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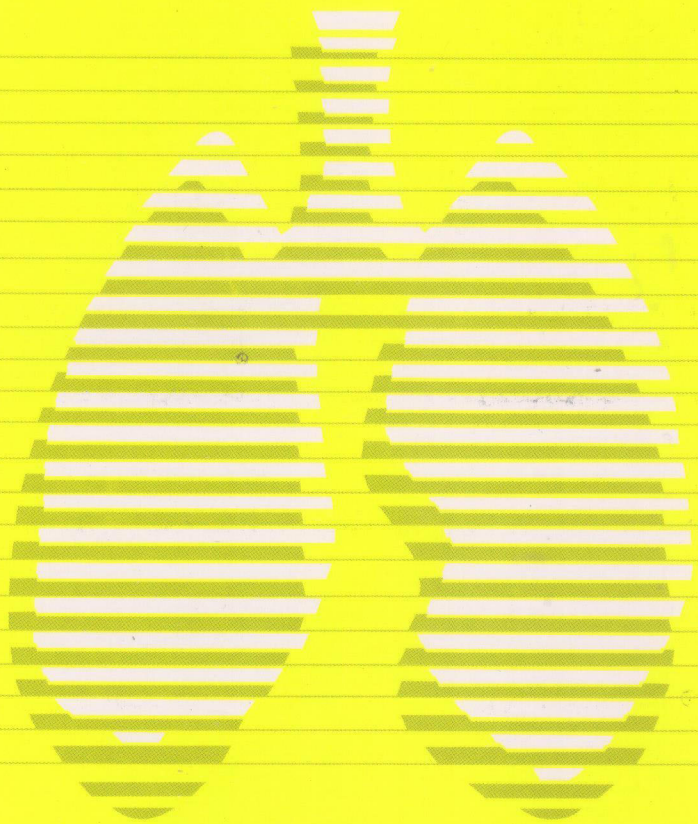

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Orginial Articles

Case Reports

Obstructive Sleep Apnea in Chronic Kidney Disease Patients

Chun-Chi Chang, Ching-Hsiung Lin, Bin-Chuan Ji, Jen-Ho Wen

Introduction: A high prevalence of sleep apnea, ranging from 45% to 80%, has been reported in dialysis patients. However, there are few data available on sleep-disordered breathing (SDB) in patients with dialysis-independent chronic kidney disease (CKD). The aim of this study was to identify the objective polysomnographic (PSG) features of consecutive CKD patients referred from the Nephrology Department that were clinically suggestive of sleep apnea.

Methods: From July 2002 to June 2005, 40 patients (24 males and 16 females) with CKD and clinical features suggestive of sleep apnea were referred from the Nephrology Department to the pulmonary physicians at Changhua Christian Hospital. Sleep history, the Epworth Sleepiness Scale (ESS) questionnaire, and in-hospital, attended full-night PSG were evaluated.

Results: Thirty-seven of 40 patients (92.5%) had an apnea-hypopnea index (AHI) of 5 or more, and were categorized as subjects with obstructive sleep apnea (OSA). The patients with a creatinine clearance rate (C_{CR}) ≤15ml/min had a shorter total sleep time (259.42±100.87 min vs. 359.09±115.35 min, *p*=0.0063), more wake time (83.02±62.51 min vs. 46.00±40.15 min, *p*=0.043), and poorer sleep efficiency (68.23±21.85% vs. 82.73±16.32%, *p*=0.0294) than those with C_{CR}>15 ml/min. Although the AHI was similar between the 2 groups, the mean time of apnea-hypopnea events was shorter in the group of patients with C_{CR}≤15 ml/min.

Conclusion: OSA clinically suggestive of SDB was very common in the CKD patients referred from the Nephrology Department, irrespective of CKD stages. Therefore, CKD patients with symptoms and signs suggestive of sleep apnea should be actively surveyed, especially those in ESRD. ***(Thorac Med 2007; 22: 153-161)***

Key words: obstructive sleep apnea, polysomnography, chronic kidney disease

Introduction

Chronic kidney disease (CKD) is a major public health problem and is associated with poor health outcomes and high medical expenditures. In the United States, more than 20 million adults have CKD [1]. In the general population, the prevalence estimates of obstructive sleep apnea (OSA) range from 2% to 4% [2]. A higher prevalence of sleep disorders, ranging from 45% to 80%, has been reported in dialysis patients [3-6]. Many factors may contribute to OSA in patients with CKD, including comorbidities such as obesity and diabetes mellitus, and renal failure

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itself. The coexistence of untreated OSA and CKD may exacerbate the cardiovascular complications of end-stage renal disease (ESRD), which are the leading causes of morbidity and mortality in these patients [7]. OSA also produces excessive daytime sleepiness and impairs neurocognitive function, which influences renal rehabilitation in ESRD patients [8]. Male gender, older age, chronic metabolic acidosis, anemia, endogenous opioids, and several cytokines have been shown in various studies to be associated with sleep disorders in dialysis patients [9-13].

The prevalence of sleep apnea appears to be similar in patients with ESRD before dialysis is started, and in those who are treated with hemodialysis or peritoneal dialysis [14-15]. However, there are few data available on sleep-disordered breathing (SDB) in patients with dialysis-independent CKD. Differences in renal functional impairment, volume status, metabolic derangement or dialysis may all have an influence on SDB. The aim of this study was to identify the objective polysomnographic (PSG) features of consecutive CKD patients referred from the Nephrology Department that were clinically suggestive of sleep apnea.

Methods

Patient Population

From July 2002 to June 2005, 40 patients (24 males and 16 females) with CKD and clinical features suggestive of sleep apnea were referred from the Nephrology Department to the pulmonary physicians at Changhua Christian Hospital for clinical assessment and overnight PSG. All the patients had a history of habitual snoring, daytime sleepiness, the partner reporting gasping or choking during sleep, or a combination of these symptoms. History-taking and physical examination, including weight, height, blood pressure and neck circumference, were recorded. All patients underwent in-hospital, attended PSG using a digital polygraph system (Healthdyne Alice 4, USA). The electroencephalogram (C3A2, C4A1, O1A2, and O2A1) was based on the 10-20 international electrode placement system. Right and left electro-oculogram and chin and leg electro-myogram were 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 (SaO2) and heart rate. Daytime sleep function was assessed subjectively by means of the Epworth Sleepiness Scale (ESS) questionnaire [16]. A total of more than 10 points was assumed to be a sign of excessive daytime sleepiness. In addition to PSG and ESS, serum creatinine and hemoglobin were measured, and whether the patient was receiving dialysis or not was also recorded.

The abnormal respiratory events during sleep consisted of apnea, defined as a 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 more than 10 seconds, a decrease of less than 50% in the amplitude of breaths associated with an arousal, or a decrease in oxygen saturation more than 3%. Obstructive apnea or hypopnea was 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 was defined as simultaneous cessation or reduction of airflow and thoraco-abdominal motion. The apnea-hypopnea index (AHI) was defined as the ratio of the number of episodes of apnea and hypopnea to total sleep time (hour). The AHI 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) [17]. Sleep efficiency was defined as the total sleep time expressed as a proportion of the total sleep duration. CKD was defined as either kidney damage or a glomerular filtration rate (GFR) below 60 ml per minute per 1.73 m² for 3 months or more. Kidney damage was defined as pathologic abnormalities or markers of damage, including abnormalities in blood or urine tests or imaging studies [18].

Classification of Patient Groups

Based on the estimated creatinine clearance rate (C_{CR})*, these patients were classified into 2 groups, C_{CR}>15 ml per minute per 1.73 m² (stage I-IV CKD) and C_{CR}≤15 ml per minute per 1.73 m² (stage V CKD).

* Cockcroft-Gault formula for estimated C_{CR} [19]:

{[(140-age) × weight (kg)]/ [72 × serum creatinine (mg/dl)]} (× 0.85 for women)

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). A *p* value less than 0.05 was considered statistically significant.

Results

The enrolled patients included 24 males (60%) and 16 females (40%), ranging from 20 to 87 years of age. Table 1 summarizes the demographic data and laboratory findings of the 2 groups

Table 1. Demographic Data and Laboratory Findings [Mean ± SD or n (%)]

	Total (n=40)	C_{CR}≤15 ml/min (n=24)	C_{CR}>15 ml/min (n=16)	*p*-value
Male, n (%)	24 (60.00)	15 (62.50)	9 (56.25)	0.6926
Age, yr	55.28 ± 14.73	51.42 ± 16.31	61.06 ± 9.85	0.0253
Weight, kg	73.81 ± 12.78	70.74 ± 11.26	78.42 ± 13.87	0.0618
Height, cm	162.48 ± 8.06	163.81 ± 8.41	160.47 ± 7.31	0.2028
BMI, kg/m²	27.92 ± 4.34	26.21 ± 2.70	30.49 ± 5.10	0.0057
SBP, mmHg	148.69 ± 21.99	154.83 ± 24.67	139.88 ± 13.85	0.0212
DBP, mmHg	79.15 ± 15.82	80.83 ± 17.16	76.75 ± 13.83	0.4359
Neck circumference, cm	38.68 ± 3.60	38.04 ± 3.69	39.59 ± 3.36	0.1890
ESS	11.05 ± 4.95	11.26 ± 4.51	10.73 ± 5.71	0.7531
Serum creatinine, mg/dl	7.52 ± 5.77	11.15 ± 4.56	2.09 ± 1.47	<0.0001
Hemoglobin, g/dl	10.48 ± 2.26	9.14 ± 1.20	12.62 ± 1.88	<0.0001
Dialyzed patients, n (%)	19 (47.50)	17 (70.83)	2 (12.50)	<0.0001
Diabetes mellitus, n (%)	14 (35.00)	6 (25.00)	8 (50.00)	0.1420
Hypertension, n (%)	26 (65.00)	17 (70.83)	9 (56.25)	0.0802
CAD, n (%)	3 (7.50)	1 (4.16)	2 (12.50)	0.3729

C_{CR}: creatinine clearance rate; BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; ESS: Epworth Sleepiness Scale; CAD: coronary artery disease

of CKD patients with features clinically suggestive of sleep apnea. The mean age of patients with C_{CR}≤15 ml/min was younger than that of those with C_{CR}>15 ml/min (51.42±16.31 years vs. 61.06±9.85 years, p=0.0253). Smaller body mass index (BMI; 26.21±2.70 kg/m² vs. 30.49±5.10 kg/m², p=0.0057), higher systolic blood pressure (154.83±24.67 mmHg vs. 139.88±13.85 mmHg, p=0.0212), and lower hemoglobin (9.14±1.20 g/dl vs. 12.62±1.88 g/dl, p<0.0001) were also found in the group of patients with stage V CKD. Two patients with C_{CR}>15 ml/min received regular hemodialysis because of diabetic nephropathy with oliguria and rapidly progressive glomerulonephritis. The differences in the body weight, body height, diastolic blood pressure, neck circumference and ESS did not achieve significance between the 2 groups of renal patients. In addition, comorbidities such as diabetes mellitus, hypertension and coronary artery disease seemed to show no significant difference between the 2 groups.

Overnight PSG was remarkably different between the 2 groups of renal patients (Table 2). The patients with C_{CR}≤15 ml/min had shorter total sleep time (259.42±100.87 min vs. 359.09± 115.35 min, p=0.0063), more wake time (83.02± 62.51 min vs. 46.00±40.15 min, p=0.043), and poorer sleep efficiency (68.23±21.85 % vs. 82.73±16.32 %, p=0.0294) than those with C_{CR}> 15 ml/min. In addition, the duration of REM sleep was shorter in stage V CKD patients. There was no significant difference in the deepest sleep duration (stages 3 and 4 of non-REM sleep) between the 2 groups. The periodic leg movement (PLM) index was higher in the group of patients with C_{CR}≤15 ml/min than in the other group (49.65 vs. 8.33, p=0.0069), but the arousal index of the 2 patient groups was similar. The heart rate of patients with C_{CR}≤15 ml/min was more rapid than

Table 2. Polysomnographic Data of Renal Patients

	Total (n=40)	C_{CR}≤15 ml/min (n=24)	C_{CR}>15 ml/min (n=16)	p-value
TST, min	299.29 ± 116.46	259.42 ± 100.87	359.09 ± 115.35	0.0063
SE, %	74.03 ± 20.88	68.23 ± 21.85	82.73 ± 16.32	0.0294
SOL, min	15.73 ± 19.92	16.73 ± 23.61	14.22 ± 13.17	0.6696
ROL, min	130.47 ± 80.45	147.00 ± 82.98	108.78 ± 73.94	0.1550
REM.SPT, min	44.26 ± 31.77	33.27 ± 22.27	60.75 ± 37.15	0.0143
REM.SPT, %	17.34 ± 39.36	19.87 ± 50.76	13.54 ± 7.14	0.5529
S1.SPT, %	27.99 ± 17.89	27.88 ± 17.74	28.16 ± 18.70	0.9619
S2.SPT, %	38.63 ± 18.71	35.09 ± 18.48	43.93 ± 18.34	0.1454
S3.SPT, %	2.25 ± 4.11	2.03 ± 2.62	2.58 ± 5.75	0.7249
S4.SPT, %	0.22 ± 0.94	0.35 ± 1.20	0.03 ± 0.10	0.2068
Heart Rate/WK	73.74 ± 15.86	79.07 ± 15.84	65.74 ± 12.48	0.0074
Heart Rate/REM	72.67 ± 13.51	76.45 ± 12.53	67.37 ± 13.43	0.0452
Heart Rate/NREM	74.13 ± 14.03	79.15 ± 12.24	66.59 ± 13.46	0.0041
Arousal index	43.39 ± 27.22	43.85 ± 23.25	42.69 ± 33.12	0.8968
PLM index	32.70 ± 54.32	49.65 ± 64.83	8.33 ± 15.42	0.0069

TST: total sleep time; SE: sleep efficiency, SOL: sleep onset latency; ROL: REM onset latency; REM. SPT: REM sleep period time; PLM: periodic leg movements

that of those with C_{CR}>15 ml/min, especially when patients were awake or during non-REM sleep. PLMs were present in 57% of patients and significantly higher in patients with stage V CKD.

AHI, maximal desaturation level and episodes of snoring in the 2 groups are summarized in Table 3. Mean AHI during total sleep time was 40.15±29.67 in the study group. Although AHI and maximal desaturation level was similar between the 2 groups, the mean time of apnea-hypopnea events was shorter in the group of patients with stage V CKD.

Table 4 shows that 37 of 40 patients (92.5%) had an AHI of 5 or more and were categorized as subjects with OSA; among those, 21 (87.5%) were in the C_{CR}≤15 ml/min group and 16 (100%) in the other group. There was no difference in the distribution of severity of OSA in these 2 groups. One patient in the C_{CR}>15 ml/min group with a periodic breathing pattern on PSG was diagnosed with central sleep apnea.

Table 4. AHI Gradient of Renal Patients

AHI	C_{CR}≤15 ml/min (n=24)	C_{CR}>15 ml/min (n=16)	*p*-value
< 5.0	3 (12.50)	0 (0.00)	0.1678
5.0 ~ 14.9	2 (8.33)	5 (31.25)	
15.0 ~ 29.9	4 (16.67)	2 (12.50)	
≥ 30.0	15 (62.50)	9 (56.25)	

Discussion

This study found that OSA was very common in CKD patients with symptoms clinically suggestive of SDB who were referred from the Nephrology Department, irrespective of CKD stages. Early recognition of sleep apnea in CKD patients is important, due to its association with cardiovascular morbidity, including hypertension, cardiac ischemia, arrhythmia, left ventricular hypertrophy and sudden death [20]. Sleep disorders, ranging from 45% to 80%, have been reported in dialysis patients. Even after exclusion of patients with symptom of OSA or with co-morbidities predisposing to OSA, the prevalence of SDB was still around 50% in ESRD patients [6]. Our study population was selected from those who had specific sleep complaints, so these results cannot be extrapolated to general CKD patients. SDB prevalence in nondialyzed CKD patients remains unknown. Markou found that nondialyzed patients with chronic renal failure (C_{CR}<40 ml/min) have a much higher prevalence (54.3%, almost exclusively obstructive events) of SDB than middle-aged adults in the general population [21]. Therefore, sleep history and symptoms

Table 3. AHI, Oxygen Saturation and Snoring Records of Renal Patients

	Total (n=40)	C_{CR}≤15 ml/min (n=24)	C_{CR}>15 ml/min (n=16)	*p*-value
AHI, TST	40.15 ± 29.67	38.51 ± 26.47	42.60 ± 34.69	0.6752
AHI, NREM	39.40 ± 30.99	38.20 ± 27.09	41.21 ± 36.96	0.7673
AHI, REM	43.31 ± 32.19	38.48 ± 32.46	50.07 ± 31.65	0.2934
AHI Max, sec	51.55 ± 27.67	44.48 ± 23.01	61.72 ± 31.24	0.0544
AHI Mean, sec	19.77 ± 6.58	17.91 ± 5.22	22.54 ± 7.55	0.0273
Max SaO2, %	77.05 ± 11.50	78.79 ± 11.59	74.44 ± 11.21	0.2457
Snoring	1380.38 ± 1009.10	1157.58 ± 913.64	1714.56 ± 1081.23	0.0873

AHI: apnea-hypopnea index; Max SaO2: maximal desaturation level

suggestive of OSA should be inquired about in CKD patients, especially those in the ESRD group.

Common striking features of OSA were its male predominance, the middle age of its victims, and their being overweight in one study [22]. We obtained similar results in this study. The male-to-female ratio of our patients with OSA was 24: 13. Most of them were middle-aged, with a BMI more than 27 kg/m² and neck circumference more than 38 cm. Chronic renal failure is commonly related to hyponutrition, which may contribute to the low BMI. The negative finding of this phenomenon may be due to the small number of renal patients in our study, so we cannot be sure if a low BMI will interfere with the results of overnight PSG. Hypertension has been reported as an important factor related to OSA [23-26], but we could not find a relationship between AHI and blood pressure, since most of the patients were hypertensive under medical control, even with AHI≥30.

The ESS score correlates closely with the intensity of daytime sleepiness and the episodes of snoring and apnea during the night in the normal population [27]. The average ESS score was 11 points in our study. The prevalence of daytime sleepiness assessed by a standardized questionnaire has been 52-67% in patients on chronic hemodialysis [28]. Investigators suggest several possible explanations for this, including subclinical uremic encephalopathy, amino acid tyrosine deficiency, inflammatory cytokines released from neutrophils by the dialyzing membrane, and persistent melatonin during the day [29].

Patients with C_{CR}≤15 ml/min had poor sleep efficiency, and shorter REM onset latency and REM sleep time than patients with C_{CR}>15 ml/min. In sum, patients with ESRD had lower sleep quality than patients with renal insufficiency. It is reasonable to assume that uremic toxin, metabolic acidosis and comorbidities contribute to poor sleep quality in patients with ESRD, but until now no strong evidence has been provided in support of these hypotheses.

Although the severity of OSA seemed similar in patients with C_{CR}≤15 ml/min and in those with C_{CR} >15 ml/min, the mean time of apnea-hypopnea events was shorter in patients with C_{CR}≤15 ml/min. This could be explained by the fact that patients with stage V CKD had lower sleep quality and aroused more frequently, which contributed to the shorter duration of apnea-hypopnea events. In one study, non-diabetic ESRD patients (calculated GFR<15 ml/min/1.73m²) had a significantly higher AHI compared to those with less severe chronic renal failure [21]. In addition, the PLM index was higher in patients with C_{CR}≥15 ml/min in this study. In a recent retrospective study of a group of dialysis patients with sleep problems, periodic limb movements rather than sleep apnea predicted death [30]. Further study is required to investigate this novel predictor to mortality of ESRD patients.

In conclusion, OSA was very common in the CKD patients with symptoms clinically suggestive of SDB referred from the Nephrology Department, irrespective of CKD stages. Patients with ESRD had lower sleep quality than patients with renal insufficiency. Early recognition and treatment of this co-morbidity may facilitate renal rehabilitation and reduce cardiovascular complications. Therefore, it is recommended that CKD patients with symptoms and signs suggestive of SDB should be actively surveyed, especially those in the ESRD stage.

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阻塞性睡眠呼吸中止症與慢性腎臟病

張竣期　林慶雄　紀炳銓　溫仁和

前言：接受透析治療的患者曾被報告過有高盛行率(45~80%)的睡眠呼吸中止症，然而卻只有少數資料關於睡眠呼吸障礙在慢性腎臟病人接受透析前之情形。本研究之目的在於探討腎臟科中慢性腎臟病患者，因臨床疑似有睡眠呼吸中止症而轉診後，藉由睡眠呼吸多項偵測儀檢查的客觀結果進行討論分析。

方法：從 2002 年七月到 2005 年六月，彰化基督教醫院腎臟科共有 40 位(24 位男性和 16 位女性)臨床疑似有睡眠呼吸中止症的慢性腎臟病患者，被轉診到胸腔科做臨床評估和睡眠呼吸多項偵測儀檢查。詢問睡眠史、填寫嗜睡量表(Epworth Sleepiness Scale, ESS)問卷和住院接受整夜的呼吸多項偵測儀(polysomnography, PSG)檢查都被執行記錄。

結果：在 40 位病人中，有 37 位(92.5%)的呼吸中止指數(apnea-hypopnea index, AHI)大於 5 ，被歸類為患有阻塞性睡眠呼吸中止症。肌酐清除率(creatinine clearance rate, C_{CR})每分鐘小於等於 15 毫升的患者比起每分鐘大於 15 毫升的患者，有較短的全部睡眠時間(259.42±100.87 分鐘 vs. 359.09±115.35 分鐘，p=0.0063)、較多的清醒時間(83.02±62.51 分鐘vs. 46.00±40.15 分鐘，p=0.043)和較差的睡眠效率(68.23±21.85% vs. 82.73±16.32% ，p=0.0294)。雖然 AHI 在這兩群體中的分佈並無差異性，但是 C_{CR} 每分鐘小於等於 15 毫升的患者有較短的呼吸中止平均時間。

結論：腎臟科慢性腎臟病患者因臨床疑似有睡眠呼吸障礙而轉診，不論其慢性腎臟病分期，阻塞性睡眠呼吸中止症仍是非常普遍的。因此，對於疑似有睡眠呼吸中止症的慢性腎臟病患者，尤其是在末期腎臟病變時期，都應該要接受積極地調查。*(胸腔醫學 **2007; 22: 153-161**)*

關鍵詞：阻塞性睡眠呼吸中止症，睡眠呼吸多項偵測儀，慢性腎臟病

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Mixed Infection by Sulfamethoxazole-Resistant *Nocardia Asteroides* and Multidrug-Resistant *Mycobacterium Tuberculosis* — A Case Report

Cheng-Shiung Hsieh*, Shih-Ming Tsao*,**, Tzu-Chin Wu*

Pulmonary nocardiosis (PN) is an infrequent but severe infection that is found most commonly in immunocompromised patients. A correct diagnosis based on clinical and radiological features is difficult, since they are nonspecific. Combined PN and *Mycobacterium tuberculosis* (MTB) infection is even rarer. We report an unusual case of a patient with nephrotic syndrome who had received corticosteroid therapy and presented with multiple cavitary pulmonary nodules. Pus and sputum cultures yielded trimethoprim-sulfamethoxazole (TMP-SMX)-resistant *Nocardia asteroides*. Multidrug-resistant (MDR) MTB was formally reported 4 weeks later. The patient was finally treated with second-line anti-tuberculosis drugs. ***(Thorac Med 2007; 22: 162-167)***

Key words: pulmonary nocardiosis, *Mycobacterium tuberculosis*

Introduction

Pulmonary nocardiosis (PN) is an infrequent but severe infection that is found most commonly in immunocompromised patients [1]. Pulmonary infection by Nocardia may be difficult to diagnose based on clinical and radiological features, as these are not specific. Chest radiography (CXR) may demonstrate air-space consolidation, pulmonary nodules, and pleural effusion [1-4]. Multiple nodules and cavitation are commonly described in AIDS patients [3, 5-6], but uncommon in non-AIDS patients [1, 3]. Mixed infection with PN and tuberculosis is even rarer. We report an unusual case of a patient with nephrotic syndrome who had received corticosteroid therapy, and presented with trimethoprim-sulfamethoxazole (TMP-SMX)-resistant PN with multiple cavitary nodules, and mixed infection with multidrug-resistant (MDR) *Mycobacterium tuberculosis* (MTB).

