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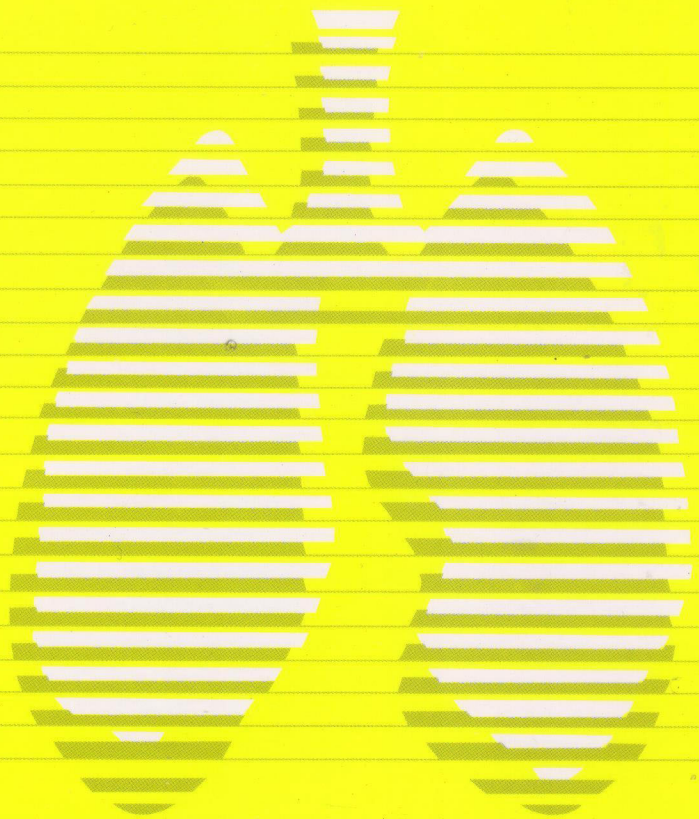

台灣胸腔暨重症加護醫學會

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病例報告

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Case Reports

Disseminated *Mycobacterium Avium Complex* Infection in a Non-HIV-infected Patient: A Case Report and Literature Review

Chor-Shen Lim, Chao-Chi Ho, Chong-Jen Yu

Disseminated *Mycobacterium-avium complex* infection (MAC) is rare in patients without acquired immunodeficiency syndrome (AIDS). Recent studies have shown that specific genetic defects have been associated with the development of disseminated nontuberculous mycobacteria infection in non-human immunodeficiency virus (HIV)-infected subjects. These genetic defects might present as susceptibility to intracellular pathogens, such as Salmonella species or severe infections due to otherwise poorly pathogenic mycobacteria. We herein report a 78-year-old non-HIV-infected man with history of pulmonary *Mycobacterium kansasii* and non-typhoidal Salmonella bacteremia, who presented with acute exacerbation of chronic obstructive pulmonary disease (COPD) and finally developed disseminated MAC infection after prolonged use of steroid. This patient subsequently died of multi-organ failure. ***(Thorac Med 2010; 25: 1-6)***

Key words: disseminated NTM infection, non-HIV, salmonellosis, steroid

Introduction

Disseminated *Mycobacterium-avium-complex* (MAC) is a disease in which *M. avium* is isolated from blood or bone marrow, from a liver biopsy specimen, or from specimens from 2 or more non-contiguous sites such as the respiratory tract, lymph node, ascites, pleural effusion, pericardial effusion, joint fluid and cerebral spinal fluid. It is common in AIDS patients and frequently occurs after the CD4+ T-lymphocyte number has fallen below 50/μL. However, it is extremely rare in non-HIV-infected patients. We herein present the case of a 78-year-old non-HIV-infected man with disseminated MAC infection and review what is currently known about this disease.

Case Report

A 78-year-old Taiwanese male ex-glass factory worker from Taoyuan was admitted to our hospital after 2 days of fever and dyspnea. He smoked 150 packs/year, and was using inhaled fluticasone/salmeterol (generic) for the control of severe chronic obstructive pulmonary dis-

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ease (COPD). One year ago, he was noted to have pulmonary *M. kansasii* infection presenting as right middle lobe consolidation on the chest radiograph. He was given isoniazid, rifampicin and ethambutol, and achieved sputum conversion 1 month after the therapy. However, he failed to continue the medications after 4 months of therapy due to generalized skin rash that was thought to be the side effect of the drugs. He was admitted once for non-typhoidal Salmonella bacteremia and was discharged after 14 days of antibiotics treatment.

On hospital admission, the patient was febrile (temperature, 39°C), and in slight respiratory distress. He was normotensive and slightly tachycardic (pulse, 10^3 beats/min). Oxygen saturation was 96% in ambient air. A physical examination demonstrated diffuse wheezing without bilateral leg edema. The WBC count was 25.8×10^3 cells/μL, the hemoglobin concentration was 8.6 g/dL, and the platelet count was 429×10^3 cells/μL. Urinalysis showed no pyuria, casts or RBCs. The admission chest radiography showed no active lesions.

He was given systemic methylprednisolone (generic), 120 mg daily, inhaled ipratropium bromide (generic), inhaled albuterol (generic), intravenous amoxicillin/clavulanate potassium (generic) and non-invasive positive pressure ventilation (NIPPV) for the treatment of acute exacerbation of COPD. Although the patient improved symptomatically and the dosage of systemic steroids was tapered, he remained NIPPV-dependent.

Thirteen weeks after admission, he was isolated for positive sputum acid-fast bacilli smears. Isoniazid, rifampicin, ethambutol and pyrazinamide were initiated. However, the same sputum sample was negative for *Mycobacterium tuberculosis* using polymerase chain reaction. One week after receiving anti-tuberculous treatment, the patient's condition deteriorated, with dyspnea, altered mental status, increasing infiltrates on chest X-ray and a marked elevation of the serum alkaline phosphatase level (2256 U/L). He was intubated for hypoxic respiratory failure. Chest CT disclosed consolidations along the bronchovascular bundle (Figure 1). Bone marrow biopsy revealed non-caseating granulomatous inflammation (Figure 2) with the presence of acid-fast bacilli. PAS staining was negative (Figure 3). Cultures of the sputum, blood, cerebrospinal fluid and bone marrow

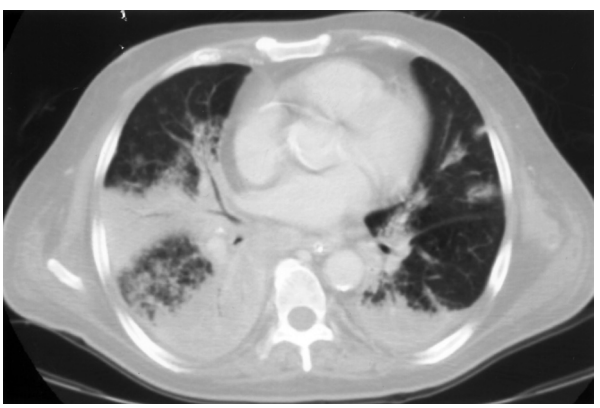

Fig. 1. Chest CT showed diffuse consolidation along bronchovascular bundles of the bilateral lung.

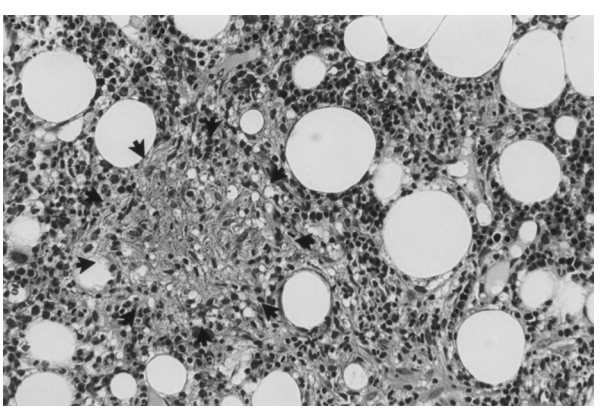

Fig. 2. Bone marrow biopsy showed hypercellularity with hemopoietic components. Multiple foci of noncaseating granulomatous inflammation were noted (arrows).

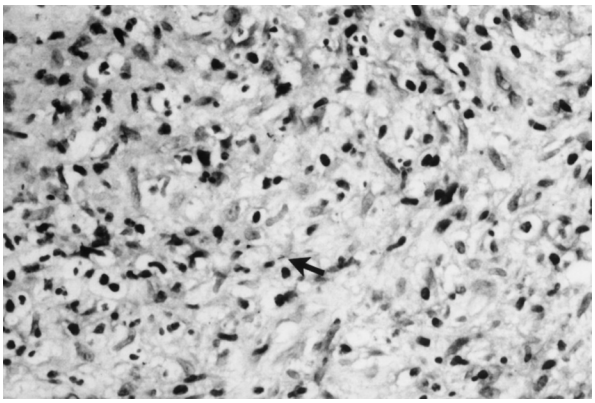

Fig. 3. PAS stain was negative. Some acid-fast-positive bacilli were demonstrated by acid-fast stain (as shown by arrow).

were positive for MAC. Repeated HIV serology was negative. After 15 days of anti-tuberculous treatment, the medications were replaced by clarithromycin (1000 mg/day), ethambutol (15 mg/kg/day) and rifabutin (150-350 mg/day) for the treatment of disseminated MAC infection. The patient subsequently died of multi-organ failure 28 days after adequate anti-MAC treatment.

Discussion

Disseminated MAC is very rare in patients without advanced HIV disease. It is also very rare in non-HIV patients with any form of immunosuppression [1]. Recent studies have shown that MAC is a definite manifestation of immunologic defects caused by defects in the interferon gamma/interleukin 12 (IFN-γ/IL-12) pathway genes [2].

Mycobacteria and salmonellae are intracellular pathogens. Human host immunity against these pathogens is dependent on an effective cell-mediated immune response [3]. Dendritic cells and macrophages are the major phagocyte populations that recognise invading bacteria by means of an innate pattern. Phagocysed bacteria induce early production of IL-12 from specific phagocyte subsets. In the early phase of the immune response, IL-12 plays a key part in driving the production of IFN-γ from natural killer (NK) cells and T-helper type 1 (Th1) cells. These cells are a major source of IFN-γ during the adaptive immune response and are necessary for the control of the chronic phase of infection [4]. The precise context in which human IFN-γ has activity against mycobacteria remains unclear. IFN-γ was able to activate antimycobacterial microbicidal mechanisms in murine macrophages [5]. Recently, patients with severe infections due to otherwise poorly pathogenic mycobacteria, such as non-tuberculous mycobacteria or Salmonella species, have been identified. Many of these patients were unable to produce or respond to IFN-γ, due to deleterious mutations in genes that encode major proteins in the IFN-γ/IL-12 pathway [6]. In the present case, genetic analysis was not performed due to family refusal. Nevertheless, with a history of high susceptibility to intracellular pathogens, we believed that the patient might have suffered from a certain level of genetic defects in the aforementioned pathway.

Previous studies have shown that disseminated MAC infection had a strong correlation with the usage of steroid [7]. Steroid was shown to have a suppressive action on the production of IL-12 via inhibition of dendritic cell functions or the immune response of Th1 cells [8-9]. However, it is still rare to see disseminated MAC infection in patients without any form of immunosuppression. We presumed that the rarity of this situation was probably due to a relatively seldom seen genetic predisposition added to an acquired predisposition.

Recent studies have shown that the severity of the defect in the IFN-γ/IL-12 pathway

correlates with the severity of the clinical and immunological phenotypes of the studied patients [10]. In partial IFN-γ receptor deficiency, residual IFN-γ signalling, IL-12 receptor deficiency and low residual IFN-γ production can account for the remaining low degree of immunity to mycobacteria [11-12]. It is clear that this remaining low degree of immunity to mycobacteria can be suppressed by steroid, and thus predispose the susceptible subject to developing disseminated infection.

The diagnosis of disseminated MAC infection is often delayed. With appropriate treatment, mortality seems to have decreased [13]. We herein presented the case of a patient with high susceptibility to intracellular pathogens that died of disseminated MAC infection with a fulminant course, even though appropriate treatment was given. Compared to previous series, we presumed that the use of steroid was probably an important factor contributing to his death [7, 13-15].

In conclusion, patients who suffer from high susceptibility to intracellular pathogens are likely to develop disseminated MAC infection. Chronic steroid use might be a risk factor for mortality. We hope to raise the awareness of physicians in identifying these high-risk patients, to be cautious while using steroids, and thus decrease the possibility of developing fatal disseminated MAC infection in such patients.

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非愛滋病引起之瀰漫性禽結核分枝桿菌感染：病例報告及文獻回顧

林祖燊　何肇基　余忠仁

瀰漫性禽結核分枝桿菌感染在非愛滋病患中是相當罕見的。既便是接受任何程度免疫抑制劑之非愛滋病病患，這樣的表現也相當罕見。近來許多研究顯示某些基因缺陷與非愛滋病患發生瀰漫性禽結核分枝桿菌感染有關。這些基因缺陷可以易感染一些胞內病原菌，像是沙門氏桿菌，或是以發生嚴重的低致病性分枝桿菌之感染來表現。我們在此報告一名78歲非愛滋病感染之男性，過去曾罹患堪薩斯分枝桿菌之肺部感染和沙門氏桿菌菌血症。病患最初以慢性阻塞性肺疾之急性發作表現，經一段時間的類固醇治療後發生瀰漫性禽結核分枝桿菌感染。病患最終死於多重器官衰竭。*(胸腔醫學* ***2010; 25: 1-6)***

關鍵詞：瀰漫性禽結核分枝桿菌感染，非愛滋病，沙門氏桿菌菌血症，類固醇

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Application of Third-Generation (3G) Mobile Videophone to the DOTS-Plus Program in Multidrug-Resistant Tuberculosis in Taiwan: Case Report

Veng-Kai Tang, Kuan-Jen Bai, Chin-Yun Wang*, Ming-Chih Yu, Taipei-MDRTB Group

Multidrug-resistant tuberculosis (MDR-TB), caused by the bacterium, *Mycobacterium tuberculosis*, is resistant to both isoniazid and rifampicin and is a phenomenon threatening to destabilize global tuberculosis control. Taiwan's Centers for Disease Control implemented a patient-centered DOTS (directly observed treatment, short-course)-Plus program for MDR-TB patients in May 2007. We report the case of a 71-year-old MDR-TB patient who successfully completed 18 months of MDR-TB treatment under the DOTS-Plus program, beginning October 2007. A third-generation (3G) mobile videophone was used to watch the patient take medicine throughout his course of treatment. His acceptance of the program and compliance with monitoring by videophone DOT (V-DOT) were excellent. We conclude that V-DOT can be an effective approach to case management for MDR-TB patients and can achieve a high level of adherence in selected cooperative cases in Taiwan. ***(Thorac Med 2010; 25: 7-12)***

Key words: multidrug-resistant tuberculosis, DOTS-Plus, 3G mobile videophone

Introduction

Multidrug-resistant tuberculosis (MDR-TB), caused by the bacterium *Mycobacterium tuberculosis* (*M. tuberculosis*), which is resistant to both isoniazid and rifampicin (with or without resistance to other drugs), is a phenomenon threatening to destabilize global tuberculosis (TB) control. The most recent estimates suggest that there were 510,545 cases of MDR-TB globally in 2007 [2]. In addition, MDR-TB requires extensive chemotherapy (up to 2 years of treatment) with second-line anti-TB drugs; second-line drugs are more costly and produce more adverse drug reactions than first-line drugs [3]. Treatment outcome has been unsatisfactory -- the rate of completion of MDR-TB treatment was only 55% (828/1513) in the United States from 1993-2002 [4].

Building on the successes of DOTS (directly observed treatment, short-course), the World Health Organization (WHO) and its partners launched DOTS-Plus in 1999 as an initiative for global management of MDR-TB, including

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the rational use of second-line drugs [5]. The DOTS-Plus strategy adapted the core components of DOTS to the needs of patients with MDR-TB -- diagnosis based on culture and drug susceptibility testing, and treatment with second-line as well as first-line drugs [6].

More than 400 MDR-TB patients were registered in Taiwan in 2008 [7]. Previous approaches to treatment outcome were unsatisfactory -- 51.2% were cured, 10.4% failed, 9.4% died, and 29.1% defaulted [8]. Therefore, Taiwan's Centers for Disease Control (CDC) organized a patient-centered treatment consortium comprising 5 medical teams to implement the DOTS-Plus program for patients with MDR-TB in May 2007.

Taipei MDR-TB groups designed the patient-centered approach programs with incentives and enablers for the patients. In order to facilitate a relationship between patients and providers, third-generation (3G) mobile videophones (instead of community care supporters) were used as 1 of the modalities to watch selected patients take medicine. We report the first known case in Taiwan of successful completion of therapy in an MDR-TB patient using 3G mobile videophone technology for direct observation of treatment.

