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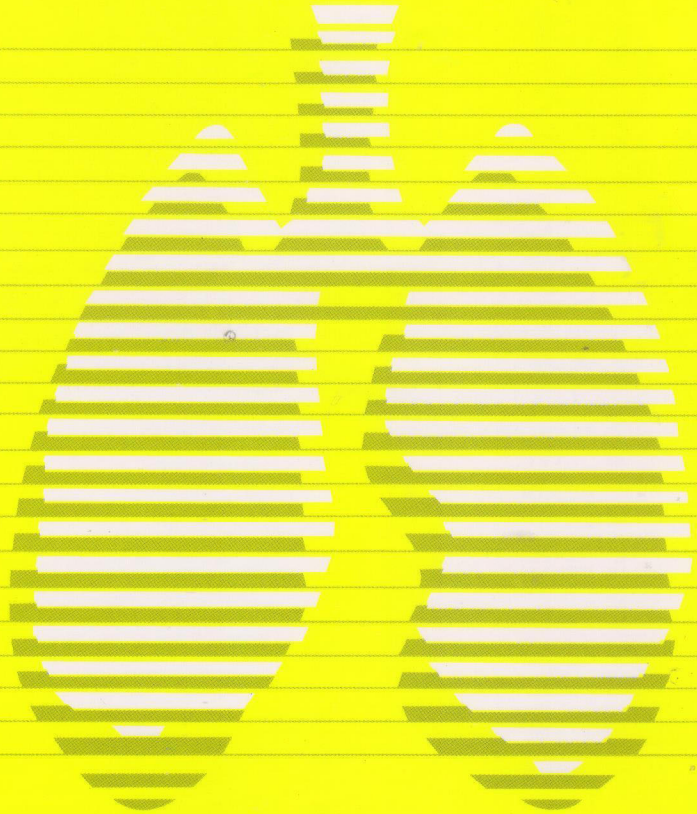

台灣胸腔暨重症加護醫學會

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Case Reports

Persistent Hypersomnolence in an Elderly Patient Treated for Obstructive Sleep Apnea Syndrome – A Case Report

Yung-Fa Lai, Chien-Hung Chin*, Mao-Chang Su*,**

Obstructive sleep apnea (OSA) is prevalent in the middle-aged and elderly population. OSA causes sleep fragmentation with intermittent oxygen desaturation and is the most common cause of excessive sleepiness, which often improves after treatment. Narcolepsy is a neurological disorder and is another common cause of excessive sleepiness. However, coexistent narcolepsy in OSA patients is uncommon. Unlike OSA, narcolepsy is rarely discovered among elderly people. Therefore, we report an elderly OSA patient co-morbid with narcolepsy, a very rare condition in clinical practice. ***(Thorac Med 2009; 24: 133-138)***

Key words: elderly, excessive sleepiness, narcolepsy, obstructive sleep apnea

Introduction

Obstructive sleep apnea (OSA) is prevalent in the middle-aged and elderly population, especially in obese male subjects [1]. It is characterized by repetitive pharyngeal collapse during sleep and is associated with intermittent oxygen desaturation and arousals. Owing to the fragmented nature of their sleep, patients with OSA usually suffer from un-restorative sleep. Thus, OSA is the most common cause of excessive sleepiness. Another common cause of excessive sleepiness is narcolepsy with or without cataplexy, of which the prevalence is much lower than that of OSA. The typical onset of narcolepsy occurs during adolescence, and is seldom diagnosed among the elderly [2]. The combination of OSA and narcolepsy might be discovered occasionally in clinical practice; however, the occurrence of such a coexistent condition is extremely rare, especially in elderly subjects. We report the case of an elderly OSA patient found to be co-morbid with narcolepsy.

Case Report

The patient was an 83-year-old man, who visited our clinic due to habitual snoring for 10

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years and excessive sleepiness, with an Epworth sleepiness scale of 13. Apart from the typical symptoms of OSA, the patient reported that he dreamed a lot every night, even during daytime naps. This phenomenon had occurred since he was young, and most of the dreams were nightmares. Detailed history-taking and a medical chart review revealed no significant neurological, psychological, or metabolic disorders. The patient was slightly obese, with a body mass index of 26.4 kg/m^2 (height: 152 cm, weight: 61 kg). Physical examination revealed no upper airway abnormality such as tonsil enlargement or oro-facial deformity.

An overnight polysomnographic study was conducted thereafter and severe OSA with an apnea-hypopnea index (AHI) of 32.8/h was revealed. The sleep stage scoring was done in 30-second intervals by experienced technicians, following the standard criteria [3] during the polysomnographic study. By definition, obstructive apnea is a cessation of airflow for at least 10 seconds, with an effort to breath during apnea. Obstructive hypopnea was defined as an abnormal respiratory event with at least a 30% reduction in thoraco-abdominal movement or airflow as compared to baseline, lasting at least 10 seconds, and with >4% oxygen desaturation. The AHI was defined as the total number of apneas and hypopneas per hour of electroencephalographic sleep [4].

After the diagnosis of OSA, therapy with routine nasal continuous positive airway pressure (nCPAP) was used with an intra-laboratory nCPAP titration to 10 cm H_2O. The patient used nCPAP regularly with a good compliance. Nevertheless, excessive sleepiness persisted, despite 5 months of nCPAP treatment. He still dreamed frequently, but most of the dreams were vivid. Although no obvious cataplexy had ever been experienced, he had experienced episodic sleep paralysis and hypnagogic hallucination. No obvious nocturnal sleep disruption or automatic behavior was noted. Due to persistent sleepiness, the patient received a multiple sleep latency test (MSLT) following a nocturnal polysomnography. The findings were consistent with narcolepsy, with an average sleep latency of 4 1/2 minutes and a sleep-onset rapid eye movement period (SOREMP) appearing during all 5 naps of the MSLT (Figure 1). Since no medication benefit had been documented for elderly patients with narcolepsy, lifestyle modification with regular nCPAP use during sleep was the only advice for this patient.

Discussion

We report an elderly OSA patient co-morbid with narcolepsy. This disease combination, with both diseases contributing to excessive sleepiness, is uncommon, and this patient might be the oldest to be reported with both OSA and narcolepsy.

OSA is characterized by repeated episodes of complete or partial upper airway obstruction during sleep, with a preservation of respiratory effort. These respiratory events often result in intermittent reductions in blood oxygen saturation and are usually terminated by brief arousals from sleep. The prevalence of OSA was estimated to be at least 2-4% [1]. It is more common in obese male subjects, particularly in the middle-aged and elderly population [1]. Since the patients' sleep is fragmented and non-restorative, excessive sleepiness is the major presenting complaint, resulting in a decline in the quality of life [5]. OSA also has strong correlations with hypertension [6], acute cardiovascular events and stroke [7-8]. The diagnosis of OSA

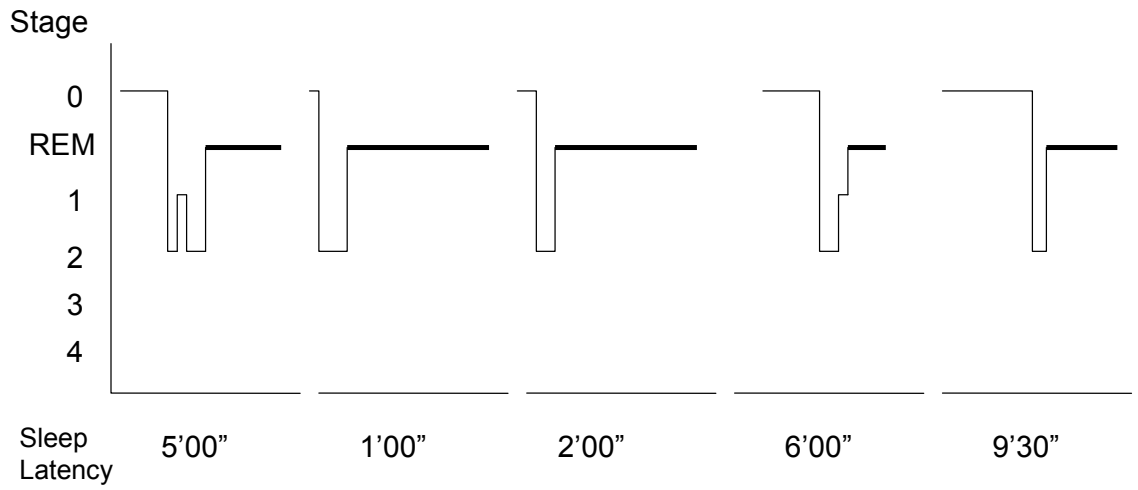

Fig. 1. Hypnogram of the multiple sleep latency test following an overnight polysomnography. This patient took 5 daytime naps with an average sleep latency of 4 1/2 minutes. A sleep onset rapid eye movement (REM) period appeared during each nap. The findings are consistent with the diagnosis of narcolepsy.

can be made by an overnight full polysomnography, and is defined as an AHI of more than 5/hr during sleep. nCPAP is by far the most effective and most frequently introduced therapy for OSA. Treating OSA with nCPAP not only reverses excessive sleepiness, but also lowers blood pressure in patients with refractory hypertension and reduces the rates of cardiovascular events [7, 9].

Narcolepsy is another disorder with the major complaint of excessive sleepiness. Its onset occurs after 5 years of age, and most typically between the ages of 15 and 25 years [2]. Diagnosis of narcolepsy can be made clinically based on the presence of cataplexy, with the assistance of the MSLT or by measurement of cerebrospinal fluid (CSF) hypocretin-1 levels [10-11]. Cataplexy is characterized by a sudden loss of bilateral muscle tone provoked by strong emotions that are usually positive, such as laughter, pride, elation, or surprise. At the genetic level, narcolepsy is closely associated with the human leukocyte antigen (HLA) subtype DQB1*0602 [12]. Other HLA subtypes might also be related to narcolepsy. Cases of narcolepsy without cataplexy represent 10 to 50% of the narcoleptic population [13]. Nocturnal sleep disruption with frequent awakening and nightmares may occur. The diagnosis of narcolepsy without cataplexy must be confirmed by nocturnal polysomnography, followed by an MSLT. The mean sleep latency for narcoleptic patients on the MSLT is less than or equal to 8 minutes, and 2 or more SOREMPs should be observed following sufficient nocturnal sleep (minimum 6 hours) during the night prior to the test [14].

The case we report herein is that of a typical patient with OSA diagnosed by standard overnight polysomnography and by the classical symptoms. Despite a good adherence to nCPAP therapy by this patient, sleepiness remained. Although some OSA patients may still experience excess sleepiness after treatment [15-16], attention to other causes of sleepiness is seldom paid. With persistent hypersomnolence after treatment for OSA, it is necessary to survey

the possible causes, such as inadequate nCPAP pressure or poor nCPAP compliance [17]. A detailed history-taking and an MSLT should be done to rule out superimposed narcolepsy. Although the appearance of 2 or more SOREMPs during MSLT is suggestive of narcolepsy, MSLT for patients with pure OSA may also yield the same findings [18]. The frequency of SOREMPs might be correlated to the severity of OSA. Perhaps the sleep deprivation due to untreated OSA is the major cause of 2 or more SOREMPs. It is highly possible that the clinical features that mimic narcolepsy can be diminished by CPAP treatment by the way of abolishing sleep apnea. The diagnosis of narcolepsy for this patient can be confirmed after proper treatment for OSA. The question remaining unanswered is whether drug therapy would be beneficial for the male patient reported in the present case.

Some aspects of this case remain to be clarified. First, the patient did not undergo a CSF study which might reveal a low hypocretin concentration, or a genetic study regarding HLA subtypes. However, the diagnosis of narcolepsy was made according to the standard diagnostic procedure, i.e. MSLT following an overnight polysomnograpgy [14]. He might be the oldest patient with narcolepsy discovered after being treated for OSA. Secondly, the transformation of nightmares to vivid dreams was reported by the patient himself, but could not be confirmed by the methods used in the present study. However, such a pleasant experience--the transformation of nightmares to vivid dreams--may imply that the use of nCPAP not only improves the physical status, but also has a positive influence on the patient's memory and mental health. A further investigation will be needed to test this hypothesis.

In conclusion, OSA is prevalent among middle-aged and elderly subjects. Narcolepsy is a neurological disease sharing a similar manifestation of excessive sleepiness with OSA. Although there is no published epidemiologic study regarding the coexistence of OSA and narcolepsy, this co-morbidity does exist. Narcolepsy should always be ruled out when sleepiness remains after optimal treatment for OSA, even though narcolepsy rarely occurs among the elderly.

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阻塞性睡眠呼吸中止症年老病患治療後之持續過度嗜睡—一病例報告

賴永發　秦建弘*　蘇茂昌*,**

阻塞性睡眠呼吸中止症較常見於年長族群，病患睡眠時其上呼吸道反覆塌陷合併氧合濃度降低，導致其睡眠受到干擾。長久以來病患多為白天過度嗜睡所苦，而過度嗜睡常因睡眠呼吸中止症治療以後獲得改善。猝睡症則是另一種造成過度嗜睡的疾病，然而與睡眠呼吸中止症不同的是它較常見於年輕族群。兩種疾病合併並不多見，合併於老年人之機率更低，因此我們報導一位八十三歲男性病患患有阻塞性睡眠呼吸中止症且合併猝睡症，藉以強調若阻塞性睡眠呼吸中止症治療以後仍然過度嗜睡，猝睡症則應該列入鑑別診斷。*(胸腔醫學* ***2009; 24: 133-138)***

關鍵詞：阻塞性睡眠呼吸中止症，猝睡症，過度嗜睡，老年人

義大醫院　內科部　胸腔內科 / 義守大學　職能治療學系，*高雄長庚紀念醫院　內科部　呼吸胸腔內科
**長庚技術學院　呼吸照護系
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F-18 FDG-Positron Emission Tomographic Scanning in Pulmonary Wegener's Granulomatosis

Yi-Ting Chen, En-Ting Chang, Kuei-Ying Su*, Shu-Hsin Liu**, Jen-Jyh Lee

Positron emission tomography (PET) with F-18 fluorodeoxyglucose (FDG) has become an important tool in differentiating benign from malignant lung lesions. But, the specificity tends to be low, especially when chronic nonmalignant inflammatory processes are prevalent.

Several kinds of vasculitis and granulomatous disease have been reported to have FDG-uptake in the scan. We presented 2 patients whose diagnosis of pulmonary Wegener's granulomatosis showed positive results with regard to the FDG-PET scan. From a literature review, we also tried to deduce the characteristics of PET scan results in Wegener's granulomatosis. ***(Thorac Med 2009; 24: 139-144)***

Key words: pulmonary Wegener's granulomatosis, FDG-PET, false-positive

Introduction

Positron emission tomography (PET) with F-18 fluorodeoxyglucose (FDG) is an important tool in differentiating benign from malignant lesions [1]. Patients with increased FDG uptake (a so-called positive PET scan) require further evaluation until the lesions are considered malignant or proven otherwise. However, false-positive scans have been reported with a number of entities, especially in infectious and inflammatory processes such as tuberculosis, histoplasmosis, cryptococcosis, sarcoidosis and rheumatoid nodules [2-5].