Case Presentation

A 65-year-old man had been retired for 1 year, and spent his time gardening. He was admitted to our hospital 3 months previous due to proteinuria and progressive edema of the legs. CXR showed some fibrotic changes in the right upper lobe (Figure 1A). Inactive pulmonary tuberculosis was considered, since all 3 sets of sputum acid-fast stain yielded negative findings. Focal

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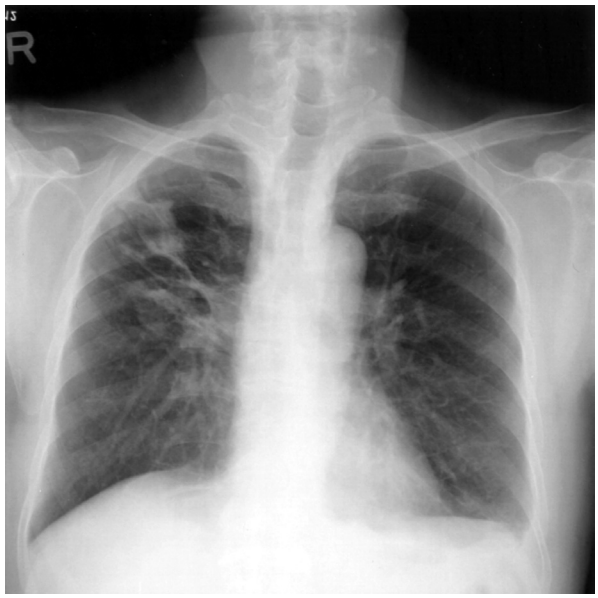
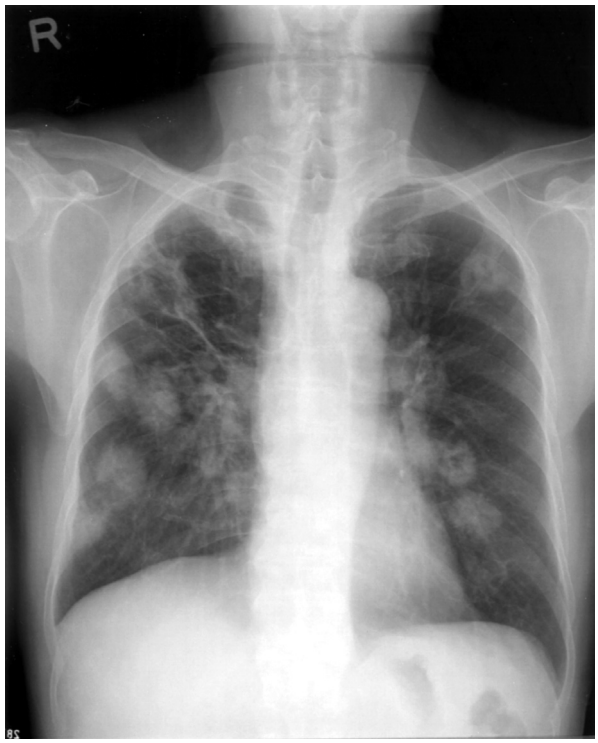


(A)



(B)

Fig. 1. (A) Initial CXR showing some fibrotic changes in the right upper lobe. (B) After receiving prednisolone therapy for nephrotic syndrome 3 months later, CXR showed newly grown multiple pulmonary cavitary nodules.

segmental glomerular sclerosis was proved by a renal biopsy. After a high-dose administration of intravenous prednisolone, the nephrotic syndrome improved. The patient then took prednisolone 40 mg daily and was followed up at the nephrology clinic.

After the appearance of productive cough with yellowish sputum, lasting 2 weeks, the patient then visited our chest clinic for help. CXR showed newly grown multiple pulmonary cavitary nodules (Figure 1B). The patient was admitted due to chills, shortness of breath, and hypotension. Leukocytosis with young cells was noted at admission, and the impression was community acquired pneumonia, favoring nocardiosis, based on the history of nephrotic syndrome with prednisolone treatment. We chose intravenous antibiotics with Septrin (400 mg sulfamethoxazole and 80 mg trimethoprim/amp) 3 amp twice daily to cover the Nocardia infection; and Augmentin 1200 mg (amoxicillin 1000 mg and clavulanic 200 mg) 3 times daily combined with Exacin

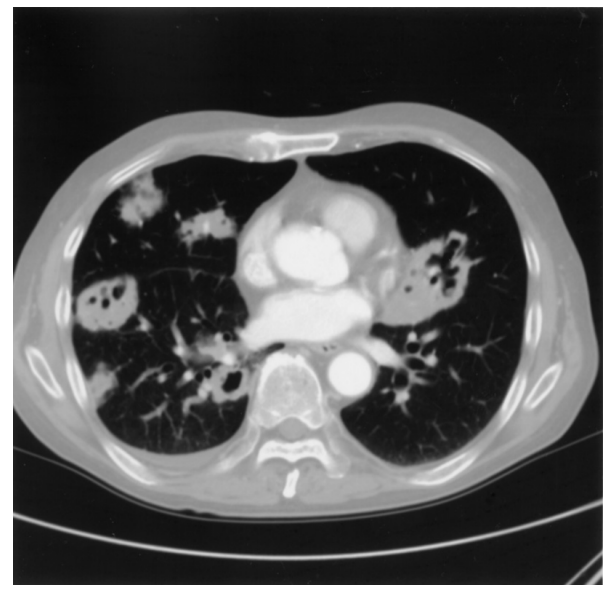
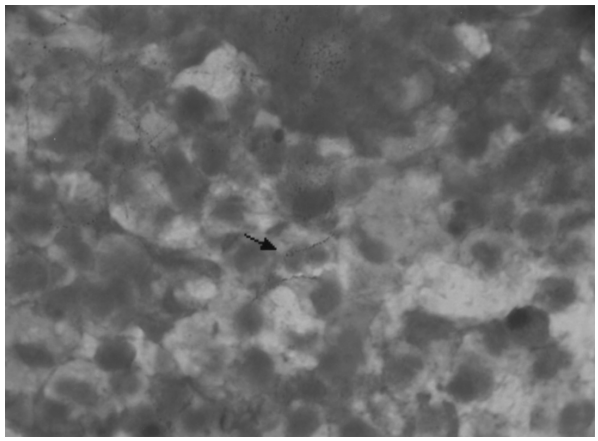
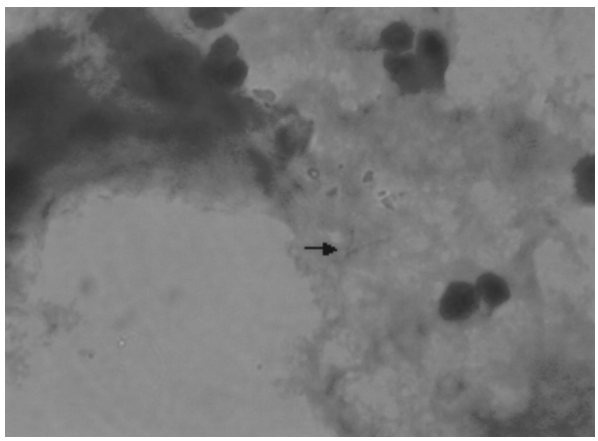


Fig. 2. Chest CT scan showing 2-3 cm sized multiple cavitary nodules in both lungs.



(A)



(B)

Fig. 3. (A) Gram stain from pus revealed Gram positive branching bacilli. (B) Acid-fast stain from pus showed a weakly positive finding.

(isepamicin) 400 mg daily to cover any other bacterial pathogen infection, as well as Nocardia infection. Chest CT scan showed 2-3-cm-sized multiple cavitary nodules in both lungs (Figure 2). Pus culture from percutaneous transthoracic needle aspiration (PTNA) revealed Gram-positive branching bacilli (Figure 3A), and acid-fast stain showed a weak positive finding (Figure 3B). Both pus and sputum cultures yielded TMP-SMX resistant *Nocardia asteroides*. TMP-SMX was still used after repeated discussion with other specialists, since there was no consensus on NCCLS (National Committee Clinical Laboratory Standards) breakpoints to the minimum inhibitory concentration (MIC) of antimicrobials for Nocardia. Administration ease, using the oral form, and cost efficiency were also considered in the clinical decision. After 3 weeks of antibiotics treatment, the general condition improved significantly. Series CXR showed a decrease in the size and extent of multiple pulmonary cavitary nodules (Figure 4). MTB derived from sputum culture, not seen in the pus culture, was informed in the third week. Anti-tuberculosis agents were added with RIF 600 mg, INH 300 mg, and EMB 800 mg daily. Pyrazinamide was not suitable for this patient with hyperuricemia. He was discharged smoothly after a 4-week course of combined antibiotics. However, rifampin and isoniazid-resistant MTB was formally reported 4 weeks later, soon after discharge. Second-line antituberculosis drugs (streptomycin 750 mg 5 days a week via the intra-muscular route, the oral forms of levofloxacin 500 mg daily, p-aminosalicylic acid

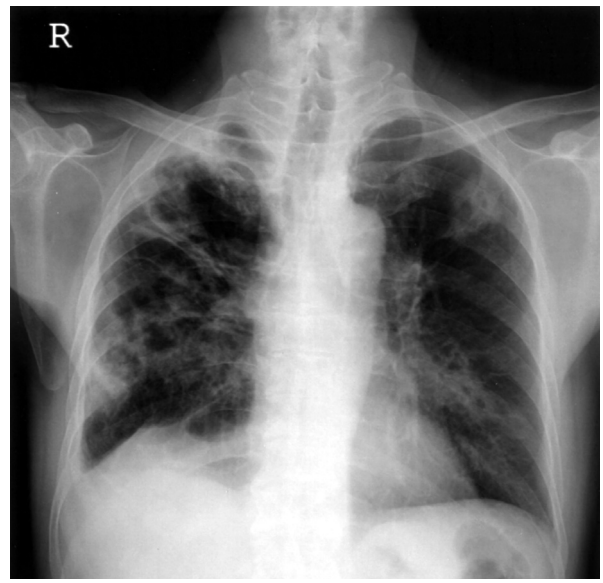


Fig. 4. CXR showing a decrease in the size and extent of multiple pulmonary cavitary nodules after a 4-week course of combined antibiotics.

2500 mg 4 times daily, and prothionamide 250 mg 3 times daily) were prescribed at our chest clinic. Three months later, his sputum converted to negative for MTB. At present (9 months after admission), multiple pulmonary cavitary nodules disappeared completely.

Discussion

Nocardia is a common natural inhabitant of the soil throughout the world. Pulmonary nocardiosis is usually acquired by direct inhalation of *Nocardia* spp. from contaminated soil. In humans, *N. asteroides* complex is the predominant pathogen, but there are several other species, including *N. brasiliensis* and *N. otitidiscaviarum* [7]. Pulmonary infection is usually produced by *N. asteroides* (85%), whereas *N. brasiliensis* causes cutaneous and subcutaneous abscess [8]. Recent studies have resulted in the identification of 3 specific subgroups of *N. asteroides*, including *N. farcinica*, *N. nova* and *N. asteroides* sensu stricto as distinct species [9]. Most Nocardia infections have predisposing factors, including corticosteroid therapy, chemotherapy for neoplasm, and acquired immune deficiency syndrome (AIDS) [10].

N. asteroides is an aerobic, Gram-positive branching filamentous bacterium which is weakly acid-fast, but not acid-alcohol fast, and that resists decolorization with 1% (but not 3%) hydrochloric acid [11]. Although susceptibility testing for Nocardia has not yet been standardized, antimicrobial susceptibility testing in 1 study showed 100% sensitivity for amikacin; 80% for imipenem; 71% for cefotaxime; and 71% for TMP-SMX [12]. However, variable susceptibility to TMP-SMX has been described in immunocompromised patients. Although TMP-SMX prophylaxis was proposed to be efficacious in heart transplant recipients, 19 nocardiosis cases have been documented. In 33% (3 of 9) of renal transplant recipients who received TMP-SMX as a *P. carinii* prophylaxis; 67% (2 of 3) of the isolates remained susceptible to the treatment [13].

In our patient, diagnosis of PN was firmly established by sputum and PTNA pus cultures. Both are resistant to TMP-SMX, ceftazidime and levofloxacin; while sensitive to amoxillin/clavulanic acid and amikacin. This unique antimicrobial susceptibility pattern requires sub-species identification and further studies. A clinical improvement was achieved in this patient by combination therapy with TMP-SMX, amoxillin/clavulani acid and aminoglycoside. Nevertheless, the recommended treatment of choice remains unclear in TMP-SMX resistant patients.

PN mimics pulmonary tuberculosis in similar clinical symptoms, being chronic in nature, overlapping radiological characteristics, and unique positive acid-fast bacilli. It might not be surprising that this patient had both pulmonary infections, even though he received high-dose steroid. In another study, 2.9% of Nocardia was isolated in a total of 209 cases of pulmonary tuberculosis [14]; hence, a mixed infection with both Nocardia species and MTB is very rare, but should be considered. Moreover, because of the slow growth and lengthy process of recognizing MDR characteristics, greater confusion regarding anti-tuberculosis therapy has arisen. In Taiwan, the prevalence of MDR MTB was reported to be as high as 7.5% [15]. We did not institute appropriate therapy until 4 weeks later, when the identification and susceptibility tests were completed.

In conclusion, mixed infection by PN and MTB rarely occurs in clinical practice, so the physician should be attentive in the management of pathogens with multiple drug resistance.

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磺胺類抗藥性土壤絲菌和多重抗藥性肺結核合併感染—病例報告

謝正雄 * 曹世明 *,** 吳子卿 *

肺部土壤絲菌症並不常見但會造成嚴重感染，最常在免疫失調病人身上被發現。土壤絲菌症造成的肺部感染由於臨床上及放射學上並無特異性而難以診斷出來。肺部土壤絲菌和肺結核合併感染更是罕見。我們報告一例並不尋常的病例在腎病症候群經類固醇治療後是以肺部多發性開洞性結節表現。膿瘍和痰液培養長出對磺胺類藥物具有抗藥性的土壤絲菌。在四週後的痰液培養正式報告，多重抗藥性的肺結核菌也被鑑定出來。抗生素治療在磺胺類抗藥性土壤絲菌和多重抗藥性肺結核合併感染方面值得加以討論並須要更多的研究。*(胸腔醫學 **2007; 22: 162-167**)*

關鍵詞：土壤絲菌症，肺結核

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Mixed Connective Tissue Disease Presenting with Chylothorax — A Case Report and Literature Review

Shung-Ru Chen, Min-De Hung*, Gwan-Han Shen, Jeng-Yuan Hsu

Mixed connective tissue disease (MCTD) was defined as a connective tissue disorder characterized by the presence of high titers of a distinct autoantibody in combination with clinical features commonly seen in systemic lupus erythematosus (SLE), scleroderma, and polymyositis (referred to as overlap syndrome).

The early clinical features of MCTD are nonspecific, and may consist of general malaise, arthralgias, myalgias, and low-grade fever. A specific clue that these symptoms are caused by a connective tissue disease is the discovery of a positive antinuclear antibody (ANA) and high RNP (ribonucleoprotein). The lung is usually involved, but pleural involvement is rare, and chylothorax has not been reported before.

The etiologies of chylothorax are: tumor (54%, with lymphoma responsible for three-quarters), trauma (25%, with surgical trauma responsible for most), idiopathic (15%), and miscellaneous (6%). Rheumatoid arthritis and systemic lupus erythematosus have been reported to have chylothorax, but in only a limited number of cases. Herein, we report a case of MCTD presenting with chylothorax, which should be considered in the differential diagnosis of chylothorax. ***(Thorac Med 2007; 22: 168-173)***

Key words: chylothorax, MCTD (mixed connective tissue disease), SLE (systemic lupus erythematosus), autoimmune disease

Introduction

Sharp and colleagues (1972) first recognized mixed connective tissue disease (MCTD) among a group of patients with overlapping clinical features of systemic lupus erythematosus (SLE), scleroderma, and myositis, with the presence of a distinctive antibody against what now is known to be U1-ribonucleoprotein (RNP). This disease has been more completely characterized in recent years and is now recognized to consist of the following core clinical and laboratory features: Raynaud phenomenon, swollen hands, arthritis/arthralgia, acrosclerosis, esophageal dysmotility, myositis, pulmonary hypertension, a high level of anti–U1-RNP antibodies, and antibodies against U1-70 kd small nuclear ribonucleoprotein (snRNP); pleuropulmonary manifestations are

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common in MCTD, and the incidence varies from 20% to 85% [1]. The pleuropulmonary complications include pleural effusion, interstitial pulmonary processes, pulmonary arterial hypertension, pulmonary vasculitis, pulmonary thromboembolic pneumonia, aspiration pneumonia, and hypoventilatory failure; pulmonary vascular pathology with progressive pulmonary arterial hypertension and cor-pulmonale is the most serious complication of MCTD.

In this report, we present a 43-year-old female suffering from dry cough for 2 months; MCTD was diagnosed and left-side chylothorax was noted.

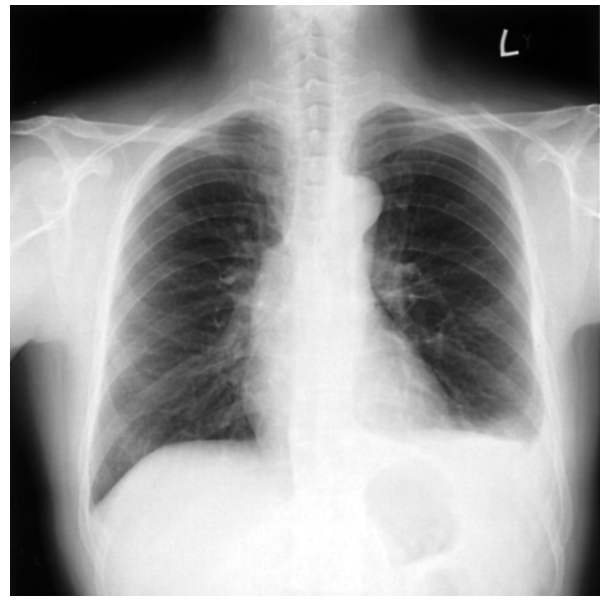

Fig 1. Chest radiography showing left-side C-P angle blunting.

Case Presentation

A 43-year-old female, a housekeeper, had been very healthy in the past, and without any known history of systemic disease. She came to our chest medicine OPD because of dry cough for 2 months. No fever or dyspnea was noted. Physical examination was essentially negative. Due to chronic cough, CXR was performed and revealed left-side C-P angle blunting (Figure. 1). The chest sonogram found pleural effusion on the same side; thus, echo-guided fine needle aspiration was performed and yielded yellowish-milky-odorless fluid (Figure.2). The following analysis revealed high TG (857mg/dl), low cholesterol (89mg/dl), and lymphocyte predominance (85%) in the differential count. Accordingly, chylothorax was established (Table.1). In addition, a high titer of pleural ANA (1:640, speckled) directed our attention to autoimmune disease. Chest CT (Figure. 3) showed only left-side pleural effusion and trivial pleural change, but no mediastinal lymphadenopathy or lung parenchymal lesion. There had been no recent traumatic accident or invasive medical procedure prior to this OPD visit. Tracing back her health history, we could find Raynaud's phenomenon (2 phases), but no swollen hands, no puffy fingers, no muscle weakness, no arthritis, etc. Serial laboratory data showed positive anti-U1RNP, positive ANA (1:1280, speckled), positive SSA/SSB, positive RF, and positive anti-ds DNA. Thus MCTD evolving to SLE was diagnosed. The renal function was within normal limits: BUN 28, Cr

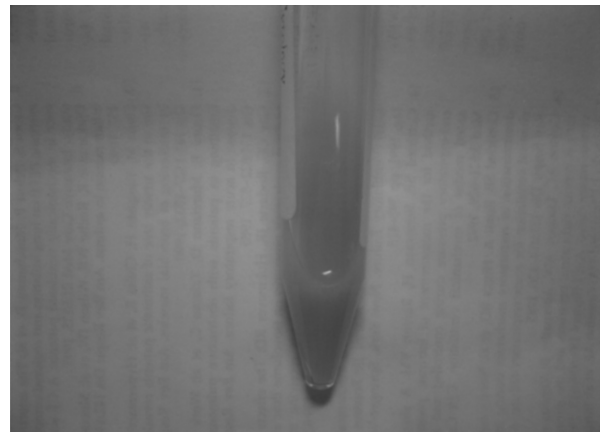

Fig 2. Yellowish-milky-odorless fluid obtained from left chest thoracentesis.

Table 1. Values obtained from pleural effusion

Variable (effusion)	Value
White-cell count (per mm^3)	6192
Lymphocytes (%)	85
Monocytes (%)	4
Neutrophils (%)	3
Monocytes (%)	4
Tissue cells (%)	3
No blood cells (%)	5
Cholesterol (mg/dl)	89
Triglyceride (mg/dl)	857
ANA	1:640, speckled

0.8, and no obvious proteinuria. Initially, we prescribed prednisone (20 mg bid), and the pleural effusion resolved completely 1 week later. Thereafter, she was followed up at our immune-rheumatologic OPD and was treated with disease modulator agents such as prednisolone and plaquenil.

