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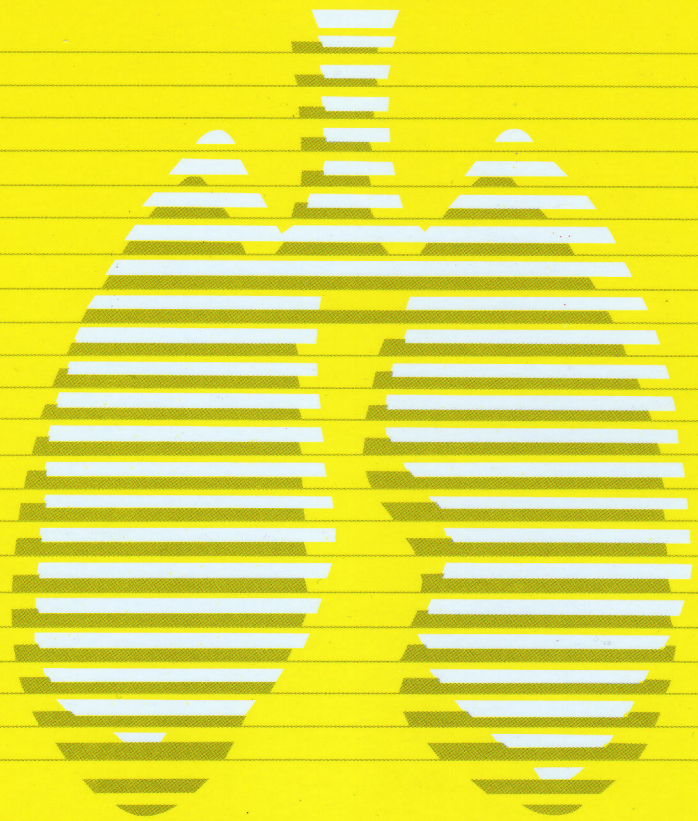

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原著

病例報告

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Orginial Articles

Case Reports

Cryorecanalization in Airway Obstruction: Initial Experience in a Medical Center

Ke-Cheng Chen, Ying-Chun Chin, Tung-Ming Tsai, Shuenn-Wen Kuo, Pei-Ming Huang, Hsao-Hsun Hsu, Jin-Shing Chen, Jang-Ming Lee, Hong-Shiee Lai

Background: Endobronchial cryotherapy is an established recanalization method for stenoses of the respiratory tract. However, previous applications of cryotherapy have seldom been reported in Taiwan. In this study we demonstrate a newly developed cryoprobe allowing recanalization of tumor stenoses during a single intervention.

Methods: We retrospectively reviewed the clinical characteristics and outcomes of 12 patients with endobronchial obstruction treated by cryosurgery between 2010 and 2012.

Results: Three women and 9 men were included in our study. The mean age was 54 ± 15.9 years. The etiology of the obstruction included tumor (n=7), post-intubation (n=3), and tuberculosis (n=2). Ten patients were treated successfully (83.3%). Re-intervention was required in 6 patients (60%).

Conclusions: This initial experience with cryosurgery for airway obstruction suggests that it can be used safely. It was effective in improving symptoms and reducing the severity of airway narrowing. Re-intervention was still required in some patients. Further study should be undertaken to determine factors that may be associated with success or failure, as well as the relative efficacy of cryosurgery compared with other endoscopic therapies. ***(Thorac Med 2014; 29: 1-7)***

Key words: cryorecanalization, cryosurgery, airway obstruction

Introduction

Cryosurgery is the controlled application of extreme cold for local destruction of abnormal living tissue. Attempts to treat malignant tumors with local application of cold were made in the mid-19th century, although the manufacturing of reliable cryosurgery equipment was not achieved until a century later [1]. Cryosurgery for the palliative treatment of endobronchial tumors was first reported in Europe in 1986 [2], and has since been used with more than 1,000 patients. Endobronchial cryosurgery is performed on patients under general anesthesia using a rigid or flexible bronchoscope. A temperature of -70°C at the end of a cryoprobe

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causes destruction of the tumor. A course of cryosurgery usually consists of 2 sessions with an interval of 2-6 weeks. Often, however, the clinical condition of the patients prevents them from undergoing more than 1 session. In this study, we analyzed the effects of palliative endobronchial cryosurgery on patients with airway stenosis who underwent at least 1 cryosurgery session. We also analyzed patient-specific characteristics in relation to outcome.

Materials and Methods

Patients

The medical records of all patients with airway stenosis undergoing cryorecanalization at National Taiwan University Hospital from January 2010 through June 2012 were reviewed retrospectively. Information collected included demographic features, clinical characteristics, microbiologic and laboratory data, radiographic studies, hospital course, intervention modality, and treatment outcomes.

Management

The procedure, benefits, and risks of endobronchial cryosurgery were explained to the patient beforehand, and informed consent was obtained. The procedure was performed under a short-acting IV general anesthesia, using a large rigid (9.2 mm) bronchoscope and a flexible bronchoscope (2.4 mm). Oxygenation was maintained with Venturi positive pressure ventilation. A Joule-Thomson-type probe (Spembly Medical; Hampshire, United Kingdom) with nitrous oxide as the cryogen was used. A temperature of approximately -70°C was achieved at the probe tip. The distal tip of the bronchoscope was placed about 5 mm or more above the lesion, and the cryoprobe was inserted through the bronchoscope and applied to the tumor. Tissue samples for histologic examination were obtained before each cryosurgery. Bleeding from the site of a biopsy or cryosurgery was contained by the local application of epinephrine (adrenaline) 1:1,000. The tumor was frozen and removed by gently pulling out the cryoprobe together with the bronchoscope. Only very mild oozing was found in the tumor bed in most cases after tumor removal. If there was more evident oozing or the tumor covered wider areas of the bronchial tree, multiple cryo-applications with epinephrine irrigation were used during the same treatment session. Patients often reported that additional necrotic-appearing material was coughed up 24 to 48 hours after cryosurgery. Most patients were discharged home on the same day (Figure 1). Patients were reviewed at the outpatient clinic 2 weeks after each cryosurgery session, and every 6 weeks thereafter. In view of the nature of the disease, regrowth of the endobronchial portion of the tumor is often rapid. Although quantification of tumor recurrence is difficult, medium-term outcome is reflected by the survival results reported in this study. Contraindications of cryosurgery include the inability of the patient to undergo general anesthesia or a previously observed poor tumor response to the procedure.

Results

Patient Demographic and Clinical Features

Twelve patients with thoracic empyema were enrolled in the study. Their mean age was 58.8 years and 9 (75%) patients were male (Table 1).

Cryorecanalization Allows Immediate Recanalization of Respiratory Tract Stenoses

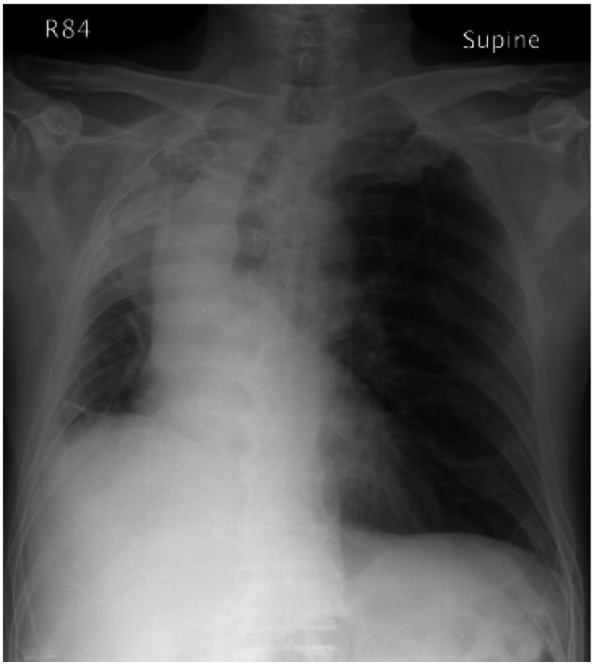
Complete recanalization was achieved in 8 (66.7%) patients. Two (16.7%) patients exhibited residual stenoses that were easily passable with a bronchoscope. Their treatment was rated as partially successful. Treatment was unsuccessful in 2 (16.7%) patients; tumor closures in these patients turned out to be too extended. No connection with the distal respiratory tract was achieved, even though large quantities of tumor tissue were extracted. The procedure lasted between 15 and 105 minutes. Seven patients required additional procedures, including stent in 4, bivona insertion in 2, and sleeve operation in 1 patient. The recurrence rate was 70%, and the average follow-up time was 13.5 months.

Cryorecanalization is a Safe Procedure

None of the patients died during the procedure. Rigid bronchoscopy to treat bleeding or other complications was needed in 1 patient. No patient had to be started on mechanical ventilation after the procedure. Six patients had light bleeding, which stopped spontaneously within a couple of minutes. One patient had more intense bleeding (amount of blood loss, 400 mL) at the tumor adhesion site after removal of the tumor tissue. In all of these patients, bleeding could be controlled with suction with a flexible bronchoscope and was stopped in all patients by using an argon plasma beamer and flexible technology.

Discussion

Cryorecanalization with a newly developed probe is immediately effective in recanalization of airway stenoses. This novel technique does not require clean-up bronchoscopy several



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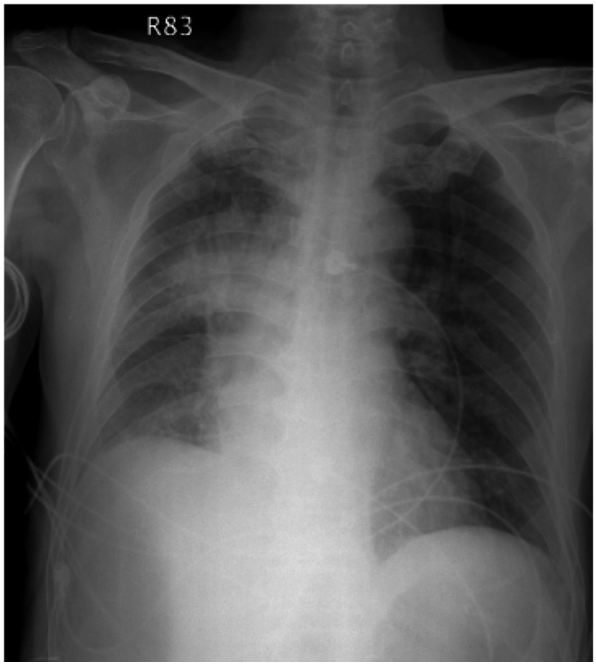

(B)

Fig. 1. A. Before cryorecanalization. B. Post-cryorecanalization day 1

Table 1. Clinical characteristics and treatment outcome of the 12 patients

Variables	Total N=12 No. (%), or Mean (SD)
Age, y	54.0 (15.9)
Male	9 (75.0%)
Ever smoker	8 (66.7%)
Comorbidity	
Hypertension	5 (41.7%)
Diabetes mellitus	5 (41.7%)
Coronary arterial disease	2 (16.7%)
Malignancy	7 (58.3%)
Chronic lung disease	4 (33.3%)
Chronic renal insufficiency	1 (8.3%)
Liver cirrhosis	1 (8.3%)
Location of obstruction	
Central	10 (83.3%)
Lobar	2 (16.7%)
Etiology of airway obstruction	
Tumor	7 (58.3%)
Post-intubation	3 (25.0%)
Tuberculosis	2 (16.7%)
Symptoms relief	10 (83.3%)
Improving in the images study	10 (83.3%)
Procedure-related mortality	0 (0%)

days after the cold treatment to remove tumor necroses. The frozen tumor tissue sticking to the cooled probe tip is extracted immediately during the procedure. Therefore this method is also suitable for patients with acute symptoms caused by airway stenosis. In 83.3% of our patients, cryorecanalization was partially or completely successful. In those patients with whom no recanalization could be achieved, tumor stenosis turned out to be too extensive and thus did not allow connection with the distal respiratory tract. However, high-grade airway strictures should be considered for cryorecanalization only when distal airway patency is preserved.

Success rates with Nd-YAG laser therapy, which is the most frequently used and best evaluated method for the immediate management of endoluminal airway obstructions, range from 50% to 90% depending on the location of the lesion [3]. In our study, cryorecanalization was successful in 83.3% of the treated patients, with no difference between tracheal or main stem bronchi and lobar bronchi lesions, respectively.

Endobronchial bleeding requiring argon plasma beam coagulation occurred in 7 patients (58.3%) after extraction of frozen tumor tissue. Cold causes vasoconstriction and capillary microthromboses in the border area between

frozen and nonfrozen tissue [4]. These effects likely contribute to the low rate of bleeding complications with this method. Visual control of the ice front is possible while the tissue is being frozen, and this allows a relatively reliable assessment of the depth of action. The rate of advance of the ice front decreases after longer freezing times, providing an additional safeguard against accidental freezing of healthy tissue. Accidental freezing of larger rings of cartilage is recognizable because the probe cannot be removed from the bronchus, even if it is very strongly pulled. The probe can then readily be released from the bronchial cartilage at the end of the freezing process. The water content of cartilage tissue is low, and this is probably the reason that cold causes little cartilage necrosis in contrast to thermal energy [5]. Furthermore, in contrast to laser therapy, with its high thermal energy release, cryorecanalization is applicable in patients with coated airway stents and can be done at high oxygen concentrations without increased risk. Cryorecanalization works through conversion of fluid-rich and vascularized tumor tissue close to the tip of the probe into an adherent homogeneous ice ball, and subsequent extraction of the frozen mass. The transition zone from the tumor ice ball to the healthy airway wall, with its unvascularized cartilage rings, represents an area of inhomogeneous ice formation [6]. This zone is believed to be the breaking area when traction is exerted on the probe, and thus preserves the healthy airway wall. Hence, this mechanism is likely to contribute to the safety of cryorecanalization.

One patient exhibited more intense bleeding (amount of blood loss, 400 mL). Bleeding could be controlled in this patient with the suction of the flexible bronchoscope and was stopped by argon plasma beam coagulation. Argon plasma coagulation was used with 7 patients, and we assume, although we cannot prove, the bleeding in these 7 patients would have stopped on its own if we had waited longer before using the argon plasma coagulator. The physiologic clotting system is indeed sufficient to stop diffuse bleeding after tissue extraction. We do not recommend argon plasma beam coagulation be included in the armamentarium required for cryorecanalization. The rate of complications with this method is low, most likely because of the relative bio-selectivity of the action of low temperatures on vascularized tumor tissue and the induction of vascular thromboses [6]. On the basis of our current experience with these patients, rigid bronchoscopy is not necessary but should be kept immediately available for potential complications with this new method.

Conclusions

In contrast to PDT and cryotherapy, cryorecanalization is immediately effective in the treatment of respiratory tract stenoses caused by exophytic tumors. Also, cryorecanalization does not require clean-up bronchoscopy. Our experience shows that cryorecanalization can be performed with flexible technology, and it is also the most inexpensive of all recanalization methods. In summary, cryorecanalization treatment with the newly developed probe is a feasible technique and offers many advantages in the interventional therapy of stenosing exophytic tumors of the respiratory tract, such as the use of flexible technology, immediate effectiveness, and a low risk of complications in comparison with other recanalization methods.

Acknowledgment

The corresponding authors, as the guarantors of the entire study, have full access to all the data in the study and take responsibility for the integrity of that data and the accuracy of the data analysis.

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冷凍再通術於呼吸道阻塞的治療：一個醫學中心的經驗

陳克誠　金盈君　蔡東明　郭順文　黃培銘　徐紹勛　陳晉興　李章銘　賴鴻緒

前言：氣管狹窄是一個嚴重的疾病，常常會造成嚴重的併發症，甚至死亡。現今針對氣管狹窄有許多的治療方式，而冷凍治療是眾多方法中的其中一個方法，但是迄今在台灣治療經驗的報導仍不多。

方法：從 2010 年一月至 2012 年六月，我們蒐集了在台大醫院裡接受冷凍治療的十二位病患，做完整的病例回顧以及統計分析。

結果：所有的病患（n=12）都有達成氣道再通的目的。雖然高達 7 位病患需要再進一步做治療，我們的死亡率是零。少出血量更是冷凍治療的優勢。只有一位病患有較多的流血量，也適當地加以止血。

結論：氣管狹窄是一個嚴重且棘手的疾病，面對氣管狹窄的病患時，可以考慮冷凍治療以及冷凍再通術。*(胸腔醫學 **2014; 29: 1-7**)*

關鍵詞：冷凍再通術，氣管腫瘤，氣管狹窄，氣管阻塞

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Severe Community-Acquired Pneumonia Caused by Methicillin-Resistant *Staphylococcus aureus*

Chung-Yen Tsai, Ming-Hsien Lin*, Chieh-Liang Wu**, Ming-Cheng Chan

Methicillin-resistant *Staphylococcus aureus* is one of the most common pathogens found in healthcare or hospital-associated infections, but it is uncommon in community-acquired infections. Although most are skin and soft tissue infections, methicillin-resistant *Staphylococcus aureus* infection may present as community-acquired pneumonia, with a high mortality rate reported. We present a case of community-acquired pneumonia due to methicillin-resistant *Staphylococcus aureus* with a rapidly progressing clinical course. In the literature review, we compare cases of community-acquired and hospital-acquired methicillin-resistant *Staphylococcus aureus*, and suggest treatment options. ***(Thorac Med 2014; 29: 8-16)***

Key words: methicillin-resistant *Staphylococcus aureus*, community-acquired pneumonia

Introduction

Methicillin-resistant *Staphylococcus aureus* (MRSA) is an uncommon pathogen in community-acquired pneumonia (CAP) [1-4], and is usually found in skin and soft tissue infections [5]. It has become an emerging pathogen in CAP and has a high mortality rate, reported at around 20% to 60% [1]. Herein, we present a case of CAP due to community-acquired MRSA (CA-MRSA) with a catastrophic clinical course. We review the literature and summarize the risk factors of CA-MRSA CAP. We also compare CA-MRSA and hospital-acquired MRSA (HA-MRSA). Although the optimal treatment of CA-MRSA pneumonia is not yet established, we provide a suggestion for antibiotics treatment choice.