Wegener's granulomatosis is a necrotizing granulomatous vasculitis. Lung involvement occurs in 90% of patients [6]. The most common findings in computed tomography (CT) are multiple pulmonary nodules or masses. Masses usually range in size from 2 to 4 cm in diameter, but may be much larger. Cavitation was noticed in 26% of detected nodules and masses [7]. Pathologic studies are planned in patients with pulmonary Wegener's granulomatosis from other causes. There are only rare reports of F-18 FDG-PET scanning in pulmonary Wegener's granulomatosis, although positive PET scans for inflammatory lesions are reasonable.

Case Reports

Case 1

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A 51-year-old male presented with fever (body temperature was 39°C) and right lower chest pain. Initial chest plain film showed a soft tissue mass near the right heart border with an air-bronchogram. The chest CT scan showed multiple nodules 40 days later. CT-guided biopsy was performed and the pathologic report showed necrotizing granulomas with a geographic pattern of necrosis surrounded by lymphocytes, plasma cells and macrophages. The c-antineutrophil cytoplasm antibody (c-ANCA) was 1:320 (normal c-ANCA range <1:20). Pulmonary Wegener's granulomatosis was diagnosed. The patient received an F-18 FDG-PET scan and a positive result was noted (Figure 1). After treatment with prednisolone and cyclophosphamide, the pulmonary lesions resolved and the patient was discharged.

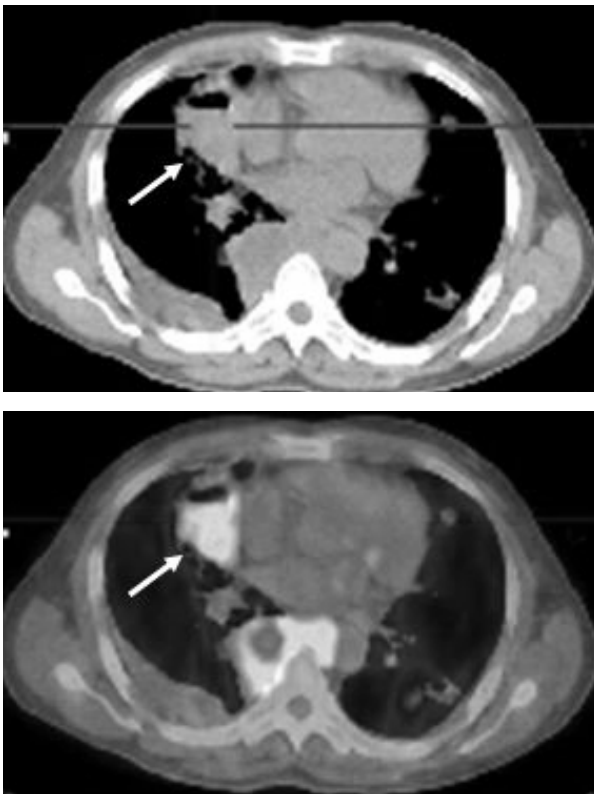

Fig. 1. Chest computed tomography showed soft tissue masses at the right heart border, posterior mediastinum and left lower lung. The F-18 FDG-PET scan showed positive uptake at these lesions.

Case 2

A 71-year-old woman was admitted due to hemoptysis without fever. Chest radiography showed multiple nodules. An F-18 FDG-PET scan was arranged, with early phase SUVmax 3.79 and delayed phase SUVmax 5.2 (Figure 2). Malignant pulmonary metastasis was diagnosed. CT-guided biopsy was performed and the pathologic report showed necrotizing granuloma with a geographic pattern. The serological c-ANCA titer was 1:1280. After treatment with steroid and cyclophosphamide, the patient was discharged with resolution of the active lung lesions.

Discussion

To identify malignant pulmonary lesions, most studies of FDG-PET operate at a point on the receiver operating characteristic curve at which sensitivity and specificity are approximately 96.8% and 77.8%, respectively [8]. The specificity tends to be even lower when chronic nonmalignant inflammatory processes are prevalent. F-18 FDG accumulates in cells with a high rate of glycolysis, a metabolic process that is present in cancer cells and inflammatory cells, such as granulocytes and activated macrophages [9]. Therefore, PET seems to be a promising imaging technique in patients with vasculitis. FDG accumulation on PET scanning has been reported in several vasculitis diseases, including giant cell arteritis, Takayasu's arteritis, polyarteritis nodosa, polymyalgia rheumatica, cardiac damage in Churg-Strauss syndrome, and pulmonary artery aneurysm in Behçet disease [10-15].

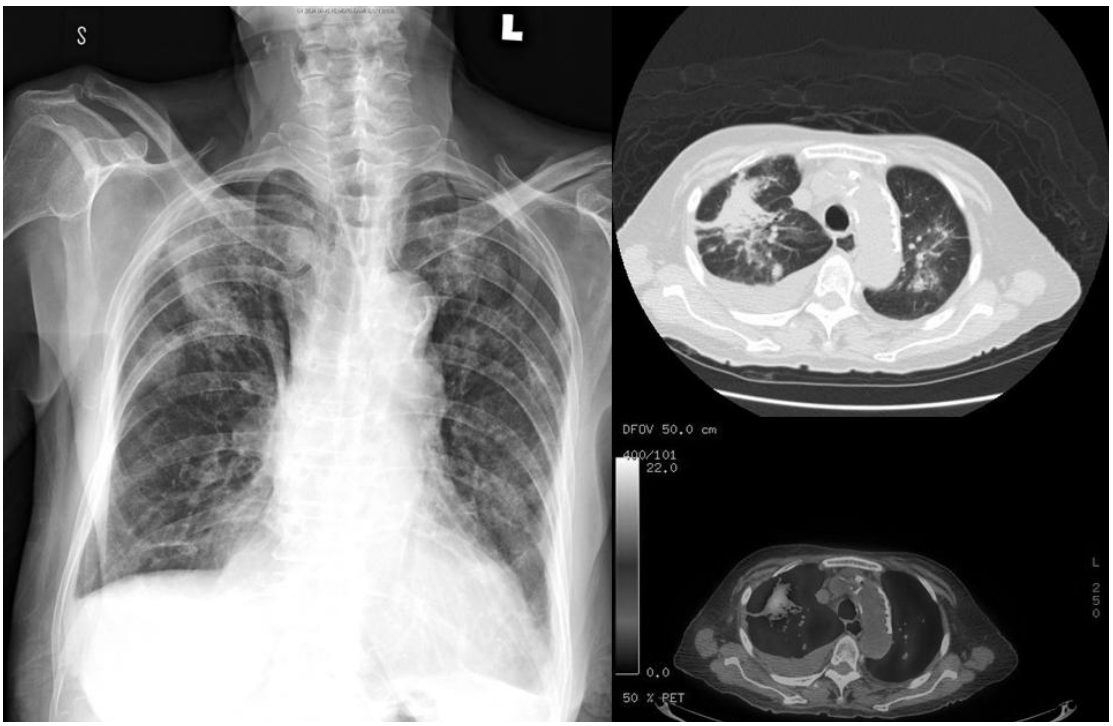

Fig. 2. Chest radiograph showed several nodules and masses in the bilateral lungs, with pleural effusion on the right side. The F-18 FDG-PET scan showed positive uptake of the right lung mass.

Wegener's granulomatosis is characterized pathologically by a necrotizing granulomatous inflammation of the lower and upper respiratory tracts, together with microabscesses. Our 2 patients both had multiple pulmonary nodules with positive FDG-uptake. Three case reports have mentioned that active Wegener's granulomatosis could appear as a positive PET scan, and 2 other cases were identified in other prospective studies (Table 1) [12-13, 16-18]. With the addition of our 2 cases, there have been 7 cases; 6 of them had pulmonary involvement: 4 presented with multifocal lung lesions with or without cavity, 1 had a solitary pulmonary nodule, and the PET scan pattern of the other patient was not described in the paper. Two of the 7 cases had uptake as nasosinusal tumor. Three cases received a 2nd PET scan after medical treatment for Wegener's granulomatosis, and all the follow-up scans showed negative or diminished uptake when the disease activity decreased.

Although there has been no large study on the role of F-18 FDG-PET scans in pulmonary Wegener's granulomatosis, these cases reveal that physicians should be careful regarding the diagnosis of patients with a positive F-18 FDG-PET scan result. In particular, about 9% of patients with Wegener's granulomatosis present disease localized to the lung [6]. This limited form may mimic pulmonary metastasis or lung cancer. The diagnostic criteria used to differentiate benign from malignant lung nodules using integrated PET/CT have been proposed in a prospective study [18], which included 76 patients with 84 pulmonary tumors suspected of malignancy and considered eligible for surgical resection. Histologically, 11 lesions (14.5%)

Table 1. Studies of F-18 Fluorodeoxyglucose Positron Emission Tomography in Wegener's Granulomatosis

First Author (Reference)	Study Design	No. *	Conclusions
Blockmans [13]	Case report	1	Uptake in both lungs, nose, and shoulders.
Beggs [16]	Case report	1	Several areas of intense uptake in the lung, with at least one cavitary lung mass. Post-treatment follow-up: decreased uptake or resolution of all lesions.
Jouret [17]	Case report	1	Severe expansion of a nasosinusal tumor into the brain, with positive uptake. Post-treatment follow-up: decreased uptake.
Quaia [18]	Prospective study	1	Solitary pulmonary nodule, 2 cm in diameter, with positive uptake.
Bleeker [12]	Prospective study	1	Positive lung uptake at diagnosis. Post-treatment follow-up: negative uptake

*Number of patients with Wegener's granulomatosis

were shown to be benign, 1 of which was Wegener's granulomatosis (1.3%). The actual role of the PET study with regard to pulmonary lesions has its limitations when the diagnosis is uncertain. The definite diagnosis of Wegener's granulomatosis still relies on the American College of Rheumatology 1990 criteria: (1) development of oral ulcers, or purulent or bloody nasal discharge; (2) the presence of nodules, fixed infiltrates, or cavities on chest radiograph; (3) microhematuria or red cell casts in urine sediment; and (4) histologic changes of granulomatous inflammation within the wall of an artery or in the perivascular or extravascular area. A patient is said to have Wegener's granulomatosis if at least 2 of these 4 criteria are present [19].

In conclusion, granulomatous diseases caused by inflammation or infection can mimic pulmonary malignancy and appear as a positive PET scan. Several kinds of vasculitis also have been reported to have an F-18 FDG uptake. Pathologically, Wegener's granulomatosis is a disease of both necrotizing granuloma and vasculitis. When reading the PET scan, if there are "positive" lung lesions, the following hints indicate the possibility of Wegener's granulomatosis: (1) nodular or tumor-like, multifocal pulmonary uptake with or without cavity; (2) concurrent positive lesions in the nasosinusal region; and (3) decreased uptake after specific treatment. To differentiate Wegener's granulomatosis from other granulomatous diseases and neoplasms, tissue proof is usual necessary [20].

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韋格納氏內芽腫的正子照影表現

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以F-18 fluorodeoxyglucose顯影的正子照影（Positron emission tomography）已經成為惡性肺部病灶鑑別診斷的重要工具。但其專一性會受到發炎性病灶影響而降低。至目前為止，已經有許多的肺部結節性病變被提出可表現為正子照影陽性，如肺結核、組織漿菌症（histoplasmosis）、隱球菌症（Cryptococcosis）、類肉芽結節（sarcoidosis）和風濕性結節（rheumatoid nodule）。也有數種血管炎會表現正子照影陽性，如巨細胞血管炎（giant cell arteritis）、高安氏動脈炎（Takayasu's arteritis）、結節性多發動脈炎（polyarteritis nodosa）等。

韋格納氏內芽腫（Wegener's granulomatosis）是一結節性血管炎。我們提出兩個多發性肺部結節的個案，診斷皆為韋格納氏內芽腫；兩位的肺部病灶在正子照影下皆為陽性。本文並回顧相關個案報告，歸納韋格納氏內芽腫可能的正子照影特徵，包括：陽性顯影之多發性肺部結節並可能有開洞表現，合併鼻部或鼻竇部位陽性顯影之腫瘤，以及針對Wegener's granulomatosis治療後，追蹤的正子照影可見原陽性顯影的減退或消失。*(胸腔醫學* ***2009; 24: 139-144)***

關鍵詞：Wegener's granulomatosis，正子照影，偽陽性

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A Case Report of Hyperbaric Oxygen Therapy for a Patient with Carbon Monoxide Poisoning and Cardiogenic Pulmonary Edema

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Wann-Cherng Perng**

Acute carbon monoxide (CO) poisoning is one of the most common causes of lethal poisoning. The incidence of acute CO poisoning has been increasing in recent years, and it may occur accidentally or intentionally. CO actively competes with oxygen (O_2) at hemoglobin (Hb) binding sites and disrupts the mitochondrial electron-transport chain. Severe CO poisoning can lead to tissue hypoxia, which can result in immediate death or in delayed neuropsychiatric sequelae. Hyperbaric oxygen (HBO_2) therapy plays an important role in the rapid elimination of CO from the body, thereby minimizing tissue hypoxia and injury. We report the case of an 18-year-old woman with severe CO poisoning and acute cardiogenic pulmonary edema who was treated successfully with HBO_2 therapy. ***(Thorac Med 2009; 24: 145-150)***

Key words: CO, acute pulmonary edema, HBO_2

Introduction

The effect of carbon monoxide (CO) poisoning may be acute (with cardiac or neurologic injuries) and delayed (with delayed neuropsychiatric sequelae). CO has approximately 200-250 times higher affinity for hemoglobin (Hb) than does O_2 [1]. When the blood CO level is high, it can displace O_2 from Hb, resulting in reduced O_2 delivery to tissues and leading to tissue hypoxia. CO can directly bind to mitochondrial cytochrome α 3 oxidase and P_{450} [1], with the resultant disruption of the mitochondrial respiratory chain and the impairment of ATP production. The effect of hypoxia is most destructive in tissues with high O_2 consumption, such as in the brain and heart. In CO poisoning, signs and symptoms of hypoxic encephalopathy and neurological sequelae have been well described, but myocardial injury and sequelae

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are rarely discussed. Herein, we report a case of CO intoxication, complicated by acute cardiogenic pulmonary edema.

Case Report

An 18-year-old woman with a history of major depression and under irregular treatment was brought to the emergency department of Kinmen Army Hospital. Her family found her unconscious in her room in the morning after she had attempted suicide by inhaling the fumes of burning charcoal.

She was in a deep coma, and her blood carboxy-hemoglobin (COHb) level was 39%. Since she was unconscious, endotracheal intubation was performed for airway protection. She was then transferred to our hospital by air transport.

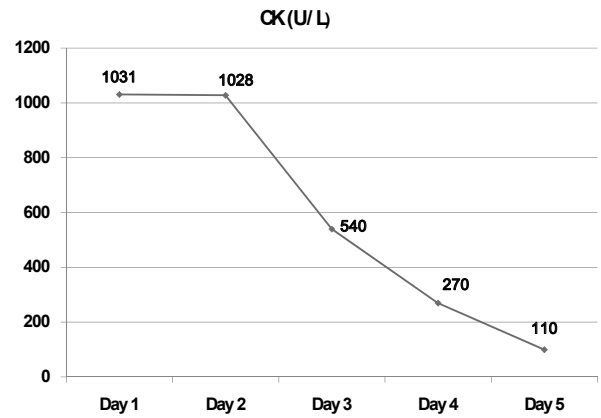
Upon arrival at our hospital, she was afebrile, and her blood pressure was 99/66 mmHg; heart rate, 115 beats per minute; respiratory rate, 28 breaths per minute; and GCS, $E1M2V_T$. In general, she was comatose and had labored respiration. Pink, frothy sputum was noticed in the endotracheal tube. Her lung fields were remarkable for bilateral diffuse crackles. Her heart beat was rapid, but regular and without murmur. Other physical findings were unremarkable.