Discussion

The early clinical features of MCTD are nonspecific and may consist of general malaise, arthralgia, myalgia, and low-grade fever, Raynaud's phenomenon, puffy hands, and fatigue. Occasionally, patients may present with an acute onset of high fever, polymyositis, arthritis, and neurologic features such as trigeminal neuralgia and aseptic meningitis. Almost any organ system can be involved in MCTD [2].

Chylothorax is characterized by pleural fluid with a turbid or milky white appearance due to the high lipid content. The lipids in chylothorax consist of triglycerides that enter the pleural space as chyle, most commonly from disruption of the thoracic duct. The miscellaneous causes of chylous effusion include lymphangioleiomyomatosis (LAM), intestinal lymphangiectasis, protein-losing enteropathy, regional ileitis, pleuritis, cirrhosis, sarcoidosis, tuberculosis, amyloidosis, thrombosis of the superior vena cava or other central veins, heart failure, filariasis, nephrotic

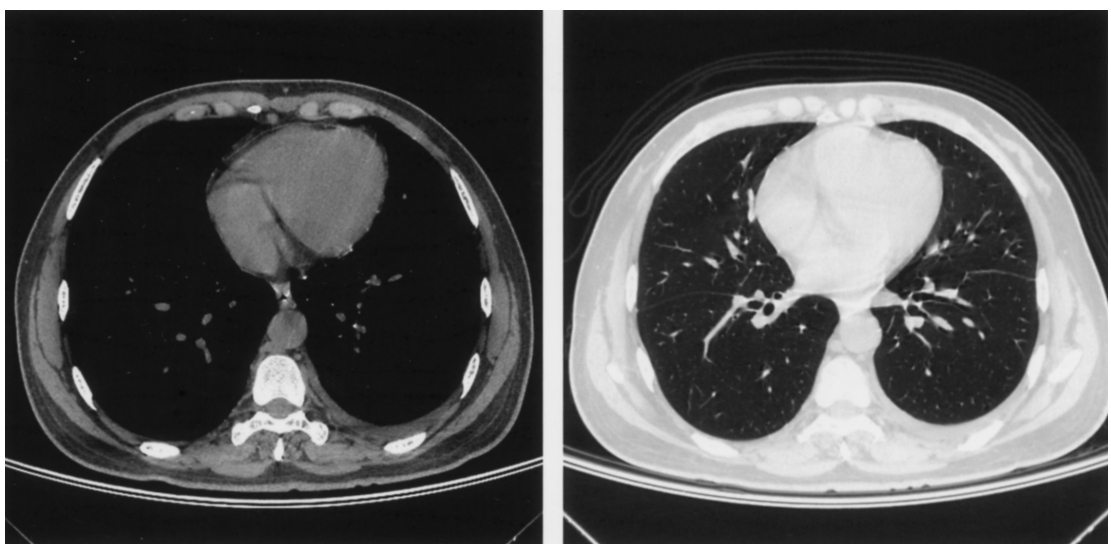

Fig 3. Chest CT showing only left-side pleural effusion and trivial pleural change, but no mediastinal lymphadenopathy or lung parenchymal lesion.

syndrome, and Behçet's disease [9]. The most common cause of chylothorax is trauma [4], but it also may result from tumors in the mediastinum [5]. Patients with chylothorax present with dyspnea, and a large pleural effusion is present on the chest radiograph; biochemical analysis reveals a triglyceride level that exceeds 110 mg/dL. Patients with chylothorax and no obvious trauma should have a lymphangiogram and a mediastinal CT scan to assess the mediastinum for lymph nodes. The treatment of choice for most chylothoraces is implantation of a pleuroperitoneal shunt [6]. Patients with chylothoraces should not undergo prolonged tube thoracostomy with chest tube drainage, because this will lead to malnutrition and immunologic incompetence.

Approximately 85% of MCTD patients have pulmonary involvement, which is often asymptomatic. Diffusing capacity for carbon monoxide may be the only abnormality. Pleurisy commonly occurs, but is seldom associated with large pleural effusions. Some patients develop interstitial lung disease. Pulmonary arterial hypertension is the most common cause of death in MCTD [7]. But lung involvement presenting with chylothorax was an extremely rare associated condition in previous reports. SLE and rheumatoid arthritis have been reported to be related to chylothorax, but only in very rare case reports. Two patients with chylothorax, chylous ascites and protein-losing enteropathy have been reported [9]. Analysis of pleural or peritoneal fluid revealed a high level of triglyceride. The antinuclear antibody (ANA) of the 2 patients was positive, as was the anti-Ro (SSA) antibody, but their anti-La (SSB) antibody, anti-RNP antibody, anti-Sm antibody, and anti-Scl-70 antibody were negative. In our patients, the anti-Ro (SSA), anti-La (SSB) antibody, anti-RNP antibody and anti-ds DNA antibody were positive. MCTD disease is a more adequate diagnosis than SLE. Our patient was the first to have chylothorax as the first presentation in MCTD disease. The pathogenesis of chylothorax in MCTD disease is unknown, but may be due to immune-related inflammation of lymphatic drainage.

Around 25% of patients develop renal disease. Membranous glomerulonephritis is most common and usually mild, but can cause nephrotic syndrome. Diffuse proliferative glomerulonephritis is unusual in MCTD, perhaps because of the protective role believed to be played by the high titers of anti-U_1 RNP [1]. Renal crisis secondary to malignant renovasculature hypertension, as occurs in scleroderma, is seen in a few patients. In our patient, the renal function was within normal limits because of high titers of anti-U_1 RNP.

Treatment of MCTD is essentially the same as would be indicated for the respective connective tissue diseases defining this syndrome [3]. Since MCTD was considered to be a steroid responsive disease, there is often a tendency to assume that all patients with MCTD should be treated with long-term corticosteroid [8]. This mistake is compounded by the assumption that all medical problems are related to MCTD. As an example, apparent flares of discomfort and pain in MCTD may instead be due to myofascial pain syndrome or fibromyalgia, and are therefore unresponsive to corticosteroids. In addition, malaise and becoming easily fatigued may be due to a reactive depression or lack of conditioning. As a result, the management of patients with MCTD requires continuing reassessment of the changing pattern of disease activity and a constant alertness to the emergence of new problems. More than half of the patients have a favorable course. The 10-year survival rate overall is approximately 80%, but varies depending on the response to medication.

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混合性結締組織疾病合併乳糜胸—病例報告及文獻回顧

陳相如　洪敏德*　沈光漢　許正園

混合性結締組織疾病是一種結締組織異常的疾病，合併有高價且明確的自體抗體,臨床上常有類似全身性紅斑性狼瘡，硬皮症及多發性肌炎的表現.。

混合性結締組織疾病早期的表現並不具特異性，常只是全身倦怠，關節肌肉酸痛及低熱,較特異的發現是抗核抗體的產生。肺部的浸潤相當常見(85%)，但少見肋膜侵犯。而以乳糜胸來表現的，在目前文獻中仍未被報導。

乳糜胸的病因如下：腫瘤(54% ，其中淋巴腫瘤占四分之三)，創傷(25% ，手術占大部分)，原因不明(15%)，其它病因(6%)。本篇報告一個呈現乳糜胸的混合性結締組織疾病病案，在以前的文獻中，鮮見類似個案的報導。乳糜胸的鑑別診斷中必須將混合性結締組織疾病納入考慮。*(胸腔醫學* ***2007; 22: 168-173)***

關鍵詞：乳糜胸，混合性結締組織疾病，全身性紅斑性狼瘡，自體免疫疾病

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Dalteparin for Severe Central Venous Catheter-Related Thrombosis in an Adult with Septic Shock: A Successful Treatment Experience

Chih-Hsiung Chen*, Han-Siong Toh*, Wen-Liang Yu*,**, Chin-Ming Chen*, Che-Kim Tan*, Kuo-Chen Cheng*

Central venous thrombosis after central venous catheter indwelling is an underestimated complication. There are far fewer reports on the clinical significance of catheter-related thrombosis in septic adults, than in hemato-oncologic, pediatric, and hemodialytic patients. Sepsis has impacts on the systemic coagulation mechanism that differ from the above diseases, and potentiates thrombosis formation. Severe catheter-related thrombosis manifesting as central venous occlusion is very rare. The safety of warfarin, thrombolytic agents, and recombinant human activated protein C in septic patients remains unclear; therefore, the treatment of choice is not well established. With the increased sepsis incidence and widespread use of central venous catheters in these patients, catheter-related thrombosis should be given more attention and discussion. We report a septic shock patient with severe femoral venous thrombosis after central venous catheter implantation. A lower extremity duplex ultrasonogram confirmed the diagnosis. The patient was treated with dalteparin subcutaneously. The endovascular thrombosis resolved completely 7 days later. This treatment experience suggests that dalteparin is safe and cost-effective for catheter-related thrombosis. ***(Thorac Med 2007; 22: 174-181)***

Key words: catheter-related thrombosis, complication, dalteparin

Introduction

Among the adverse effects of the central venous catheter (CVC), much more attention is paid to catheter-related infections than other mechanical complications, such as catheter misplacement, vascular rupture, arterio-venous fistula, or hematoma formation. Catheter-related thrombosis has been rarely reported in septic adults, with research focused only on the incidence, morbidity, and mortality. Severe sepsis and septic shock resulting in systemic coagulopathy, as well as microthrombosis, potentiate catheter-related thrombosis formation, the mechanism [1] of which differs from the thrombotic events of hemato-oncologic, pediatric, and hemodialytic populations [2]. Disseminated intravascular coagulopathy associated with sepsis, massive fluid challenge during treatment, and vasoconstriction after the use of a vasopressor, causes ele-

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vation of d-dimer and FDP, trunk and extremities edema, and lower limb coldness, respectively, resembling clinical venous thrombosis presentations [3]. These conditions make the early diagnosis and suspicion of venous thrombosis difficult. With the increasing sepsis incidence and the development of critical care medicine, we will encounter more and more catheter-related thrombosis events in septic adults. More discussion about early recognition, medication considerations, and treatment experience is needed.

Lower limb duplex ultrasonography is a potentially useful diagnostic method. Recombinant human activated protein C (rhAPC) has been documented to be effective for sepsis-related thrombotic events and coagulopathy modulation. However, it is much more expensive than low molecular weight heparin. Lack of clinical experience with rhAPC, as well as thrombolytic agents like urokinase, streptokinase, and tissue plasminogen activator, in the treatment of catheter-related thrombosis limits the clinical indications. We report the successful treatment of a septic adult with CVC-related thrombosis using a low molecular weight heparin, dalteparin, rather than other agents.

Case Report

A 67-year-old man with type 2 diabetes mellitus, hypertension, and severe obesity was brought to the emergency department of this hospital because of low back pain, chills, and high fever. The patient was a retired factory worker and had quit smoking 3 years earlier. He had been admitted to our ward for necrotizing fasciitis of the left leg, which was treated with antibiotics and surgical debridement, in March 2005, and was discharged uneventfully. He was then regularly followed up at our diabetes mellitus clinic. He had no trauma or other abdominal surgery, did not use alcohol, and reported no known allergies.

About 10 days earlier, he noticed that he had low back pain. A renal ultrasonographic examination performed in the genitourinary clinic of the previous hospital revealed left renal stones. Extracorporeal shock wave lithotripsy for left-side renal stones was performed there, but his low back pain recurred 1 week later. Several episodes of chills and high fever with a temperature that peaked at 39°C developed 3 days before admission. Because of progressive anorexia, diffuse weakness, and mild confusion, he was brought to the emergency department and admitted on October 26, 2005.

On examination, the patient appeared tired and somnolent. His temperature was 39.2°C. The pulse was regular at 127 beats per minute, the blood pressure 83/42 mmHg, and the respiratory rate 32 breaths per minute. He was 163 cm tall, and weighed 106 kg. His neck was supple and there was no palpable cervical lymphadenopathy. The chest was clear to auscultation and there was no heart murmur. Knocking tenderness at the left costo-vertebral area was noted. The remainder of the examination showed no abnormalities.

Laboratory data were as follows. The electrocardiograph revealed sinus tachycardia. Chest radiography showed an elevated diaphragm, probably due to the obesity, and no other remarkable findings. The white cell count was 15,700 cells/μL and C-reactive protein was >250.0 mg/L. Biochemical laboratory tests included a blood urea nitrogen level of 55 mg/dL, creatinine of 2.6 mg/dl, sodium of 137.5 mEq/L, potassium of 4.42 mg/dL, and glucose of 195 mg/dL. Arterial blood gas examinations showed a pH of 7.275; PCO2, 61.4 mmHg; PO2, 26.9 mmHg; bicarbonate, 27.9 mmole/L; and oxygen saturation, 41.3%. Prothrombin time (PT) was 13.5 seconds

over a control value of 11.4 seconds with an international normalized ratio (INR) of 1.2, and activated partial thromboplastin time was 24.4 seconds over a control value of 29.1 seconds in his coagulation profile. D-dimer and fibrin degradation products were 1141 ug/L and 27.7 g/mL respectively.

The patient was endotracheally intubated and a CVC was emplaced via the right jugular vein. A continuous intravenous infusion of dopamine was initiated to maintain adequate blood pressure, despite the administration of normal saline (about 3 liters) resuscitation. Intravenous hydrocortisone 300 mg daily divided into 3 doses and flumoxef 1000 mg every 8 hours was begun. He was transferred to the medical intensive care unit with suspected septic shock and was mechanically ventilated. Magnetic resonance imaging (MRI) of the abdomen disclosed a left psoas muscle abscess, 3.0 × 2.5 × 2.3 cm, extending to the preexistent L4-5.

On the 4th hospital day, blood cultures obtained at the emergency department and pus cultures drained from the left-side psoas muscle abscess grew *Proteus mirabilis*, susceptible to flumoxef with an improving clinical condition.

His right jugular venous central catheter was removed 3 days later and another CVC was implanted via the right femoral vein. One day later, however, swelling on the entire right lower extremity developed. Pedal pulsation of the right foot was still noted. The central femoral venous catheter was immediately removed. Right lower extremity duplex ultrasound examination showed a focally distended venous lumen, non-compressible pattern, and internal echogenicity in the

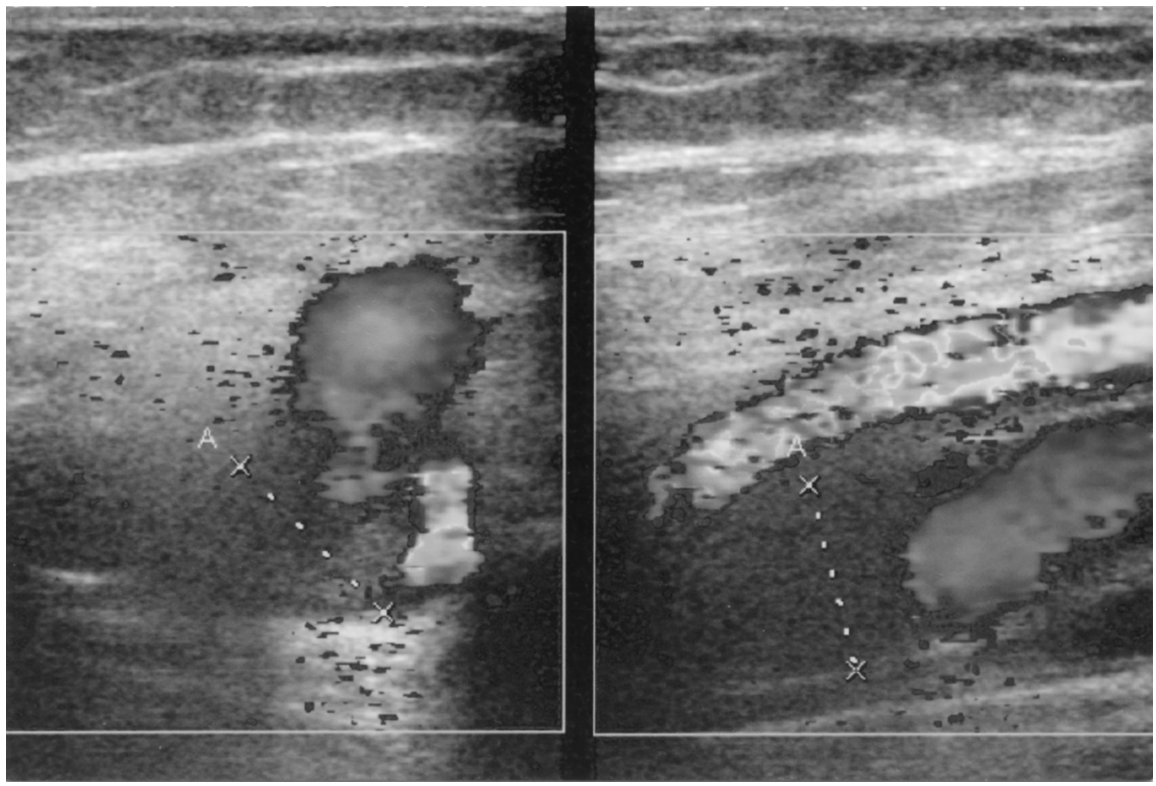

Fig. 1. Endovascular focal and partial thrombosis of the right common femoral vein (12 mm × 13 mm).

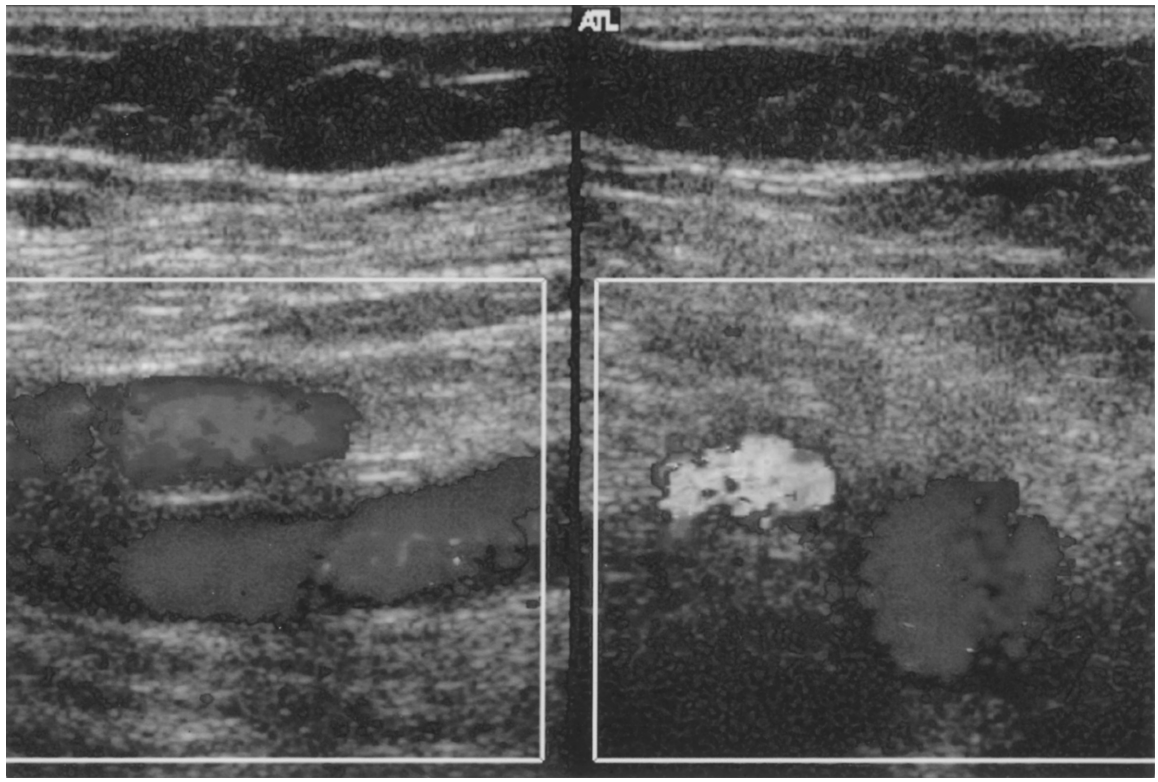

Fig. 2. After treatment with dalteparin for 7 days, complete resolution of the right common femoral venous thrombosis was noted.

right common femoral vein, about 1.2 × 1.3 cm in size, compatible with focal and partial thrombosis. (Figure 1)

Subcutaneous dalteparin (5000 units every 12 h) and oral omeprazole (20 mg per day) as prophyaxis for the stress-related gastro-intestinal tract ulcer bleeding were begun. After 7 days of dalteparin therapy, the patient was treated with oral warfarin 2.5 mg daily; he had a PT of 24.9 seconds over 11.5 seconds with an INR of 2.2, 5 days after starting warfarin. A follow-up ultrasonogram revealed a normal venous flow pattern. (Figure 2) The partial thrombosis, previously detected in the right common femoral vein, no longer existed. The swelling of the right lower limbs completely resolved, although slowly, over the next 20 days. Finally, the patient was transferred to the respiratory care center for the ventilator weaning program. There was no recurrence of right common femoral venous thrombosis or treatment-associated bleeding during the dalteparin therapeutic course and subsequent hospital days.

Discussion

Severe sepsis, including septic shock, has been proven to trigger the events of microthrombosis, which lead to multiple organ dysfunction syndromes. Sepsis-related coagulopathy and shock-related endothelial dysfunction play major roles in systemic microthrombosis formation [1, 9]. The central venous catheter (CVC) decreases intravascular blood flow along the line and provides a surface for thrombosis formation. Nevertheless, there is little discussion about the rela-

tionship between catheter-related thrombosis and sepsis-associated coagulopathy. The Surviving Sepsis Campaign guidelines published in 2004 recommended intravenous corticosteroids 200-300 mg per day for 7 days for shock reversal [7]. The use of steroids is another risk factor contributing to the formation of the venous thrombosis [4].

Central venous catheterization is a routine practice used in intensive care units. It is used as a vascular access for intravenous fluid infusion, as well as blood products transfusion, and pharmacological therapies. It is very important in hemodynamics monitoring as guidance for shock management. Many complications, including blood-stream infections, arterio-venous fistula, vascular pseudoaneurysm, pneumothorax via the subclavian vein, and subcutaneous hematoma formation, have been reported [5]. In 1 study, CVC-associated thrombosis was usually asymptomatic and rarely caused severe occlusion [6]. Therefore, more attention has been paid to CVC-related infections than to catheter-related thrombosis in adults with sepsis.

There are many factors that make the diagnosis of thrombotic events difficult. Elevation of serum d-dimer and FDP occurs in deep vein thrombosis [3], but it is also caused by disseminated intravascular coagulation in severe sepsis. The lower limbs swell after aggressive fluid resuscitation and prolonged bed rest. Pallid color changes with decreased pulsation of the extremities due to hypovolemia and vasopressor support are usually found in septic shock patients. Hypoalbuminemia in disease progression precipitates these conditions and leads to difficulties in diagnosis and clinical suspicion of catheter-related thrombosis. These factors are good reasons why most catheter-related thrombosis is underestimated and thought to be “asymptomatic”.