Case Report

A 71-year-old man had a history of pulmonary TB and had completed a full course of anti-TB treatment several decades ago. He was diagnosed with pulmonary TB on August 7, 2007, with positive culture of *M. tuberculosis*. Initially, Rifater (isoniazid 80 mg, rifampin 120 mg, and pyrazinamide 250 mg in each tablet) 5 tablets per day and ethambutol 800 mg per day were given at another hospital. However, drug susceptibility testing (DST) revealed MDR-TB, which was confirmed by the national mycobacteriology reference laboratory of the CDC. The patient was then referred to our hospital for further MDR-TB treatment. His initial chest radiograph (Figure 1) showed minimal pulmonary infiltrates that were compatible with pulmonary TB. Another *M. tuberculosis* isolate was obtained at our hospital, and DST showed it to be resistant to isoniazid, rifampin, streptomycin, and rifabutin, and susceptible to ethambutol, kanamycin, ofloxacin, *p*-aminosalicylic acid (PAS), and ethionamide. Rifater was discontinued due to significant arthralgia, poor appetite, and elevation of AST (114 U/L) and ALT (107 U/L) on October 8, 2007. Ethambutol was discontinued because of a complaint of blurred vision by this patient. A new anti-TB regimen was designed, consisting of kanamycin 750 mg per day, levofloxacin 750 mg per day, cycloserine 250 mg twice daily, and prothionamide 250 mg twice daily. The patient tolerated this regimen

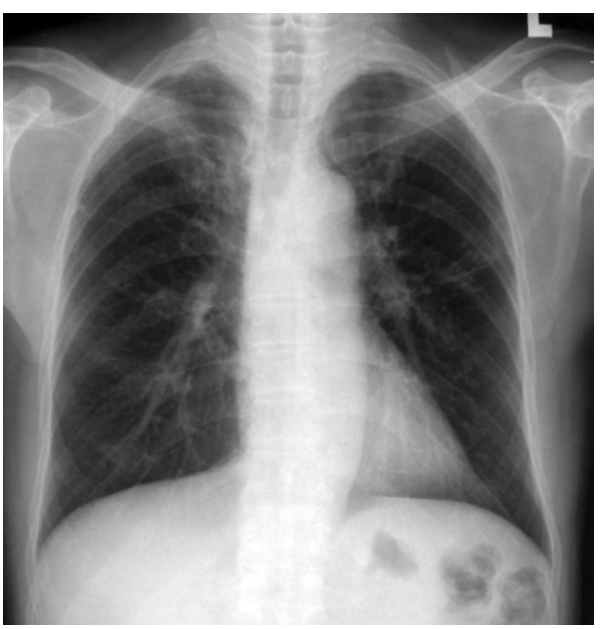

Fig. 1. Chest radiograph shows minimal pulmonary infiltrates in both upper lung fields.

well and was discharged with outpatient clinic follow-up on 15 October 2007.

On follow-up, the patient complained of poor appetite, and liver enzymes were elevated (AST 144 U/L and ALT 232 U/L); prothionamide was discontinued on 28 November 2007. Liver enzymes gradually returned to normal values, and ethambutol 800 mg per day was given again on January 2, 2008. Kanamycin was discontinued after 6 months. Thereafter, his clinical course was smooth. Monthly sputum smear and culture for *M. tuberculosis* were consistently negative after initiation of second-line anti-TB treatment in October 2007. He successfully completed 18 months of treatment after sputum culture conversion.

After discharge from our hospital, medications were dispensed monthly at the patient's routine visit to our chest clinic. Each day's dosage was separately packaged and dated by a DOTS-Plus nurse. In addition to kanamycin injected at a nearby health station, a third-generation (3G) mobile videophone was used to watch the patient take his medication; the patient called the DOTS-Plus nurse at prearranged times, identified himself, and displayed the daily dosage of medication. All pills were swallowed in view of the 3G mobile videophone. The DOTS-Plus nurse asked about problems or adverse reactions during every videophone-DOT (V-DOT). Any questions or problems were referred to the doctor. Dates of treatment, time required for therapy, and any problems, including adverse drug reactions, were recorded. His adherence rate (1006/1006=100%) on V-DOT and acceptance of this technology were excellent.

Discussion

The development of MDR-TB is a complex multifactorial process. Although its causes are microbial, clinical, and programmatic, MDR-TB is essentially a man-made phenomenon. From a microbiological perspective, resistance is caused by a genetic mutation that makes a drug ineffective against mutant bacilli. From a clinical and programmatic perspective, it is an inadequate or poorly administered treatment regimen that allows a drug-resistant strain to become the dominant strain in a patient infected with TB [9]. In 2006, the World Health Organization published general treatment principles for MDR-TB: (1) regimens should consist of at least 4 drugs with certain, or almost certain, effectiveness; (2) an injectable agent (an aminoglycoside or capreomycin) is used for a minimum of 6 months and at least 4 months past culture conversion; (3) the minimum length of treatment is 18 months after culture conversion; and (4) each dose is given as directly observed therapy (DOT) throughout the treatment [9-10].

Adherence to MDR-TB therapy is particularly difficult because of its prolonged treatment regimens with larger numbers of drugs that have serious adverse effect profiles [11]. Adherence to treatment is a critical factor in the management of MDR-TB, and a previous study showed a 29% default rate in Taiwan [8]. Higher rates of adherence can be achieved if patients are offered a comprehensive package of services, including disease education, DOT, socioeconomic support, emotional support, management of adverse effects, and monitoring systems [9].

Telemedicine, including the 3G mobile videophone, allows patients and health-care providers to interact both verbally and visually over large distances. It creates a multi-way

interaction between patient and providers and facilitates the dynamic nature of this relationship [12]. The most significant advantage of a 3G mobile videophone is that it minimizes the significance of the distance between the patient and the health-care provider. Videophone visits are brief, lasting several minutes, and allow flexibility in scheduling. This flexibility is convenient for both the patients and the DOTS-Plus nurse [13]. DOT may affect the patient's private life and must therefore be conducted with sensitivity. If treatment takes place at home, the privacy of the patient and his or her family may be compromised; whereas if treatment occurs in a public place known for the treatment of TB, there may be stigma or discrimination [14]. Patients have reported that V-DOT is less intrusive than DOT by community care supporters [13]. Therefore, V-DOT can be provided in a way that does not place undue burdens on patients and their families. As has been seen with other patients in our study as well as in previous reports [13, 15], our patient's acceptance of videophone technology was high. This patient was very cooperative and achieved 100% compliance with V-DOT.

Current videophone technology showed generally good transmission quality in Taiwan. The technology was relatively simple and easily explained to patients. However, videophone technology still does have some limitations. In some areas, the transmission quality is not satisfactory; therefore, we must evaluate the transmission quality of the patient's environment before using the 3G mobile videophone for DOT.

The successful application of videophone to DOT for TB requires careful patient selection [13]. V-DOT is most appropriate for patients who have good adherence and who simply need a reminder to take their medication. V-DOT is not appropriate for patients who are making an active effort to avoid therapy. It would be possible for a patient to place the pills in his or her mouth while on mobile videophone but not swallow them [13]. The Taipei MDR-TB group has established a standard procedure to carry out each V-DOT and avoid this situation.

Conclusion

The DOTS-Plus strategy can be provided in a way that does not place undue burdens on patients and their families. The successful experience of this patient shows that the 3G mobile videophone minimizes the effect of distance between the patient and the health-care provider. Videophone visits were brief and allowed great flexibility in scheduling. This flexibility and minimal intrusiveness made the process convenient for the patient and the DOTS-Plus nurse. However, the successful application of the 3G videophone to DOTS-Plus for MDR-TB requires very careful patient selection. Therefore, we conclude that V-DOT is 1 of the useful modalities for patient care in the management of MDR-TB and can achieve a high level of adherence in selected cooperative cases in Taiwan.

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3G 影像手機應用於多重抗藥結核病的進階都治計畫：病例報告

鄧穎佳　白冠壬　王錦雲*　余明治　台北區多重抗藥結核病小組

對於isoniazid及rifampin同時具有抗藥性的多重抗藥結核病會威脅全球的結核病防治，因此，台灣疾病管制局於民國96年5月開始實施以病人為中心的進階都治計畫。在此，我們報告一位71歲多重抗藥結核病人於民國96年10月開始接受抗結核藥物治療並完成18個月的進階都治計畫。在整個治療過程中，我們運用3G影像手機直接觀察病人服藥。病人對於進階都治計畫的接受度極佳，並且對於3G影像手機的接受度也非常好。我們認為對於特定合作的多重抗藥結核病人，3G影像手機可有效的應用於進階都治計畫並能達到相當好的服藥順從性。*(胸腔醫學* ***2010; 25: 7-12)***

關鍵詞：多重抗藥結核病，進階都治計畫，3G影像手機

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Hypertrophic Osteoarthropathy (HOA) as the Initial Presentation of Squamous Cell Carcinoma of the Lung: A Case Report

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Hypertrophic osteoarthropathy (HOA) is a clinical syndrome consisting of periostitis, arthritis and clubbing. HOA is associated with a variety of diseases, the malignancies of which are the major cause, especially pulmonary malignancies. The mechanism of HOA may be associated with platelets, VEGF, PDGF, or other cytokines. The therapy for HOA should be directed at the underlying disease. We herein report the case of a 33-year-old woman who suffered from squamous cell carcinoma of the lung with the initial presentation of arthritis and clubbing. The symptoms of HOA resolved after 6 courses of chemotherapy and curative radiotherapy. ***(Thorac Med 2010; 25: 13-18)***

Key words: hypertrophic osteoarthropathy, lung cancer

Introduction

Hypertrophic osteoarthropathy (HOA) is a clinical syndrome consisting of periostitis, arthritis and clubbing. The association of HOA with lung and heart disease was first described by von Bamburger in 1889 [1]. Herein, we report the case of a patient who presented with clubbing and arthritis, and who was diagnosed with squamous cell carcinoma of the lung. The symptoms improved after chemotherapy and curative radiotherapy.

Case Presentation

A 33-year-old woman who had smoked 1 pack of cigarettes per day for 10 years suffered from progressive swelling and pain in the joints of the hands and toes for 2-3 months (Figure 1). She visited the outpatient department of a local hospital, and was told she had arthritis. She visited another local hospital, where abnormalities on the chest X-ray were found incidentally (Figure 3). Chest CT scan was performed and showed a 3×3 cm soft tissue mass at the right upper lobe of the lung, right hilar and mediastinal lymphadenopathy with nodal compression of the right main bronchus, and stenosis of the

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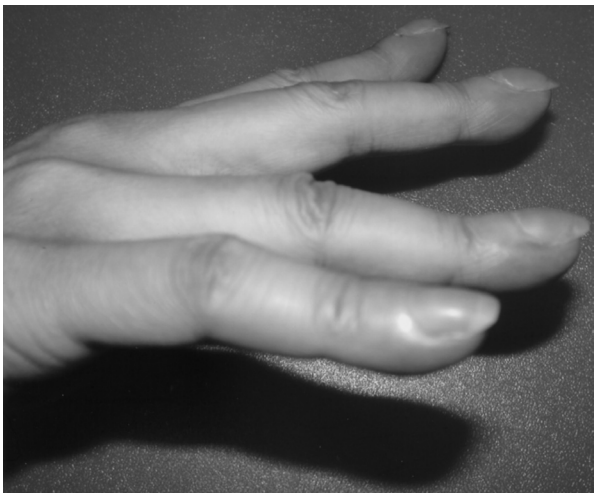

Fig. 1. The clubbing fingers of the patient at the initial presentation.

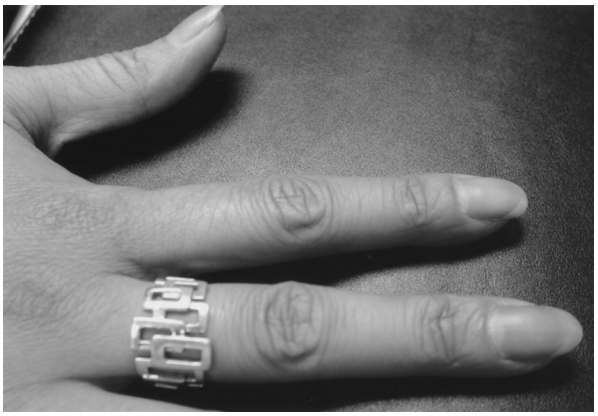

Fig. 2. The clubbing fingers resolved after chemotherapy.

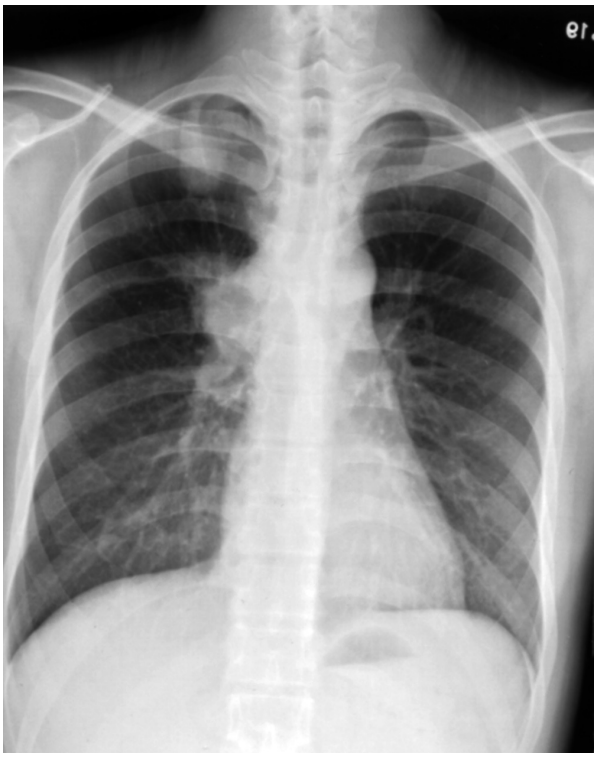

Fig. 3. The initial chest X-ray film (2006/3/15) of the patient, which showed a RUL mass lesion suggestive of lung cancer.

right main bronchus (Figure 4). Fiberobronchoscopy was performed on 2006/3/10 and showed marked stenosis of the right main bronchus, but the brushing cytology had a negative finding. She was referred to our chest surgery department for further management.

After admission, a whole body positron emission tomography (PET) scan was performed and showed fluorodeoxyglucose (FDG) uptake in the right upper lobe of the lung, compatible with lung cancer involving the right upper lobe with right pulmonary hilum lymph node metastasis. Mediastinoscopy with lymph node sampling from the right upper paratracheal region was performed and the pathology report showed poorly-differentiated squamous cell carcinoma. The whole body bone scan performed on 2006/3/16 showed radioactive uptake in the elbows, wrists, hips, knees and ankles.

Under the diagnosis of squamous cell carcinoma of the lung, right upper lobe, with mediastinal lymph node metastasis, pT2N2M0, stage IIIa, 60Gy radiotherapy was directed at the tumor and the mediastinal lymph node. Concurrent chemotherapy with paclitaxel and carboplatin was performed as well. After 4 courses of chemotherapy, her arthritis improved, and after the completion of 6 courses of chemotherapy, her clubbing fingers showed much improvement (Figure 2). In addition, the RUL tumor and the mediastinal lymph node showed significant

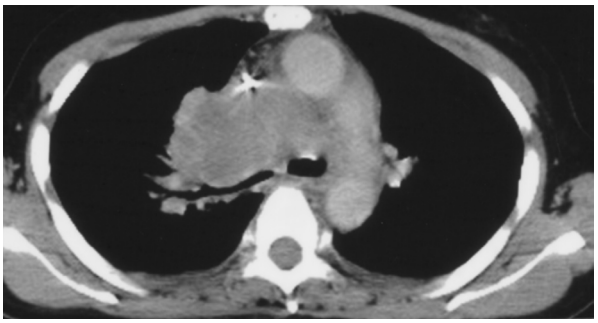

Fig. 4. The chest CT image at the time of diagnosis (2006/3/23), which showed a RUL mass compatible with lung cancer.

