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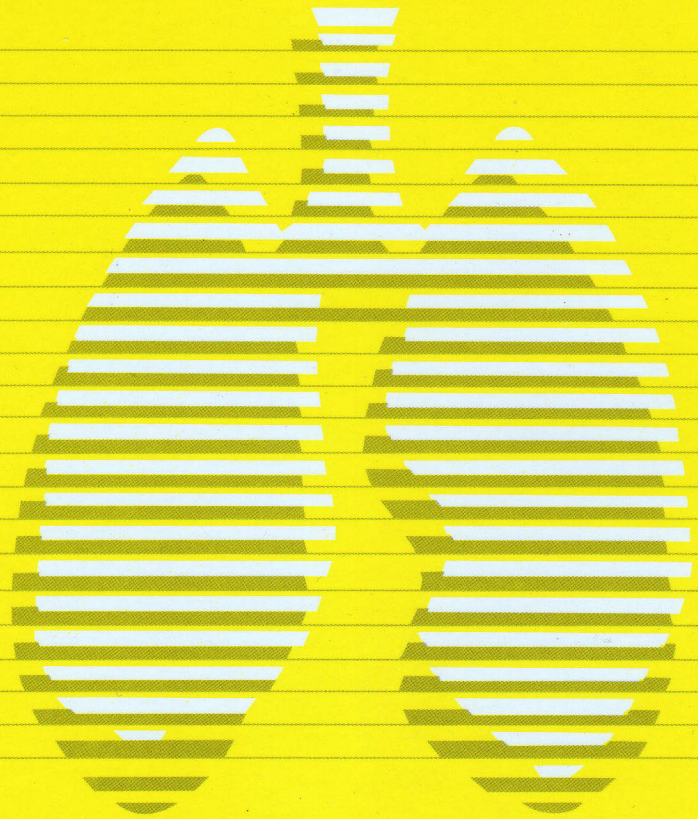

台灣胸腔暨重症加護醫學會

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## 原著



## 病例報告

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# 胸腔醫學
# Thoracic Medicine

The Official Journal of Taiwan Society of Pulmonary and Critical Care Medicine

## Orginial Articles



## Case Reports

# The Effect of Extracorporeal Membrane Oxygenation Treatment on Patients with Severe Acute Respiratory Distress Syndrome Caused by Influenza Virus

Yen-Tin Chen*,****, Chien-Wei Hsu*,**, Guan-Sheng Wu***, Ruay-Sheng Lai****

**Objectives:** We compared the clinical outcomes of patients with virus pneumonia and severe acute respiratory distress syndrome (ARDS) status treated with or without extracorporeal membrane oxygenation (ECMO) support.

**Methods:** We retrospectively reviewed the hospital courses of patients who were admitted to intensive care unit (ICU) with severe ARDS ($PaO_2/FiO_2$ <100 under positive end expiratory pressure >5 $cmH_2O$) due to influenza virus pneumonia and who had a period ≤7 days between the onset of influenza and intubation from January 2008 to December 2011. Clinical characteristics and outcomes were compared between patients with and without ECMO support.

**Results:** A total of 13 patients with refractory hypoxemia and severe ARDS status were enrolled. Eleven of the 13 patients had a diagnosis of influenza confirmed by PCR test (8 influenza A (swH1), 2 influenza A (H3) and 1 influenza B), 1 by the influenza rapid test (influenza A) and 1 by bronchoalveolar lavage (BAL) virus isolation (influenza A). Six patients were provided with veno-venous ECMO (vv-ECMO) support and 7 patients received only conventional ventilatory support. Patients who were provided with ECMO support had a higher successful ventilator weaning rate (83.3% vs. 29%, $p$=0.048) than patients without ECMO support. The hospital mortality rate between patients with and without ECMO support did not differ (17% vs. 57%, $p$=0.135).

**Conclusions:** In patients with influenza virus pneumonia-related severe ARDS, ECMO support may be an effective rescue treatment strategy for refractory severe hypoxemia and lead to a significantly higher successful ventilator weaning rate, a lower hospital mortality rate, and better long-term outcome. ***(Thorac Med 2013; 28: 200-208)***

Key words: acute respiratory distress syndrome, critical care, extracorporeal membrane oxygenation, influenza viral pneumonia, mechanical ventilation

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## Introduction

A novel swine-origin influenza A (H1N1) virus pandemic occurred in April 2009 in Mexico [1]. Most patients diagnosed with the H1N1-2009 virus had a self-limited respiratory illness, and a few patients suffered from severe illness and were hospitalized in intensive care unit (ICU). Of these ICU patients, 14-46% died because of influenza-associated pneumonia and acute respiratory distress syndrome (ARDS) with refractory hypoxemia or hypercapnia. For patients with severe ARDS refractory to maximal conventional therapies, extracorporeal membrane oxygenation (ECMO) could be considered as a rescue therapy [2]. However, the role of ECMO in ARDS remains uncertain. Some previous randomized studies revealed negative results [3-4] and 1 study showed a better survival rate for ARDS patients treated with ECMO [5]. This study was conducted to compare the clinical outcomes of patients with virus pneumonia-related severe ARDS who failed conventional mechanical ventilation therapy and were treated with or without ECMO support.

## Methods

We included all patients with a diagnosis of influenza and acute respiratory failure with mechanical ventilator support in an adult ICU between January 2008 and December 2011. Only those patients with severe ARDS and an onset of influenza-to-intubation period of less than 7 days were enrolled. Severe ARDS was defined according to the definition of the American-European Consensus Conference [6] and the presence of $PaO_2/FiO_2$ <100 before endotracheal intubation or ECMO cannulation under positive end expiratory pressure (PEEP) >5 $cmH_2O$. The diagnosis of influenza was made based on the results of the influenza rapid test, polymerase chain reaction (PCR) test or bronchoaveolar lavage (BAL) virus isolation.

