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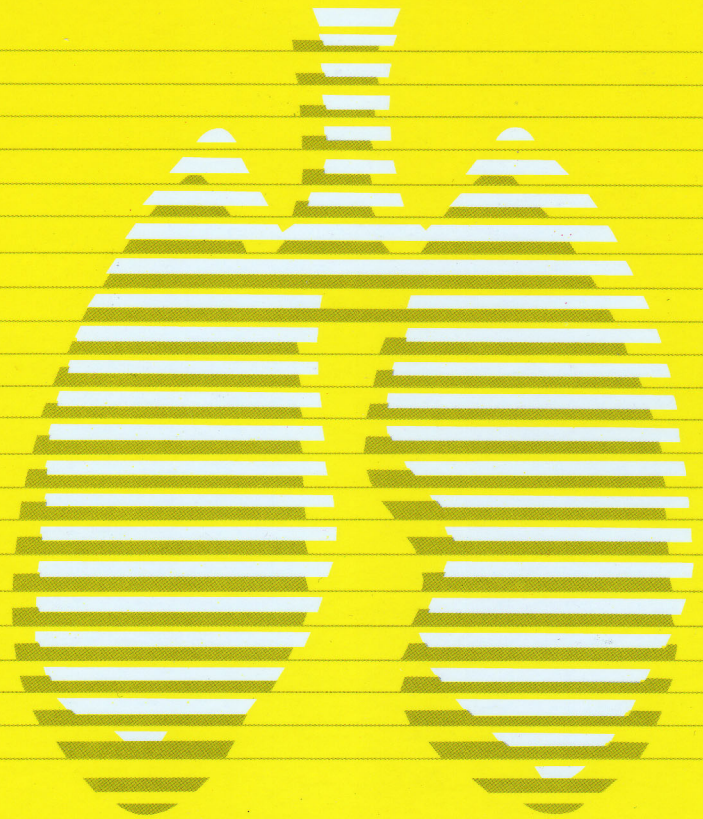

台灣胸腔暨重症加護醫學會

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原著

病例報告

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Orginial Articles

Case Reports

Evaluation of Exhaled Nitric Oxide in Patients with Sauropus Androgynus-Related Bronchiolitis Obliterans

Ting-Yun Ou*, Shieh-Yi Shen*, Ruay-Sheng Lai*,**

Background: In Taiwan, there was an outbreak of bronchiolitis obliterans (BO) in 1995. Based on an epidemiological study, the disease was associated with the consumption of a vegetable, Sauropus androgynus. The goal of this study is to determine whether nitric oxide (NO) plays a role in Sauropus androgynus-- related BO.

Methods: Twenty cases of Sauropus androgynus related--BO, 38 cases of asthma and 10 cases of healthy volunteers were included. Cases with upper respiratory tract infection in the most recent 6 weeks and allergic rhinitis were excluded. The exhaled nitric oxide (eNO) level was measured by an offline method, and the levels from 3 exhalations were analyzed immediately after the completion of the last exhalation. The exhaled NO was measured before spirometry or on different days, and was then calculated as the mean of 3 values.

Results: The BO, asthma and healthy volunteer case numbers were 20, 38 and 10 individually. The youngest mean age was in the asthma group (37 years old), compared with the BO group (51 years old) and the healthy volunteers (51 years old). The male-to-female ratios in the 3 groups were 1/19, 27/11 and 4/6. There were no smokers in either the BO or healthy volunteer group, but there were 9 smokers among the 38 subjects with asthma. The forced expiratory volume in 1 second (FEV1) in the 3 groups (BO, asthma, healthy volunteer) were 0.49 ± 0.13, 2.50 ± 1.10 and 2.26 ± 0.64L (mean ± SD), respectively. FEV1 was significantly low in the BO group (p<0.001). The exhaled NO level was significantly lower in the BO subjects than in those with asthma (p=0.006), but without statistical difference from the healthy volunteers (p=0.843). The eNO level did not correlate with FEV1 among the 3 groups.

Conclusions: The eNO level was not elevated in the subjects with Sauropus androgynus-related BO; however, it was significantly elevated in the asthma subjects, as in other reports. The possible reasons may be: 1) The eNO level does not elevate in stable patients with Sauropus androgynus-related BO. 2) NO plays an insignificant role in the pathogenesis of Sauropus androgynus-related BO. 3) There was extended damage to the epithelial cells, the main production site of eNO. ***(Thorac Med 2011; 26: 120-126)***

Key words: bronchiolitis obliterans, nitric oxide, sauropus androgynus

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Introduction

Sauropus androgynus was used as a weight-reducing vegetable in Taiwan, and was related to an outbreak of bronchiolitis obliterans (BO) in 1995 [1]. In our hospital, we saw about 120 patients who were suffering from Sauropus androgynus-related BO. Most victims were young to middle-aged females with persistent cough and respiratory distress.

Nitric oxide (NO) is synthesized from L-arginine in various cell types by nitric oxide synthase [2]. In the lung, NO is produced by the bronchial nerve, vascular endothelium, airway epithelium, smooth muscle, resident inflammatory cells and alveolar macrophages [3]. An increase in respiratory NO production, as measured by the exhaled NO (eNO) level, has been regarded as a marker of inflammation. Elevated eNO has been reported in patients with asthma, bronchiectasis, viral respiratory tract infection, systemic lupus erythematosis, liver cirrhosis and acute lung allograft rejection [4]. Some studies [5-7] have suggested that elevated eNO is an early marker of BO post-heart and lung transplantation. However, the association between the eNO level and Sauropus androgynus-related BO has rarely been reported in the literature, due to the small case numbers. Our study sought to reveal the difference in eNO levels between Sauropus androgynus-related BO patients and subjects with asthma and healthy nonsmoking volunteers.

Materials and Methods

Subjects

Cases of Sauropus androgynus-related BO that occurred a decade ago were collected by chart reviewing. The patients fulfilled the diagnostic criteria of BO in our pilot studies. Cases of asthma were defined by history plus a reported 12% improvement of FEV1 following a bronchodilator test, or a positive response to bronchial challenge with methacholine. Healthy volunteers were lifetime nonsmokers who had a normal spirometery. Subjects were excluded if they had had a respiratory tract infection 6 weeks before the study and allergic rhinitis.

NO Measurement

NO was measured by a rapid-response chemiluminescence analyzer (model 280, Sievers Instrument; Boulder, Co), which was calibrated daily. About 20 ml of gas was required for a reliable reading in Mylar balloon samples. Exhaled NO was collected using a controlled-flow restricted offline technique. Before each eNO collection, subjects performed tidal breathing 2 times via a NO scrubbing filter in order to control ambient NO. Without a nose clamp, the subjects inserted the mouthpiece, inhaled to total lung capacity, and then immediately exhaled for 15 seconds via expiratory resistance into the balloon while targeting a pressure of 20 mmHg. The NO levels in 3 balloons from 3 exhalations were analyzed immediately after the completion of the last exhalation and were calculated as mean values.

Statistical Analysis

Because of the non-normal distribution, eNO levels were reported as median values, shown as a 25-75% range. Other variables were reported as mean ± standard deviation (SD). The differences among the 3 groups were examined by Kruskal-Wallis 1-way analysis of variance on ranks and the Mann-Whitney rank sum test. The correlations between eNO and FEV1 were measured by Spearman rank order

correlation.

Results

The demographic characteristics of the 3 groups of subjects are shown in Table 1. The Sauropus androgynus-related BO patients were significantly older than the asthma subjects (51.2 ± 10.2 and 37.7 ± 18.9 years, p=0.004), but no different from the healthy volunteers (51.2 ± 10.2 and 51.3 ± 16.2 years, p=0.982). The male-to-female ratios among the 3 groups (Sauropus androgynus-related BO, asthma, healthy volunteers) were 1/19, 27/11 and 4/6, respectively. There were no smokers among the BO subjects and healthy volunteers, but 9 of 38 (23.7%) subjects in the asthma group were smokers. Patients with Sauropus androgynus-related BO had a worse pulmonary function during FEV1 than the asthma group (0.49 ± 0.13, 2.50 ± 1.10L, p<0.001) and healthy volunteers (0.49 ± 0.13, 2.26 ± 0.64L, p<0.001). The eNO level, shown in Figure 1, was lower in the Sauropus androgynus-related BO group than in the asthma group (median: 5.25 vs 8.40 ppb, p=0.006), but no different from that of the healthy volunteers (median: 5.25 vs 5.35 ppb, p=0.843). Moreover, no significant correlations of eNO and FEV1 were found by Spearman rank order correlation (Table 2).

Discussion

NO, a gaseous free radical, is synthesized from L-arginine in various cell types by nitric oxide synthase (NOS) with 3 isoforms. Constitutive NOS includes NOS I and NOS III, which are calcium-dependent. They are not only predominantly expressed in nerve (NOS I) and endothelial cells (NOS III), but also at low levels in airway epithelium. NO produced specifically by endothelial cells is important in the regulation of vascular tone, blood flow and inhibition of platelet aggregation in vessels. NOS II is a calcium-independent inducible enzyme found in alveolar macrophages, and occasionally in lymphocytes, neutrophils, eosinophils, Kupper's cells, hepatocytes of the liver, airway epi-

Table 1. Demographic Data

	SABO	Asthma	Healthy volunteer
No. of cases	20	38	10
Age (years)	51.2 ± 10.2	37.7 ± 18.9	51.3 ± 16.2
Sex (M:F)	1:19	27:11	4:6
No. of smokers	0	9	0
FEV1 (L)	0.49 ± 0.13	2.50 ± 1.10	2.26 ± 0.64

Data are presented as mean ± SD; SABO: Sauropus androgynus-related BO

Table 2. Correlation between Exhaled NO and FEV1

	SABO		Asthma		Healthy volunteers	
	R	*p*	R	*p*	R	*p*
FEV1	-0.057	0.811	0.115	0.491	0.285	0.425

R: correlation coefficient; p: *p*-value; FEV1: forced expiratory volume in 1 second

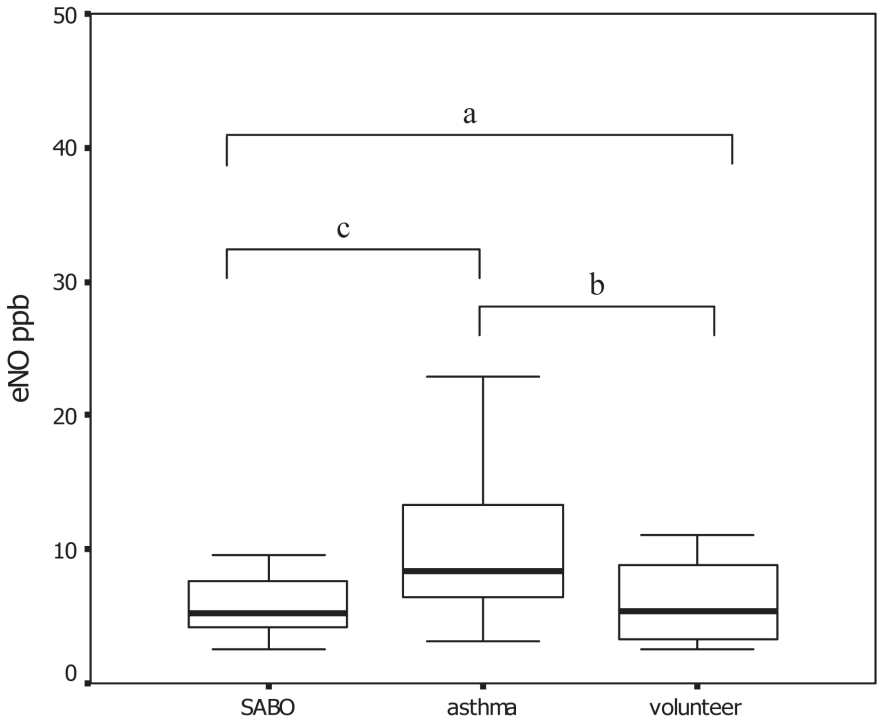

Fig. 1. Boxplots of eNO among 3 groups shown as median value with a 25-75% range; a: p=0.843, b: p=0.020, c: p=0.006; SABO: Sauropus androgynus-related BO

thelial cells, etc. NOS II works as an important element in the host defense system, in which cytokines play a role in its up-regulation.

NO plays diverse roles, including as a neurotransmitter, endothelium-derived relaxing factor, immune-mediated agent and mediator of cytotoxicity. In the lung, it is produced by the bronchial nerve, vascular endothelium, airway epithelium, smooth muscle, resident inflammatory cells and alveolar macrophages. In addition to the cytotoxic potential in the host defense system, higher levels of NO produced by inducible NOS have been implicated in the pathogenic mechanism of diseases such as atherosclerosis, arthritis and asthma. Respiratory NO production, measured by the eNO level, has been regarded as a marker of inflammation, and is increased in asthma, bronchiectasis and active tuberculosis.

BO is represented as a form of chronic rejection, and is a major morbidity and mortality complication post-transplantation; it develops in >50% of lung transplant recipients within 3 years after transplantation and is the commonest cause of late graft failure [8]. It is clinically characterized by progressive dyspnea with an unexplained fall in expiratory flow rate, and is histologically recognized by the recruitment of inflammatory cells, damage to the airway epithelium, granulation formation, and fibrosis. Complete loss of the epithelium and extension of fibrosis into the lumen ultimately lead to obliteration of the terminal and respiratory bronchioles. Because of the sampling limitation, histological proof of BO is difficult. Therefore, the diagnosis is based on symptoms and objective changes in pulmonary function tests. Some studies have suggested that eNO is el-

evated in patients with BO post-heart and lung transplantation [5-7]. The eNO level could be a marker related to the stability of BO, instead of the stage [9]. Therefore, an elevated eNO level might help in the early detection of BO in lung transplant patients, leading to a timely modification of immunotherapy and the prevention of undesirable outcomes.

In Taiwan, there was an outbreak of BO in 1995 that was associated with consumption of a vegetable (Sauropus androgynus) in an epidemiological study [1]. There were about 120 BO patients in our hospital. Most of them were young to middle-aged females who suffered from persistent cough and respiratory distress. The pulmonary function tests revealed irreversibly obstructive ventilatory impairment. Only 3 patients had undergone exploratory thoracotomy for tissue diagnosis and 3 had received lung transplantation. The pathological changes were all compatible with BO. After a decade, the survivors still endured a respiratory-distressed life and were in a chronic stable status. Using the diagnostic criteria of BO syndrome post-transplantation, the Sauropus androgynus-related BO patients recruited for this study were all allocated to stage 3, without significant differences in eNO level from that of the healthy volunteers. The following were the possible reasons for this phenomenon. First, the Sauropus androgynus insult occurred a decade ago. All 20 patients were relatively stable and tolerated the chronic hypoxic status well when they were recruited for this study. None of them had had an upper respiratory tract infection in the most recent 6 weeks that would cause an elevation of the eNO level. Second, the reactive oxygen-nitrogen species might not play a major role in the pathogenesis of Sauropus androgynus-related BO. The immunohistochemical stain of the lung tissue for inducible NOS revealed only weakly positive, which could partly explain why the eNO levels did not increase in these Sauropus androgynus-related BO patients. Third, our patients had advanced disease with a more severely obstructed airway and more extended destruction of the epithelial cells, the main site of NO production.

In conclusion, our study is the first to explore the eNO levels in Sauropus androgynus-related BO. We cannot infer a change in eNO levels in the early stage of Sauropus androgynus-related BO because there were no available new cases after a thorough epidemiological study and public education. However, the pathologic change in the Sauropus androgynus-associated lung damage was undoubtedly BO [1]. Whether Sauropus androgynus and transplantation-related BO share the same pathogenesis is not clear, but both diseases have the same patterns in eNO levels, namely, eNO was not elevated in stable, uncomplicated and late-stage BO.