Deep vein thrombosis is traditionally treated with anticoagulant therapy, such as heparin or warfarin, but the optimal treatment for catheter-related thrombosis remains uncertain [6]. A new drug, rhAPC, also called drotrecogin alfa, reduces mortality in patients that have a high risk of dying from severe sepsis. It has well-known antithrombotic, anti-inflammatory, and profibrinolytic properties in severe sepsis that reduce systemic microthrombosis. There is no clinical report of catheter-related thrombosis treated with rhAPC in the literature. The price of rhAPC should be taken into consideration in such an indication [8].

CVCs are implanted in cancer, pediatric, and hemodialytic patients. Although the mechanism of thrombotic events differs from sepsis populations, various medications and investigations in these cases provide us reference materials [2]. Underlying thrombophilia, plasma homocysteine levels, cytotoxic chemotherapeutic agents, such as 5-fluorouracil, and CVC-related infections increase the risk of thrombotic events in cancer patients [10-12]. Several studies have been conducted to evaluate the efficacy of thromboprophylaxis with long-term warfarin in cancer patients. Warfarin protects cancer patients from venous thrombosis; however, the risk of hemorrhage increases [13]. Due to its delayed anticoagulation effect, warfarin plays a more prophylatic than treatment role.

Low-dose streptokinase was reported to manage thrombus in 3 cancer patients with catheter-related septic thrombophlebitis [14]. In a Children’s Oncology Group study, an every-2-week administration of fibrinolytic therapy with urokinase could decrease these complications, compared with standard heparin flushes [15]. Thrombolytic agents have been used when anticoagulants failed in only a few cases [14-15]. Besides, thrombolytic therapy during sepsis may

lead to more severe uncontrolled bleeding and is contraindicated with multiple invasive procedures.

Unfractionated heparin and low molecular weight heparin, such as enoxaparin and dalteparin, were used as an anticoagulant prophylaxis with a lower bleeding rate [16-18]. The treatment of choice for these patients without previous thromboprophylaxis in the intensive care unit remains uncertain [19]. Only a few reports on these anticoagulation agents have been published [20].

This patient was obese and his BMI was 39.9. Hydrocortisone, vasoconstrictive doses of dopamine, and a normal saline challenge contributed to the thrombosis formation, but could not be discontinued because of the septic shock status. We used lower extremities color Doppler as a diagnosis tool, and subcutaneous-administered dalteparin to treat catheter-related thrombosis. Prior to anticoagulant therapy, the bleeding tendency and occult foci were investigated and all invasive procedures, for example, psoas muscle abscess drainage, another CVC recannulation, and insertion of a Foley catheter and nasogastric tube, were performed. Another clinical finding in treating this patient was slow resolution of the lower extremity swelling. This may have been because of the longterm bed rest and hypoalbuminemic status after vigorous fluid administration in treating septic shock. A lower extremity duplex ultrasonogram should be performed in the follow-up study after anticoagulant therapy.

Based on our successful experience, a proton pump inhibitor begun for prophylaxis of gastrointestinal tract bleeding and a lower extremity duplex ultrasonogram are both essential to thrombosis detection. Dalteparin in the treatment of catheter-related thrombosis is safe, effective, and cost-effective.

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在一敗血症成年病人使用 Dalteparin 治療中央靜脈導管引起的嚴重血栓併發症：病例報告

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中央靜脈導管造成的中央靜脈血栓是一個被低估的併發症。相較於血液腫瘤科、小兒科、和洗腎病人等，在敗血症病人這一部分，只有非常少的文獻討論放置中央靜脈導管後的血栓併發症。敗血症對於全身凝血會有影響，不只和上述疾病的機制不一樣，並且會促成血栓的形成。造成中央靜脈阻塞的嚴重中央靜脈導管血栓併發症是相當罕見的，傳統如 warfarin 和血栓溶解劑以及新一代的 recombinant human activated protein C 用於敗血症病人的安全性未明，故目前仍無確定的治療準則。隨著敗血症發生率上升和廣泛使用中央靜脈導管，中央靜脈導管血栓症值得多加注意和討論。本文報告一個罹患敗血症的成人於股靜脈處放置中央靜脈導管後出現嚴重的股靜脈血栓，使用下肢 duplex 超音波確定診斷後，在採用皮下注射 dalteparin 治療病人七天之後血管內血栓完全消除。本病例經驗指出，使用 dalteparin 治療中央靜脈導管血栓併發症是安全、方便、以及經濟有效的。*(胸腔醫學 **2007; 22: 174-181**)*

關鍵詞：中央靜脈導管，血栓併發症， dalteparin

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Respiratory Failure Induced by Myxedema — A Case Report

Yen-Wen Chen, Jia-Horng Wang

Respiratory failure in myxedema is a complex medical emergency and may require prolonged ventilatory assistance. Chronic hypothyroidism is easily neglected by clinician due to the lack of specific symptoms and signs. It is also easily misdiagnosed as heart failure. We report a 55-year-old woman with chronic hypothyroidism. She had been treated for congestive heart failure for years. Myxedematous coma was not diagnosed until respiratory failure occurred. After replacement with levothyroxine, she was successfully weaned from prolonged mechanical ventilation. ***(Thorac Med 2007; 22: 182-186)***

Key words: myxedema hypothyroidism respiratory failure

Introduction

Hypothyroidism is a common medical problem encountered in the primary care setting. The most common causes of hypothyroidism include autoimmune thyroiditis, previous thyroid ablation, lithium or amiodarone use, and rarely a pituitary tumor or hypothalamic dysfunction [1] Severe hypothyroidism may result in cardiovascular compromise, respiratory failure, psychosis and obtundation. Despite adequate hormonal replacement, patients who present with the severe manifestations of hypothyroidism often die. Profound hypothyroidism causes impaired ventilatory response to hypoxia and hypercapnia [2], neuromuscular dysfunction [3], hypoventilation [4], obstructive sleep apnea [5], and pleural effusions [6]. Respiratory failure as a component of myxedema coma has a high mortality.

Case Report

A 55-year-old woman treated as congestive heart failure was irregularly followed up at a local hospital for 3 years. She had been in relatively stable condition and was ambulatory. Her medical history was otherwise noncontributory.

She suffered from slowly progressive bilateral lower leg weakness and difficulty in breathing for about 2 months. She fell to the ground occurred on August 24, 2005 without major complications, and then visited our neurosurgery and orthopedic OPD for help. A lumbar computed tomography (CT) scan on September 2, 2005 showed herniation of the intervertebral disc over L5/S1. However, persistent progressive shortness

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of breath, dyspnea on exertion, and chest discomfort were noted. On the morning of September 3, 2005, she suffered from severe dyspnea, severe chest discomfort and consciousness disturbance. She was sent to the emergency department of our hospital where her blood pressure was 133/91 mmHg, heart rate was 74/minute, respiratory rate was 20 and body temperature was 35.3°C. There was periorbital edema. Heart sounds were distant with a regular rate and rhythm. Bilateral basilar rales were audible,and nonpitting edema of the extremities was present. Deep tendon reflexes had marked a relaxation delay. The Glasgow coma scale of the eye was 1, verbal was 1,and motor was 1. Endotracheal tube insertion was perfomed with mechanical ventilation .

Laboratory data revealed normocytic anemia, and no leukocytosis. Liver function test, renal function test, C-reactive protein and electrolyte revealed no abnormal findings. The arterial blood gas (ABG) showed a pH of 7.26, a PCO_2 of 89.4 mmHg, a PO_2 of 75.9 mmHg, a saturation of oxygen of 92%. Chest radiograph (Figure 1) revealed cardiomegaly and low lung volumes with intubation. Electrocardiogram showed low voltage and sinus bradycardia. Echocardiogram demonstrated severe hypokinesia in the inferior and posterior wall, a left ventricle ejection fraction (LVEF) around 32%, and a small to moderate amount of pericardial effusion without tamponade. The thyroid function study revealed thyroid stimulating hormone (TSH) of 68 uIU/ml (reference range, 0.4~4.0), and free thyroxine (free T4) of 0.12 ng/dL (reference range, 0.8~1.7). The clinical and laboratory pictures were compatible with myxedema coma and respiratory failure. Oral levothyroxine was given. The titer of antithyroid peroxidase (anti-TPO) was 228.40 U/ml (reference range <60) and the antithyroiglobulin (anti-TG) was 208.30 U/mL (hospital day 3). Hashimoto's disease was diagnosed. On hospital day 5, the patient's consciousness became clear. Levels of free thyroxine checked on hospital day 3 and day 12 were still low. The levothyroxine dose was adjusted twice. Free thyroxine checked on day 31 was in euthyroidism (Table 1). Tracheo-

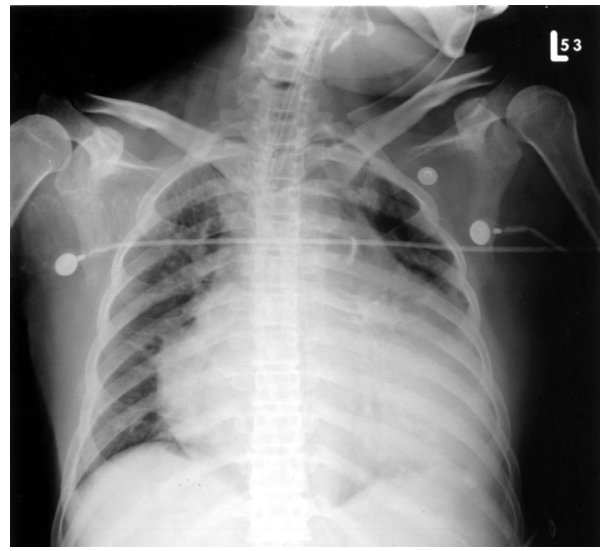

Fig. 1. Chest radiograph taken in emergency room revealing cardiomegaly, bilateral pleural effusion and low lung volumes with intubation.

Table 1. Thyroid Function Laboratory Data

Hospital day	Day 1	Day 3	Day 12	Day 31
T3 ng/dL (reference 60~181)		40		
T4 ug/dL (reference 4.5~10.9)		1		
Free T4 ng/dL (reference 0.8~1.7)	0.12	0.16	1.07	2.17
TSH uIU/ml (reference 0.4~4.0)	68	30.6	13.2	0.77

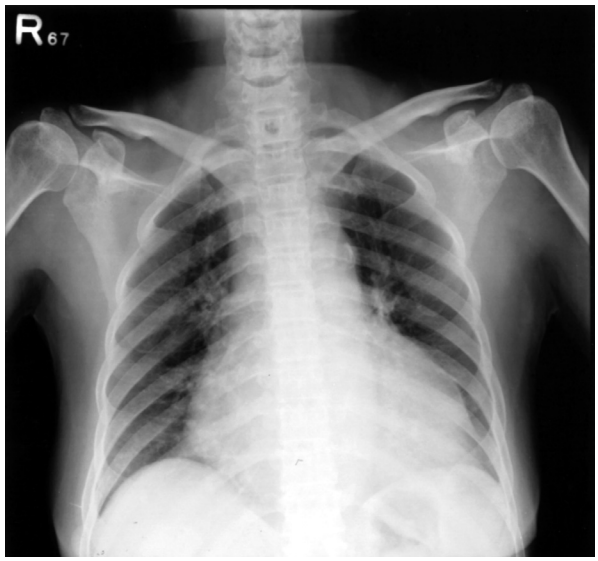

Fig. 2. Chest X-ray on day 44 showing mild cardiomegaly, but no pleural effusion.

stomy was suggested to the patient due to poor expectoration and excess sputum. Prolong intubation and ventilator dependence were also found after the weaning profile was not passed. A tracheostomy was done on day 27. Repeated echocardiogram demonstrated moderate hypokinesia in the inferior and posterior wall, LVEF around 57%, and no evidence of pericardial effusion. A T-piece was tried on hospital day 32, and a tracheal button was inserted on day 34. She was then transferred to the general ward. Chest X-ray (Figure 2) on day 44 showed mild cardiomegaly, but no pleural effusion. She was discharged on hospital day 47.

Discussion

This case clearly demonstrated that severe chronic hypothyroidism was easily neglected and treated as congestive heart failure for years and highlights the need for physicians to understand the respiratory consequences of hypothyroidism: impaired ventilatory response to hypercapnia and hypoxemia; subsequent respiratory alkalosis despite low mechanical minute ventilation and a prolonged ventilatory course from severe neuromuscular compromise.

Hypothyroidism alters ventilation in 2 ways. One feature is diminished central response to hypoxia and hypercapnia, resulting in respiratory acidosis. Nordqvist *et al.* first reported CO_2 narcosis in myxedema in 1960 [2]. The second feature of hypothyroidism is a propensity for respiratory alkalosis. Iatrogenic alkalosis is common after the initiation of overaggressive mechanical ventilation. Immediately after induction and intubation, the end-tidal CO_2 was between 18 and 20 mmHg. These investigators attributed these findings to a reduced basal metabolic rate and diminished CO_2 production brought about by depressed levels of thyroid hormone [7]. Decreased levels of PCO_2 may trigger an adjustment in the central respiratory drive [3]. No investigations on humans have determined the duration of hormonal replacement needed to normalize metabolic rates and consequently, CO_2 production and minute ventilation. Our patient had a similar clinical presentation. At presentation, her acid-base disorder was consistent with chronic respiratory acidosis. After mechanical ventilation use, she developed respiratory alkalosis. This was caused by iatrogenic hyperventilation and by a very low metabolic rate with diminished CO_2 production. We were unable to correct respiratory alkalosis even by using low minute ventilation in this patient. Added anatomic dead space was used with some improvement.

In addition to the altering ventilation, hypothyroidism also affects the neuromuscular system by causing weakness of the diaphragm and other respiratory muscles. Diaphragmatic dysfunction causes a restrictive respiratory pattern that may contribute to hypoxia and hypercapnia [8]. Defici-

ency of thyroid hormone causes demyelination and fibrosis of the phrenic nerve. Hormone replacement improves phrenic nerve conduction and normalizes transdiaphragmatic pressure within 3 months [9].

Several other factors may contribute to difficult weaning and should be investgated in severely hypothyroid patients. Patients may have a combination of hypothyroid-induced diaphragmatic and peripheral neuropathy, myopathy, or concomitant critical illness polyneuropathy [10]. Other complicating factors include congestive heart failure [11], anemia [12], and electrolyte imbalance. Hypothyroidism may exacerbate angina or congestive heart failure. It may also induce a normochronic nomocytic anemia that reduces oxygen-caring capacity [13]. As with all patients requiring prolonged mechanical ventilation, electrolyte should be monitored and corrected if abnormality is present. Balanced nutrition is also necessary. Physical therapy is necessary to prevent further muscular atrophy.

In conclusion, this case suggests that in a patient with symptoms and signs of heart failure, thyroid function needs to be checked. Myxedematous patients with respiratory failure need hormone replacement as soon as possible. Tracheostomy should be considered due to prolonged mechanical ventilator assistance. Full recovery may take several months.

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黏液水腫導致呼吸衰竭—病例報告

陳燕溫　王家弘

呼吸衰竭發生在黏液水腫的病人身上是極具複雜性的急症而且治療需要長期的呼吸器協助。慢性甲狀腺功能低下由於沒有明顯的症狀，常常被臨床醫師忽略，並以心臟衰竭的藥物來治療。我們報告一個 55 歲女性病人因為長期慢性甲狀腺功能低下，卻以心臟衰竭藥物來治療，直到呼吸衰竭，意識不清，插管治療並使用呼吸器後才診斷出來。經過荷爾蒙的補充及長期時間呼吸器輔助,我們成功的將她脫離呼吸器。*(胸腔醫學* ***2007; 22: 182-186)***

關鍵詞：黏液水腫，甲狀腺功能低下，呼吸衰竭

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Clubbing Fingers in a Patient as an Initial Presenting Symptom of Lung Adenocarcinoma — A Case Report

Hugo You-Hsien Lin, Inn-Wen Chong, Tung-Heng Wang, Mee-Sun Tsai, Ming-Shyan Huang, Jhi-Jhu Hwang

Clubbing finger is a characterized physical finding in many diseases. Its pathophysiology is still uncertain. But this striking symptom and sign gives the physician an important clue to make the differential diagnosis. We report the case of a 57-year-old female who was admitted to our hospital with chief complaint of clubbing fingers and bone pain. The serial examinations showed possible hypertrophic pulmonary osteoarthropathy (HPOA) throughout the bilateral pelvic bones and the long bones of both lower limbs, with a lobulated nodule in the right middle lung and multiple small nodules in both lung fields. The CT-guided biopsy pathologic study of this pulmonary nodule was adenocarcinoma. Due to the advanced stage of the lung cancer, she received chemotherapy, after which, the clubbing fingers improved. We conclude that the HPOA of this patient was probably caused by the lung cancer. ***(Thorac Med 2007; 22: 187-192)***

Key words: clubbing finger, hypertrophic pulmonary osteoarthropathy (HPOA), adenocarcinoma

Introduction

Clubbing fingers is associated with a number of neoplasm, pulmonary, cardiac, gastrointestinal, infectious, endocrine, psychiatric, and multisystem diseases. We report a patient with lung adenocarcinoma with the initial symptom of clubbing fingers.

Case Presentation

A 57-year-old female with a past history of pulmonary tuberculosis with complete treatment about 10 years ago, a hepatitis B carrier who had had a right femur bone trauma about 1 month previous, suffered from swelling in all digits with bone pain since March 2006, and came to the Kaohsiung Medical University Hospital (KMUH) outpatient department. The laboratory initially only showed an inflammatory reaction with CRP of 39.27 μg/ml (normal < 5.0 μg/ml); she was admitted for further evaluation.

After admission, the physical examination revealed clubbing fingers. (Figure 1) The roentgenography of the 4 limbs (April 24, 2006) only showed a small bony fragment with a sclerotic

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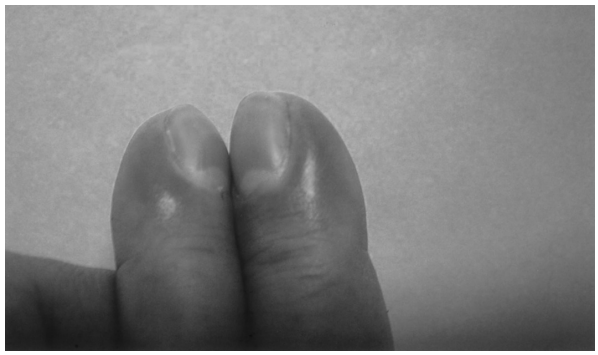

Fig. 1. Clubbed fingers, obliterated fingers, Schamroth's sign in clubbing

margin adjacent to the styloid process of the distal ulna.

Laboratory examination of the immune profile showed that complement 3 (C3) was 138 mg/dl (normal 104.3 ± 21.2 mg/dl). Other surveys, including antinuclear body and anti-Ds DNA, were all negative. The tumor marker survey with SCC was 0.0 ng/ml (normal <1.5 ng/ml), and CEA was 4.22 ng/ml (normal 0-5 ng/ml).

The whole body bone scan (April 28, 2006) revealed an irregular pericortical uptake in the long bones of both lower limbs, which suggested hypertrophic pulmonary osteoarthropathy (HPOA) (Figure 2A) (Figure 2B). The follow-up chest computed tomography showed a lobulated nodule in the right upper lobe with multiple small nodules in both lungs and low attenuation fluid collection in the pericardial and right pleural spaces (Figure 3). Thoracocentesis of the pleural effusion showed that PMN (polymorphonucleocytes/monomorphonucleocyte) was 5%/95%. The effusion cytology was positive with few clusters of large hyperchromatic cells. The CT-guided biopsy proved that the mass lesion was adenocarcinoma. After a discussion with the patient and her family, chemotherapy with cisplatin 70 mg/m^2 and nalvelbine 20 mg/m^2 was given. After 3 cycles chemotherapy, the clubbing fingers improved: we concluded that the patient's HPOA was probably caused by the lung cancer.