Pneumonia was diagnosed according to the National Nosocomial Infection Surveillance (NNIS) system clinical pneumonia diagnosis criteria [7]. We excluded patients who had evidence of bacterial pneumonia, such as positive sputum and blood culture or any positive atypical pneumonia serological test. Those who received other rescue therapy, such as inhaled nitrous oxide, prone positioning, high frequency oscillator ventilation or partial liquid ventilation, were also excluded. All patients received the same lung protective strategy. We reviewed their medical records and recorded clinical characteristics, including age, gender, underlying comorbidities, Acute Physiology and Chronic Health Evaluation II (APACHE II) score, $PaO_2/FiO_2$, laboratory values at the beginning of ICU admission, and medications and outcomes of patients treated with or without ECMO. Vasopressor use was defined as a vasopressor requirement after ICU admission. Use of corticosteroids was defined as an administration of corticosteroids for >3 days. Hemorrhagic complications were defined as bleeding from whole body organs, including the central system, lung, gastroenteral tract, kidney, skin or puncture site.

### *Statistical analysis*

All data were analyzed by SPSS version 19. Data are presented as medians with interquartile range or number with percentages. Mann-Whitney tests were used to compare continuous variables with non-normally distributed data. Chi-square tests were used to compare dichotomous

variables. The Kaplan-Meier curve was used to estimate the probability of survival. The log-rank test was used to compare the difference in survival between patients with and without ECMO support. All *P* values were 2-tailed. A *P* value <0.05 was considered significant

## Results

### *Characteristics of study patients*

From January 2008 to December 2011, a total of 719 patients were admitted to our hospital with a diagnosis of influenza. Among them, 27 patients (27/719, 3.8%) received ICU care due to acute respiratory failure under mechanical ventilator support. Thirteen (13/27, 54%) patients had severe ARDS with $PaO_2/FiO_2$ <100 under a ventilator PEEP level >5 $cmH_2O$, and ≤7 days between the onset of influenza and intubation (Figure 1). None of the 13 patients had bacterial pneumonia. Superinfection was diagnosed at the beginning of the ICU course with positive results on microbiological sputum or blood culture or the atypical pneumonia serological test. Eleven of the 13 patients were confirmed to have influenza by PCR test (8 influenza A (swH1), 2 influenza A (H3) and 1 influenza B), 1 by the influenza rapid test (influenza A) and 1 by bronchoalveolar lavage (BAL) virus isolation (influenza A). There was no significant difference in clinical characteristics between patients with and without ECMO support (Table 1). Six patients were supported with venous-venous ECMO (vv-ECMO) and 7 were managed with conventional ventilatory support only. The clinical care characteristics of the ECMO support group patients are presented in Table 2.

### *Outcome and complications*

Patients who were provided with ECMO support had a higher mechanical ventilator

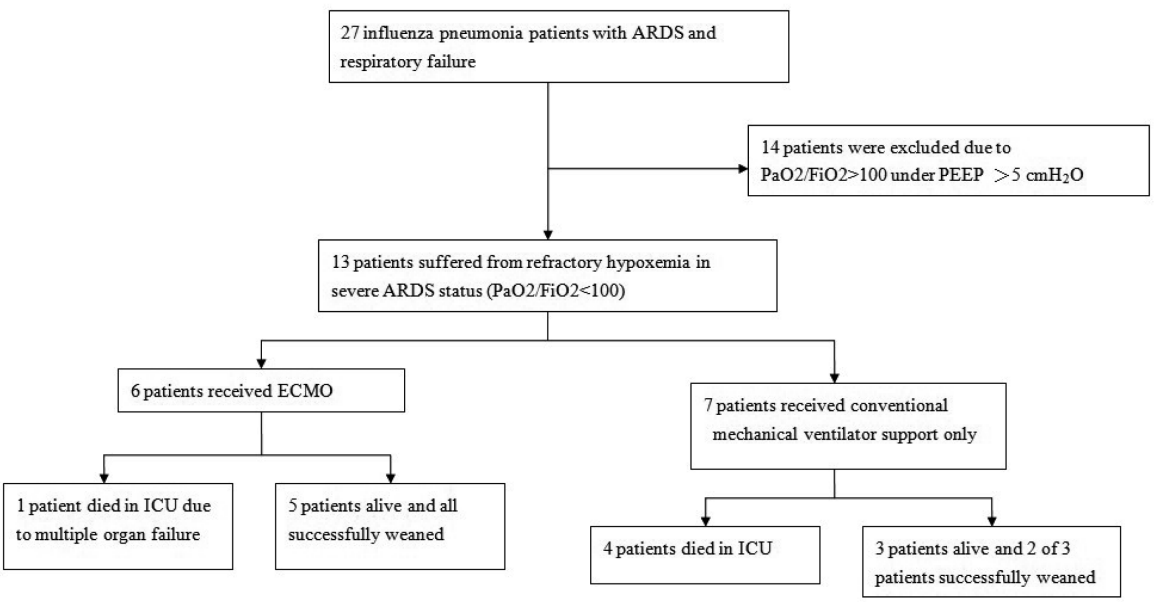


**Fig. 1.** Flow diagram of critically ill patients who were admitted to our intensive care units due to acute respiratory failure under mechanical ventilator support with a diagnosis of influenza.