Case Report

A 75-year-old male Taiwanese was presented to the emergency department with severe respiratory distress in March 2010. One week before this admission, he had cough, watery diarrhea and poor appetite, and was symptomatically treated at a local clinic. However, the symptoms did not improve and he became more

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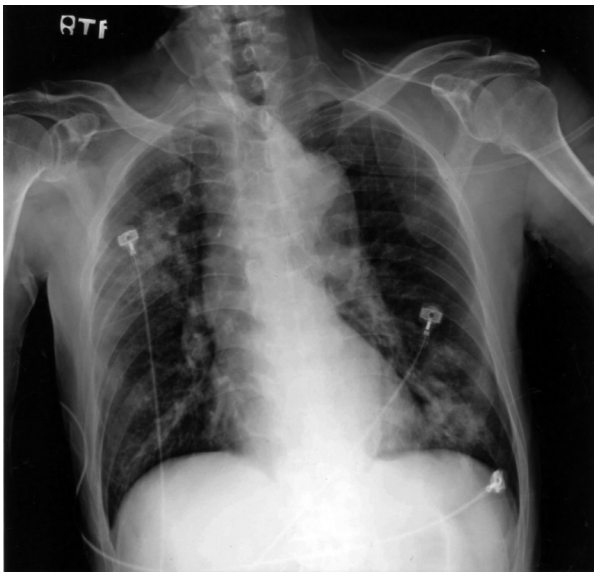
and more dyspneic. At the emergency room, his blood pressure was 188/102 mmHg, pulse rate 114 beats/min, body temperature 38.4ºC, and respiratory rate 18 breaths/min. Auscultation revealed rhonchi in the right lung field and regular rapid heart sounds without audible murmurs. Chest X-ray showed patchy consolidation in the right and left upper lobes (Figure 1A). Laboratory tests disclosed white blood cells 4.7×10^3 cells/mm^3, hemoglobin 11.5 g/dL, platelet 190,000/mm^3, creatine kinase 341 U/L, troponin I less than 0.034 ng/mL, creatinine 3.9 mg/dl, blood urea nitrogen 72 mg/dL, aspartate aminotransferase 50 U/L, alanine aminotransferase 49 U/L, lactate dehydrogenase 299 U/L, and C-reactive protein 24.4 mg/dL. Arterial blood gas examination revealed pH 7.326, SO_2 95.2%, PCO_2 30.6 mmHg, HCO_3^- 15.6 mmol/L, and PaO_2 79.9 mmHg. Serum lactate was 25.6 mg/dL and a rapid screen of influenza by nasal swab was negative. He was intubated immediately due to severe respiratory distress and was sent to the respiratory intensive care unit (ICU).

At ICU admission, fluid resuscitation was started for hemodynamic stabilization. A protective lung ventilation strategy was implemented with a mechanical ventilation tidal volume setting of 360 ml, fraction of inspired oxygen (FiO_2) 40%, respiratory rate 26/min, and positive end-expiratory pressure (PEEP) of 14 cmH_2O. The patient began receiving antibiotics with ceftriaxone 2000 mg QD and erythromycin 500 mg Q6H empirically for severe CAP at admission. In addition, inotropic agents were administrated due to shock status on the day of admission. Bronchoscopy was performed on the second day of admission and vancomycin 1000 mg QW was added on the same day due to numerous Gram-positive cocci in groups yielded from the bronchoalveolar lavage. The patient also underwent renal replacement therapy with continuous veno-venous hemofiltration due to acute renal failure on the second day of admission. His condition deteriorated rapidly on the



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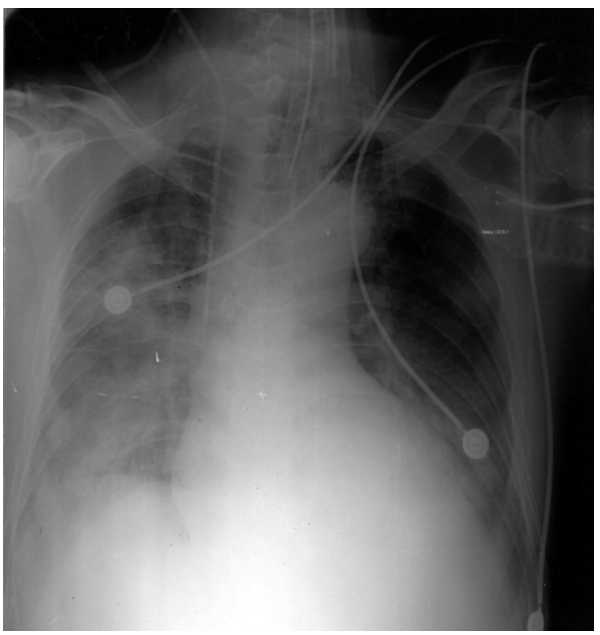

(B)

Fig. 1. Imaging studies of the presented case. A. Chest radiography shows multilobar infiltrates. B. Chest radiography shows rapid progression within 1 day.

second day of ICU admission. His lung oxygenation and hemodynamic parameters worsened. Chest X-ray revealed rapid progression with widespread bilateral alveolar infiltrates (Figure 1B). Lung recruitment was performed every 4 hours due to acute respiratory distress syndrome (ARDS) with PEEP 40 cmH_2O for 40 seconds on the second day. The patient unfortunately passed away 3 days after ICU admission due to multi-organ failure. The relationship between the treatment and the rapidly deteriorating clinical picture during the admission course is presented in Figure 2. The bacterial culture from sputum and broncholavage both revealed *Staphylococcus aureus* (>10^5 CFU/mL) 3 days later. The susceptibility profile is shown in Table 1.

The patient's past medical history was not remarkable, except nasopharyngeal cancer of a squamous cell-type diagnosed 5 years before this admission. He received chemotherapy and radiotherapy then. No tumor recurrence was noted in the subsequent follow-up.

Discussion

Methicillin-resistant *Staphylococcus aureus* (MRSA) was first described in the 1960s, after the introduction of methicillin into clinical practice [6]. It has been regarded as a nosocomial pathogen and not normally present in the community. However, MRSA was detected in the community for the first time in the mid 1990s, and was known as community-acquired MRSA (CA-MRSA). It became the leading cause of identified skin and soft tissue infections in US emergency departments [5]. There has been an increasing number of case series reports of CAP

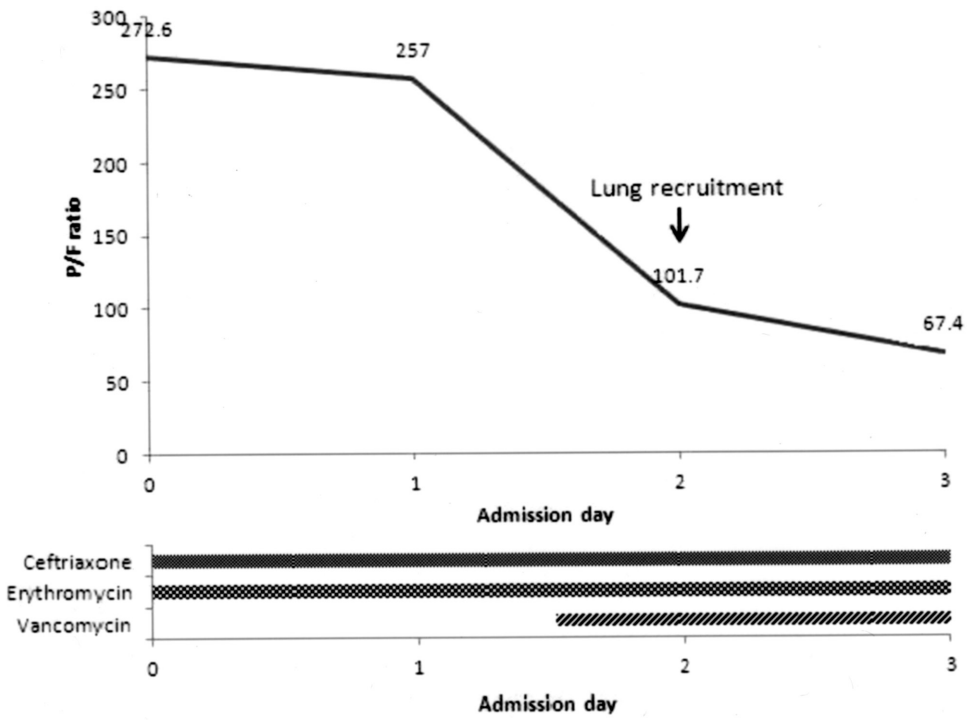

Fig. 2. Time course of the P/F ratio and antibiotics.

Table 1. Antibiotics susceptibility of MRSA in the presented case

Antibiotics	Susceptible	Resistant
Cefazolin	-	R
Clindamycin	S	-
Gentamicin	S	-
Ampicillin-sulbactam	S	-
Penicillin	-	R
SMX-TMP	S	-
Vancomycin	S (MIC=1.0)	-
Oxacillin	-	R
Ciprofloxacin	S	-
Teicoplanin	S	-
Erythromycin	S	-

MRSA: methicillin-resistant *Staphylococcus aureus*; MIC: minimal inhibitory concentration; SMX-TMP: trimethoprim-sulfamethoxazole; S: susceptible; R: resistant

due to CA-MRSA recently, describing severe, necrotizing pneumonia with high mortality in previously healthy individuals [7-8]. Thus, the emergence of CA-MRSA as a cause of life-threatening, invasive infections in the community has becoming an important public health problem.

Published data has suggested that MRSA was not a frequent cause of CAP, and the prevalence and incidence of invasive CA-MRSA infections, such as CA-MRSA pneumonia, probably varies geographically. The published data also suggest that CA-MRSA pneumonia is associated with a high mortality rate, ranging between 20% and 60% [1]. A study from the United States reported that MRSA was responsible for 8.9% of culture-positive CAP requiring hospitalization and 34.8% of staphylococcal CAP [3]. Another study reported that 6% of CA-MRSA infections in the United States caused invasive disease, and pneumonia accounted for 2% overall [9]. CA-MRSA accounts for 14% of invasive MRSA infections and 14% of these infections are CA-MRSA pneumonia [10]. In Canada, *S. aureus* accounts for less than 10% of CAP, and is the second or third most common etiology in CAP requiring ICU admission [11]. According to the 2007 Clinical Practice Guidelines for Pneumonia in Taiwan, the incidence of *S. aureus* in CAP is between 1.0% and 1.8% [12-14]. However, the actual prevalence and incidence of CA-MRSA in CAP remains unknown.

CA-MRSA pneumonia frequently occurs in young and previously healthy adults, with up to 75% of cases having a preceding flu-like illness [8,15]. In a recent study of CA-MRSA pneumonia, 38% of cases had documented evidence of influenza infection and 57% had symptoms consistent with influenza [4]. Patients with CA-MRSA pneumonia rapidly develop severe respiratory symptoms, including hemoptysis, high fever, and leukopenia, and may progress to ARDS. Radiographic features of multi-lobar necrotizing cavitary lesions are common in CA-MRSA pneumonia. The at-risk groups with increased rates of CA-MRSA colonization are the following: children aged < 2 years, athletes

(mainly contact sports), injected drug users, males who have sex with males, military personnel, inmates of correctional facilities, residential homes and shelters, veterinarians, pet owners and pig farmers, patients with post-flu-like illness and/or severe pneumonia, patients with concurrent skin and soft tissue infection (SSTI), a history of colonization or recent infection with CA-MRSA, and a history of antibiotic consumption in the previous year (particularly quinolones or marcolides) [16]. Although these nonspecific findings are helpful in raising a suspicion of CA-MRSA, they have not been shown to reliably distinguish CA-MRSA from community-acquired methicillin-susceptible *S. aureus* [17].

There are several differences between CA-MRSA and nosocomial MRSA. Compared with nosocomial MRSA, CA-MRSA isolates are often resistant to β-lactams only, but sensitive to most other antibiotic classes such as clindamycin, fluoroquinolones, trimethoprim-sulfamethoxazole, tetracyclines and rifampicin. The methicillin resistance of MRSA is mediated by the penicillin-binding protein PBP2A, which is encoded by the *mecA* gene located in the staphylococcal cassette chromosome mec (SCCmec). CA-MRSA strains carry SCCmec type IV, and the most common CA-MRSA strain lineages in the United States are USA 300 and USA 400 clones. In contrast, nosocomial MRSA strains carry SCCmec types I, II, and III, and the most common lineages in the United States are USA 100 and USA 200 clones [18]. Panton-Valentine leukocidin (PVL), a *S. aureus* toxin that creates pores on host cell membranes, is a major virulence factor for CA-MRSA, causing lysis and apoptosis of neutrophils and tissue necrosis, and also mediates initial pulmonary injury [19-20]. The PVL cytotoxin is encoded by genes *lukS-PV* and *lukF-PV*. The PVL gene is found frequently in CA-MRSA strains (>95%) and rarely in hospital-acquired MRSA (HA-MRSA) strains (<5%) [21]. Patients with CAP who harbor PVL-positive *S. aureus* isolates had more sepsis, hemoptysis and higher mortality [20]. A comparison of clinical, epidemiological and microbiological characteristics of CA-MRSA and HA-MRSA is presented in Table 2 [16,22].

At present, there have been no treatment trials for CA-MRSA pneumonia. Most experts recommend vancomycin or linezolid for empirical treatment in cases of severe CAP, especially when CA-MRSA is considered [23]. However, the optimal therapy has not yet been defined. The latest IDSA/ATS CAP guidelines do not recommend covering CA-MRSA for patients routinely admitted to the ICU. However, there was a recommendation to consider this pathogen in patients with severe CAP and compatible clinical pictures. In this case, we used vancomycin as the first-line treatment for CA-MRSA isolates from sputum and broncholavage culture, but rapid progression was noted. Treatment with vancomycin alone may not be sufficient, and possibly leads to treatment failure. This is due presumably to the lack of activity against the PVL toxin; thus therapy may need to involve both an antibacterial agent and an antitoxin-producing agent [24]. For this consideration, it is suggested that adding clindamycin to vancomycin or using linezolid (with rifampin in severe illness) can inhibit toxin production [25] by suppressing translation of genes producing PVL, toxic shock syndrome toxin-1, and α-hemolysin [26]. This has led some experts to recommend the use of clindamycin and linezolid as the preferred antibiotic in the treatment of CA-MRSA pneumonia [27-28]. Another concern with vancomycin is the increasing minimal

Table 2. Comparison of community-acquired (CA-) and hospital-acquired (HA-) MRSA

Characteristic	HA-MRSA	CA-MRSA
Affected patient	Elderly Immunocompromised Hospital/healthcare/nursing home patients/ residents	Young, healthy people Athletes and military service personnel
Medical history	Permanent indwelling catheter or dialysis History of MRSA colonization, infection, recent surgery Prolonged hospitalization or nursing home care Long-term antibiotic use	Close physical contact Activities associated with poor communal hygiene No significant medical history or healthcare contact
Transmission	Within healthcare setting	Community-acquired with shared facilities (families and sports teams)
Infection site	Bacteremia Wound infection Catheter infection Respiratory tract infection (VAP)	Mainly skin and soft tissue May cause necrotizing community-acquired pneumonia, septic shock and bacteremia
Antibiotic susceptibility	Often multiresistant Choice of agents often limited	Often susceptible to most antibiotic classes such as clindamycin, fluoroquinolones, trimethoprim-sulfamethoxazole, tetracyclines and rifampicin
Presence of PVL gene	Low (<5%)	High (>95%)
SCCmecA type	Mainly type I, II, or III	Mainly type IV, V

MRSA: methicillin-resistant *Staphylococcus aureus*; VAP: ventilator-associated pneumonia

inhibitory concentrations (MICs) of MRSA in recent years. A statistically significant study about vancomycin MICs of MRSA revealed that for MRSA isolates with vancomycin MICs of 0.5 μg/ml or less, vancomycin was 56% successful in the treatment of bacteremia, whereas it was only 9.5% effective in cases in which vancomycin MICs were from 1 to 2 μg/ml [29]. Therefore, in patients with a MRSA isolate with an increasing vancomycin MIC (>1 μg/ml), linezolid may be an alternative treatment of choice.

In conclusion, CA-MRSA pneumonia is uncommon in CAP and mortality may be high. Keeping alert to a suspicion of CA-MRSA pneumonia in patients with compatible clinical pictures was recommended in all kinds of recent CAP guidelines, though there were no optimal treatment recommendations. Herein, we provide a notion of an antibiotic treatment choice with both an antibacterial agent and an antitoxin-producing agent for severe CA-MRSA pneumonia. Further investigations are necessary to establish optimal treatment strategies.

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抗藥性金黃色葡萄球菌導致之嚴重社區型肺炎

蔡仲晏　林明賢 *　吳杰亮 **　詹明澄

抗藥性金黃色葡萄球菌是院內感染最常見的致病菌之一，但在社區型感染中是很少見的。雖然其中大部分是皮膚及軟組織感染，抗藥性金黃色葡萄球菌也可以造成社區型肺炎，並且合併高致死率。我們報告一位因抗藥性金黃色葡萄球菌引起嚴重社區型肺炎並導致死亡的案例。經由文獻審查，我們比較社區型和院內型抗藥性金黃色葡萄球菌，並提供一個治療上抗生素選擇的新想法。*(胸腔醫學 **2014; 29: 8-16**)*

關鍵詞：抗藥性金黃色葡萄球菌，社區型肺炎

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Tuberous Sclerosis Complex-Lymphangioleiomyomatosis Initially Presenting as Acute Abdominal Pain: A Case Report and Literature Review

Chun-Wei Lin, Jeng-Yuan Hsu, Kun-Yuan Cho*, Ming-Cheng Chan, Chen-Hui Lee**

Abdominal pain is a common complaint at the emergency room. Rare congenital disorders, like tuberous sclerosis complex-lymphangioleiomyomatosis (TSC-LAM), may initially present as abdominal pain. But, the underlying disease is often neglected. Herein we report a patient with severe acute abdominal pain and hypovolemic shock due to massive bleeding from renal angiomyolipoma. The patient underwent surgical excision of the left kidney after failure of transcatheter arterial embolization. One year post-surgery, the patient developed progressive dyspnea. The initial impression was TSC-LAM, based on clinical manifestations, and imaging and pathology studies. The pulmonary function test revealed mixed restrictive and obstructive ventilatory defects. Her symptoms improved with bronchodilator use. ***(Thorac Med 2014; 29: 17-24)***

Key words: lymphangioleiomyomatosis, tuberous sclerosis complex, transcatheter arterial embolization, long acting beta-agonist

Introduction

Lymphangioleiomyomatosis (LAM) is a rare, progressive, and often fatal cystic lung disease that almost exclusively affects women [1-2]. In previous case series, the average age at the diagnosis of LAM was approximately 35 years [3]. LAM consists of a diffuse proliferation of smooth muscle cells. It can occur alone (sporadic LAM) or in association with tuberous sclerosis complex (TSC), which is an autosomal-dominant tumor suppressor gene syndrome characterized by seizures, mental retardation, and tumors in the brain, heart, skin, and kidneys [4]. The most common manifestations of LAM are pulmonary symptoms, such as progressive dyspnea, recurrent pneumothorax, and pleural chylous effusions. However, TSC-LAM may have a different initial presentation: abdominal pain. There is no effective medical treatment at

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this time. Herein, we report the case of a patient with TSC-LAM initially presenting as acute abdominal pain.