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評估吐氣之一氧化氮在守宮木引起之阻塞性細支氣管炎的表現

歐亭芸* 沈協益* 賴瑞生*,**

背景：台灣在民國84年時有爆發一波阻塞性細支氣管炎，經流行病學調查後發現與服用減肥菜—守宮木有關，本研究的目的在於了解一氧化氮在守宮木引起之阻塞性細支氣管炎所扮演之角色。

方法：利用化學發光分析法測量吐氣之一氧化氮濃度。共有20位守宮木相關之阻塞性細支氣管炎，38位氣喘及10位健康的志願受測者接受測量。本實驗排除過敏性鼻炎及測量前6週有上呼吸道感染之病人。個案於肺功能檢測前即接受吐氣之一氧化氮檢測，共執行三次並取其平均值。

結果：用力吐氣第一秒量（FEV1）於阻塞性細支氣管炎個案明顯低於氣喘組及健康受測者（<0.001），分別為阻塞性細支氣管炎組0.49 ± 0.13L，氣喘組2.50 ± 1.10L，及健康受測者2.26 ± 0.64L（平均值±標準差）。阻塞性細支氣管炎之吐氣一氧化氮濃度較氣喘患者來的低（平均值：5.25 vs 8.40 ppb, p=0.006），但與健康受測者則無差異（平均值：5.25 vs 5.35 ppb, p=0.843）。而吐氣之一氧化氮濃度與用力吐氣第一秒量在三組間皆無統計學上之相關性。

結論：守宮木引起的阻塞性細支氣管炎其吐氣一氧化氮濃度並不若氣喘病人有上升現象，可能原因為：一）病人接受一氧化氮測量時皆處於穩定期；二）一氧化氮於守宮木引起的阻塞性細支氣管炎並無扮演重要角色；三）廣泛性呼吸道上皮細胞損傷導致一氧化氮合成減少。*(胸腔醫學* ***2011; 26: 120-126)***

關鍵詞：阻塞性細支氣管炎，一氧化氮，守宮木

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Pulmonary Coccidioidomycosis Diagnosed after Thoracoscopic Lobectomy — Case Report and Literature Review

Ching-Kai Lin, Ping-Hung Kuo, Jang-Ming Lee*

Coccidioides spp. is endemic to certain lower deserts in western regions of the United States of America. All patients with coccioidomycosis reported in Taiwan have had a history of travel to endemic areas. In this report, we describe the case of a 60-year-old woman who presented with right middle lobe consolidation that was not responsive to empiric antibiotic treatment. Laboratory examinations of sputum and bronchial washing specimens failed to reveal any microbiological pathogens. She underwent video-assisted thoracoscopic lobectomy of the right middle lobe, and the pathology confirmed the diagnosis of coccidioidomycosis. To our knowledge, this is the first case of pulmonary coccidioidomycosis diagnosed after thoracoscopic lobectomy in Taiwan. ***(Thorac Med 2011; 26: 127-132)***

Key words: Coccidioidomycosis, video-assisted thoracoscopic lobectomy

Introduction

Coccidioidomycosis is an infection caused by the dimorphic fungi of *Coccidioides* spp. (*C. immitis* and *C. posadasii*). It was first described in Argentina by Alexandro Posadas in 1892 [1]. In the United States of America, these fungi are endemic to some lower deserts of the west, including those in southern Arizona, central California, southwestern New Mexico, and west Texas [2-3]. Arizona Department of Health Services data have shown a substantial increase in the incidence of coccidioidomycosis in recent years [4].

Surgical intervention was indicated in only a few patients. The most common indications for surgery are diagnostic dilemmas involving nodular disease, symptomatic cavitary disease that is not responsive to treatment, and complications [5].

With the closer contact between Taiwan and the United States, some Taiwanese citizens may contract coccidioidomycosis, although only 2 severe cases have been reported to date [6-7]. In this report, we describe a case of pulmonary coccidioidomycosis diagnosed after thoracoscopic lobectomy in Taiwan.

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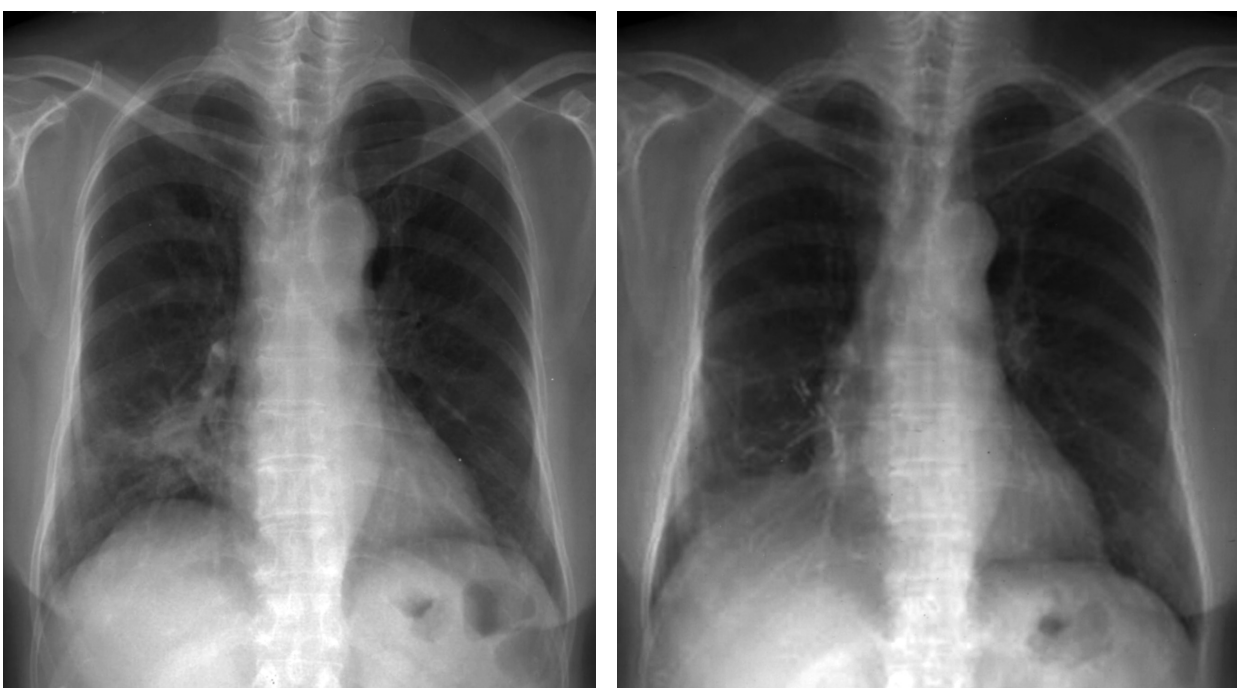
Case Report

A 60-year-old woman who had had intermittent cough with whitish sputum for about 3 months presented to our outpatient clinic in December 2009; she showed no fever, malaise, night sweats, or weight loss. No remarkable findings were revealed in her medical history, except hypertension, which was controlled by medication. The patient was a Taiwanese citizen but had lived in California for many years. She frequently traveled between the 2 locations and was a non-smoker.

The patient's chest radiograph showed right middle lobe consolidation (Figure 1, Panel A). Her leukocyte count was 8.21×10^9/L (neutrophils, 49.4%; eosinophils, 10.7%; lymphocytes, 34.8%) and the C-reactive protein level was 1.01 mg/dL (reference value, <0.8 mg/dL). Sputum culture did not show significant pathogens. Unfortunately, the patient's symptoms and chest radiographs showed no improvement after empiric antibiotic therapy with oral azithromycin. Chest computed tomography (CT) showed right middle lobe consolidation with air bronchograms and central necrosis (Figure 2). Bronchoscopy revealed hyperemic mucosa at the right middle lobe bronchus. A culture of the bronchial lavage fluid from the right middle lobe was also negative for pathogens. The patient underwent video-assisted thoracoscopic surgery (VATS), which revealed a yellowish and elastic lesion, about 2.5 cm in size; therefore, lobectomy of the right middle lobe was performed. The tentative diagnosis was pulmonary tuberculosis, and anti-tuberculosis agents were administered immediately after surgical intervention. Unexpectedly, the pathology re-



(A) (B)

Fig. 1. Panel A: Chest radiograph showing right middle lobe consolidation and mild widening of the mediastinum. Panel B: Chest radiograph after antifungal therapy for 9 months.

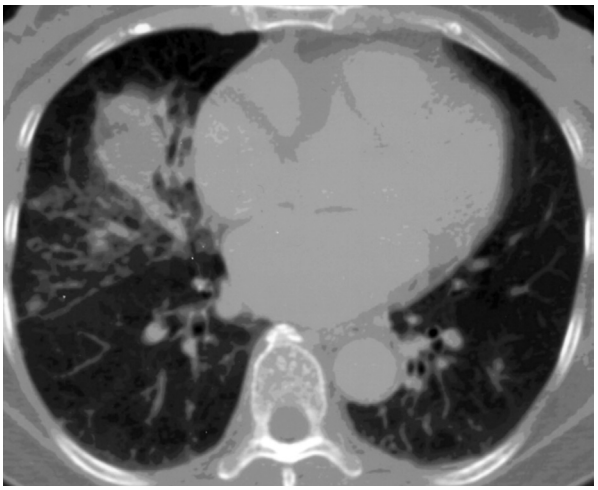
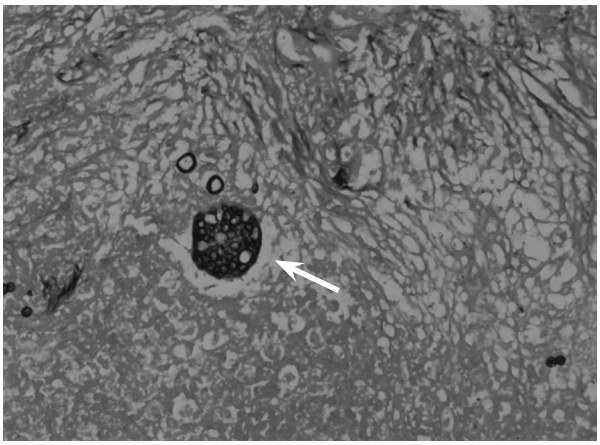
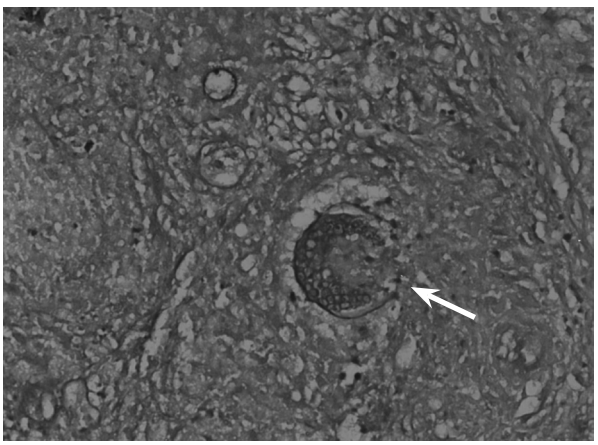


Fig. 2. Chest CT showing right middle lobe consolidation with air bronchograms and multiple pulmonary nodules.

port revealed numerous spherules filled with endospores in the necrotic lesion (Figure 3, Panel A and B). Acid-fast staining yielded negative results. The tissue culture finally yielded *C. immitis* growth on the 7th hospital day, and antifungal therapy with fluconazole 400 mg per day was initiated. The postoperative course was uneventful, and 1 week after VATS, the patient was discharged in a stable condition. The follow-up chest radiograph did not reveal any evidence of recurrence.



(A)



(B)

Fig. 3. Panel A: Pathological analysis of the biopsy specimen showing numerous spherules (arrow) filled with endospores. Panel B: Ruptured spherule (Panel A: Dako Grocott's methenamine silver stain; panel B: periodic acid-Schiff stain)

Discussion

The spectrum of diseases caused by *Coccidioides* spp. is very broad and is almost completely dependent on host defenses, inoculum size, and possibly other specific virulence or resistance factors that are not clearly understood [2]. There are 5 major clinical manifestations of coccidioidal infection, i.e., acute pneumonia, chronic progressive pneumonia, pulmonary nodules and cavities, extrapulmonary non-meningeal disease, and meningitis [3]. The primary clinical manifestation is an acute respiratory infection that occurs 1-3 weeks after inhalation of arthroconidia. About 40% of patients may present with an acute or subacute spectrum of illness, ranging from "flu-like" symptoms to progressive pneumonia [2]. A small percentage of cases may present with persistent illness for more than 3 months, and this condition may be called a chronic progressive pneumonia [3].

In this case, the patient presented with a

chronic progressive pneumonia. Patients with this type of presentation comprise only a small percentage of coccidioidomycosis patients. For these patients. treatment with oral azole antifungal agents for at least 1 year is recommended [9].

To our knowledge, only 2 cases of coccidioidomycosis in Taiwanese patients have been reported to date [6-7]. In the first case, a 28-year-old man initially presented with right lower lobe pneumonia after traveling to Arizona. He was treated with antifungal therapy for 3 months with a good response, but then showed a relapse of symptoms with disseminated lymphadenopathy after discontinuing antifungal therapy for 1 month. [6] In 2003, Wang *et al*. reported the case of another Taiwanese patient who developed disseminated coccidioidomycosis complicated with coccidioidal meningitis after traveling to Los Angeles and the San Joaquin Valley. He died in spite of receiving intravenous fluconazole and intrathecal amphotericin B [7].

Coccidioidal infection can be diagnosed using any of several methods: (1) culture from any body fluid or tissue; (2) identification of coccidioidal spherules in a cytology or biopsy specimen; and (3) serologic testing for coccidioidal-related antigens. In this case, the final diagnosis was not established until the patient underwent a thoracoscopic lobectomy. Surgical intervention for diagnosis or treatment is indicated in only a few patients. A previous report showed that only 86 (6%) of 1496 patients underwent operations. The common reasons for surgical intervention were diagnostic dilemmas involving nodular disease, symptomatic non-responsive cavitary disease, and complications [5]. Among the 86 patients with cavitary lesions, 18 (21%) underwent surgical intervention because the lesions showed no response to long-term antifungal therapy or increased in size in spite of the therapy. The most common complications indicating an operation were cavity rupture complicated with empyema or pneumothorax.

Antifungal therapy is typically administered before and after surgical resection. The most common agent used is fluconazole [2]. On the basis of the findings obtained over a period of 10 years at the Mayo Clinic, postoperative antifungal therapy for at least 2-3 months was recommended for patients with large nodular lesions, clinically significant cavitary disease, or multiple satellite lesions that showed a high probability of active coccidioidal infection in histologic evaluation [5]. However, the optimal duration of antifungal therapy for post-surgical intervention remains unclear. One previous report described the relapse of coccidioidomycosis with disseminated lymphadenopathy 1 month after completion of a 3-month-long antifungal treatment [6]. In this case, fluconazole therapy was maintained for 9 months. The follow-up chest radiograph (Figure 1, Panel B) showed nearly full expansion of the right lung, and no relapse was observed.

In conclusion, coccidioidomycosis is an endemic infection in the southwestern region of the United States of America. With the increase in globalization and global travel, it is possible that more cases will be diagnosed in Taiwanese subjects. This disease should be listed in the differential diagnosis for patients who have previously traveled to endemic areas. The outcomes of these patients may be improved by early diagnosis with culture or pathology and adequate antifungal treatment.

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胸腔鏡肺葉切除手術診斷肺部球胞子菌感染──一病例報告及文獻回顧

林敬凱　郭炳宏　李章銘*

球胞子菌是美國西南部沙漠特有之地區性黴菌。所有在台灣報告之球胞子菌感染皆有疫區的旅遊使。我們報告一個60歲女性因右肺中葉實質化，痰液及支氣管鏡檢查之細菌培養查皆無發現且對完整的經驗性抗生素治療無明顯效果。病人最後接受影像胸腔鏡肺葉切除手術並由病理診斷為球胞子菌感染。據我們所知，這是台灣第一位由影像胸腔鏡肺葉切除手術診斷為肺球胞子菌感染之病例。*(胸腔醫學* ***2011; 26: 127-132****)*

關鍵詞：球胞子菌感染，影像胸腔鏡肺葉切除手術

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Pulmonary Granulomatous Inflammation and Unexplained Repeated Infections — A Case of Chronic Granulomatous Disease

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Chronic granulomatous disease (CGD) is a rare inherited disorder caused by a failure of intracellular superoxide production by phagocytes. It is usually identified in early childhood with severe recurrent bacterial and fungal infections. We present a case of CGD in a young male adult in whom the disease initially presented with left middle lung consolidation with cavitation. The patient had a history of unexplained repeated infection (including liver abscess and submandibular cellulitis at the age of 17 and 19 years). A specimen of cutting biopsy of the lung showed granulomatous inflammation. Pulmonary granuloma is a common manifestation of tuberculosis in Taiwan, but no acid-fast bacilli were identified by Ziehl-Neelsen staining in a specimen of sputum and cutting biopsy. In addition, no autoimmune disease was detected. The patient had negative respiratory burst activity in the polymorphonuclear leukocyte function test, a low response in the chemiluminescence test, and a normal finding in the chemotaxis assay, so the diagnosis of CGD was finally established. CGD rarely starts presenting in adulthood, either because it is not well-recognized in non-pediatric chest wards or because of the administration of potent antimicrobials that unintentionally treat many CGD-associated infections, postponing the diagnosis until more severe infections occur. Therefore, any adolescent or adult with unexplained and repeated infections that are accompanied by granuloma formation should be checked for phagocyte function defects. Early diagnosis of CGD is important because of the benefits of timely treatment and infection prophylaxis. ***(Thorac Med 2011; 26: 133-139)***

Key words: chronic granulomatous disease, granulomatous inflammation

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Introduction

Chronic granulomatous disease (CGD) is a group of disorders of the granulocyte and monocyte oxidative metabolism. The frequency of CGD in the United States is approximately 1 in 200,000 live births [1]. The disease primarily affects males, since most mutations are X-linked. CGD may present at any time from infancy to late adulthood, but the majority of patients are diagnosed as toddlers and children before the age of 5 years. In several series, the median age at diagnosis was 30-36 months after birth [2-5].

The 20-year survival rate is 40-50% [6-7]. Only rare cases of CGD diagnosed in adults have been reported [8-11]. Recently, however, patients increasingly have been diagnosed later in childhood or in adulthood. This is due, in part, to the recognition of milder cases of autosomal recessive CGD [12], as well as delayed diagnosis in some patients. Diagnosis may be delayed because of the administration of potent antimicrobials that unintentionally treat many CGD-associated infections, postponing diagnosis until more severe infections occur. X-linked CGD tends to have an earlier onset and to be more severe than a p47phox deficiency [5].

When patients with CGD become infected, they often have extensive inflammatory reactions, and lymph node suppuration is common, despite the administration of appropriate antibiotics. Excessive inflammation probably reflects failure to inhibit the synthesis or degradation of chemoattractants and antigens, leading to persistent neutrophil accumulation. Impaired killing of intracellular microorganisms by macrophages may lead to persistent cell-mediated immune activation and granuloma formation. We can arrive at a diagnosis of CGD on the basis of an abnormal polymorphonuclear leukocyte function, which can be determined via a nitro-blue tetrazolium (NBT) dye test, a simple and rapid (but largely qualitative) determination of phagocyte NADPH oxidase activity, and a chemiluminescence response, followed by confirmatory tests such as immunoblotting and genotyping.