**Table 1.** Characteristics of severe ARDS patients receiving ECMO or not

| Parameter | | | ECMO (N=6) | Non- ECMO (N=7) | *P* value |
|---|---|---|---|---|---|
| Age, years, median (IQR) | | | 49.5 (28.8-55.2) | 60 (48-78) | 0.086 |
| Gender | Male (%) | | 2 (33) | 6 (86) | 0.053 |
| | Female (%) | | 4 (66) | 1 (14) | |
| Underlying disease | Hypertension (%) | | 1 (17) | 5 (83) | 0.048 |
| | Type 2 DM (%) | | 3 (50) | 3 (42) | 0.797 |
| | CAD (%) | | 0 (0) | 1 (14) | 0.335 |
| | Pregnancy (%) | | 1 (17) | 0 (0) | 0.261 |
| Cause of ARDS | Influenza type A | swH1 (%) | 5 (83) | 3 (57) | |
| | | H3 (%) | 1 (17) | 1 (14) | |
| | | Non-subtype | 0 (0) | 2 (29) | |
| | Influenza type B (%) | | 0 (0) | 1 (14) | |
| Disease severity | APACHE II score, median (IQR) | | 31 (23.5-38.5) | 22 (20-37) | 0.173 |
| | $PaO_2/FiO_2$, median (IQR) | | 59 (53-66) | 73 (54-86) | 0.223 |
| | PEEP, $cmH_2O$, median (IQR) | | 10 (7.5-15) | 10 (8-12) | 0.882 |
| | Lactate, mg/dL, median (IQR) | | 10.6 (7.1-59) | 13.2 (9.9-21) | 0.749 |
| | WBC,1000/Cumm, median (IQR) | | 6.1 (4.1-20.7) | 4.6 (2.9-11.5) | 0.475 |
| | ≥3 organ dysfunction | | 1 (17) | 3 (57) | 0.308 |
| Medications | Use of vasopressor (%) | | 6 (100) | 4 (57) | 0.067 |
| | Use of Tamiflu (%) | | 6 (100) | 6 (85) | 0.335 |
| | Use of corticosteroids (%) | | 3 (50) | 5 (71) | 0.429 |

Data are presented as number (%) or median (interquartile ranges), ECMO: extracorporeal membrane oxygenation, ARDS: acute respiratory distress syndrome, CAD: coronary artery disease, APACHE II score: Acute Physiology and Chronic Health Evaluation II score, PEEP: Positive end expiratory pressure

**Table 2.** Characteristics of 6 patients under ECMO support

| Parameter | 1 | 2 | 3 | 4 | 5 | 6 |
|---|---|---|---|---|---|---|
| Age, years | 25 | 54 | 45 | 30 | 56 | 55 |
| Sex | F | F | M | M | F | F |
| APACHE II score | 24 | 24 | 38 | 40 | 22 | 38 |
| Type of ECMO | V-V | V-V | V-V | V-V | V-V | V-V |
| $PaO_2/FiO_2$ before ECMO | 57 | 53 | 65 | 69 | 53 | 61 |
| PEEP level before ECMO, $cmH_2O$ | 10 | 15 | 6 | 10 | 15 | 8 |
| Ventilator setting during ECMO | PCV | PCV | PRVC | PCV | PCV | PCV |
| Time from the onset of influenza to intubation, days | 4 | 5 | 3 | 2 | 3 | 5 |
| Time from intubation to ECMO, days | 0 | 2 | 0 | 0 | 5 | 1 |
| Duration of ECMO, days | 24 | 29 | 13 | 16 | 14 | 2 |
| 1-2 organ dysfunction before ECMO | Yes | Yes | Yes | Yes | Yes | - |
| ≥3 organ dysfunction before ECMO | No | No | No | No | No | Yes |
| Outcome | Survived | Survived | Survived | Survived | Survived | Expired |

ECMO: extracorporeal membrane oxygenation, APACHE II score: Acute Physiology and Chronic Health Evaluation II score, PEEP: Positive end expiratory pressure

weaning rate (83.3% vs. 29%, $p$=0.048), and a non-statistically significant trend toward lower hospital mortality (ECMO vs. non-ECMO, 17% vs. 57%, $p$=0.135) and ICU mortality (ECMO vs. non-ECMO, 17% vs. 57%, $p$=0.135) compared with those without ECMO support. Only 1 of the 6 patients who received vv-ECMO support died due to multiple organ failure. Four of the 7 patients who received conventional ventilatory support with the ARDS protocol died of refractory hypoxemia and multiple organ failure (Table 3). The Kaplan-Meier survival curve showed that patients with ECMO support tended to have a better chance of survival than patients without ECMO support (Figure 2). Patients who received ECMO support had more days of ICU stay (31 vs. 10, $p$=0.062), hospitalization (40 vs. 17, $p$=0.15) and ventilator use (30 vs. 10, $p$=0.063) than patients without ECMO use, but the differences were not statistically significant. Hemorrhagic complications were more common in the ECMO group than in the non-ECMO group. Four of the 6 patients had upper gastroenteral tract bleeding and 2 had significant respiratory tract hemorrhage under ECMO support (Table 3). Two patients in the non-ECMO support group also suffered from upper gastroenteral tract bleeding episodes. In terms of long-term outcome, none of the surviving ECMO support group patients had a home $O_2$-dependent status or had expired at the 6-month follow-up. Two of the 3 survivors in the non-ECMO support group were lost to follow-up and the third was alive at the 6-month follow-up without home $O_2$-dependence (Table 3).