Case Report

A 28-year-old woman came to the emergency room due to severe, progressive abdominal dull pain with an acute onset at the left lower quadrant. The pain quickly extended to the entire abdomen, causing the patient to wake up at midnight. The pain was not relieved by position change. The patient had fluent speech, could walk and jog without discomfort, and had no cognitive or psychological disorders or congestive heart failure. On physical examination, the patient had a pale face and lips, drowsy consciousness, and tachycardia. Laboratory exams revealed anemia with hemoglobin of 9.2 mg/dl, so she received an emergency blood transfusion. Computed tomography (CT) scan of the abdomen revealed bilateral renal angiomyolipomas (AMLs) with active bleeding of the left kidney (Figure 1). She underwent transcatheter arterial embolization, but this failed. She eventually underwent excision of the left kidney for recurrent bleeding. Pathological studies revealed AML, classic type, with a recent infarct and old hemorrhage (Figure 2).

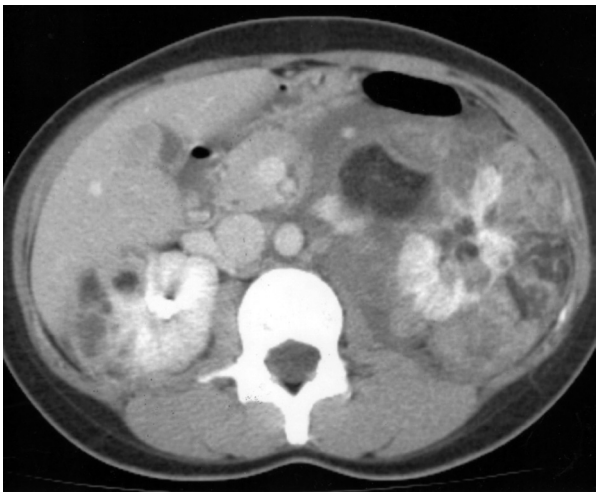


Fig. 1. Abdominal CT showed 2 heterogeneous masses in both kidneys with blood clot accumulation around the left kidney.

One year after the surgery, the patient began to have progressive exertional dyspnea, even with only a short distance of walking. There was no productive cough, wheezing, or muscle soreness. She then visited the chest medicine

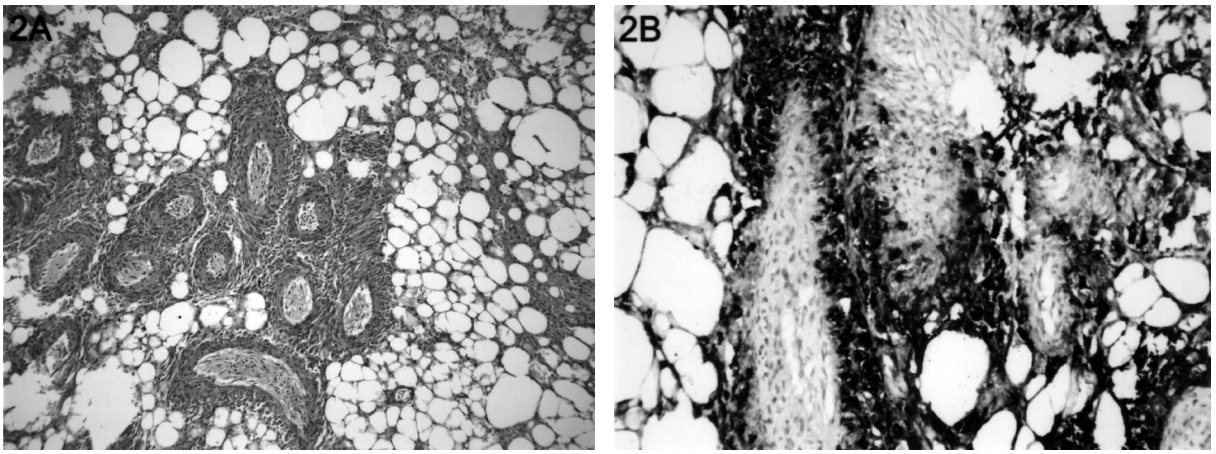
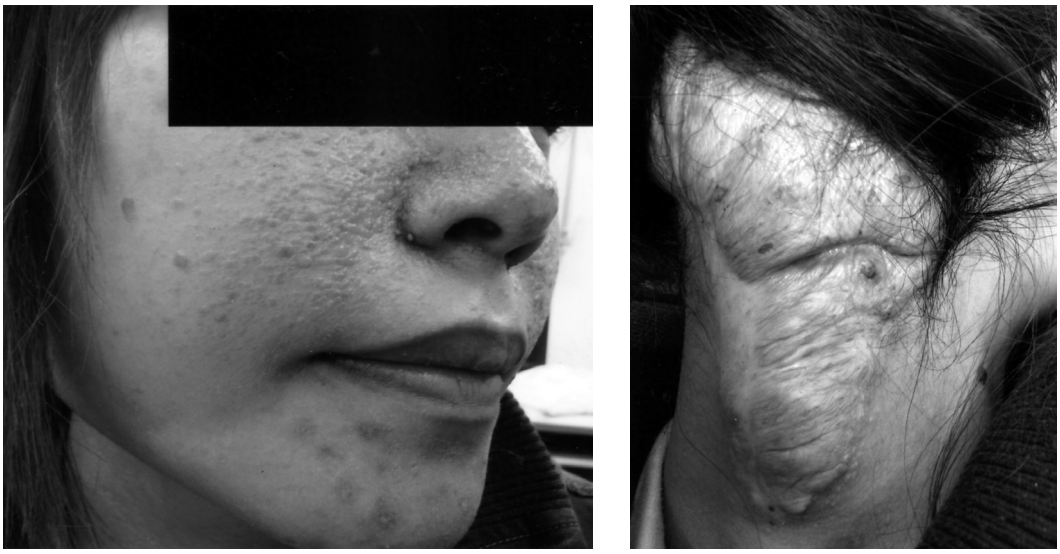


Fig. 2. Pathology of the present case. (A) Angiomyolipoma is composed of blood vessels, smooth muscle cells and fat cells, with the specific feature of muscle cells perpendicular to the vascular wall (H&E stain, 200X). (B) HMB-45 staining was positive.



(A) (B)

Fig. 3. Abnormal appearance of the present case. (A) Adenoma sebaceum, a misnamed cutaneous disorder consisting of angiofibromas, had developed since childhood (2-5 years of age) and presented clinically as facial papules. (B) Shagreen patches/collagenoma, thick leathery skin that is dimpled like an orange peel; pigmentation was noted on the patient's nape. The frequency of the lesions increases with age.

outpatient department. On examination, she had multiple soft erythematous papules on the bilateral cheeks (Figure 3A) and a soft 5×3 cm linear excrescency on her nape (Figure 3B). The skin lesions had developed since childhood. Chest X-ray showed cystic lesions in the bilateral lung fields with large bullae (Figure 4), which was confirmed by chest CT scan (Figure 5A). Brain magnetic resonance imaging revealed several nodules at the bilateral lateral ventricular wall and calcification at the subependymal layer (Figure 5B). No other family member had a similar disorder. Pulmonary function test showed mixed obstructive and restrictive ventilatory impairment (Table 2), with FEV_1 1.20 L (38% of reference value), FVC 1.89 L (52% of reference value), and FEV_1/FVC 64% and total lung capacity 4.22 L (79% of reference value [5.36 L]). She also had impaired gas transfer with low diffusion capacity. The DLco was 7.2 mL/mmHg/min (36% of reference value) (Table 2). She was started on a long-acting beta-2 agonist (Indacaterol) for the impaired lung function

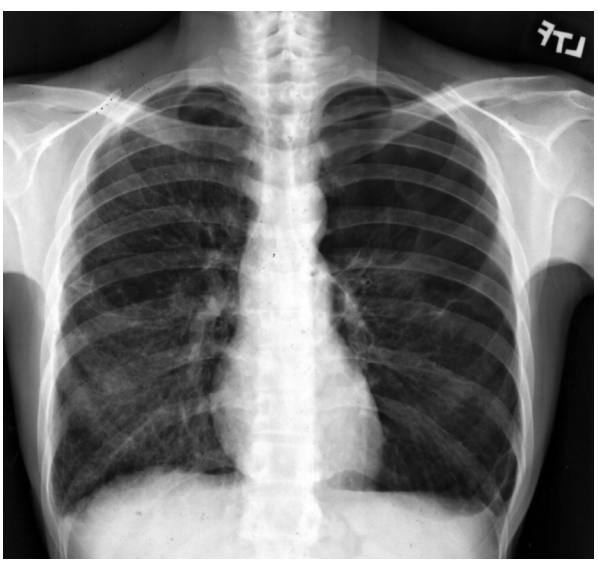
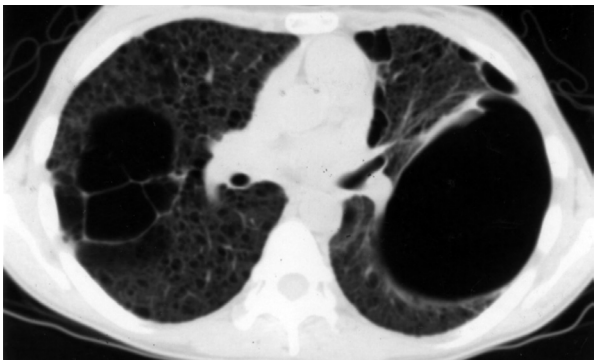
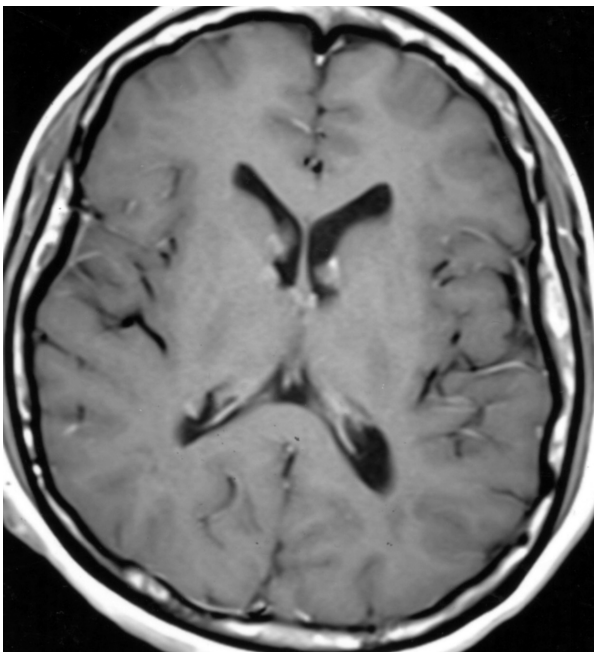


Fig. 4. Bilateral cystic lesion in both lungs, accompanied with large bullae



(A)



(B)

Fig. 5. Imaging studies of the present case. (A) Chest CT showed multiple cystic lesions in both lungs. (B) Brain MRI revealed several nodules at the bilateral lateral ventricular wall and calcification at the subependymal layer.

and dyspnea. Her symptoms and lung functions improved with treatment.

Discussion

The diagnostic criteria for TSC consist of a set of major and minor diagnostic features (Table 1). In the present case, the patient had several typical characteristics, including diffuse bilateral lung cysts (LAM), subependymal nodules in the lateral ventricle, renal AML, adenoma sebaceum (angiofibromas) on the face, and Shagreen patches/collagenoma on the neck. These confirmed the diagnosis of TSC-LAM.

TSC is a multi-systemic disorder with autosomal-dominant heredity and a female predominance. The mean age of diseased females is 28 years. The most common clinical presentations of TSC are extra-pulmonary complications, skin lesion (98.8%), subependymal nodules (77%) and renal AML (61%) [5]. Renal AML can grow rapidly during the teenage years [6]. These renal tumors contain abnormal vasculature and aneurysms, which will make them prone to life-threatening bleeding, especially when the tumor size is greater than 3 cm in diameter [7]. In general, embolization is the first choice of intervention to stop the bleeding [8-9] and save the renal function. Surgical resection is preserved as the last choice for refractory bleeding.

The prevalence of LAM varied from approximately 2% to 40% in several reports [10-11]. The clinical symptoms and signs are dyspnea, recurrent pneumothorax, hemoptysis and ultimate respiratory failure. Pulmonary symptoms do not develop until an average age of 33 years (range, 22-46 years). There was an average delay of 8 years before the correct diagnosis was made [10]. High-resolution CT and pulmonary function tests are the only methods to evaluate early LAM. Airflow limitation is the most common manifestation of impaired lung function. According to the "NHLBI" LAM registry, 34% of patients have normal lung function. Among them, 57% have obstructive ventilatory impairment, 11% have a restrictive-type

Table 1. Revised Diagnostic Criteria for Tuberous Sclerosis Complex

Major Features	Minor Features
Facial angiofibromas or forehead plaque	Multiple randomly distributed pits in dental enamel
Non-traumatic ungual or periungual fibroma	Hamartomatous rectal polyps
Hypomelanotic macules (more than 3)	Bone cysts
Shagreen patch (connective tissue nevus)	Cerebral white matter migration lines
Multiple retinal nodular hamartomas	Gingival fibromas
Cortical tubera	Non-renal hamartoma
Subependymal nodule	Retinal achromic patch
Subependymal giant cell astrocytoma	"Confetti" skin lesions
Cardiac rhabdomyoma, single or multiple	Multiple renal cysts
Lymphangiomyomatosis	
Renal angiomyolipoma	

Note: Definite TSC, 2 major features or 1 major feature with 2 minor features

Probable TSC, 1 major plus 1 minor feature

Suspected TSC, either 1 major feature or 2 or more minor features

Table 2. Pulmonary function test before and after long-acting bronchodilator

		2012/07/24		2012/09/17		2012/10/19	
FV Loop	Pred	Actual	% Pred	Actual	% Pred	Actual	% Pred
FVC(L)	3.63	1.89	52	2.19	60	2.31	64
FEV_1(L)	3.11	1.20	38	1.49	47	1.60	52
FEV_1/FVC	86	64		68		69	
$FEF_{25-75\%}$(L/s)	3.68	0.69	19	1.00	27	1.08	29
PEF(L/s)	6.68	3.45	52	4.04	61	4.12	62
Lung volume							
TLC(L)	5.36	4.22	79				
RV(L)	1.63	2.33	143				
FRC(L)	3.27	2.92	89				
ERV(L)	1.28	0.59	46				
IC(L)	2.56	1.30	51				
Diffusion							
DLCO	20.0	7.2	36				
DLCO/VC	4.58	2.84	62				

Note: The patient had been on a long-acting beta-agonist (Indacaterol) since 2012/8/10 and long-acting cholinergic antagonist (Tiotropium) since 2012/9/7.

defect, and only 2% have a mixed pattern. Only 17% of patients with an obstructive ventilatory defect have a positive bronchodilator response. Reduced single-breath diffusing capacity is as common as airflow limitation [2]. Although the pulmonary function test results are similar those of chronic obstructive pulmonary disease (COPD), hospitalization for acute exacerbation

of the underlying obstructive disease or respiratory failure is not seen. The earliest manifestation is the increase in residual volume due to air trapping and the decrease of D_LCO, resulting in an oxygenation defect. Exercise-related dyspnea and hypoxemia may be a complaint even in patients with near-normal diffusing capacity and FEV_1. The rapid decline in FEV_1 and poor outcome are correlated with a positive bronchodilator response. The predominant smooth muscle proliferation in lung biopsy may be responsible for the patho-physiologic manifestations [12].

This patient experienced progressive dyspnea on exertion, which limited her daily activity, such as taking a shower, climbing the stairs, and walking for a short distance. She had mixed obstructive and restrictive ventilatory defects. Nonetheless, her lung function improved after using a long-acting beta-agonist, which also alleviated her dyspnea. We assume the dyspnea can be attributed to the partly reversible airway obstruction, a finding that is compatible with the improved FEV_1 (from 1.2 to 1.6 L) in the following pulmonary function tests (Table 2). The bronchodilator relieved her symptoms. Should disease progression be delayed by the treatment? There is no clinical study or literature exploring this issue, as of now.

Although the frequency of LAM in patients with TSC is high, only 19% of patients with LAM worsen rapidly. The remaining 81% do not progress or worsen slowly [5]. However, there is no way to distinguish severe LAM from mild LAM in the early stages of the disease. Regular follow-up of all patients is necessary. For cases with rapid deterioration of LAM, lung transplantation is a choice of treatment. The drug sirolimus has shown promise as a therapeutic agent, but it has a high number of intolerable side effects [13].

In summary, we reported a relatively rare case of TSC-LAM presenting with severe, dull abdominal pain and life-threatening intra-abdominal bleeding. Dyspnea and impaired lung function can both be improved by long-acting bronchodilators. However, the underlying mechanism remains unclear.

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肺淋巴管平滑肌增生症以不尋常的急性腹痛表現：病例報告

林俊維　許正園　裘坤元 *　詹明澄　李貞慧 **

腹痛在急診室是很常見的問題，在罕見的肺淋巴管平滑肌增生症也可能以腹痛來表現。我們提出一個病患她因為急性腹痛伴隨有休克的症狀被送至急診，經診斷為左側腎臟血管脂肪瘤出血。因為經導管動脈栓塞術止血失敗，病人接受腎臟切除。一年後，病人開始有活動性喘不適的表現。病人肺功能有阻塞性與限制性的混合表現，經過長效 ß 受體激動劑的治療，病人症狀明顯改善。*(胸腔醫學 **2014; 29: 17-24**)*

關鍵詞：肺淋巴管平滑肌增生症，結節性硬化症，動脈血管栓塞治療術，阻塞性肺疾，長效 ß 受體激動劑

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Gefitinib-Related Interstitial Lung Disease with Pleural Effusion Successfully Treated with Medium Dose of Steroid: A Case Report and Literature Review

Shu-Fan Lin, Ming-Tai Lin, Ching-Hsing Lin

Gefitinib, an epidermal growth factor receptor tyrosine kinase inhibitor, is effective for patients with non-small cell lung cancer. However, the serious adverse effect of interstitial lung disease has been reported with its use. We present the case of a patient with lung adenocarcinoma with re-challenge gefitinib-induced interstitial lung disease with pleural effusion. The patient was then initially treated for atypical pneumonia and gefitinib was stopped, however re-administration of gefitinib led to the same symptoms re-occurring. The patient recovered from the interstitial lung disease with pleural effusion after steroid therapy. Re-administration of gefitinib should be considered cautiously in patients who have previously developed gefitinib-induced interstitial lung disease. ***(Thorac Med 2014; 29: 25-31)***

Key words: gefitinib, lung adenocarcinoma, interstitial lung disease, pleural effusion

Introduction

Compared with platinum-based chemotherapy, the adverse effects of gefitinib are modest [1], and commonly include diarrhea, skin rash, acne, dry skin, nausea and vomiting [2]. Interstitial lung disease (ILD) is an infrequent but life-threatening and toxic pulmonary adverse effect [3].