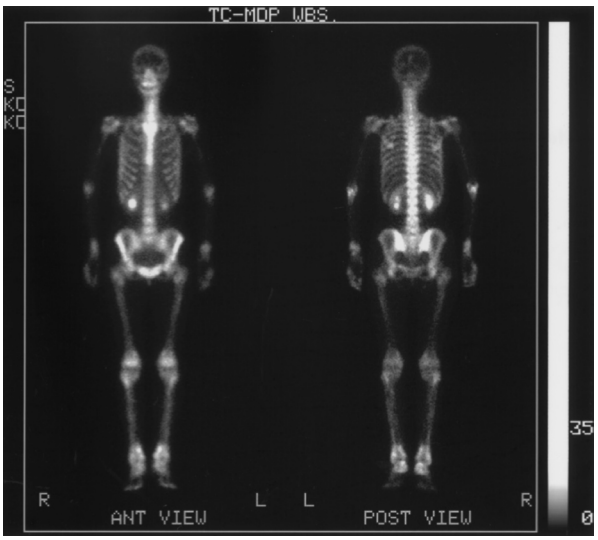

Fig. 5. The Tc-99m MDP whole body bone scan showed an uptake of radioactivity in the elbows, hips, knees and ankles, suggestive of arthritis.

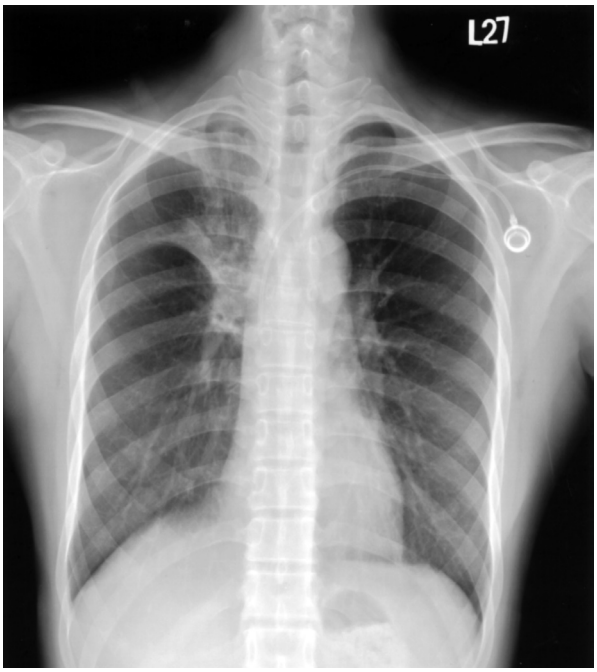

Fig. 6. The chest X-ray film of the patient after completion of concurrent radiotherapy and 6 courses of chemotherapy (on 2006/8/14), which showed regressive change of the RUL mass lesion.

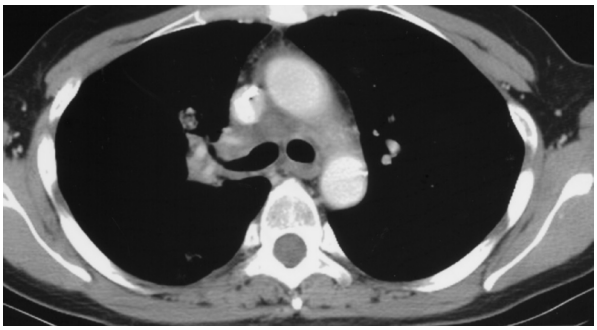

Fig. 7. The chest CT image after completion of concurrent radiotherapy and 6 courses of chemotherapy (on 2006/8/17), which showed regressive change of the tumor.

regressive change after radiotherapy and chemotherapy (Figure 6, Figure 7). She was regularly followed up at our outpatient clinics and the follow-up imaging studies showed a stable condition without evidence of recurrence or distant metastasis.

Discussion

HOA is associated with a variety of diseases, and its prevalence depends on the underlying disease. The primary form of HOA was first described by Touraine in 1935 as autosomal-dominant genetic disease [2]. The secondary form of HOA is associated with a variety of diseases, and 80% of HOA cases have malignancies [3]. Pulmonary malignancies are the major cause of secondary HOA, and the majority of these malignancies are non-small cell lung cancer, such as adenocarcinoma and squamous cell car-

cinoma [4]. The incidence of HOA in primary lung cancer has varied in different investigations: A Japanese study [5] showed HOA to be a rare condition, and a Romanian study [6] found a 30% incidence.

Classic HOA includes the triad of periostitis, clubbing and arthritis. Clubbing is the best-known characteristic of HOA, and it presents with an increase in the Lovibond's angle between the nail bed and the proximal nail fold, which is normally 160 degrees [7]. The periostitis of HOA may occur in the upper or lower limbs, but the lower limbs are more commonly afflicted, especially in secondary HOA associated with malignancies [1]. The arthritis in HOA usually involves the large weight-bearing joints, especially the knees and the ankles, but the finger joints may also be involved symmetrically [1].

The histopathology of clubbed fingers showed diffuse endothelial hyperplasia and dilatation of the vessels, and partial occlusion of the capillary lumen with platelet clusters [8]. The histopathology of the periosteum showed proliferative vasculitis of the small vessels and bony remodeling. The mechanism of HOA is not exactly clear, but Dickson and Martin have proposed a possible mechanism [8]. Normally, the megakaryocytes are fragmented into platelets in the pulmonary capillaries. Many diseases, such as cardiac right-to-left shunting and lung disease, would result in failure of megakaryocytes fragmentation in the pulmonary circulation. The megakaryocytes enter the systemic circulation and reach the capillaries of the digits. The platelet aggregation may release platelet-derived growth factor (PDGF). In addition, hypoxic lung diseases and malignancies may result in overexpression of the vascular endothelial growth factor (VEGF). Elevation of VEGF and PDGF has been reported in several studies of HOA patients [9-10], and is considered to contribute to the periostitis and clubbing.

The therapy for HOA varies, based on the underlying disease. Surgery and chemotherapy of the malignancies associated with HOA can improve the condition [11]. Gefitinib, an epidermal growth factor receptor tyrosine kinase inhibitor (EGFR-TKI), has been reported to resolve lung cancer-associated HOA [12]. In this case, we treated the patient's underlying lung cancer with radiotherapy and chemotherapy. As her lung cancer regressed, the symptoms of HOA improved. Analgesics can be prescribed to relieve the pain of HOA For those patients refractory to analgesics, pamidronate therapy has been reported to resolve the pain of HOA [13], and the mechanism may be its anti-tumor and anti-inflammatory effects [14].

In conclusion, HOA is associated with a variety of diseases through the effects of platelets, VEGF, PDGF, and other cytokines. Treatment of HOA is directed at its underlying disease. The patient we have described showed much improvement of the lung cancer after radiotherapy and chemotherapy, as did her clubbing and arthritis. We concluded that her HOA was associated with the lung cancer.

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以肥厚性骨頭關節病變（hypertrophic osteoarthropathy, HOA）爲初始表現之肺鱗狀上皮細胞癌—病例報告

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肥厚性骨頭關節病變（hypertrophic osteoarthropathy, HOA）是一包含杵狀指、骨膜炎及關節炎之臨床徵候。大多數之肥厚性骨頭關節病變是次發性的，大部份跟惡性腫瘤有關，尤其是肺部的惡性腫瘤。肥厚性骨頭關節病變之成因被認為是跟血小板、血管內皮生長因子（vascular endothelial growth factor, VEGF）、血小板衍生性生長因子（platelet-derived growth factor, PDGF）等有關。肥厚性骨頭關節病變之治療須針對其原發疾病作治療。這裡我們提出一個33歲之女性，一開始表現出杵狀指及關節炎，經過詳細檢查後診斷為肺鱗狀上皮細胞癌之病人。經過化學治療後病人之肥厚性骨頭關節病變明顯改善。*(胸腔醫學* ***2010; 25: 13-18)***

關鍵詞：肥厚性骨關節病變（hypertrophic osteoarthropathy），肺癌（lung cancer）

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Remission of Clubbing Fingers after Chemoradiotherapy in a Patient with Locally Advanced Non-small Cell Lung Cancer

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Digital clubbing is a clinically sign that typically indicates pulmonary or cardiac disease. It is not uncommon and can occur in all cell types of lung cancer [1]. The exact mechanism for clubbing is still not fully understood. A reversal of clubbing after resection of the lung cancer has been reported in several publications [2], but improvement in digital clubbing after chemotherapy or radiotherapy is seldom reported. We herein report a lung cancer patient whose clubbing fingers improved simultaneously with the clinical response after chemotherapy and radiotherapy. A 50-year-old man was diagnosed with non-small cell lung cancer and the initial presentation was productive cough for 2 months. Chest radiography showed a mass 9 cm at the right upper lobe. Cytology of the transthoracic needle aspiration revealed adenocarcinoma. The clinical stage was T4N0M0 with mediastinal invasion, using a CT scan. The clubbing fingers were also remarkable. He received 6 courses of chemotherapy with paclitaxel 180 mg/m^2 plus cisplatin 75 mg/m^2 every 3 weeks followed by radiotherapy 52 Gy. The tumor shrank significantly after treatment. The clubbing fingers also improved simultaneously. The patient was followed up for 12 months after treatment without recurrence.
(Thorac Med 2010; 25: 19-25)

Key words: clubbing finger, lung cancer, hypertrophic osteoarthropathy (HOA)

Introduction

Clubbing of the digits is a common and well recognized physical sign which is frequently seen in infections, inflammatory disease, and cyanotic heart disease, or with a neoplasm. Most cases of hypertrophic osteoarthropathy (HOA) are correlated with non-small cell lung cancer (NSCLC) [1]. In a retrospective study, clubbing fingers were present in as many as 32 (29%) of 111 patients with lung cancer. They were more predominant in women (40%) than men (19%) and in NSCLC (35%) than in small-cell lung cancer (SCLC) (4%) [3]. Digital clubbing is usually painless, unless it is associated with hypertrophic osteoarthropathy.

Although the pathogenesis of clubbing fingers is still unknown, a common consensus is that clubbing fingers occur because of vasodilation of vessels in the fingertip, including the

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formation of the arteriovenous connections. In addition, clubbing fingers are characterized by a proliferation of the connective tissue between the matrix and nail and the distal phalanx [4]. Generally clubbing fingers is thought to be a poor prognostic sign of some certain diseases, such as sickle cell anemia [5], cystic fibrosis [6], pulmonary fibrosis [7], and Grave's disease [8].

However, the reversal of digital clubbing after resection of lung cancer has been reported. Forty patients with NSCLC in 1 study had clubbing fingers, which resolved in 33 of the patients after surgery [2]. However the reversal of digital clubbing after chemotherapy or radiotherapy in lung cancer is seldom reported relatively. We herein report an NSCLC patient with clubbing fingers that improved simultaneously after the clinical response to chemotherapy and radiotherapy.

Case Report

A 50-year-old man was a smoker, consuming 1 pack per day for 30 years. He was admitted to the chest department of Taichung Veteran General Hospital due to productive cough for 2 months. Chest radiography (Figure 1a) showed a 9 cm mass in the right upper lobe. He had no systemic disease such as hypertension, diabetes mellitus, or cardiovascular disease. Besides cough, progressive swelling of the face and arms was also found during this period, and dyspnea on exertion and shortness of breath were mentioned. Clubbing fingers were noted by physical examination initially (Figure 3a). There was no palpable lymph node in the neck, axilla, or inguinal areas. Chest CT scan (Figure 1b) showed a mass, 9 cm in diameter, at the right upper lobe, accompanied with invasion of the mediastinum. The tumor had also invaded

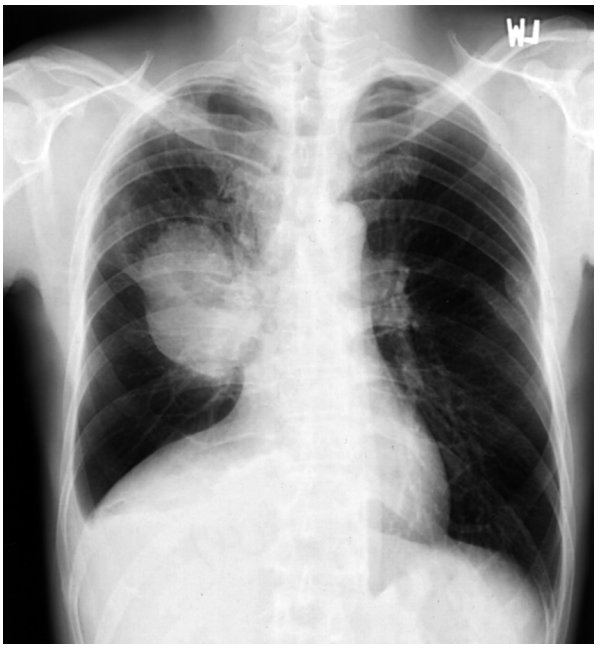

Fig. 1a. Chest radiography showed a huge mass in right hilar region before treatment

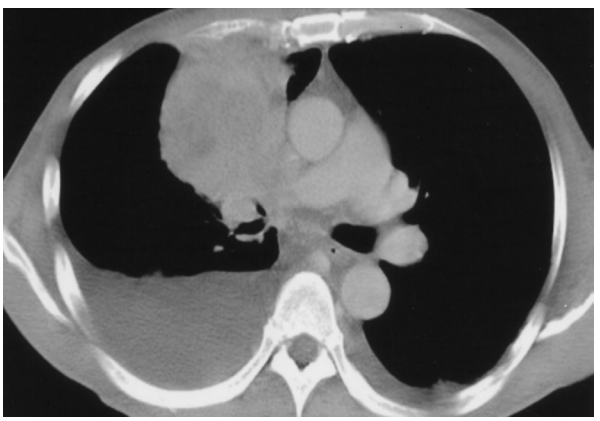

Fig. 1b. CT scan showed a huge mass in right upper lobe with pleural effusion before treatment with chemotherapy plus radiotherapy

the superior vena cava, right main bronchus and right pulmonary artery. Some pleural effusion was noted in the right chest. The cytology of the lung mass based on the transthoracic aspiration revealed adenocarcinoma. The pleural effusion cytology revealed no malignant cells. There was no evidence of distal metastasis in a series

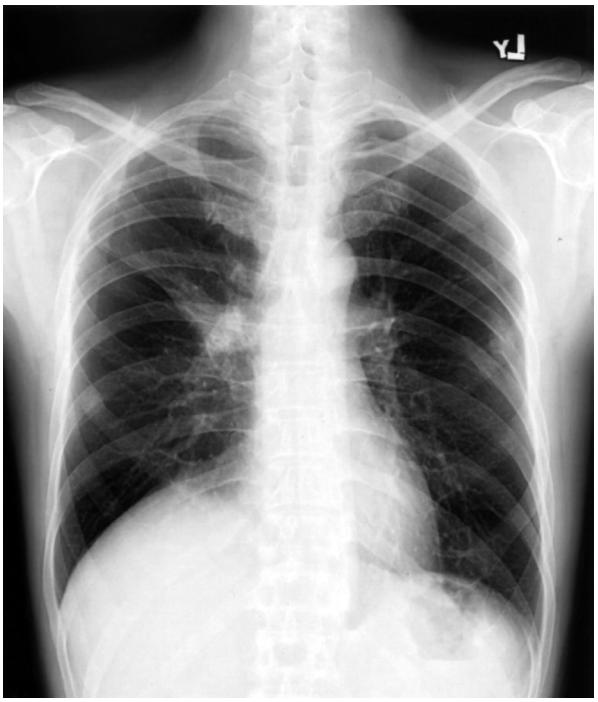

Fig. 2a. Chest radiography showed the mass shrank in right hilar region after 6 month's treatment

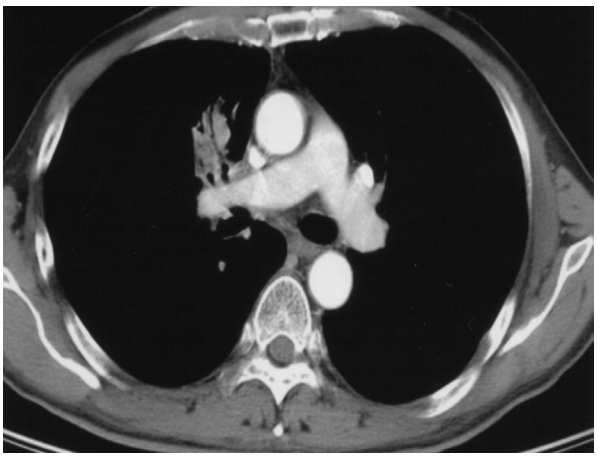

Fig. 2b. CT scan showed the mass shrank in the right upper lobe and pleural effusion disappeared after 6 months' treatment with chemotherapy plus radiotherapy

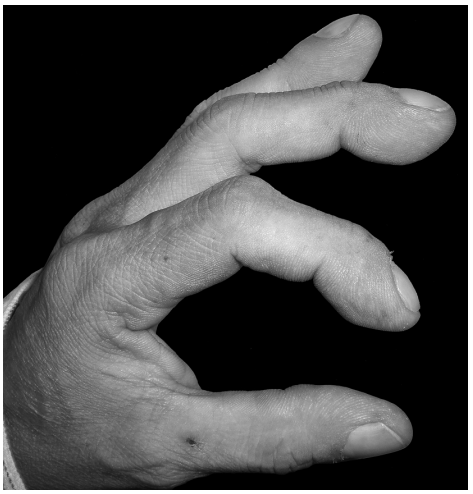

Fig. 3a. Clubbing fingers of patient were noted while initial diagnosis without treatment

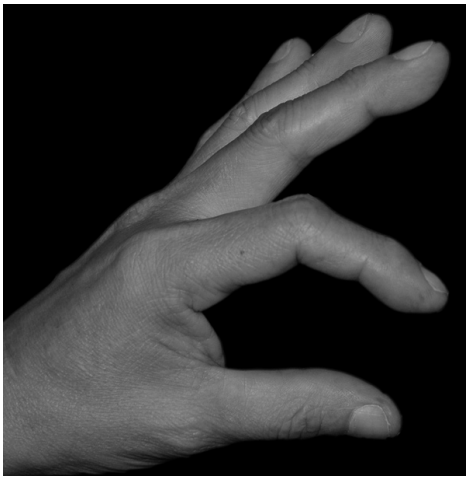

Fig. 3b. Remission of clubbing fingers was noted after 6 months' treatment with chemotherapy plus radiotherapy

of examinations including abdominal sonography, whole body bone scan, and brain computed tomography. Lung cancer, adenocarcinoma, in the right upper lung, T4N0M0, stage IIIb, with mediastinal invasion and superior vena cava syndrome was diagnosed in this patient. His performance status was ECOG grade 1.

