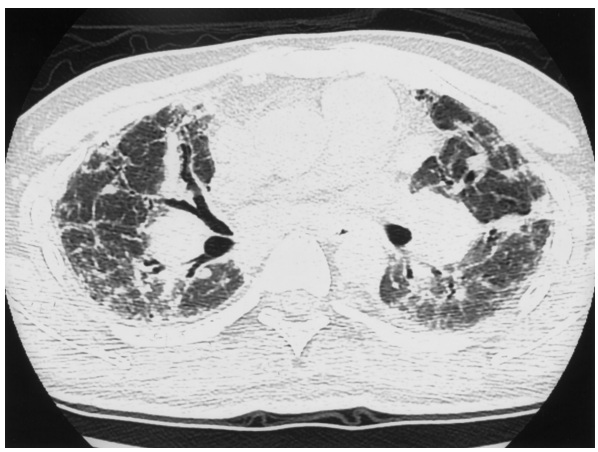


Fig. 1. Chest radiography showing decreased lung volume and diffuse haziness interspersed with fibrotic bands over bilateral lung fields.

The pulmonary function test results were: forced vital capacity, 1.07 L (24.4% of predicted value [pred]); FEV1, 1.01 L (26.5% of pred); total lung capacity, 1.81 L (30.8% of pred); and PEFR, 4.62 L/S (46.4% of pred). Severe impairment of diffusion capacity was also found (9.17 ml/min/mmHg, STPD, 29.35% of pred). Arterial blood gases in room air were: pH 7.393; arterial oxygen tension (PaO2), 53.6 mmHg; arterial carbon dioxide tension, 41.2 mmHg; sodium bicarbonate, 25.4 mEq/l; and oxygen saturation, 87%. Chest computed tomography revealed bilateral diffuse interstitial lung changes with reticulation (Figure 2A) and ground glass opacity at the peripheral and subpleural regions (Figure 2B). Fiberoptic bronchoscopy showed no endobronchial lesion, and a transbronchial lung biopsy was done from the right posterior bronchus. The pathology results disclosed scattered giant cells engulfing foreign bodies (Figure 3). The acid fast and Gomori methenamine silver (GMS) stains were negative for microorganisms. The bronchial washing was negative for malignant cells. Sputum cultures for mycobacteria, aerobic, anaerobic and fungal microorganisms were all negative.



(A)



(B)

Fig. 2. Chest computed tomography of the lung window, revealing: (A) bilateral diffuse interstitial parenchymal change with predominant reticulation, and (B) ground glass opacity at the peripheral and subpleural regions, more prominent at the upper lung zones, and pleural thickening also seen more evidently at the upper lung fields with prominent mediastinal and hilar lymphadenopathy.

Considering the patient's occupational history, and radiographic and pathologic findings, pneumoconiosis with interstitial pneumonitis was suspected.

The patient received methylprednisolone 80 mg a day (2mg/kg/day). The dyspnea and oxygenation desaturation improved gradually with PaO2 of 74.3 mmHg in room air. However, the

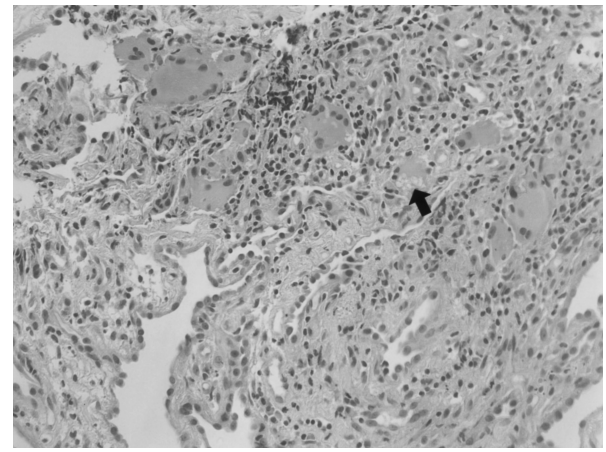


Fig. 3. The transbronchial lung biopsy specimen showing lymphocyte infiltration in the interstitium with an aggregation of scattered foreign body giant cells (arrowhead) containing crystal-like material. (H X E, 66X, original magnification)

patient complained of a sudden onset of substernal dull pain on the 14th day of his hospital stay. The pain extended upwardly to the entire sternum and lower neck bilaterally. Chest radiography showed pneumopericardium and pneumomediastinum. High-concentration oxygen was given to relieve the symptoms. In addition, elevated alamine transaminase (ALT: 232 U/L) was noted. Viral hepatitis markers showed positive for HBsAg, and negative for anti-HBs antibody and anti-HCV antibody; Steroid-induced hepatitis B flare was suspected. Methylprednisolone was tapered to oral prednisolone with a maintenance dosage of 20 mg per day. The liver function test results decreased back to the level of chronic hepatitis (AST: 24 U/L and ALT: 105 U/L). The patient was discharged with follow-up at the outpatient department.