However, the clinical manifestations of tyrosine kinase inhibitor (TKI)-induced ILD are nonspecific, and include cough, fever, dyspnea, and hypoxemia. The computed tomography (CT) features of target agent-related ILD can be (a) diffuse alveolar damage or acute interstitial pneumonia; (b) bronchiolitis obliterans; (c) cryptogenic organizing pneumonia or a cryptogenic organizing pneumonia-like pattern; (d) hypersensitivity pneumonitis; (e) interstitial pneumonia with either a nonspecific interstitial pneumonia or usual interstitial pneumonia pattern; and (f) progressive disease of underlying ILD [4]. Making a differential diagnosis among lymphangitis carcinomatosis, pneumonia, allergy, cardiogenic edema and pulmonary hemorrhage is sometimes difficult [5]. In addition, no gefitinib-induced pleural effusion has been reported in the literature [4,6].

We report the case of a patient with gefitinib-induced ILD with pleural effusion that

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initially could not be confirmed and was diagnosed after re-challenge with gefitinib.

Case Report

A 40-year-old man who was a heavy smoker for more than 20 years presented in October 2012 with dry cough for 2 years and swelling of the neck for 2 weeks. He was diagnosed with right middle lung (RML) adenocarcinoma, with a tumor size of 2.6 cm, and with contralateral and supraclavicular region lymph node metastasis and brain metastasis, T1bN3M1b stage IV, (American Joint Committee on Cancer 7th edition criteria), epidermal growth factor receptor (EGFR) L858 R(+), and Eastern Cooperative Oncology Group performance status: 0. He was given the TKI erlotinib 150 mg/d (self-paid) for first-line therapy beginning October 29, 2012 and switched to gefitinib after a health insurance agreement on November 12, 2012. Whole brain radiation therapy was performed from October 30, 2012 to November 7, 2012. He complained of cough, chest pain and exertional dyspnea for 1 week with a mild fever up to 37.5^{o}C and visited our chest out-patient department on December 7, 2012. His chest X-ray (CXR) showed diffuse central peribronchovascular bundle thickness in both hilar regions, more on the right side, and a new onset of right pleural effusion (Figure 1).

Levofloxacin 500 mg/d was prescribed, due to suspected pneumonia. However, the symptoms persisted and chest CT on December 17 showed: (1) ground-glass opacities with central peribronchial wall thickening and small consolidations in both upper lungs, the RML and the lingular lobe, and (2) decreased lobulated neoplasm size in the RML (from 2.6 cm to 1.5 cm) (Figure 2). TKI-related pneumonitis was suspected, and gefitinib was stopped on December 15. He was then treated with steroid therapy (prednisolone 40 mg/d) for 10 days, beginning December 17. Cytology of the right pleural effusion on December 19 showed negative findings, so malignancy of the pleural effusion was less likely. The symptoms and CXR (Figure 1) improved. We explained to the patient the benefits and risks of re-challenge with gefitinib, which was necessary to prove gefitinib-induced

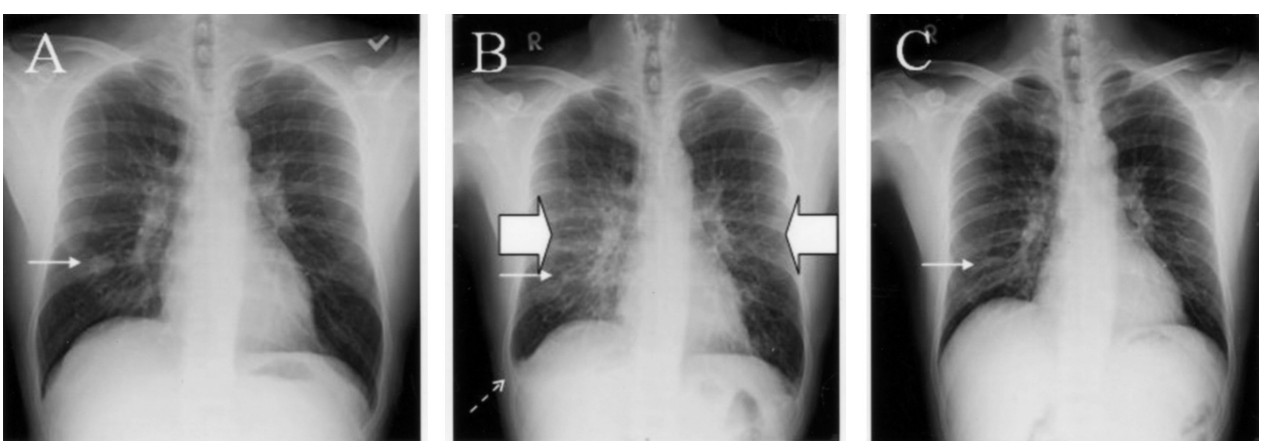

Fig. 1. (A) The initial diagnosis of lung cancer. CXR showed a soft tissue nodule about 2.3 cm in size in the right lower lung field (white arrow). (B) After 43 days of TKI treatment, the chest plain film showed diffused central peribronchovascular bundle thickness (large white arrows) in both hilum regions, more on the right side, and a new onset of right pleural effusion (white dashed arrow). (C) After 9 days of steroid treatment.

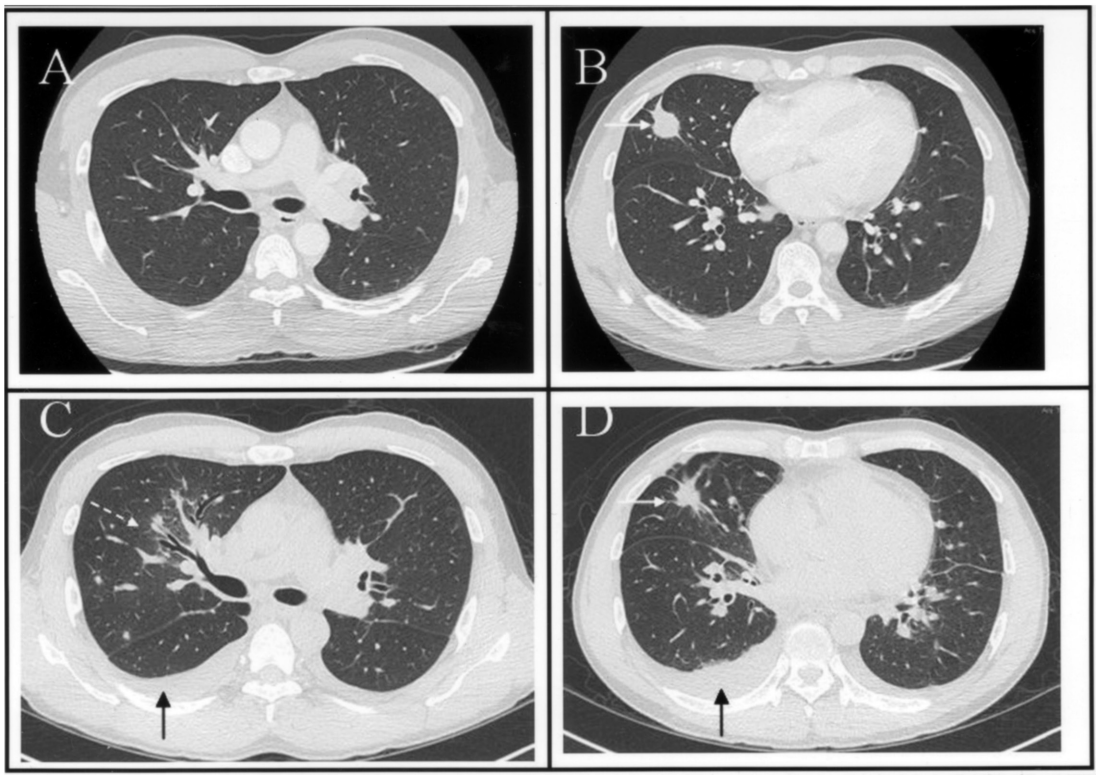

Fig. 2. Before gefitinib treatment: (A) Chest CT scan before gefitinib treatment and through the carina level, demonstrated normal lung parenchyma. (B) Chest CTthrough the right middle lobe (RML) demonstrated a 2.6 cm lobulated nodule (white arrow) in the RML with heterogeneous enhancement and pleural tail sign. Two days after stopping the 50-day gefitinib treatment: (C) Chest CT scan showed ground-glass opacities with central peribronchial wall thickening and small consolidations (white dashed arrow). (D) Chest CT through the RML, showed small consolidations in the RML and left inguinal lobe, right pleural effusion (black arrow) and a decrease in the size of the lobulated neoplasm (white arrow).

ILD. The patient, agreed to go ahead with the test of the drug. We re-challenged gefitinib 150 mg/d beginning December 27, and mild fever and cough developed on December 28. Dyspnea occurred after 3 to 4 days of gefitinb re-challenge, and the patient then stopped taking the drug himself. A CXR (Figure 3) showed infiltration in both hilum regions with thickness of the bronchial wall more on the right side with right pleural effusion, similar to the previous presentation of pneumonitis. Prednisolone 30 mg/d was administered beginning January 3, 2013. The CXR (Figure 3) on January 19, 2013 showed recovery. The patient then started chemotherapy with pemetrexed plus cisplatin because of the re-challenge gefitinib-induced ILD.

Discussion

The incidence of ILD during gefitinib treatment has been reported to be as high 2% in Japan and 1% worldwide [7], with a reported mortality rate of 31.6%, and an adjusted odds ratio of 1.05 versus chemotherapy [3]. In more than 75% of cases, complications occur within 3 months of drug use, and the majority of these complications arise within 4 weeks of the thera-

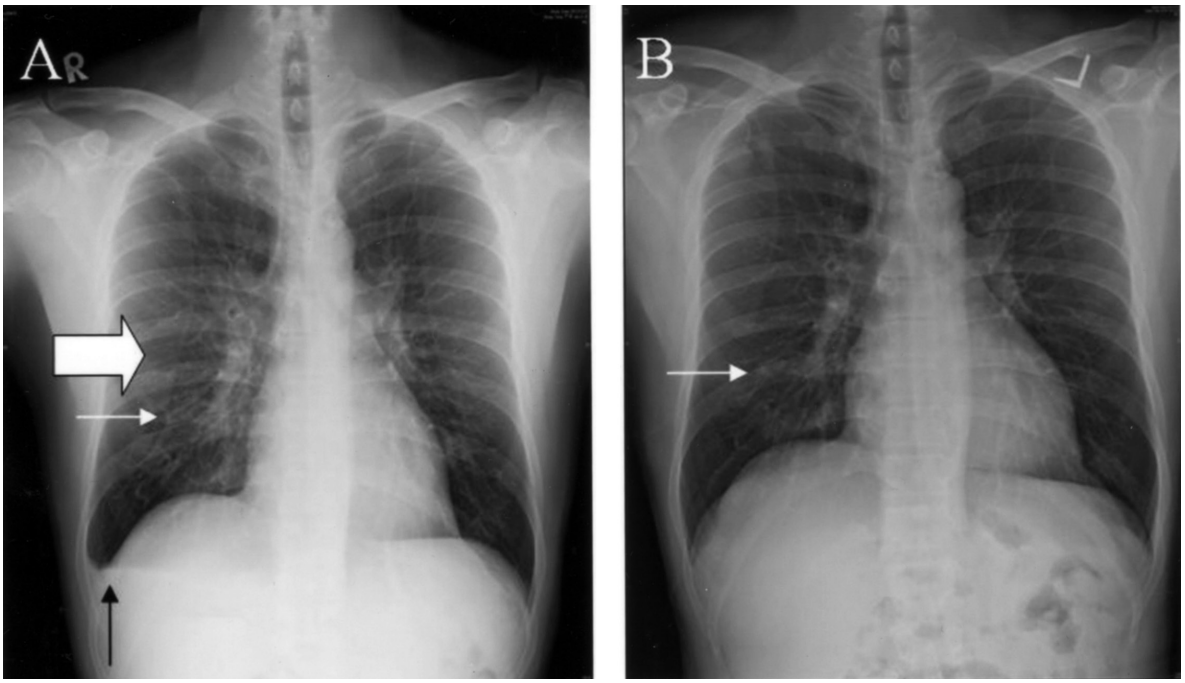

Fig. 3. (A) CXR after 1 week of gefitinib re-challenge demonstrated small opacity lesions at the right lower lung field (lower white arrow), and infiltration in both hilar regions with a thicker bronchial wall on the right side (white thick arrow) with right pleural effusion (black arrow). (B) After 19 days of stopping gefitinib and with steroid use, CXR revealed infiltration in the right hilum region with greater resolution than the prior CXR and small opacity lesions (white arrow) in the right lower lung field.

py [8]. The risk factors for gefitinib-related ILD include male gender, a history of smoking, poor functional status, concomitant radiation therapy, no history of chemotherapy, and a reduction in serum albumin [4]. In our case, the risks were male gender, a smoking history and an absence of chemotherapy.

The mechanism of gefitinib-induced ILD has not been fully elucidated. Previous findings suggest that gefitinib inhibits EGFR-mediated signaling and impairs the repair of lung injury, thereby exacerbating the injury [9].

CXR is often the first diagnostic imaging study conducted. CT is particularly useful for diagnosis of the subacute or chronic appearance of ILD based on the pattern [4]. The chest CT of our patient revealed a hypersensitivity pneumonia-like pattern with pleural effusion. The pleural effusion was less likely to be malignant because the cytology was negative for malignancy and the effusion resolved after steroid treatment, but re-appeared during drug re-challenge. Many drugs (including some TKIs) can induce pleural effusions through various mechanisms [10-12]. However, there has been evidence that EGFR TKI might induce pleural effusion [4,6], and the association between gefitinib and drug-induced pleural effusion is still unclear.

For the assignation of TKI-induced ILD, 4 specific findings are required: (1) new onset of dyspnea with or without cough or fever, (2) lack of evidence of infection, (3) radiographic findings consistent with drug-induced ILD, and (4) consistent pathologic findings if available [4]. Infection is a very common cause of

pulmonary infiltrates and respiratory failure in cancer patients [13]. The diagnosis of TKI-induced ILD can be made when pneumonitis develops shortly after the initiation of treatment (i.e., hours to weeks), when there is a lack of an alternative explanation for respiratory failure, and with the resolution of pneumonitis after corticosteroid treatment and withdrawal of the presumed agent [4].

No randomized controlled trials have been performed with regard to the management of gefitinib-induced acute interstitial pneumonia. Immediate withdrawal of gefitinib, and the use of intravenous corticosteroid and oxygen therapy are currently recommended [14]. Successful treatment with high-dose corticosteroids has been reported [15]. In our case, we initially stopped gefitinib and treated the patient with medium-dose corticosteroid, and the symptoms and CXR image improved dramatically. Medium-dose corticosteroid may help in the treatment of early-onset gefitinib-induced ILD.

Recurrent gefitinib-induced ILD has been previously reported [16]. Reducing the dose of gefitinib with initiation of corticosteroid treatment or switching to other kinds of EGFR TKIs such as erlotinib may be considered as a potential therapeutic option in patients with EGFR-mutant non-small-cell-lung carcinoma who develop gefitinib-related ILD [8,17-21]. However, further investigations are needed to clarify this issue.

In conclusion, early recognition and early intervention in TKI-induced ILD are very important for the prognosis, and will prevent irreversible changes in the ILD and mortality. The association between gefitinib and drug-induced pleural effusions is still unclear, and further studies are warranted.

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經中劑量類固醇成功治療的艾瑞莎再激發引起之間質性肺炎併肋膜積水：病例報告與文獻回顧

林書帆　林明泰　林慶雄

艾瑞莎是種有效治療非小細胞肺癌的表皮生長因子酪氨酸激酶抑制劑。然而，此藥物仍有可能產生如間質性肺炎等嚴重的種副作用。我們提出一個肺癌的案例，一開始無法明確診斷是治療過程中發生非典型肺炎還是艾瑞莎所引起的管直性肺炎合併肋膜積水，經由再次使用艾瑞莎導致間質性肺炎亦合併肋膜積水，進而確診此病例為艾瑞莎引起之間質性肺炎及肋膜積水。*(胸腔醫學 **2014; 29: 25-31**)*

關鍵詞：艾瑞莎，肺腺癌，間質性肺炎，肋膜積水

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Pulmonary and Rhino-orbito-cerebral Mucormycosis in a Patient with Diabetic Ketoacidosis: A Case Report and Review of the Literature

Jing-Yao Jhan, Chun-Chi Chang, Ying-Ming Shih, Hui-Chun Tai*, Ching-Hsiung Lin

Mucormycosis is an opportunistic fungal infection mainly occurring in patients with poorly controlled diabetes mellitus or neutropenia, in recipients of corticosteroids or other immunosuppressive medications, and in those with iron overload. The infection begins in the nose and paranasal sinuses and then rapidly spreads to pulmonary, orbital, and intracranial structures. Herein, we report a case of pulmonary and rhino-orbito-cerebral mucormycosis in a patient with diabetic ketoacidosis to emphasize the importance of an early diagnosis of this potentially fatal fungal infection. We also review the recent literature on the management of mucormycosis. ***(Thorac Med 2014; 29: 32-38)***

Key words: diabetic ketoacidosis, mucormycosis, rhino-orbito-cerebral

Introduction

Patients with phagocytic dysfunctions caused by neutropenia or ketoacidosis, high iron serum concentrations, use of corticosteroids or other immunosuppressive medications, hematologic malignancies, and bone marrow transplantation are at high risk of developing zygomycosis (mucormycosis) [1]. Mucormycosis is classified as having rhinocerebral, pulmonary, cutaneous, gastrointestinal, disseminated, and uncommon presentations [2]. A rhino-orbito-cerebral presentation in patients with poorly controlled diabetes is the predominant form [3].

We present a case of pulmonary and rhino-orbito-cerebral mucormycosis in a 48-year-old woman with diabetic ketoacidosis. There have been few case reports of combined pulmonary and rhino-orbito-cerebral mucormycosis in patients with diabetic ketoacidosis. This is also the first case in our hospital.

Case Report

The patient was a 48-year-old woman with diabetes mellitus and hypertension for more than 5 years that was not being controlled by any medication. She had been well until 3 weeks before presentation, when dry cough and dyspnea developed. She also had right retro-orbital and facial pain for 3 weeks. Two days before admission, she became aware of blurred

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vision in the right eye. She was admitted to the chest ward via the emergency department under the impression of right lower lobe pneumonia.