He underwent 6 courses of paclitaxel 180 mg/m^2 and cisplatin 75 mg/m^2 every 3 weeks with a good response on the follow-up image studies. He also received radiotherapy at 52 Gy (200 cGY each time, on 26 occasions) after chemotherapy. After chemotherapy and radiotherapy, the tumor shrank significantly (Figure 2a and 2b), and the clubbing fingers were also

resolved (Figure 3b).

Discussion

Hippocrates was the first person in the literature to describe digital clubbing as a sign of disease. He wrote "the patient has fever and cough; the respiration is fast; the feet become edematous; the nails appear curved and the patients suffers as if he had pus inside …". Digital clubbing is also known by the eponym "Hippocratic fingers" for this reason [9].

Lovibond [10] observed that the nail projects from the nail bed at an angle of about 160° in normal fingers, but this angle changes to 180° in clubbing fingers. With the introduction of radiologic imaging in the late nineteenth century, clubbing fingers were thought to be a unique finger deformity, often accompanied by periosteal proliferation of the tubular bones. Focal proliferation and bulbous swelling of the digital connective tissue developed on the dorsal surface of the terminal phalanges [11]. Bamberger [12] and Marie [13] named the fully developed expression pulmonary HOA. The prefix "pulmonary" was later given up when it was discovered that the skeletal syndrome may also appear as a response to severe diseases without the lungs and even may be present in individuals not having underlying illnesses ("primary HOA"). Digital clubbing and HOA display different stages of the same syndrome [14]. A conference in 1992 attempted to reach a consensus on the definition of HOA. The rare primary form and the more frequent secondary form of HOA should be distinguished from each other. (Table 1)

Digital clubbing is associated with a variety of diseases, including cancer, cirrhosis, cyanotic congenital heart disease, cystic fibrosis, and bronchiectasis [11]. Digital clubbing is thought to be a kind of paraneoplastic syndrome of lung cancer, such as HOA, hypercalcemia, hypoglycemia, and others. Patients with NSCLC were found to be more likely to have clubbing fingers than those with SCLC [15].

The mechanisms involved in finger clubbing remain unclear and many hypotheses have been put forward. The first hypothesis was that vascular endothelial growth factor (VEGF) may play an important central role in the development of clubbing, as reported in several studies [16-17]. VEGF is a platelet-derived factor induced by hypoxia and is produced by diverse malignancies. VEGF produces vascular hyperplasia, edema, and fibroblast/osteoblast proliferation [18]. Dickinson and Martin also thought that megakaryocytes and platelet clumps might

Table 1. Classifications of hypertrophic osteoarthropathy

Primary Form	Secondary Form
Primary Pachydermoperiostosis (Friedreich-Erb-Arnold syndrome, Touraine-Solente-Golé syndrome) a rare disease, autosomal dominant	Secondary Pachydermoperiostosis (Pierre-Marie-Bamberger Syndrome) Often, a complete form in 90% of NSCLC
Clinical features: Clubbed digits of the hands and feet with watch-crystal nails, periosteal hyperostosis, Pachydermia, hyperhidrosis, seborrhoea, Differential diagnosis: Thyroid acropachy and acromegaly	Clinical features: Clubbing fingers, periosteal hyperostosis, arthralgia/arthritis

be involved in the formation of digital clubbing and they suggested that the platelet-derived growth factor (PDGF) could be a likely factor in the pathogenesis of digital clubbing [19]. Both PDGF and VEGF are released by platelets on aggregation [20], and a previous study demonstrated that digital clubbing presents with stromal and vascular changes through the synergy of VEGF and the PDGF [17].

Another study hypothesized digital clubbing was correlated with hypoxia, but showed only that the lung function had a correlation with digital clubbing in patients with cystic fibrosis. Hypoxia had no relationship with digital clubbing [18]. A study of chronic obstructive pulmonary disease patients also reported that hypoxemia was not correlated with the existence of clubbing [21].

The secretion of growth hormones was initially thought to be a cause of digital clubbing [22-23], but later, other growth factors were suspected of playing a major role in its development [24]. A hypothesis involving lung cancer was that a tumor-derived growth factor would gain direct access to the systemic circulation, and then induce digital clubbing [24-25].

One study reported that clubbing fingers was the initial presentation of lung cancer, and then, resolved after resection of the neoplasm [26]. In a review [2] of 52 cases (1954-2007), digital clubbing reversed after treatment of the underlying disease. Five of the cases were lung cancer, and digital clubbing was resolved after surgery; only 1 case received chemotherapy and another was treated with resection plus chemotherapy. Forty NSCLC patients were enrolled in another study and all received surgery for lung cancer; the digital clubbing was resolved in 33 of the patients after surgery. Moreover, there were no significant differences in the reversal of digital clubbing, including age, preoperative symptoms, tumor histology, clinical staging, and site of the pulmonary lesion [2]. Another study reported a poor post-treatment prognosis if clubbing fingers were not reversed after resection of lung cancer [27].

In conclusion, clubbing fingers are an important physical sign, and call our attention to the possibility of lung cancer. Although the mechanism and pathogenesis of digital clubbing is still unclear, it can be reversed in a patient with lung cancer after the tumor is removed. Furthermore, the clubbing can also be resolved by chemotherapy and radiotherapy, as we have reported herein.

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非小細胞肺癌病患接受化學治療後，杵狀指的明顯消散

林聖皓　楊宗穎　張基晟　許正園

杵狀指是一個臨床常見的現象，通常是在肺部或心臟疾病中的病人表現。這種情況並非罕見，可發生在所有細胞類型的肺癌 [1]。導致杵狀指的確切機轉還沒有完全理解。在某些研究報告指出，肺癌切除後會看到杵狀指的改善 [2]。至於肺癌接受化學治療或放射治療後，杵狀指的改善的報導則相當稀少。我們報告一位肺癌患者的杵狀指，在臨床肺癌對化學及放射治療有反應的同時，也看到杵狀指的改善。一位50歲的男子被診斷出非小細胞肺癌，他的初步症狀是咳嗽有痰持續約2個月。胸部X光顯示，大約有一個9公分的腫瘤在右上肺葉。經細針穿刺胸部的細胞學報告顯示為腺癌。臨床分期為T4N0M0，同時伴隨有縱隔腔的侵襲。杵狀指也同樣明顯。這位患者接受六次的化學治療平均每三週施打一次，紫杉醇180 mg/m^{2}和順鉑75 mg/m^2，以及放射治療52 Gy。腫瘤治療後顯著縮小。杵狀指同時也改善。病人治療後已追蹤12個月並無復發。*(胸腔醫學* ***2010; 25: 19-25)***

關鍵詞：杵狀指，肺癌，肥厚性骨頭關節病變

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Foreign Body Aspiration with a Movable Suction Tube Shifted from Left to Right Bronchus – A Case Report

Yueh-Lan Huang, Cheng-Yi Wang, Hen-I Lin, Shih-Tze Chung, Yen-Teh Chang

Foreign body aspiration (FBA) usually occurs in children and the elderly. We report a 69-year-old man who had left-side massive pleural effusion and empyema secondary to a movable foreign body, without knowing the exact time of the FBA. A suction tube, 11 cm in length, was initially found by chest radiography and computed tomography (CT) in the lower trachea extending to the left bronchus. However, 4 days later, the suction tube was retained between the lower trachea and right bronchus, using flexible bronchoscopy, and then removed successfully. Empyema in the left side persisted, so video-assisted thoracoscopic surgery for decortication was performed, and his pneumonia then improved. FBA may be undetected due to an atypical history or misleading clinical and radiological findings. It can be unrecognized for a long time until symptoms and signs occur or persist. FBA is sometimes a life-threatening emergency and requires prompt attention. Flexible fiberoptic bronchoscopy can be chosen as the first-line approach to remove the foreign body. ***(Thorac Med 2010; 25: 26-30)***

Key words: foreign body, suction tube, empyema

Introduction

Foreign body aspiration (FBA) is a condition seen all over the world and can occur in children, as well as adults or the elderly [1]. It can present in a variety of ways, ranging from no or trivial symptoms to irreversible damage to the lungs which may be life-threatening [2]. FBA in adults is more common in the setting of advanced age, underlying neurological disorder, poor dentition, alcohol consumption and sedative use [3-4]. Sometimes it may remain undetected due to an atypical history or misleading clinical and radiological findings [5-6]. Pneumonia atelectasis and empyema are significantly more common in patients with an atypical history or misleading clinical and radiological findings with a delayed diagnosis. Herein, we present a case of FBA of a piece of broken movable suction tube.

Case Report

A 69-year-old man who had bed-ridden for

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10 years presented with old pulmonary tuberculosis, diabetes mellitus, hypertension and an old cardiovascular accident (CVA). He lived in a nursing home and relied on a nasogastric tube for feeding. Sputum suction was also required. He had suffered from fever with shortness of breath on and off for about 2 weeks. He had a yellowish productive cough, without hemoptysis, and was sent to our emergency room. Chest radiography revealed left-side pleural effusion with leukocytosis, and he was subsequently admitted to our chest ward.

After admission, chest auscultation revealed bilateral inspiratory wheezing and rhonchi, and antibiotics with cefuroxime and gentamicin were given. Chest thoracentesis was performed in the left lung fields, and the extracted fluid was turbid, with specific gravity>1.035, WBC 7450/ul, L:N%=9:84%, and protein 5 g. Exudative pleural effusion was diagnosed, but bacterial culture yielded no growth. The follow-up chest radiography revealed recurrent massive pleural effusion with atelectasis of the left lung, the possibility of bronchogenic carcinoma could not be ruled out, so chest computed tomography (CT) was arranged 2 days after admission. The CT scan revealed left massive pleural effusion with atelectasis of the left lung and a broken tube-like structure within the left main bronchus to the lower branch (Figure 1). Under anesthesia, flexible bronchoscopy was performed and diffuse mucosal swelling with a polyp-like lesion at the left main bronchus and entrance to the left lower lobe, with no lumen obstruction, was noted. A suction tube about 11 cm in length that was retained in the lower trachea extending to the right bronchus was found (Figure 2A) and immediately removed via the flexible bronchoscope (Figure 2B). Bronchial biopsy revealed chronic inflammation, no malignancy was noted. The antibiotic was changed to piperacillin. A follow-up chest radiograph showed haziness of the left lung. Chest thoracentesis was performed again and empyme was found. Video-assisted thoracoscopic surgery (VATS) with decortications and chest tube insertion at the left lower lung zone with endotracheal tube intubation showed chronic inflammation with reactive atypia, the patient was transferred to the surgical intensive care unit for critical care.

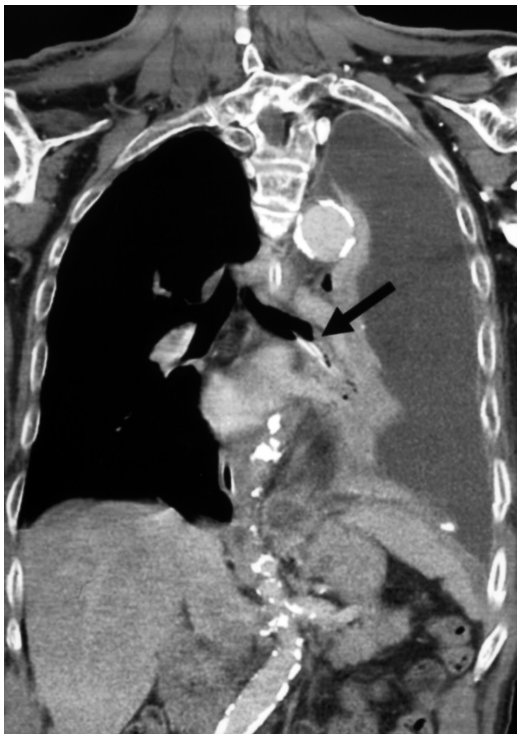
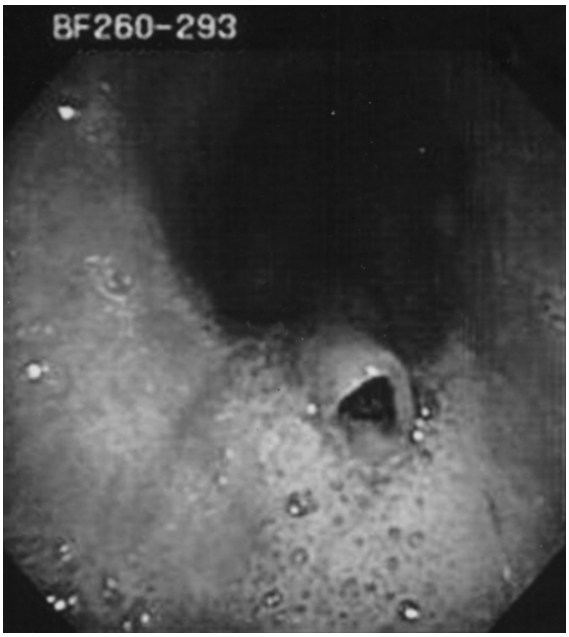


Fig. 1. Chest computed tomography revealed a foreign body in the left main bronchus. (Arrow)

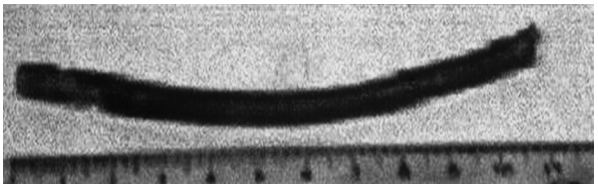
After his condition had stabilized, the chest tube and endotracheal tube were removed and he was transferred to an ordinary ward. He was discharged after 15 days of antibiotic treatment without recurrence of the symptoms.

Discussion

Foreign bodies in the airway are the result



(A)



(B)

Fig. 2. A piece of broken movable suction tube (10-11 cm) was found by flexible bronchoscopy (A) in the right 2nd carina to right intermediate carina and was removed (B).

of aspiration or inhalation and can be a life-threatening emergency [7]. The severity of foreign body aspiration depends on whether the airway obstruction is complete or partially complete. Complete airway obstruction occurs in the airway at the levels above the carina; it causes an acute onset of respiratory distress in which the patient is unable to speak or cough. Unfortunately, complete airway obstruction may rapidly proceed to death if the foreign body is not immediately dislodged or removed. Partial airway obstruction occurs when the airway is partially occluded or if the obstruction occurs distal to the carina. Patients with partial airway obstruction may present weeks to months after the foreign body aspiration, and the condition may be diagnosed because of the sequelae, such as recurrent pneumonia, persistent cough, hemoptysis, wheezing and atelectasis [8].