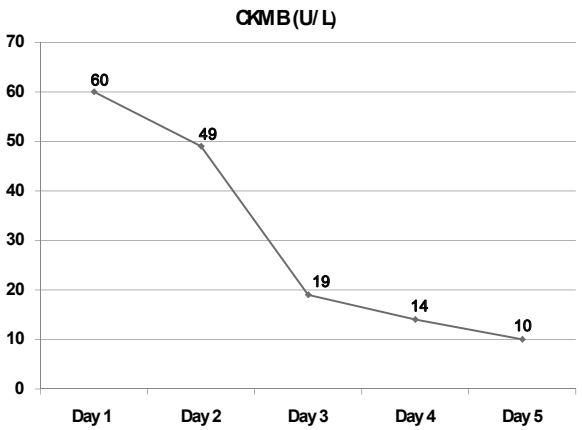
Laboratory findings showed leukocytosis (WBC count: 19000/mm^3) with neutrophil predominant (85%), increased CRP (17 mg/dl) and elevated cardiac enzyme levels (troponin-I: 10.24 ng/ml, CPK: 1031 U/l, CKMB: 60U/l, AST: 94 U/l, and ALT: 52 U/l). Arterial blood gas analysis, which was performed using the blood sample drawn while the patient was on endotracheal intubation with 100% oxygen, showed the following results: pH: 7.353, PCO_2: 25.5 mmHg, PO_2: 76 mmHg, HCO_3: 14 mEq/l, and SaO_2: 94%. The COHb level was 3%. The chest X-ray (CXR) revealed bilateral perihilar infiltration with a normal heart size, which was compatible with acute pulmonary edema. Electrocardiogram showed sinus tachycardia (109/min). The trans-thoracic echocardiogram showed mild global hypo-kinesis with an ejection fraction (EF) of 35%. She was diagnosed as acute pulmonary edema caused by CO-related cardiac injury. A single dose of diuretic was given immediately, followed by 1 session of HBO_2.

After 8 hours of admission, a Swan-Ganz catheter was emplaced, revealing high central venous pressure (24 cmH_2O) and high pulmonary capillary wedge pressure (23 cmH_2O), which indicated congestive heart failure. She was treated with HBO_2 at 2.5 atmospheres absolute (ATA) for 90 minutes per session, 1 session per day. After the 3rd session of HBO_2 therapy, a follow-up echocardiogram showed EF of 60%. Cardiac enzymes returned to a normal range within 5 days (Figure 1). Daily monitoring of cardiac function and the Swan-Ganz catheter showed significant improvement (Table 1). The patient regained complete consciousness on the 3rd day of admission, and her lungs were clear of congestion on the CXR (Figure 2A, B). She was extubated on the 5th hospital day. HBO_2 therapy was continued for another 6 sessions, and the patient was discharged from our hospital after complete recovery. The patient was last followed up 1 year after discharge, and she had suffered neither delayed neuropsychological nor cardiac sequelae.

Discussion

CO is a colorless, odorless, tasteless and no-





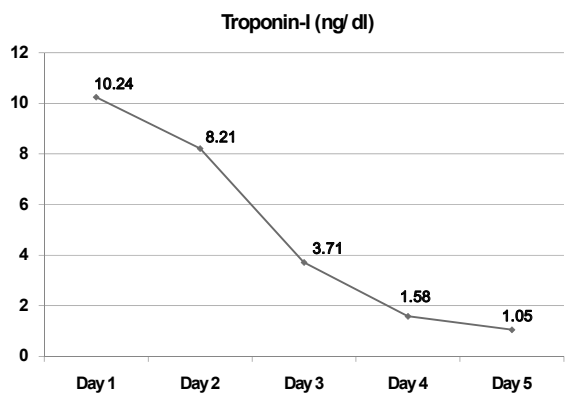


Fig. 1. Recovery of cardiac enzymes after HBO_2

nirritating gas produced by the incomplete combustion of any carbon-containing fuel [2]. CO has a high affinity for Hb, and a lethal concentration of COHb can be achieved within 10 minutes in the confines of a closed garage [3]. Sources of CO poisoning are either endogenous or exogenous. The endogenous source of CO production is heme degradation by heme oxygenase, and a higher rate of production is seen in hemolytic anemia and sepsis [4-5]. The exogenous sources include microbial activity in plant life, automobile exhaust, defectively functioning heaters and cooking appliances, industrial exhaust, mining accidents, fire, methylene chloride poisoning, cigarette smoking and suicide attempts.

The central nervous system involvement and delayed neuropsychiatric sequelae in CO poisoning have been well described before. Myocardial injury is frequently found on admission of patients with moderate to severe CO poisoning, and the mortality rate has increased, even in low-risk populations. Henry *et al*. reported that the hospital mortality rate from CO poisoning with myocardial injury was about 5% [6].

Myocardial injury by CO occurs through a combination of tissue hypoxia and direct CO-related damage at the cellular level. CO competes with O_2 for binding to Hb; this causes an O_2-Hb dissociation curve shift to the left, thus impairing the release of O_2 at the tissue level, and resulting in tissue hypoxia. Myoglobin and mitochondrial cytochrome α 3 oxidase are other heme-containing proteins that bind CO; when this occurs, it directly impairs cellular respiration [1]. Oxygen free radical formation and lipid peroxidation are also implicated in tissue death [7].

The affinity of myoglobin for CO is 30 to

Table 1. Swan-Ganz catheter data for our patient

Date	Day 1 (after 8h)	Day 2	Day 3
Mode	ASV	ASV	PS
FiO2	100%	80%	50%
HR (beat/min)	115	108	93
Arterial pressure (S/D/M) (mmHg)	124/41/67	122/53/72	104/40/57
CVP (mean) (mmHg)	24	7	7
PAP (S/D/M) (mmHg)	47/31/37	33/20/25	35/20/25
PCWP or LAP (mmHg)	23	13	7
C.O (L/min)	4.91	5.23	
C.I (L/min/ M^2)	3.30	3.51	
SVI (ml/beat/ M^2)	42.7	48.4	
SVRI (dynes-sec-cm^{-5})	700	1435	
PVRI (dynes-sec-cm^{-5})	228	199	

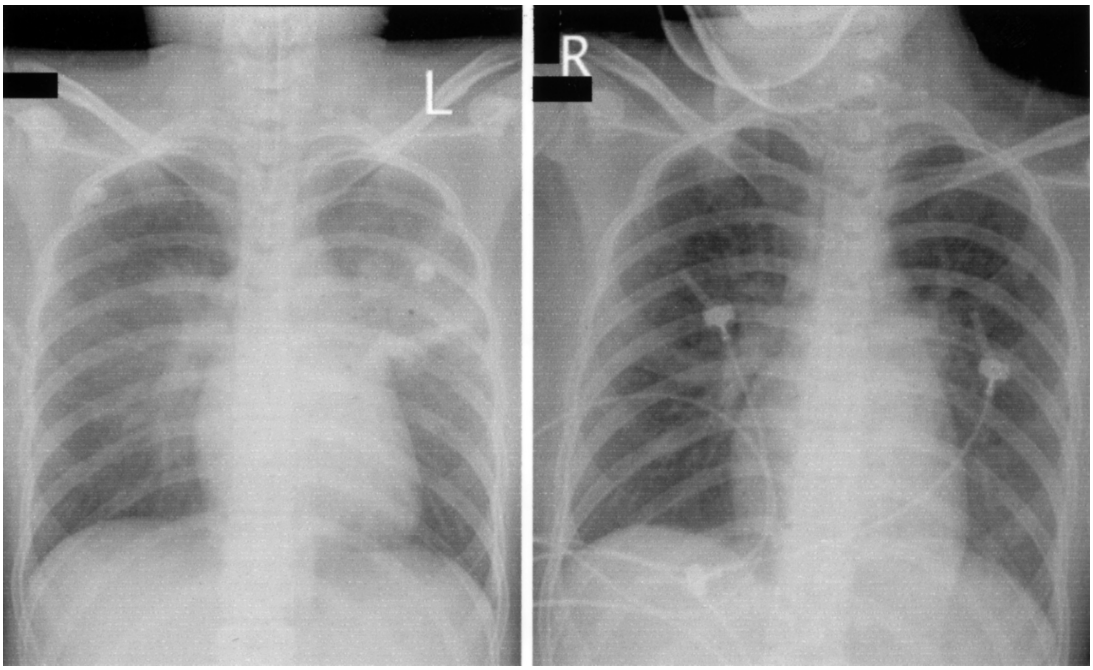


Fig. 2A, B. CXR, AP views on admission showed bilateral pulmonary edema and improvement on the 3rd day

50 times greater than its affinity for O_2, whereas cytochrome α 3 oxidase binds CO and O_2 equally [8]. The heart is a highly O_2-consuming tissue, and CO binding to cardiac muscle occurs 3

times more than binding to skeletal muscle [1]; thus, the heart is particularly vulnerable to hypoxia.

Clinically, the cardiovascular effects of CO include myocardial ischemia, pulmonary edema, ventricular dysfunction and arrhythmias. Pulmonary edema occurs in 10% to 30% of acute CO poisoning cases [9]. Pulmonary edema is possibly due to tissue hypoxia, toxic effects on the alveolar membrane, left ventricular failure, and aspiration after loss of consciousness [10]. Myocardial involvement is noted by changes in ECGs with and without elevation of cardiac biomarkers (Troponin-I and CK-MB). Thus far, the number of sessions of HBO_2 therapy that is required to ameliorate CO poisoning remains unclear. Serial evaluation of cardiac biomarkers and ECG can be used to monitor the recovery from myocardial injury, as in our patient.

The mainstay of therapy in CO poisoning is to provide O_2 supplementation, ventilator support as necessary and cardiac function monitoring. The half-life of COHb is 5 hours in room air, 90 minutes with 100% normobaric oxygen therapy, and as short as 20 minutes with HBO_2 [1]. Thus, HBO_2 therapy is an important adjunctive therapy in CO poisoning with myocardial injury, for both life-saving and the prevention of sequelae. In our hospital, HBO_2 is administered to patients with moderate to severe CO poisoning as indicated, in up to 3 to 10 sessions depending on the clinical condition.

The decision to administer HBO_2 can not be made solely on the basis of the COHb level [11-12]. In this patient, we administered HBO_2 therapy regardless of her normal COHb level. We witnessed a complete recovery from CO-induced cardiac and neurological injury after a total 10 sessions of HBO_2, without apparent sequelae in the 1-year follow-up. The study of a larger number of cases is needed to gain more information about long-term cardiac sequelae, such as delayed neuropsychiatric syndrome.

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以高壓氧治療一氧化碳中毒合併心因性肺水腫

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急性一氧化碳（CO）中毒是常見的致命中毒原因之一，近年來，其發生率（不論是意外或故意造成）一直不斷在增加。一氧化碳會積極的和氧氣競爭位於血紅蛋白的結合點，也會擾亂粒腺體的電子傳遞鏈。如不施與緊急治療，重度一氧化碳中毒可導致組織缺氧，引起立即死亡或延遲性神經精神後遺症。高壓氧治療對於迅速消除體內一氧化碳以減少組織缺氧和傷害是非常重要的。在此，我們報告一位重度一氧化碳中毒併有急性心因性肺水腫的18歲女子成功以高壓氧治療康復的案例。***(胸腔醫學 2009; 24: 145-150)***

關鍵詞：一氧化碳中毒，急性肺水腫，高壓氧治療

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Intramural Esophageal Bronchogenic Cyst – Report of a Case

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Bronchogenic cyst is a relatively rare mediastinal tumor. As the name implies, most of these tumors arise from the broncho- pulmonary tract. In very rare cases, they may present in the esophageal muscular layer. After progressive dysphagia of 6 months' duration, our patient sought treatment. Esophagogram and chest computed tomography revealed an esophageal cyst with lumen compression. To alleviate the symptoms, we performed cyst removal by enucleation through a right thoracotomy. During operation, we suggested emplacing a nasogastric tube to render the dissection safer. The diagnosis was revised to bronchogenic cyst after receiving the pathology results. ***(Thorac Med 2009; 24: 151-155)***

Key words: bronchogenic cyst, mediastinal tumor, esophagus

Introduction

Bronchogenic cyst is derived from abnormal budding of the primitive foregut. Most cysts are located in the mediastinum, but others may present in the lung parenchyma. The location of the cyst depends on the timing of bud formation. In very rare conditions, a bronchogenic cyst may be found in the esophagus, pericardium, thymus and retroperitoneum. About two-thirds of adult cases have milder respiratory or digestive symptoms, but symptoms in neonates are life-threatening. Total removal of the cyst is suggested because of likely recurrence with incomplete resection.

We report a case of bronchogenic cyst located between the trachea and the esophagus, below the aortic arch. After suffering progressive dysphagia for 6 months, the patient decided to undergo an operation to remove the mediastinal cyst. The thoracoscopy approach was difficult to perform, so a right thoracotomy was done. Intraoperatively, the tumor was located within the esophageal muscular layer and was removed smoothly. Postoperatively, the patient recovered uneventfully and the dysphagia had not recurred during a 10-month follow-up period.

Case Report

This patient was a 58-year-old male with-

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out systemic disease. He had been drinking and smoking for 30 years. Because of a sore-throat and worsening dysphagia in the most recent 6 months, he went to the hospital for examination. No tumor was found at the nasopharynx or hypopharynx, but leukoplakia in the left arytenoid- epiglottitis fold was noted with laryngoscopy. Biopsy from the leukoplakia revealed parakeratosis and squamous epithelial hyper-plasia. The dysphagia was evaluated by water-soluble esophago- graphy and endoscopy, with both demonstrating a bulging lesion with a smooth mucosa, 22 cm from the upper incisor. Extrinsic compression of the esophagus by the tumor was found. Further chest computed tomography (CT) was done to localize the site and to measure the tumor size (Figure 1). A round tumor was found between the esophagus and trachea, and below the aortic arch. The tumor had low density with homogenous content (20-30 Housefield units), so an enterogenous cyst was highly suspected.

To relieve the symptoms, a resection of the cyst was prepared. Under selective 1-lung ventilation, a right thoracotomy was performed along the 5th intercostal space. Intraoperatively, we emplaced a nasogastric tube for guidance in the dissection. The nasogastric tube was also a good tool to check the integrity of the esophagus, which was placed underwater and filled with air through the tube. The azygos vein was divided for better exposure. We found the tumor located within the muscle layer of the esophagus. Since the tumor was medial to the esophagus and protruding to the left side, turning the tumor to the opposite side following muscle-splitting helped the dissection. Therefore, the tumor was removed completely by enucleation without rupture. There was no fistula between the cyst and the esophageal lumen. The esophageal mucosa was intact and the muscle was approximated to prevent diverticulum formation.