Her initial vital signs were a body temperature of 36.8°C, sinus tachycardia of 155 beats/minute, respiration rate of 24 breaths/minute, and blood pressure of 204/147 mmHg. There was white necrotic material coating the right upper hemipalate, and rales in the right lower lung field. A neurological examination revealed complete ophthalmoplegia and ptosis in the right eye. Her white blood cell count was 5900/cubic millimeter, with 84% neutrophils, 6% lymphocytes, and 8% monocytes. Her hematocrit level was 38.8%. Serum glucose level was 325 mg/dL, and serum creatinine and blood urea nitrogen levels were normal. The sodium level was 130 mmol/L, potassium was 4.6 mmol/L, and arterial blood gas analysis revealed metabolic acidosis (pH 7.252, HCO_3^- 8.5 mmol/L). Urinalysis revealed a glucose level greater than 1 g/dL, specific gravity 1.031, proteinuria 300 mg/dL and 4-plus ketone bodies.

Chest X-ray revealed a dense patchy opacity in the right lower lung field below the horizontal fissure (Figure 1A). A computed tomographic (CT) scan of the thorax showed confluent, patchy opacities in the right middle lobe and right lower lobe. A CT scan of the orbital and para-nasal sinuses revealed thickness and good enhancement of the right upper nasopharynx with obliteration of the adjacent right Rosenmuller fossa (Figure 2A). Microscopic examination of a stained sputum specimen showed yeast-like cells with pseudohyphae.

As mucormycosis was suspected, intravenous amphotericin B 60 mg once daily was initiated. Emergency surgical resection was

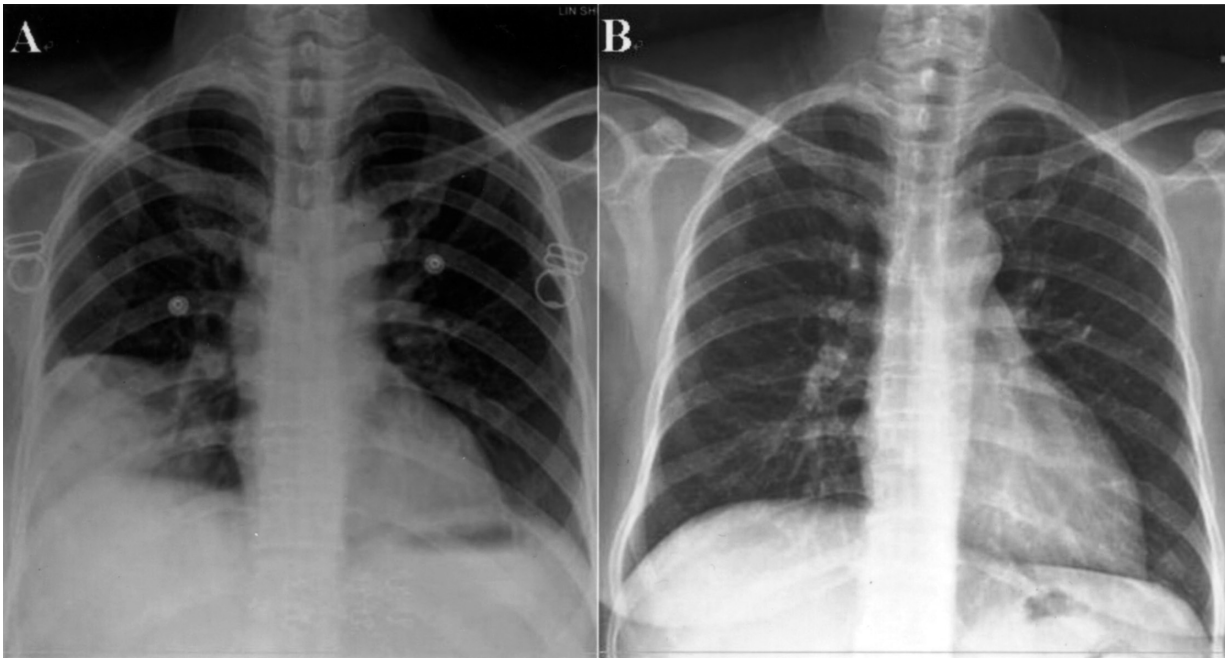

Fig. 1. Serial chest X-rays before and after antifungal therapy: (A) Initial chest X-ray revealed patchy opacity in the lateral aspect of the right lower lung field. (B) A subsequent chest X-ray 108 days later showed complete resolution of the consolidation after effective antifungal therapy.

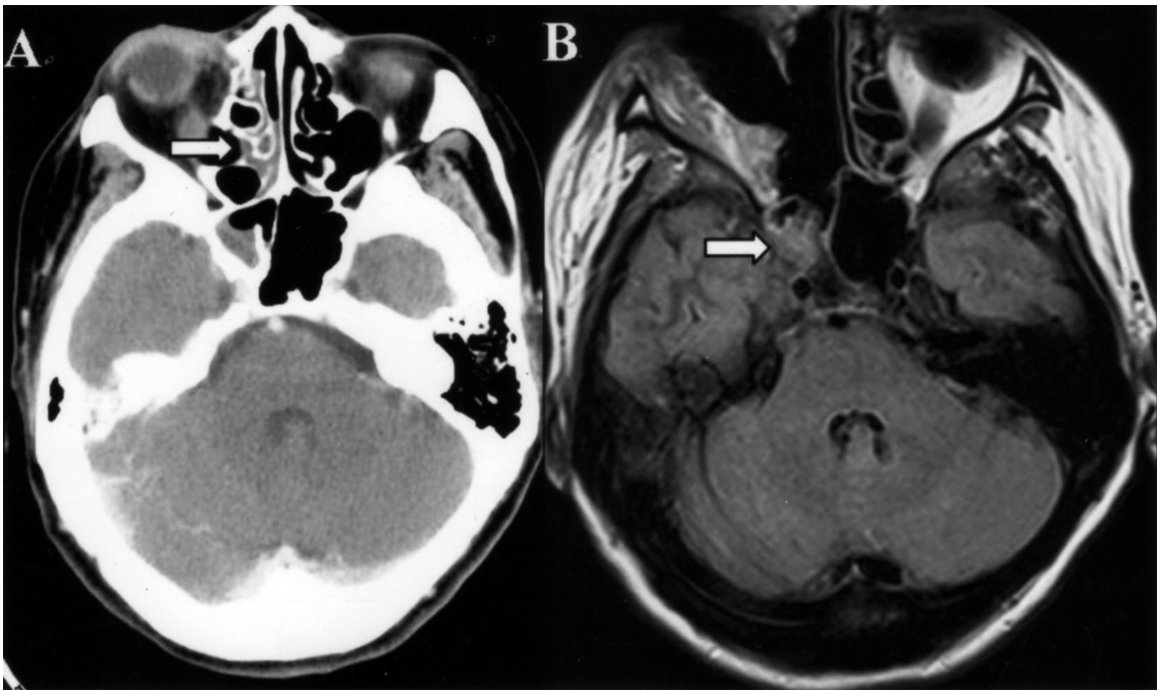

Fig. 2. Findings of head imaging examinations before treatment: (A) CT scan of the orbital and paranasal sinuses revealed thickness and good enhancement of the right upper nasopharynx (white arrow). (B) Axial T2-weighted MRI scan showed fungal sinusitis with intracranial parasellar extension (white arrow).

performed by the otolaryngologist and ophthalmologist, including total resection of the right inferior turbinate and partial right-side mucosa of the septum. In addition, the lamina papyracea was broken for orbital decompression, and enucleation and debridement of the right eye were performed. A histological examination with Grocott-Gomori methenamine silver and periodic acid-Schiff staining identified septated fungal hyphae with narrow-angled branching and angioinvasion (Figure 3).

On the 13th hospital day, the intravenous amphotericin B 60 mg once daily was replaced with intravenous liposal amphotericin 300 mg once daily because of deterioration of her renal function. Magnetic resonance imaging (MRI) examinations of the brain showed abnormal signal lesions in the right parasellar region and right cavernous sinus, with thickness of the dura adjacent to the right prepontine cistern, right orbital apex, right nasopharyngeal region, sphenoid sinus wall, and right pterygomaxillary recess, and obliteration of the right Meckel's cave (Figure 2B). Surgery with sinoscopy to remove the crust and fungal tissue in the right nasal cavity and sinus, sequestrectomy (removal of sequestra which are small pieces of necrotic bone that are avascular and harbor microorganisms) and saucerization (excision of the margins of necrotic bone overlying the focus of osteomyelitis) of the right palate granulation tissue and sequestrum, and endoscopic transsphenoidal parasellar removal of fungal infection materials were performed by an otolaryngologist, oral surgeon, and neurosurgeon on the 69th hospital day.

After 11 days of intravenous amphotericin B and 86 days of intravenous liposal ampho-

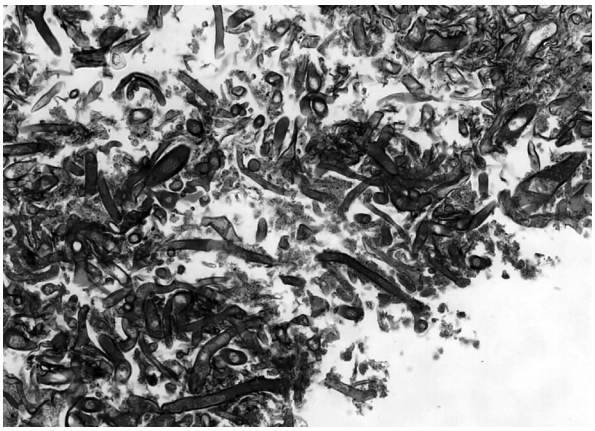

Fig. 3. Histological evaluation of the resected tissue showed coagulative necrosis of respiratory epithelial tissue. Septated fungal hyphae with narrow-angled branching are seen with angioinvasion in periodic acid-Schiff staining.

tericin treatment combined with broad surgical debridement, a chest X-ray revealed resolution of the patchy opacity (Figure 1B). On the 123rd hospital day, the patient was discharged with oral posaconazole. The final microbiological culture of both sputum and necrotic tissue in the rhino-orbito-cerebral area yielded Rhizopus spp.

Discussion

Mucormycosis is a fungal infection caused by fungus of the phycomycetos order, and the main pathogens are the Rhizomucor, Rhizopus, Absidia, and Mucor species. Rhizopus is the most frequently seen. A study in France revealed an increasing incidence, from 0.7 per million in 1997 to 1.2 per million in 2006 (p<0.001), and also reported an increasing incidence in patients with diabetes mellitus [1]. Opportunistic pathogens usually infect immunocompromised patients such as those with diabetes mellitus (especially those with acidosis) or hematologic malignancies with neutropenia, solid-organ-transplant recipients, recipients of corticosteroids or other immunosuppressive medications, and those with an iron overload [2]. The fungus also invades blood vessels and causes vascular thrombosis, which reduces the blood supply and causes tissue necrosis [3]. Mononuclear and polymorphonuclear phagocytes can eliminate the fungal spores and hyphae by oxidative and non-oxidative killing mechanisms [3]. Quantitative or qualitative defects in phagocytic cell activity induce growth of the hyphae and invasive infection [2]. Hyperglycemia and acidosis impair chemotaxis and the killing activity of phagocytic cells against Mucorales [3]. Corticosteroids impair the migration, ingestion, and phagolysosome fusion in human macrophages [3]. Patients with iron overload are also predisposed to mucormycosis [3-4]. Thus, mucormycosis in patients with diabetic acidosis is attributed to the increased availability of serum iron due to the diminished affinity of transferring free iron at a low pH (<7.4) [5-6]. Our patient had diabetes with ketoacidosis, which was a predisposing factor for mucormycosis.

Mucormycosis is classified into 6 forms: rhino-orbito-cerebral, respiratory, gastrointestinal, cutaneous, disseminated, and mixed [4,7]. Pulmonary mucormycosis is often noted in neutropenic patients with cancer undergoing chemotherapy, or in patients undergoing hematopoietic stem cell transplantation with graft-versus-host disease [2-3]. Pulmonary mucormycosis presents as an endobronchial or tracheal lesion, especially in patients with diabetes mellitus, and may cause airway obstruction, lung collapse and invasion of the hilar vessels with subsequent massive hemoptysis [8]. Tedder *et al*. reported that isolated pulmonary mucormycosis had a 65% mortality rate, but the

disseminated form had a mortality rate of up to 96% [9]. Rhino-orbito-cerebral mucormycosis is the most frequent form of mucormycosis in patients with diabetes mellitus [10]. After inhalation of fungal sporangiospores into the sphenoid sinuses, the invading fungus spreads to the palate, sphenoid sinus, and cavernous sinus, and then to the orbits or brain [11]. The symptoms of rhino-orbito-cerebral mucormycosis are consistent with those of sinusitis and periorbital cellulites, including eye pain, facial pain, and facial numbness followed by blurred vision [12].

The diagnosis of mucormycosis is difficult and is often made after a delay or even postmortem, because it is based on cultures or microscopy of clinical specimens [13]. The definite diagnosis is confirmed by histological and microbiological studies. Hematoxylin and eosin, periodic acid-Schiff and Gomori silver staining are used. Microscopy reveals large non-septate hyphae that branch at right angles [7]. McAdams *et al*. reported that pulmonary mucormycosis manifests as consolidation on chest radiographs, and cavitations are seen in 40% of patients [14]. Jamadar et al. have reported the CT halo sign to be a common finding in pulmonary mucormycosis, seen in 78% of nodules studied with CT [15]. Head CT scans and brain MRI studies reveal the involvement of the sinuses, orbits, and central nervous system. Although we performed a sputum culture instead of a lung biopsy for our patient, pulmonary mucormycosis was indirectly diagnosed according to the clinical presentations and complete response to antifungal therapy. Contamination of sputum cultures from the orbital and paranasal sinuses may also yielded Rhizopus spp.

The treatment of mucormycosis requires an early diagnosis, reversal of the underlying predisposing factors, early and broad surgical debridement, and administration of effective antifungal therapy [3]. Intravenous amphotericin B is the mainstay of treatment. However, it has numerous side effects such as fever, chills, or renal toxicity. In our case, deterioration of renal function developed after administration of amphotericin-B for 11 days. We therefore replaced amphotericin-B with liposomal amphotericin, which has a better solubility in the central nervous system and fewer adverse effects. Posaconazole is used in patients who are resistant or intolerant to amphotericin in the USA. It is an oral broad-spectrum triazole and is well tolerated with a high response rate [16]. Surgical treatment with extended resection is necessary because mucormycosis causes angioinvasion, extensive thrombosis and tissue necrosis, and antifungal agents have poor penetration at these sites of infection. Tedder *et al*. reported a mortality rate of 11% among patients with mucormycosis treated surgically and medically, which was significantly lower than the 68% in those treated only medically (p=0.0004) [9]. Repeated resections of small residual fungal foci from the margins of the wound during the postoperative period are often needed to ensure paranasal sinus drainage.

In conclusion, physicians should keep in mind that a prompt diagnosis is important for pulmonary and rhino-orbito-cerebral mucormycosis in patients with diabetic ketoacidosis. Adequate treatment should focus on correcting the underlying acidosis, comprehensive antifungal treatment, and wide surgical resection. In the current case, we arranged multidisciplinary management including chest, infection, and endocrinology specialists, an otolaryngologist, ophthalmologist, and neurosurgeon, and the disseminated mucormycosis was resolved after a hospital stay of 123 days.

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一位糖尿病酮酸血症患者併發肺部及鼻眼腦白黴菌病：病例報告與文獻回顧

詹景堯　張竣期　施穎銘　戴蕙君 *　林慶雄

白黴菌病是一種伺機性黴菌感染，主要發生在糖尿病控制不良、嗤中性白血球低下、接受類固醇或者其他免疫抑制劑、及鐵質過度攝取的患者身上。感染開始於鼻部及鼻竇，然後快速的蔓延到肺部、眼部、及腦部內構造。在此我們報告一位糖尿病酮酸血症患者併發肺部及鼻眼腦白黴菌病，以強調早期診斷這個潛在致命性黴菌感染的重要性。我們也回顧最近關於白黴菌病處置的文獻。*(胸腔醫學 **2014; 29: 32-38**)*

關鍵詞：糖尿病酮酸血症，白黴菌病，鼻眼腦

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Bronchial Asthma and Septic Lung in a Patient with Hyperimmunoglobulin E Syndrome

Hsuan-Fu Ou, Jiunn-Min Shieh, Shian-Chin Ko

Hyperimmunoglobulin E syndrome (HIES), or Job's syndrome, is a rare and complex primary immunodeficiency disorder characterized by a spectrum of abnormalities related to the immune system, connective tissue, and bones. Despite more than 40 years of research, the etiology of HIES is still unclear. Most cases are sporadic, but autosomal dominant (AD) and autosomal recessive (AR) inheritances have been reported. HIES is characterized by a particular susceptibility to staphylococcal and mycotic infections. Therapy for HIES is directed at prevention and management of infections through the use of sustained systemic antibiotics and antifungals along with topical therapy for eczema and drainage of abscesses. Anti-staphylococcal antibiotic prophylaxis is useful. We present the case of a patient with HIES syndrome who had a long history of bronchial asthma. She was admitted due to recurrent oxacillin-resistant *Staphylococcus aureus* (ORSA) bacteremia, infectious spondylodiscitis (L2-3) and septic lungs. ***(Thorac Med 2014; 29: 39-45)***

Key words: hyperimmunoglobulin E syndrome (HIES), bronchial asthma, *staphylococcus aureus* infection

Introduction

Hyperimmunoglobulin E syndrome (HIES), also known as Job's syndrome, was first reported by Davis SD, *et al*. in 2 red-haired girls with recurrent pneumonia and skin boils [1]. Job's syndrome is reminiscent of the biblical character Job, who was smitten by Satan "...with sore boils from the sole of his foot unto the crown"; the skin boils manifested the skin hallmark of this syndrome. HIES is a rare and complex primary immunodeficiency disorder with diverse clinical manifestations and heterogeneous genetic origins. Most cases are sporadic, but it can be inherited in either autosomal dominant (AD) or autosomal recessive (AR) patterns [2].

Dominant-negative mutations in the DNA-binding domain of signal transducer and activator of transcription 3 (STAT3) are the cause of AD-HIES [3]. STAT3 is integral to T helper cell (Th17) differentiation and interleukin (IL)-17 production. Th17 CD4 cells are thought to be important in host defense through recruitment of neutrophils and upregulation of antimicrobial peptides [4]. Impaired Th17 function is postulated as the cause of impaired clearance of fun-

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gal and extracellular bacterial infections. Most immunological manifestations of AD-HIES are driven by *Staphylococcus aureus* infection of the skin and lung. Forty percent of patients also have fungal infections, including mucocutaneous candidiasis, histoplasmosis, and *Cryptococcus neoformans*. AD-HIES and the sporadic type of HIES are observed with a cluster of facial, dental, skeletal, and connective tissue abnormalities and post-infection pneumatocele formation, which are not observable in the recessive type. The characteristic constitutional features include coarse face, rough skin, deep-set eyes, prominent forehead, prognathism, thick lower lip and auricles, a wide nose and increased interalar distance [5].