Case Report

A 24-year-old male student, a non-smoker with a history of repeated infection (including liver abscess and submandibular cellulitis at the ages of 17 and 19 years) was admitted to our chest ward twice, due to right lung consolidation on 21 April 2006, and left middle lung consolidation with a cavitation lesion (Figures 1A and 1B) on 9 May 2006. At the admission in early April 2006, no anatomic deficit or endobronchial lesion was found during bronchoscopy, and cutting lung biopsy revealed active chronic inflammation with abscess and granuloma formation (Figure 2). The patient was prescribed anti-tuberculosis medicine (rifampicin 480 mg, isoniazid 320 mg, pyrazinamide 1000 mg and ethambutol 800 mg qd) from 27 April to 28 August 2006, which seemed to have no effect, as seen in the serial follow-up of the posterior-anterior chest roentgenological view. On investigation, the hemogram and renal and liver function tests yielded normal results, except for hypoalbuminemia. A pulmonary function test revealed severe restrictive ventilatory impairment (forced vital capacity = 1.08 L). A computerized tomography scan of the chest (Figure 3) obtained on 27 July 2006 showed consolidation in the left lower lobe, which differed from the site of consolidation seen on the film obtained in May 2006. Sputum culture to

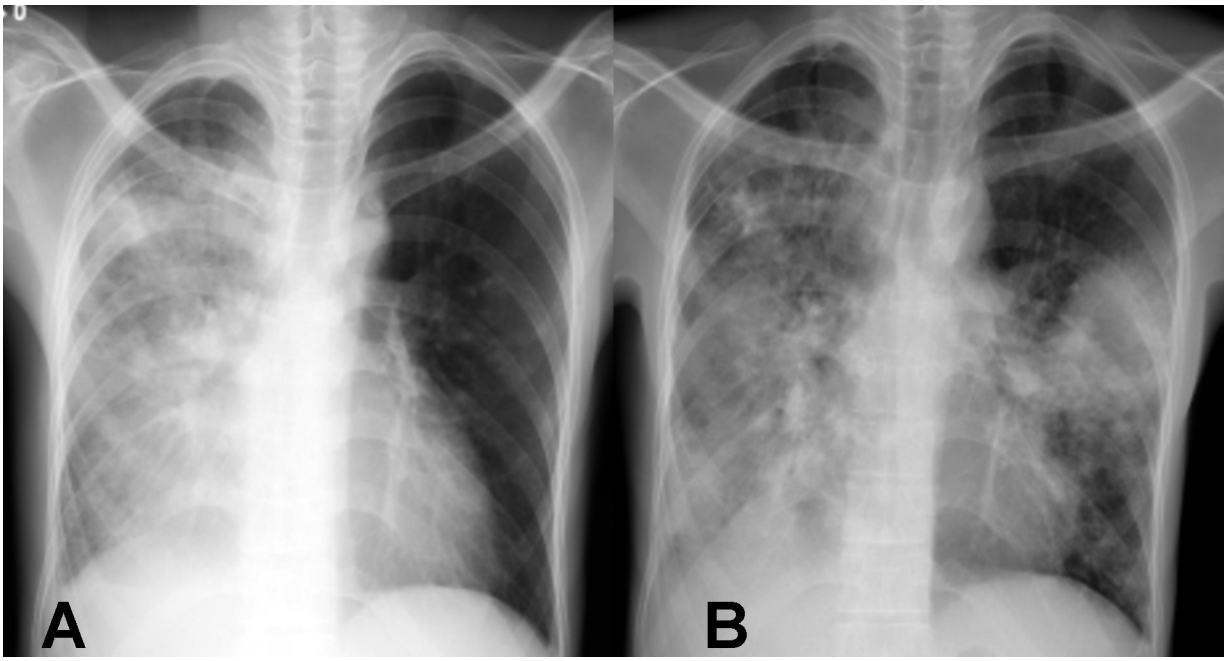

Fig. 1. A. The initial chest roentgenology scan obtained on 21 April 2006 revealed right lung consolidation; B. The roentgenology scan obtained on 9 May 2006 revealed bilateral lung consolidation with cavitation of the left lower lung. The lung consolidation was in a location different from that of Fig. 1A.

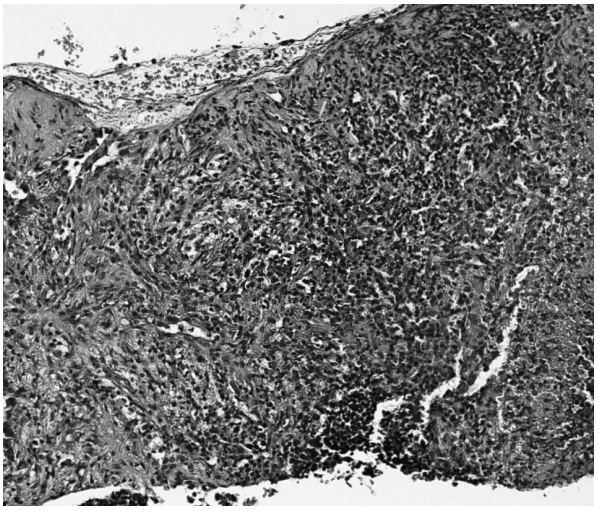

Fig. 2. The lung specimen of the cutting biopsy showed lung tissue with necrosis, acute and chronic inflammatory cell infiltration, focal abscess formation and histiocytic aggregation forming granuloma-like lesions were also found.

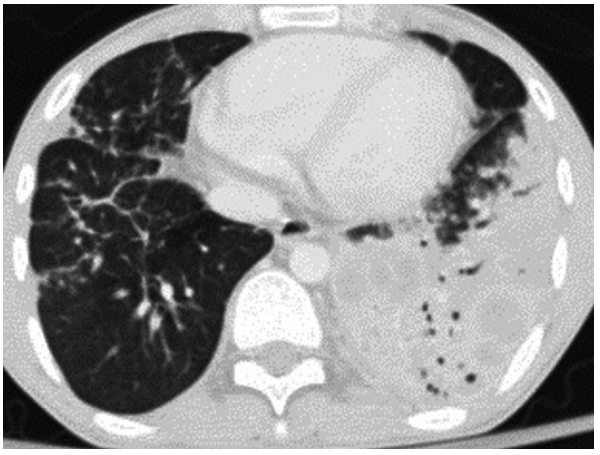

Fig. 3. The computerized tomography scan of the chest showed consolidation in the left lower lobe.

isolate bacterial pathogens and tuberculosis was negative. Polymerase chain reaction (PCR) assay of bronchoalveolar lavage (BAL) fluid was negative for *Mycobacterium tuberculosis*.

The lymphocyte surface marker study showed a normal ratio of CD4/CD8 (CD: cluster of differentiation), but only suboptimal total

T cell counts. Due to the repeated abscess and pulmonary granuloma, primary immune deficiency disease, especially deficits in phagocyte function, was highly suspected. The patient had negative respiratory burst activity in the NBT test, a polymorphonuclear leukocyte function test, post-stimulation with phorbol myristate acetate (0% pre-stimulation and 0.5% post-stimulation for the patient compared with 95% and 98% post-stimulation for his younger sister and mother, respectively; normal limits: more than 50%). The patient also had a low response in the chemiluminescence test stimulated with phorbol myristate acetate (compared with the normal response post-stimulation exhibited by his mother and younger sister). However, the chemotaxis assay yielded normal findings (2 hours post-stimulation with *N*-formyl-L-methionyl-L-leucyl-L-phenylalanine, FMLP; 25.7, 40.3, and 32.8 cells/high power field in the patient, his mother, and his sister, respectively). Finally, we arrived at the diagnosis of CGD, and the patient was discharged after antibiotics treatment was completed. Subsequently, he was started on interferon gamma therapy in our pediatric outpatient clinic.

Discussion

Our patient was a 24-year-old man with a history of unexplained repeated infection (including liver abscess and cellulites) who initially presented with granulomatous inflammation. In Taiwan, tuberculosis is endemic, so anti-tuberculosis treatment was started because pulmonary tuberculosis was highly suspected. However, it had little effect, and Ziehl-Neelsen staining of the sputum and cutting biopsy was negative for acid-fast bacilli; PCR of BAL fluid was also negative for tuberculosis.

On the basis of the patient's history of repeated infections (including liver abscess, pneumonia, and cellulitis) and granuloma inflammation, an immunodeficiency disease was highly suspected. There was no history of asthma, diabetes, human immunodeficiency virus (HIV) infection, liver cirrhosis, nephrotic syndrome, autoimmune disease, splenectomy, malignancy, hemoglobinopathy, multiple myeloma, or chronic lymphocytic leukemia. The patient also denied any family history of congenital inherited disease or use of immunosuppressive agents such as glucocorticoids or immunomodulatory agents. In addition, a subsequent test for HIV antibody, and serum and urine electrophoresis tests were negative. The initial immunoassay (used to determine the serum immunoglobunin level and IgG subclass) was normal, except an elevation of IgE (patient: 1319 ku/L, normal limits: 80-120 ku/L) and eosinophil cationic protein without specific allergen-antigen detection. There was also negative detection for antinuclear antibody and anti-extractable nuclear antigen (ENA). Because of the negative finding for c-anti-neutrophil cytoplasmic antibodies (ANCA) in serum, Wegener's granumatosis was less likely.

For an adolescent or adult with repeated abscess and granuloma formation in the respiratory tract without evidence of secondary immune deficiency, primary immune deficiency disease, especially deficits in phagocyte function, is highly suspected. The initial immunologic evaluation includes determination of IgG, IgA, and IgM levels and IgG subclass, which in our patient, were found to be within normal limits. Further, in our patient, the movement of neutrophils was not impaired; they showed normal chemotaxis with FMLP stimulation. Phagocytic disorders may be divided into ex-

trinsic and intrinsic defects. This patient had no history of anatomic deficits or extrinsic deficits, which are secondary to diabetes mellitus, metabolic storage disease, malnutrition, immaturity, and burns, associated family history, or autoimmune disease. Intrinsic disorders of chemotaxis include leukocyte adhesion defects, but the chemotaxis of neutrophils in this patient was normal, making neutrophil movement dysfunction less likely as the underlying cause. The findings of a subsequent autoimmune study were also unremarkable. If CGD is suspected, neutrophil function should be tested. Since there was no respiratory burst activity by the polymorphonuclear leukocytes as evidenced by the chemiluminescence assay and NBT test as stated in the case report, we finally arrived at the diagnosis of CGD.

The most common manifestations of CGD are pulmonary infections and skin involvement, followed by generalized lymphadenopathy. The pulmonary radiologic findings of CGD include consolidation, nodules, areas of scarring, traction bronchiectasis, emphysema, air trapping, mediastinal and hilar lymphadenopathy, pulmonary artery enlargement, and pleural effusion [13].

The screening examinations for CGD, including the chemiluminescence test and the NBT test that determine phagocyte NADPH oxidase activity, are simple to perform and produce results rapidly. Patients with CGD usually reveal no or profoundly low activity in these tests.

The cornerstones of CGD management are an early diagnosis of infections, antimicrobial and immunomodulatory prophylaxis, and aggressive management of infectious complications. Survival of patients with CGD has dramatically improved, with many now living well into middle age. Prophylactic and therapeutic measures are still needed to further increase life expectancy and quality of life for these patients [14].

The presentation of CGD rarely starts in adulthood, and delays in diagnosis may occur because the disease is not well-recognized in non-pediatric chest wards, or because the potent antimicrobials that are administered also treat many CGD-associated infections, postponing diagnosis until more severe infections are present. In conclusion, in view of the possibility of timely treatment, infection prophylaxis, and genetic counseling for affected families, CGD should not be excluded as a possible diagnosis in adolescents or adults presenting with unexplained infections or granulomas.

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肺部肉芽性發炎及不明原因反覆感染—慢性肉芽腫病個案報告

陳泓丞* 楊崑德** 林安伸* 王金洲* 黃琬婷*** 賴建豪*

慢性肉芽腫病（CGD）是一種罕見因細胞內superoxide製造功能衰竭所造成的遺傳性及先天免疫功能不全症候群疾病。它通常於出生後第一年即有嚴重反覆性細菌和黴菌感染。

我們提出一個案為一年輕男性患有慢性肉芽腫病於初就診的胸部X-ray表現為左下肺實質化與空洞化。患者曾有反覆不明原因感染病史（包括肝膿瘍，蜂窩組織炎分別在患者17歲和19歲）。此患者切割活檢標本顯示為肺肉芽腫發炎。在台灣肺肉芽腫發炎常於肺結核病患者出現，此患者的痰標本及切割活檢檢體中抗酸桿菌鑑定皆呈陰性表現。相關自體免疫疾病檢測亦呈現陰性。在刺激後的多發性多形性白血球功能測試及chemiluminance測試顯示為低反應，加上趨化檢測為陰性結果，故診斷為慢性肉芽腫病。慢性肉芽腫病罕見在成年才開始表現，推測延遲診斷原因是目前強效抗生素藥物治療及在成年胸腔科相關知識的缺乏。因此，任何青少年或成人不明原因的肺部反覆感染，並伴隨著肉芽腫的形成，應考慮顆粒球白血細胞缺陷所導致的免疫不全症候群及慢性肉芽腫病。對於慢性肉芽腫病早期診斷給予及時治療和預防感染是相當重要的。*(胸腔醫學 2011; 26: 133-139)*

關鍵詞：慢性肉芽腫病，慢性肉芽腫性發炎

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Colonic Metastasis from a Primary Lung Carcinoma: A Case Report

Chih-Hao Chang, Chih-Wei Wang*, Meng-Heng Hsieh, Fu-Tsai Chung, Chih-Teng Yu, Horng-Chyuan Lin

Lung cancer with clinically demonstrated colonic metastasis is very rare, and only a few case reports have been published in the English literature. Colonic metastasis from lung malignancies occurs almost exclusively in male patients, with only 1 case involving a female patient being reported in the literature. The most common symptoms of colonic metastasis are bleeding and abdominal pain. Different malignant cell types have been reported, including large cell carcinoma, small cell carcinoma, adenocarcinoma, squamous cell carcinoma, and adenosquamous carcinoma. Such colon metastases may present with solitary lesions or disseminated masses. Determining the origin of a metastatic cancer on the basis of a morphologic examination alone is a difficult task. By using reliable immunohistochemical markers, clinical physicians can make an accurate diagnosis with appropriate staging and effective treatment for patients with lung cancer and colonic metastasis. Herein, we reported a 73-year-old woman with colonic metastasis from pulmonary adenocarcinoma, which was confirmed by an immunohistochemical study. A literature review is also included. ***(Thorac Med 2011; 26: 140-146)***

Key words: lung cancer, colonic metastasis, immunohistochemical study

Introduction

Lung cancer is the most common cause of cancer-related deaths worldwide [1]. The brain, liver, and bone are the most common sites of metastatic disease in patients with lung cancer [2]. Lung cancer with gastrointestinal (GI) tract metastasis is relatively rare, and the small intestine is the most commonly involved GI site [3]. The most common histologic type among these patients is squamous cell carcinoma [4-5]. Primary lung adenocarcinoma with colonic metastasis is extremely rare, and it can be mistaken as colon cancer with lung metastasis. We present a case of primary lung adenocarcinoma with colonic metastasis confirmed by an immunohistochemical study.

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Case Report

A 73-year-old woman was admitted due to malignancy with liver metastasis. The patient, a non-smoker, had been well until approximately 8 months before this admission, when she developed a cough with mucoid sputum. Six months before this admission, abdominal fullness, constipation, poor appetite, and weight loss (10 kg in 6 months) had developed gradually. Her body temperature was 36.1ºC, blood pressure 142/75 mmHg, pulse 93 beats/min, and respiration 18 breaths/min. Chest auscultation revealed symmetrical breathing sounds, and an abdominal examination was normal. Laboratory studies were all within normal limits, except the presence of leukocytosis.

Chest X-ray (Figure 1) showed an opacity occupying the left lower lung field. Chest computed tomography (CT) (Figure 2) revealed a consolidation in the left lower lobe, metastasis in the liver, and multiple lymphadenopathies in the bilateral mediastinum, gastro/duodenohepatic ligaments and abdominal para-aortic area.

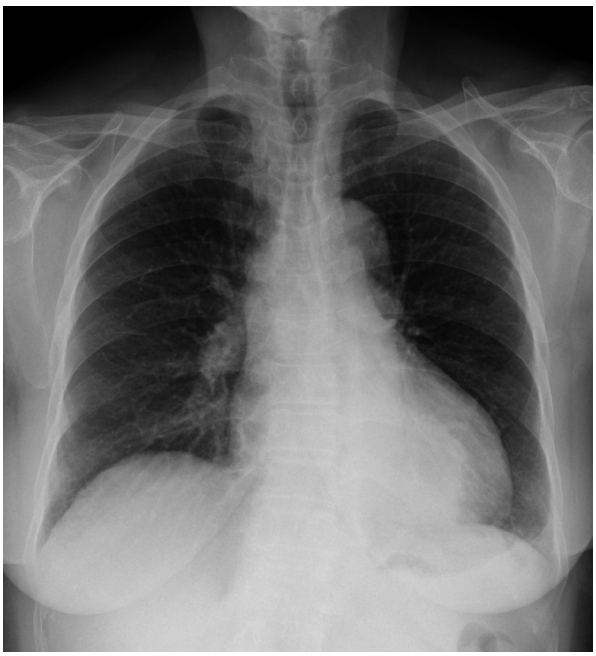

Fig. 1. Chest X-ray showed an opacity in the left lower lung field.