Unfortunately, a history consistent with foreign body aspiration is usually available in only 70% of patients. After an acute episode of airway distress, patients may continue to experience episodes of persistent coughing and wheezing, or they may be asymptomatic [9]. Chronic debilitating symptoms with recurrent infection might occur with delayed extraction, or the patient may remain asymptomatic [10]. In our case, the patient was a bed-ridden elderly person, and the timing of when the suction tube broke off into the bronchus was unknown. This explains why he had experienced the fever, productive cough and dyspnea on and off at the nursing home. Because of the delay in sending the patient to the hospital for treatment, the suction tube was already retained in the lower trachea extending to the right and left bronchus when he was finally admitted, and empyema had already occurred. Because of the diversity of clinical presentations in the elderly population [11], inhalation of a foreign body into the bronchial tree rarely occurs asymptomatically and, if it leads to recurrent pneumonia [12], it can be very difficult to diagnose. Empyema usually occurs as an extension of an infectious process [13]. Bronchoscopy was first developed largely in response to the need to extract items such as suction tubes.

In conclusion, the clinical manifestation of bronchial foreign bodies is often unrepresentative in aged patients [14], and chest radiographic manifestations often result in misdiagnosis

or delayed diagnosis [15]. Accurate diagnosis often requires a detailed history, early use of CT imaging, and flexible bronchoscopic evaluation. Bronchoscopy is indicated with an appropriate history and suspicion. To prevent delayed diagnosis, characteristic symptoms, signs and radiological findings of foreign body aspiration should be checked in all suspected cases [16].

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吸入性異物—抽痰管在左右氣管內遊走—病例報告

黃月蘭　王誠一　林恆毅　鍾世哲　張炎德

吸入性異物常發生在小孩及老年人身上。我們報告一位65歲男性病患。因不知吸入異物多長時間而導致左側大量胸水及膿胸。在胸部X光及電腦斷層掃描下證實了一支約11公分長的抽痰管在左側氣管，但四天後安排支氣管鏡取出時卻發現抽痰管在右側氣管。在不明確的病史及胸部X光沒任何發現下，吸入性異物常常難被發現，且往往會讓症狀持續而不見改善。吸入性異物偶會危及生命並需要盡快取出。支氣管鏡是取出異物的初步選擇。*(胸腔醫學* ***2010; 25: 26-30)***

關鍵詞：異物，抽痰管，膿胸

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Lemierre's Syndrome, a Forgotten Disease: Case Report and Review of the Literature

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Lemierre's syndrome is an ancient and rare disorder with a fatal potential. It is an infection usually caused by the anaerobe *Fusobacterium necrophorum* and spreads from the oropharynx to the thrombosed internal jugular vein, eventually resulting in sepsis via the hematogenous route. We report a healthy 29-year-old male who developed acute respiratory distress syndrome (ARDS) after an upper respiratory tract infection 2 weeks previous. The initial Gram stains all showed Gram-negative rods, which only grew in anaerobic blood culture bottles. After the diagnosis of Lemierre's syndrome was made and the antibiotic regimen adjusted accordingly, the patient began to improve. However, subsequent chest radiographs showed septic emboli and empyema; chest computed tomography (CT) supported the diagnosis and confirmed the presence of internal jugular vein thrombi. After chest tube drainage in addition to continued antibiotic treatment, the patient was successfully weaned off the mechanical ventilator and discharged from the hospital.

After the introduction of antibiotics, the incidence rate of Lemierre's syndrome decreased. With the appearance of drug-resistant bacteria associated with the overuse of antibiotics, however, general practitioners are now discouraged from prescribing antibiotics for uncomplicated upper respiratory tract infections. With the changes made in the antibiotics prescribing pattern, the incidence rate of this almost forgotten disease seems to be on the rise again. Correct and timely antibiotics usage improves the prognosis of Lemierre's syndrome. Beta-lactamase-containing penicillins are the drugs of choice. Lemierre's syndrome should remain in the differential diagnoses when treating patients with pneumonia preceded by upper respiratory tract infection and neck fullness or discomfort. ***(Thorac Med 2010; 25: 31-37)***

Key words: Lemierre's syndrome, pneumonia, upper respiratory tract infection, thrombophlebitis, *Fusobacterium necrophorum*

Introduction

Lemierre's syndrome, also called post-anginal septicemia or necrobacillosis, was first reported in the medical literature in 1900 by Courmont and Cade. [1] The disease is named after Andre Lemierre, who published a report describing 20 cases in 1936. [2] The popula-

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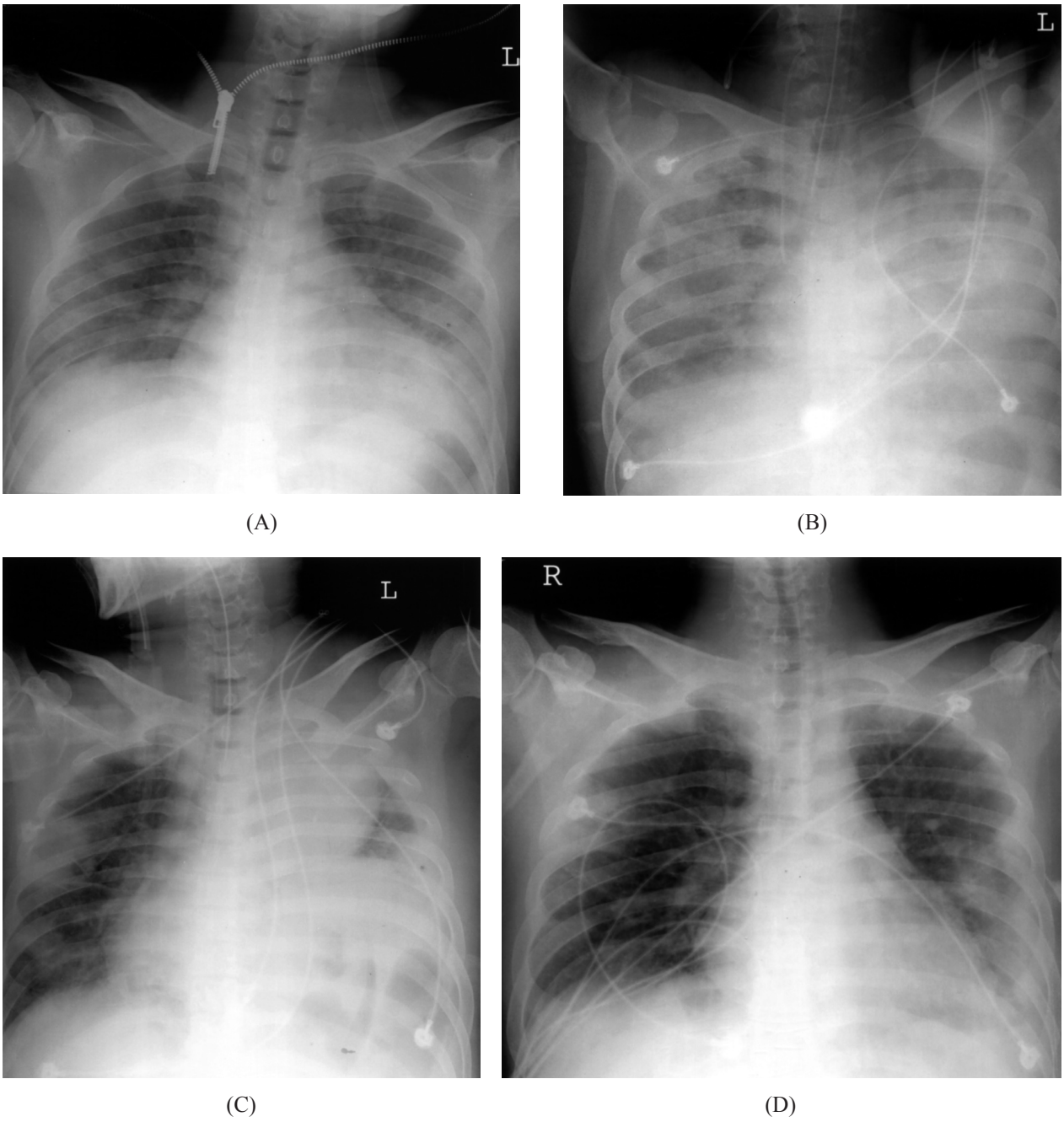
tion most at risk is adolescents and young adults. Lemierre's syndrome usually starts as an oropharyngeal infection which spreads into the surrounding soft tissue, causing thrombophlebitis of the internal jugular vein. It then spreads hematogenously to other organs, most often the lungs. The usual pathogens are anaerobes, especially *Fusobacterium necrophorum* or *Fusobacterium nucleatum*. In addition, *Streptococcus* sp., *Bacteroides* sp., *Peptostreptococcus* sp., *Eikenellacorrodens* and *Staphylococcus aureus* have all been reported to cause Lemierre's syndrome. [3-6]

In pre-antibiotic years, Lemierre's syndrome was common and often fatal. After the introduction of antibiotics, the incidence rate dropped precipitously -- only 39 cases were reported between the years 1974 and 1987. [7] In the last few decades, the concept that uncomplicated upper respiratory tract infections do not require antibiotics has been emphasized so much that this disease that once was so rare is on the rise again. We report a 29-year-old male who developed respiratory distress 2 weeks after contracting an upper respiratory tract infection. His illness progressed to acute respiratory distress syndrome (ARDS) with septic embolism complicated by empyema. After appropriate antibiotic treatment and surgical drainage, he was discharged in good health.

Case Report

A 29-year-old male presented with cough for 2 weeks and the subsequent development of fever for 3 days. He was treated for an upper respiratory tract infection initially at a local medical clinic. He was a bank clerk and had smoked 1 pack of cigarettes per day for 3 years. He denied recent travel and had no remarkable past medical history.

He was brought in to the emergency department after a sudden onset of right upper chest pain. The pain was sharp, without radiation, or precipitating or relieving factors. His temperature was 38.1^{o}C, heart rate 126/min, respiratory rate 18/min, blood pressure 109/52 mmHg, and oxygen saturation (SpO_2) 92% while breathing room air. He was diaphoretic and cyanotic around the lips upon presentation. He also had bilateral rhonchi and crackles, and several pustules on his left flank area. Electrocardiogram showed normal sinus rhythm without ST-T changes. Chest radiograph revealed a bilateral diffuse alveolar process (Figure 1A). His white count was 10,000/μl (segments: 71%, band forms: 20%). C-reactive protein was 36.3 mg/dl. We sampled blood for bacterial cultures and started intravenous levofloxacin. The patient was then intubated. Septic shock with acute renal failure soon followed. ARDS occurred on the 2nd day of hospitalization (Figure 1B). High positive end-expiratory pressure and low tidal volume settings on the mechanical ventilator were used to avoid further lung injury. Arterial oxygenation improved. The initial Gram stain of the sputum (Figure 2) and the aspirates from the skin pustules both revealed Gram-negative bacilli. The antibiotics were changed from levofloxacin alone to imipenem plus erythromycin and oseltamivir. The patient's general condition started to improve. By the 7th day of hospitalization, only anaerobes had grown from the blood culture bottles. Metronidazole was then added to the antibiotics regimen. On the 10th day, his chest radiograph showed a rapid accumulation of multi-loculated pleural effusion at left side and multiple cavitary nodules (Figure 1C). Chest computed tomography (CT) showed similar findings. Thoracentesis disclosed empy-



(A) (B)

(C) (D)

Fig. 1. (A) Initial CXR revealed a bilateral alveolar process. (B) ARDS developed on the 2nd day of hospitalization. (C) Accumulation of loculated pleural effusion and multiple peripheral nodules with a cavity were noted on the 10th day. (D) After surgical drainage.

ema thoracics. Septic embolism with empyema formation was diagnosed. In addition, intravascular thrombus in the left internal jugular vein was noted on both the chest CT (Figure 3) and neck sonogram. Cardiac sonogram showed no valvular vegetation. Decortication under video-assisted thoracoscopic surgery was performed. Fever subsided after surgical drainage and the

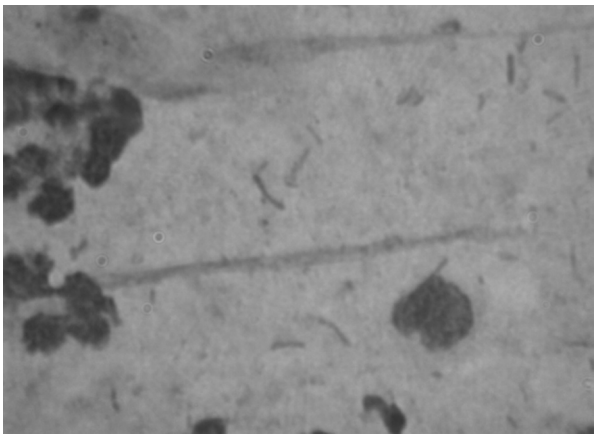


Fig. 2. Gram stain of the patient's sputum revealed Gram-negative bacilli.

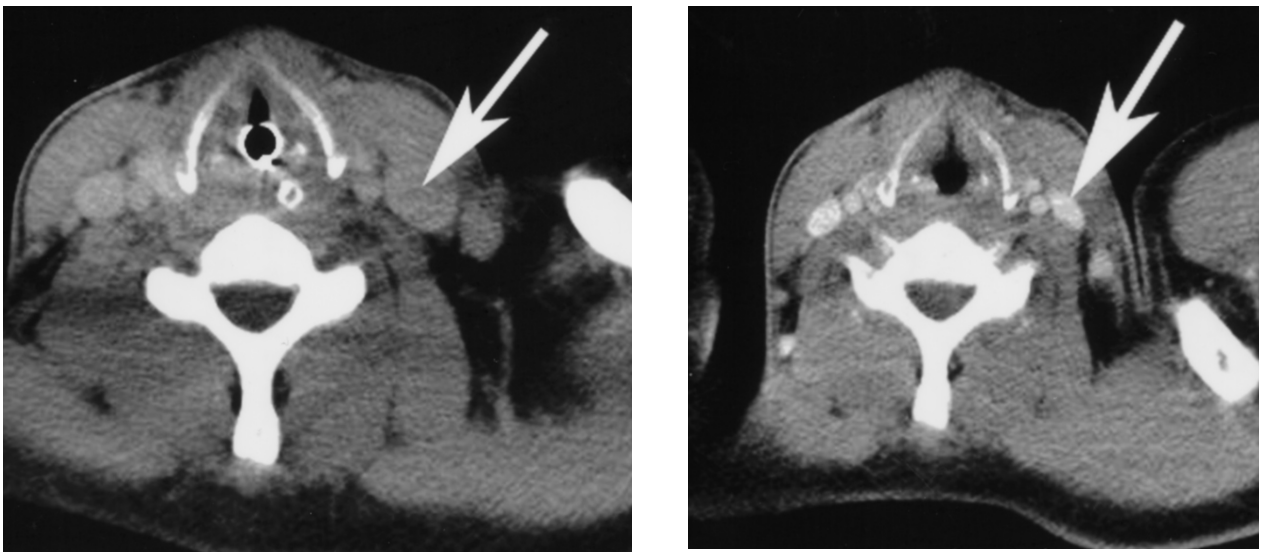


Fig. 3. CT revealed engorgement of the left internal jugular vein (arrow). The thrombophlebitis improved on the follow-up CT image 2 months later.

patient was successfully extubated 2 days after surgery (Figure 1D). The blood culture confirmed growth of *Fusobacterium necrophorum* on the 14th day of hospitalization. High-dose penicillin was given for another 7 days, and the patient was discharged.

Discussion

The population most at risk for Lemierre's syndrome is adolescents and young adults; it can occur occasionally in children or the elderly. Most of the patients are in good health before the onset of their illness. There is no predilection for either sex. A Danish study indicated that the incidence rate for Lemierre's syndrome is around 0.8/million persons. [8]

Fusobacterium necrophorum causes more than 80% of Lemierre's syndrome. Other bacteria are less frequently reported. *Fusobacterium necrophorum* is part of the normal flora in the oropharynx, the female genitals, and the gastrointestinal tract. It is a non-motile, non-spore forming, Gram-negative, obligate anaerobe. It produces lipopolysaccharide endotoxins like Gram-negative aerobes. In addition, it produces leukocidin and hemolysin, both of which potentiate its toxicity. [9] Recent reports have indicated that *Fusobacterium necrophorum* can escape being killed by complements by binding with complement inhibitor factor H. This enables it

to be pathogenic even in healthy young adults who are not immunocompromised by injury or cancer. [10]

The initial portal of infection is usually the tonsils and their adjacent tissue. However, otitis media, mastoiditis, parotitis, and tooth infection have also been reported to be the initial event. [11] The bacteria then invade the parapharyngeal space. Some reports have indicated that Epstein-Barr virus infection or infectious mononucleosis may weaken the usual physiological barriers, thereby facilitating invasion by the bacteria. However, the actual mechanism is still unclear. [12-13] Involvement of the parapharyngeal space leads to thrombophlebitis of the neck vessels, which in turn results in hematogenous spread of the infection.