AR-HIES is associated with mutations in the dedicator of cytokinesis 8 (DOCK8) gene encoding a protein implicated in the regulation of the actin cytoskeleton. A high rate of neurological complications, autoimmune diseases and malignancy is found in AR-HIES patients [6]. Severe chronic cutaneous viral infections are distinctive features of AR-HIES. The most common pathogens are herpes simplex virus (HSV), human papillomavirus (HPV), molluscum contagiosum virus (MCV), and varicella-zoster virus (VZV). AR-HIES patients are also susceptible to recurrent sinopulmonary infections caused by a wide variety of pathogens.

We report the case of a patient with HIES syndrome with a history of asthma, recurrent oxacillin-resistant *Staphylococcus aureus* (ORSA) bacteremia, infectious spondylodiscitis (L2-3) and septic lung.

Case Report

A 57-year-old woman, a non-smoker, had a history of bronchial asthma and chronic eczema for more than 40 years. A pulmonary function test taken 3 years before this admission showed forced expiratory volume in 1 sec (FEV_1) of 39% predicted with significant bronchodilator reversibility (220 ml, 24% improvement), confirming the diagnosis of asthma. She had a left distal radius fracture due to minor trauma and underwent open reduction and internal fixation (ORIF) 7 years ago. An episode of pneumonia developed 6 years ago and she was admitted to our hospital for 6 days. She also had a secundum type of atrial septal defect (ASD) and received device occlusion 2 years prior to this admission.

She had suffered from generalized itching erythoderma with exfoliative changes for 2 months after taking some anti-inflammatory drugs prescribed by an orthopedist. Oral steroid and antihistamine were given at a rheumatologist's clinic, but in vain. After admission, physical examination showed erythematous papular lesions with scaling and vesicle formation on her face, trunk and extremities. Areas of lichenification and ecchymosis were also found (Figure 1). Oral candidiasis was detected on the buccal mucosa and tongue surface. Bilateral diffuse expiratory wheezes with scattered coarse crackles were heard at chest auscultation. Lab data revealed WBC 16,600 cells/L with a left-shifted differentiation (band forms 7%, segments 85%), CRP 119.2 mg/L (normal <6), and IgE 15,200 IU/mL (normal 10-80). Chest radiography revealed multiple cavitary infiltrates in the bilateral lung fields. An enlarged cardiac silhouette, bilateral engorged hila and widened carinal angle were also noted (Figure 2). Chest computed tomography (CT) revealed multiple consolidative lesions with cavitation in the bilateral lung fields. Air-fluid levels within the cavities indicated lung abscess formation

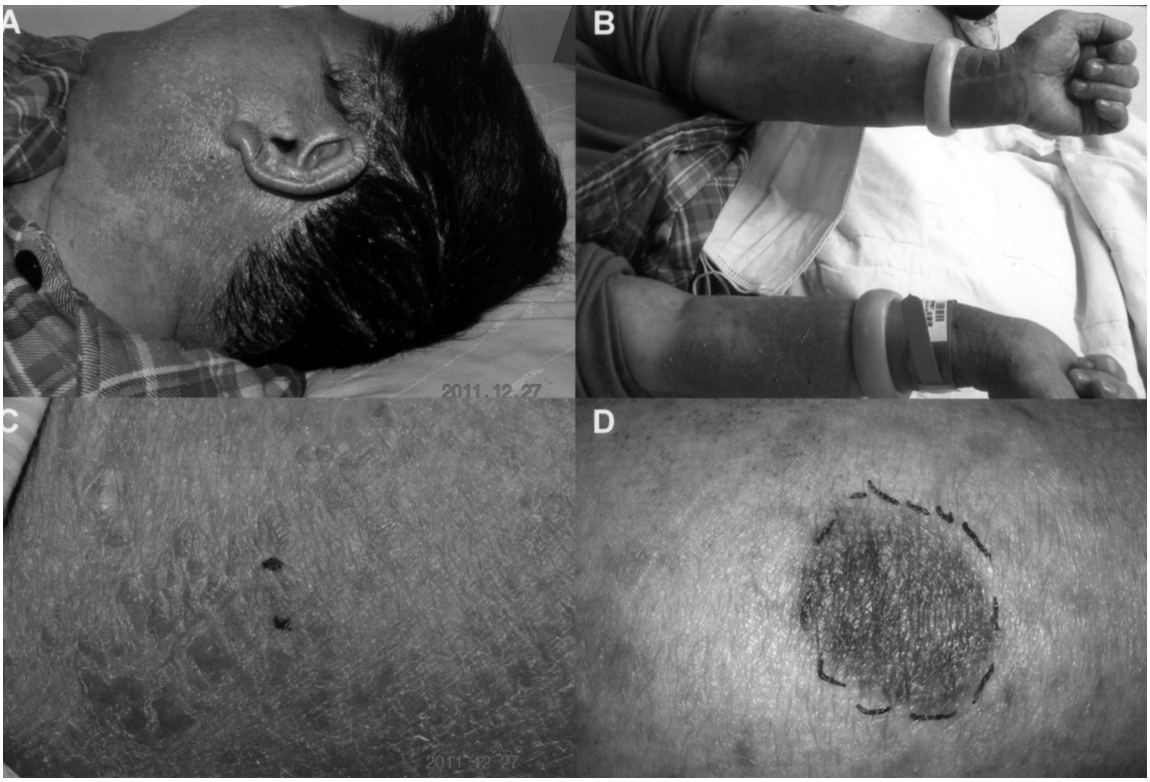

Fig. 1. Skin manifestation: (A,B) Erythematous papular lesions with scaling and vesicle formation on the face, extremities and trunk; (C) Lichenified lesions; (D) Areas of ecchymosis.

(Figure 3). Skin biopsy showed chronic active dermatitis with psoriasiform hyperplasia.

She complained of severe lower back pain, and a high fever of up to 39°C developed during admission. Blood culture yielded ORSA on 3 occasions on separate days. Spinal magnetic resonance imaging (MRI) showed abnormal signal intensity in the L2-3 endplates and disc with disc deformity and endplate irregularity. Infectious spondylodiscitis was suspected. Because of the severe staphylococcal infection, vancomycin, tigecycline and fosfomycin were given for more than 14 days. She underwent spinal surgery, including laminectomy, bone graft (left tibia plateau), cage fixation, and debridement of the paraspinal abscess. ORSA was recovered from the pus culture. Systemic corticosteroid was also prescribed for an acute asthmatic attack. Her serum IgE level was decreased to 953.0 IU/mL 1 month later. She was discharged on the 39th day of hospitalization.

Discussion

HIES is characterized by immunologic and non-immunologic findings such as recurrent sinopulmonary infections, recurrent skin infections, multiple fractures, atopic dermatitis and characteristic facial features [7]. Extra-immunologic features are important in distinguishing HIES from other primary immunodeficiencies. The clinical triad of HIES includes: 1) recurrent staphylococcal abscesses, 2) recurrent airway infections, and 3) an increased concentration of

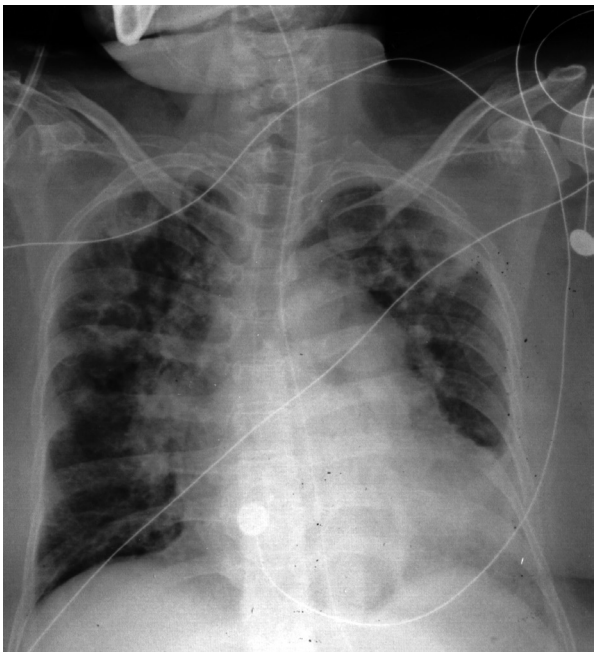

Fig. 2. Chest radiography showed multiple cavitary infiltrates in bilateral lung fields. Enlarged cardiac silhouette, bilateral engorged hila and widened carinal angle are also noted.

IgE in serum. Increased serum IgE level is the hallmark of the syndrome, and a value of 2,000 IU/mL is considered to be the cut-off value. A scoring system comprising both clinical and laboratory diagnostic criteria has been proposed by Grimbacher B and colleagues [8]. High serum IgE level, skin abscesses or eczema, recurrent pneumonia, parenchymal lung anomalies (bronchiectasis or pneumatocele), characteristic facial features, scoliosis and retained primary teeth are the important criteria.

In our case, the patient's serum IgE level was 15,200 IU/mL, much higher than the cut-point value 2,000 IU/mL. HIES is characterized by particular susceptibility to staphylococcal and mycotic infections. In addition to the past history of minimal trauma fracture and pneumonia with pneumatocele formation, our patient's

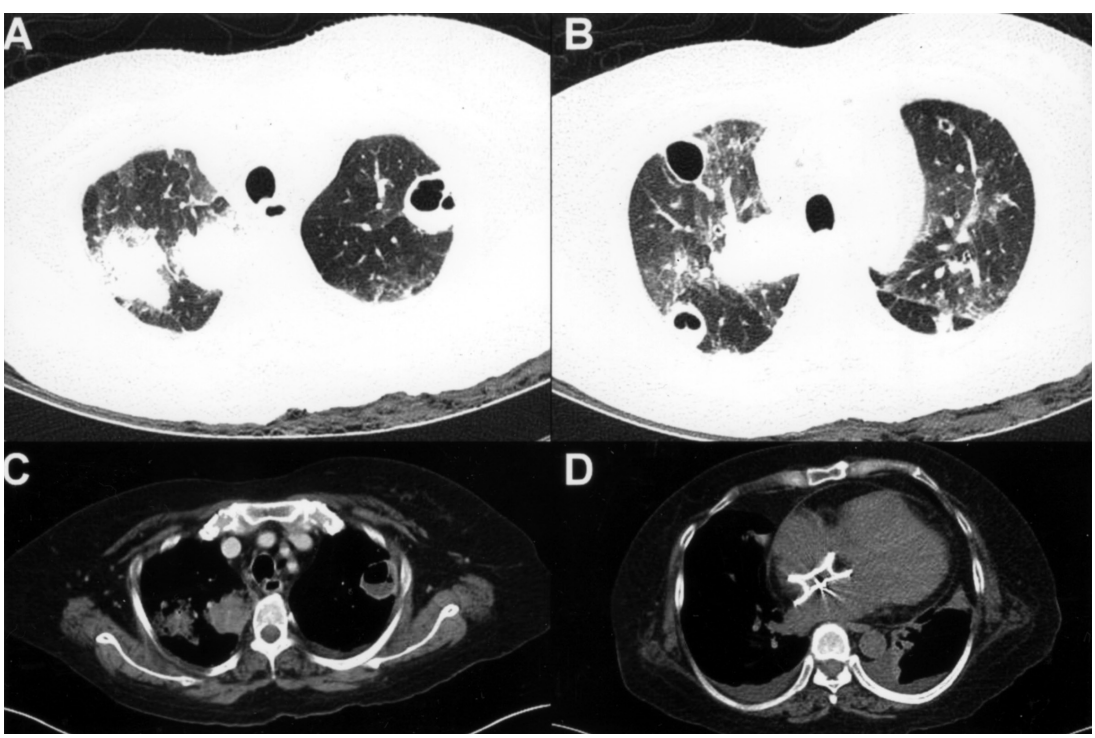

Fig. 3. Chest CT scan. (A,B) Lung window setting: multiple consolidative lesions, and infiltrates with cavitation in the bilateral lung fields; (C) Mediastinal window setting: air-fluid levels in the cavities indicating lung abscess formation; (D) Interatrial obstructor: An obstructive device in the interatrial septal area.

characteristic skin manifestations, oral candidiasis and severe staphylococcal infection made the diagnosis of HIES highly probable. Tracing back her family history, no other family member had had a similar presentation. Although molecular biological evidence was unavailable, we suspected the patient had the sporadic type of HIES.

To our knowledge, there have been few reports referring to the association between HIES and asthma. However, a defective T helper 1 (Th1)-dependent cytokine response and a skewed Th1/Th2 cell ratio were detected in patients with HIES [9]. These situations facilitate the development of allergic asthma. Of interest, when the asthmatic attack was controlled by anti-inflammatory agents, the serum IgE level was reduced.

Complications of pulmonary infections, including bronchiectasis and pneumatocele, are the most common causes of death in hyper-Ig E syndrome [10]. As in our case, severe pulmonary infections are the major problems in HIES. With a late diagnosis, the respiratory function will worsen significantly [11].

As with most primary immunodeficiencies without a cure, HIES management focuses on preventative measures to limit the number and severity of infections. The introduction of regular long-term intake of systemic antibiotics and antifungal drugs is of great importance. Zhang Q and colleagues suggested molecular diagnosis of HIES for optimal patient management [12]. Infections in AD-HIES are usually well controlled by antibiotics. By contrast, the viral infections in AR-HIES are difficult to manage. Potentially curative hematopoietic cell transplantation is considered for AR-HIES patients. However, the molecular biological technique needed to distinguish different types of HIES is usually unavailable in most hospitals.

Conclusion

In the absence of a definitive test, the diagnosis of HIES must be made based on a combination of clinical and laboratory findings. A serum IgE level greater than 2,000 IU/mL in association with characteristic skin lesions and recurrent sinopulmonary infections suggests the diagnosis of HIES. Since HIES is a multisystemic disorder with a broad constellation of clinical manifestations, interdisciplinary care by specialists in infection, pneumonology, dermatology, immunology, and even surgery is mandatory.

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高免疫球蛋白E症候群併發氣喘與敗血性肺炎：病例報告

歐軒甫　謝俊民　柯獻欽

高免疫球蛋白E症候群是一種先天性、罕見的免疫功能缺陷疾病、可以體染色體顯性或隱性方式遺傳，二者在臨床上表現不同。高免疫球蛋白E症候群最常見的表現為復發性的皮膚感染、復發性肺炎伴隨肺囊腫的形成、與血清免疫球蛋白E濃度增高，顯性遺傳患者常合併臉部、牙齒及骨骼特徵，如：臉型粗獷、皮膚粗糙、額頭明顯、下巴前凸、鼻翼距離增加、乳牙不易脫落等。皮膚特徵包括：異位性皮膚炎與間歇性葡萄球菌膿瘍。復發性感染為此病的主要特色，特別是金黃色葡萄球菌與黴菌感染。處置上首重感染的預防與治療，減少合併症的產生，藥物包括：抗生素、抗黴菌劑、與抗病毒劑。本文報告一例高免疫球蛋白E症候群併發氣喘、反覆性菌血症、細菌性骨髓炎、與敗血性肺炎，長期抗生素治療合併脊椎手術，終使病人順利出院。高免疫球蛋白E症候群影響多個器官系統，故需各個相關學科協調處置，方可使病人得到最好的照顧。*(胸腔醫學 **2014; 29: 39-45**)*

關鍵詞：高免疫球蛋白E症候群，敗血性肺炎，葡萄球菌感染

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Melioidosis with Lung Mass and Mediastinal Lymphadenitis: A Case Report

Chun-Li Chen*, Jeng-Yuan Hsu*,**, Chun-Shih Chin*,**

Melioidosis, caused by *Burkholderia pseudomallei*, is highly endemic to northern Australia and northeast Thailand. An outbreak of melioidosis was identified in southern Taiwan after a rainy season in 2005. The lung is the most commonly affected organ. Acute pulmonary melioidosis is commonly presented with pneumonia. Subacute or chronic infection has diverse lung manifestations, such as abscess, cavitation, and calcified node. Lung mass and mediastinal lymphadenopathy are rarely seen. The radiographic pattern of chronic pulmonary melioidosis can mimic pulmonary tuberculosis or lung cancer.

Herein, we report a 67-year-old man with a history of diabetes mellitus who presented with productive cough and loss of body weight. The radiographic finding was a mass at the right hilum with mediastinal lymphadenopathy. A detailed survey revealed no malignancy or pulmonary tuberculosis. The patient was admitted for fever 2 months later. Blood cultures yielded *Burkholderia pseudomallei*. Antibiotics with intravenous ceftazidime for 2 weeks and imipenem/cilastatin for 2 weeks were prescribed. He was discharged 1 month later with good improvement of clinical symptoms and chest x-ray findings. Oral tetracycline was continued for 6 months. ***(Thorac Med 2014; 29: 46-51)***

Key words: melioidosis, *Burkholderia pseudomallei*, mediastinal lymphadenopathy

Introduction

Melioidosis, caused by the Gram-negative bacterium *Burkholderia pseudomallei* (*B. pseudomallei*), is highly endemic to northern Australia and northeast Thailand [1]. An outbreak of melioidosis was identified in southern Taiwan after a rainy season in 2005 [2]. The disease may be localized or disseminated and virtually any organ system can be affected. There are diverse clinical manifestations including pneumonia (51%), genitourinary infection (14%), skin infection (13%), septic arthritis/osteomyelitis (4%), and neurologic melioidosis (3%) [3]. The clinical features of pulmonary melioidosis can be acute, subacute or chronic [4]. Chronic pulmonary melioidosis rarely has the radiographic pattern of lung mass and mediastinal lymphadenopathy.

Herein, we report a man with poorly-con-

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trolled diabetes who presented with a lung mass at the right hilum and mediastinal lymphadenopathy. His radiographic findings mimicked lung cancer.

Case Report

A 67-year-old man with a history of heavy smoking and type 2 diabetes mellitus with poor control presented with productive cough and whitish sputum for 1 month. The accompanying manifestations included malaise, poor appetite and body weight loss of about 4 kg in 1 month. He was a farmer and lived in southern Taiwan. He denied any travel history in the past year. Physical examination was unremarkable, and clubbing of the fingers was not detected. Laboratory test results, including urinalysis, complete blood counts, and liver and renal function, were normal. Chest radiography revealed a mass lesion with an irregular border at the right hilum and a widened mediastinum (Figure 1A). Contrast computed tomography (CT) scan of the chest showed a mass lesion about 3 cm in diameter at the right hilum, with mildly irregular margination and multiple mediastinal lymphadenopathy (Figure 2). Bronchoscopy showed only swelling mucosa with a bulging lesion at the right upper lobe. However, the pathology results of the transbronchial biopsy revealed fibrinous exudate with chronic inflammation and were negative for malignant cells. We performed endobronchial ultrasound bronchoscopy with transbronchial needle aspiration for paratracheal lymphadenopathy. The pathology report showed granulomatous inflammation. The results of tuberculous cultures from the sputum, bronchoalveolar lavage and biopsy sample were all negative. Ordinary cultures from the sputum and bronchoalveolar lavage revealed no positive finding, as well. The patient was then discharged and received regular follow-up at our outpatient department.