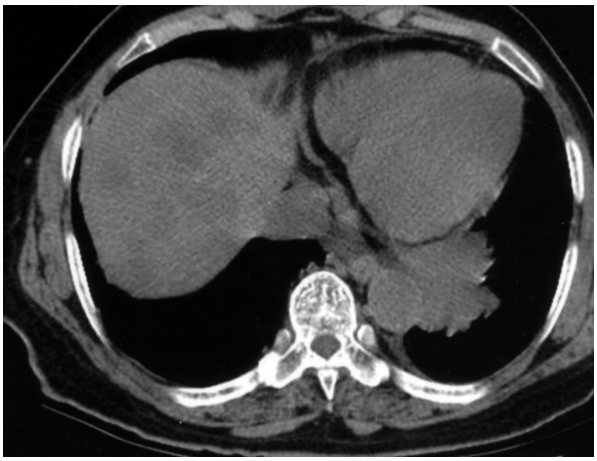

Fig. 2. Computed tomography showed a consolidation in the anteromedial basal segment of the left lower lobe, with multiple liver metastasis.

Bronchoscopy of the left lower lobe consolidation demonstrated multiple endobronchial masses located on the left main bronchus. Bronchial biopsies were performed and adenocarcinoma was diagnosed. Because the patient had GI symptoms, gastrointestinal malignancy with multiple metastases could not be excluded. A colonoscopy with biopsy was performed which revealed 2 cecum sessile polyps (Figure 3), 1 at the ascending colon, 0.2 cm in size, and the other at the proximal transverse colon, 0.3 cm in size. A colonoscopic biopsy of these 2 polyps was then performed. The pathology showed nests of poorly differentiated adenocarcinoma within the lymphatic spaces. The overlying mucosa was intact without dysplastic change. Immunohistochemical staining was performed and the adenocarcinoma was found to be positive for thyroid transcription factor 1 (TTF-1) and negative for CDX-2, confirming a diagnosis of metastatic adenocarcinoma from the lung (Fig-

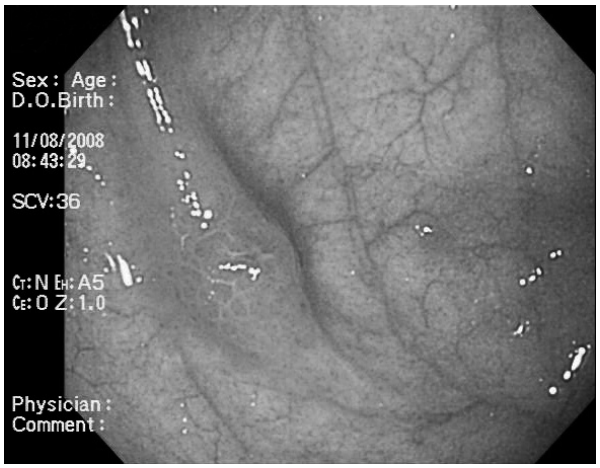

Fig. 3. Colonoscopic view showing polyps in the cecum

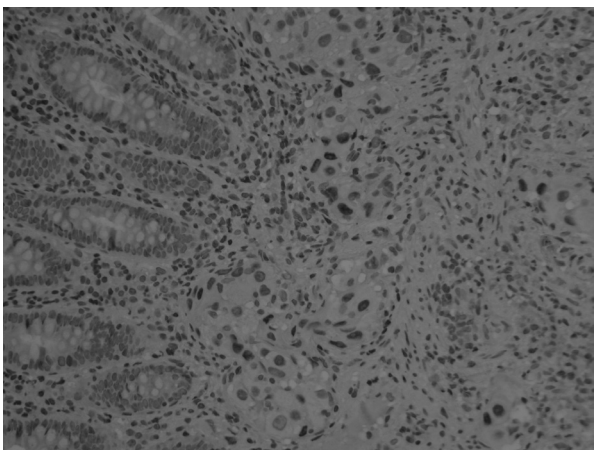

Fig. 4. Immunohistochemical staining for TTF-1. The adenocarcinoma cells within the lymphatic spaces show positive nuclear staining (X200).

ure 4).

The patient was finally diagnosed with stage IV (T4N3M1) lung adenocarcinoma with colon, brain, bone, and liver metastases. She refused systemic chemotherapy and was lost to follow-up 1 month later.

Discussion

Lung cancer is the most commonly diagnosed cancer and is the most common cause of cancer-related deaths in both men and women [1]. Common sites of metastasis include the brain, bone, liver, and contralateral lung. Gastrointestinal metastasis from lung carcinoma has been reported in 0.19-1.77% of lung cancer patients [3, 6], but according to several autopsy series, this kind of metastasis might not be as rare as previously thought [7-8]. The small bowel is the most common site of GI metastatic lung carcinoma involvement [3, 6], and colonic metastasis of primary lung cancer is extremely rare. We have reviewed the English literature, and to the best of our knowledge, this the first case report of an immunohistochemically-confirmed case of lung adenocarcinoma with colonic metastasis in a Taiwanese woman.

Cases of lung cancer with colonic metastasis have been reported since 1978 [9]. In our review of the literature, we found that these patients were almost always male, with only 1 female reported (Table 1). These patients presented with intermittent or continuous colonic obstruction, abdominal pain, lower gastrointestinal tract bleeding, or anemia, and the colonic metastases were synchronous or metachronous with respect to diagnosis of the lung lesion. The liver and brain metastases in our patient occurred synchronously at the time of diagnosis of colonic metastasis. However, colonic metastasis can be a solitary metastasis in lung cancer patients.

Kim *et al*. [4] and Yang *et al*. [3] reported that squamous cell carcinoma was the dominant tumor cell type for GI metastasis in lung cancer patients. However, the histologic types of lung cancer causing colonic metastasis have varied, with large cell carcinoma, small cell carcinoma, adenocarcinoma, and squamous cell carcinoma all being reported. In our patient, the pathologic results revealed predominant adenocarcinoma,

Table 1. Clinicopathologic findings of lung cancer patients with colon metastases between 2001 and 2010; a literature review

Author	Date	Age/ sex	Pathology of primary lung cancer	Metastatic site	GI symptoms	Treatment	Survival
Carroll, D. [16]	2001	68/M	SCC	Colon	Diarrhea, weight loss	Colectomy and C/T	6 months
John, A. K. [17]	2002	73/M	Large cell carcinoma	Colon	Diarrhea, rectal bleeding, weight loss	No active treatment	3 months
Habesoglu, M. A. [18]	2005	67/M	SCC	Colon and bone	Abdominal pain, constipation, nausea and vomiting	C/T	190 days
Stinchcombe, T. E. [14]	2006	60/M	SCC	Ascending colon	None, detected on PET	C/T	ND
Marinella, M. A. [19]	2007	76/M	Poorly differentiated carcinoma confirmed by IHC stain	Cecum, bone, adrenal mass	Melena	C/T	ND
Goh, B. K. [20]	2007	63/M	Large cell carcinoma	Cecum, ileum, Brain, bone, cervical and mesenteric LN	GI Hemorrhage	Rt Hemicolectomy	2 months
Rossi, G. [5]	2007	73/F	Large cell carcinoma, confirmed by IHC stain	Colon	Rectal bleeding	Hemicolectomy	4 months
Rossi, G. [5]	2007	73/M	Adenocarcinoma	Cecum	None, incidental finding by colonoscopy	ND	2 months
Lau, C. P. [21]	2008	59/M	Small-cell neuroendocrine carcinoma, confirmed by IHC stain	Cecum and brain	Abdominal pain, constipation, and anemia	C/T	ND
Hirasaki, S. [22]	2008	74/M	SCC	colon	Anemia, positive fecal occult blood test	C/T	23 weeks
Kim, M. S. [6]	2009	79/M	Adenosquamous carcinoma	Colon	Abdominal pain, with GI obstruction	Operation for the intestinal obstruction	91 days
Kim, M. S. [6]	2009	78/M	Adenocarcinoma	Colon, Lung, neck LN, adrenal gland, and spleen	Abdominal pain, hematochezia	ND	133 days
Weng, M. W. [23]	2010	53/M	Adenocarcinoma, confirmed by IHC stain	Descending colon	Abdominal pain, nausea, vomiting, bloody stool	Operation for intestinal obstruction	6 months

M=Male; F=Female; ND=not determined; IHC=immunohistochemical; LN=lymph node; PET=Positron emission tomography; C/T=chemotherapy; SCC=squamous cell carcinoma

either from the lung or the colon.

The distinction between adenocarcinoma of pulmonary origin and that of colorectal origin is crucial because of the differences in treatment strategy and chemotherapy regimen. CDX-2 is the product of the CDX-2 homeobox gene. It is a reliable marker to distinguish between primary and metastatic lung malignancies [10-11]. TTF-1, positive in primary lung and thyroid adenocarcinoma, is a highly specific marker of pulmonary adenocarcinoma [12-13]. In our patient, a diagnosis of metastatic adenocarcinoma from the lung was confirmed, because the tumor was positively stained for TTF-1 and negatively stained for CDX-2. Immunohistochemical studies play a significant role in differentiation between primary and metastatic adenocarcinoma.

Precise staging for lung cancer patients is also important in determining the appropriate treatment, especially in patients with a potentially resectable lung cancer. Positron emission tomography (PET) with radiolabeled [18F]-2-fluoro-deoxy-d-glucose (FDG) imaging is widely used in non-small cell lung cancer staging. Stinchcombe *et al*. [14] reported a case of lung cancer presenting with solitary colonic metastasis detected on a PET scan, and the patient's treatment plan changed because of a different clinical stage. Although its specificity is not high because of the wide range of standardized uptake values, PET scanning may reveal a higher incidence of colonic metastasis than previously suspected. PET scans following a tissue sampling may assist in diagnosing metastatic lung carcinoma involving the colon. Furthermore, some reports have suggested that combined PET/CT may be clinically significant in the detection of gastrointestinal foci [15].

Lung cancer with colonic metastasis has been reported to have a poor prognosis, with a survival of 2-6 months (Table 1) under management with chemotherapy or supportive care. However, none of the cases received targeted therapy (erlotinib or gefitinib) treatment. Whether targeted therapy can improve the survival of lung cancer patients with colonic metastasis is not known.

In summary, lung cancer with colonic metastasis may be more common than previously thought. Immunohistochemical markers and PET scans are useful diagnostic tools, permitting accurate diagnosis and precise staging, and avoiding unnecessary operations for lung cancer patients.

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原發性肺癌併結腸轉移：一個病例報告

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肺癌伴隨結腸的轉移在臨床非常罕見。在過去幾十年來的的英文文獻裡，只有少數零星的病例報告被發表過。幾乎所有肺癌併結腸轉移的病例都是男性患者，只有一例文獻是女性。最常見的臨床症狀是出血和腹痛。不同類型的惡性腫瘤細胞，包括大細胞癌、小細胞癌、肺腺癌、鱗狀細胞癌，腺鱗癌都有被報導過。有些案例是單一的結腸轉移，而有些案例是同時伴隨其他器官的轉移。只靠著細胞型態來判斷癌症的原發處是一項困難的工作。靠著使用免疫組織化學染色法，可以幫助臨床醫師對肺癌做出正確的診斷、分期、及有效的治療。在此我們報告一名73歲女性病患，以肺腺癌併結腸轉移表現，經免疫組織化學染色法來確定診斷的病例。並回顧歷年來與此種病歷相關的文獻報告。*(胸腔醫學* ***2011; 26: 140-146)***

關鍵詞：肺癌，癌症結腸轉移，免疫組織化學染色法

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Severe Acute Respiratory Distress Syndrome Caused by Influenza B Virus in a Healthy Adult

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Primary influenza pneumonia is characterized by fever, cough, progressive dyspnea, and even respiratory failure in severe cases. Acute respiratory distress syndrome (ARDS) due to influenza pneumonia is rare and is associated with a very high mortality rate. Most reported cases of primary influenza pneumonia were caused by influenza A virus. There are rare reports of influenza B pneumonia, and most of the cases have occurred in children with underlying disease. We report a case of ARDS associated with influenza B pneumonia in a 28-year-old man without underlying disease. The pathologic features of the open lung biopsy were consistent with diffuse alveolar damage. The patient received oseltamivir and methylprednisolone therapy, but oxygenation deteriorated, and the patient was refractory to prone position ventilation and high frequency oscillatory ventilation. Extracorporeal membrane oxygenation was used as a life-sustaining modality, but the patient developed ventilator-associated pneumonia and died. Although rarely found, influenza B pneumonia could develop in adults without underlying disease and cause refractory ARDS. ***(Thorac Med 2011; 26: 147-152)***

Key words: acute respiratory distress syndrome, influenza B virus, open lung biopsy, prone position, high frequency oscillatory ventilation, extracorporeal membrane oxygenation

Introduction

Influenza virus usually causes tracheobronchitis in healthy older children and young adults. Most of the mortality and morbidity associated with influenza infections result from pulmonary complications. Influenza-associated pneumonia ranges from severe primary viral pneumonia to secondary bacterial pneumonia. Primary influenza pneumonia is characterized by cough, progressive cyanosis, respiratory failure and diffuse infiltration on chest radiography. These symptoms begin within 24 hours of the onset of febrile illness, and the patients deteriorate despite antibiotic treatment [1]. Most patients who develop influenza pneumonia are

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older and have comorbidities such as chronic obstructive pulmonary disease, heart disease, diabetes, renal disease, and immunosuppression [2]. Acute respiratory distress syndrome (ARDS) associated with influenza pneumonia is rare, but is associated with a very high mortality rate [3]. Most reported cases of primary influenza viral pneumonia are caused by the influenza A virus [4]. There are rare reports of ARDS associated with influenza B pneumonia, and most cases have occurred in infants or children with underlying disease [5-8]. We report herein a case of influenza B pneumonia-associated severe ARDS in a young adult without underlying disease.

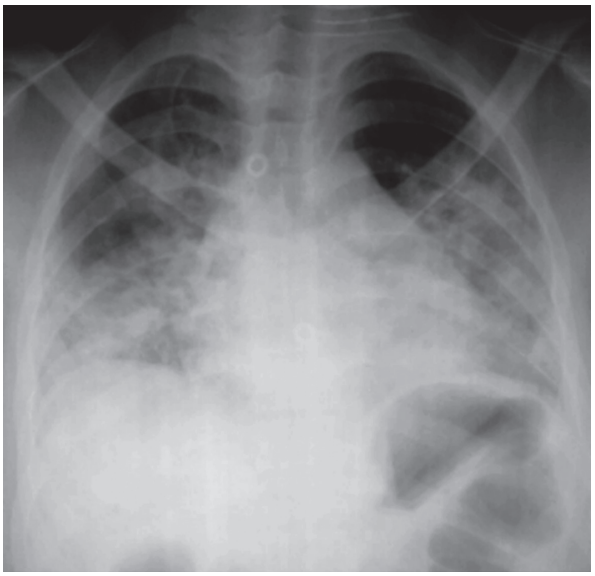

Fig. 1. Chest radiography on the 1st day of hospitalization showed bilateral diffuse infiltration.

Case Report

A 28-year-old man was admitted to a hospital because of fever, cough, and progressive dyspnea for 3 days. He had been in good health prior to this admission. His body temperature was 40°C upon arrival, and arterial blood gas analysis (under 2 L/min nasal O_2 cannula) showed pH: 7.388; PCO_2: 43.7 mmHg; PO_2: 49.9 mmHg; HCO_3^- concentration: 25.8 meq/L; and SaO_2: 84.8%. The chest radiography showed bilateral diffuse infiltration (Figure 1). ARDS of unknown origin was highly suspected, and the patient was admitted to the intensive care unit. Progression of the bilateral diffuse lung infiltration was found despite antibiotic treatment with cefotaxime and ciprofloxacin. Sputum culture and blood culture failed to detect a causative pathogen. Hypoxemic respiratory failure occurred 4 days after the onset of symptoms, and so the patient was intubated and placed on mechanical ventilation on the 1st day of hospitalization. The PaO_2/FiO_2 ratio on the first day of mechanical ventilation was 81.7. Respiratory system compliance was 31.9 ml/cm H_2O. Since the patient still needed a high FiO_2 (90%) after being mechanically ventilated for 5 days, he was referred to our institution on the 5th day of hospitalization.

Upon arrival, the patient was oriented and bilateral lung field fine rales were heard on auscultation. He needed FiO_2 of 100% to maintain adequate oxyhemoglobin saturation. A high resolution computed tomography (HRCT) scan of the chest (Figure 2) on the 7th day of hospitalization showed diffuse ground-glass attenuation and airspace opacities in bilateral lungs. A bronchoalveolar lavage (BAL) was performed the same day. All bacterial cultures, fungus cultures, CMV (identify), *pneumocystitis carinii*, legionella, iron stain, and cytology examinations of the BAL fluid were negative. A throat swab for virus identification revealed the presence of influenza B virus by reverse transcription polymerase chain reaction (RT-PCR), and an elevated serum influenza B antibody titer

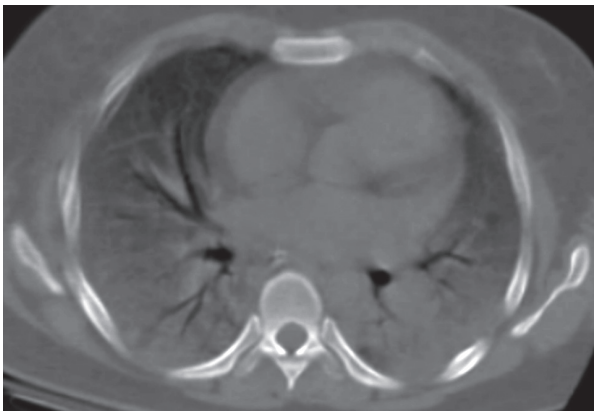

Fig. 2. High resolution chest tomography of the lung on the 7th day of hospitalization showed diffuse ground-glass opacity and consolidation on both the dependent and non-dependent parts of the bilateral lungs.