The size of the tumor was 3.5 x 2.4 x 1.6 cm. On cross section, a cystic lesion with a smooth inner surface and milky fluid was found. The microscopic finding revealed a cyst lined with ciliated respiratory epithelium. Smooth muscle fibers surrounded the cyst wall (Figure 2). From the pathological findings, bronchogenic cyst

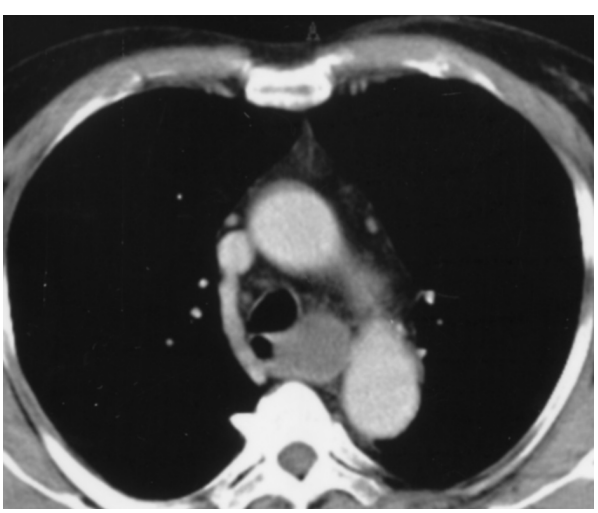

Fig. 1. A round tumor with homogenous content of lower density was located between the esophagus and the trachea, and beneath the azygos vein. The tumor was difficult to approach by thoracoscopy.

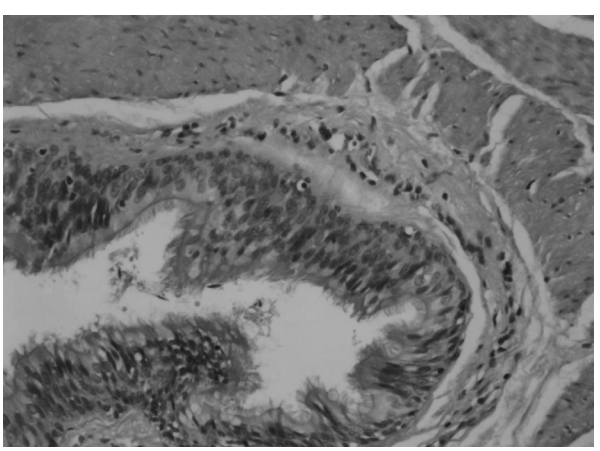

Fig. 2. Under microscopic view, pseudo-stratified epithelium lined with cilia was clearly seen, and was surrounded by smooth muscle. The hyaline cartilage was not seen in our case. (200X, H&E stain)

was diagnosed. The patient returned to oral intake on the 3rd postoperative day. After a 10-month follow-up, the patient no longer complained about swallowing.

Discussion

At the end of the 3rd week of gestation, the laryngo- tracheal groove is present in the embryonic foregut. The dorsal portion elongates to form the esophagus. The respiratory tract is differentiated from the ventral portion. Abnormal budding from any site of the foregut can form cysts, including bronchogenic cysts, enteric cysts and neuroenteric cysts. Among these, bronchogenic cysts are the most frequent. In 1948, Maier described the pathologic characteristic of bronchogenic cysts as their being lined with respiratory epithelium with cilia [1]. But other authors pointed out that the embryonic esophagus and trachea are both lined with ciliated epithelium. The component of the cyst wall is more specific in separating esophageal cysts from bronchogenic cysts, such as in cartilage [2].

Distinguishing esophageal from the bronchial cysts is sometimes difficult, especially when there is a lack of cartilage within the cyst wall. According to a statement from Rosai and Ackerman, the best evidence that a cyst in the esophagus is of the esophageal type is the presence of a definite double layer of smooth muscle in the wall [3]. In our case, there was no double smooth muscle layer present in the cyst wall; therefore, the esophageal duplication cyst might be excluded.

If an intramural esophageal cyst was found, it was often misdiagnosed as leiomyoma, gastrointestinal stromal tumor, or even leiomyosarcoma. These intramural esophageal cysts are usually found in the middle and lower part of the esophagus, and rarely in the upper part [4].

Various tools are available that can be used to make a preoperative approach to mediastinal tumor, of these, chest CT can localize and characterize the tumor. Magnetic resonance imaging has good sensitivity in detecting fluid-filled tumor on T2-weighted images. Moreover, MRI can provide a more precise location of the tissue adjacent to the tumor than can chest CT. Endoscopic ultrasound has a good ability to distinguish cystic from solid lesions and to confirm the invasion depth of the tumor [5].

Most patients with intramural esophageal bronchogenic tumor have symptoms. One report revealed that the most common was dysphagia (61%), followed by chest pain (35%) [6]. The operation is more complicated when these cysts become infected, ulcerated, or fistulized to the aerodigestive tracts. Thus, earlier surgical intervention is recommended, if these patients are operable [7].

These bronchogenic cysts have a tendency to recur if they are managed by aspiration, so a complete resection is strongly suggested [8-9]. The tumor can be removed by open thoracotomy or thoracoscopy or even by transoral endoscopic resection for small tumors [10]. In our case, with the unusual location compared with other cases, right thoracotomy may be a safer method. To prevent the esophageal mucosa from perforating, continuous transillumination by esophagoscope was used for better control in dissection [11]. We used a nasogastric tube for our patient, instead of the esophagoscope.

In conclusion, the presence of pseudostratified ciliated epithelium lining the inner wall can define the cyst as a bronchogenic cyst. This type of cyst is rarely found in the muscular layer of the esophagus. The best management of

choice is to remove it completely. We suggest using a nasogastric tube intraoperatively, which may be useful in helping to prevent the esophagus from perforating during the dissection.

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食道平滑肌內的支氣管源性囊腫—病例報告

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支氣管源性囊腫是種罕見的縱膈腔腫瘤。此類囊腫大多數發生於肺部或是支氣管旁。但是在極罕見的情形下，它可能出現在食道肌肉層中。在此個案中，因患者於半年內感覺吞嚥逐漸困難而就醫。經由食道攝影及胸部電腦斷層攝影檢查，發現食道肌肉層中有一囊腫向內壓迫。經過右側開胸後，將此囊腫完全取出。在手術中，我們建議置放鼻胃管以利囊腫分離更安全，不會破壞食道的黏膜層。經由病理檢查後，診斷修正為支氣管源性囊腫。*(胸腔醫學 **2009; 24: 151-155**)*

關鍵詞：支氣管源性囊腫，縱膈腔腫瘤，食道

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Pulmonary and Gastric Mucosa-associated Lymphoid Tissue Lymphoma in a Patient with Sjögren's Syndrome: A Case Report

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Mucosa-associated lymphoid tissue (MALT) lymphoma may arise from certain autoimmune diseases (Sjögren's syndrome, systemic lupus erythematosus, Hashimoto's thyroiditis) or infections (Helicobacter pylori). MALT lymphoma is indolent and often localized for a long time. Coexistence of MALT lymphomas in 2 or more sites is rare. We reported a patient with long-term symptoms of dry eyes and dry mouth who was admitted for evaluation of lung lesions. The computed tomography (CT) guided biopsy specimen was too small to yield a definite diagnosis. The diagnosis of pulmonary MALT lymphoma is based on the pathological examination, often needing a larger specimen obtained through surgery. This patient was diagnosed with Sjögren's syndrome and unexpected gastric MALT lymphoma during this hospitalization. The diagnosis of pulmonary MALT lymphoma was made using the polymerase chain reaction (PCR) technique. ***(Thorac Med 2009; 24: 156-162)***

Key words: pulmonary MALT lymphoma, gastric MALT lymphoma, Sjögren's syndrome

Introduction

MALT lymphoma is thought to be derived from the marginal zone B-cells. It was first described as occurring in the gastrointestinal tract, and is now known to play a role in a significant proportion of extranodal B cell lymphomas. MALT lymphoma can arise in many organs and shares common clinical and histological features. Because of its indolent nature, dissemination to another extranodal organ is not usual. We describe herein a patient with long-term symptoms of Sjögren's syndrome who presented coexisting pulmonary and gastric lymphomas at diagnosis.

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Case Report

A 56-year-old female without a history of medical disease presented with a 2-week history of productive cough and left chest pain, and a 2-day history of blood-tinged sputum. She also had a 5-year history of dry eyes and dry mouth. She denied having had fever or body weight loss. Her chest radiography showed diffuse tiny centrilobular opacities and irregular, consolidated and nodular lesions in both lung fields (Figure 1). Contrast-enhanced computed tomography (CT) of the chest showed diffuse tiny centrilobular opacities, pulmonary cysts (less than 1.5 cm), irregular consolidations with calcified nodules in them, and nodular lesions in both lung fields with lower lung zone predominance (Figure 2). She underwent CT-guided biopsy, and pathologic examination of the lung tissue revealed a large deposit of eosinophilic material, a few B lymphocytes, and plasma cell infiltration. A conclusive diagnosis was difficult to reach because of the limited specimen. She refused invasive procedures, such as video-assisted thoracoscopic surgery (VATS) or thoracotomy. Sialoscintigraphy demonstrated moderately to severely impaired function of the bilateral parotid glands and submandibular glands. A positive Shirmer's test, anti-Ro (>240.0 U/ml) and anti-La (82.5 U/ml) were also noted. Thus, she was diagnosed as having Sjögren's syndrome. She developed epigastric pain and nausea during the same hospitalization. Upper gastrointestinal endoscopy incidentally revealed a 2.0-cm gastric IIa lesion on the lower body, and a biopsy was done. Pathologic examination of the specimen showed infiltrating lymphoplasmacytic cells in the lamina propria associated with focal lymphoepithelial lesions of the gastric tissue (Figure 3), and also disclosed Helicobacter pylori (HP) infection of the mucosal surface. Immunohistochemically, the specimen showed CD20 positivity and kappa immunoglobulin light chain restriction. Based on the gastric lesion finding and the diagnosis of Sjögren's syndrome, the specimen of lung was restudied. Immunohistochemically, the specimen of lung showed CD20 positivity and kappa immunoglobulin light chain restriction.

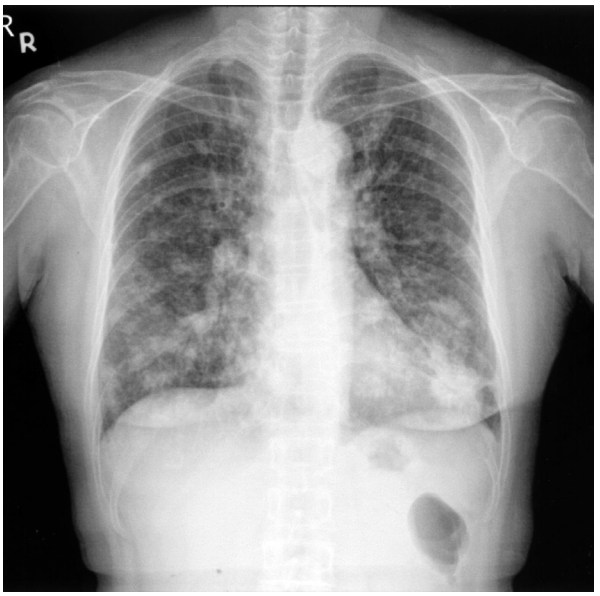

Fig. 1. Chest radiography showed diffuse tiny centrilobular opacities and irregular, consolidated and nodular lesions in both lung fields.

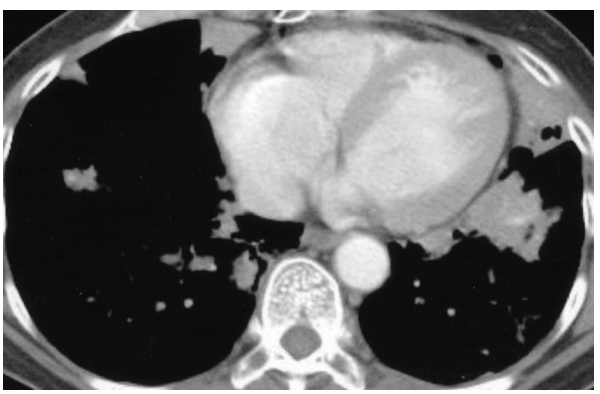

Fig. 2. Contrast-enhanced CT of the chest disclosed irregular consolidations with calcified nodules in them, and nodular lesions in both lung fields with lower lung zone predominance.

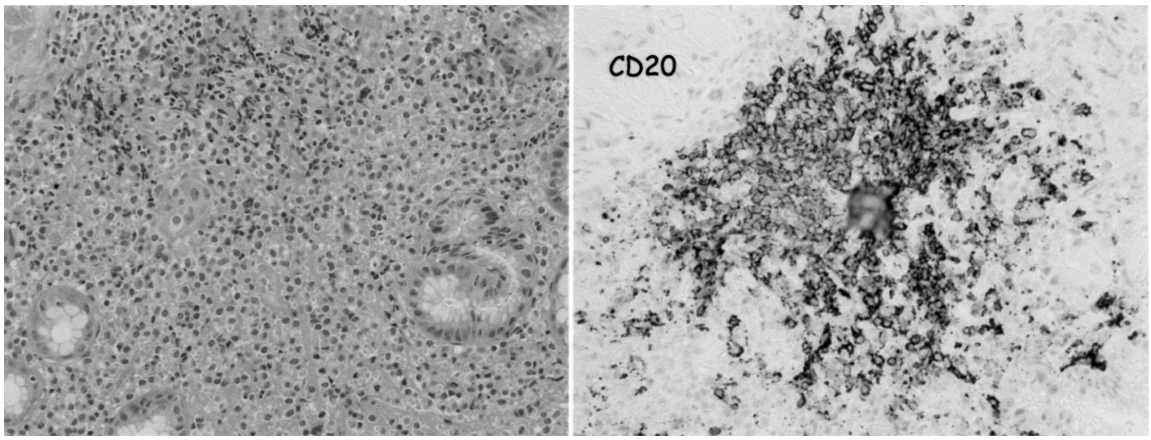

Fig. 3. A picture of infiltrating lymphoplasmacytic cells in the lamina propria, associated with focal lymphoepithelial lesions of the gastric tissue, CD20(+).

PCR analysis showed B-cell receptor overexpression (Figure 4). The patient was diagnosed with gastric and pulmonary MALT lymphomas. 18-fluoro-2-deoxyglucose (18F-FDG) positron emission tomography (PET)/CT showed multiple (>10) nodular lesions with moderately increased FDG uptake in both lungs, but not in the stomach (Figure 5). Bone marrow aspiration disclosed no lymphoma involvement. The patient then received HP eradication therapy and chemotherapy. The MALT lymphomas in both the lung and stomach were smaller in size 6 months later.

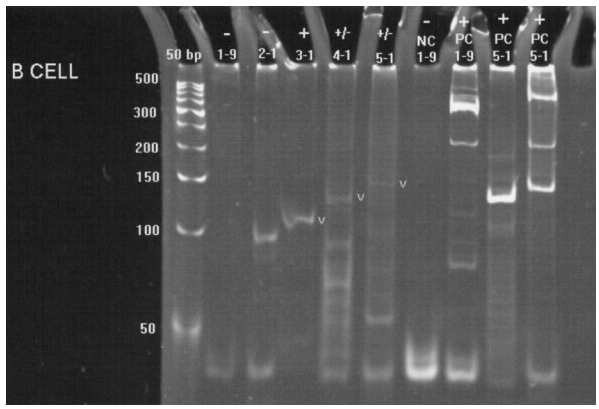

Fig. 4. PCR analysis showed B cell receptor overexpression. (arrowhead: consistent with positive control; NC: negative control; PC: positive control).