After the dissemination of the bacteria, most of the clinical manifestations occur in the lungs. Septic emboli to the lungs may cause chest pain, hemoptysis, dyspnea, or respiratory failure. Most patients exhibit 1 or 2 of these symptoms. Empyema and lung abscess are also common. Septic arthritis and other less common complications, such as meningitis, sigmoid sinus thrombosis, liver abscess, hepatic venous thrombosis, acute renal failure, pyomyositis and fasciitis have also been reported. ARDS as a complication of Lemierre's syndrome was first reported in 1993. It is generally managed by a low tidal volume just as in ARDS of other etiologies in order to support the patients while waiting for the antibiotics to take effect. [14] This is how our patient was managed. Extracorporeal carbon dioxide removal has been used to deal with carbon dioxide retention in a patient with intractable pneumothorax and ARDS. [15] Endotoxins may be the culprit in ARDS caused by *Fusobacterium necrophorum*, and hemoperfusion with polymyxin B-immobilized fiber has been used successfully to reduce the concentration of endotoxin in the serum of these patients. [16]

In his original report, Lemierre wrote, "the appearance and repetition several days after the onset of a sore throat (and particularly of a tonsillar abscess) of severe pyrexial attacks with an initial rigor, or still more certainly the occurrence of pulmonary infarcts and arthritic manifestations, constitute a syndrome so characteristic that mistake is almost impossible." [1] Therefore, clinical suspicion of Lemierre's syndrome should be raised in all patients with pharyngitis or tonsillitis complicated by swollen or painful neck and lower respiratory tract symptoms. The diagnosis is established by obtaining a blood sample for culture, and confirming thrombophlebitis in the internal jugular vein. [17] The severity of disease is often correlated with the delay in giving appropriate antibiotics. Early diagnosis and timely administration of antibiotics is most important for a good outcome.

Antibiotics treatment of sufficient duration is also important. Penicillin, clindamycin, and metronidazole are all traditionally effective agents against *Fusobacterium necrophorum*; however, some bacteria produce ß-lactamase. Therefore, the safer option is to give combination ß-lactam and ß-lactamase before drug sensitivity is established. Surgical drainage is necessary if there are pockets or deep neck tissue infection. Disease dissemination, although uncommon, may progress despite of appropriate antibiotics, so ligation of the internal jugular vein or tonsillectomy may have to be considered. [9] The use of anticoagulants in Lemierre's syndrome is controversial. It may speed up the resolution of thrombophlebitis and bacteremia, and is probably appropriate if there is

a cerebral infarct or sinus venous thrombosis. Aspirin, enoxaparin and warfarin have all been tried. As there is no large-scale study to support its benefits, the potential risk of bleeding needs to be taken into consideration before using anticoagulants. [18]

Lemierre's syndrome is a rare disorder mostly caused by the anaerobe *Fusobacterium necrophorum*. We should include Lemierre's syndrome in the differential diagnoses when febrile patients with swelling of the neck and previous throat infection present with septic emboli. Early diagnosis and appropriate antibiotics lead to a good prognosis.

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Lemierre 氏症候群：病例報告與文獻回顧

賴君宇* 葉育雯*,** 林鎮均*

Lemierre氏症候群，一個古老，罕見，但卻有潛在性致命危險的疾病，主要是由厭氧菌壞死細梭桿菌造成口咽部的感染，進而侵犯到內頸靜脈造成栓塞性靜脈炎，最後經由血行性傳染造成全身性轉移的敗血症(主要是以肺部的表現為主)，我們報告一個29歲的健康男性，在兩週的上呼吸道感染症狀之後，於短短的時間內就進展到呼吸衰竭與急性呼吸窘迫症候群，一開始所有檢體的染色都顯示是革蘭氏陰性桿菌，但只有在厭氧瓶的血液培養中有細菌生長，在有了初步方向與Lemierre氏症候群的診斷，選用適當的抗生素治療之後，病人情況開始改善，但是接下來的的胸部X光片顯示敗血性栓塞與膿胸的形成，胸部電腦斷層也有同樣的發現，除此之外，還發現病人的內頸靜脈有血管內的栓塞，雖然病人在臨床上並沒有脖子腫痛的症狀，在外科引流膿胸與持續的抗生素治療之後，病人成功的脫離呼吸器，於幾天後健康的出院。

因為抗生素的發明以及廣泛的被使用，Lemierre氏症候群的發生率的確有下降的趨勢，但最近不斷的宣導上呼吸道感染不應例行性的使用抗生素之後，這個被遺忘的疾病有病例增加的趨勢，使用正確的抗生素治療決定此疾病的預後，含有乙型內醯胺酶抑制劑的盤尼西林維治療的首選，對於合併有脖子腫脹，上呼吸道症狀與肺部病變的病人，鑑別診斷時應該把此疾病列入考慮。*(胸腔醫學 **2010; 25: 31-37**)*

關鍵詞：Lemierre氏症候群，肺炎，上呼吸道感染，血栓性靜脈炎，壞死細梭桿菌

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Bilateral Pulmonary Mass as a Clinical Presentation of Primary Pulmonary Leiomyosarcoma: A Case Report

Jen-Siong Yip, Jiunn-Min Shieh, Shian-Chin Ko

Leiomyosarcoma is a malignant soft tissue tumor predominantly affecting the uterine and gastrointestinal tract. Primary pulmonary leiomyosarcoma is very rare. It is diagnosed only after other primary origins have been excluded. Less than 100 cases have been reported worldwide in the literature. Most of the reported cases involved a unilateral lung, and only a few cases had bilateral lung involvement on diagnosis. We herein report a case of pulmonary leiomyosarcoma with bilateral lung involvement and no other detectable primary origin. Although the patient had a good performance status initially, the poor prognosis was inevitable in this unresectable condition. Palliative chemotherapy was given. Ultimately, the patient succumbed to the disease. ***(Thorac Med 2010; 25: 38-43)***

Key words: pulmonary tumor, leiomyosarcoma

Introduction

Leiomyosarcoma is an aggressive soft tissue sarcoma derived from smooth muscle cells typically of the uterine and gastrointestinal tract. Soft tissue sarcomas account for 0.7% of malignancies, and approximately 5-10% of all soft tissue sarcomas are leiomyosarcomas [1]. Primary pulmonary leiomyosarcoma is very rare. Less than 100 cases have been reported worldwide in the literature. The rarity of these tumors makes definitive studies difficult to perform. A multi-specialty treatment plan is needed and a grave prognosis is inevitable for those who are unresectable. Lymph node metastasis or bilateral lung involvement is extremely rare, even though distant metastasis is present [2]. Herein, we report a case of primary pulmonary leiomyosarcoma with bilateral lung involvement.

Case Report

A 55-year-old woman presented with progressive dyspnea on exertion. She had had productive cough with whitish sputum for a few weeks. A poor appetite with body weight loss of 5 kilograms was noted during the previous 3 months. She was a housewife and had no history of smoking or alcohol consumption. There was no fever, chest pain, hemoptysis, or dysphagia. The symptoms progressed, and she was

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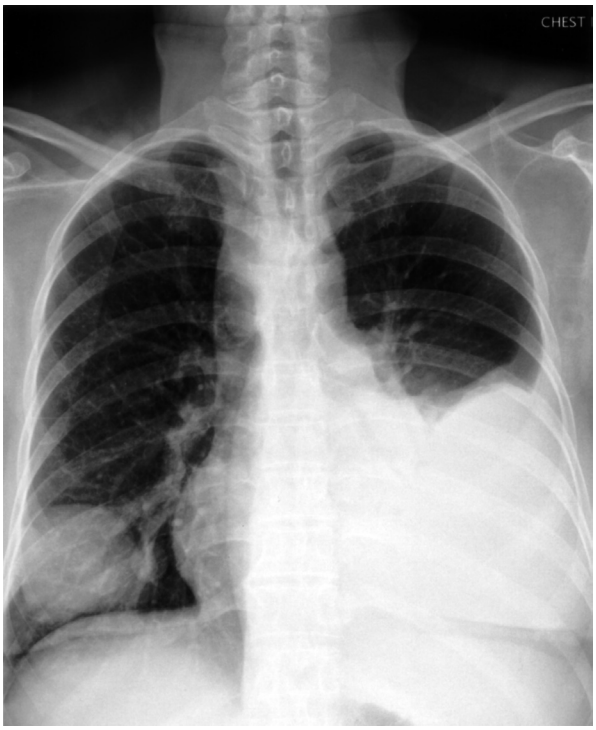

Fig. 1. Chest radiograph shows mass-like lesions in the bilateral lower lung zone with a blunting left heart border and hemidiaphragm.

brought to our emergency department for help.

On physical examination, her body temperature was 36.5°C, pulse rate was 96 beats per minute, respiratory rate was 18 per minute, and blood pressure was 125/60 mmHg. The conjunctiva was slightly pale. There was no palpable neck or axillary lymphadenopathy. On auscultation, the breathing sound was decreased with rales in the left lower thorax. There were no positive findings in the abdominal region and no clubbing of the fingers.

The chest roentgenogram examination revealed a well-defined mass-like lesion at the right lower lung zone. There was radiopacity in the left lower lung zone with blunting of left the heart border and left hemidiaphragm (Figure 1). Chest computed tomography (CT) was performed, and a huge tumor about 11.1 cm in the left lower lung, with lung-to-lung metastasis

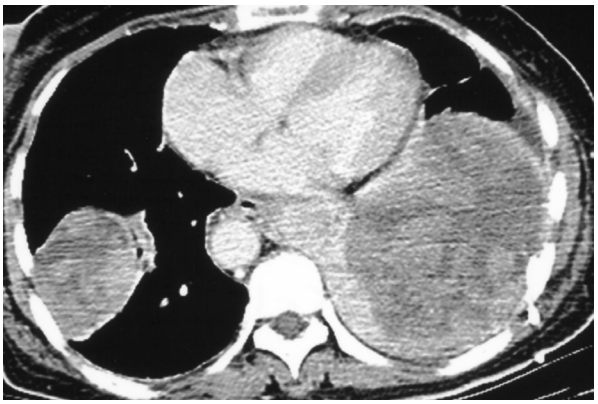

Fig. 2. Chest CT scan reveals a huge tumor in the left lower lung with lung-to-lung metastasis.

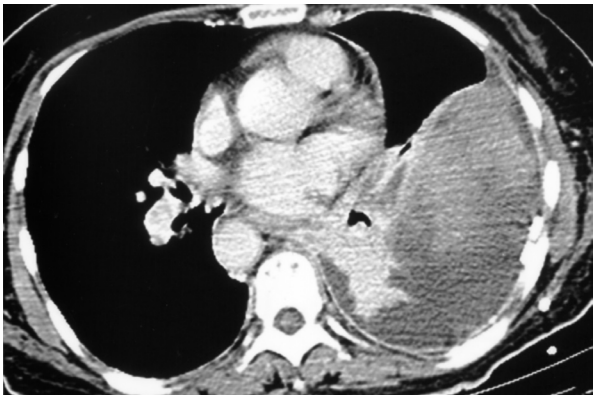

Fig. 3. Chest CT scan shows a small amount of pleural effusion with no significant lymphadenopathy.

was disclosed. No significant hilar lymphadenopathy was found (Figure 2). The main tumor was well marginated with large necrotic masses. A small amount of pleural effusion was noted (Figure 3). Laboratory assays showed mild anemia. Other blood routines and biochemistry studies were within normal limits. The serum CEA was normal (1.44 ng/ml), but CA-125 was elevated (251.0 U/ml).

Echo-guided thoracocentesis was arranged. A huge mass with heterogeneous echotexture in the left lower lung field was observed. The pleural effusion studies disclosed exudative bloody pleural effusion with lymphocytes predominant.

Then, echo-guided lung biopsy with 7 passes of a TruCut needle was performed smoothly. The histology revealed pulmonary tissue infiltrated by spindled neoplastic cells in fascicles, with focal necrosis (Figure 4). These neoplastic cells exhibited pleomorphic nuclei and eosinophilic cytoplasm (Figure 5). Immunohistochemically, these tumor cells expressed desmin (Figure 6), smooth muscle actin (Figure 7), and vimentin, but not AE1/AE3, CD34 or S-100. The diagnosis of leiomyosarcoma was confirmed.

To exclude the possibility of pulmonary metastasis, CT scan of the abdomen was performed. There was no evidence of intra-abdominal tumor or lymphadenopathy. Both bone scan and CT of the brain showed negative findings. Since the patient was not suitable for surgical resection, she received palliative chemotherapy with a regimen of epirubicin and cyclophosphamide. As her symptoms improved, she was then discharged and scheduled for out-patient department follow-up. Unfortunately, the dyspnea exacerbated again 2 weeks later, she was re-admitted and informed of the expected poor outcome. She expired under hospice care about 2 weeks after admission.

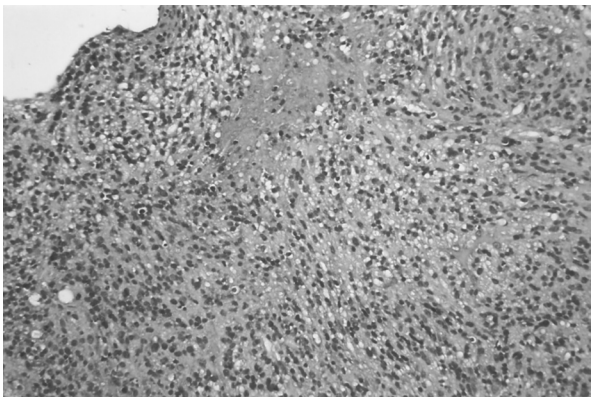

Fig. 4. The pathologic findings of the tumor revealed pulmonary tissue infiltrated by spindled neoplastic cells in fascicles, with focal necrosis (hematoxylin and eosin stain, 400X).

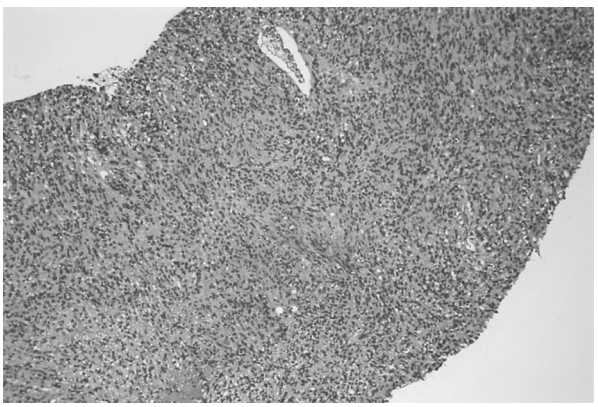

Fig. 5. The pathologic findings of the tumor revealed pleomorphic nuclei and eosinophilic cytoplasm (hematoxylin and eosin stain, 200X).

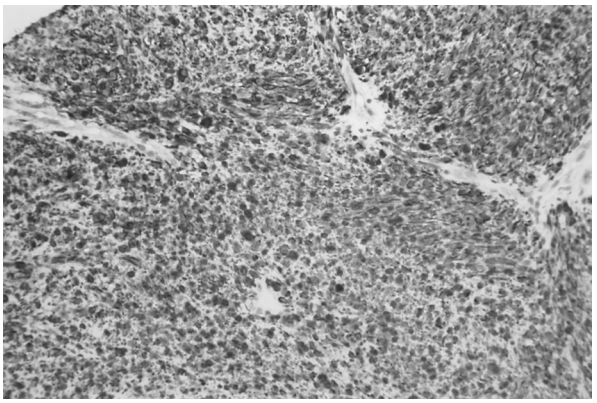

Fig. 6. The immunohistochemical staining of the lung tumor was positive for desmin (400X).

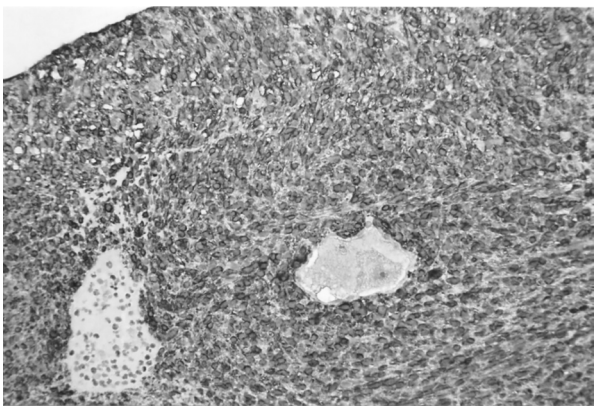

Fig. 7. The immunohistochemical staining of the lung tumor was positive for smooth muscle actin (400X).