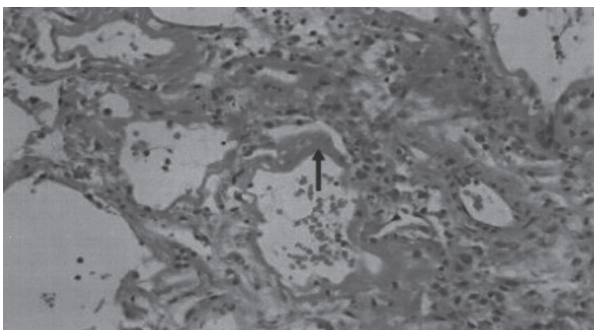

Fig. 3. Pathological examination of the open lung biopsy showed marked alveolar cell hyperplasia and hyaline membrane formation (arrow). The pathological findings were consistent with diffuse alveolar damage.

(1:1024) was also found on the 8th day of hospitalization. The patient was ventilated using a pressure control mode with high positive end-respiratory pressure (PEEP) and low tidal volume (ventilation rate: 30/min; pressure control: 20 cmH_2O; PEEP: 20 cmH_2O; tidal volume: 200 mL; peak airway pressure: 42 cmH_2O; plateau pressure: 39 cmH_2O). The pressure-volume (P-V) curve of the lung showed a lower inflection point of 23 cmH_2O via the P-V tool II of the GALILEO GOLD ventilator (Hamilton Medical AG, Via Nova, Switzerland). The pulmonary artery was catheterized and the cardiac index was 8.43 $L/min/m^2$. The pulmonary capillary wedge pressure was 19 mmHg under a PEEP of 20 cmH_2O.

Open lung biopsy with a wedge resection from the left upper lobe was performed on the 8th day of hospitalization. Pathological examination of the biopsy showed marked alveolar cell hyperplasia, interstitial edema, and hyaline membrane formation (Figure 3). There were also an interstitial lymphoplasma cell infiltration and a proliferation of fibroblasts. The pathological findings were compatible with diffuse alveolar damage. Oseltamivir (150 mg daily) and methylprednisolone (40 mg intravenous infusion every 6 hours) were started on the 8th day of hospitalization. We tried high frequency oscillatory ventilation (HFOV) on the 9th day of hospitalization. The HFOV settings were FiO_2: 1.0, an oscillation frequency of 5Hz, a percent inspiratory time of 33%, and a bias flow of 40 L/min. Mean Paw was set 3 to 5 cm H_2O greater than the mean airway pressure before conversion to HFOV. The initial pressure amplitude of oscillation was set to achieve mechanical vibration to the midthigh. After 30 minutes, arterial blood gas analysis showed pH: 7.37; PCO_2: 49.9 mmHg; PO_2: 65.8 mmHg; HCO_3^- concentration: 23.5 meq/L; SaO_2: 85.5%. The PaO_2/FiO_2 ratio decreased from 81.7 to 65.8. Hypoxemia deteriorated and the patient was refractory to prone position ventilation and HFOV. Venovenous extracorporeal membrane oxygenation (ECMO) was started on the 11th day of hospitalization because of severe oxygenation failure. Ventilator-associated pneumonia was diagnosed, since new infiltration of the right upper lung field was seen on chest radiography and positive sputum culture grew *Pseudomonas aeruginosa* on the 12th day of hospitalization.

The patient died of multiple organ failure after using ECMO as a life-sustaining modality for 16 days.

Discussion

The influenza B virus is less virulent than influenza A because of the slow rate of mutation of its hemagglutinins, and because of the absence of major antigen shifts. Most cases of primary influenza B pneumonia occur in children with underlying disease. The present case was of 28-year-old man who had been in good health prior to this admission. ARDS was diagnosed because of the acute onset of illness, diffuse infiltration on chest radiography, and severe hypoxemia. Influenza B virus was identified by RT-PCR, and the high serum influenza B antibody titer (1:1024) confirmed the influenza B viral infection. Tanaka *et al*. reported marked ground-glass opacities with lobar distribution on HRCT of the chest in patients with influenza pneumonia [9]. The HRCT finding in this case showed diffuse ground-glass opacities in bilateral lungs, similar to the findings described by Tanaka. The ground-glass attenuation was found in both the dependent and non-dependent part of the lung, which accounted for the poor response to oxygenation in the prone position.

There are only a few reports discussing the pathological changes in influenza pneumonia. Yeldandi, *et al*. reported the pathological features of lung biopsy specimens from 6 sporadic influenza pneumonia cases [10]. Acute changes varied from patchy fibrinous alveolar exudates and hyaline membranes with interstitial edema, to severe diffuse alveolar damage and necrosis of the bronchiolar mucosa. Reparative changes included proliferation of type II cells, mild interstitial chronic inflammatory infiltrates, and organization within the air spaces and interstitium. The present case received open lung biopsy on the 7th day of hospitalization. The pathological findings showed hyaline membrane formation, alveolar cell hyperplasia, and interstitial edema, which were consistent with diffuse alveolar damage. Most of the alveoli were obliterated because of alveolar cell hyperplasia and fibroblast proliferation. This resulted in high critical opening pressure for the majority of the alveoli, and accounted for the significantly elevated lower inflection point of 23 cmH_2O on the P-V curve of the mechanical ventilator, and for the need for a higher PEEP to keep the alveoli open.

Our study group has reported that open lung biopsy in ARDS patients is relatively safe in elective cases [11]. The role of open lung biopsy in these ARDS patients is to exclude specific etiologies and change the treatment as needed immediately. In this case, PCR and serology-based tests for the virus were not obtained until 3 days later. However, open lung biopsy results can be available the day after the procedure.

The use of an antiviral agent is recommended for influenza infections. It is difficult to distinguish influenza A from B virus based on the clinical presentation, and methods to identify the infecting virus are not widely available. Therefore, treating influenza infection with amantadine or rimantadine should be discouraged, since these 2 agents are only active against influenza A. Neuraminidase inhibitors are approved for use within the first 48 hours of symptom onset and are effective against both influenza A and influenza B virus. Jefferson, *et al*. reported that oseltamivir 150 mg daily is effective at preventing lower respiratory tract complications in influenza cases, especially bronchitis and pneumonia [12]. Our patient received osel-

tamivir therapy, but the symptoms deteriorated. This may due to the delayed use of oseltamivir, since it was started 11 days after the onset of symptoms.

Patients with features suggestive of influenza infection and shortness of breath should receive chest radiography to exclude pneumonia. Rapid diagnosis of influenza infection may be helpful for the early use of neuraminidase inhibitors to reduce the incidence and severity of influenza pneumonia. This report indicated that although rarely found, influenza B virus could cause influenza pneumonia and severe ARDS in adults without underlying disease.

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成年人 B 型流感病毒感染造成嚴重呼吸窘迫症候群：病例報告

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流感病毒感染造成急性呼吸窘迫症候群常常會造成嚴重的併發症和很高的死亡率。大部分都是導因於A型流感病毒感染，而B型流感病毒大部分發生在小孩及健康的年輕成人。茲報告一位28歲健康男性感染B型流感並導致嚴重呼吸窘迫症候群。肺部病理切片顯示瀰漫性肺泡破壞。個案後來有接受抗病毒藥物oseltamivir及類固醇使用，但是血氧濃度並沒有明顯改善即使用了高頻震盪通氣和俯臥姿。後來這位病人有使用葉克膜改善血氧交換，但是發生嚴重的呼吸器相關肺炎和死亡。雖然B型流感病毒造成的呼吸窘迫症候群相對少見，健康成人若是有病毒性肺炎相關症狀仍須早期診斷及投藥。*(胸腔醫學* ***2011; 26: 147-152)***

關鍵詞：B型流感病毒，呼吸窘迫症候群，開肺切片，高頻震盪通氣，俯臥姿，葉克膜

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Spontaneous Pneumomediastinum — A Rare Complication in Dermatomyositis

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Dermatomyositis is a generalized disorder characterized by myositis and typical cutaneous findings. Dermatomyositis is commonly associated with interstitial lung disease. However, spontaneous pneumomediastinum has been reported as a rare complication in dermatomyositis. Herein, we describe a 57-year-old female patient with dermatomyositis who had the complications of spontaneous pneumomediastinum and extended subcutaneous emphysema. The progressive ulcerative skin lesions were accompanied by refractory pneumomediastinum despite relatively high-dose corticosteroids. The ulcerative skin lesions and pneumomediastinum resolved successfully after treatment with oxygenation therapy and corticosteroids in combination with cyclosporine-A. The patient remained well during more than 6 months of outpatient follow-up after discharge. According to previous studies, spontaneous pneumomediastinum is not associated with interstitial lung disease, but with bronchial necrosis. Necrosis of the bronchial wall caused by focal ischemia due to vasculopathy could result in air leakage with resultant pneumomediastinum. ***(Thorac Med 2011; 26: 153-159)***

Key words: spontaneous pneumomediastinum, dermatomyositis, polymyositis, interstitial lung disease, corticosteroid, cyclosporine-A

Introduction

Dermatomyositis (DM) is a systemic and inflammatory disease affecting skeletal muscles, skin and other organs, including the lungs [1]. Interstitial lung disease (ILD) develops in DM in about 10-43% of cases and is associated with a poor outcome [2].

Pneumomediastinum (PnM) consists of air or other gas in the mediastinum. It mostly occurs after traumatic injury, mediastinitis, esophageal rupture or mechanical ventilation. PnM may also arise spontaneously. Spontaneous pneumomediastinum (SPnM) has been reported as a rare complication of various types of ILD, including interstitial pneumonia associated with connective tissue diseases [3]. Inflammatory myositis (polymyositis/dermatomyositis) (PM/DM) is the connective tissue disease most frequently associated with PnM [2-3].

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The disease mechanism, outcome, and prognostic factors of PnM in DM have not been fully understood. We report a case of DM-associated SPnM in a 57-year-old female with DM who received successful treatment with relatively high-dose prednisolone and cyclosporine-A (CYA) without recurrence of SPnM during 6 months of follow-up. We also review other case reports of PnM in PM/DM and discuss the mechanisms of the disease and the benefit of immunosuppressant administration.

Case Report

A 57-year-old woman was first admitted to our hospital complaining of fever, polyarthralgia (wrists, interphalangeal joints, ankles), proximal muscle weakness and multiple skin lesions in October 2007. Erythematous-to-violaceous infiltrating plaques were observed on the face, upper back, lower anterior neck and upper anterior chest, with some maculopapules and scaly changes. She was suspected to have DM based on proximal muscle weakness, typical cutaneous manifestations and skin biopsy. She had periungual telangiectasia and typical Gottron's signs at the proximal interphalangeal joints. A muscle strength test demonstrated symmetric proximal weakness of the limbs. No focal neurological sign was observed. Laboratory data showed a raised level of aspartate aminotransferase (AST) (50 U/L, normal range: 0-39 U/L) and lactic dehydrogenase (LDH) (222 U/L, normal range: 100-200 U/L), but no elevation of serum creatinine kinase (CK) (62 U/L, normal range: 30-135 U/L) was noted. Tests for antinuclear antibodies, anti-double stranded DNA, anti-Jo-1, and rheumatoid factor were all negative. Electromyography suggested no obvious myopathic changes. Skin biopsy was taken from the erythematous plaque of the right middle finger, and pathological examination revealed slight vacuolar interface dermatitis with a mucin deposit.

The patient was initially treated with prednisolone (20 mg/day) and hydroxychloroquine (400 mg/day), and the proximal muscle weakness and skin erythema then improved. However, 11 months later, she experienced dry cough, neck swelling, odynophagia and hoarseness. Crepitus resulting from subcutaneous emphysema was felt on the anterior chest extending to the supraclavicular fossa and neck. Breathing sounds revealed fine basal crackles in the right lower lung. Chest roentgenogram revealed cervical subcutaneous emphysema and PnM (Figure 1, A). Compatible image findings on chest computed tomography (CT) scans were noted (Figure 1, B & C). Pulmonary fibrosis in the bilateral lower lobes was also noted. DM with ILD was diagnosed. The pulmonary function test showed a restrictive pattern, with a total lung capacity (TLC) of 2.76 L (71% of the predicted value), a vital capacity (VC) of 1.98 L (80% of predicted) and a forced expiratory lung volume in 1 second (FEV1) of 1.24 L (61% of predicted). The diffusion coefficient (DLco/VA) was 76% of the predicted value, but the pulmonary fibrosis lesion was stationary in light of an old imaging report. DM with SPnM and subcutaneous emphysema was diagnosed. A high concentration of oxygen and prednisolone at a dosage of 45 mg/day were given initially, and the subcutaneous emphysema and SPnM resolved rapidly.

Despite the initial response to treatment, relapse with similar symptoms occurred 1 month later, and was refractory to corticosteroid therapy at that time. Because her symptoms of skin ulceration and SPnM were progressive, she

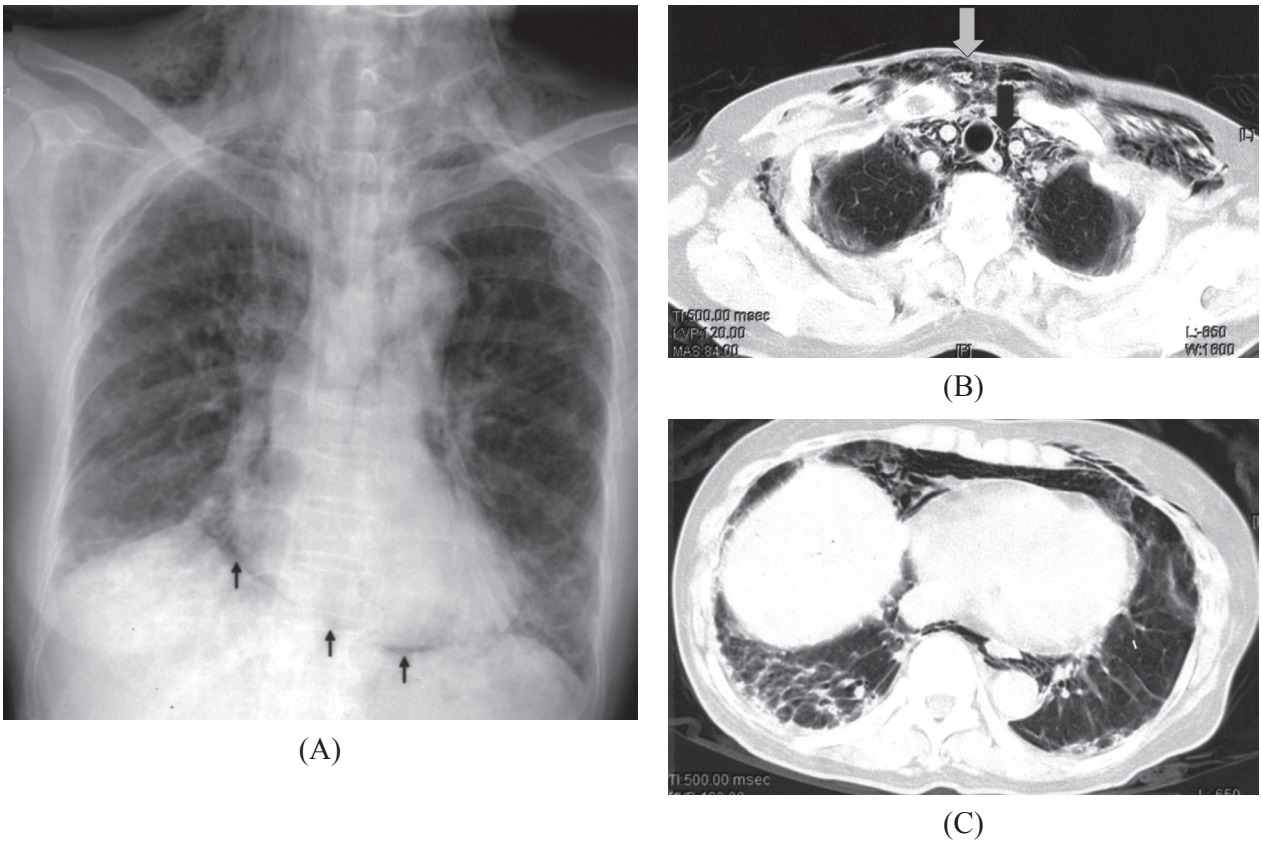

Fig. 1. (A) Chest X-ray showing a continuous diaphragm sign indicating PnM (thin arrow). Subcutaneous emphysema in the bilateral neck area (B) Chest CT showing air in the mediastinum (around the trachea and the aorta) and subcutaneous emphysema (red thick arrow) (C) Pulmonary fibrosis with traction bronchiectasis in the right lower lobe and left lower lobe was also noted.

received combination therapy with prednisolone and CYA at a dosage of 30 mg and 150 mg daily, respectively. Her symptoms, including skin and SPnM, were resolved without further recurrence for more than 4 months. The patient was well without recurrence of SPnM or cervical subcutaneous emphysema during outpatient department follow-up for 6 months.