## Discussion

Viral pneumonia, which is typically associated with disease in childhood, is increasingly recognized as a cause of problems among adults. Certain viruses, such as influenza virus, can attack immunocompetent adults, but other viruses take advantage of vulnerable patients only. A swine influenza pandemic occurred in

**Table 3.** Clinical outcomes

| Outcome | | ECMO (N=6) | Non- ECMO (N=7) | *P* value |
|---|---|---|---|---|
| Successful weaning from ventilator (%) | | 5 (83) | 2 (29) | 0.048 |
| ICU days, median (IQR) | | 31 (19.25-40.5) | 10 (1-12) | 0.062 |
| Hospital days, median (IQR) | | 40 (26-51.75) | 17 (5-46) | 0.150 |
| Ventilator days, median (IQR) | | 30 (18.5-36.8) | 10 (1-13) | 0.063 |
| Mortality | In ICU (%) | 1 (17) | 4 (57) | 0.135 |
| | In hospital (%) | 1 (17) | 4 (57) | 0.135 |
| Complication | Hemorrhage (%) | 4 (67) | 2 (29) | 0.170 |
| 6 months' survival | (%) | 5 (83) | 1 (14)* | |
| Bedridden status | (%) | 0 (0) | 0 (0)* | |
| Home $O_2$-dependent (%) | | 0 (0) | 0 (0)* | |

Data are presented as number (%) or median (interquartile ranges), ICU: intensive care unit

*One survivor in the non-ECMO support group was transferred to the long-term care unit under ventilator support on day 17 and was lost to follow-up; the other survivor was discharged home without an $O_2$ support requirement and was lost to follow-up on day 30.

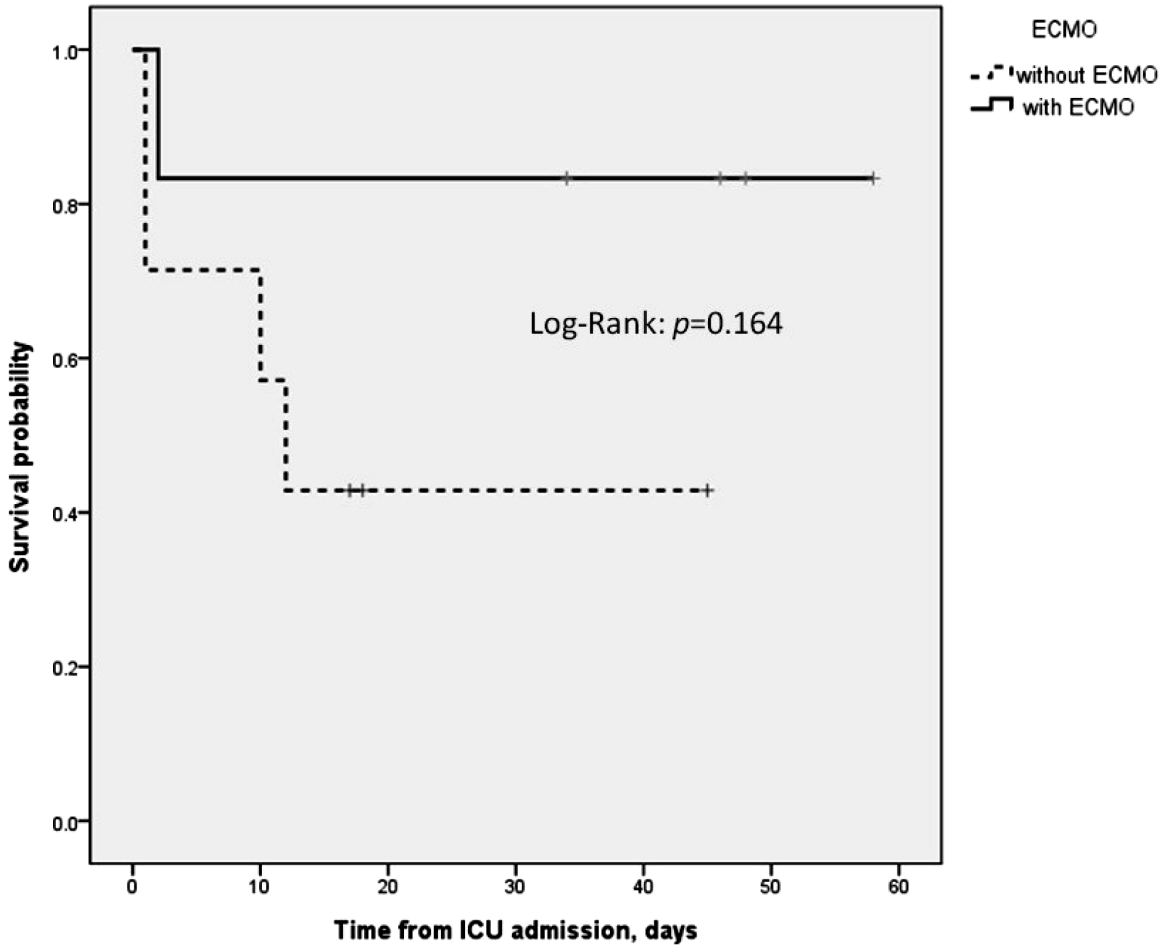


**Fig. 2.** Survival curves of critically ill patients who were admitted to our intensive care units with influenza-related severe ARDS. (Log Rank: $p$=0.164)

2009 during which the rate of hospitalization reached 7% and the rate of pneumonia was reported as 0.4% [8]. Among patients admitted to hospitals, 9-31% required ICU admission [2] and more than 80% of these patients required mechanical ventilation due to influenza-associated pneumonia with ARDS [9]. The mortality rate among patients admitted to the ICU with respiratory failure varied from 17-28% [9].