Discussion

Primary thoracic leiomyosarcoma may occur in the mediastinum, heart, and lung [3]. Mediastinal leiomyosarcoma typically manifests clinically as a local mass effect [4], whereas cardiac leiomyosarcomas differ from angiosarcomas in that they occur typically in the left atrium [5]. The leiomyosarcoma of the lung may arise from the pulmonary artery or lung parenchyma, and has a different clinical presentation and radiographic characteristics. Pulmonary artery leiomyosarcoma mimics pulmonary embolism, in that it presents with chest pain, dyspnea or right-side heart failure. Gadolinium enhancement on magnetic resonance imaging (MRI) allows a distinction from thrombus [6]. Patients with primary pulmonary leiomyosarcoma are often asymptomatic, but they can present with cough and hemoptysis if bronchial involvement exists [7].

Leiomyosarcoma is 1 of the common histologic subtypes of sarcoma occurring in the lung [8]. Primary pulmonary leiomyosarcoma usually occurs in the sixth decade, with male predominance [2]. The radiologic characteristics of these neoplasms are well-marginated smooth or lobulated homogeneous nodules. Large area of necrosis or hemorrhage in the mass can be found in the advanced stage [9]. These neoplasms occur with an equal frequency in the right and left lungs: 2.63-3.13% of patients had bilateral lung involvement when the tumors were recovered [2, 10]. Since blood-borne spreading is the main route of metastasis, lymphadenopathy is extremely rare. Contrast-enhanced dynamic MRI is an alternate method to facilitate an accurate preoperative diagnosis [11].

The lung is 1 of the favored metastatic sites for soft tissue sarcomas; primary pulmonary sarcomas should be confirmed after excluding the possibility of an alternate primary source by clinical history and radiographic evaluation [5]. We arranged the abdominal CT scan to exclude the most common origins of leiomyosarcoma (uterine and gastrointestinal tract). In addition, pulmonary sarcomas must be distinguished from a number of sarcoma-like primary lung neoplasms, including spindle and giant cell carcinoma, and from mixed epithelial/mesenchymal lesions such as pulmonary blastoma and carcinosarcoma. Immunohistochemistry has an important role and supports the diagnosis by demonstrating the presence of muscle-specific markers, including vimentin (intermediate filament protein of mesenchymal cells), desmin (marker for muscles), and smooth muscle actin; and the absence of other markers, including AE1/AE3 (cytokeratin antibody in carcinoma), CD34 (endothelial marker), S-100 (marker for all nerve sheath tumors) [12].

Surgical resection remains the most effective potentially curative treatment for soft tissue sarcomas regardless of their site of origin. Pulmonary metastasectomy for leiomyosarcoma is an acceptable treatment to improve survival [13]. The prognosis is poorer when the tumor is unresected or incompletely resected. Achieving wide surgical margins is important in preventing local recurrence [14]. The primary role of chemotherapy is in the treatment of metastatic disease, and no survival benefit has been demonstrated. Chemotherapy is sometimes used as an adjunct to the treatment of localized sarcomas. The agents that are used include doxorubicin, gemcitabine, taxotere and ifosfamide. There may be a survival benefit for adjuvant chemotherapy using doxorubicin-based regimens [15]. Patients with unresected sarcomas,

particularly with a tumor size <5 cm, can be treated with high-dose radiation therapy with or without chemotherapy [16].

In summary, primary pulmonary leiomyosarcoma may manifest with a bilateral lung mass, like other primary lung cancers. We should be aware of this rare differential diagnosis via chest CT or contrast-enhanced MRI. The immunohistochemical study is an efficient tool in diagnosis. Further studies are needed to determine the optimal treatment.

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以兩側肺部病灶爲臨床表現的原發性肺部平滑肌肉瘤：病例報告

葉子洪　謝俊民　柯獻欽

平滑肌肉瘤是一種影響子宮和腸胃道為主的惡性軟組織腫瘤。原發性肺部平滑肌肉瘤更是非常罕見。診斷前必須先排除其他原發部位。目前在全世界曾經被報導的病例不到一百個。大部分被報導的病例都只有單側肺部病灶，只有少數的病例在診斷時已經有兩側肺部病灶。本病例是一個以兩側肺部病灶為表現的平滑肌肉瘤，而且沒有發現其他原發部位。儘管病人剛開始時的狀態不錯，其預後卻因無法切除而很差。我們只能給予姑息性的化學治療。最終病人還是因疾病而死亡。*(胸腔醫學 **2010; 25: 38-43**)*

關鍵詞：肺腫瘤，平滑肌肉瘤

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Pseudo-Meigs' Syndrome Presenting as Lymphocytic Pleural Effusion with Elevated Adenosine Deaminase Activity – A Case Report

Zhung-Han Wu*, Chi-Li Chung*,**

Pseudo-Meigs' syndrome is defined as the association of nonmalignant hydrothorax and ascites with any benign or malignant pelvic tumor other than benign solid ovarian tumor. We reported a 38-year-old obese woman who was admitted for massive right-side pleural effusion. The analysis of the pleural fluid revealed an exudate with lymphocyte predominance and an increased adenosine deaminase (ADA) level (49 IU/L). The patient was treated as having tuberculous (TB) pleurisy initially. However, the pleural effusion did not resolve and further examinations disclosed ascites and ovarian cancer. After surgical resection of the ovarian tumor, both the hydrothorax and the ascites resolved markedly and did not recur during the 1-year follow-up. This report described mildly elevated ADA activity in pleural effusions associated with pseudo-Meigs' syndrome. Although a relatively uncommon etiology, pseudo-Meigs' syndrome should be included in the differential diagnosis of a lymphocytic pleural exudate with high ADA activity. ***(Thorac Med 2010; 25: 44-50)***

Key words: adenosine deaminase, hydrothorax, pleural effusion, Pseudo-Meigs' syndrome

Introduction

In 1937, Meigs described a syndrome characterized by the presence of ascites and pleural effusion in patients with ovarian fibroma [1]. Meigs also defined pseudo-Meigs' syndrome as the association of nonmalignant hydrothorax and ascites with any benign or malignant pelvic tumor other than a benign solid ovarian tumor [2]. Both the ascites and pleural effusion resolved spontaneously when the pelvic mass was removed, which confirmed the diagnosis. Pseudo-Meigs' syndrome is usually not identified before surgery, and some cases presented initially with pleural effusions of unknown origin [3-4].

Adenosine deaminase (ADA) levels are elevated in the pleural effusion of tuberculous (TB) pleurisy, and measurement of ADA activity is of value in the approach to idiopathic pleural effusions to rule out TB pleuritis [5]. However, to the best of our knowledge, ADA activity has never been reported in the pleural fluid of patients with Meigs' or pseudo-Meigs'

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syndrome. We report a case of pseudo-Meigs' syndrome due to ovarian carcinoma presenting with a large amount of lymphocytic pleural effusion with an elevated ADA level, which masqueraded as TB pleuritis.

Case Report

A 38-year-old female was admitted to the hospital because of palpitation and progressive dyspnea for 2 weeks. She was a nonsmoker, without a history of systemic diseases. The patient's menstruation was regular, and she did not have a history of malaise, fever, weight loss, night sweats, abdominal pain, or swelling of the extremities. She was a well-developed, but obese young female. Her body height was 160 cm and body weight 102 kg. Her consciousness was oriented. Initial examination revealed her temperature was 36.2°C, blood pressure 138/88 mmHg, pulse rate 102 beats per minute and respiratory rate 24 cycles per minute. Physical examination revealed dullness to percussion and diminished breathing sounds in the right lower lung zone and a distended non-tender abdomen with no shifting dullness. No abdominal masses were palpable. The rest of the physical examination was unremarkable.

The results of blood tests, including complete blood count, coagulation tests, electrolytes, liver function tests and renal function tests were all within the reference range. The electrocardiogram revealed regular sinus tachycardia and diffuse non-specific T wave changes. The chest radiograph (Figure 1) showed cardiomegaly and a massive pleural effusion occupying more than half of the right hemithorax. The echocardiography revealed moderate-to-severe pulmonary hypertension, but the chamber size, wall thickness, and contractility of the left ventricle were normal.

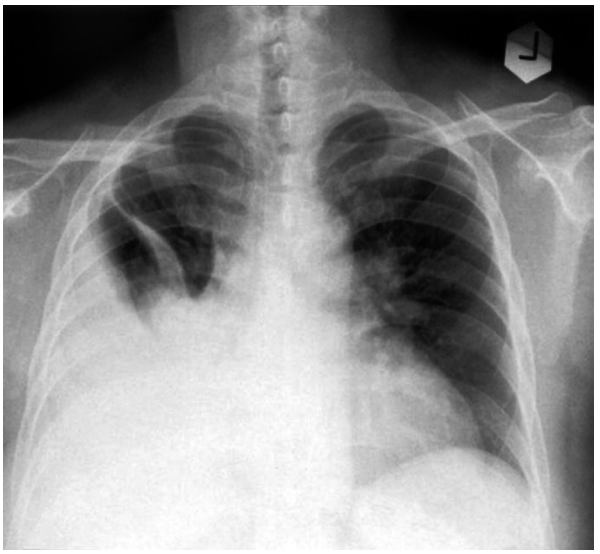

Fig. 1. The chest radiograph at admission showed massive right-side pleural effusion.

She was placed in a sitting position. Chest ultrasonography was performed and disclosed a massive amount of complex, non-septated pleural effusion in the right pleural space. Thoracentesis was performed and 30 ml of brown-colored, mildly cloudy pleural fluid was drained. Biochemical analysis of the pleural fluid showed: LDH 298 U/L; glucose 299 mg/L; total protein 4.8 g/dL; amylase 32 IU/L. Pleural fluid pH was 7.43. The total pleural fluid white blood cell (WBC) count was 890 cells/μl. The differential cell count showed lymphocyte predominance (neutrophil 19%, lymphocyte 81%). Using the colorimetric method of Giusti and Galanti [6], the level of ADA activity measured in the pleural fluid was 49 IU/L. The Gram's stain, acid-fast stain, and bacteria culture of the pleural fluid revealed no significant finding. Repeated cytological examination showed no evidence of malignant cells. Pleural fluid carcinoembryonic antigen (CEA), antinuclear antigen (ANA), and rheumatoid factor (RF) were

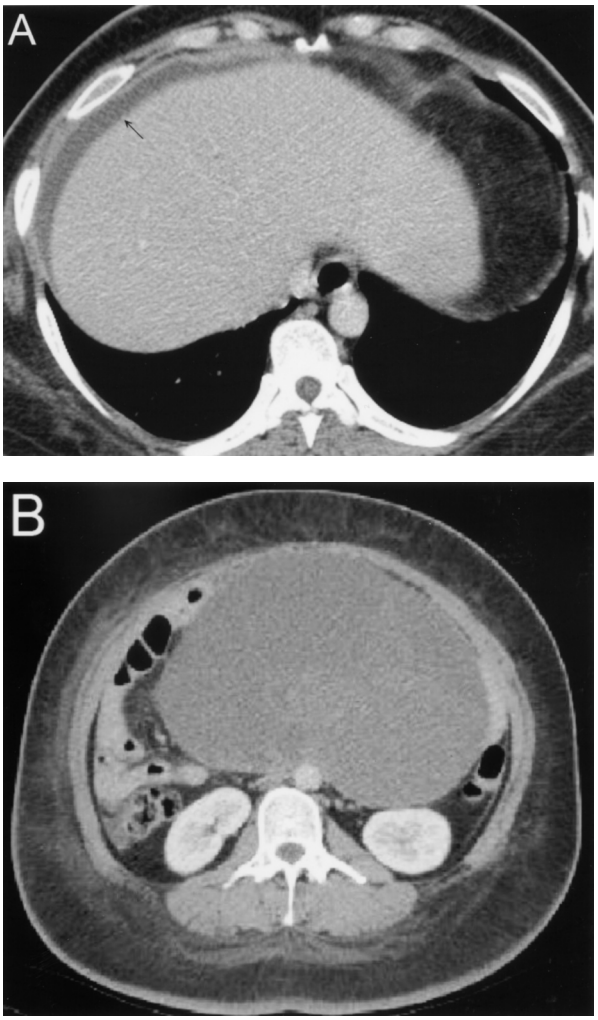

Fig. 2. CT imaging of the chest and whole abdomen. In 2A. After pigtail drainage of the right-side pleural effusion, chest CT revealed a small amount of ascites (arrow) in the perihepatic space and no pleural or parenchymal lung lesion. In 2B. The whole abdominal CT disclosed a huge well-defined cystic mass, about 30 cm in diameter, in the pelvic cavity. The thick subcutaneous fat layer of the abdominal wall was also noted.

all within the reference range. Pleural biopsy was performed and the pathological finding showed chronic inflammation, and no evidence of granuloma or malignancy. Since the massive pleural effusion was causing respiratory embarrassment, a pigtail tube was inserted to drain the pleural fluid as completely as possible. As the pleural effusion was characterized by a lymphocytic pleural exudate with an ADA level above 40 IU/L, the diagnosis of TB pleurisy could not be excluded [7]. Therefore, the patient was started on anti-TB therapy on the 4th day of admission, using isoniazid, rifampicin, emthambutol and pyrazinamide [5]. However, daily drainage of massive amounts of pleural fluid (ranging between 1100 and 1800 ml per day) persisted during the next 12 days. Computed tomography (CT) scanning of the chest was performed and revealed no pleural or parenchymal lung lesions, but a small amount of ascites in the perihepatic space was found (Figure 2A).

The patient underwent a whole abdominal CT examination to search for the cause of the ascites, and the results disclosed a huge cystic pelvic mass, about 30 cm in diameter, suggestive of an ovarian tumor (Figure 2B). The serum level of cancer antigen-125 (CA-125) was 1124 U/ml. The patient underwent laparotomy, incision of the pelvic mass and left salpingo-oophorectomy, which revealed 1400 ml of straw-colored ascitic fluid in the peritoneal cavity. There was no palpable pelvic or periaortic adenopathy; the liver, diaphragm, bowel, and omentum were grossly free of disease. The pathologic examination of the pelvic mass confirmed the diagnosis of ovarian adenocarcinoma, and the cytological examination of ascites showed reactive mesothelial cells and no evidence of malignancy. The pigtail tube was removed and anti-TB therapy was discontinued postoperatively. Two days after surgery, the follow-up chest radiograph revealed marked resolution of hydrothorax (Figure 3). The patient was discharged uneventfully and regularly and underwent 6 cycles of adjuvant chemotherapy (cisplatin and cyclophosphamide). The chest radiograph obtained 1 year later revealed no recurrence of pleural effusion (Figure 4).

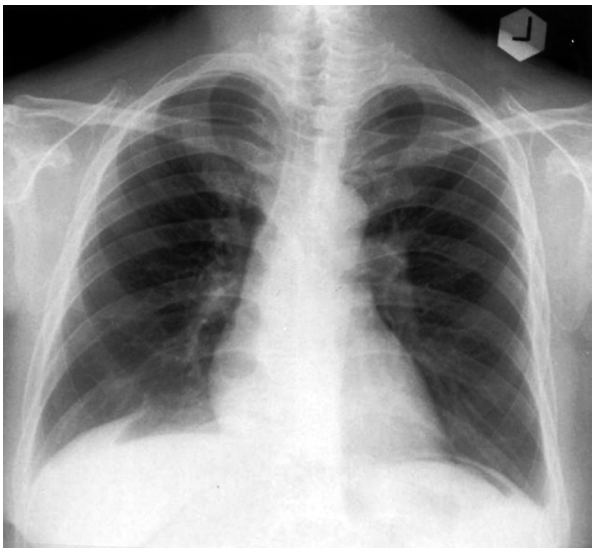

Fig. 3. The chest radiograph obtained 2 days after resection of the ovarian tumor revealed marked resolution of the right-side pleural effusion and residual free air in the left subphrenic area.

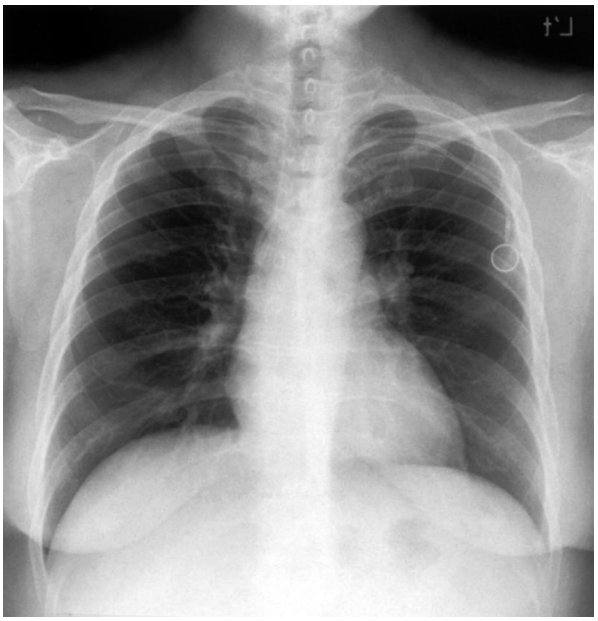

Fig. 4. The chest radiograph taken 1 year later showed no recurrence of pleural effusion. The port-A catheter was in place.