Discussion

DM is a generalized disorder characterized by myositis and typical cutaneous manifestations [1]. Systemic symptoms, including arthritis, dysphagia, gastrointestinal symptoms and pulmonary dysfunction may be presented to a varying degree in patients with DM. This disorder is commonly associated with pulmonary disease, including aspiration pneumonia, hypoventilation resulting from inflammation of the respiratory muscles, and ILD [2]. SPnM is a rare complication of various types of ILD, including interstitial pneumonia associated with connective tissue diseases [3]. Although the pathogenesis of SPnM has not yet been clarified, Kono *et al*. [4] have suggested that it is not associated with interstitial pneumonitis but with the complication of vasculopathy appearing as skin lesions in DM. It has been estimated that 39% of patients with PM/DM have ILD [5]. Patients

with ILD such as idiopathic pulmonary fibrosis are at risk of developing PnM [6]. In fact, retrospective studies have estimated that PnM was detectable by CT scan in 5-14.7% of patients with idiopathic pulmonary fibrosis [7-8].

Bradley *et al*. [9] first reported SPnM in adult DM in 1986, acknowledging that it was rarely a complication of connective tissue disease (e.g., rheumatoid arthritis, lupus erythematosus, scleroderma) and primarily associated with pulmonary involvement and a poor prognosis. Two hypotheses have been proposed to explain the etiology of SPnM in patients with DM. The first is that SPnM might be related to ILD. Due to previously damaged lungs, episodic increases in intra-alveolar air pressure may result in rupture in a weakened respiratory tree. Further, ILD could be complicated by PnM according to a previous study [11]. The second hypothesis suggests that SPnM is caused by active pulmonary vasculitis. Cicuttini *et al*. hypothesized that vasculitis was the common denominator leading to PnM in patients with DM [10]. Kono *et al*. [4] reviewed 48 patients with inflammatory myositis (20 PM, 24 DM), of which, 4 cases of SPnM were reported. In the SPnM group, 3 patients had signs of active cutaneous vasculopathy (ulcerative lesions, periungual erythema), but in the non-SPnM group, only 6 patients had cutaneous vasclopathy. A higher prevalence rate of cutaneous vasculopathy was detected in the SPnM group compared with the group without SPnM (75% vs. 14%). Moreover, to our knowledge, there are no reports of SPnM in PM. Further evidence to support the association between cutaneous vasculopathy and SPnM came from a case report in which a patient with bronchial necrosis was identified via bronchoscopy [4].

Yoshida *et al*. [12] reviewed 21 cases of PnM associated with DM. Among them, 6 resulted in death complicated by ILD. The direct cause of death was respiratory failure, due to progressive ILD or pulmonary infection rather than PnM. In another study, Le Goff *et al*. [13] reported 11 PM/DM patients complicated by ILD and PnM. A high prevalence rate of amyopathic DM, a variant and rare form of DM manifesting without muscle involvement, was noted in patients with PM/DM associated with PnM (5 of 9 DM patients). Furthermore, a poor prognosis was associated with an absence of muscle weakness, initial low vital capacity, and initial low carbon monoxide diffusion capacity [13]. Amyopathic DM is characterized by the presence of DM for 6 months or more in individuals who have normal muscle enzymes and no clinically significant muscle weakness. One retrospective study revealed that patients with amyopathic DM are at risk for developing the same potentially fatal disease complications as those patients with DM (e.g., ILD and internal malignancy) [18].

Randomized controlled trials are not available to guide the management of DM-related SPnM. Up to 50% of symptomatic patients with myositis respond to treatment with corticosteroids. Most clinicians may initiate immunosuppressants (e.g., azathioprine, methotrexate, cyclosporine-A or cyclophosphamide) after a failure to respond to steroids or in cases of fulminant respiratory disease [14]. Neves *et al*. [15] reported favorable outcomes in patients who received immunosuppressants in contrast to patients who received corticosteroids only. Yamanashi et al. [16] suggested that vasculitic activity associated with DM was important in the development of PnM. Hence, immunosuppressive agents might be beneficial to DM complicated by PnM.

Recently, CYA was reported to be a possibly effective treatment for DM complicated by PnM. Kim *et al*. [17] reviewed 6 patients with DM complicated by PnM who received combination therapy with steroids and CYA. The disease resolved in 5 patients and prednisolone was tapered off successfully [17].

We reported a patient with DM who developed SPnM and was treated successfully with combined prednisolone and CYA. During 6 months of follow-up, the SPnM and multiple skin lesions resolved without recurrence. Based on previous studies, SPnM caused by vasculopathy was suspected, despite the lack of direct evidence from bronchoscopic findings. To date, a standard treatment is lacking due to the rarity and heterogeneity of the cases. From our experience, CYA may be an effective therapeutic agent in DM refractory to corticosteroid therapy. In addition, we suggest that CYA may be considered as an initial immunosuppressant for patients with DM complicated by SPnM.

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自發性氣縱膈—皮肌炎之罕見併發症

陳昭宏　陳炯睿　張漢煜

皮肌炎普遍以肌炎與典型的皮膚症狀來表現，且常見與間質性肺病相關。然而自發性氣縱隔在皮肌炎已被發現是一種罕見的併發症。在此，我們描述一個57歲的女性被診斷為皮肌炎，有潰瘍性皮膚損傷與間質性肺炎的表現，並且發生罕見的自發性氣縱隔合併厲害的皮下氣腫之併發症。儘管用高劑量之類固醇，漸進性的潰瘍性皮膚損傷與頑固性自發性氣縱隔依然發生。當合併類固醇、氧氣，與環孢靈的治療，潰瘍性皮膚損傷與自發性氣縱隔之情形獲得改善。病人出院六個月後依然在門診追蹤。根據過去的研究，自發性氣縱隔與支氣管壞死相關而非之前所認定是間質性肺病造成。血管病變造成支氣管壁壞死被認為才是造成氣縱隔的原因。*(胸腔醫學* ***2011; 26: 153-159****)*

關鍵詞：自發性氣縱隔，皮肌炎，多發性肌炎，間質性肺病，類固醇，環孢靈

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Small Intestine Intussusceptions Secondary to Metastasis from Adenocarcinoma of the Lung – A Case Report

Juei-Yu Cheng*, Chih-Jen Yang*,****,*****, Jong-Rung Tsai*,****, Chee-Yin Chai**, Jaw-Yuan Wang***, Jhi-Jhu Hwang*,****

Lung cancer is the leading cause of cancer death in the world [1-2]. In patients with lung cancer, metastasis to the bone, brain, liver and adrenal gland is most frequently found [2]. Gastrointestinal metastasis is not as frequently reported [1]. Among these patients, bleeding, anemia, and acute abdomen were the common presentations. Intussusception is a relatively rare but emergent condition. Aggressive investigation and early surgery are the only methods for providing palliation to patients with gastrointestinal metastasis. However, morbidity and mortality remain high and the prognosis is poor. Herein, we report a lung adenocarcinoma patient who presented acute abdomen; the final diagnosis was the unexpected small bowel intussusception caused by metastasis. We report this rare case and review the literature. ***(Thorac Med 2011; 26: 160-164)***

Key words: lung cancer, gastrointestinal metastasis, intussusception

Introduction

Lung cancer with gastrointestinal metastasis is not common and often asymptomatic, or patients may have only some vague symptoms such as nausea and vomiting which may be confused with the side effects of chemotherapy [1]. However, symptomatic gastrointestinal metastasis is extremely rare and may cause severe complications such as hemorrhage, acute abdomen, perforation, obstruction, and rarely, intussusception [1-4]. As reported in several studies [6], the survival duration of patients with perforated small intestine metastasis is often less than 16 weeks, implicating small bowel metastasis as a poor prognostic indicator of lung carcinoma. Lack of attention to gastrointestinal metastasis in lung cancer leads to a delayed diagnosis, but

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early diagnosis remains challenging.

Case Report

A 68-year-old man with severe and progressive abdominal pain with vomiting was sent to our emergency department with a suspected intestinal obstruction. Six weeks earlier, lung adenocarcinoma with left supraclavicular lymph node, multiple bone and left adrenal gland metastases were diagnosed (Figure 1). Because of the patient's poor Eastern Cooperative Oncology Group (ECOG 2) performance status, gefitinib 250 mg per day was initiated, though a wild-type epidermal growth factor receptor (EGFR) mutation was later detected. Before this admission, gefitinib had been administered for 30 days.

On this admission, his temperature was 36.6°C, blood pressure 151/77 mmHg, respiratory rate 18 cycles/min, and pulse 88 beats/min. Physical examination revealed periumbilical area tenderness and muscle guarding. Laboratory tests showed 9200 leukocytes/ mm^3 with 9% bands and 86% neutrophils, C-reactive protein 168.34 mg/L (N<5), aspartate transaminase 19 IU/L (N=10-42), alanine transaminase 12 IU/L (N=10-40), blood urea nitrogen 11.3 mg/dL (N=7-18), creatinine 0.05 mg/dL (N=0.6-1.3), amylase 52 U/L (N=36-123), and lipase 20 U/L (N=7-58).

Plain abdomen demonstrated much fecal material impaction in the recto-sigmoid colon with an increased bowel gas pattern, so mechanical ileus was suspected. An abdominal computed tomography (CT) scan revealed small bowel intussusception at the ileus, with a tumor mass as the leading point causing mechanical ileus (Figure 2). Emergency exploratory laparotomy with segmental resection and small intestine anastomosis was performed. A firm tumor mass measuring 2.3 × 2.2 cm at the largest diameter was detected at the leading edge of the intussusceptions, 200 cm from the ileocecal valve. The tumor appearance was polypoid and ulcerated with extension to the muscularis propria. Pa-

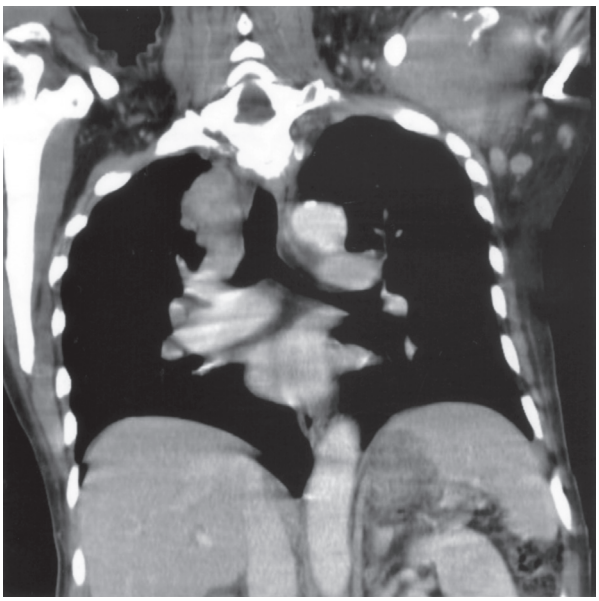

Fig. 1. Chest CT scan showed a primary lung cancer measuring 4.6 cm x 3.3 cm in the right upper lung field and a huge mass in the supraclavicular area with bony destruction.

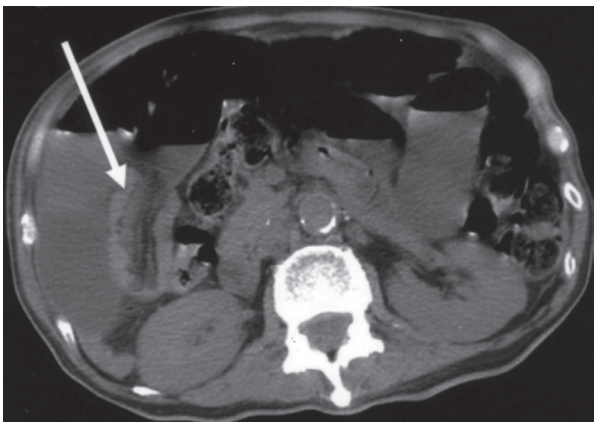

Fig. 2. Abdominal CT scan demonstrated dilated intestinal loops with a sausage-shaped mass lesion (white arrow), suggesting small bowel intussusceptions.

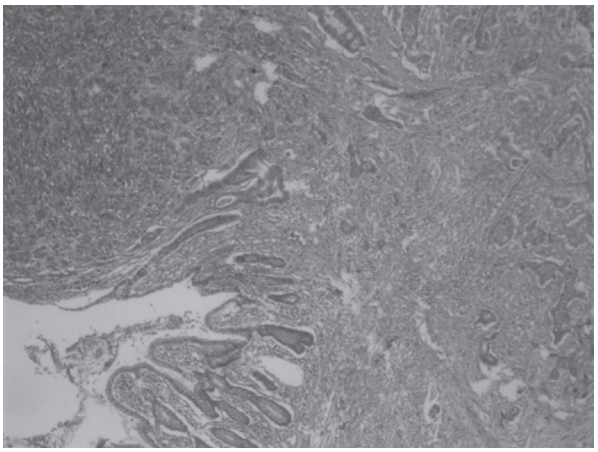

Fig. 3. Some cuboidal cancerous cells arranged in irregular tubules and a nested pattern within desmoplastic stroma indicated adenocarcinoma (H&E stain 40X).

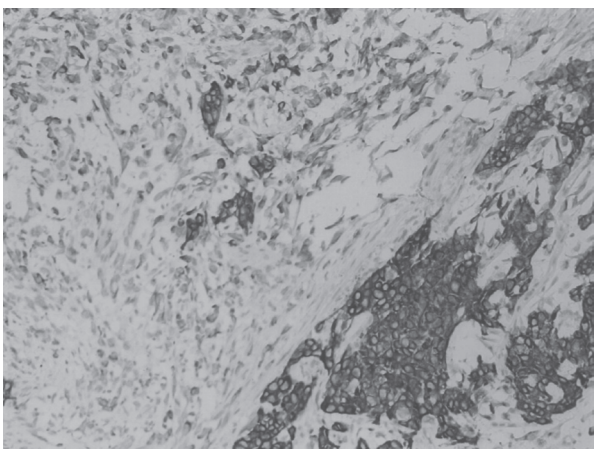

Fig. 4. Positive for CK7 in the immunohistochemical stain of the small bowel mass (100X).

thology yielded metastatic adenocarcinoma that was positive for CK7 but negative for TTF-1, CK20 and CDX2; the IHC panel was the same as that of the patient's lung cancer, confirming lung cancer with unexpected gastrointestinal metastasis (Figure 3, 4).

However, pneumonia and sepsis developed a few days after operation. Acute respiratory distress syndrome occurred and emergent intubation with mechanical ventilation support was also performed. His clinical condition deteriorated, and septic shock and multiple organ failure soon followed. He passed away 34 days after operation.

Discussion

Lung cancer is a major cause of cancer-related death in the world, with approximately half of patients presenting with metastatic disease [2]. However, lung cancer with symptomatic gastrointestinal metastases is found in only 1.77% of living patients, as compared with 11.9-14% of autopsies after death due to lung cancer [2, 5]. This discordance may be attributed to the fact that gastrointestinal metastases from lung cancer very rarely give rise to symptoms or complications [2]. Survival duration in perforated small intestine metastasis was often less than 16 weeks in several studies, indicating that small bowel metastasis is a poor prognostic indicator of lung carcinoma.

The most common metastatic site is the small bowel, with sporadic case reports of metastasis to the stomach, large bowel and anus. Within the small bowel, the jejunum had a slightly higher prevalence and occurrence in the duodenum was relatively infrequent. The pathogenesis of gastrointestinal metastases has been summarized by Leidich and Rudolph [6]. Lung cancer cells spread via the hematogenous and lymphatic route to the bowel and then replace the bowel wall, resulting in various complications. Necrotic tumors tend to perforate, bulky tumors cause obstruction, ulcerative tumors bleed, and extensive mucosal involvement causes malabsorption. Therefore, in clinical practice, patients present with obstruction, hemorrhage, intussusception and perforation [1-4].

Intussusceptions are classified according

to location as enteroenteric, colocolonic and ileocolonic [5], with the former type being the least common [5]. In terms of the histological subtypes of lung cancer, lung adenocacrinoma and lung squamous cell carcinoma have been reported [1, 4-5]. The classic triad of intussusception includes cramping abdominal pain, bloody diarrhea and a palpable tender mass, and is infrequently observed in adults [5]. However, in patients with lung cancer and presenting with acute abdomen, gastrointestinal metastasis should also be considered as 1 of the differential diagnoses [5].

Despite the poor prognosis, early and appropriate therapy will occasionally yield successful surgical palliation. Patients with known lung cancer who develop abdominal complaints should be examined thoroughly and treated quickly [2].

Our patient had advanced lung adenocarcinoma with a poor performance status under targeted therapy, and suffered from a rare small intestinal intussusception. He underwent emergent operation due to mechanical ileus but progressed to nosocomial pneumonia-related death.

In conclusion, small bowel intussusception caused by metastatic lung cancer is rare but possible. We should pay attention to lung cancer patients that have unexplained abdominal discomfort and take such life-threatening complications into consideration.