In the past 2 decades, the technical evolution of ECMO has led to significant improvement in the survival of critically ill patients. ECMO effectively improved survival in selected acute failed cardiac or pulmonary function patients who would normally have a 100% mortality rate due to severe illness [10]. Therefore, ECMO was used with patients with ARDS in order to reduce lung injury and give the lung more time to recover. However, the use of and the indications for ECMO in the most severe cases of ARDS remain highly debated [11-13]. Only 1 multicenter, prospective, randomized controlled trial showed significant improvement in survival without disability in patients with severe illness but potentially reversible respiratory failure with ARDS (defined as a Murray

score ≥3 or pH <7.2 despite optimal conventional treatment) [5].

In our study, the ECMO support group had a lower hospital mortality rate (17%) than the non-ECMO support group, although without a statistically significant difference. This result is close to the reported mortality rate (21%) of influenza A patients associated with respiratory failure with ECMO support during the H1N1 pandemic in the observational study published in JAMA 2009 [14], but better than the mortality rate of 56% (5/9) in a prospective observational study published in Intensive Care Medicine 2010 [15]. The patient characteristics of the ECMO support group, such as age, gender and $PaO_2/FiO_2$ level, were similar to those of the latter study [15]. Multiple organ failure contributed to the death of most of the ECMO non-survivors in both our study and the latter prospective observational study [15]. That fewer patients in our study received ECMO support while in an ongoing multiple organ failure status may be the reason why we had a lower mortality rate in the ECMO support group. The only expired patient in the ECMO group had multiple organ failure due to refractory hypoxemia before ECMO implantation. This patient was transferred for further ECMO support management from another hospital where she received conventional mechanical therapy. However, multiple organ failure developed when she arrived at our hospital. Even with ECMO support, she still died of multiple organ failure within 1 day. When she arrived, it was probably too late to set up ECMO for this patient. The other survivors had received ECMO support before multiple organ failure occurred. In the group without ECMO, the 4 patients that presented multiple organ failure expired quickly. When patients present hypoxia under conventional mechanical ventilation therapy, they may progress to multiple organ failure and die without rescue therapy. That was why the patients without ECMO support tended to have shorter ICU stays, and fewer hospital days and ventilator days than patients with ECMO. In addition, there was a significantly better mechanical ventilator weaning rate in the ECMO support group in our study. With regard to the long-term outcome of our study, limited data were acquired to analyze the difference with ECMO support because 2 of the non-ECMO support survivors were lost to follow-up on day 17 and day 30. All of the survivors in the ECMO support group were successfully weaned from the ventilator during hospitalization, and none of them required home $O_2$ therapy or a bedridden status due to deteriorated lung condition after recovery from severe ARDS. That mechanical ventilator support could be immediately weaned allowing the lungs rest under ECMO support and minimizing ongoing secondary lung injury in the ARDS lungs may be the reason [16].

There are several limitations in this study. First, the case number is small. No statistically significant difference in patient mortality was shown between the ECMO and the non-ECMO support group due to the limited patient number in both arms. Further large, prospective studies are needed to confirm this result. Second, this was a retrospective study and the timing of ECMO set up could not be controlled. Based on the results of this study, it would be better in future prospective studies to set up ECMO before multiple organ failure appears.

## Conclusion

In patients with influenza virus pneumonia-related severe ARDS, ECMO support may be an

effective rescue treatment strategy for refractory severe hypoxemia, and lead to a significantly higher successful ventilator weaning rate, a lower hospital mortality rate and better long-term outcome.

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# 流感病毒性肺炎引起嚴重急性呼吸窘迫症候群病患使用體外循環維生系統支持治療之效果

陳彥廷 *,**** 許健威 *,** 吳冠陞 *** 賴瑞生 ****

**目標**：對於流感病毒性肺炎合併嚴重急性呼吸窘迫症候群，比較使用體外循環維生系統與否對於臨床預後之不同。

**方法**：我們回溯性分析這些於西元 2008 年 1 月至 2011 年 12 月中，曾因流感病毒性肺炎合併嚴重急性呼吸窘迫症候群（$PaO_2/FiO_2$ <100 under PEEP >5 cm $H_2O$）而於加護病房接受治療之病患，並比較分析其曾接受體外循環維生系統支持治療與否的病患臨床特徵及預後。

**結果**：全部有 13 位病患被納入分析，其中 11 位乃經由聚合酵素鏈鎖反應證實感染（8 位為 A 型流行性感冒（swH1），2 位為 A 型流行性感冒（H3），1 位為 B 型流行性感冒），1 位經由流感快速篩檢測試證實為 A 型流行性感冒，1 位經由支氣管肺泡灌洗術病毒分離證實為 A 型流行性感冒。其中 6 位病患接受靜脈循環式的體外循環維生系統治療，其他 7 位病患僅接受傳統呼吸器支持治療。在接受體外循環維生系統治療對於沒有使用體外循環維生系統的病患有較高的呼吸器脫離率（83.3% vs. 29%, $p$=0.048）還有較低的死亡率，雖然沒有達到統計學上的意義。

**結論**：對於這些流感病毒性肺炎合併嚴重急性呼吸窘迫症候群病患，體外循環維生系統的使用於那些難矯正的低血氧或許是個有效的治療策略，並且可以提供病患之後較好的呼吸器脫離率，較低的死亡率及較佳的長期預後之趨勢。*( 胸腔醫學 **2013; 28: 200-208**)*