Discussion

Pseudo-Meigs' syndrome is relatively uncommon and usually manifests with a chronic illness characterized by a pleural effusion, ascites and a pelvic mass [2]. The symptoms include fatigue, shortness of breath, increased abdominal girth, and body weight loss. Tachypnea and tachycardia are usually noted. Chest examination reveals dullness to percussion and decreased breathing sounds on the side affected by the pleural effusion [2]. However, physical examination of the abdomen and pelvis may or may not reveal ascites and a pelvic tumor. [3-4, 8]. The pleural effusion is usually located on the right side (70%), and is less common on the left (15%) and bilaterally (15%) [8-9]. The pleural and ascitic fluids are of a similar nature and may be either transudate or exudate; they are usually positive for reactive mesothelial cells and negative for malignant cells on cytological examination [1, 4, 10]. Diagnosis of the syndrome requires a demonstration of resolution of both the pleural effusion and ascites once the pelvic tumor has been surgically removed. A few patients, as with ours, have been reported to present initially with pleural effusion of an unknown etiology [3-4].

The pleural effusion in the present case manifested as an exudate with lymphocyte predominance. Evaluation of exudative pleural effusion usually includes a complete clinical examination, appropriate blood tests, radiographs, studies of the pleural fluid, and needle biopsy of the pleura [11]. Furthermore, the ADA level should be measured in the approach for lymphocytic pleural effusions [5]. ADA is an enzyme found in most cells and is important in the metabolism of purine nucleotides. It is required for lymphoid cell differentiation, particularly T lymphocytes, and the maturation of monocyte-macrophages [12]. Therefore, the ADA level is a good parameter for identifying pleural TB, in which T lymphocytes and mono-

cytes play essential roles in the inflammatory response. In general, levels of ADA activity in pleural fluid >40 IU/L have high sensitivity (81-100%) and specificity (83-100%) for TB pleural effusion [13], while a level below 40 IU/L virtually excludes the diagnosis [7]. High levels of ADA also have been reported in other conditions associated with pleural fluid lymphocytosis, including malignancy and collagen vascular diseases, which make the test less useful in countries with a low prevalence of TB [14]. In contrast, in areas of high prevalence, ADA measurement is a very useful test for TB pleurisy because it is inexpensive, minimally invasive, rapid and readily accessible, and the sensitivity and specificity may reach 95% and 90%, respectively [15].

The present case was initially mistaken for TB pleurisy. There are several reasons as to why a misdiagnosis would occur. First, this patient presented with the symptom of dyspnea only and right-side pleural effusion. Owing to her obesity, the pelvic mass could be shielded by the thick subcutaneous fat layer of her abdominal wall (Figure 2B) and, as in previous reports [3-4], was not detected on initial physical examination. Second, the small amount of ascites was not detectable by the chest ultrasonography because the patient was placed in a sitting position to receive the examination, and the ascites could shift to the dependent part of her peritoneal cavity. Third, except for the elevated pleural ADA level, the results of the laboratory tests and cytopathological examinations of the lymphocytic pleural fluid were all inconclusive, which presented us with a dilemma as to the cause of the intractable pleural effusion. Fourth, in areas with a high prevalence of TB, as in Taiwan, the pleural ADA level false positive rate would obviously be lower [14], so it is reasonable to consider TB pleurisy as the cause of lymphocytic pleural effusions with the presence of an elevated ADA level (>40 IU/L). Fifth, we did not perform CT imaging studies to search for an occult etiology of the pleural effusion before we started the anti-TB therapeutic trial. Nevertheless, to the best of our knowledge, this is the first report to demonstrate elevated ADA activity in pleural effusion associated with pseudo-Meigs' syndrome, and reminds us that further careful abdominal and pelvic physical examinations and imaging studies of the chest and abdomen are required in the management of any patient with unexplained or recurrent pleural effusions, even with high ADA activity.

In conclusion, this report has described elevated ADA activity in pleural effusion associated with pseudo-Meigs' syndrome. Although a relatively uncommon etiology, pseudo-Meigs' syndrome should be included in the differential diagnosis of a lymphocytic pleural exudate with high ADA activity.

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以 ADA 活性偏高之淋巴球性肋膜積水爲表現的 Pseudo-Meigs 症候群—病例報告

吳宗翰* 鍾啟禮*,**

Pseudo-Meigs症候群的定義是，除了良性實體卵巢腫瘤外，凡其它任何良性或惡性之骨盆腔腫瘤之患者，合併發生非惡性之肋膜積水及腹水。我們報告一位三十八歲的肥胖女性患者，因大量右側肋膜積水而住院；其肋膜積水之數據顯示為以淋巴球為主，且腺苷酸脫氨基酶（adenosine deaminase, ADA）活性高之滲出液（exudate）。這位患者起初被懷疑為結核性肋膜炎接受抗結核藥物治療，然而其肋膜積水並未改善，每天仍有高達1100~1800 ml 從胸管引流出來；進一步檢查發現了合併產生的腹水及卵巢癌。經外科手術切除卵巢腫瘤後，肋膜積水及腹水皆明顯減少，且經過一年的持續追蹤後，並無復發的情況。這份病例報告顯示在pseudo-Meigs症候群患者的肋膜積水為以淋巴球為主且ADA的活性是增加的。雖然pseudo-Meigs症候群是一相對少見的疾病，但是當發現有高ADA活性與淋巴球為主之滲出性肋膜積水時，仍應將其列為鑑別診斷之一。*(胸腔醫學* ***2010; 25: 44-50)***

關鍵詞：腺苷酸脫氨基酶，胸水，肋膜積水，Pseudo-Meigs症候群

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Left Chylothorax Following Subtotal Gastrectomy and Vagotomy – A Case Report

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Chylothorax is a rare postoperative complication of general surgery. It has never been reported to occur after subtotal gastrectomy and vagotomy. We described a 66-year-old man who developed left chylothorax resulting from subtotal gastrectomy and vagotomy. Conservative treatment was tried first. Then, surgical intervention through right-sided video-assisted thoracoscopic surgery with clipping of the right thoracic duct was performed, but failed. Finally, left thoracotomy with ligation of the branch of the thoracic duct at the supradiaphragmatic region resolved the left chylothorax. ***(Thorac Med 2010; 25: 51-55)***

Key words: chylothorax, subtotal gastrectomy, vagotomy, left thoracotomy, thoracic duct ligation

Introduction

Chylothorax can contribute to significant morbidity and mortality. Loss of chylous fluid can lead to nutritional deficiency and metabolic disturbance. However, the underlying primary disorder is different. Identifying the causes is important in planning treatment, which can consist of conservative and surgical management [1]. Surgical intervention emphasizes 2 key factors: reducing the chylous leak and providing good lung re-expansion. Several surgical techniques, including direct ligation of the thoracic duct, supradiaphragmatic mass ligation of the thoracic duct, infradiaphragmatic mass ligation, and fibrin glue application, have been discussed [2]. These techniques can be performed by either an open approach or video-assisted thoracoscopic surgery (VATS). We report the first left chylothorax resulting from subtotal gastrectomy and vagotomy. The patient was cured finally by left thoracotomy intervention with ligation of the branch of the thoracic duct.

Case Report

A 66-year-old man was sent to a hospital with the presentation of fresh bloody vomiting. Gastric ulcer with active bleeding was diagnosed, and a subtotal gastrectomy with Billroth II anastomosis and vagotomy were done at another hospital. A large ulcer at the lower antrum with adherent blood clot was found. The patient was discharged on the 20th postopera-

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tive day uneventfully. Two months later, he was admitted to the same hospital for repair of a ventral hernia. The chest film showed left massive pleural effusion. The left thoracocentesis revealed chylous pleural effusion. Right-sided VATS supradiaphramatic thoracic duct clipping and left tube thoracostomy were performed. Left chemical pleurodesis was also done twice after operation. The patient was discharged on the 29th postoperative day.

Two months later, the patient felt progressive shortness of breath. The follow-up chest film showed left recurrent massive pleural effusion with a compressed trachea, and the mediastinum and heart pushed to the right side (Figure 1). He was referred to our hospital for the further management. Chest computed tomography (CT) showed huge loculated fluid in the left pleural cavity, about 18.1 × 8.6 × 29.8 cm in length (Figure 2). After hospitalization, a pig-tail catheter was inserted into the left pleural space and up to 2000 ml of milky pleural effusion was drained the first day. The concentration of triglyceride in the pleural effusion was 1462 mg/dl. The pig-tail catheter broke and the follow-up chest film showed increased left pleural effusion. Total parenteral nutrition failed. Then, olive oil, 200 ml, was administered through a nasogastric tube 2 hours before operation in order to identify the thoracic duct. Under general anesthesia with single-lung ventilation, the patient was placed in the right decubitus position. Posteriolateral thoracotomy via the left 6th intercostal space was performed. About 3200 ml of milky pleural effusion was drained when entering the pleural space. Peel formation with pleural adhesion in the left pleural cavity was detected during operation. The inferior pulmonary ligament was dissected, and the parietal pleura lying over the site between the descending thoracic aorta and the esophagus was divided. The thoracic duct was difficult to find between the aorta and the azygos vein. We carefully searched for the source of the milky pleural effusion. Finally, the major branch of the thoracic duct was identified at the left side of the descending thoracic aorta on the diaphragm. We ligated the major branch of the

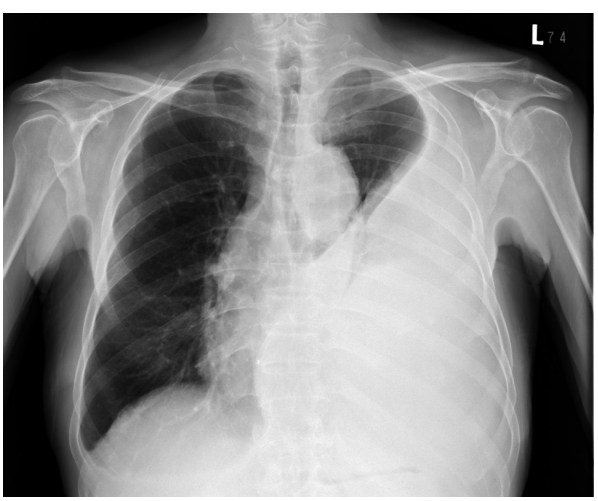

Fig. 1. The frontal chest plain film showed left massive pleural effusion with lung volume reduction and the mediastinum pushed to the right side.

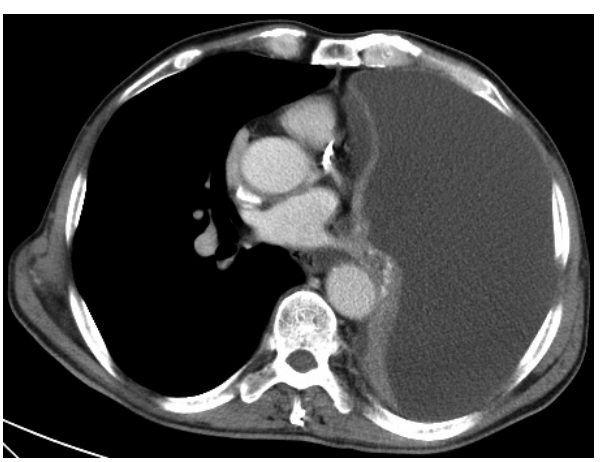

Fig. 2. The chest computed tomography disclosed a huge mass of loculated fluid in the left pleural cavity, 18.1 × 8.6 × 29.8 cm, with passive atelectasis of the left lung and compression of the mediastinum.

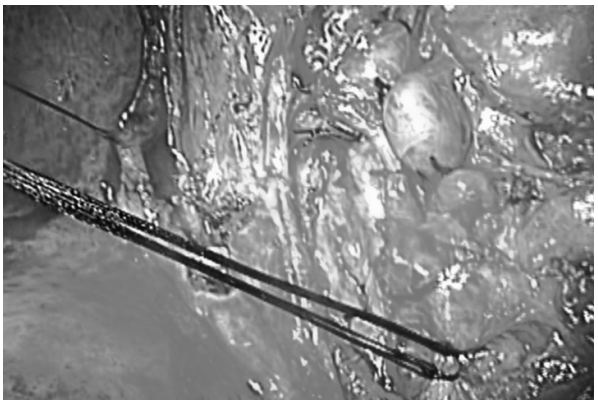

Fig. 3. The operative picture showed that the major branch of the thoracic duct on the diaphragm was ligated with double silks.

thoracic duct with double silks (Figure 3). Postoperatively, dirty pleural effusion from the left chest tube was noted, and grew *Staphylococcus aureus*. We withdrew the chest tube slowly day by day, and it was finally removed on 23rd postoperative day. The patient came back to the outpatient department for follow-up 1 month later, and the chest film demonstrated full expansion of bilateral lungs.

Discussion

Chylothorax is the accumulation of lymphatic fluid in the pleural spaces, usually as a result of a leak from the thoracic duct or 1 of its major branches. The causes are variable and include neoplasms, trauma, infection, and venous thrombus. Chylothorax can be a complication of general thoracic surgical procedures, at a frequency of 0.42% [3]. The accumulation of chyle in the chest can compromise pulmonary function, resulting in respiratory distress. A persistent chyle leak can contribute to nutritional deficiencies, immunosuppression, serious metabolic disturbance, and death. Due to the serious symptoms, treatment of chylothorax is indicated.

The treatment of chylothorax is divided into 2 general categories: conservative (non-surgical) and surgical [1]. The important principles of treatment are (1) respiratory care, (2) prevention of dehydration and malnutrition, (3) reduction of chyle production, and (4) treatment of the underlying disease. Surgical intervention is usually augmented by conservative modalities, but there is no consensus about the indications for surgery. When the chyle leakage remains higher than 200 ml/day after 2 weeks of conservative treatment, surgical intervention may be indicated [2]. The standard surgical approach was right thoracotomy in the past. In recent years, surgery has been widely performed through the right pleural space using VATS [4], which provides excellent visualization of intrathoracic structures and less postoperative pain. However, thoracic duct anatomy varies among subjects, with an incidence up to 28.6% [5]. Instillation of olive oil or cream through the nasogastric tube 2 to 3 hours before the operation has been suggested to easily identify the thoracic duct [6]. Watanabe first reported a new technique for supradiaphragmatic thoracic duct ligation using left-sided VATS [7]. Accessing the thoracic duct through the left side can be relatively technically difficult, but it should still be considered as a surgical option for patients with left chylothorax.

Surgical morbidity has occurred in about 9% of subtotal gastrectomy patients [8], but left chylothorax resulting from subtotal gastrectomy and vagotomy have never been reported before. With regard to this patient, the major branch of the thoracic duct over the infradiaphragmatic region may have been damaged accidentally during the first operation. The initial surgical treatment was right-sided VATS with endoclipping of the right supradiaphragmatic thoracic

duct, but it failed. Left-sided thoracotomy was attempted to control the chyle leakage. The thoracic duct between the descending aorta and the azygos vein was difficult to recognize. With preoperative administration of olive oil via a nasogastric tube, we were able to find the chyle leakage at the left side of the descending aorta on the diaphragm. A major branch of the thoracic duct was identified and ligated with double silks. The rare complication resulting from subtotal gastrectomy and vagotomy was managed by left-sided thoracotomy with thoracic duct ligation.

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亞全胃切除和迷走神經切斷手術後引起左側乳糜胸—病例報告

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乳糜胸在胸腔手術中為一罕見之併發症。而亞全胃切除和迷走神經切斷手術後引起左側乳糜胸未曾被報告過。我們提出一位66歲男性病人，因為接受亞全胃和迷走神經切斷切除手術後，引起左側乳糜胸，先給予保守性治療無效後，經由右側胸腔鏡輔助下，予以手術金屬夾夾住胸管後，病人乳糜胸未見改善。最後，經由左側開胸手術，在降主動脈左方於橫隔膜上找到胸管分支並結紮之，成功治療病人乳糜胸。*(胸腔醫學* ***2010; 25: 51-55)***

關鍵詞：乳糜胸，亞全胃切除，迷走神經切斷，左側開胸手術，胸管結紮

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