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由肺腺癌引起的罕見小腸轉移併發腸套疊之一個案報告

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肺癌是世界重要癌症死因。骨骼、腦部、肝臟、腎上腺是肺癌轉移最常見的地方，而胃腸道轉移則甚少被報導。這些病人往往以出血、貧血、急性腹痛表現。在胃腸道轉移中，腸套疊是相對罕見但緊急的狀況。積極介入、及早手術對這些病人而言是唯一可行的解決之道。即便如此，併發症以及死亡率仍居高不下，且預後欠佳。這裏，我們報導一位肺腺癌病患表現急性腹痛，其最終診斷為肺癌之小腸轉移造成之腸套疊。我們報導這位病人並作文獻回顧。*(胸腔醫學* ***2011; 26: 160-164)***

關鍵詞：肺癌，胃腸道轉移，腸套疊

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Urinothorax Following Percutaneous Nephrolithotripsy – A Case Report

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We presented an unusual case of transudative pleural effusion. Urinothorax developed in a young man who underwent percutaneous nephrolithotripsy (PCNL) for obstructive hydronephrosis caused by renal stones. Urinothorax was confirmed by biochemistry study. The anatomic defect could be identified from computerized tomography (CT) of the abdomen. The pleural effusion resolved rapidly and the dyspnea was relieved after drainage. We reviewed the literature and focused on the diagnostic processes. ***(Thorac Med 2011; 26: 165-170)***

Key words: urinothorax, percutaneous nephrolithotripsy

Introduction

There are many causes of transudative pleural effusion. Urinothorax is a rare condition, and is an unusual cause of pleural effusion; mostly, it is a transudate. It can be attributed to anatomic defects in the renal collecting system and the diaphragm. Urine might leak into extrarenal spaces and then extravasate from the retroperitoneal space into the pleural cavity. This condition is reversible and the pleural effusion might disappear rapidly following appropriate treatment. Urinothorax is diagnosed by a pleural fluid creatinine-to-serum creatinine ratio greater than 1. Scintigraphy or a computerized tomography (CT) scan is recommended to demonstrate the anatomic defect, if it is present.

Case Report

A 36-year-old man presented to the emergency room with left flank pain and progressive dyspnea. Nine days before this presentation, a left renal stone was diagnosed that was complicated with obstructive hydronephrosis, which was resolved by percutaneous nephrolithotripsy (PCNL). The day after PCNL, the percutaneous nephrostomy (PCN) tube was clamped, and then removed on the following day. No complications, such as bleeding, fluid extravasating from the wound, chest pain or dyspnea were noted. He could urinate well by himself, and was discharged uneventfully. His chest radiograph and renal function before PCNL were normal. Biochemistry revealed blood urea nitrogen

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(BUN) 14 mg/dL and creatinine (Cr) 1.1 mg/dL.

After this discharge, the urine amount gradually decreased and progressive dyspnea was noted. He visited our emergency department with shortness of breath and left flank pain. Physical examination revealed decreased breathing sounds in the left lower lung field. There was no fluid discharge from the PCN wound. Chest radiography showed left-sided pleural effusion, and chest ultrasonography confirmed massive pleural effusion. Thoracocentesis disclosed a light red and urine-like fluid. Biochemistry of the pleural fluid revealed transudative effusion with a pH of 7.0, glucose 72 mg/dL, protein 0.45 g/dL, lactate dehydrogenase (LDH) 305 U/L, and creatinine 14.2 mg/dL. Renal function showed BUN 32 mg/dL and creatinine 2.4 mg/dL. The effusion-to-serum creatinine ratio (14.2/2.4) was 5.9, which confirmed the diagnosis of urinothorax. The effusion was drained by tube thoracostomy, and the dyspnea disappeared rapidly after drainage.

Abdominal CT showed a small tract communicating with the left renal collecting system through an extrarenal space extending to the left pleural cavity (Figure 1). In addition, a calculus leading to dilatation of the left upper ureter was present in that area (Figure 2). The formation of a nephro-pleural fistula which resulted in ipsilateral urinothorax was confirmed by this imaging study. The left hydroureter disappeared rapidly after a Double J stent was implanted. The chest tube was removed 5 days later. Follow-up renal function was normal with BUN 15 mg/dL and Cr 0.9 mg/dL. Ten days after removing

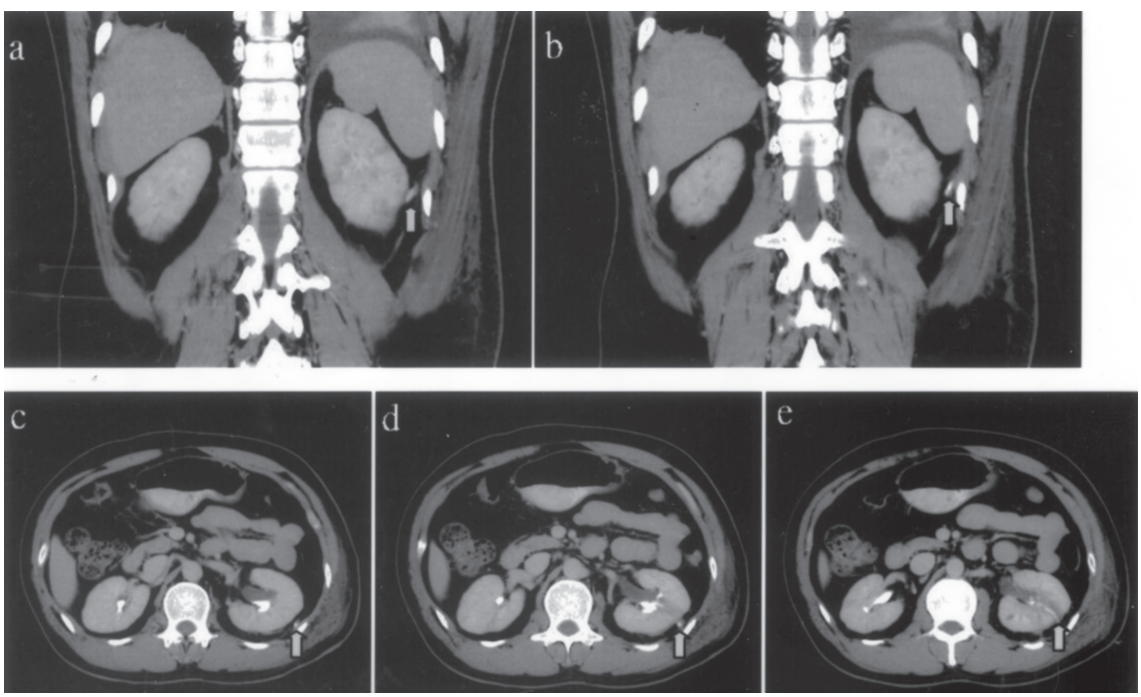

Fig. 1. The abdominal CT disclosed nephropleural fistula. Coronal sections (a and b) show the left kidney is beneath the level of the 10th to the 12th rib. The lower portion of the pleural reflection can be identified in the transverse section (c). Hydroureter can be identified in the transverse sections (c, d and e). Contrast medium leaking from the calyx to the pleural cavity was observed in the transverse sections.

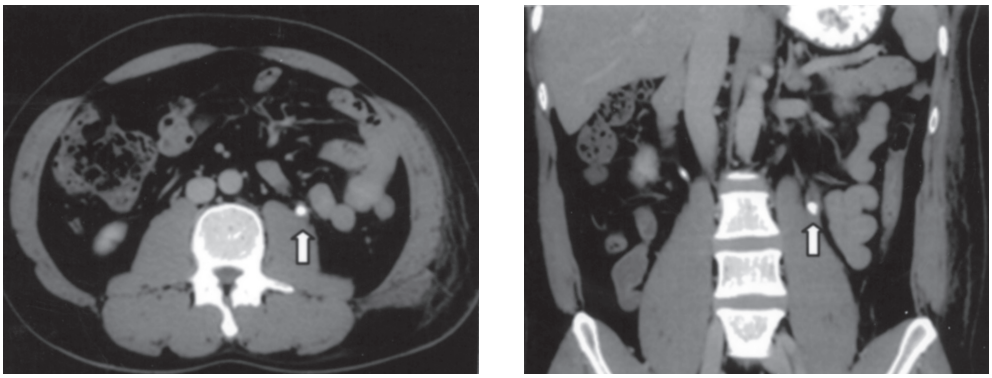

Fig. 2. The transverse and coronal sections of the abdominal CT disclosed a left ureteral stone. The stone occluded the left-side ureter and was complicated with hydroureter.

the chest tube, no evidence of recurrent pleural effusion was present in follow-up chest X-ray film.

Discussion

Urinothorax is rarely recognized. It is a condition in which there is an accumulation of urine in the pleural space. In routine examinations of pleural effusion, creatinine is usually not checked, although it is present more frequently than recognized. The etiology of urinothorax can be obstructive or traumatic [1]. The former results from bilateral or common distal obstructive uropathy. Urine leaking into the abdominal space moves into the pleural space through a diaphragm defect. Ascites can be observed in this type. One study reported a patient with non-Hodgkin's lymphoma complicated with urinothorax. The extrathoracic lymphadenopathy induced urinary tract obstruction and rapidly resulted in urinothorax. It was inferred that urinothorax resulted from the abdominal fluid directly leaking into the pleural space through defects in the diaphragm [2].

Traumatic urinothorax is usually related to unilateral traumatic injury. In addition to blunt trauma, iatrogenic events have been reported. Kidney biopsy, renal calculi lithotripsy and acute obstruction secondary to renal calculi with hydronephrosis have been reported. Urinothorax following iatrogenic events usually presented with unilateral pleural effusion in a rapid course. Symptoms depended on the rate of accumulation of the fluid [3]. It is estimated that 0.5-1% of patients requiring peritoneal nephrostomy placement may develop nephropleural fistula [4]. One study reported the observation that 1% of 375 patients developed nephropleural fistula after PCNL. Of the 87 patients with supracostal-12th rib access, 2.3% developed a nephropleural fistula; 6.3% of the 32 patients with supracostal-11th rib access developed the same complication. The overall incidence of nephropleural fistula in a reported analysis was 0.87% per access tract placed, and increased to 3.3% when considering supracostal access only. The study disclosed that nephropleural fistula formation could be attributed to anatomic embarrassment [5].

An explanation for this anatomic embarrassment is that the pleural reflection is usually at the level of the 10th rib in the mid-axillary line and the 12th rib at the lateral border of the sacros-

pinal muscle. The upper pole of the kidney could be at the level superior to the lower border of the 10th rib. Puncture to create a nephrostomy at the intercostal space could go through the pleural reflection and result in a nephropleural fistula. Sometimes, repeated punctures to dilate the PCNL tract are necessary. This also dilates the nephropleural fistula. Otherwise, the pressure gradient between the renal calyx and the pleural cavity drives the urine flow to move into the pleural cavity [6].

With our patient, we inferred that the urinothorax was attributed to the left upper ureteral calculi occluding the urine drainage. With normal urine flow blocked by the calculi, the urine leaked into the pleural space following the pressure gradient through the existent nephropleural fistula. Abdominal CT (Figure 1) showed contrast medium leaking from the left renal calyx into the pleural space through the extrarenal space. This imaging study confirmed our inference: the nephropleural fistula might have been created during PCNL.

The urinothorax showed transudate mostly. The appearance, odor and biochemistry of the fluid were similar to urine. Exudative effusion has also been reported. Urinothorax with an increased protein level can be found in patients with blunt abdominal trauma and bleeding in the urinary tract [7]. With a traumatic origin, a pale red appearance and red blood cells can be observed [8]. In view of the above, exudative effusion and an elevated effusion protein level are not exclusion criteria for the diagnosis of urinothorax.

An effusion-to-serum creatinine ratio greater than 1 was proposed in 1982 [9]. Another researcher suggested that a ratio close to 1 should be interpreted cautiously, since it could be found in pleural effusion other than urinothorax. In a 2003 literature review, the average effusion-to-serum ratio in 12 urinothorax cases was reported to be 9.15. When obstructive uropathy is not present, the creatinine ratio is rarely greater than 1. If the ratio is greater than 1, the value is usually much lower than in urinothorax [10].

As in urine examinations, a low pH and low glucose level can be observed in most urinothorax. The pH of the fluid is usually low, depending on the pH of the urine [11]. In a literature review including 54 cases of urinothorax, 71% had a pH lower than 7.3. The glucose level could be less than 60 mg/dL; a trend indicating that the higher the creatinine ratio, the lower the glucose level has been observed [10].

In our case, symptomatic dyspnea with radiographic evidence of new pleural effusion soon followed. The fluid was similar to urine. A high degree of suspicion of urinothorax was taken into consideration after diagnostic thoracocentesis. The biochemical data consolidated the diagnosis. The urinothorax was rapidly resolved after tube thoracostomy and Double J stent implantation.

Imaging study to confirm the presence of nephro-pleural fistula is important. In addition to intravenous contrast medium studies which can show contrast medium extravasation, Tc-99m diethylenetriamine pentaacetic acid (DTPA) renal scintigraphy was reported to demonstrate nephro-pleural fistula. This procedure could be taken into consideration when massive effusion following blunt abdominal trauma or surgery on the urinary tract [12-14].

Conclusion

Urinothorax is a rare etiology of pleural effusion. However, including urinothorax in the

list of differential diagnoses for transudative effusion is crucial to obtaining the correct diagnosis, especially when pleural effusion develops concurrently with obstructive uropathy soon after urology-related procedures. Urinothorax may occur due to obstruction or trauma. Tc-99m DTPA renal scintigraphy helps to confirm the nephropleural fistula. Once the correct diagnosis is made and the obstruction is resolved, the effusion will disappear rapidly.

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Urinothorax：病例報告

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Urinothorax是一種少見的肋膜腔漏液積水。我們報告一位36歲男性在進行過percutaneous nephrolithotripsy一週後出現同側大量肋膜漏液。由漏液的外觀及生化檢查數據的分析診斷為urinothorax。電腦斷層影像可以看到顯影劑經由腎臟流出進入肋膜腔，證實了nephro-pleural fistula的存在。病人情況在正確診斷後，施予胸管引流及Double J stent置放而快速緩解。核子醫學的標記也可以用來協助找nephro-pleural fistula的存在。當臨床快速出現大量肋膜漏液於曾經接受手術處置obstructive nephropathy之病患，urinothorax需列為必要之鑑別診斷。*(胸腔醫學* ***2011; 26: 165-170****)*

關鍵詞：Urinothorax，Percutaneous Nephrolithotripsy

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Ruptured Mediastinal Mature Teratoma Mimicking Difficult Asthma: A Case Report

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The clinical presentation of central airway obstruction may mimic asthma. If a patient fails to respond to standard asthma treatment, an alternative diagnosis should always be considered. We described a 61-year-old female who initially presented diffuse wheezing and was treated for asthma. The patient had a poor response to asthma treatment and respiratory distress persisted. Endotracheal intubation and mechanical ventilator support had to be initated. A mediastinal abscess was found 7 days after endotracheal intubation and required catheter drainage. After successful weaning from the ventilator, serial imaging studies revealed a tracheal tumor. Bronchofiberscopic biopsy was performed and the pathology disclosed squamous dysplasia. Nd-Yag laser tumor ablation was performed several times, but rapid recurrence of the tumor was observed. The patient underwent removal of the tumor and segmental tracheal resection. The pathology confirmed the tumor as a ruptured mediastinal mature teratoma. After surgery, the patient's symptom completely disappeared. ***(Thorac Med 2011; 26: 171-178)***

Key words: difficult asthma, mediastinal mature teratoma

Introduction

"Difficult asthma" is defined as a condition in which there is a failure to achieve control when maximum recommended doses of anti-asthmatic therapy are prescribed. Approximately 5% of patients who are diagnosed with asthma do not respond to this regime, and further investigations are required to establish the reasons for the lack of response [1]. Several factors contribute to the poor response to conventional therapy, and incorrect diagnosis should always be considered. We present a case of ruptured mediastinal teratoma with invasion to the trachea that was initially treated as asthma.