Table 1. Diseases associated with bilateral clubbing

Neoplastic
Bronchogenic carcinoma
Pleural tumors
Lymphoma
Nasopharyngeal carcinoma
Mesothelioma
Pulmonary
Cystic fibrosis
Asbestosis
Hypersensitivity pneumonitis
Idiopathic pulmonary fibrosis
Pulmonary arterial-venous malformation
Hanta virus pulmonary syndrome
Sarcoidosis
Cardiac
Cyanotic heart disease
Gastrointestinal
Inflammatory bowel disease
Liver disease
Celiac sprue
Juvenile polyposis coli
Infectious
Mycobacteria tuberculosis
Infective endocarditis
Chronic parasite infection
Human immunodefficiency virus infection
Endocrine
Thyroid disease
Vascular
Venous stasis
Psychiatric
Laxative abuse

Discussion

Clubbing has been described as occurring in stages [1]. There is a periungual erythema and a softening of the nail bed, yielding a spongy sen-

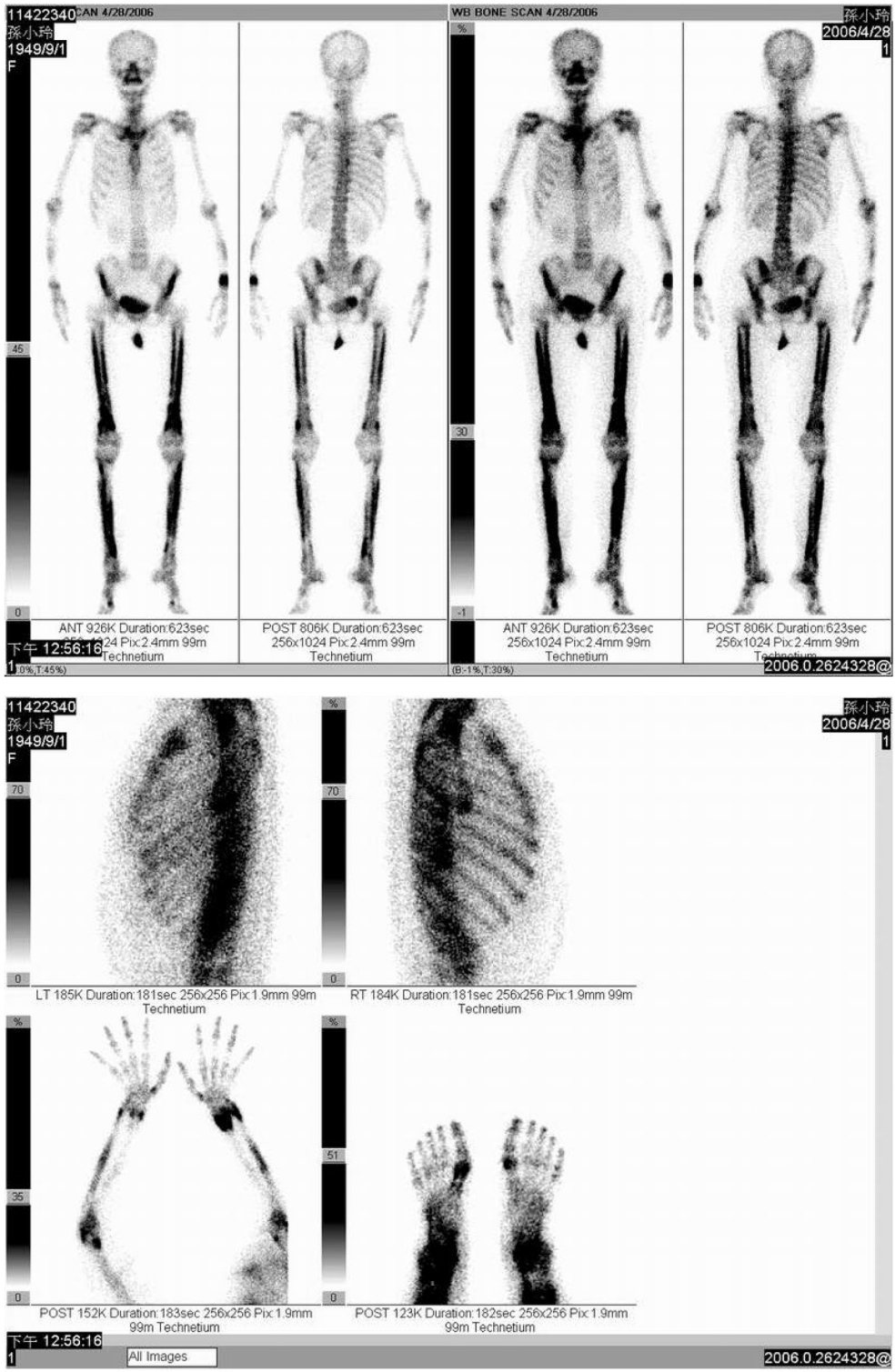

Fig 2A, 2B. The Tc-99m MDP (methylene diphosphomate) whole body bone scan revealed irregular pericortical uptake throughout the bilateral pelvic bones (especially along the iliac crests), and the long bones of both lower limbs (especially along the distal end of the left ulna, radius, bilateral femoral, tibial shafts, and the right 1st metatarsal bone), which may indicate a characteristic "tramline sign" (distinctive parallel tracks) that suggest hypertrophic pulmonary osteoarthropathy (HPOA)

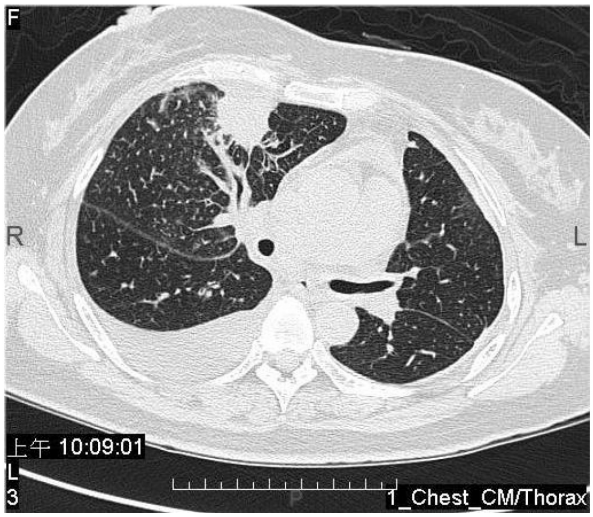

Fig 3. The follow-up chest computed tomography showed a lobulated nodule about 2.36 × 1.8 × 2.17 cm in the right upper lobe with multiple small nodules in both lungs; low attenuation fluid collection is noted in the pericardial and right pleural spaces.

sation on palpation, followed by an increase in the normal 160° angle between the nail bed and the proximal nail fold. Clubbing usually develops over years, but in certain conditions may develop subacutely. Many researchers have tried to develop techniques to diagnose clubbing fingers, including the Lovibond sign [2], which is the same as the "profile sign" of the thumb, defined as the angle made by the nail as it exits the proximal nail fold. Schamroth [3] observed that the normal diamond-shaped window created by placing the back surfaces of the opposite terminal phalanges together was obliterated in clubbing (Figure 1). As for imaging, plain radiography of clubbed nails is not recommended as the first choice for proving HPOA. Arteriography or magnetic resonance angiography are reported for diagnosing clubbed fingers, but still not widely used in clinical diagnosis [5-7]. The pathophysiology of clubbing fingers is still unknown, by far the most acceptable hypothesis has been that of Dickinson and Martin [8], who based their proposal on emerging evidence of physiological platelet production, which showed that megakaryocytes are normally fragmented into platelets in the lungs. Another platelet-derived, growth-promoting cytokine, vascular endothelial growth factor, is elevated in the serum of patients with lung cancer and secondary HPOA, compared with patients with lung cancer without HPOA [9], and likely contributes to the vascular hyperplasia seen in clubbing pathology.

Many diseases are associated with bilateral clubbing fingers (Table 1) [10]. Physicians should do a complete physical examination and history-taking to narrow the differential diagnosis. A review of the system should focus on constitutional, pulmonary, gastrointestinal, and musculoskeletal symptoms for evidence of malignancy, infection, or inflammation. A family history should screen for primary HPOA or familial clubbing, which may preclude the need for further evaluation. A social history should screen for occupational exposure to asbestos, coal mine dust, and pigeon breeding, and risk factors for lung cancer [11], HIV, and tuberculosis.

Lung cancer is increasing its incidence and mortality in Taiwan; the initial symptoms before diagnosis vary. The major symptoms of lung cancer include hemoptysis, loss of weight, loss of appetite, dyspnea, thoracic pain, fatigue and cough [12]. In our case, this remarkable symptom led us to evaluate the possibility of underlying disease.

Since her HPOA was much improved after chemotherapy treatment, we concluded that the lung cancer was the etiology of her HPOA.

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肺腺細胞癌病人以杵狀指爲初始表現—個案報告

林祐賢　鍾飲文　王東衡　蔡米山　黃明賢　黃吉志

杵狀指在許多疾病中是個極有特色的理學徵像，它的病理生理學機轉依然未獲定論，但這個極富特色的症狀提供臨床醫師一個重要的線索來做鑑別診斷。我們報告一位 57 歲女性因為杵狀指，合併骨頭疼痛而住院。經詳細檢查，發現骨骼掃描呈現兩邊骨盆以及下肢長骨骨增生性病變，並且在胸部 X 光以及斷層掃描發現右上胸肺葉有一小葉狀腫瘤與數個小結節遍布兩邊肺葉。病理檢查報告為腺細胞癌，由於肺癌後期，經過了化學治療，杵狀指獲得了改善，因此我們認為造成此病患處狀指的病因是肺癌。*(胸腔醫學* ***2007; 22: 187-192)***

關鍵詞：杵狀指，增生性肺性骨關節病，腺癌

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Primary Endobronchial Minute Leiomyoma — A Case Report

Chin-Chou Wang*, Chien-Hao Lie*, Fang-Ying Kuo**, Meng-Chih Lin*,***

Primary endobronchial minute leiomyoma is a rare benign tumor of the lung. In this report, we discuss a case of this rare tumor in a 78-year-old male who presented with hemoptysis and was diagnosed as endobronchial leiomyoma based on the histopathological examination of a bronchial biopsy from the posterior segmental bronchus of the left upper lobe. Bronchofiberscopy revealed a polypoid tumor (0.1 × 0.1 cm) in the posterior segmental bronchus of the left upper lobe, which was easily extirpated by transbronchial forceps biopsy. We could not find another primary lesion or metastases in any other organ. Following treatment, this patient has been asymptomatic with no recurrence of haemoptysis. ***(Thorac Med 2007; 22: 193-197)***

Key words: bronchofiberscopy, primary endobronchial leiomyoma, pulmonary leiomyoma

Introduction

Primary endobronchial minute leiomyoma is a rare entity with few documented cases in the medical literature [1-2]. Pulmonary leiomyoma accounts for less than 2% of all benign tumors of the lung [3]. Pulmonary leiomyoma can present as either an endotracheal/endobronchial or intraparenchymal lesion, and may be primary or metastatic [3-4]. We encountered a case of primary endobronchial minute leiomyoma in an older male without malignancy; herein, we present the bronchofiberscopic finding and review the literature.

Case Report

A 78-year-old non-smoking ethnic Chinese man with a peptic ulcer history was admitted to our ward with the chief complaint of cough with bloody sputum for 6 months. His chest radiography showed bilateral emphysematous change, and no definite mass or nodule lesion (Figure 1). On admission, body temperature was 37ºC, with a pulse rate of 78 beats per minute and a respiratory rate of 22 breaths per minute; blood pressure was 120/80 mmHg. On physical examination, the bilateral breathing sound was clear; peripheral blood examination and routine biochemical tests

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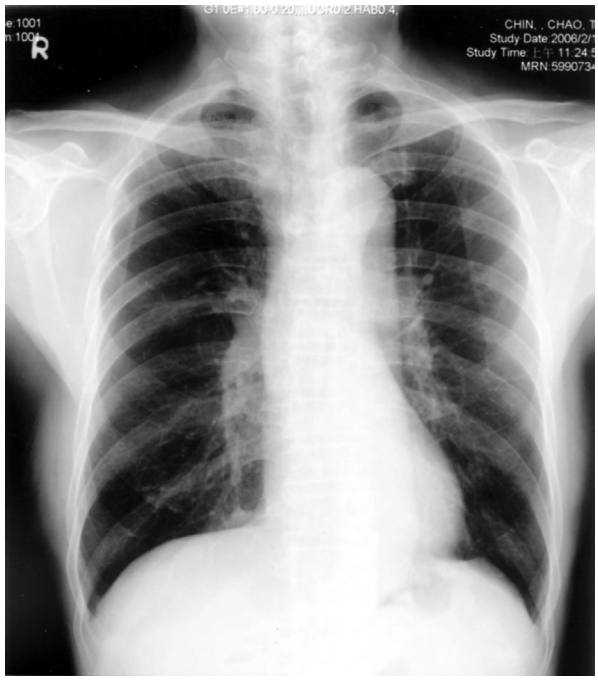

Fig. 1. Chest radiography showing emphysematous change, but no definite lung nodule or mass.

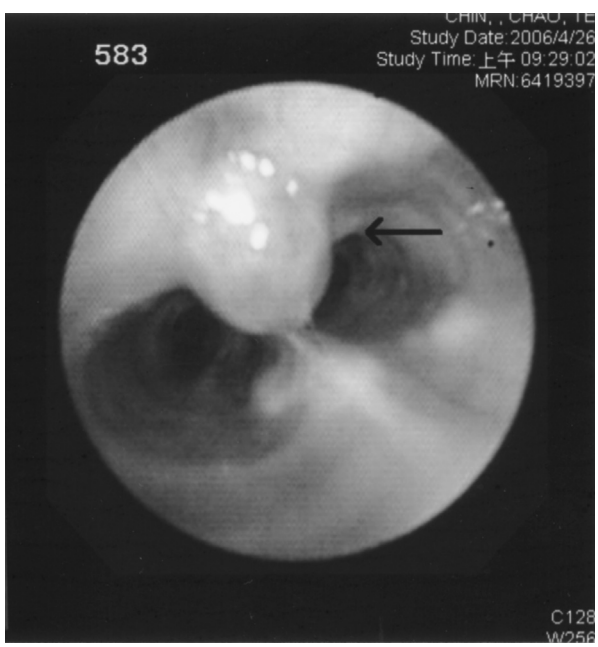

Fig. 2. Bronchofiberscopic examination showing an endobronchial polypoid tumor in the posterior segmental bronchus of the left upper lobe.

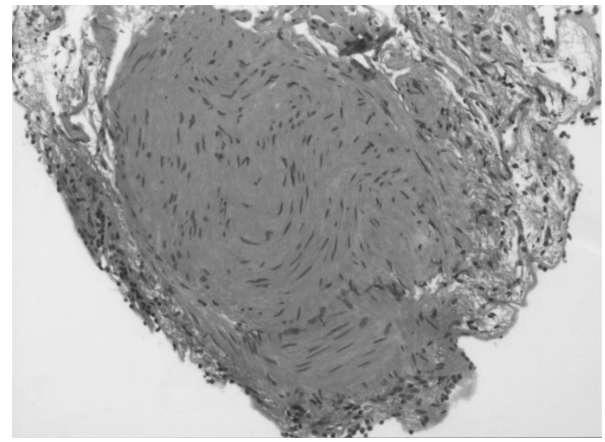

Fig. 3. This image shows a myomatous nodule composed of interlacing bundles of spindle cells without cytologic atypia or mitotic activity (Hematoxylin and Eosin, 40X).

were within normal limits. Due to persistent hemoptysis during admission, bronchofiberscopy was performed to evaluate the condition of the tracheo-bronchial tree; a polypoid tumor (0.1 × 0.1 cm) was noted in the posterior segmental bronchus of the left upper lobe and was easily extirpated by transbronchial forceps biopsy (Figure 2). Microscopically, the resected specimen was leiomyoma with no evidence of malignancy (Figure 3). Later, enhanced chest and abdomen computed tomography (CT) scans were performed, and showed no evidence of other mass lesion. We could not find another primary lesion or metastases in any other organ. The diagnosis was primary endobronchial leiomyoma. After local resection of the leiomyoma, the patient no longer complained about hemoptysis.

Discussion

Benign tumor of the lung is rare, and leiomyoma accounts for less than 2% of all benign tumors of the lung [3]. Histopathologically, over half of these lesions were from the pulmonary parenchyma, one-third from the bronchi, and fewer from

the trachea [1-4]. Furthermore, these lesions can be primary or metastatic, and uterine leiomyoma was the most common metastasized origin [3-4]. Clinically, pulmonary leiomyoma can present as either an endotracheal/endobronchial or intraparenchymal lesion; the latter presents as a solitary or multiple nodule/mass on chest radiography and CT scan. In contrast, the endotracheal/endobronchial lesion presents as a polypoid nodule/mass that protrudes intralumenally and might have a wide base [1, 5].

Endotracheal/endobronchial leiomyomas are derived from the smooth-muscle layer of the tracheal/bronchial wall, and intraparenchymal leiomyomas originate from smaller airways and/or vascular muscle. However, patients with either endotracheal/endobronchial or intraparenchymal leiomyoma should be investigated for the possibility of a primary extrapulmonary leiomyoma metastasizing to the lung [3-4].

We describe a 78-year-old male patient with endobronchial leiomyoma. Leiomyomas are commonly found young and middle-aged patients, with a mean age of around 40 years [3, 6-7]. Since most metastasizing leiomyomas were from the uterine leiomyoma, intraparenchymal leiomyomas occurred twice as often in females as in males; otherwise, endotracheal/endobronchial leiomyomas showed no sex predilection [3, 6-7]. One-third of pulmonary leiomyomas are without any significant symptoms. Intraparenchymal leiomyomas rarely cause symptoms; however, 92.9% of patients with endobronchial leiomyoma have respiratory symptoms due to partial or total obstruction of the bronchus, and superimposing infections resulting from atelectasis or bronchiectasis distal to the obstruction [6-8]. Endobronchial leiomyoma presenting with hemoptysis is rarely reported [6]. This was a case with recurrent hemoptysis, but, this symptom subsided after removal of the endobronchial leiomyoma.

In most cases, the exact diagnosis of pulmonary leiomyoma can be made by bronchofiberscopy. For endobronchial lesions, bronchofiberscopy provides visualization of the bronchial tree and direct biopsy for histopathological examination; for intraparenchymal lesions, endobronchial ultrasound sonography can also provide visualization of the lung parenchyma, and a transbronchial lung biopsy can be done for histopathological examination under bronchofiberscopy [4, 6-7, 9]. The diagnosis of leiomyoma was established by light microscopy, electron microscopy and immunohistochemical studies, which included antibodies to desmin and smooth muscle actin [7-8]. In the present case, direct bronchofiberscopic biopsy revealed a definitive diagnosis of leiomyoma. Histopathological examination of the biopsy specimen and immunohistochemical studies with antibodies to smooth muscle actin confirmed the diagnosis.

Treatment of pulmonary leiomyoma depends on the location, size, and width of the base of the lesion and secondary lung destruction. Surgical resection of pulmonary leiomyoma should be considered because leiomyoma is benign, and recurrence is rare after surgical resection [6, 9-11]. Lobectomy and pneumonectomy were the main conservative methods for most patients with pulmonary leiomyoma [4, 12-13]. For endobronchial lesions, bronchofiberscopic removal of the tumor, bronchotomy, and segmental resection may be considered [6, 9-11]. In our patient, a direct forceps resection via bronchofiberscopy was done due to the minute lesion.

In conclusion, our patient had atypical clinical and imaging pictures, but typical histopathologic pictures. Primary endobronchial minute leiomyoma is a very rare entity; it may also cause respiratory symptoms. Leiomyoma should be

taken into consideration in the differential diagnosis when patients have an endobronchial minute lesion and present with hemoptysis.

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原發性支氣管內細平滑肌瘤—病例報告

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原發性支氣管內平滑肌瘤為一罕見的肺部良性腫瘤，我們在此報告一位罹患原發性支氣管內平滑肌瘤的 78 歲男性病人。病人因為咳血至醫院求診，給與安排支氣管內視鏡檢查，於左上肺葉的位置發現一個 0.1 × 0.1 公分的囊性腫瘤，病理報告為一“平滑肌瘤”。此一個囊性腫瘤於支氣管內視鏡下，利用 forceps 完整將其完全切除。我們給與進一步的檢查，並沒有發現其他原發性或轉移病灶，故確定此囊性腫瘤為一個原發性支氣管內平滑肌瘤。經過支氣管內視鏡下切除此囊性腫瘤，病人不再發生咳血現象。*(胸腔醫學* ***2007; 22: 193-197)***

關鍵詞：支氣管內視鏡，原發性支氣管內平滑肌瘤，肺平滑肌瘤

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Prostate Adenocarcinoma with Pleural Metastasis: A Case Report

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Tumors of the pleural space can be of primary or secondary origin. Pleural mass is a rare presentation of metastatic adenocarcinoma of the prostate.

We report the case of an 84-year-old male, a patient with a history of end-stage renal disease (ESRD) and pulmonary tuberculosis. He suffered from progressive dyspnea for several months, and the chest radiograph revealed a left pleural mass. The diagnosis of prostatic adenocarcinoma with pleural metastasis was made after true-cut biopsy from the mass. We treated the patient with diethylstilbesterol and the pleural lesion resolved after 6 weeks of hormonal therapy. Prostate adenocarcinoma is often asymptomatic in patients with ESRD, however, we should not ignore this disease in these patients with a pleural mass. ***(Thorac Med 2007; 22: 198-202)***

Key words: pleural mass, prostatic adenocarcinoma

Introduction

Tumors of the pleural space can be of primary or secondary origin, although primary tumors of the pleural space are uncommon. Those of secondary origin are the most common and are discussed first. Certain tumors appear to have a predilection for metastasis to the pleura, particularly in lung cancer, breast cancer, and lymphomas, and less commonly in gastrointestinal and genitourinary malignancies [1]. A review of the literature showed that the pleura is the second rarest site of involvement after the adrenals in soft tissue metastases of prostate adenocarcinoma [2].

We report the case of an 84-year-old male with prostate adenocarcinoma, with an initial presentation of a pleural mass. The pleural mass regressed after 6 weeks of hormonal therapy.

Case Report

This patient was an 84-year-old man with a diagnosis of pulmonary tuberculosis post-chemotherapy over 10 years ago; he also had end-stage renal disease in maintained hemodialysis for 16 years. He was a retired ophthalmologist and denied an allergic or other systemic disease history, except the old pulmonary tuberculosis and ESRD. He suffered breathlessness for several months before admission. He was sent to our

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emergency room because of worsened respiratory distress and orthopnea that had occurred for several days. He was tachypneic (23/min) without fever and needed Bipap support at our hospital. Chest radiograph (Figure 1) revealed a left-side pleural mass and effusion. No other related symptoms, such as fever, cough, chest tightness, body weight loss or other specific complaints, were presented during this period.

We arranged a chest echo-guided thoracocentesis and pleural biopsy for study. Exudative effusion was obtained and the fluid cytology showed negative findings. The pleural fluid had a total protein concentration of 3.5 gm/dl and a lactate dehydrogenase (LDH) level of 41U/L; acid-fast stain and bacterial culture showed negative findings. On microscopic examination, the fluid demonstrated the presence of 220 cells per cubic mm. These were predominantly neutrophils (76%). No organisms or malignant cells were seen. The pleural biopsy pathology revealed chronic inflammation. After the fluid was drained and the pleural mass had been identified by chest computed tomography (CT) (Figure 2), we performed true-cut biopsy, which yielded the diagnosis of metastatic prostate adenocarcinoma. [Pathology: metastatic carcinoma; prostatic origin: low molecular weight cytokeratin (+++); strong positive for prostate specific antigen (PSA)] Bone scan showed that left-first-rib active-lesion bony metastasis should be considered. The PSA level was 5343 ng/ml (normal range <5 ng/ml). After yielding the diagnosis of prostate carcinoma, we treated the patient with hormonal therapy (diethylstilbesterol 1 mg tid po). The symptom of breathlessness improved slowly after hormonal therapy. The follow-up chest radiograph showed regressive change of the pleural lesion (Figure 3). The follow-up PSA was downgraded to 6.63 ng/ml 6 weeks after diethylstilbesterol was prescribed. The pleural lesion did not recur again after hormonal therapy.

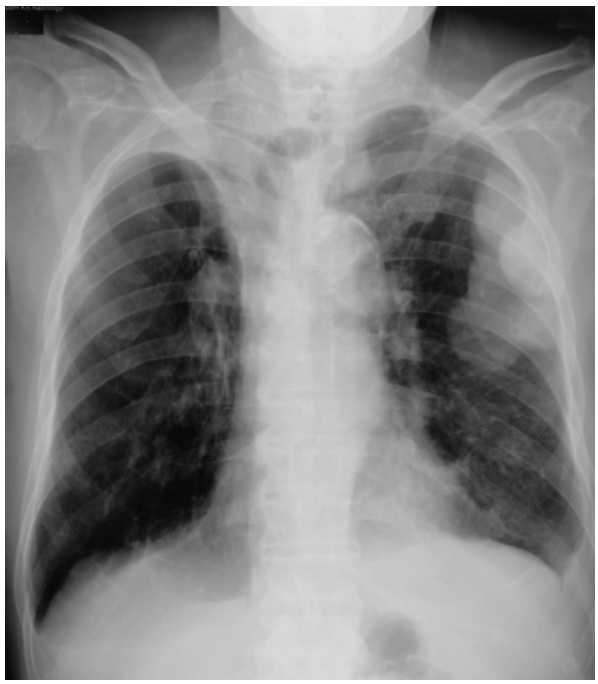

Fig. 1. Initial chest radiograph: Several masses and pleural effusion in the left pleura; right upper lung volume reduction that was related to the old pulmonary tuberculosis.