關鍵詞：急性呼吸窘迫症候群，重症照護，流感病毒性肺炎，體外循環維生系統

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# Micropapillary-Predominant Invasive Adenocarcinoma with Aerogenous Spread – A Case Report

Hui-Hsuan Shih, Yu-Chung Kung, Chi-Yuan Tzen*, Ming-Jen Peng

Micropapillary components of lung adenocarcinoma are classified into 2 types, aerogenous and stromal invasive, based on their pattern of dissemination. Aerogenous spread is characterized by the presence of tumor cells floating within the alveolar spaces rather than invading the stroma, and is more frequently encountered than the stromal invasive type. This suggests that metastasis of tumor cells occurs via the alveolar spaces by intercellular and cell-matrix interactions, and involves a neutrophil-mediated process and subsequent signaling cascades. The clinical presentation includes multifocal intrapulmonary metastases, the shedding of tumor cells that are found in the bronchoalveolar lavage, and an inflammatory process in the non-neoplastic lung tissue. Aerogenous spread therefore indicates a rather poor prognosis. We presented a 68-year-old woman with T4N0M1a adenocarcinoma and multifocal intrapulmonary metastases. The pathological examination of resected tissue showed micropapillary-predominant invasive adenocarcinoma with an aerogenous spread within the alveolar space. The non-neoplastic lung tissue showed marked inflammation and necrosis. ***(Thorac Med 2013; 28: 209-214)***

Key words: aerogenous spread, micropapillary components, invasive adenocarcinoma

## Introduction

Travis and colleagues proposed a new classification for adenocarcinoma in IASLC/ATS/ERS Adenocarcinoma Multidiciprinary Panel, March 12-13, 2009: preinvasive, minimally invasive and invasive adenocarcinoma [1]. Micropapillary pattern is added as a new histology subtype in invasive adenocarcinoma. It exhibits multifocal involvement, resulting in multifocal peripheral adenocarcinomas, relapsing and even advanced stage disease. Aerogenous spread makes an important contribution to this phenomenon [2].

Aerogenous spread often occurs in micropapillary invasive adenocarcinoma [3] of the lung and is characterized by the presence of tumor cells floating within alveolar spaces without invading the fibrotic stroma [4]. This suggests that metastases may occur through the alveolar space by intercellular and cell-matrix interactions [5-6], in a process that involves

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neutrophil infiltration and soluble mediators [3,6]. The clinical presentation includes multifocal intrapulmonary metastasis [2], the shedding of tumor cells found in the bronchoalveolar lavage (BAL) fluid [3], and an inflammatory process in the non-neoplastic lung tissue. Even further vascular invasion due to a neutrophil-mediated reaction and increased vascular endothelial growth factor (VEGF) expression with the appearance of fenestrations in the capillary endothelium may occur without lymph node metastasis [7]. Aerogenous spread may indicate a rather poor prognosis [8].

## Case Report

A 68-year-old woman who had never smoked presented with productive cough with watery sputum for 3 months. She had hypertension and diabetes mellitus with nephropathy (stage 4 chronic kidney disease) and was treated with regular medications. She also presented decreased appetite and had lost 3 kg during the previous 3 months. While coughing, the patient experienced chest pain and shortness of breath.

Chest radiography showed multifocal ill-defined opacities in both lungs and consolidation in the left lower lung field (Figure 1). Chest computed tomography (CT) showed multifocal ground-glass opacities in the bilateral upper lobes (Figure 2A). Mixed consolidation and ground-glass opacities were also noticed in the left lower lobe (LLL) (Figure 2B). No enlarged lymph nodes or metastasis to the liver or adrenal glands were found. The bone scan was negative for metastasis. Pulmonary function tests revealed neither obstructive nor restrictive defects. Cytological examination of the BAL fluid obtained from the LLL showed adenocarcinoma. Wedge resection by video-assisted thoracoscopic surgery (VATS) of the left upper lobe (LUL) and LLL was performed to obtain tissue biopsies for the genetic analysis of the epidermal growth factor receptor (EGFR) mutation.

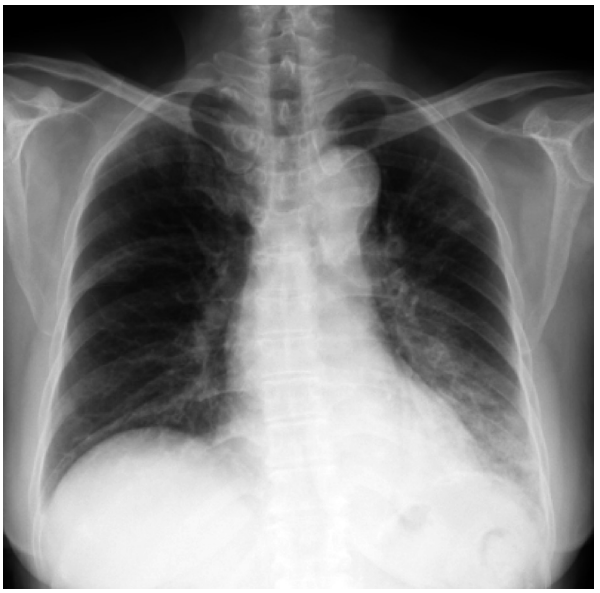

**Fig. 1.** Chest radiograph showing multifocal ill-defined opacities in both lungs and consolidation in the LLL field.

Pathological examination of specimens from both the LUL and LLL showed micropapillary components-predominant invasive adenocarcinoma. Only minor (<5%) foci of lepidic growth and mucinous differentiation were present. Immunohistochemistry stains were positive for TTF-1 and napsin A. Lymphatic and vascular invasion were absent, but aerogenous spread was present (Figure 3). The remaining non-neoplastic lung tissue showed marked inflammation and fibrosis. The endothelial growth factor receptor (EGFR) mutation study revealed the presence of polymorphism at codon 787 in exon 20; the EGFR mutation was negative. The patient unfortunately had septic shock during the postoperative hospital course and died.