Discussion

MALT lymphoma is usually a very indolent lymphoma that often is localized at diagnosis. It was first described in the gastrointestinal tract, and now can be recognized in the respiratory tract, salivary gland, ocular adnexa, breast, kidney, prostate, skin, gall bladder, thyroid uterine cervix and thymus. The disease may arise as a result of chronic inflammation or autoimmune diseases such as HP-associated chronic gastritis, Hashimoto thyroiditis or Sjögren's syndrome. Chronic inflammation by exoantigens or autoantigens may play an important role in the development of the disease by driving the proliferation of specific B-cells and increasing the frequency of their transformation. In the discussion below, we will focus on the clinical issues surrounding pulmonary MALT lymphoma.

Disseminated or localized

There is no organized lymphoid tissue in the normal lung, but some conditions lead to the accumulation of MALT in relation to the small

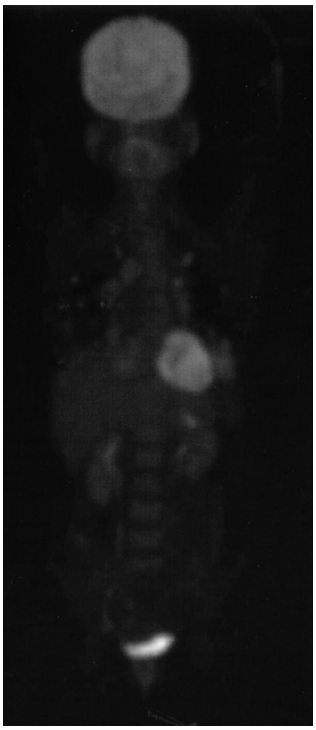

Fig. 5. Multiple (>10) nodular lesions with moderately increased FDG uptake in both lungs.

bronchi or bronchioles. The typical features of pulmonary MALT lymphoma are lymphoepithelial lesions produced by a lymphomatous invasion of the bronchiolar epithelium. Dissemination to local nodes, systemic spread and high-grade transformation are rare. The clinical behavior of low-grade pulmonary MALT lymphoma is remarkably indolent. However, more and more studies, including case reports and retrospective analyses, have shown the early dissemination of this disease at diagnosis. In a study that enrolled 158 patients with MALT lymphoma [1], 22 (13.9%) patients had pulmonary MALT lymphoma; 7 (31.8%) of the 22 patients had multiple MALT lymphomas, and up to 5 (22.7%) patients had gastric MALT lymphoma. In another study of 72 patients with non-gastric MALT lymphoma [2], 8 (11.1%) patients had pulmonary MALT lymphoma; 4 (50%) of the 8 had additional lymphoma locations, and 3 (37.5%) had additional gastric lymphoma. The researchers concluded that more thorough staging procedures would reveal that non-gastric MALT lymphoma is often a multifocal disease. The abnormalities of pulmonary MALT lymphoma on chest radiography are easy to identify, though often not specific. Tumor staging, especially for stomach involvement, should always be done if a patient has been diagnosed with pulmonary MALT lymphoma.

Imaging and Diagnosis

Patients with pulmonary MALT lymphoma are often asymptomatic, but a few have cough, hemoptysis and dyspnea; they are often seen at the age of 60 [3]. The disease is detected by routine chest radiographs incidentally. Because of the indolent feature of the disease, patients with MALT lymphoma might be misdiagnosed as having other diseases, or have no definite diagnosis, if the diagnostic procedure is inadequate. The initial chest radiograph is not specific. The most common radiographic features are solitary or multiple nodules and multiple consolidations [3-5]. Some specific features, such as rare hilar and mediastinal lymphadenopathy, are not like those of secondary pulmonary lymphomas [3-4, 6]. To stage or monitor MALT lymphoma, 18F-FDG-PET may be a useful tool [7], but in our case there was no increased FDG uptake in the stomach.

The diagnosis of pulmonary MALT lymphoma is based on the pathological examination. Open thoracotomy, thoracoscopy and CT-guided biopsy are common methods to obtain specimens. The diagnosis of the disease often requires a larger specimen by surgery. The positive predictive rate of the CT-guided biopsy is

only 25% [8]. Pulmonary MALT lymphoma that presents with a solitary pulmonary lesion can be resected surgically; if the MALT lymphoma presents with multiple pulmonary lesions, bronchial, transbronchial or transthoracic biopsy is often the first diagnostic procedure. The diagnostic studies of limited specimens obtained by CT-guided or transbronchial lung biopsy should be included in the PCR analysis, if surgery (VATS, thoracotomy) is relatively contraindicated clinically for patients with suspected pulmonary lymphoma.

Most B-cell lymphomas have rearranged immunoglobulin heavy chain (IgH), and the PCR methods are often designed to amplify IgH gene rearrangements. Many studies showed variable sensitivity (62% [9], 84% [10], 92% [11]) and high specificity (87% [9], 96.6% [10], 100% [11]) using primers to framework III (FrIII) of the variable (V) segments and to conserved sequences from the joining (J) regions of the IgH genes. The variability of sensitivity might be due to deletions and extensive somatic mutations within the FrIII regions. PCR as the primary method for immunoglobulin gene rearrangement analysis is gradually becoming accepted and many strategies have been devised to enhance the detection sensitivity of PCR techniques for B-cell clonality.

Treatment

The clinical outcome of pulmonary MALT lymphoma is favorable, with the 5-year survival rate exceeding 80% and a median survival time of more than 10 years [12-13]. Current treatment options are surgery, single or combined chemotherapy and radiotherapy. Patients with localized pulmonary MALT lymphoma can be treated with surgery, local radiotherapy and single chemotherapy with chlorambucil. Some authors have even proposed clinical observation in the early stage of the disease. Disseminated disease should be treated with chlorambucil as first-line chemotherapy. Combined chemotherapy with cyclophophamide, doxorubicin, vincristine and prednisone (CHOP) is recommended in patients with MALT lymphoma transforming to high grade or a large tumor mass. HP eradication therapy should be proposed if HP-related gastric MALT lymphoma is considered. The patient who underwent CHOP and HP eradication therapy in this case report showed a good clinical response.

Conclusion

MALT lymphoma, especially pulmonary MALT lymphoma, is an indolent disease, although dissemination is often noted at diagnosis. More thoroughgoing diagnostic studies are necessary for those patients who have similar imaging findings and clinical pictures, as discussed above. Further staging procedures, especially upper gastrointestinal endoscopy, should be performed if a patient presents with pulmonary MALT lymphoma. Chemotherapy for pulmonary MALT lymphoma is patient-tailored. Long-term follow-up is necessary.

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一位罹患修格蘭氏症候女性合併有肺及胃粘膜相關淋巴組織淋巴瘤：病例報告

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粘膜相關淋巴組織淋巴瘤可能會因為特定的自體免疫疾病（修格蘭氏症候、全身性紅斑性狼瘡、橋本氏甲狀腺炎）或感染（幽門螺旋桿菌）而引起。粘膜相關淋巴組織淋巴瘤是相當良性的腫瘤，常侷限在某一器官很久的時間，很少有同時發生兩處以上的情形，我們報告一位長時間有眼乾及口乾症狀的56歲女性因咳血住院，以電腦斷層導引穿刺術評估肺部病灶，因檢體太小無法作確定診斷，住院中意外發現胃粘膜相關淋巴組織淋巴瘤，進而以聚合酵素鏈鎖反應方法診斷肺部病灶亦為粘膜相關淋巴組織淋巴瘤。在肺部診斷此疾病需要較大的檢體，電腦斷層導引穿刺術的診斷率並不高，但我們可以根據臨床上相關的疾病及影像學的特徵，懷疑此疾病並輔以聚合酵素鏈鎖反應方法，減少需要手術的風險並提高診斷率。*(胸腔醫學* ***2009; 24: 156-162)***

關鍵詞：胃粘膜相關淋巴組織淋巴瘤，肺粘膜相關淋巴組織淋巴瘤，修格蘭氏症候

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Real-time Endobronchial Ultrasound-guided Transbronchial Needle Aspiration is Useful for Diagnosing Recurrent Hypopharyngeal Carcinoma Located in the Upper Paratracheal Space – A Case Report

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Recurrent hypopharyngeal carcinoma is usually not diagnosed until it has reached an advanced stage, and so carries a poor prognosis. The most common sites of recurrence of hypopharyngeal carcinoma are the local and neck areas. However, these sites sometimes present a challenge to the surgeon because they are difficult to approach. Herein, we report the case of a 59-year-old man who was diagnosed with left hypopharyngeal squamous cell carcinoma (pT3N2M0 stage IVa) in September 2006. He underwent bilateral salvage neck dissection and concurrent chemoradiotherapy to prevent recurrence. The follow-up neck computed tomography (CT) in December 2007 revealed a tumor in the right upper paratracheal space which was not seen in the July 2007 CT. We describe a feasible method to diagnose recurrent hypopharyngeal carcinoma located adjacent to the central airway using real-time endobronchial ultrasound-guided transbronchial needle aspiration and avoiding surgery. ***(Thorac Med 2009; 24: 163-167)***

Key words: carcinoma, hypopharynx, diagnosis, endobronchial ultrasound

Introduction

Early-stage hypopharyngeal cancers are usually asymptomatic; thus, most patients present with advanced disease and a poor prognosis. Many patients at an advanced stage receive multidisciplinary treatment with neck radiotherapy, chemotherapy, neck dissection, or a combination to prevent regional recurrence. In a past study, 34.9% of patients had recurrence and the most likely sites of recurrence were local and neck areas [1]. Numerous follow-up imaging studies, including chest X-ray, computed tomography (CT), and magnetic resonance imaging, are available for early recurrence detection. However, biopsies of all suspicious lesions are

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necessary to establish a diagnosis of recurrent hypopharyngeal carcinoma. Although it is difficult to approach the paratracheal lesion without surgical intervention, many patients are very poor surgical candidates. We report the successful diagnosis of recurrent hypopharyngeal carcinoma located in the right upper paratracheal space using real-time endobronchial ultrasound (EBUS)-guided transbronchial needle aspiration (TBNA) under local anesthesia, and without surgical intervention, that may serve as a solution to this problem.

Case Report

A 59-year-old man with hypopharyngeal squamous cell carcinoma (pT3N2M0 stage IVa) diagnosed in September 2006 had received concurrent chemoradiotherapy till 14 December 2006. On 1 March 2007, he underwent salvage neck dissection, and was regularly followed up with fibroscopy and neck CT (Figure 1A), which showed no evidence of residual or recurrent hypopharyngeal cancer. Unfortunately, the neck CT (Figure 1B) in December 2007 revealed an ill-defined tumor (26 mm x 15 mm) in the upper paratracheal space. Because of its location, we inserted an EBUS through the patient's oral cavity under local anesthesia and sedation (*i.e.*, midazolam). Convex probe EBUS-TBNA was performed using a bronchoscope equipped with a distal 7.5-MHz linear ultrasound transducer probe (CP-EBUS, model XBF-UC260F; Olympus; Tokyo, Japan) (Figure 2A) and a dedicated ultrasound image processor (model EU-C2000; Olympus). A 22-gauge, 4-cm cytology needle (Olympus) was used to obtain specimens. Figure 2B shows a hypoechoic density mass as seen by the convex probe EBUS with the TBNA needle in the patient's right paratracheal tumor. The needle was moved back and forth inside the tumor, and was finally retrieved and pushed out of the histologic core. The histology from the EBUS-TBNA core biopsy specimens confirmed squamous cell carcinoma. The patient tolerated the procedure well and without complication.

Discussion

Basic histopathological features of cervical metastasis of hypopharyngeal cancer, such

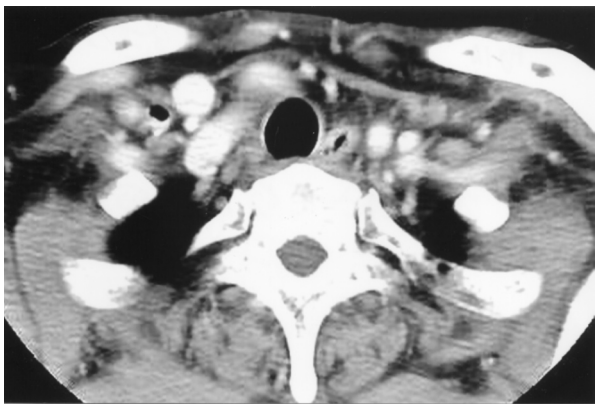

Fig. 1A. The neck computed tomography (CT) in July 2007 revealed no evidence of residual or recurrent tumor.

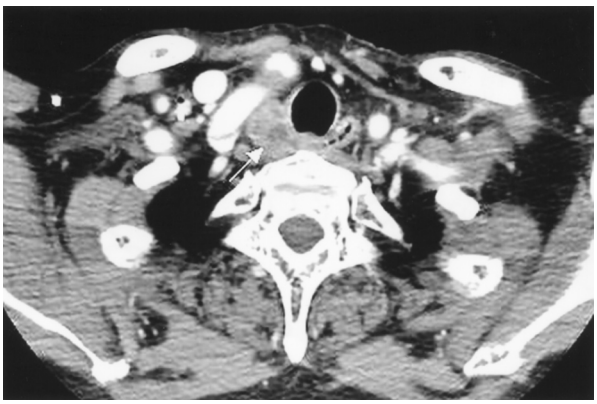

Fig. 1B. The follow-up neck computed tomography (CT) in December 2007 revealed a recurrent tumor (arrow) in the right upper paratracheal space.

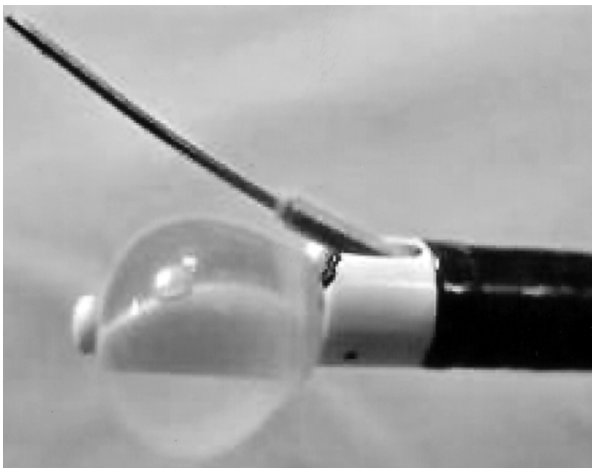

Fig. 2A. Distal end of the convex probe EBUS showing the curved array ultrasound transducer with balloon inflated and a 22-gauge aspiration needle protruding from the biopsy channel.