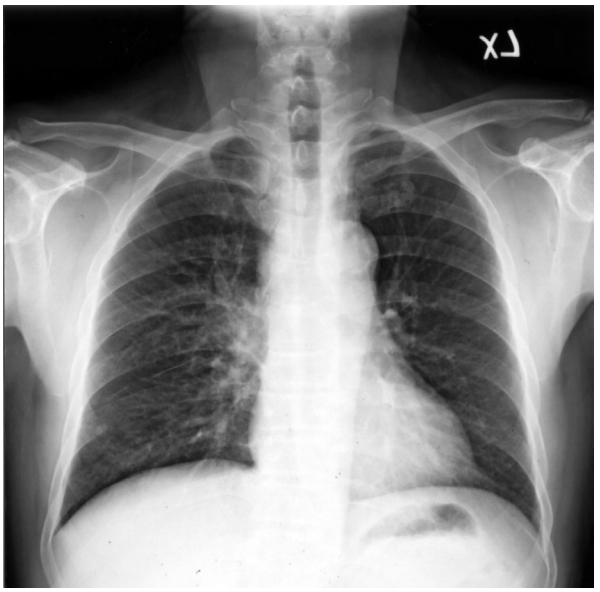

Fig. 1A. Initial chest x-ray revealed a mass lesion with an irregular border at the right hilum and a widened mediastinum.

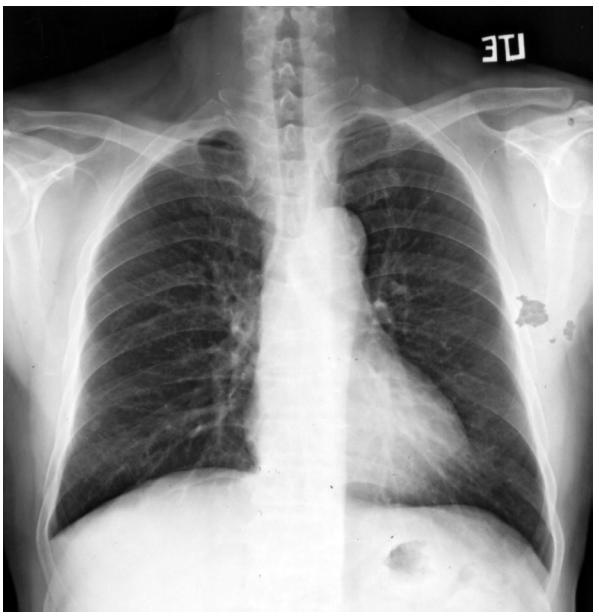

Fig. 1B. One week after discharge, chest x-ray revealed complete resolution of the right hilar mass and subsidence of the widened mediastinum.

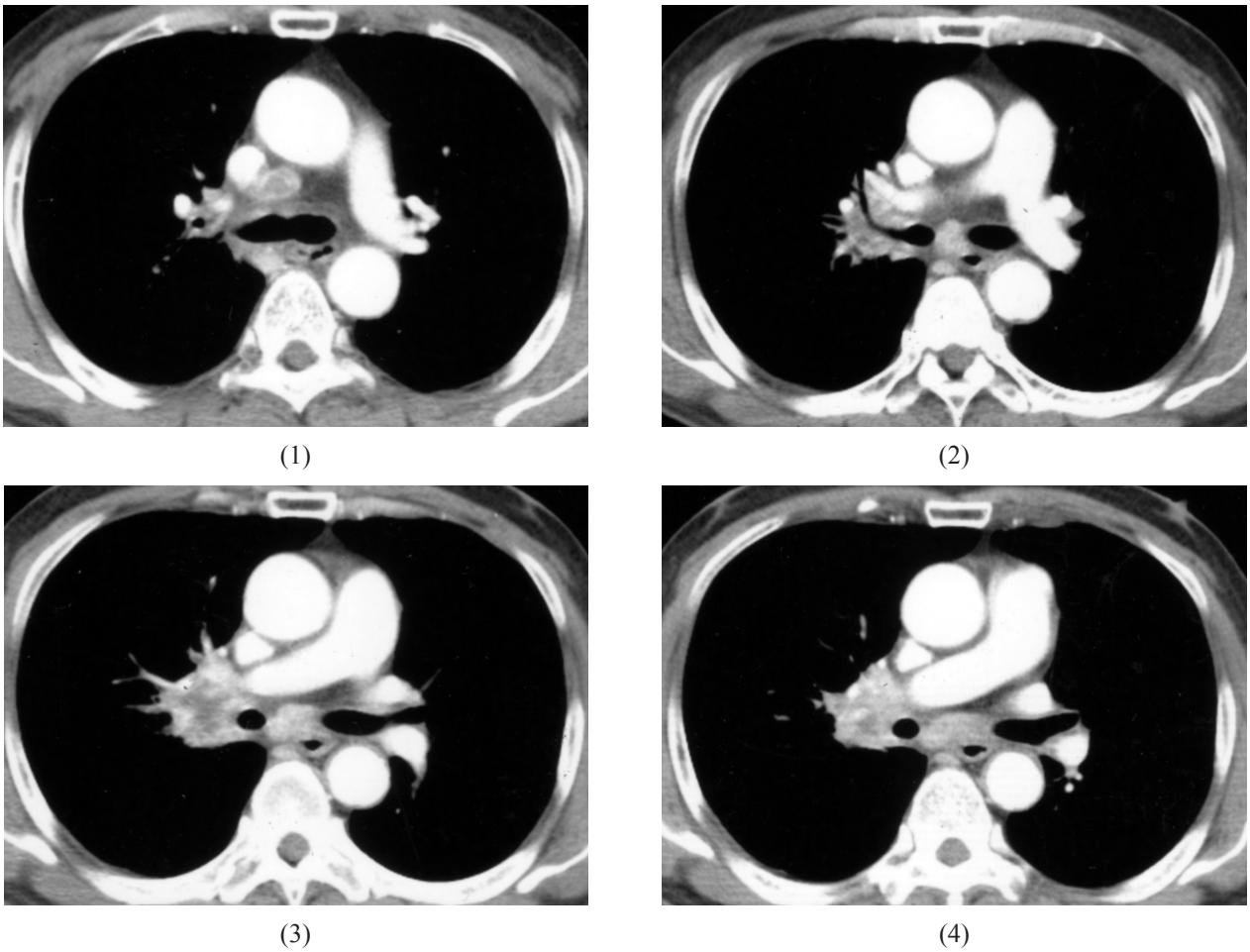

Fig. 2. Chest CT scan series showed a mass lesion about 3 cm in diameter in the right hilum, with mildly irregular margination and multiple lymphadenopathies in the right paratracheal, pretracheal and subcarinal regions of the mediastinum, as well as the right parahilar area.

Two months later, he visited our hospital complaining of fever and chills for 2 days. Neither skin wound nor abdominal discomfort was noted. He still had the symptom of productive cough. Physical examination was unremarkable except for tachycardia. On admission, his vital signs were: temperature 39.5°C, pulse 128/minute, respiration 20/minute, and blood pressure 140/92 mmHg. Chest x-ray did not reveal a new active lesion. The right hilar mass and widened mediastinum were still noted. Laboratory data showed a white cell count of 9000/mm^3, C-reactive protein of 22.25 mg/dl, erythrocyte sedimentation rate of 60 mm/hour, hyperglycemia (blood glucose level of 351 mg/dl), and glycated hemoglobin 9.7%. Pelvic CT scan did not reveal an abscess formation of the internal organs. Gram's stain of the blood isolated Gram-negative rods. Therefore, sepsis of an unknown origin was suspected. Empiric antibiotics with ciprofloxacin were used, but the fever did not subside. Three days later, 4 sets of blood cultures yielded *B. pseudomallei*. The *B. pseudomallei* were sensitive to ceftazidime and

imipenem, but resistant to trimethoprim-sulfamethoxazole (TMP-SMX). Antibiotic treatment was immediately shifted to intravenous ceftazidime 2 g every 8 hours for 14 days. His fever was relieved on the second day of ceftazidime usage. Because the repeated chest x-ray findings did not resolve completely, we prescribed intravenous imipenem/cilastatin for another 14 days. The patient was discharged after 30 days of hospitalization. One week later, the chest x-ray showed complete resolution of the right hilar lesion and subsidence of the widened mediastinum (Figure 1B). Oral tetracycline was continued for 6 months.

Discussion

Melioidosis, a potentially fatal disease, is transmitted by ingestion, inhalation or percutaneous inoculation [1]. Diabetes mellitus is the most common underlying disease. Other risk factors for melioidosis include heavy alcohol use, chronic lung disease, chronic renal disease, and immunosuppression [3]. Patients with these risk factors more frequently present with either primary pneumonia or bacteremia [3]. Our patient worked as a farmer in southern Taiwan, so he may have more easily come in contact with soil or water contaminated with *B. pseudomallei*. A survey of the prevalence of *B. pseudomallei* in soil in Taiwan showed a more frequent isolation rate from the soil in southern Taiwan than in central or northern Taiwan [5]. The patient also had a greater likelihood of infection because of his age, poorly-controlled diabetes and chronic lung disease.

The diagnostic "gold standard" is the isolation of *B. pseudomallei* from any sample, such as blood, urine, sputum, or pus. The serodiagnostic test by indirect hemagglutination assay is poorly standardized worldwide and is neither sensitive nor specific in highly endemic areas [6]. Leukocytosis and high C-reactive protein are common, but they do not reflect the severity of the disease. The diagnostic rates from sputum culture and blood culture in patients with chronic pulmonary melioidosis were 22% and 37.5%, respectively [7]. Our patient was diagnosed by positive blood culture, but the cultures from sputum and bronchoalveolar lavage were negative. The application of polymerase chain reaction for direct detection of the specific sequence in bronchoalveolar lavage may be helpful in diagnosing melioidosis [8].

Pulmonary disease is the most common clinical manifestation of melioidosis. Acute pneumonia with septic shock resulted in a mortality rate as high as 49% in melioidotic cases [3]. Acute pneumonia has the symptoms of high fever, dyspnea, pleuritic chest pain, or hemoptysis. The acute chest radiographic findings include alveolar infiltration in single or multiple lobes, nodular densities by hematogenous spread, and lung abscess [9]. Upper-lobe involvement is common [10]. The chronic form, which accounts for less than 9% of cases of pulmonary melioidosis, has more diverse patterns in the lungs, including cavity formation, calcified node, mass-like lesion, atelectasis, lung abscess, or hilar adenopathy [7]. Pleural effusion occurs in approximately 15% of cases [7]. Both lung mass and mediastinal lymphadenopathy are rarely seen; they are found in chronic melioidosis more frequently. The coexistence of mediastinal lymphadenopathy, lung abscess, atelectasis and lung mass is possible. The radiographic findings can resemble tuberculosis or lung cancer. Therefore, infection with *B. pseudomallei* is a differential diagnosis if a patient is suspected of having lung cancer with-

out a positive pathologic report after detailed survey and repeated biopsies.

The treatment for melioidosis includes intravenous ceftazidime, meropenem, or imipenem for at least 10 to 14 days, followed by oral eradication therapy with TMP-SMX for 3 to 6 months [1]. Since the patient was resistant to TMP-SMX, we administered tetracycline for 6 months. The rate of resistance to TMP-SMX was reported to be approximately 13% for isolates in Thailand [11]. In Taiwan, the antibiotics for melioidosis, including ceftazidime, meropenem, imipenem, and TMP-SMX, are almost all effective [2].

In conclusion, subacute or chronic pulmonary melioidosis presents with diverse clinical symptoms and radiographic patterns. Although lung mass and mediastinal lymphadenitis are seldom seen, melioidosis can mimic tuberculosis or lung cancer. The diagnosis of melioidosis is achieved by isolation of *B. pseudomallei* from any clinical sample. Drug resistance to TMP-SMX is rarely seen in Taiwan. With adequate antimicrobial therapy, clinical symptoms and chest radiographic findings can both show dramatic improvement.

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類鼻疽合併肺部腫瘤及縱膈腔淋巴結炎：病例報告

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類鼻疽（melioidosis）是由類鼻疽伯克氏菌（*Burkholderia pseudomallei*）所造成的疾病，且多盛行於澳洲北部及泰國東北部。台灣南部在2005年的雨季時曾出現群聚感染的病患。肺部是最常被感染的器官。急性肺部感染多以肺炎表現。亞急性和慢性感染則有多樣的肺部變化，像是肺膿瘍、肺開洞、肺塌陷以及鈣化結節。縱膈腔淋巴結病變是極少見的肺部變化。因此，慢性肺部感染在影像學上可能會和肺結核或是肺癌混淆。

在此，我們報告一位67歲有糖尿病史的男性，表現為咳嗽有痰和體重減輕。影像學上發現右側肺門的肺部腫瘤合併縱膈腔淋巴結病變，經檢查無惡性細胞或是肺結核的可能。病人於兩個月後因發燒再次入院，血液培養發現感染類鼻疽伯克氏菌，經使用靜脈注射抗生素ceftazidime兩週及imipenem/cilastatin兩週，病人1個月後，在臨床症狀及胸部X光改善下出院。出院後繼續使用6個月的口服抗生素tetracycline。*(胸腔醫學* ***2014; 29: 46-51)***

關鍵詞：類鼻疽，類鼻疽伯克氏菌（*Burkholderia pseudomallei*），縱膈腔淋巴結病變

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Primary Angiomyolipoma with Coincident Adenocarcinoma of the Lung

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Extrarenal angiomyolipomas are benign tumors that have been reported in several different organs including the liver, oral cavity and skin, but rarely in the thorax. We herein report the clinical and radiographic presentation, and pathological data of a primary angiomyolipoma of the lung in a 46-year-old female. In addition to the primary angiomyolipoma, an adenocarcinoma was incidentally found during surgery. No evidence of tuberous sclerosis or renal angiomyolipoma was noted in this patient. Previous cases of primary angiomyolipoma of the lung reported in the literature are also reviewed. ***(Thorac Med 2014; 29: 52-57)***

Key words: angiomyolipoma, adenocarcinoma, lung

Introduction

Angiomyolipomas are rare mesenchymal tumors that are usually found in the kidney, and are composed of an admixture of fat, smooth muscle, and blood vessels. Reports indicate that approximately half of renal angiomyolipomas occur in patients with tuberous sclerosis, while the others occur sporadically and are not associated with other conditions. Extrarenal angiomyolipomas are even rarer, and have been described in the liver, oral cavity, skin, and lungs [1-5]. We herein report a case of pulmonary angiomyolipoma with coincident adenocarcinoma of the lung, which we believe is the first case in the literature. The clinical and histological presentations of patients with pulmonary angiomyolipoma reported in the literature were also collected and reviewed.

Case Report

A 46-year-old female was referred to Taipei Veterans General Hospital, Taipei, Taiwan, because of an incidental finding of a small nodule in the upper lobe of the left lung revealed on chest X-ray taken during a routine physical check-up. Chest computed tomography (CT) showed a well-circumscribed nodule, approximately 0.9 × 0.7 cm in size (Figure 1A). No en-

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larged lymph nodes were found in the bilateral neck and mediastinum, and no focal nodular lesions were noted in the visible portions of the kidneys, adrenal glands, liver, gallbladder, spleen, and pancreas. She underwent a left mini-thoracotomy and wedge resection of the left upper lobe for excision of the tumor. The frozen section revealed the lesion was benign. Another palpable small nodule in the lower lobe of the left lung, about 3 mm in diameter, was also removed by wedge resection. The postoperative course was uneventful, and no tumor recurrence was noted 24 months after surgery.

Final results of the histopathological examination revealed the lesion in the left upper lobe was an angiomyolipoma, and the lesion in the left lower lobe was adenocarcinoma of the lung. The tumor in the left upper lobe was well-demarcated, rubbery, tan-yellow in color and measured 0.9 × 0.8 × 0.6 cm (Figure 1B). Histological examination results were consistent with an angiomyolipoma; the lesion was composed of a mixture of spindle cells, adipocytes, and blood vessels (Figure 1C, D). The tumor cells were immunoreactive for S100, SMA, HMB-45, and focal CD68, and negative for cytokeratin (Figure 1E). The nodule in the lower lobe measured 0.3 × 0.3 × 0.2 cm in size and was consistent with adenocarcinoma of the lung with acinar growth patterns and moderate differentiation (Figure 1F). No angiolymphatic or perineural invasion was noted.

Discussion

Most angiomyolipomas occur in the kidney, and approximately 50% of cases are associated with tuberous sclerosis. A relationship between renal angiomyolipoma and lymphangioleiomyomatosis in females has also been reported. Extrarenal angiomyolipomas are found most frequently in the liver. Primary pulmonary angiomyolipoma is extremely rare. Only 5 cases of primary pulmonary angiomyolipomas have been reported in the literature, including a non-English-language case report. The clinical data of these 5 cases and the present case are summarized in Table 1.

We believe that the present case is the first case with coincident adenocarcinoma reported in the literature. Papla *et al*. [3] stated that preoperative diagnosis of angiomyolipomas using fine needle aspiration biopsy is important; however, in our case a preoperative biopsy was not performed. During surgery, in addition to resection of the pulmonary angiomyolipoma in the left upper lobe, a thorough inspection and palpation of the left lung was also performed. Another small nodule in the left lower lobe was palpated and removed, and proved to be adenocarcinoma. The type of adequate management for stage IA lung cancer with a tumor size less than 1 cm has been debated. Nakamura *et al*. reported that survival after limited resection of stage I lung cancer was comparable to that after lobectomy [6]. Kates *et al*. concluded that in stage I lung cancer less than 1 cm in size, limited resection and lobectomy may lead to survival rates equivalent to those of patients with stage I non-small cell lung cancer tumors less than 1 cm in size [7]. In this case, no further resection was attempted. The patient remained free of disease 2 years after operation.