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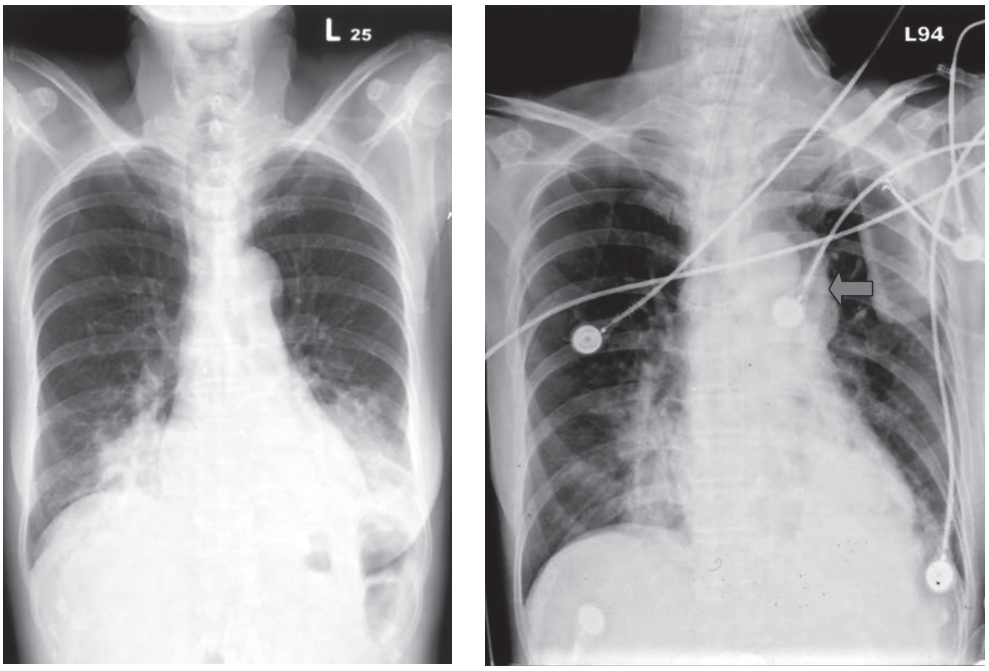
Case Report

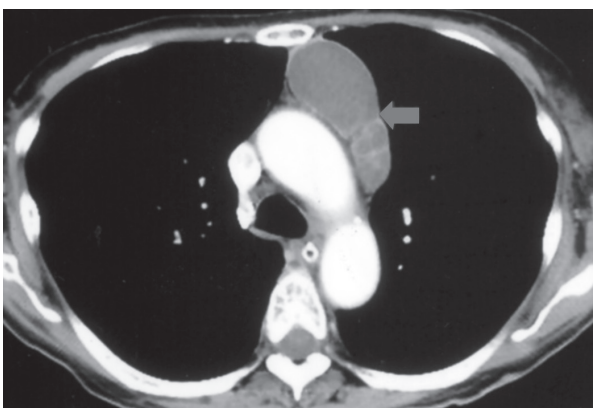
A 61-year-old retired female nurse who had a history of asthma without regular medication control, presented to the out patient department with progressive dyspnea 1 month before admission. On physical examination, forced expiratory wheezing in the bilateral lung fields was noted. The pulmonary function test showed the forced vital capacity (FVC) was 1.90 liters, forced expiratory volume in 1 second (FEV1) was 1.06 liters/second and the FEV1/FVC ratio was 55%. The flow-volume curve showed reduction in the peak flow rate and curvilinear shape of the descending limb, with no obvious flattening of both the inspiration and expiration limbs. Under the impression of asthma with acute exacerbation, oral prednisolone 40 mg twice daily and an inhaled bronchodilator were prescribed. However, her symptoms deteriorated after 1 week of treatment and FEV1 declined. She was then admitted to our hospital for further management. Intra-venous methylprednisolone 125 mg per day and bi-level positive airway pressure (BiPAP) were used, but her symptoms worsened. Severe respiratory distress developed 3 days after admission and emergent endotracheal intubation with mechanical ventilator support was performed immediately. Chest X-ray (CXR) showed increased infiltration in the bilateral lower lung filed (Figure 1A). Brochoalveolar lavage (BAL) was performed in the superior segment of the left lower lobe bronchus and the lavage fluid culture yielded K*lebsiella pneumoniae*. The trachea was passed by the endotracheal tube and could not be evaluated.

Intermittent fever persisted after 7 days of antibiotic treatment and CXR revealed a newly developed mediastinal soft tissue density (Figure 1B). Chest computed tomography (CT) showed a bulky mass with cystic and solid components in the left anterior mediastinum compatible with abscess formation, with the level ranging from the T2-T6 (Figure 1 C). CT-guided pigtail catheter insertion was performed for pus drainage, and the pus culture yielded *Klebsiella pneumoniae* and *Serratia marcescens*. The pigtail catheter was removed 10 days later and she was successfully weaned from the ventilator after her general condition had improved.

However, several episodes of dyspnea with wheezing occurred around 1 month after extubation. Chest CT with 3-dimensional reconstruction imaging was performed again and showed a 2.4 cm soft tissue density lesion with rim-calcification at the left anterior mediastinum, and adjacent to the previous abscess site, and 2 intra-luminal nodules (1.2 cm and 0.7 cm) at the left lateral wall of the trachea at the T3-T4 level (Figures 2A, B). Bronchoscopy was performed and showed 2 overlapping endotracheal tumors arising from 11 cm above the carina that were 1.5 cm in length and caused tracheal obstruction (Figure 2C). These tumors arose from the left anterior-lateral wall of the trachea. Nd-Yag laser treatment for tumor ablation was performed. The pathology of these tumors showed submucosal granulation tissue and fibrosis. Her symptoms improved initially, but progressively deteriorated 1 month after the procedure. Follow-up bronchoscopy showed a recurrent nodular tumor at the anterior-lateral wall of the trachea, causing 50% airway stenosis. External compression of the upper trachea with erythema and swelling of the mucosa was also noted. Nd-Yag laser tumor ablation was performed again for symptom relief. Due to the rapid growth of these tumors, surgical intervention was suggested, but the patient refused ini-



(A) (B)



(C)

Fig. 1. (A) Anteroposterior CXR showing patchy opacities in bilateral lower lung fields. (B) A newly-developed soft tissue density at the left upper mediastinum near the aortic arch. (C) Chest CT showed a bulky mass with solid and cystic components in the retrosternal region of the left anterior mediastinum, ranging from level of T2 to T6, compatible with abscess formation.

tially.

Two months later, the patient agreed to undergo surgical intervention because of persistent dyspnea. Pre-operative chest CT revealed a low-density soft tissue mass about 2.6 cm in size with rim calcification that was contiguous with the previous abscess site. Bronchoscopy showed a recurrent protruding mass about 1.5 cm in size at the left anterior-lateral wall of the trachea. Operation was then performed. During operation, a calcified tumor, 2.5 × 2 cm in size, located at the upper left anterior mediastinum with direct invasion to the trachea, was found. Segmental resection of the trachea, about 3 cm in length, with primary anastomosis was done. The pathology showed the tumor had an aggregation of pancreatic tissue, cartilage, smooth muscle, bone and adipose tissue (Figure 3). The

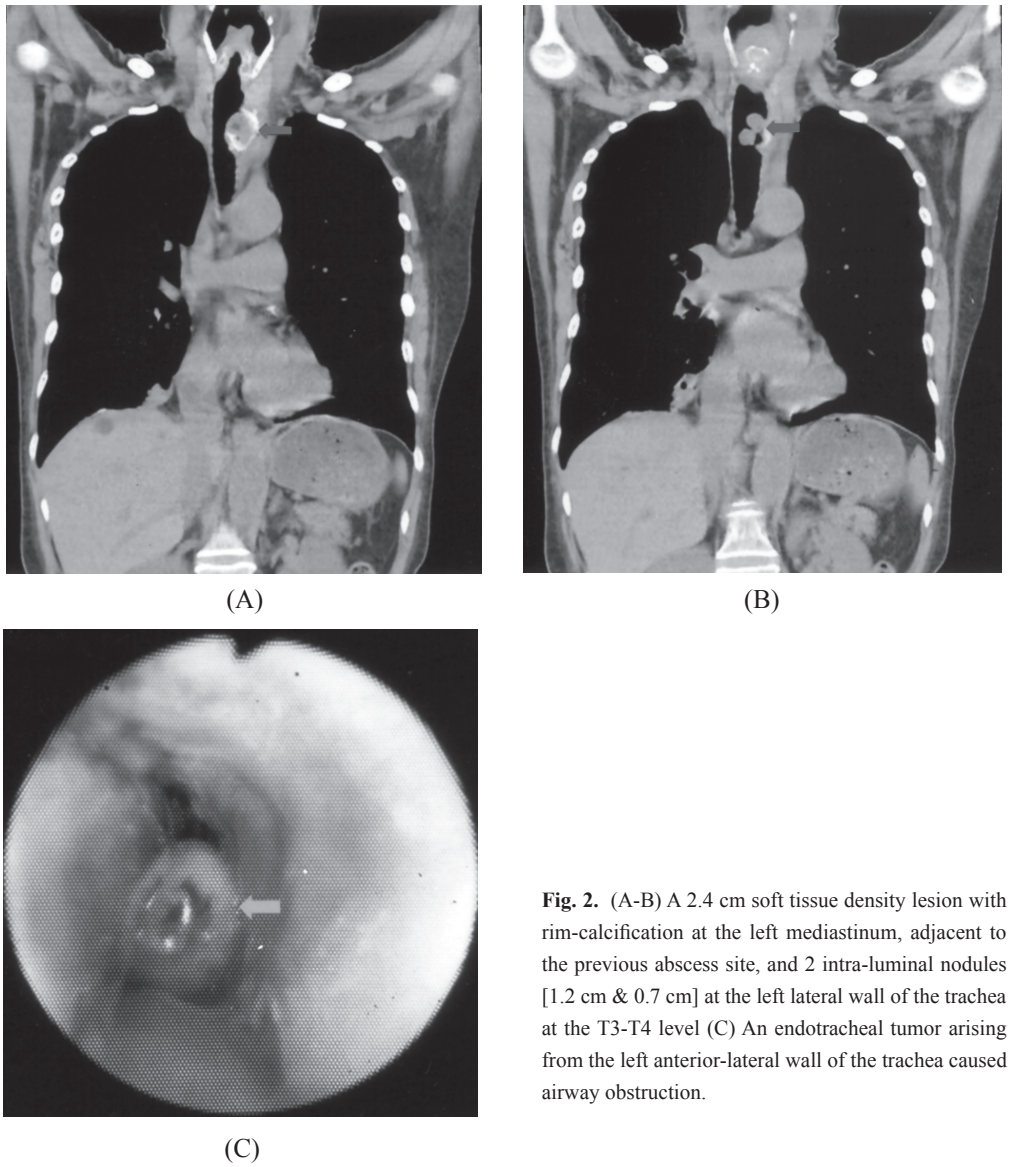


Fig. 2. (A-B) A 2.4 cm soft tissue density lesion with rim-calcification at the left mediastinum, adjacent to the previous abscess site, and 2 intra-luminal nodules [1.2 cm & 0.7 cm] at the left lateral wall of the trachea at the T3-T4 level (C) An endotracheal tumor arising from the left anterior-lateral wall of the trachea caused airway obstruction.

trachea showed squamous metaplasia of the lining epithelium. No immature component was identified. The pathology picture was consistent with mature teratoma. No respiratory symptom and no tumor recurrence were noted 3 months after the surgery.

Discussion

Most patients with asthma are easily diagnosed and respond to standard treatment with a short-acting inhaled β2- agonist for symptom relief and long-term control with an inhaled corticosteroid. However, about 5% of patients failed to respond to medical treatment even with the maximum recommended dosage [1]. Failure to respond to anti-asthma therapy may suggest the presence of diseases other than asthma [2]. Obstruction of the large airways by an intraluminal tumor or by extrinsic compression

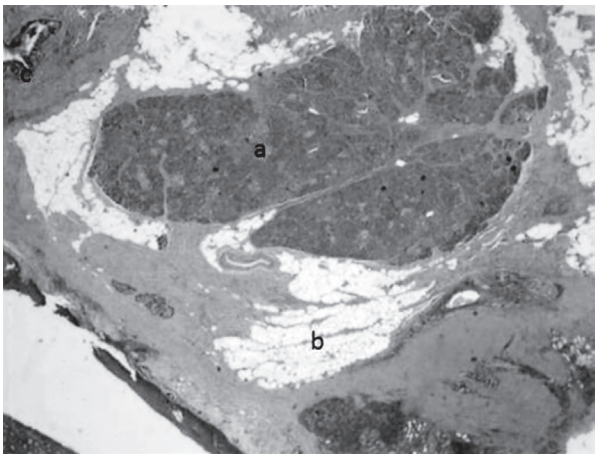


Fig. 3. Pathologic exam of the endotracheal tumor showed aggregation of pancreatic tissue (a), cartilage, smooth muscle, bone, and adipose tissue (b) and intestinal epithelium (c). The picture was consistent with mature teratoma.

may also mimic asthma. Establishing the correct diagnosis of central airway obstruction (CAO) is challenging.

Signs and symptoms develop when the CAO impairs airflow to the point of increasing the work of breathing or altering cardiopulmonary interactions. Exertional dyspnea develops when the tracheal lumen diameter is narrowed to 8 mm. Once the lumen is less than 5 mm, symptoms present at rest [3]. The primary sensation of air hunger in patients with CAO was not related to hypoxia or hypercapnia, but rather to the increased effort required to obtain the normal velocity of air delivered to and from the lungs. With an anatomically fixed obstruction, shortness of breath and wheezing are typically unresponsive to standard anti-asthma therapy, and the failure of a patient to improve with these measures should prompt the physician to consider the presence of CAO. Although wheezing indicates airflow through a narrowed orifice, its location does not always correspond to the site of airflow obstruction [3-4]. Pulmonary function can detect obstruction in the central airway with the finding of flattening of both the inspiratory and expiratory phases of the flow-volume loop. But the typical finding present only when the central airway narrows to about 50-75%. Most patients showed only obstructive ventilatory impairment [4]. CXR is unable to determine airway invasion or aid in procedure planning. Standard CT scans provide much more information. Advances in airway imaging, now allow multiplanar and 3- dimensional reconstruction with internal (virtual bronchoscopy) and external rendering, providing better characterization as to whether the lesion is intraluminal, extrinsic to the airway, or has the features of both types of lesions, and whether the airway distal to the obstruction is patent [5]. Bronchoscopy is always necessary in evaluating airway obstruction and allows the nature or extent of the obstruction to be determined and a tissue proof to be made [6].

CAO can be caused by either malignant or benign tracheal neoplasms, due to Intraluminal or extraluminal growth. About 1/3 of all primary tracheobronchial tumors are squamous cell carcinomas, and 1/3 are adenoid cystic carcinomas. The other 1/3 is a heterogeneous group composed of malignant, intermediate, and benign lesions [6]. Benign tumors of the trachea represent approximately 1.9% of all lung tumors. Many benign neoplasms are slow-growing and often go unrecognized for a long period [7]. Therefore, patients often undergo prolonged treatment for obstructive lung disease or asthma, like our patient.

Teratomas contain elements of all 3 germinal layers: ectoderm, mesoderm and endoderm; the anterior mediastinum is the most common site. These tumors are histologically classified as mature, immature, and malignant. Mature teratomas represent 60-70% of all mediastinal

germ cell tumors that usually occur within or near the thymus gland [8]. Mediastinal mature teratomas typically occur in patients younger than 40 year old. There is a slight female predominance, with a male: female ratio of 1:1.4. Around 53% of mediastinal mature teratomas are left-sided and have thymic origin, since the left lobe of the thymus is larger and extends more inferiorly than the right [9]. On CT, mediastinal mature teratomas most commonly appear as a well-defined unilocular or multilocular cystic lesion containing fluid, soft tissue, and fat attenuation [8]. Mediastinal mature teratomas are usually asymptomatic, but may cause symptoms and signs when a large mass compresses the mediastinal structure, or by functional activity, including sebaceous secretion, insulin production, secretion of chorionic gonadotropin, or exocrine secretion of pancreatic, salivary, or intestinal tissue.

Rupture of mediastinal teratomas may cause significant clinical symptoms such as hemoptysis, severe chest pain, and dyspnea, and sometimes results in acute respiratory distress. About 36% of mediastinal mature teratomas may rupture into the adjacent organs, most frequently into the lung and bronchial tree, followed by the pleural space, pericardial space, or great vessels [10]. The signs and symptoms are determined by which structure is involved.

The differential diagnosis between rupture matured teratomas and malignant teratomas is sometimes difficult to reach based on radiologic study. With malignant tumors, imaging may reveal the tumor's spiculated borders, thick capsules, heterogeneous contents, fat plane obliteration around the tumor, or direct invasion into the adjacent structures with or without effusion. But these findings are similar to those of ruptured mature teratomas. A sudden onset of symptoms after rupture may suggest the correct diagnosis [11-12].

Several mechanisms have been proposed as causes for the rupture of mediastinal mature teratomas. The most common acceptable explanation is autolysis. Some kinds of digestive enzymes such as pancreatic tissue, salivary gland tissue, or intestinal epithelium released from tumor tissues may cause noninfectious inflammation and necrosis of the tumor. Pancreatic tissue is present more frequently in mediastinal mature teratomas than teratomas in other locations [13]. Infection also can be a cause of rupture. Mediastinal mature teratomas are characterized as cysts lined with mature stratified squamous epithelium, and infection makes the tumor wall fragile and leads to tumor rupture [10]. Prompt treatment of ruptured mediastinal teratomas is necessary, because acute respiratory distress can develop. Surgical resection is still the best option and local recurrence is uncommon [12].

The case present herein is a good example of the clinical pitfalls of asthma treatment. An unidentified ruptured mediastinal teratoma in the central airway with prolonged standard asthma treatment may cause secondary infection and respiratory distress. Encountering a patient with wheezing that fails to respond to asthma medication should always raise the suspicious of an etiology other than asthma. When CAO is 1 of the causes of wheezing, we have to manage it more aggressively and rapidly.

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以困難性氣喘來表現之縱膈腔錯構瘤：一病例報告

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臨床上大氣道阻塞可以氣喘急性發作來表現，若是病人以標準氣喘治療方式治療後仍無法獲得有效的改善時，就要考慮是否有其他可能之致病因包括大氣道阻塞。本案例是一名61歲女性一開始即以氣喘發作來表現，在類固醇及氣管擴張劑治療數週後症狀反而加重, 進而發生呼吸衰竭的情形。在插管使用呼吸器後一週，發現一縱膈腔膿瘍而緊急接受導管引流。在拔管後病人一直有反覆出現之呼吸道症狀而接受系列之影像追蹤，且發現有一快速生長之氣管內腫瘤。一開始的病理切片只有鱗狀上皮異化，病人接受多次雷射腫瘤燒灼，但此腫瘤仍持續快速生長。最後病人接受氣管內腫瘤摘除術及部分氣管切除，而手術病理顯示為一縱膈腔良性錯構瘤。手術後病人症狀完全消失。*(胸腔醫學* ***2011; 26: 171-178)***

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