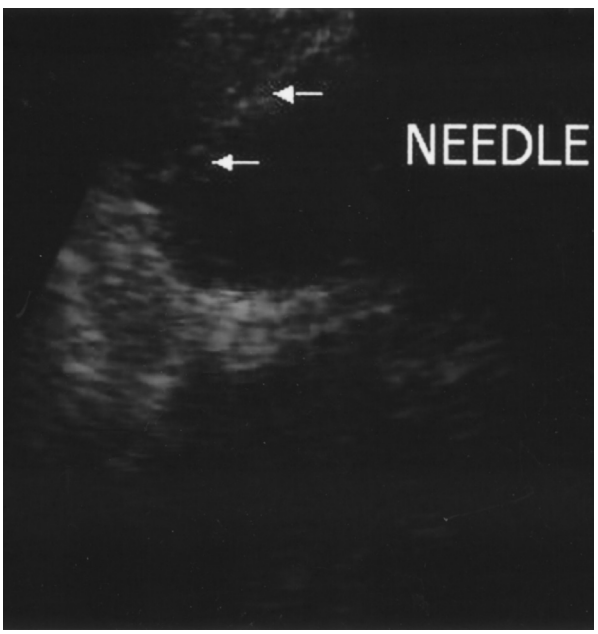

Fig. 2B. Real-time EBUS-guided transbronchial needle aspiration was performed in the right upper paratracheal space tumor. A hypoechoic tumor was seen by the convex probe EBUS. A 22-gauge needle (arrow) is seen within the hypoechoic tumor.

as the node level, number and size, and the presence of extracapsular extension have been shown to be independently associated with an increased risk of recurrence [1]. Hypopharyngeal cancer with negative lymph node disease involvement recurred significantly less frequently than that with positive lymph node disease involvement, and the most likely site of recurrence was the local area, followed by the neck [2]. Early pathologic diagnosis of recurrent hypopharyngeal cancer in the paratracheal space is challenging, because the location in the paratracheal space makes biopsy with traditional endoscopic equipment difficult.

CT-guided transthoracic needle aspiration is the most commonly used modality by interventional radiologists for tissue diagnosis of pulmonary nodules, when the lesion is not visible on bronchoscopy. However, compared with transbronchial biopsies, complications including pneumothorax are seen at a fairly high rate [3]. Moreover, the yield is lower for centrally located tumors compared with peripheral lesions [4]. Bronchoscopic TBNA is a widely accepted and safe diagnostic tool for evaluating suspect mediastinal and hilar masses [5-6]. The overall sensitivity of the conventional bronchoscopic modality ranges around 70%, with large deviations depending on size and location [7-8]. However, due to the anatomy and the size of the tumor, tissue from lesions located in certain areas may be difficult to obtain with the conventional bronchoscopic modality. Real-time EBUS-TBNA that can access centrally located tumors not visible on conventional bronchoscopy seems to solve most of these problems.

EBUS-TBNA is a feasible approach for the evaluation of mediastinal and hilar lymph node metastasis in patients with lung cancer [9-12]. Aside from the potential utility of EBUS-TBNA in lymph node staging in lung cancer patients, the technique can also be used to obtain biopsy specimens in some patients with paratracheal tumors that usually require a surgical procedure for definitive diagnosis.

This is the first report of a one-step ap-

proach for the pathologic diagnosis of recurrent hypopharyngeal squamous cell carcinoma in the upper paratracheal space using a minimally invasive technique under consciousness sedation. We believe that for hypopharyngeal carcinoma patients, a combined EBUS-TBNA approach can circumvent general anesthetic and surgical procedures with potential savings, in terms of both time and cost. This technique may allow diagnosis for patients who are medically unfit to undergo surgical diagnostic procedures and who have recurrent hypopharyngeal carcinoma around the paratracheal space.

Although we have reported only 1 case to illustrate this technique in diagnosing upper paratracheal recurrent hypopharyngeal carcinoma, we believe that this case report will assist the pulmonologist and otolaryngologist in their approach to paratracheal tumor. EBUS-TBNA offers the possibility of a minimally invasive biopsy, and has the potential to accurately sample masses in the paratracheal space. Larger studies of this new technique to further define its role in diagnosing recurrent hypopharyngeal carcinoma around the paratracheal space are warranted.

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支氣管內視鏡超音波指引經氣管細針抽吸來診斷位於氣管旁邊復發性之轉移下咽癌—病例報告

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復發性下咽癌通常不易在早期被發現，所以預後差。復發性下咽癌最常見的復發位置為局部及頸部。然而，有時這些復發位置之組織取得對臨床醫師而言是一項挑戰。在此，我們報導一位59歲的男性病患在2006年9月被診斷出罹患stage IVa之下咽癌。之後他接受頸部外科手術及同時化療放射線治療處置。在2007年7月頸部電腦斷層掃描無異常病灶，於2007年12月之追蹤電腦斷層掃描發現氣管附近有一顆腫瘤.本篇我們陳述利用內視鏡超音波指引經氣管細針抽取氣管周邊腫瘤成功診斷復發性下咽癌之病患。
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關鍵詞：下咽癌，診斷，支氣管內視鏡超音波

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Nodular Lymphoid Hyperplasia: A Case Report and Literature Review

Lan-Eng Tan, Chi-Yuan Tzan*, Pei-Jan Chen, Chien-Liang Wu

Pulmonary nodular lymphoid hyperplasia (NLH) is an uncommon disease, and is considered to be a benign lesion of polyclonal lymphoid proliferation. It was originally known as pseudolymphoma. This term is no longer used after the finding of morphologically low-grade lymphoid proliferation. Patients that present with NLH have no specific clinical symptoms, and chest film mostly reveals single or multiple nodules. The diagnosis of this disease is through the surgical approach, and the prognosis is fair, with long-term follow-up required as the etiology is not clear. We herein reported a 53-year-old man who presented with a lung nodule, and the final pathology revealed nodular lymphoid hyperplasia. The patient was discharged uneventfully. No recurrence of the mass lesion was noted after 1 year of follow-up. ***(Thorac Med 2009; 24: 168-174)***

Key words: nodular lymphoid hyperplasia, reactive lymphoid follicle, germinal center

Introduction

Pulmonary nodular lymphoid hyperplasia (NLH) is an uncommon disease, and is considered to be a benign lesion of polyclonal lymphoid proliferation. This term was first suggested by Kradin and Mark [1]. Patients that present with NLH usually are asymptomatic, with an incidental finding of single or multiple mass lesions on chest film. NLH can be found in any patient age group, but the majority of patients are middle-aged or older from age 50 and 69. The differential diagnosis includes bronchioalveolar cell carcinoma (BAC) and mucosa-associated lymphoid tissue (MALT) lymphoma. The diagnosis of this disease is through the surgical approach, and the prognosis is fair, with long-term follow-up required as the etiology is not fairly clear. We herein present the case of 53-year-old man with nodular lymphoid hyperplasia, and review what is currently known about this disease.

Case Report

This 53-years-old man was a chronic smoker, at 30 packs per year, and had a history of frequent upper respiratory tract infection lasting

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for years. He came to our outpatient department (OPD) on 17 October 2007 due to occasional shortness of breath and dull pain in the left upper chest since April. This gentleman stated he went to another hospital in April for his chest pain. Two opaque patches were noted in the chest film at that time, 1 in the left upper and the other in the right lower lung field. Initially, antibiotics were given for possible infection. Follow-up chest film after antibiotics treatment revealed a subsiding of the right lower patch of opacity, but a persistence of the left upper patch. The patient's chest pain persisted for several months. Chest film after 4 months later revealed the left upper patch had increased in size (Figure 1).

Physical examination and blood test disclosed no abnormalities. Tumor markers including beta-HCG, alpha-fetoprotein, and SCC were within normal limits. Chest CT revealed 1 3-cm ill-defined non-calcified soft tissue mass with moderate enhancement and central necrosis in the left apical lung, with 2 borderline enlarged lymph nodes from 8 mm to 1 cm in diameter in the aorto-pulmonary (AP) window (Figure 2).

Bronchogenic carcinoma was highly suspected, based on the chest CT. However, since the lesion was in left upper lung field, pulmonary tuberculosis (TB) could not be totally excluded. We checked the sputum TB stain and culture, and the data revealed negative results, as did serum Cryptococcus antigen and the sputum and the percutaneous needle biopsy. Bronchoscopy showed nodulation on the left main bronchus above the 2nd carina, but biopsy data revealed stroma cells only. Wedge resection was performed in October 2007. Grossly, the resected specimen was soft and whitish with central necrosis, and adhesive to the pleural (Figure 3). Microscopic examination showed dense infiltration of numerous lymphocytes, with reactive lymphoid follicles and germinal centers.

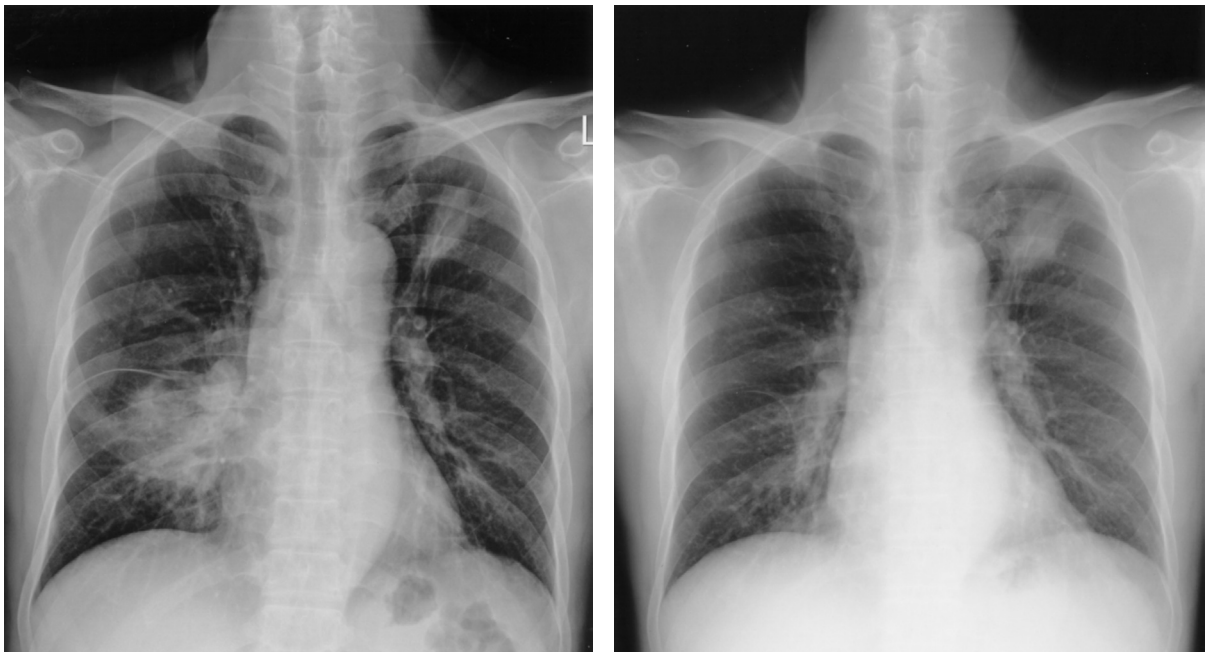

Fig. 1. Initial CXR (left panel) revealed RML and LUL opacity. Antibiotics treatment was given. CXR 4 months later (right panel) showed resolving of the RML opacity, but persistence of the LUL opacity with mild progression.

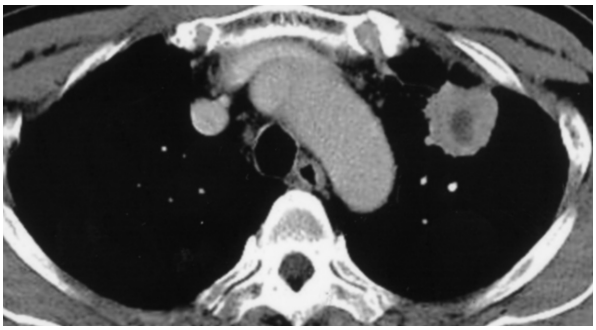

Fig. 2. A 3-cm ill-defined soft tissue mass without calcification and with central necrosis in the left apical lung.

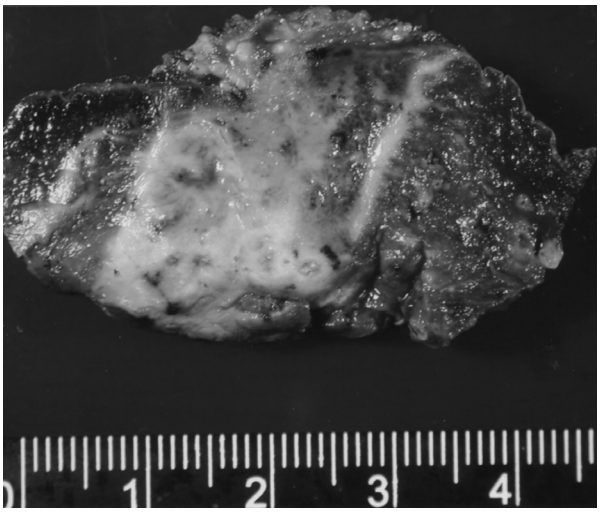

Fig. 3. A 3x3x3-cm solid mass with pleural adhesion resected from the LUL.

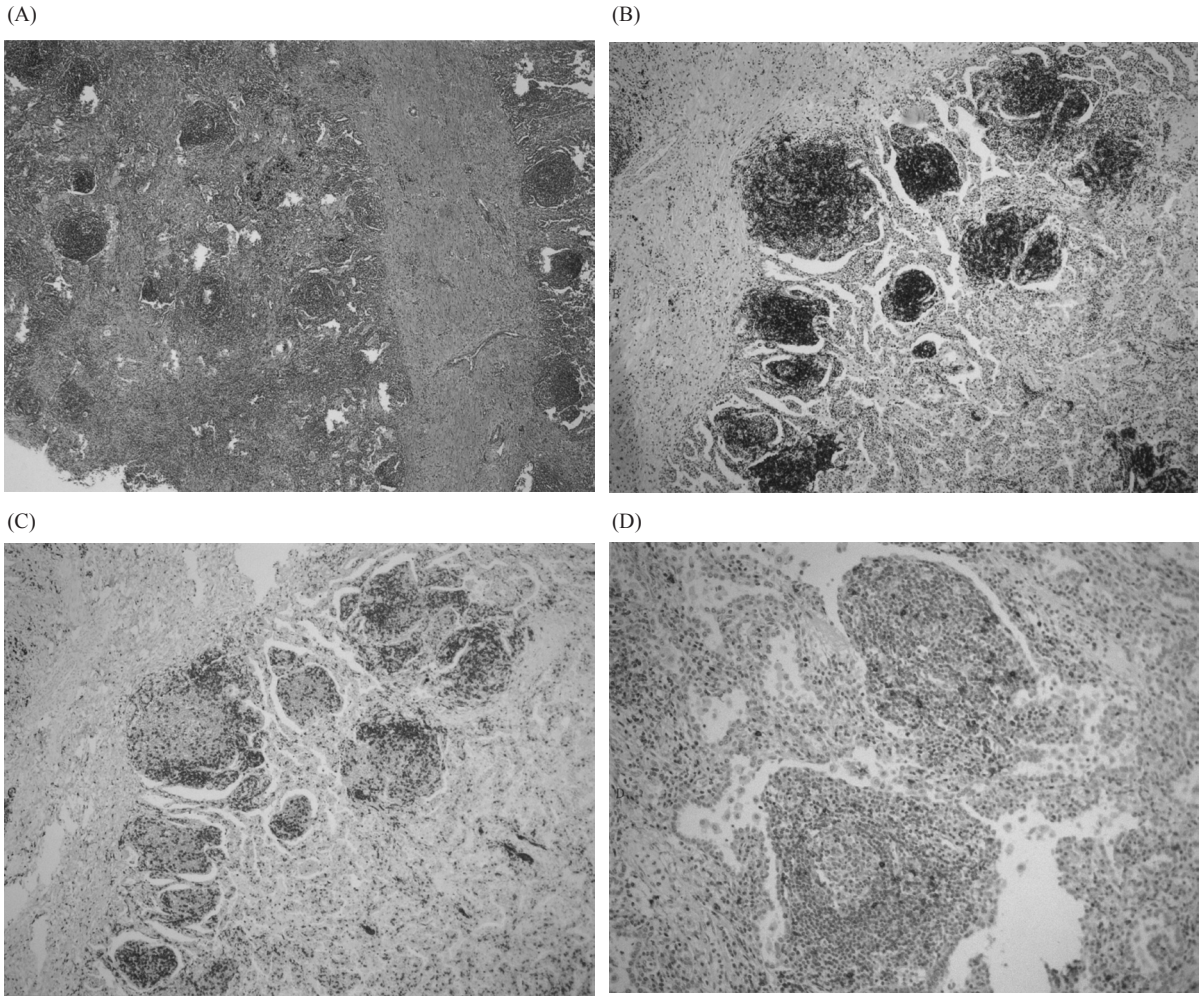

Fig. 4. Histology finding showed dense infiltration of numerous lymphocytes, with reactive lymphoid follicles and germinal centers (A), filled with B cells which were immunoreactive to antibody to CD20 (B), and interfollicular lymphocytes with CD3 and CD5 antibodies (C, D).