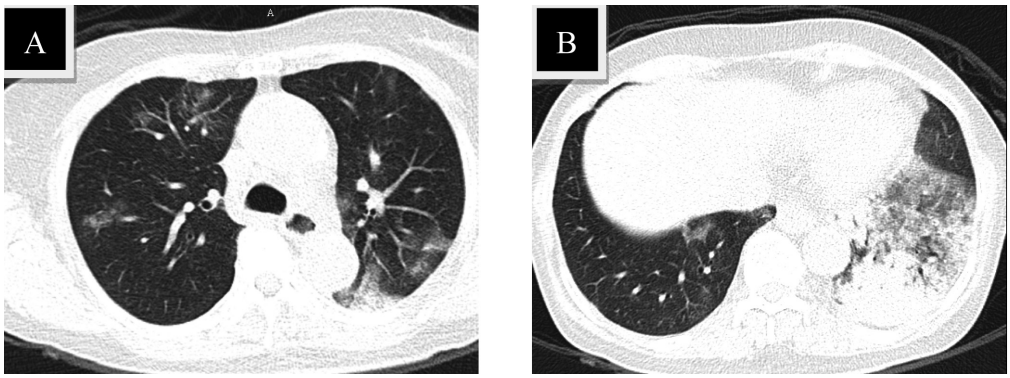


**Fig. 2.** (A) Chest CT showing multifocal ground glass opacity in the bilateral upper lobes. (B) Mixed consolidation and ground glass opacity is seen in the LLL.

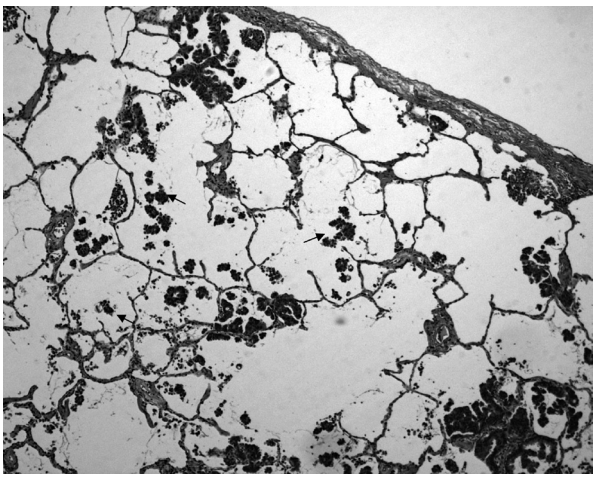

**Fig. 3.** Micropapillary-predominant adenocarcinoma with notable aerogenous spread, characterized by floating tumor cells (arrows) within the alveolar spaces.

## Discussion

The term of "micropapillary adenocarcinoma" of the lung was proposed as early as 2002 [9] and did not receive much attention, but it has been widely discussed with regard to breast, colon, ovarian and bladder cancers. Articles subsequently discussing micropapillary adenocarcinoma of the lung mentioned the possibility of metastasis. "Micropapillary adenocarcinoma of the lung" was formally proposed in 2011 by Travis and colleagues [1]. Micropapillary-predominant adenocarcinoma was further classified into an aerogenous micropapillary component (AMPC; tumor cells floating within alveolar spaces; aerogenous spread) and a stromal invasive micropapillary component (SMPC; tumor cells invading fibrotic stroma) by Ohe and colleagues [4,10]. AMPC, which suggests that cancer metastasizes through the alveolar spaces, is more frequently seen than SMPC [4,11], which is significantly associated with pleural, lymphatic and vascular invasion and spread.

Aerogenous metastasis can occur by processes in which cancer cells first grow and spread on the basement membrane (BM), and subsequently detach from the BM and survive in an anchorage-independent manner in the alveolar space (aerogenous spread), a stage at which they could be detected by BAL [3]. This is followed by their re-attachment and growth on the BM at another site in the lung [5]. In invasive breast micropapillary adenocarcinoma, the tumor cells lose their cell polarity, a phenomenon that is also observed in micropapillary adenocarcinoma of the lung [6]. The loss of cell polarity facilitates cell detachment from the BM. Normally, when displaced from the

extracellular matrix, epithelial cells undergo apoptosis (anoikis) [5-6]. In neoplastic cells, the altered expression of cell-matrix adhesion molecules, integrins, integrin-associated signaling molecules or apoptosis regulators may lead to anoikis resistance [5,12]. Animal models showed that cells with laminin-5 (LN5) overexpression exhibited resistance to anoikis and activation of the EGFR by overexpressing the LN5-integrin-FAK (focal adhesion kinase) signaling pathway [5]. Neutrophils also facilitated the aerogenous spread by secreting soluble mediators and by direct cell-to-cell contact with epithelial cells [3]. K-Ras activation in lung adenocarcinoma induces IL-8 secretion, eliciting a local inflammatory reaction with neutrophils, which is critical for neovascularization and sustained tumor growth [2-3,6]. Neoplastic cells also express more VEGF than normal cells, and alveolar capillaries express more proliferating cell nuclear antigen (PCNA). The lumina of alveolar capillaries are distended like venules, and certain intercellular junctions remain open with fenestrations. Capillary sprouting then occurs [7]. Therefore, aerogenous spread suggests further vascular invasion and multifocal intrapulmonary metastases, even without nodal involvement [3,7].