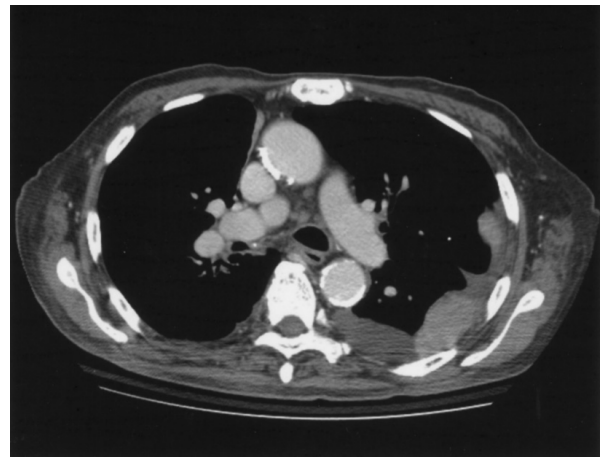

Fig. 2. Chest CT revealed left pleural effusion and masses.

Discussion

Prostate adenocarcinoma with pleural

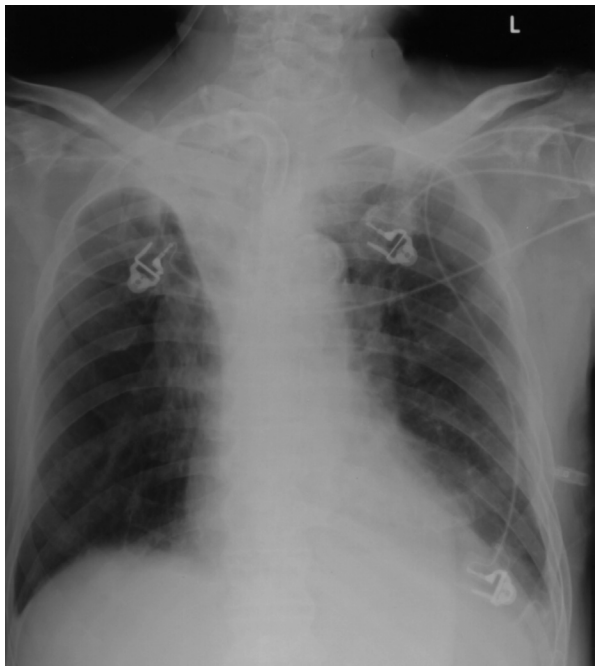

Fig. 3. 6 weeks after hormonal therapy. The left pleural masses and effusion regressed after hormonal therapy.

metastasis is a very rare presentation of soft tissue metastasis [2]. Most cases are reported by urologists and pathologists. Patients with prostate cancer may be asymptomatic or may present with symptoms of advanced disease with frequent urination, increased urination at night, blood in the urine, painful urination, body weight loss, bladder outflow obstruction, and bone pain. The specific causes of prostate cancer remain unknown [3]. The possible risk factors for prostatic cancer include diet, genetics, occupation, race, and other factors.

There is no evidence to prove the relationship between ESRD and prostate carcinoma. Anuria or oliguria is common in patients with ESRD. Prostatic disease in patients with ESRD may be overlooked because it is often asymptomatic. Once prostate carcinoma develops, it is difficult to detect at an early stage.

Primary tumors of the pleural space are uncommon. The most common primary tumor is malignant mesothelioma [4]. Metastatic, secondary tumors of the pleura are a common clinical problem for the pulmonologist [2]. Some tumors appear to have a predilection for metastasis to the pleura, particularly lung cancer, breast cancer, and lymphomas [1]. Diagnosis is now often made from core needle specimens obtained using CT or ultrasound guidance, or from biopsies obtained under direct visualization during pleuroscopy [4].

The diagnosis of our patient was reached after ultrasound-guided biopsy and biomarker examination (PSA). Since the advent of PSA screening, prostatic cancer is being detected and treated earlier. PSA is a sensitive and specific method of detection of metastatic prostatic adenocarcinoma, but there have been case reports showing that it can be negative in some cases [7]; therefore, it should not be taken as a confirmatory test. The definite diagnosis should be made from the tissue pathology.

In approximately half the cases of metastatic pleural disease, the patient will have an associated pleural effusion; most of the effusions were exudative [5]. The most common symptom associated with malignant pleural disease is dyspnea; cough, dull chest ache and pleuritic chest pain are also often noted [6]. Our patient presented breathlessness and exudative pleural effusion as the initial presentation, without other associated chest or bony discomfort. This was compatible with the presentation of most cases.

Androgen ablation therapy (so-called hormonal therapy) is the treatment of choice for the palliation of patients with advanced prostate cancer. More recent data show that orchidectomy alone is as effective in advanced stage cancer with similar palliation and survival [8]. Cytotoxic chemotherapeutic agents have also been tried in conjunction with endocrine therapy; however, no survival advantage has been demonstrated [9].

We treated the patient with androgen deprivation therapy due to the patient's advanced age and also the advanced stage of the prostate cancer. However, hormonal therapy alone does not cure this type of cancer; it is referred to as a palliative therapy. The pleural lesion regressed after we treated the patient with hormonal therapy (diethylstilbesterol) and the PSA level returned to a normal range within 6 weeks. He was then discharged with an oxygen supply of 2 liter/minute.

Although the pleura is the second rarest site of soft tissue metastasis of prostate carcinoma, a prostate lesion should be considered if malignant pleural effusion is suspected. This case illustrates the importance of including prostatic carcinoma in the differential diagnosis of pleural effusions.

In conclusion, prostatic adenocarcinoma is often asympto-matic in the early stage, especially in patients with ESRD. It is difficult to detect the disease at an early stage because the patients often have anuria or oliguria (asymptomatic).

Although the pleural space is a very rare site of soft tissue metastasis in prostate carcinoma, it should be listed in the differential diagnosis in patients with a pleural mass.

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攝護腺癌合併肋膜腔轉移；罕見的肋膜腔積水及腫瘤之致病因—一個案例報告

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肋膜腔腫瘤的成因大多數是轉移性的癌症，這些病人常合併有肋膜積水以及肋膜腫瘤，並造成呼吸困難以及咳嗽等症狀。攝護腺癌合併肋膜腔轉移非常罕見。我們報告的這位病人本身是末期腎臟病須長期血液透析的病人，病人一開始的表現是以呼吸困難為主，影像學診斷發現有肋膜積水以及肋膜腫瘤,經切片診斷為轉移性攝護腺癌。

雖然末期腎病的病人通常不會表現出泌尿道方面的症狀，但是我們藉由這位病人臨床上的表現，彰顯出來攝護腺腫瘤在肋膜轉移時所表現的症狀以及將攝護腺癌列入鑑別診斷的重要性。*(胸腔醫學 **2007; 22: 198-202**)*

關鍵詞：肋膜腔腫瘤，攝護腺癌

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Thoracic Endometriosis — A Case Report and Literature Review

Jiun-Ting Wu*, Meng-Chih Lin*,**, Chien-Hao Lai*, Chao-Chien Wu*, Yung-Che Chen*

Hemoptysis can be caused by a variety of pulmonary diseases, including infection, cardiovascular disorders, systemic disorders, trauma and malignancy. If it recurs and correlates with the time of menstruation in a pre-menopausal woman, a diagnosis of thoracic endometriosis should be highly suspected. We report the case of 49-year-old woman who presented with recurrent episodes of hemoptysis and dyspnea, coincident with the time of menstruation, for 1 year. Chest X-ray and computed tomography (CT) yielded significant right-sided hydropneumothorax. Thoracentesis revealed bloody pleural effusion. An elevated tumor marker cancer antigen-125 (CA-125) level was noted. Chest echo-guided pleural biopsy and thoracotomy led to a diagnosis of endometriosis. The patient underwent decortication of the right involved pleura and received danazol (Ladogal®) treatment after surgery. No recurrence of hemoptysis was noted during 6 months of follow-up. In this report, we also review the various presentations, pathogeneses and therapies of thoracic endometriosis, and discuss the role of CA-125 in thoracic endometriosis. ***(Thorac Med 2007; 22: 203-208)***

Key words: thoracic endometriosis, catamenial hemoptysis, hemothorax, pneumothorax

Introduction

Hemoptysis is a nonspecific sign associated with many pulmonary diseases, and common causes include airway diseases, parenchymal diseases and vascular disorders. The incidence of nontraumatic hemothorax is rare, and it usually correlates with pleural malignancy, anticoagulant therapy for pulmonary embolism, hematologic disorders and complication of pneumothorax. If recurrent episodes of hemoptysis, hemothorax or pneumothorax occur in a woman, coincident with the time of menstruation, thoracic endometriosis should be highly suspected.

Thoracic endometriosis is a rare disorder with varying clinical presentations. The term "thoracic endometriosis syndrome", proposed to refer to the varying clinical and radiological manifestations, includes 4 well-recognized clinical entities (namely, catamenial pneumothorax, catamenial

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hemothorax, catamenial hemoptysis and lung nodules). The etiological mechanisms of this syndrome are not well understood and the treatment strategy remains controversial [1]. In this report, we present a patient with thoracic endometriosis characterized by catamenial hemoptysis, spontaneous pneumothorax, and hemothorax. Pathological examination of the pleura was consistent with endometriosis.

Case Report

A 49-year-old woman (gravida 3, para 3) had experienced right-sided spontaneous pneumothorax and been treated with tube thoracostomy 5 years earlier. In the most recent year, she presented with episodes of cough with blood-streaked sputum, exertional dyspnea, and right-sided pleuritic chest pain. She noted a 3-kg unintentional weight loss over the past year. She had no fever, chills, easy bruising, limb edema, or trauma. These symptoms recurred and were associated with the occurrence of menstruation and subsided during the intermenstrual period. Five months prior to this hospitalization, she came to the outpatient clinic for medical first aid. Physical examination revealed mild pale conjunctiva and diminished breathing sounds on the right side. Chest radiography and CT demonstrated right-sided hydropneumothorax with partial collapse of the right middle and lower lobes (Figure 1, 2). The blood carcinoembryonic antigen (CEA) level was 1.6 ng/ml (normal range <5 ng/ml). Thoracentesis revealed bloody pleural fluid with a lactate dehydrogenase (LDH) level of 1297 U/L and a protein level of 8.4 g/dL. Further analysis of the pleural fluid was negative for acid-fast bacilli and bacterial culture. Cytologic examination demonstrated acute and chronic inflammatory cells infiltration, and no evidence of malignancy. Later, she underwent bronchoscopic examination and echo-guided pleural biopsy. She was then lost to follow-up and began eating health foods. Four months later, she visited the outpatient clinic again because the previous symptoms had persisted. Follow-up chest X-ray and CT revealed right-sided hydropneumothorax, local pleural thickening, progressive change of

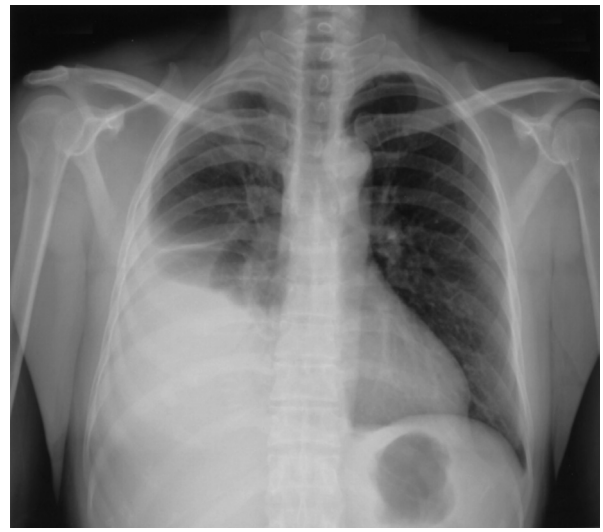

Fig. 1. Chest radiography reveals right pleural effusion.

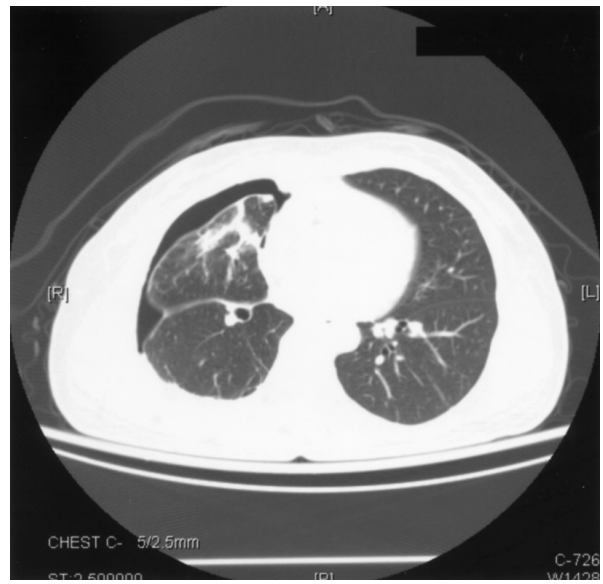

Fig. 2. Chest CT shows right hydropneumothorax, as well as partial collapse of the right middle and lower lobes.

the right middle lobe, and right lower lobe consolidation. Gynecological echo demonstrated unremarkable findings. At that time, her CA-125 level elevated to 246 U/ml (normal range: <35 U/ml) and the CEA level was 34.3 ng/ml. Therefore, she was admitted for surgical intervention to exclude malignancy.

Severe pleural adhesion with trapped lung and thickening of the visceral and parietal pleura with diffuse bloody pigmentation were noted during operation. Wedge resection of the right lower lung, multiple biopsies of the parietal pleura, evacuation of a loculated blood clot and decortication of thickening pleura were performed. No palpable lung nodules were found. The wedge resection pathology showed old and fresh hemorrhage with acute and chronic inflammation, and decortication of the thickening pleura showed necrosis. Pathology of the pleural biopsy and immunohistochemical study revealed endometriosis without malignancy (Figure 3).

After surgery, danazol (200 mg) twice daily was administered. The CEA level returned to normal range 1.4 ng/ml and the CA-125 level decreased to 44.85 U/ml 2 months later. No recurrence of hemoptysis was noted during 6 months of follow-up.

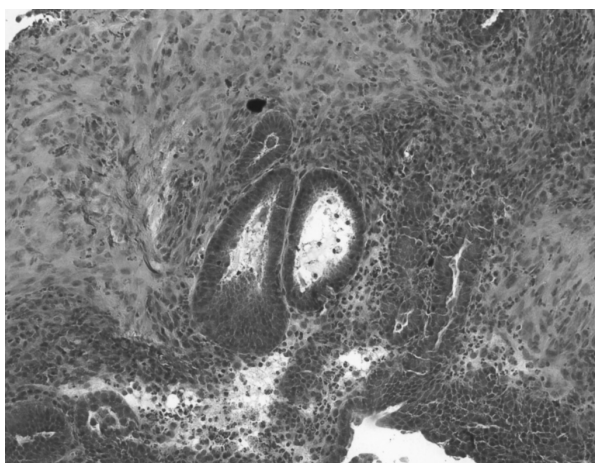

Fig. 3. Pathology of the pleura reveals endometrial gland and stroma. (Hematoxylin and eosin stain, 100X)

Discussion

Thoracic endometriosis is a rare disorder with varying clinical and radiological manifestations. The largest series reviewed 110 cases of thoracic pathology associated with menstruation presenting as hemoptysis, hemothorax, pneumothorax, or pulmonary nodules [1]. The term thoracic endometriosis syndrome (TES) was proposed. The mean age at diagnosis was 35±0.6 years, with a range from 15 to 54 years. Pneumothorax occurred in 73% of these cases, hemothorax in 14%, hemoptysis in 7%, and pulmonary nodules in 6%. In 90% of patients, the symptoms occurred within 2 days after the onset of menstruation. The symptoms, signs, and pathologic state that recur in the chest with menses are hallmarks of the disease. Such phenomena were termed catamenial by Lillington in 1972 [2].

Two types of thoracic endometriosis have been described: pleural and parenchymal [3]. The right side was involved predominantly in more than 90% of cases [1, 4]. Pleural endometriosis usually causes chest pain, cough and shortness of breath, and it may be associated with catamenial pneumothorax, catamenial hemothorax, or both. Parenchymal endometriosis usually results in catamenial hemoptysis. Chest radiography may reveal pulmonary opacities or nodular infiltrates, and sometimes even a normal picture in the presence of current bleeding [5].

Three theories have been proposed to explain the presence of thoracic endometriosis: coelomic metaplasia, lymphatic or vascular embolization from the uterus or pelvis, and retrograde menstruation with subsequent transperitoneal-transdiaphragmatic migration of endometrial tissue [1].

None of these theories can explain all the clinical manifestations of TES, and the disease probably has a multifactorial etiology [6-7].

The most effective treatment strategy remains controversial because of the lack of therapeutic trials. Treatment of thoracic endometriosis includes immediate intervention followed by long-term control of thoracic endometriosis syndrome. The immediate treatment for a significant pneumothorax or a large hemothorax is lung re-expansion with tube thoracostomy. Medical treatments focus on the suppression of the existing thoracic endometrial tissue and the prevention of further seeding by blocking the action of estrogen. Although various hormonal agents are utilized to achieve this objective, including danazol, progesterone, gonadotropin-releasing hormone (GnRH) agonists and oral contraceptives, recurrence rates greater than 50% have been reported [1, 8]. At present, no specific drug has been shown to be superior to another; the decision is influenced by cost, side effects, duration of treatment and the will to become pregnant.

In general, medical therapy alone is not sufficient for the treatment of thoracic endometriosis [9]. Segmental lung resection or wedge resection of endometrial implanted tissue could be potentially effective if a single focus of thoracic endometriosis or foci confined to a small area were definitely detected. Hysterectomy with bilateral oophorectomy is the definitive treatment of endometriosis, but it may be ineffective if hormone replacement therapy is undertaken. Repair of diaphragm fenestration and chemical pleurodesis are also shown to be effective in the treatment of thoracic endometriosis complicated with pneumothorax or hemothorax [10]. In this case, the patient underwent pleural decortication combined with danazol treatment. Her symptoms subsided and the serum CA-125 level returned to a nearly normal range 2 months later. This may imply that the simpler operative procedure is effective, but long-term follow-up is necessary.

This patient presented with catamenial hemoptysis, hemothorax and pneumothorax that included all possible manifestations of thoracic endometriosis. Wedge resection of the right lung consolidation revealed old and fresh hemorrhage with acute and chronic inflammation, and pleura biopsy proved endometriosis. However, it is difficult to correlate the whole clinical picture if only pleural endometriosis is suspected. We supposed that there was a parenchymal endometrial lesion, but the lesion was not detected during operation and the subsequent pathological examination.

The CA-125 antigen is a high molecular glycoprotein produced by normal cells of different tissues derived from the celomic epithelium, such as the epithelium of the Fallopian tubes, the endometrium, endocervix, pleura, peritoneum, and pericardium. The serum CA-125 level correlates with the amplitude of serosal involvement, and a possible role should be considered for this glycoprotein as a marker of clinical evolution and response to treatment [12]. Serum CA-125 concentrations can be elevated in patients with thoracic endometriosis, but the sensitivity and specificity of the test in this setting are unknown [11]. In our case, a high-level CA-125 presented initially, and decreased gradually after surgery and danazol treatment; meanwhile, the patient became asymptomatic. CA-125 may have indicated the degree of thoracic endometriosis and the response to treatment in this case. We suppose that CA-125 could be a marker to follow up the extent of thoracic endometriosis.

In conclusion, thoracic endometriosis should be suspected in any case of recurrent spontaneous pneumothorax, hemoptysis and blood-stained

pleural effusion, especially if it is right-sided, occurring in women of reproductive age during the menstrual period. Serum CA-125 levels may correlate with the extent of involvement and imply the treatment response of thoracic endometriosis; however, further studies are required to determine the sensitivity and specificity.

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胸腔子宮內膜異位症—病例報告及文獻回顧

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咳血是肺部疾病非特異性的徵象。但若其發生於停經前婦女且與經期相關，則需考慮胸腔子宮內膜異位症之可能性。胸腔子宮內膜異位症是一種罕見疾病。依據子宮內膜異位的位置可區分為肺實質及肋膜子宮內膜異位。臨床及影像上主要的表現，包括：月經性氣胸、月經性血胸、月經性咳血及肺結節。治療的方法仍未有定論，在所有文獻報告中，目前仍然是以手術治療，以及術後合併使用荷爾蒙治療以抑制排卵及子宮內膜的活性最為有效。在此，我們報告一位 49 歲的女性病人以月經性咳血和呼吸困難為最初表現，影像上呈現右側氣胸併肋膜積水，同時血中 CA-125 上升。經一系列檢查及手術肋膜切片，證實為胸腔子宮內膜異位症。在本文中同時回顧胸腔子宮內膜異位症的臨床表現、病理機轉及治療策略，並探討 CA-125 在胸腔子宮內膜異位症的相關角色。*(胸腔醫學* ***2007; 22: 203-208)***

關鍵詞：胸腔子宮內膜異位症，月經性咳血，血胸，氣胸

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Morgagni Hernia Presenting as Heart Failure: A Case Report

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Morgagni hernia is a subcostosternal diaphragmatic hernia, and is the rarest form of disease related to diaphragmatic defects. Most Morgagni hernias are congenital, but are rarely diagnosed in childhood. Specific examinations are needed because of reducible symptoms and herniation. Surgical correction is the golden rule for cure of this complicated disease. We report a 57-year-old male patient with diabetic obesity and Morgagni hernia who presented as heart failure and acute renal insufficiency. Dramatic recovery of clinical symptoms and systemic complications occurred after surgical repair. Roentgenographic studies and operative findings are demonstrated as well. ***(Thorac Med 2007; 22: 209-214)***

Key words: Morgagni hernia, systemic complications, surgical repair

Introduction

Subcostosternal diaphragmatic hernia is the least common form of diaphragmatic hernia, accounting for 2~3% of all cases [1]. In 1769, Morgagni first described a diaphragmatic hernia which originated from the sternocostal trigone, and thus it bears his name [2]. Most Morgagni hernias are congenital diseases and are rarely detected in children. The hernia is asymptomatic in about one-third of patients and is frequently diagnosed by chest radiography. Those with compression of vital organs often show non-specific complaints, such as gastrointestinal or respiratory symptoms. In some cases, they might present with bowel obstruction or acute respiratory distress. In practice, more than half of Morgagni hernias are detected incidentally during investigation for related problems. We reported a patient with Morgagni hernia who presented as heart failure associated with acute renal insufficiency.