The specimen was negative to CK stain, which is a marker for epithelial growth. Lymphocyte subset markers such as CD3, CD5 and CD20 showed an admixture of T and B cells (Figure 4). A final diagnosis of nodular lymphoid hyperplasia was made.

The post-operative course was uneventful. The patient was discharged and followed up at the OPD. We performed a whole body gallium scan 2 months after discharge, and the results revealed no abnormality. Chest film taken 1year later showed no evidence of pulmonary relapse.

Discussion

Pulmonary "pseudolymphoma" was first proposed by Saltzstein in 1962. Pathologically, pseudolymphoma is characterized by an infiltration of mature lymphocytes and plasma cells without involvement of lymph nodes [2]. However, this term was no longer used after the finding of morphologically low-grade lymphoid proliferation, which included mucosa-associated lymphoid tissue (MALT) lymphoma, NLH and other low-grade lymphoproliferative diseases. Kradin and Mark used pulmonary lymphoid hyperplasia in 1983 to describe 1 or more nodules or localized lung infiltrates consisting of reactive lymphoid proliferation [1]. NLH is considered a benign lesion with a polyclonal lymphocyte population.

NLH can be found in any patient age group, but the majority of patients are middle-aged or older and between the age of 50 and 69. There is also no sex predominance [3-4]. Patients with NLH can present with no symptoms, shortness of breath, cough, and/or pleuritic chest pain [4]. The most frequent radiographic finding of NLH is a solitary pulmonary nodule, as in our case, mostly measuring from 2 to 4 cm. However, multiple lesions were found in 36% of patients, as shown in a report of 14 cases [3]. Approximately 90% of NLH lesions were located at the subpleura. Chest CT mostly showed discrete nodules or ill-defined nodular opacities associated with air-bronchograms and vascular involvement, but ground glass attenuation has been reported as well [4]. NLH lesions usually have no pleural indentation on CT, despite their subpleural location.

The etiology is still not fully understood. NLH in the lung usually occurs as an isolated finding, and it does occur in patients with collagen-vascular disease. NLH was also once reported in a familial systemic autoimmune disorder [5].

The differential diagnosis includes mainly of BAC and MALT lymphoma. BAC is a type of lung cancer that presents as a patchy opacity, often with air-bronchograms. MALT lymphoma is a primary extranodal lymphoma, often presenting as multiple lesions on imaging [4]. However, based on the radiologic features only, differentiation among these entities is difficult.

NLH often does not invade the bronchial mucosa, and cytologic study of sputum or bronchoscopic washing or brushing specimens may be negative. Diagnosis through transbronchial biopsy or transthoracic needle biopsy is often difficult because reactive lymphoid proliferation can be detected in inflammation, as well as primary lung cancer or lymphoma. Surgical confirmation is therefore the diagnostic procedure of choice [4, 7-8]. Differentiation between benign and malignant lymphoproliferative lesions of the lung is impossible by light microscopic examination of the specimen only. Now with modern immunofluorescent techniques and molecular biologic analysis, we can distinguish polyclonal cell populations of benign lymphoid

proliferation from monoclonal B-cells or T-cell lymphomas [8].

Grossly, most of the lesions were gray, white, or tan nodules or masses with firm, rubbery, or fleshy consistency, as in our case. Histologic findings were a well-demarcated mass, comprised of prominent reactive germinal centers, well-preserved mantle zones, and sheets of interfollicular mature plasma cells [3, 6]. The germinal centers were immunoreactive with antibody to CD20, and the interfollicular lymphocytes with CD3 and CD5. CD20 is a marker for B cells, while CD3 and CD5 are markers for T cells. As in our case, the specimen was stained with CD3, CD5 and CD20, representing the simultaneous presence of T and B cells which was indicative of a reactive reaction. We can exclude lymphoma from the immuno-staining results, as lymphoma usually is a disease of monoclonal proliferation, and also exclude MALToma, a tumor of monoclonal B cells, which is a differential diagnosis that needs to be considered. The B cells of NLH can secrete an immunoglobulin light chain, which is polyclonal with a kappa to lambda ratio of 3-5:1. However, we did not perform this kind of stain in our case.

The prognosis of NLH after surgical resection is fairly good, but long-term follow-up is needed because this disease is still not fully understood. We need to keep in mind that some cases of MALT lymphoma may show reactive germinal centers, which probably developed around the marginal zones of preexisting reactive lymphoid hyperplasia [3]. Modern immunohistochemical and molecular studies are always required to confirm the diagnosis of NLH [7, 9].

In our case, we performed a gallium scan 2 months after operation to detect any recurrent lesion. Gallium can accumulate in both inflammatory and tumor lesions. A possible explanation for the accumulation of ^{67}Ga is that it binds weakly to plasma transferrin, and translocates to lactoferrin in tumor or inflammatory cells [10]. Gallium-67 scintigraphy is now a useful clinical technique for assessment of post-treatment lymphoma, but there is no report on post-treatment NLH, probably due to rarity of the disease. However, the interpretation of ^{67}Ga scintigraphy is not without problem, as ^{67}Ga can accumulate in non-malignant tissue or post-operation fibrotic tissue. Other imaging studies are still needed for follow-up [11].

In conclusion, NLH is a benign lymphoproliferative disease. The clinical presentation of this disease is always atypical, and patients always presented with single or multiple nodules. Surgery is the diagnostic modality of choice, with modern immunohistochemical and molecular studies for confirmation. Long-term follow-up is suggested, since the etiology of the disease is not fully understood.

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肺結節性淋巴組織增生：病例報告及文獻回顧

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肺結節性淋巴組織增生是一種罕見的疾病，主要是良性的淋巴組織的增生。最初是被命名為偽淋巴瘤。肺結節性增生的病人沒有特定的症狀，影像上是以單顆或多顆結節為主。肺結節性增生可見於任何年齡層，但主要常見於中年及老年人。鑑別診斷包括支氣管肺泡癌及淋巴組織淋巴瘤。診斷方式主要以手術切除及病理判讀。目前這種疾病的預後良好，但因為這種疾病的成因仍不明確，需要長期追蹤病人。我們在此報告一個53歲病人被診斷得了肺結節性淋巴組織增生，以及這疾病的相關知識。*(胸腔醫學 **2009; 24: 168-174**)*

關鍵詞：肺結節性淋巴組織增生，反應性淋巴濾泡，生長中心

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Endobronchial Metastasis from Rectal Adenocarcinoma without Liver Involvement: A Case Report

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The lungs are common sites for secondary metastases. However, endobronchial metastases from extrapulmonary primary sites are rare, and their definition and developmental modes have not yet been fully elucidated. The liver is the most common site of hematogenous spread from colon tumors, which then progresses to pulmonary sites. Herein, we report a case of adenocarcinoma of the rectum, status post-radical proctectomy and postoperative chemotherapy. After a 2-year disease-free interval, the patient was brought to the emergency department and hospitalized with pulmonary symptoms similar to pneumonia. Computed tomography disclosed lobar consolidation of the right upper lobe and obstruction of the right main bronchus. Metastatic lung cancer was confirmed with histopathology of a biopsy specimen obtained through bronchoscopy. Hematogenous dissemination was most likely because of the additional pulmonary nodule at the right lower lobe. Due to the tumor being unresectable, the patient received radiation therapy for palliative treatment. We also reviewed the literature on endobronchial colorectal metastasis. The median time of metastasis to the lung from the primary site at the colon is about 4 years, and treatment is variable on account of the individual condition. ***(Thorac Med 2009; 24: 175-180)***

Key words: colorectal, endobronchial, metastasis, extrapulmonary

Introduction

The lungs are the most common sites for secondary metastases, and autopsy series of patients with known extrapulmonary malignancies have demonstrated pulmonary parenchymal metastases in approximately 50% of patients [1-2]. Endobronchial metastases (EBM) are much less common, with autopsy series finding endobronchial lesions in just 2% of metastatic lung cancers [2-4]. They mostly present with parenchymal pulmonary secondaries, and the rates of bronchial metastatic involvement at the time of pulmonary resection were estimated at 27% [5-6]. The developmental modes of EBM have not been fully described previously, and the definition of EBM varies according to the author. One definition includes only direct metastasis to the tracheobronchial wall [4]; and another, secondary involvement as well as direct invasion [7].

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Colorectal carcinoma frequently spreads to the liver and lung by the hematogenous route. Liver involvement is usually earlier than involvement of the lung, and advanced progression from the liver to the lung was assumed [4].

Case Report

A 46-year-old male truck driver was referred from a local hospital because of a 10-day history of nonproductive cough, and then was admitted via the emergency department due to suspected pneumonia in the right upper lobe. He had a significant past history, including cigarette smoking 30 packs per month for 40 years and adenocarcinoma of the rectum, stage III C, status post-radical proctectomy, low anterior resection and postoperative chemotherapy (a fluorouracil and leucovorin regimen 14 times weekly) 2 years prior to this admission.

The clinical evaluation was unremarkable except for coarse breathing sounds bilaterally. Routine biochemical and hematological profiles were within physiological limits. Sputum study for bacteria and tuberculosis bacillus yielded negative findings. The serum level of carcinoembryonic antigen was 25.6 IU/L. Chest radiography showed lobar consolidation in the right upper lobe (Figure 1), which was not seen in the last chest radiography. Endobronchial metastasis was highly suspected due to the incompatible presentation of pneumonia. Computed tomography (CT) of the chest with radio-contrast was performed 1 day later, and pulmonary consolidation and collapse of the right upper lobe, a pulmonary nodule at the medial basal segment of the right lower lobe, and mediastinal necrotic lymphadenopathies were found (Figure 1). He

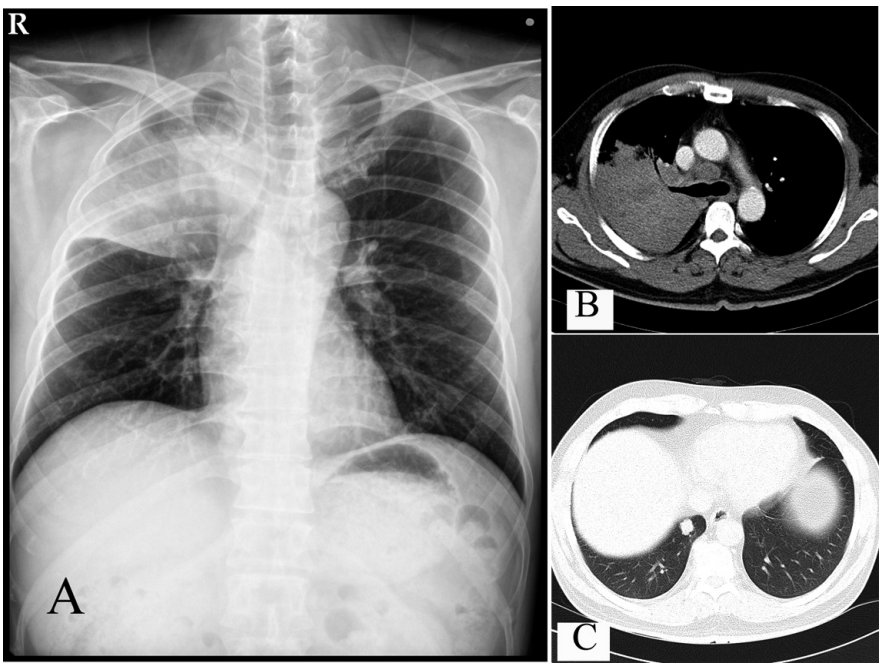

Fig. 1. Chest radiography. Left: Lobar consolidation, right upper lobes with a specific golden-S curve. Computed tomography of the chest. Right top: Consolidation and collapsed lung at the right upper lobe surrounding the right main bronchus. Right bottom: A pulmonary nodule at the medial basal segment of the right lower lobe.

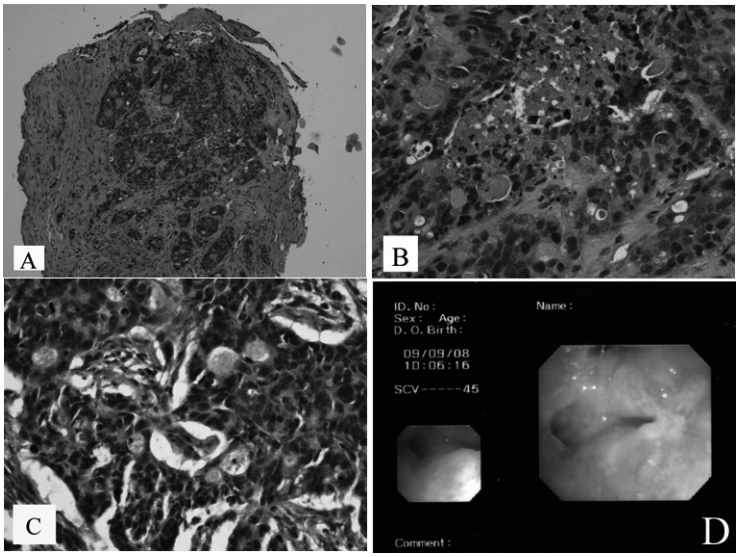

Fig. 2. Left top, A: Biopsy specimen of the right bronchus shows papillary growth of neoplastic cells with mucosal invasion. (hematoxylin-eosin, × 40). Right top, B: Lung tissue; colonic adenocarcinoma (hematoxylin-eosin, × 200) Left bottom, C: Last histopathology of the surgical specimen of rectal adenocarcinoma (hematoxylin-eosin, × 200). Right bottom: Bronchoscope; tumor growth resulting in obstruction in the orifice of the right upper lobe.

then underwent flexible bronchoscopy, which revealed tumor growth with nearly total obstruction of the orifice of the right upper lobe (Figure 2). Histopathology of the biopsy specimen was consistent with colonic adenocarcinoma (Figure 2). Endobronchial colorectal metastasis was diagnosed. Because of the consolidation of the right upper lobe and the additional pulmonary nodule at the right lower lobe, hematogenous dissemination of metastasis from rectal cancer was most likely. However, the mass lesions could not be resected completely, so the patient underwent radiation therapy for palliative treatment. He then suffered from obstructive pneumonitis related to progression of the lung carcinoma, and 3 months later died of respiratory failure status post-endotracheal tube with mechanical ventilation.