The first case of pulmonary angiomyolipoma in the literature was reported by Guinee *et al*. in 1995 [1]. However, unlike that case, immunohistochemical staining for HMB-45 was positive in our case, similar to the case reported by Gloeckner-Hofmann *et al*. in 2000 [4]. HMB-45 expression has been identified in the

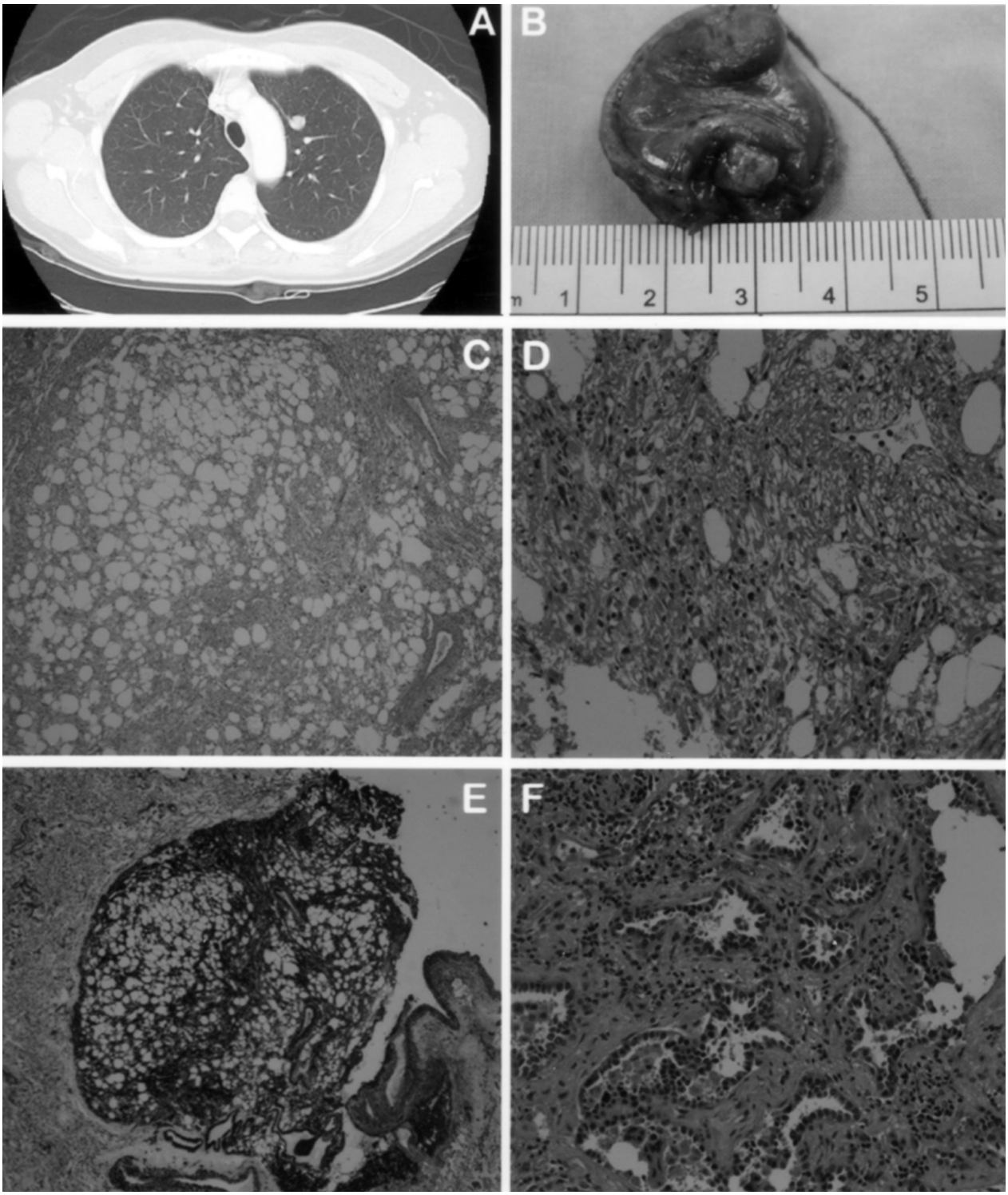

Fig. 1. (A) Chest computed tomography showed a well-defined nodule, about 1 cm in size, in the upper lobe of the left lung. (B) The tumor was well-demarcated, rubbery, tan-yellow in color, and measured 0.9 × 0.8 × 0.6 cm after resection. (C,D) The tumor was consistent with an angiomyolipoma, and was composed of a mixture of spindle cells, adipocytes, and blood vessels (hematoxylin-eosin x40, x100, respectively). (E) The tumor cells were positive for HMB-45. (F) Coincident adenocarcinoma in the lower lobe of the left lung showing an acinar growth pattern and moderate differentiation (hematoxylin-eosin x200).

Table 1. Summary of the clinical data of patients with primary angiomyolipoma of the lung reported in the literature and the present case

Patient	Age (years)	Sex	Location	Tumor diameter (cm)	Operative procedure	Immunohistochemical staining	Comment
Guinee *et al*. [1]	68	F	LLL	2.0	Wedge resection	HMB-45(-)	None
Ito *et al*. [2]	67	M	LLL	2.5	Wedge resection	HMB-45(-)	None
Palpa *et al*. [3]	28	F	LUL	2.0	Pneumonectomy	HMB-45(-)	None
Gloeckner-Hofmann *et al*. [4]	48	M	LLL	9.5	Lobectomy	HMB-45(+), S-100(+)	None
Marcheix *et al*. [5]	63	F	RLL	2.3	Lobectomy	HMB-45(-)	None
Present case	46	F	LUL	0.9	Wedge resection	HMB-45(+), S-100(+)	Coincident adenocarcinoma of the lung

LLL, left lower lobe; LUL, left upper lobe; RLL, right lower lobe.

smooth muscle cells of renal and hepatic angiomyolipomas associated with tuberous sclerosis. The 4 other reported cases of pulmonary angiomyolipomas were all negative for HMB-45. Four of the reported cases of primary pulmonary angiomyolipomas were in females who varied in age from 28 to 68 years. The tumor location was predominantly in the left lung, and 4 were in the left lower lobe. The size of the lesions ranged from 0.9 to 9.5 cm at the greatest diameter. All patients underwent tumor resection, and the operative procedures included wedge resection, lobectomy, and pneumonectomy. No tumor recurrence was reported, and none of the cases were associated with tuberous sclerosis. Some authors have reported that regional lymph node involvement may be present with renal angiomyolipomas, and have suggested sampling of the regional lymph nodes. Data regarding lymph node involvement was not available in the reported cases of pulmonary angiomyolipomas.

In summary, primary pulmonary angiomyolipoma is extremely rare. The present case is the first reported case of primary pulmonary angiomyolipoma with coincident adenocarcinoma of the lung. An analysis of all 6 cases reported in the literature showed that primary pulmonary angiomyolipoma is solitary, noninvasive, and not associated with tuberous sclerosis. Surgical resection for primary pulmonary angiomyolipomas can be performed with excellent outcomes.

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肺部原發性血管肌脂瘤合併肺腺癌－案例報告

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發生在腎臟以外的原發性的血管肌脂瘤，大多為良性的腫瘤，在過去文獻中有被報告過發生於肝臟、口腔、皮膚，但僅有極少數案例發現於胸腔內。這篇案例報告介紹了一名四十六歲女性於健康檢查發現左上肺葉有一 0.9 × 0.7 公分結節，此外在腎臟、腎上腺、肝臟及膽囊均無發現異常，頸部及縱膈腔淋巴結也沒有異常增大的情形。患者接受手術切除左上肺病兆，術中冰凍切片顯示為良性，術中於左下肺觸診到另一處約 0.3 公分大小之病兆亦予以切除，術後患者順利出院，於兩年追蹤期間也沒有任何腫瘤復發跡象。最後病理組織報告顯示左上肺病兆為血管肌脂瘤，而左下肺病兆為肺腺癌。

大多數血管肌脂瘤發生於腎臟，約有一半的患者可能合併結節性硬化症的病史。腎臟以外原發血管肌脂瘤最常發生在肝臟，而發生在肺部的案例極少，根據文獻上記載只有五例原發性血管肌脂瘤被報告過。我們這位患者是第一位合併有肺腺癌發生的患者。過去報告過的患者多數為女性，腫瘤大小不一，最小直徑有 0.9 公分大，到最大有 9.5 公分大；發生位置有四位是發生於左下肺葉；患者診斷當時的年紀分布也從二十八歲到六十八歲不等；病理免疫組織生化染色發現 HMB-45 多為陰性，而我們的案例為陽性。所有患者皆接受手術切除，沒有任何腫瘤復發的情形被報告過，所有患者中，沒有任何人有結節硬化症的病史。

肺部原發性血管肌脂瘤是極少見的，我們報告的這案例除了血管肌脂瘤外，還合併發現肺腺癌。分析目前發現的案例中，可知道肺部原發性血管肌脂瘤常以單一、非侵襲性的病兆來表現，與結節性硬化症沒有相關，治療還是以手術切除為主，且預後通常都很好。*(胸腔醫學* ***2014; 29: 52-57)***

關鍵詞：血管肌脂瘤，肺腺癌，肺

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Bronchial Diverticula in a Patient with Asthma – A Case Report and Literature Review

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Bronchial diverticula are sometimes asymptomatic and are widely under-diagnosed; they are often incidentally found in patients who have undergone bronchoscopy or chest computed tomography (CT). We reported the case of a 59-year-old female with a history of asthma who presented to our outpatient department with chronic productive cough and intermittent hemoptysis for over 2 months. Chest CT scan and bronchoscopy exam showed multiple bronchial diverticula at the subcarinal region and the left main bronchus. She was treated with antitussive drugs and inhaled budesonide/formoterol combination therapy, which improved her symptoms. This was a rare case, with numerous diverticula (more than 10) located at the subcarinal region and the left main bronchus. Although clinical diagnosis of bronchial diverticula can be delayed due to the absence of symptoms, no specific treatment or intervention is necessary. ***(Thorac Med 2014; 29: 58-62)***

Key words: asthma, bronchial diverticula

Introduction

Diverticulum (plural: diverticula) is a medical term for an out-pouching of a hollow (or fluid-filled) structure in the body. The most common diverticular disease is colon diverticulum. Over 65% of older patients (age >65) have colon diverticula [1]. Bronchial diverticula, on the other hand, are rare and seldom diagnosed by clinical physicians because most patients have limited symptoms, other than a nonspecific chronic cough. Therefore, this disease is often incidentally found by computed tomography (CT) scan or bronchoscopy [2]. The presence of bronchial diverticula might induce turbulence of airflow and promote the attachment of bacteria and viruses to ciliated epithelial cells, resulting in local recurrent inflammation, which consequently causes productive cough or blood-tinged sputum [3].

Case Report

A 59-year-old, non-smoking female presented to the hospital with a 2-month history of worsening cough and mucoid sputum production, as well as a small amount of blood-tinged sputum. She complained of cough, dyspnea

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on exertion, and several asthma exacerbations, none of which required hospitalization in the previous 6 months. Her medical history included atopy and asthma since childhood, and cough with several episodes of hemoptysis over the past decades. Her medication included an anti-histamine agent (ebastine) and oral beta-2 agonist (procaterol). Her spirometry reading during periods of stability showed a normal forced vital capacity (FVC) of 2.8 L (99% predicted), a forced expiratory volume in one second (FEV_1) of 1.84 L (78% predicted), and an FEV_1/FVC of 66% predicted. When she inhaled a bronchodilator, the FEV_1 increased 19%.

Physical examination revealed pink conjunctiva and clear breathing sounds in both lung fields, and the cardiovascular, abdominal, and neurological examinations were normal. The chest radiograph was also normal. A 16-detector multislice CT (SOMATOM® Sensation 16, Definition Flash, Siemens Healthcare, Forchheim, Germany) scan of the chest revealed several out-pouching air cysts at the subcarinal region (Figure 1A) and spotty air foci at the left main bronchus (Figure 1B). Bronchoscopy showed multiple small bronchial diverticula, located in a linear fashion between cartilages at the left main bronchus (Figure 2). Mild bronchial mucosa congestion without bleeding or oozing was observed. The patient was diagnosed with bronchial diverticula and treated with antitussive drugs, tranexamic acid and inhaled budesonide/formoterol. For the next 3 months, the patient's symptoms of cough and sputum production improved, and there was no more hemoptysis.

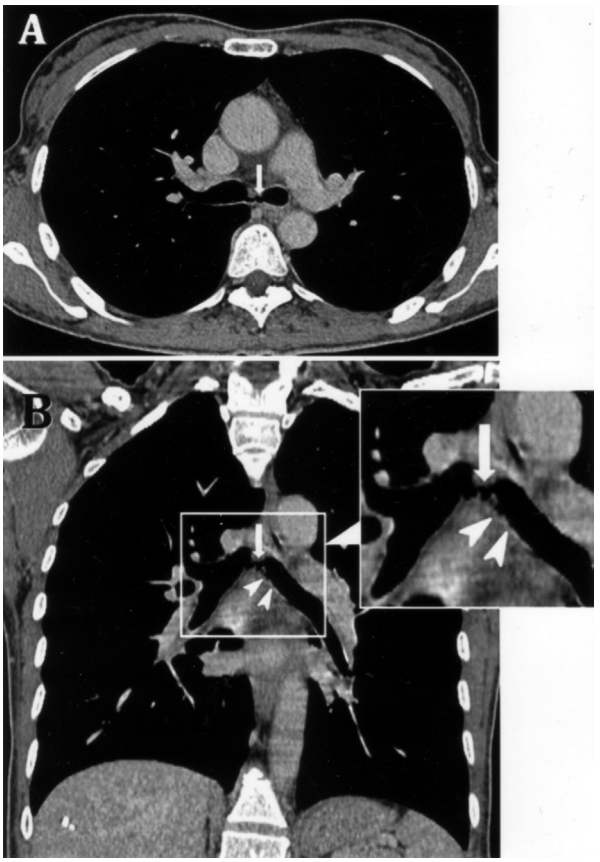

Fig. 1. Chest CT scan (with contrast) of a 59-year-old female with bronchial diverticula. (A) Transaxial view of air cysts pouching out from the left and right main bronchus mucosa to the subcarinal region (arrow). (B) Coronal view of air cysts at the carina area (arrow) and spotty air foci at the left main bronchus (arrowhead).

Discussion

Bronchial diverticula are sometimes asymptomatic and are widely under-diagnosed; they are often incidentally found in patients who have undergone bronchoscopy or chest CT [2,4]. Some cases have been reported previously, but the majority of them had a single diverticulum, with less than 1% of patients having 5 or more diverticula [5]. To the best of our knowledge, numerous diverticula (more than 10) located at the subcarinal region and the left main bronchus in an asthmatic patient has never been reported.

The rapid technical advances in chest CT over the past few years have assisted physicians in gaining access to more anatomic details, and allowed small pathologic structures, such as

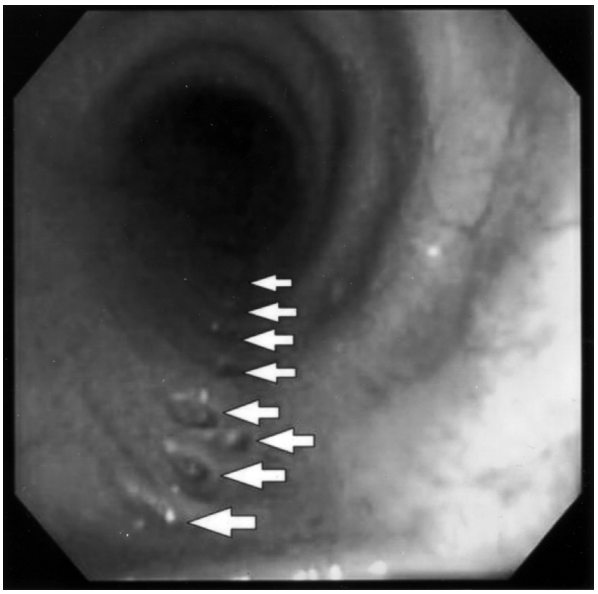

Fig. 2. Bronchoscopy shows multiple small bronchial diverticula (arrow), located in a linear fashion between cartilages at the left main bronchus.

bronchial diverticula, to become visible [6-8]. In a recent report of 1122 patients with a smoking history [5], bronchial diverticula were found in 242 patients (22%) using chest CT scans. Of these 242 patients, 64% had a single diverticulum, and the mean number of diverticula per patient was 1.65. The bronchial diverticula ranged in size from 1 to 8 mm (mean, 1.56 mm) and were located most frequently at the subcarinal region (59%), followed by the left main bronchus (29%).

The causes of bronchial diverticula are not clear. One study [7] reported that bronchial diverticula could be seen in patients with chronic obstructive pulmonary disease (COPD), bronchiectasis, or asthma. Patients with these diseases had the common symptom of chronic cough, which might induce elevation of intrabronchial pressure, leading to a mucosal herniation through the weakened portion of the bronchial wall [8-9]. On the other hand, bronchial diverticula might in turn induce cough. It has been hypothesized that the presence of bronchial diverticula might induce turbulence of airflow and promote the attachment of bacteria and viruses to ciliated epithelial cells [3]. This might result in recurrent local mucosal inflammation, which would consequently cause productive cough and blood-tinged sputum.

Published information on any direct relationship between bronchial diverticula and respiratory diseases is still limited. Goo *et al*. [10] reported that the presence of diverticula on CT could be a sign of obstructive lung disease. In contrast, Polverosi *et al*. [8] maintained that no clear cause and effect relationship existed between COPD and tracheobronchial diverticula. Only smoking was thought to be a risk factor that increased the incidence of bronchial diverticula formation [5,11].

Determining the best treatment approach for bronchial diverticula is still a matter of controversy, although the majority of cases do not require any specific intervention or treatment. In the present case, chronic cough not only arose from the diverticula themselves, but also indicated a partly controlled asthma. The recommended therapies were inhaled glucocorticoid (ICS) and a long-acting beta-agonist (LABA). These therapies improved the patient's symptoms of cough and sputum production.

Despite the possible delay in the clinical diagnosis of bronchial diverticula, due to its rarity and the absence of symptoms in some cases, and the fact that specific treatment or intervention is not necessary, outcomes are usually very good.

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氣喘合併支氣管憩室－病例報告與文獻回顧

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支氣管憩室通常是沒症狀而且偶然在支氣管鏡或胸部斷層掃瞄中發現，因此臨床上常常沒有被診斷出來。我們報告一位過去有氣喘病史的五十九歲女性，因為持續慢性咳嗽合併有輕微的血痰兩個月而來門診求診，安排胸部電腦斷層掃瞄跟支氣管鏡檢查發現在氣管隆凸下和左主支氣管黏膜有多個支氣管憩室。我們使用止咳藥，吸入性類固醇及長效型支氣管擴張劑治療後病人的症狀獲得改善。這個病例是一個罕見病例，在氣管隆凸下和左主支氣管發現超過十個支氣管憩室。雖然支氣管憩室常常因為沒有症狀被延遲診斷，臨床上並不需要特殊的治療。*(胸腔醫學 **2014; 29: 58-62**)*

關鍵詞：氣喘，支氣管憩室

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