Case Report

A 57-year-old male patient with diabetic obesity (body mass index: 30 kg/m^2) was admitted to our hospital with progressive edema of bilateral lower legs, oliguria, general weakness and abdominal distention for 2 weeks. His physical examination showed decreased breathing sounds with dullness by percussion in the right lower chest. Blood test revealed elevated serum creatinine

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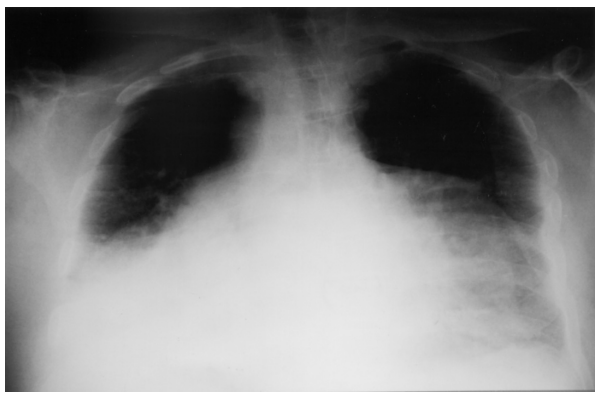
(13.3 mg/dL) and azotemia (blood urea nitrogen, 121 mg/dL). Chest radiography showed a large radiopacity in the right lower lung field with bowel gas in the thorax (Figure 1). Computed tomography of the chest demonstrated a large occupying lesion with the colon and omentum in the right-side hemi-thorax (Figure 2). Therefore,



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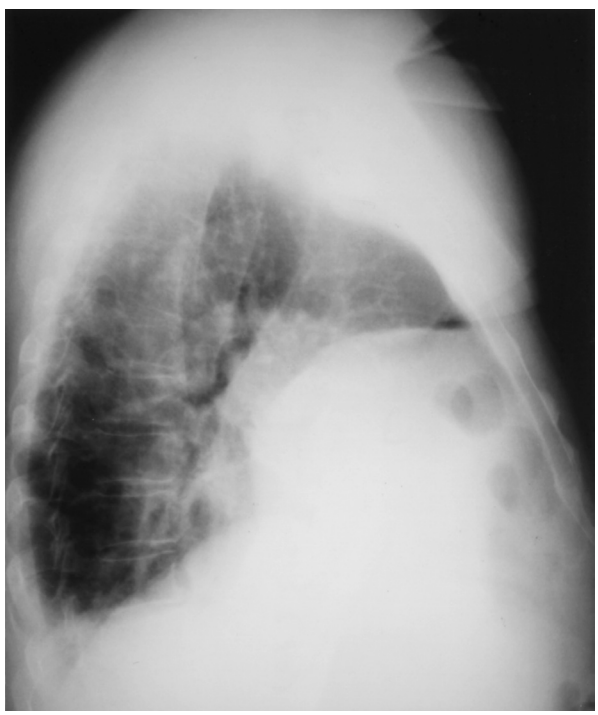

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Fig. 1. A. Posteroanterior radiography shows large opacity in the right lower lung field. B. Lateral view reveals the opacity at the retrosternal area with bowel gas.

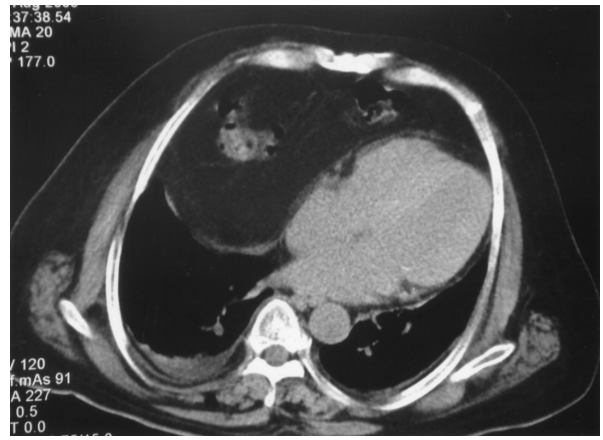


Fig. 2. Computed tomographic scan shows a right retrosternal hernia containing both omentum and colon. The heart is compressed by the hernia sac and shifts to the left side of the thorax.

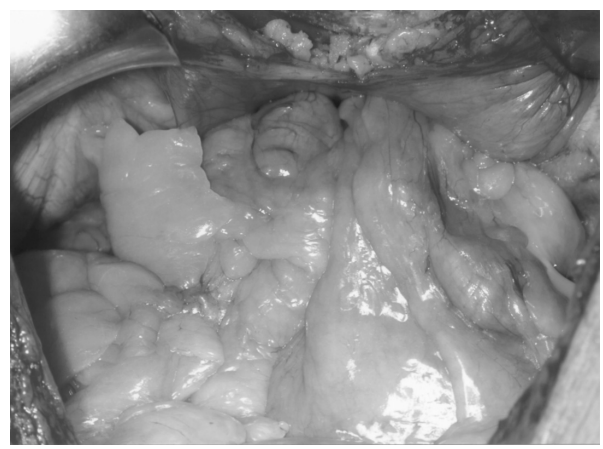
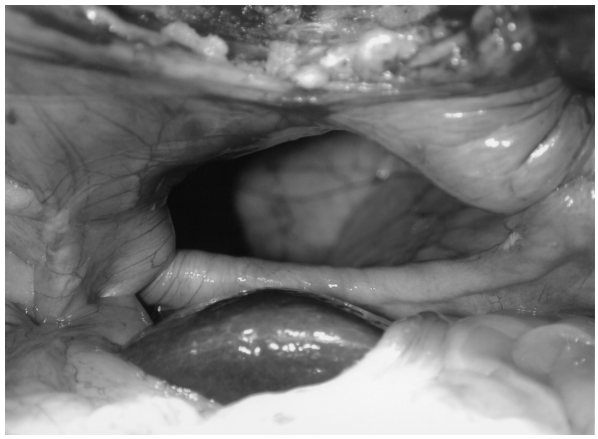


Fig. 3. Through a transabdominal approach, the omentum and transverse colon were noted in front of the liver and pulled into the right thorax.

a diaphragmatic Morgagni hernia with hemodynamic suppression was diagnosed.

The patient received surgical intervention with an upper midline laparotomy. Operative findings showed the hernia with a sac filled with the omentum and colon (Figure 3). The incarcerated and herniated contents were reduced smoothly, and the hernia sac and diaphragmatic defect were repaired with interrupted nonabsorbable stitches (Figure 4).



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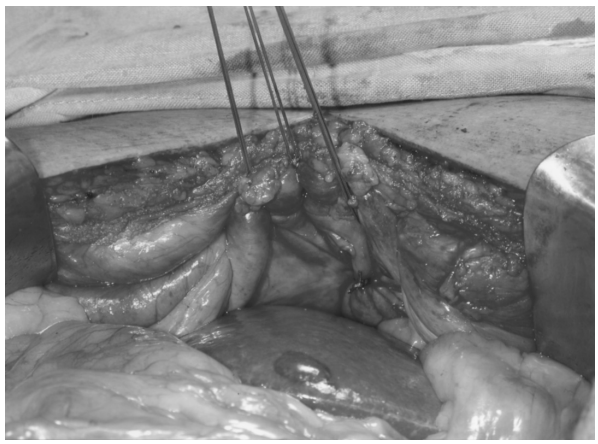

(B)

Fig. 4. A. After reducing the viscera, the defect in the diaphragm was noted and the sac was found in the right thorax. B. The sac was retained and the defect was repaired with interrupted sutures.

The postoperative course was uneventful. Dramatic improvement of the heart failure was noted, including an adequate urine output and no presence of edema. The levels of serum creatinine and blood urea nitrogen were all back to normal (0.7 mg/dL and 17 mg/dL respectively), and the patient recovered well about 10 days after operation.

Discussion

Morgagni hernia is an unusual defect of the anterior part of the diaphragm, and accounts for about 1% to 6% of surgically-removed diaphragmatic hernias. It is located anteromedially on either side of the junction of the septum transversum and thoracic wall [3], and is caused by unsuccessful fusion between the fibrotendinous portions of the sternal and costal parts of the diaphragm [4]. Such failed fusion creates weakness in the diaphragm and is later stretched loose by the rapid rise in intra-abdominal pressure, which gives rise to a hernia. This is the reason that Morgagni hernias are usually not found in children [5]. About 90% of Morgagni hernias are located on the right side, 2% are located on the left, and 8% are bilateral [6-7]. The lesser incidence of left-side Morgagni hernias is due to cardiac compression forming a natural barrier on the sternocostal trigone [8].

Pathogenetically, a Morgagni hernia is caused by incomplete development of the diaphragm. Other secondary factors, including trauma, stressful effort, and obesity, may also contribute to formation of the Morgagni hernia, and these factors are thought to be caused by the increased abdominal pressure [9]. The typical presentations are abdominal pain, intestinal obstruction, chest tightness and/or shortness of breath [5]. In complicated conditions, as in the current case, the patient presents with heart failure and non-specific abdominal distention. We suspected that the huge herniated occupancy induced compression of the heart and later, unstable hemodynamics. Reviewing the literature, only 1 report has ever mentioned a similar condition [10].

Due to the non-specific presentations of Morgagni hernia, it is difficult to diagnose clinically. Most Morgagni hernias are diagnosed by chest

radiography, with evidence of gas-filled bowel loops or a soft tissue mass above the right dome of the diaphragm [7, 11]. However, if the herniated contents are reversible, the radiography may sometimes be normal. Morgagni hernia can also be mistaken as a lung collapse, pneumonic consolidation, pericardial fat pad, pericardial cyst, or mediastinal mass. Specific studies, such as bowel contrast roentgenography, ultrasound, computed tomography, and magnetic resonance imaging, can contribute to the diagnosis [12-14].

Surgery is the only way to treat the herniated viscera of Morgagni hernia. The management of Morgagni hernia is controversial in asymptomatic patients. However, for the prevention of incarceration and related complications, surgery should be considered in all patients when the diagnosis is made [4]. Both transabdominal and transthoracic approaches have been recommended [8, 15]. Chin et al advised a transthoracic approach because it provided a wide exposure and easy repair of the hernia sac [4]. However, an abdominal approach would be suggested if bilateral or complicated herniation was apparent [15]. In patients whose hernia presents as a homogenous density on X-ray, or when the differential diagnosis with a chest tumor is difficult, the thoracic approach is preferable, as it may provide better preparation and reduction of the herniated liver or appropriate management of an unsuspected chest lesion [4]. Recently, endoscopic surgery with primary repair with or without mesh has been reported as a safe and effective option for treatment of Morgagni hernia [16-19].

Conclusion

Morgagni hernia is a rare type of diaphragmatic hernia. Its diagnosis is often made by imaging studies. The value of surgical repair is in preventing the incarceration or strangulation of the herniated viscera, and to relieving hemodynamically compressive syndromes, such as heart failure and cardiac tamponade. Transabdominal or transthoracic approaches in surgery are recommended, and either thoracoscopic or laparoscopic repair may be another choice of management.

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以心臟衰竭表現之 Morgagni 橫隔疝氣一病例報告

陳百璽　劉洪彰　黃文傑　陳兆弘　黃常哲

Morgagni 疝氣唯一少見之橫隔膜缺損疾病，大多數病因為胚胎時期橫隔膜封閉不全所導致的橫隔缺損，少數病患為後天因素所造成，例如：創傷、肥胖等。此病的臨床表現，多半以呼吸道和腸胃道的癥狀為主。也由於症狀不明顯，且缺乏特異性，因此在診斷上添加了困難度。一般來說，此疾病常因影像學檢查而偶然發現。我們在此報告一個 57 歲的肥胖男性，因出現心衰竭併急性腎衰竭入院求診。在常規的胸部影像學檢查中發現右下肺野大區塊之不透亮陰影；胸部電腦斷層掃瞄確立 Morgagni 疝氣之診斷，且心臟因為疝氣的存在而造成明顯的左側偏移。病患在接受開腹手術修補 Morgagni 疝氣後，其腎衰竭及心衰竭症狀皆獲得顯著的改善。我們回顧並整理過去的相關文獻提出此報告。*(胸腔醫學* ***2007; 22: 209-214****)*

關鍵詞：Morgagni 疝氣，全身性併發症，外科修復

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Acute Respiratory Distress Syndrome Caused by *Mycoplasma Pneumoniae* Infection: A Case Report

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The clinical course of *Mycoplasma pneumoniae* (*M. pneumoniae*) pneumonia is generally benign. Unfavorable outcomes have been reported in some patients, and most of them have involved extrapulmonary sites. Acute respiratory distress syndrome (ARDS) caused by *M. pneumoniae* infection is very rare; only a few cases have been reported in the literature. This type of ARDS has a different clinical course from other bacteria-induced ARDS. In this report, a 40-year-old previously healthy woman with initial right lower lung pneumonia and parapneumonic effusion is presented. Moxifloxacin was administered after she had been hospitalized, but ARDS developed on the fifth hospital day. Two weeks later, *M. pneumoniae* antibodies were present at a titer of 1:640, a 4-fold increase compared to the serologic test before hospitalization. Although the patient was discharged and her condition remained uneventful, moderately restrictive ventilatory impairment and moderately reduced gas exchange were noted in the lung function test during the chest clinic follow-up. *M. pneumoniae* should be considered as a possible pathogen in a slowly progressing course of ARDS after community-acquired pneumonia. ***(Thorac Med 2007; 22: 215-221)***

Key words: *Mycoplasma pneumoniae*, acute respiratory distress syndrome

Introduction

Mycoplasmas are the smallest free-living organism, and are of the class Mollicutes. They lack a cell wall and require sterols to stabilize their cytoplasmic membrane, making them unique among bacteria. All mycoplasmas are facultatively anaerobic, but not *Mycoplasma pneumoniae* (*M. pneumoniae*), which is the exception because of its strict aerobic nature. Eaton *et al.* first discovered this causative agent in their studies on the etiology of primary atypical pneumoniae in 1945 [1].

M. pneumoniae accounted for 20% of all community-acquired pneumonia in Taiwan in a recent study, and was the second most common etiologic pathogen after *Streptococcus pneumoniae* [2]. Infection with this bacterium produces mild upper airway disease, such as atypical pneumonia or tracheobronchitis. The diseases are mild and follow a benign course. Unfavorable outcomes such as acute hemolytic anemia [3],

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myocarditis [4], or various degrees cerebral involvement [5] have been reported, and most of them involve extrapulmonary sites. Acute respiratory distress syndrome (ARDS) caused by *M. pneumoniae* infection is very rare; only a few cases have been documented.

We present a rare condition, in which ARDS developed in a 40-year-old previously healthy woman 5 days after admission for right lower lung pneumonia. The diagnosis was made by an over 4-fold increase in the antibody titer to *M. pneumoniae*. No pathogen in the blood or sputum culture was identified during the course. The clinical significance of an atypical bacterial infection, such as *M. pneumoniae,* in certain patients with ARDS should be emphasized.

Case Report

A 40-year-old woman was admitted to the hospital because of dry cough, spiking fever, and chills. She was in good health without systemic disease, previous admission, or surgical intervention. She had no allergies, and never smoked or drank. She worked as a nursing specialist in the pediatric department of a teaching hospital. Three days before admission, dry cough, spiking fever up to 39.5 degrees, and chills developed. She was seen by the pediatrician at Chi-Mei Hospital and had a chest radiography which showed right lower lobe pneumonia (Figure 1). Amoxicillin 500 mg 3 times per day was prescribed after a single dose of cefuroxime 1500 mg was administered intravenously in the clinic. The immunoglobulin G (IgG) of the *M. pneumoniae* antibodies titer was negative in the blood drawn on that day.

Dry cough, high fever, and chills persisted. She visited the chest clinic at this hospital because there were no signs of improvement after 3 days of medication. Repeated chest radiography revealed a deteriorated pneumonia patch in the right lower lobe (Figure 2). The white cell count was 4,300 cells/μL, with 92% segment neutrophils, and the C-reactive protein level was 157.2 mg/L. Biochemical laboratory tests included a blood urea nitrogen level of 6 mg/dL, creatinine of 0.7 mg/dl, sodium of 137.4 mEq/L, potassium of 3.44 mg/dL, glucose of 133 mg/dL, aspartate aminotransferase of 44 IU/L, and alanine aminotransferase of 27 IU/L, all within normal range.

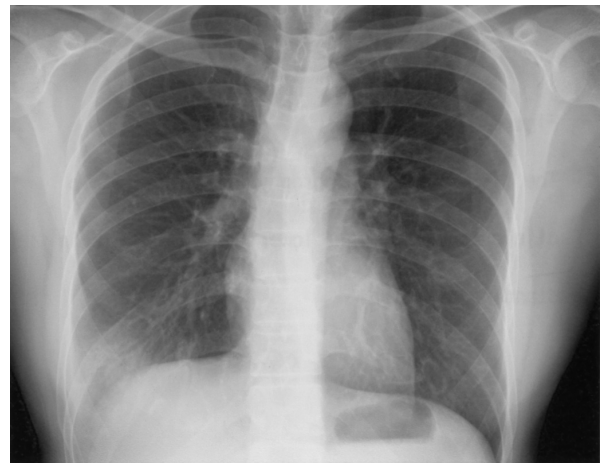

Fig. 1. The first chest radiograph at the pediatric clinic, revealing right lower lobe pneumonia in the standing position

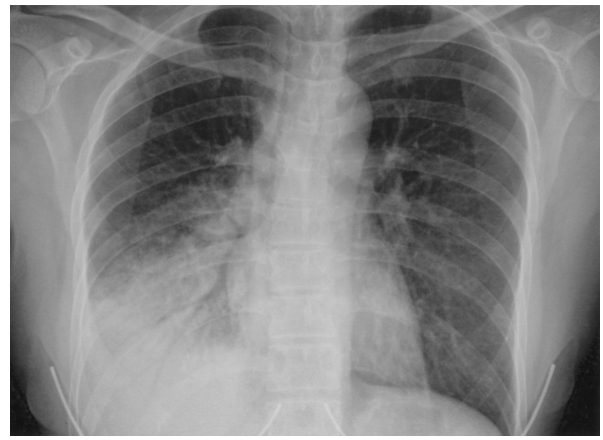

Fig. 2. Repeated standing chest radiograph after medication, revealing a progressive pneumonia patch in the right lower lobe

She was treated with intravenous moxifloxacin 400 mg daily after hospitalization. The ultrasonography of her chest showed right side pleural effusion. Tube thoracostomy with a pigtail into the right pleural cavity was performed for drainage. The pleural effusions were serosanguous in appearance and analyzed as follows: red cell count: 63,000 cells/μL, white cell count: 1980 cells/μL, with a differential fraction of lymphocytes : neutrophils : mesothelial cells : histocytes = 57 : 43 : 0 : 0. A lactic dehydrogenase (LDH) level of pleural effusion of 580 IU/L, total protein of 3.2 g/L, and carcinoembryonic antigen (CEA) of 4.51 ng/mL were noted. The bacterial and acid-fast bacilli cultures were all negative, compatible with her negative findings in Gram's and acid-fast stains of the pleural effusion.

Her spiking fever subsided, but progressive shortness of breath was noted on the third hospital day. The chest radiograph revealed more severe bilateral air-space infiltrates (Figure 3) compared with the previous film on admission. Her oxygen saturation was 85-90% with the patient breathing 100% supplemental oxygen delivered by a non-rebreathing mask on the fifth hospital day. Arterial blood gas results under FiO2 100% were as follows: pH 7.497, PCO2 35.6 mmHg, PO2 45.4 mmHg, and HCO3 27 mmol/liter. Echocardiography showed adequate left ventricle performance.

The patient refused elective endotracheal intubation and was transferred to the medical intensive care unit with the impression of ARDS. Repeated bacteriology workups, such as blood culture, sputum culture, and urine culture, were all performed; however, no pathogen was identified during the course of hospitalization. The immunoglobulin M (IgM) of *Chlamydia pneumoniae* and *Legionella pneumophila*, as well as the *Streptococcus pneumoniae* antigen, were also negative. Moxifloxacin was continued due to adequate blood pressure without septic shock and the lack of evidence of any other potential pathogen infection. After 2 days of non-rebreathing mask supplement, the patient slowly improved and survived. She was treated with hydrocortisone 100 mg every 8 hours after transfer to the general ward on the 10th hospital day. Her lung condition improvement was noted in her chest radiograph (Figure 4).

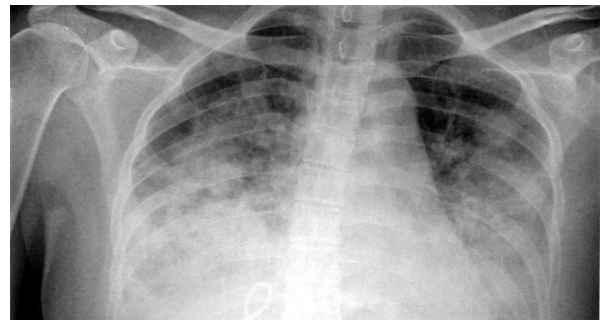

Fig. 3. More severe bilateral air-space infiltrates on the third hospital day in the supine chest radiograph

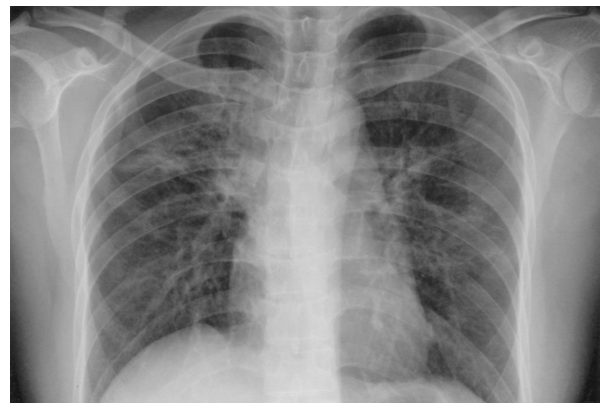

Fig. 4. The standing chest radiograph, revealing resolution after steroid administration

M. pneumoniae antibodies were present at a titer of 1:640 2 weeks after the previous *M. pneumoniae* serologic test. Moderately restrictive ventilatory impairment (FVC 2.2 liters, 65% of predicted value) and moderately reduced gas exchange (Dlco 9.2 mL/mmHg/min, 44% of

predicted value) were noted in the lung function test in the chest clinic. The patient's condition was uneventful after discharge.