Discussion

A variety of primary tumors have been associated with EBM, although breast, colon, and renal carcinomas predominate [7-9]. The symptoms and roentgenographic manifestations of patients with EBM are identical to those associated with primary bronchogenic carcinomas, so it is difficult to differentiate between the 2 diagnoses based on the symptoms and radiographic signs alone. The most common symptoms are hemoptysis and cough with dyspnea. However, the lesions may be asymptomatic in some patients. The radiographic findings are quite variable; CT was sensitive in detecting and localizing endobronchial neoplasms, including metastatic lesions, and correlated well with bronchoscopic findings [10]. Diagnosis of EBM with fiberoptic bronchoscopy is usually precise [4].

Bronchoscopy should be performed early in patients with breast, colon, and renal cancer who have pulmonary symptoms. The histologic identification of the tissue can be correlated with previously documented primary tumors or as a guideline for further investigation in those patients in whom the underlying primary tumor site has not been identified [4]. Immunohistochemistry, such as thyroid transcription factor-1 (TTF-1), cytokeratin 7 (CK 7) and cytokeratin 20 (CK 20), could provide further confirmation in differentiating primary lung cancer from metastatic lung lesion [12].

EBM tend to occur at a significant interval from the diagnosis of the primary tumor, indicating a relatively slow disease progression [4, 7]. Takuji K, *et al*. reported the free interval from the diagnosis of primary colorectal tumor to the discovery of EBM ranged from 1 to 112 months [11], and Bar-Gil Shitrit A, *et al*. reported a median time of 4 years [13]. However, survival after the diagnosis of EM is poor, since it is generally a manifestation of a far-advanced disease stage. Therefore, it should be emphasized that treatment plans must be individualized, because some patients can achieve long-term survival [7-9].

Treatment for and management of EBM are determined by the histologic identification of the primary tumor, biological behavior, anatomic location, evidence of other metastatic sites, and the patient's performance status [4, 7]. Survival is dependent to a great degree on the biological behavior of the particular tumor and its responsiveness to the palliative measures available [4]. The therapeutic options include surgical excision, local radiotherapy, chemotherapy, and transbronchial endoscopic procedures, such as photodynamic therapy, electrocoagulation, intratumoral ethanol injections, Nd-YAG laser-debulking therapy, diathermic snares, and prosthetic stents [8]. Surgical resection should be reserved for patients with localized disease, because most patients have extrabronchial metastatic disease at the diagnosis of EBM [8], and mediastinal lymph node involvement is frequently present during the postmortem examination [2, 8]. Long-term survival after surgical resection is expected for some patients with localized disease.

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直腸癌病人術後多年後併發遠端肺支氣管內癌症轉移—案例報告

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肺部是常見的癌症轉移處，然而肺外腫瘤併發支氣管內轉移的個案機率卻是少見，尤其此類轉移的機轉與過程目前尚無定論。依目前所推論的癌症轉移路徑而言，原發大腸直腸惡性腫瘤應先轉移至肝臟，而後再由血液循環路線至肺內。本次報告一位男性直腸癌病人，於接受直腸切除手術及化學治療後，因疑似肺部感染症狀住院診察，最後診斷為直腸癌併支氣管內癌症轉移，但無肝臟轉移情形。因個案之肺部轉移病灶超過手術切除適應症（縱膈腔淋巴轉移），僅能接受放射治療緩解。本篇案例報告蒐集相關文獻，簡介此類病例之發生率、診斷方式、治療策略以及存活機會。*(胸腔醫學 **2009; 24: 175-180**)*

關鍵詞：大腸直腸癌，癌症轉移，支氣管

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Salmonella: A Rare Cause of Fatal Emphysematous Aortitis – A Case Report

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In rare cases, *Salmonella* infection may be associated with extra-intestinal manifestations. Of these, an endovascular invasion of *Salmonella* to the thoracic aorta, manifesting as non-aneurysmal aortitis, is seldom seen. Nonetheless, it poses a risk of rupture and mortality equal to the aneurismal form. We describe the case of an 86-year-old man who had a medical history of hypertension and prostate cancer under treatment with hormone therapy, and who presented with *Salmonella* bacteremia and a rare combination of infectious thoracic aortitis and left-side empyema. When pneumomediastinum and loculated pleural effusion are encountered on chest radiography, the possible origins of the air should include thoracic organ invasion by gas-forming bacteria. The characteristic chest radiographic abnormalities presented in our case can aid clinicians in the differential diagnosis, including aortitis and esophageal rupture. Emergency chest CT is the best diagnostic modality for identifying these abnormalities clearly, and led to a quicker diagnosis of the rare combination of *Salmonella* aortitis and empyema in our case. ***(Thorac Med 2009; 24: 181-185)***

Key words: emphysematous, aortitis, *Salmonella*

Introduction

The etiologies of acute mediastinitis include perforation of a thoracic organ and direct extension of infection from elsewhere. Infectious thoracic aortitis, which is defined as inflammation of the thoracic aortic wall by an infection, is seldom diagnosed as the cause of acute mediastinitis. *Salmonellae*, together with *Streptococcus* and *Staphylococcus*, are among the most commonly detected bacteria to seed the aorta, with *Salmonellae* being the most common [1]. *Salmonellae* have a predilection for diseased arterial walls, especially atherosclerotic arterial walls. Aneurysm formation, enlargement of an existing aneurysm, and simple vascular inflammation are 3 characteristically vascular manifestations [2]. Vascular infection due to *Salmonellae* usually involves the thoracic and abdominal aorta. In such cases, the abdominal aorta is particularly involved [3], but a higher mortality is associated with thoracic aortic involvement [4]. Involvement of the thoracic aorta in *Salmonellae* bacteremia is an extremely rare

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complication [5-6], especially in the form of non-aneurysmal aortitis, as in our patient.

Computed tomography (CT) with contrast medium is the diagnostic modality of choice because it detects changes in the aortic arterial wall and peri-aortic tissue, including aneurysm, fluid, gas, and blood components. Nonetheless, few cases of non-aneurysmal bacterial aortitis have been reported, with most past reports describing mycotic aneurysms of the aorta. In 1990, Michael *et al*. reported 2 cases of non-aneurysmal bacterial aortitis with subsequent rupture documented on CT; they concluded that the diagnosis of acute aortic infection on CT, even in the absence of aneurysmal dilatation, heralds a high risk of impending rupture [7]. Furthermore, a previous report of aortic infection due to *Salmonella* described complications such as pneumonia, aortobronchial fistula, thoracic or lumbar osteomyelitis, and psoas muscle or pelvic abscess [8]. Empyema caused by *Salmonella* has been reported only once before (in 1991) as a complication of simultaneous aortitis [9]. The coincidence of fatal thoracic aortitis and left-side empyema caused by *Salmonella* is very rare in clinical practice.

Case Report

An 86-year-old man with a history of hypertension and prostate cancer under treatment with hormone therapy presented to the emergency room (ER) because of progressively drowsy consciousness and poor appetite at home. About 2 weeks earlier, the patient complained of nonspecific tenderness in the anterior chest wall that improved after taking an analgesic agent. He had no fever or other associated symptom such as cough, abdominal pain, or back pain. On arrival in the ER, his temperature was 37.4°C, pulse rate was 133 beats/minute, and respiratory rate was 22 breaths/minute. His blood pressure was 102/76 mmHg. Neurological and physical examinations revealed nothing remarkable, except crackles heard in the left lower lung field. A complete blood count showed leukocytosis with a left shift (10,400 WBC/μl, 67% segmented neutrophils, 32% bands). He had no anemia. Biochemistry showed acute renal insufficiency with pre-renal azotemia (99 mg/dl blood urea nitrogen, 2.9 mg/dl creatinine) and elevated C-reactive protein (276 mg/L). All other tests were non-contributory. His arterial blood gases in room air showed a pH of 7.454, PCO_2 of 27.2mmHg, PO_2 of 51 mmHg, and HCO_3^- of 19.1 mmol/L, which was compatible with hypoxemia and respiratory alkalosis. An emergency chest radiograph (Figure 1) revealed air within the mediastinum and left-side loculated pleural effusion. Thoracentesis was performed and empyema was diagnosed due to apparent frank pus. Several episodes of hypotension were evident, and improved after a normal saline challenge. Empiric antibiotic

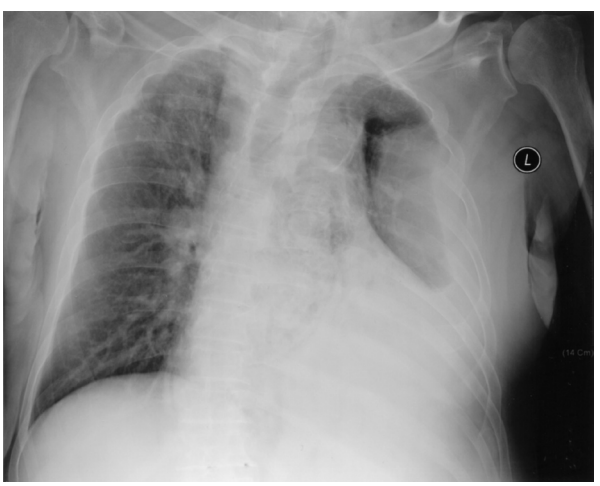

Fig. 1. Chest radiograph obtained in the emergency room. Note the presence of air within the mediastinum and left-side loculated pleural effusion.

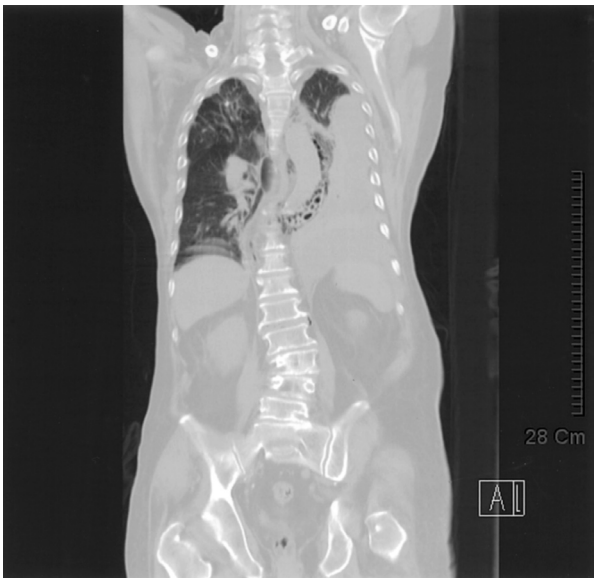

Fig. 2. Emergency non-contrast computed tomography of the chest shows emphysematous change along the thoracic aorta and neighboring loculated pleural effusion (coronal view).

with Ceftriaxone was prescribed and emergency non-contrast CT of the chest (Figure 2) was arranged. The emphysematous change along the thoracic aorta and the neighboring loculated pleural effusion suggested infectious aortitis as the primary source of infection. Blood and pleural effusion were submitted for culture, and *Salmonella* enteritidis group B was identified 2 days later. Surgical intervention was suggested by the cardiovascular surgeon, but the family refused due to the patient's advanced age. Unfortunately, the patient experienced a sudden hemodynamic collapse resulting in the performance of emergent cardiac pulmonary cerebral resuscitation (CPCR). The patient expired due to failed resuscitation the next day.

Discussion

Most patients with aortitis caused by *Salmonella* have preexisting atherosclerotic disease and the most common predisposing factor for *Salmonella* aortitis is diabetes mellitus, which could serve as a marker of preexisting atherosclerotic disease of the aorta [8]. Although there was no medical history of diabetes mellitus in our patient, obvious calcification on the arterial wall, as seen on chest CT, indicated evidence of underlying atherosclerosis in this patient. In addition to the risk factors mentioned above, endovascular infection may also complicate patients older than 50 [10], as with our patient. Other underlying diseases include hypertension, which was also noted in our case.

In general, the symptoms and signs of *Salmonella* vascular infections are often nonspecific. Prolonged fever, back or abdominal pain, and relapsing bacteremia are the clinical hints of a vascular infection. The results of laboratory tests are also of little help, except for positive blood cultures. Nearly all of the reported cases of *Salmonella* aortitis have resulted in aneurysm formation or, more rarely, enlargement of a preexisting aneurysm [2]. Widening of the mediastinum on a chest radiograph is suggestive of an aneurysm, but it is usually nonspecific. CT plays a pivotal role in detecting aortic aneurysm. In our patient with non-aneurysmal aortitis, loss of contiguous intimal calcification and the gas surrounding the aorta on CT (Figure 2) were diagnostic. Nonetheless, the characteristic feature on the chest CT in our case, emphysematous formation along the descending aorta, was of great educational value and a clue for differentiating aortitis from esophageal rupture, despite the latter being more frequently encountered in our clinical practice.

In a comprehensive review of the literature, the overall mortality due to *Salmonella* aortitis was found to be 53%, but mortality was 95% among patients treated medically and only 41% when patients were treated surgically [2]. The

earlier the diagnosis of *Salmonella* aortitis was made, the less subsequent morbidity and mortality there were. Depending on its location, infectious aortitis with or without aneurysm often progresses undiagnosed, resulting in recurrent bacteremia from an unidentified source; eventually, the aorta ruptures, and leading to cardiovascular collapse.

Surgical intervention is the treatment of choice and can greatly increase survival. Because involvement of the thoracic aorta produces a more complex surgical challenge and surgeons have little experience with this type of intervention, an early diagnosis is even more important, so as to reduce life-threatening complications.

In conclusion, when we encounter pneumomediastinum and loculated pleural effusion on chest radiography, the possible origins of the air usually are the respiratory or gastrointestinal tract, and may be the result of inflammation, trauma, or iatrogenic procedures. Although most patients with *Salmonella* aortitis present without distinctive clinical symptoms, obtaining a comprehensive history, including recent trauma or iatrogenic procedures, the presence of significant abnormal radiographic findings, and a high index of suspicion will help to manage the mediastinitis with greater confidence. In our patient, the isolation of *Salmonella enteritidis group* B from the blood cultures and pleural effusion samples, coupled with radiographic evidence of gas surrounding the thoracic aorta and loculated pleural effusion, highlighted the rare combination of *Salmonella* aortitis and empyema.

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造成致命縱膈腔炎的罕見原因—病例報告

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一般沙門氏桿菌很少會造成胃腸道以外的症狀。其中，沙門氏桿菌侵犯到胸腔主動脈並且以非動脈瘤表現的主動脈炎更是少見。然而，它和以動脈瘤表現的主動脈炎有同樣高的破裂和死亡的機率。我們報告一位86歲有高血壓病史和接受賀爾蒙治療的攝護腺癌男性，被發現合併了感染性的胸腔主動脈炎，左側膿胸還有沙門氏桿菌菌血症。臨床上，當胸部X光片發現縱膈腔氣腫和多處肋膜積水時，我們要把會侵犯到胸腔器官的產氣細菌當作可能造成氣腫的來源。典型的胸部X光異常可以幫助我們在鑑別診斷上需要將主動脈炎和食道破裂納入考慮，緊急的胸部電腦斷層是區分這些病灶的最好工具並且進一步快速診斷罕見合併沙門氏桿菌感染的主動脈炎和膿胸。*(胸腔醫學* ***2009; 24: 181-185)***

關鍵詞：產氣的，主動脈炎，沙門氏桿菌

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