Discussion

A dental technician with pneumoconiosis due to exposure to silicosis was first reported in 1939 [1]. With advancements in science and techno-

logy, more materials have been incorporated in the manufacture of dental prostheses, such as silica, aluminum, asbestos fibers, and non-precious metal alloys which include beryllium, cobalt, chromium, molybdenum and nickel [2-3, 7-9]. Dental technicians might possibly be exposed to and inhale these toxic substances in the laboratory, causing dermatological lesions, pulmonary diseases, neurotoxicity and malignancy [3]. Because of their exposure to a wide variety of inorganic dusts, it is difficult to identify a specific causal agent [1-2, 6, 11].

The incidence of this disease was related to the dose-response relationships, including the duration of exposure and type of particles [1-3, 9]. Epidemiological studies have found that the prevalence of pneumoconiosis in dental technicians with 20 or more years of exposure was significantly higher than in those with less than 20 years of exposure (16.7 *vs*. 1.4%) [1, 8-10]. Many studies have revealed the factors that increase the incidence of disease, such as poor airway protection equipment, and substandard ventilation or local exhaust systems. [2] The pathogenesis of dental technician's pneumoconiosis is complex. Many inorganic substances used in dental laboratories for abrasions and impressions were noted to contain a fibrogenic compound, such as Co-Cr-Mo or Ni. [4-5, 8, 11]. In cases of severe interstitial fibrosis, continual progression of the disease is observed, even after cessation of exposure. It has been suggested that cobalt-induced fibrosis with lymphocyte stimulation is associated with an immunological base [12-15]. In addition, the release of macrophage-derived mediators from macrophage stimulation may also cause fibrosis of the lung [12]. As with our case, some patients have a disease progression which presents initially with interstitial pneumonitis of unknown origin [12-15].

Chest roentgenograms have revealed diffuse bilateral micronodular and reticulonodular infiltration located mainly in the upper lobes [4-5, 11]. Computed tomography scans showed extensive fibrotic change, millimetric nodular densities, emphysematous blebs in the upper lung, and compensatory emphysema in the lower lungs [4, 11]. Patients present with respiratory symptoms, such as chronic productive cough and dyspnea [2]. Although the BAL (broncho-alveolar lavage) fluid was found to have a normal cell distribution, the macrophages were dust-laden. BAL fluid is not diagnostic for all cases, so open lung biopsy remains the gold standard for the diagnosis of pneumoconiosis. The specimens could be examined by Energy Dispersive X-ray Spectrometer (EDS) and Scanning Electron Microscopy (SEM) for mineralogical and metal content analysis [5, 7]. Evaluation of the lung function tests presented a mixed type (restrictive and obstructive pattern) or a restrictive type pulmonary function test [1, 5-7, 10]. The diffusion capacity for carbon monoxide was also decreased [2, 6].

To date, there are no reports correlating the details of dental technicians' pneumoconiosis and its prognosis. Lung function was more affected in cigarette smokers than in non-smokers and ex-smokers [1, 5, 9]. The consequences were highly variable and may have depended on the total amount of dust inhaled. It is suggested that early diagnosis with periodic radiological surveys may be of value to prevent overt disease [4].

Conclusion

Pneumoconiosis in dental technicians, if developed, can cause marked morbidity and an impaired quality of life. It also presents with ongoing inflammation and fibrosis, even after the

exposure has ceased. Reduced hazardous dusts within a well-ventilated area, or local exhaust ventilation, adequate airway protection, decreased exposure periods, and the replacement of dangerous materials (such as silica, heavy metal, beryllium) should be seriously taken into consideration to prevent occupationally related disorders in these workers [1, 3, 9, 11].

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以間質性肺炎爲表現的牙體技術員塵肺症：一病例報告

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塵肺症很少發生於牙體技術人員。由於他們獨特的工作環境本質，這些技術員常被暴露在各種各樣的無機物質中，主要包括一些重金屬和化學製品之粉塵。這些物質目前認為是造成牙體技術人員肺部傷害的潛在原因。過去的研究報告指出這類塵肺症發生的原因與吸入粉塵的種類、暴露的時間與劑量有關。並且會導致肺功能降低、呼吸症狀惡化乃至於癌症的形成。我們報告一個病例以不明原因間質性肺炎為表現，經診斷為牙體技術員塵肺症。本案例點出牙體技術員塵肺症會以間質性肺炎的反覆性發作來表現，而導致病人肺功能的急速惡化。*(胸腔醫學* ***2007; 22: 299-304)***

關鍵詞：牙體技術人員，塵肺症，職業暴露，間質性肺炎

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