Discussion

As noted in the studies done by Eaton in 1945, the clinical course of *M. pneumoniae* pneumonia is generally benign. Most patients with *M. pneumoniae* infection develop upper airway diseases like tracheobronchitis and atypical pneumonia that are usually self-limited. Acute exacerbation of asthma in some children [6], and more severe bronchopneumonia, or even empyema [7], are reported. Extrapulmonary manifestations are reported to be its severest complications, and if at all, most of them are hemolytic anemia [3], myocarditis [4], and varied neurologic deficits [5]. In 1978, Fischman, *et al*. first reported 2 cases of ARDS due to *M. pneumoniae*. These were 2 previously healthy young adults, and the diagnosis of *M. pneumoniae* infection was made by a 4-fold rise in the complement fixation to *M. pneumoniae* [8]. Chian CF, *et al*. reported the first *M. pneumoniae*-related ARDS in Taiwan [9] in 1999. The patient was also a previously healthy young man of 20. He required mechanical ventilation due to hypoxemia on the third hospital day and fulfilled the criteria of ARDS on the seventh day. The positive tests for *M. pneumoniae* IgM and cold agglutinin confirmed the diagnosis.

An adequate antibiotics choice is crucial for pneumonia therapy, either community or hospital-acquired. In several cases with *M. pneumoniae* infection, the patients were treated with adequate antibiotics but still deteriorated to ARDS [9-11]. ARDS caused by *M. pneumoniae* in previous reports was believed to be a cell-mediated hyperimmune response [12]. In our case, moxifloxacin was effective due to an afebrile status without progression to septic shock after administration. *M. pneumoniae* does not produce classical bacterial toxins, so the reasons for respiratory epithelial damage are still being studied, with no definite conclusions [13].

The observations of the ARDS Clinical Trials Network do not support the routine use of methylprednisolone for ARDS [14]. Does the same apply for *M. pneumoniae*-related ARDS? McGonigle, in 1980, put an emphasis on the potential role of steroid pulses in the treatment of severe acute lung injury caused by *M. pneumoniae* in his early case experience [15]. A small sample study carried out by Lee, *et al*. reached the same conclusion in children with severe *M. pneumoniae* pneumonia [16]. For adult patients, there are only case reports, and no randomized double-blinded study on steroid therapeutic experiences [17-19]. The role of steroid for other bacterial ARDS remains unclear; however, steroid administration may be beneficial in these patients, based on the pathophysiology induced by *M. pneumoniae*. The first case in Taiwan was discharged with normal pulmonary function. Our reported patient's lung function test in the chest clinic revealed moderately restrictive ventilatory impairment and reduced gas exchange. Affected patients have recovered to various degrees from full resolution without lung sequelae, requiring treatment ranging from intermittent positive pressure ventilation [10] to lung fibrosis [20]. The mechanism and determining factors in individual differences of lung functioning impairment after *M. pneumoniae* ARDS are still a mystery.

M. pneumoniae rarely causes parapneumonic effusion. In a clinical analysis of *M. pneumoniae* pneumonia by Hwang, *et al*. [21], only 7% of patients developed parapneumonic effusions. The presence of pleural effusions led to the mistaking of *M. pneumoniae* pneumonia for other com-

munity-acquired bacterial pneumonia. Although the antibiotics of choice for this patient affected by *M. pneumoniae* are macrolides, new quinolones such as moxifloxacin, gatifloxacin, or gemifloxacin are reasonable for monotherapy in community-acquired pneumonia before the definite pathogen is identified. *M. pneumoniae*-related ARDS is rare, and all patients are diagnosed by serologic tests in the later course. Because many different pathogens can cause ARDS, initial monotherapy with only macrolides for these ARDS patients, before *M. pneumoniae* is confirmed, is risky.

In conclusion, severe lung injury is possible clinically with evidence of these cases. *M. pneumoniae* should be considered as an etiologic pathogen in a delayed onset of ARDS after pneumonia. The role of steroid therapy remains undetermined, but is worthy of clinical trials with these patients.

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肺炎黴漿菌感染引起的急性呼吸窘迫症：病例報告

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肺炎黴漿菌的臨床病程一般比較良性。曾有文章報告過不佳的預後，大部分是肺臟外面的表現。肺炎黴漿菌感染所引起的急性呼吸窘迫症相當罕見，過去只有幾個病例報告過。在本篇文章，我們報告一個過去身體健康的 40 歲女性，因為右下葉肺炎合併肺炎積水而住院。儘管給予有效的抗生素 moxifloxacin ，病人依然在住院後第五天發生急性呼吸窘迫症。兩個星期後肺炎黴漿菌的血清抗體值高達 1:640 ，和住院前追蹤的血清抗體值有四倍以上的上升。這是一個相當罕見的肺炎黴漿菌感染所引起的急性呼吸窘迫症。雖然病人最後出院並且無嚴重不適發生，在胸腔科門診追蹤的肺功能檢查仍然有中等程度侷限性換氣功能和氣體交換能力的下降。我們認為在一個相對上病程進行比較緩慢的急性呼吸窘迫症，應該要考慮肺炎黴漿菌感染是一個可能原因。*(胸腔醫學* **2007; 22: 215-221)**

關鍵詞：肺炎黴漿菌，急性呼吸窘迫症

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The Diagnosis of Pulmonary Arteriovenous Malformation by Multi-Detector Computed Tomography — A Case Report and Literature Review

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Owing to advances in computer technology, non-invasive examinations for diagnosing diseases have been further developed. The previous diagnostic procedure for pulmonary arteriovenous malformation (PAVM) was pulmonary angiography, but multi-detector computed tomography (MDCT) of the chest, which can display pulmonary vascular disease clearly, is now used. MDCT was used for diagnosing coronary artery disease initially and then for studying other aspects, including pulmonary physiologic problems and pulmonary vascular diseases. Herein, we present a 55-year-old woman who was found unintentionally by chest X-ray to have a lung mass. Physical examination of the chest revealed a bruit in the left posterior lower lung field, and a PAVM was highly suspected. The PAVM with feeding artery and drainage vein was diagnosed clearly by MDCT. The patient received a transcatheter embolism with metallic coils, which treated the PAVM successfully.

After patients with PAVMs are diagnosed, their family history of hereditary hemorrhagic telangiectasia (HHT) must be traced carefully. Although the PAVM is a benign lesion, its behavior is not benign. There are some complications of PAVMs, including brain abscess and embolic stroke, so PAVMs should be treated aggressively. ***(Thorac Med 2007; 22: 222-228)***

Key words: pulmonary arteriovenous malformation, multi-detector computed tomography

Introduction

Churton first reported a pulmonary arteriovenous malformation (PAVM) in 1897 [1]. It has various names, including pulmonary arteriovenous fistula, pulmonary arteriovenous aneurysm, cavernous angioma of the lung, and pulmonary telangiectasis. The PAVM involves capillary-free communication between the pulmonary artery and the pulmonary vein. The size of the communication varies from small to large complexes consisting of bulbous aneurysmal sacs. PAVMs occur sporadically or are associated with hereditary hemorrhagic telangiectasia (HHT), also called Osler-Weber-Rendu syndrome. About 70% of multiple PAVMs occur with HHT [2], and sporadic PAVMs are usually single.

The methods for diagnosing PAVM include

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pulmonary angiography, chest MRI or chest CT. Angiography for viewing pulmonary vessels is an invasive procedure, and it can be replaced by less-invasive technologies for diagnosing PAVMs. Chest CT is one of these less-invasive technologies, and it has the ability to create three-dimensional (3D) data sets that have greater diagnostic possibilities than standard angiographic images. Spiral CT provides these advantages, and multi-detector computed tomography (MDCT) is similar to spiral CT in structure and principle. MDCT systems have 2 or more parallel detector arrays and use a third-generation technology with a synchronously rotating tube and detector array. MDCT provides a huge gain in performance that can reduce scan time, reduce section collimation, or increase scan length substantially [3]. MDCT can be used in coronary artery disease surveys in patients with hemoptysis who have nonbronchial systemic collateral arteries [4], or in patients with intralobar pulmonary sequestration of the right upper lobe [5]. Herein, we report a patient with a large PAVM; MDCT of the chest displayed the clear structure of the lesion, including the feeding and draining pulmonary vessels.

Case Report

This 55-year-old female patient had no previous systemic disease. She had developed progressive dyspnea on exercise in the most recent year. The dyspnea was improved after resting and was not related to sitting or lying down, so she paid no attention to it. She suffered a sudden onset of consciousness disturbance with right-sided weakness 2 weeks before being admitted to our hospital. She was sent to a local hospital and a left middle cerebral arterial infarction was diagnosed. During that admission, a mass lesion in the left lower lung was found incidentally by CXR. She visited our hospital for the lung tumor survey after the stroke episode. At that time, she had no symptoms, such as chest tightness or hemoptysis. There was no clubbing of the fingers, recurrent spontaneous nasal bleeding, mucocutaneous telangiectasia, or family history of HHT. The physical examination revealed bruit in the left lower lung field and clear consciousness. The CXR (Figure 1) showed a mass lesion in the left lower lung field, and a lateral view of the CXR (Figure 2) showed a mass with feeding vessels in the posterior lower lobe. Lab data were: ABG: pH: 7.426, PaCO2: 32.8 mmHg, PaO2: 76 mmHg, and SaO2: 95.2%. The scintigraphy showed that the ratio of right to left shunting was about 33%. MDCT (Figure 3, 4) was done and showed a huge PAVM in the left lower lobe. Embolotherapy of the PAVM was achieved with 19 metallic coils 1 day later. After embolization (Figure 5), the follow-up ABG in room air showed pH: 7.426, PaCO2: 34.1 mmHg, SaO2: 99.1%, and PaO2:133 mmHg, and the bruit of the lung could not be heard. She was discharged 2 days after the procedure without complications. CXR was taken several weeks later for follow-

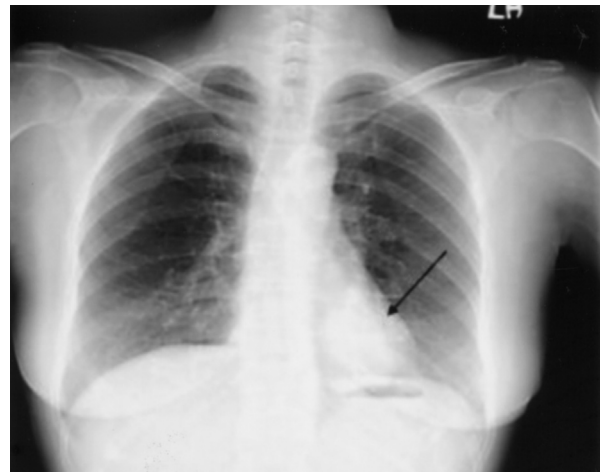


Fig. 1. PA view: mass lesion in the left lower lobe.

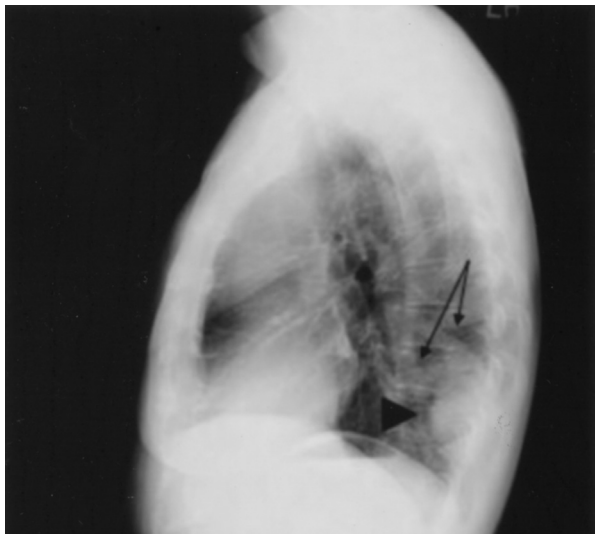
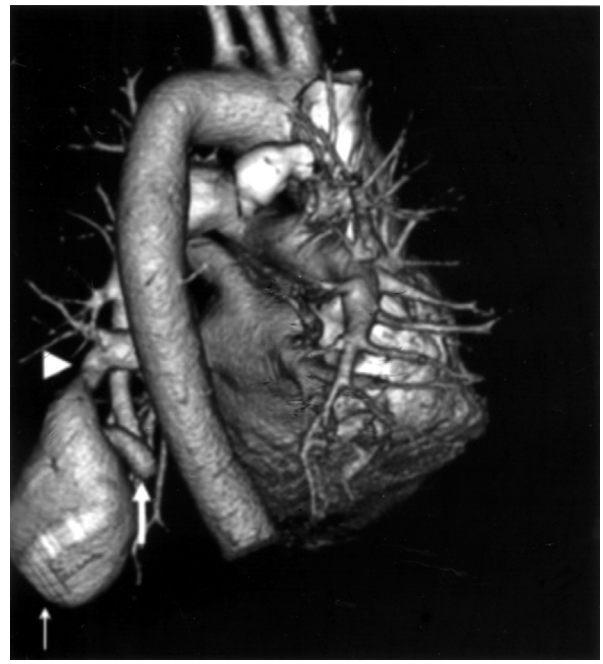


Fig. 2. CXR: lateral view, mass lesion with feeding vessels in the posterior lower lung field.
→ : feeding pulmonary vessels
▶ : mass lesion



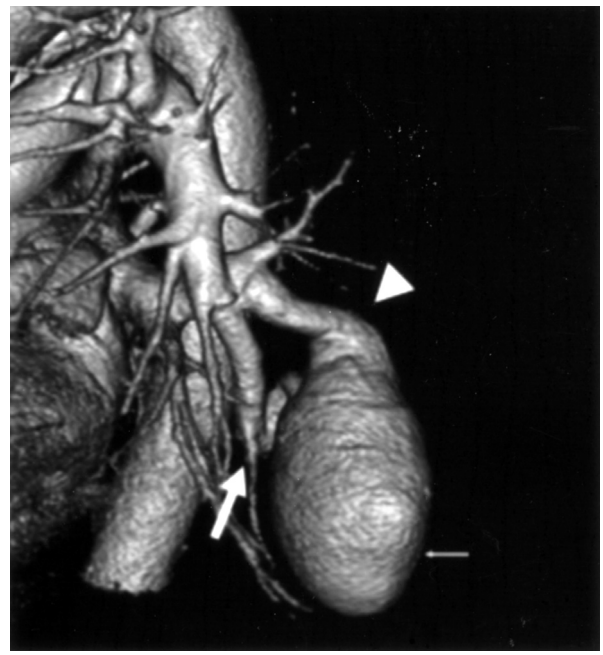


Fig 3, 4. MDCT of the chest reveals a large PAVM with a draining pulmonary vein and feeding pulmonary artery.
▶ : draining pulmonary vein
→ : PAVM
➡ : feeding pulmonary artery

up, and revealed that the metal coils were in position, but the size of the PAVM had not changed very much.

Discussion

The Mayo Clinic has reported 194 cases of PAVM over a period of 45 years, at an incidence of 4.3 cases a year [6]. However, small PAVMs can easily be missed and may have contributed to the low documented prevalence. PAVMs occur twice as often in women as in men. PAVMs are uncommonly identified at a young age, and gradually increase in incidence through the fifth and sixth decades.

The clinical respiratory features of PAVMs include dyspnea, cyanosis, pleuritic chest pain, hemoptysis, clubbing finger, and bruit. The embolic phenomena of PAVMs include cerebral abscess, or young stroke. However, half of PAVMs are asymptomatic. In this case, the patient did not have clubbing fingers or cyanotic change in the limbs, despite the large PAVM. Her manifestations were stroke, dyspnea and bruit, which were heard in the left posterior lower lung field.

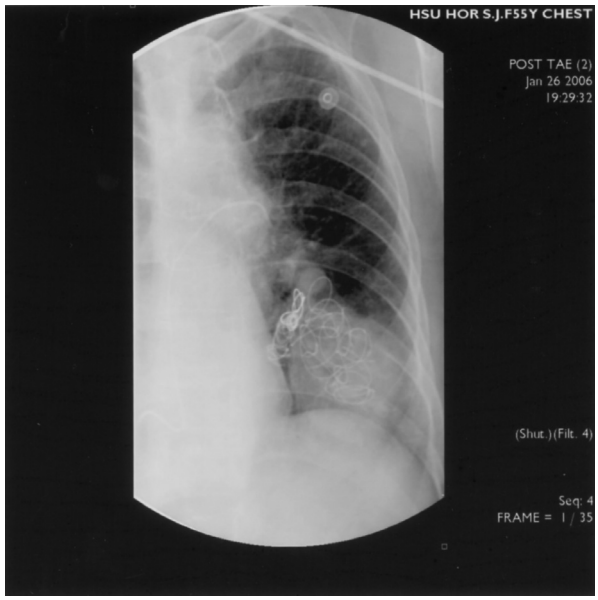


Fig. 5. Pulmonary angiography with embolism. Patient received percutaneous transcatheter embolization with metallic coils.

Her CXR was not specific, so a PAVM was considered due to bruit and stroke. PAVMs are sometimes associated with HHT, but this patient did not have epistaxes, mucocutaneous telangiectasia, or a family history of HHT, so HHT was not likely a diagnosis. Although a large right to left shunt was found by scintigraphy, her working capacity was relatively preserved. Embolization of this huge PAVM was performed with 19 metallic coils. After embolization, her PaO2 was improved.

As many as 60% to 90% of PAVMs have abnormal CXRs [7] and 53% to 70% of PAVMs occur in the lower lobes. The CXR typically shows a mass with feeding and draining vessels. The other imaging studies used include MRI, CT and angiography. The use of MRI in the diagnosis of PAVM was studied, but it had low sensitivity due to its poor expression of blood flow [8]. Pulmonary angiography remains the gold standard for confirming PAVMs in cases where uncertainty persists after using other tests, such as CT or MRI. Conventional chest CT is useful for the detection of pulmonary AVMs [9], but it has false-negative results due to variations in respiratory depth, partial volume averaging effects, and motion artifacts. MDCT was the next breakthrough in CT technology. It transformed conventional CT into a true 3D imaging modality that allows excellent 3D displays of the data volume [10]. This technique is becoming widely available and has progressively replaced digital pulmonary angiography as the standard diagnostic imaging modality for pulmonary vascular diseases.

MDCT is similar to spiral CT in structure and principle. MDCT of the chest evaluates pulmonary vascular disease and determines the number of PAVMs. In treating pulmonary AVMs, we are interested in PAVMs that include the numbers of feeding arteries and vascular pedicles. In the embolization procedure, the number and orientation of the feeding arteries are important anatomic data that determine the technical difficulty, and thus the duration of the embolization procedure [11]. The angioarchitecture of the PAVM, which is analyzed on 3D chest CT, revealed 76% of cases on the reference standard of spiral CT and unilateral selective pulmonary angiography [12]. The accuracy of 3D spiral chest CT for PAVM angioarchitecture is considerably improved when using cross-sectional images and a 3-D view. In this case, we used MDCT for evaluating the huge PAVM. The feeding and draining vessels of the PAVM were displayed clearly. This image can help the radiologist to manage the PAVM.

A screening test is not appropriate for patients with symptoms that include dyspnea or hemoptysis, because half of PAVMs do not have symptoms. These manifestations usually occur in the non-PAVM population. The patient with HHT, cerebral abscess, or young embolic stroke should

have a screening test for PAVMs because right-to-left shunt may exit. The screening tests include CXR, 100% oxygen breathing, SaO2 in the standing position, and ^{99m}Tc-MAA shunt ratio or contrast cardiac echo [13]. The ^{99m}Tc-MAA lung and kidney scan uses radio-labeled human serum albumin particles. The right-to-left shunt is the ratio of (brain+kidney/total injected doses). One study found that the normal population had a mean shunt fraction of 3%, while patients with PAVM had a mean shunt fraction of 23% [14]. The radionuclide method, although expensive and not routinely available at many hospitals, has several potential advantages over the 100% oxygen method.

PAVMs lack capillary filtering, which leads to paradoxical embolism. There is an association between a single PAVM and neurological manifestations; however, the greater the numbers of PAVMs, the greater the prevalence of cerebral infarction [15]. The benefit of therapeutic PAVM occlusion in preventing ischemic events has been well documented [16].

"Wait and see" is not the correct policy for the treatment of PAVMs, because even a very small PAVM still poses a risk of paradoxical embolism. PAVMs are not malignant, but their behavior is not benign. Even with no symptoms, the patient with PAVMs has a substantial risk of brain abscess, embolic stroke, and TIA. There is no evidence of medical treatment for reducing thromboembolic risk. The major role of medical treatment is prophylactic antibiotics for preventing brain abscess [17]. Pregnancy should be deferred by advice, because of the relatively high risk of PAVM rupture. PAVMs tend to increase in size during pregnancy, bringing on the risk of pulmonary hemorrhage, which may be fatal [18]. In 1942, pneumonectomy for PAVM was performed successfully by Hepburn *et al*. However, the treatment of choice for PAVMs today is percutaneous transcatheter embolization. Metallic coils or balloons are usually used for embolotherapy. Post-procedural complications are infrequent and self-limiting, and include pleuritic chest pain (13%), transient air embolization (5%), pulmonary infarction (3%), deep venous thrombosis (1.5%), and stroke (<1%) [19].

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肺動靜脈畸型之診斷的新工具—病例報告

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由於時代的進步，很多儀器及科技的研發都是為了減少病人暴露在危險的環境及提高準確性。以前診斷肺動靜脈畸型(PAVM)需要做血管攝影，危險性較大，目前電腦斷層檢查大大減低其危險性，而多切面電腦斷層(MDCT)則提供更準確的資訊，有關於 MDCT 的使用，它最早是運用在冠狀動脈疾病的診斷，之後有人將它推廣運用在其他方面，如：肺生理的研究及肺血管疾病的診斷。在本報告病例為一最近罹患中風的病人，其胸部 X 光意外發現一顆腫瘤，而在胸部理學檢查中發現有 bruit 雜音，由此高度懷疑病人患有 PAVM ，在 MDCT 的影像上可以很清楚的看出支配的肺動脈、肺動靜脈畸型本身及輸出的肺靜脈，之後病人接受血管栓塞治療。 PAVM 的病人很多都是沒有症狀，診斷出 PAVM 時，要再仔細問家族史及過去病史，因為 PAVM 有一部份會同時合併有 HHT (hereditary hemorrhagic telangiectasia)。而雖然 PAVM 不是惡性腫瘤，但是它的行為卻不是良性，沒有處理的 PAVM 會有很高的比例產生併發症，如：腦膿瘍。所以 PAVM 診斷後不能只做觀察的動作，一般仍建議使用栓塞甚至是手術的方式來治療。*(胸腔醫學* ***2007; 22: 222-228)***

關鍵詞：肺動靜脈畸型，多切面電腦斷層

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