In our case, adenocarcinoma was found in the BAL fluid and chest CT showed multifocal peripheral tumors (lung-to-lung metastasis) without nodal involvement. The pathological examination showed invasive adenocarcinoma with micropapillary components-predominant without pleural, nodal or vascular involvement, and notable aerogenous spread in the alveolar space. The non-neoplastic lung tissue showed marked inflammation. All these findings were compatible with the above-mentioned findings characteristic of aerogenous spread.

## Summary

Aerogenous spread plays a crucial role in the “air metastases” of micropapillary invasive adenocarcinoma, causing multifocal tumors and advanced-stage disease without lymph node metastases. This possibility was suggested by the malignant cytology of the BAL. The mechanism includes intercellular and cell-matrix interaction, a neutrophil-mediated process and subsequent signaling cascades. Therefore, aerogenous spread suggests a more advanced stage of the disease or predicts the possibility of relapse after surgical resection.

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# 微乳突型侵襲性肺腺癌的氣行性散佈之病例報告

施慧瑄　龔昱中　曾岐元*　彭明仁

肺腺癌中微乳突型病理分類具有兩種成份：氣行性散佈或基質侵襲，其中氣行性散佈較基質侵襲性分類為多。氣行性散佈定義為肺泡空間中看到癌細胞漂浮在其中，而沒有基質的侵襲。這顯示癌細胞經由肺泡空間以細胞與細胞、細胞與基質之間的交互作用、嗜中性白血球中介之過程以及後續的訊息傳遞而導致的擴散。臨床上的表現是多發性的肺內擴散、癌細胞因脫落而可在氣道灌洗液中發現，以及在非癌肺組織中可看見發炎的現象。因此氣行性散佈的發現顯示較差的預後。

我們提出一位 T4N0M1a 第四期肺腺癌的 68 歲女性，具有多發性的肺轉移。切除下來的組織病理顯示微乳突型侵襲性肺腺癌且具有氣行性散佈。而非癌肺組織中則顯示顯著的發炎及壞死現象。*(胸腔醫學* ***2013; 28: 209-214)***

關鍵詞：氣行性散佈，微乳突型成份，侵襲性腺癌

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# *Fusobacterium nucleatum* Infection Manifesting as Simultaneous Psoas Muscle and Lung Abscesses: Report of a Case

Han-Sheng Huang, Gwan-Han Shen, Jeng-Yuan Hsu

Lung abscess is usually initiated by aspiration pneumonia and results from necrosis of pulmonary parenchyma. The most commonly aspirated pathogens are anaerobes from the oropharyngeal cavity. However, the bacteriology of community-acquired lung abscess (CALA) is different in present-day Taiwan. *Klebsiella pneumoniae* is now the most commonly isolated pathogen in CALA. We reported a 59-year-old man who had an initial presentation of back pain for 6 months. A rapidly growing lung abscess within 3 days and a psoas muscle abscess were revealed on chest X-ray and abdominal computed tomography (CT) scan. The lung aspirate culture yielded *Fusobacterium nucleatum*, corresponding to the patient's history of periodontitis, but this pathogen is not commonly seen in psoas muscle abscess. The patient did not have an impaired swallowing mechanical defect or immunocompromised status. Empirical treatment with intravenous Flomoxef was used initially, and then intravenous amoxicillin/clavulanic acid was started based on the drug sensitivity test. The follow-up chest X-ray and chest CT scan revealed improvements in the lung and psoas muscle abscesses during hospitalization. The patient was prescribed a course of oral amoxicillin/clavulanic acid and was discharged home. The lung abscess had resolved completely on chest X-ray when the patient visited the hospital outpatient department. ***(Thorac Med 2013; 28: 215-221)***

Key words: lung abscess, psoas muscle abscess, anaerobes, periodontitis, *Fusobacterium nucleatum*

## Introduction

Lung abscess is a process involving necrosis of pulmonary parenchyma and cavity lesion formation. Primary lung abscess is typically initiated by aspiration pneumonia caused by anaerobic pathogens from the upper respiratory tract or oropharyngeal cavity [1]. Most subjects with lung abscess are immunocompromised or have a mechanical defect associated with alcoholism, drug abuse or dysphagia. Anaerobic species, the most common of which are *Peptostreptococcus*, *Fusobacterium* species, and *Prevotella*, are normally present in the gingival crevices [2-4]. Although the predominant organisms are anaerobic bacteria, other aerobic

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bacteria such as *Streptococci milleri*, *Staphylococcus aureus*, and *Klebsiella pneumoniae* may also cause monomicrobial or mixed lung abscess with anaerobes [4]. Herein, we report the case of a patient who did not have an impaired mechanical defect or immunocompromised status, but developed simultaneously psoas muscle and lung abscesses.

## Case Report

A 59-year-old man was an ex-smoker (2.5 PPD for 30 years) who had quit smoking for 3 years. He reported a daily alcohol intake of 3 glasses of sorghum liquor for 15 years. He appeared otherwise healthy and denied major systemic disease, but had a history of periodontitis. He had noticed progressive low back pain for 6 months. Poor appetite and body weight loss of about 10 kg then developed over the most recent 6 weeks. He came to the hospital outpatient department and chest X-ray (CXR) was taken (Figure 1). The initial CXR did not show an active lung lesion. Chest sonography revealed no pleural effusion bilaterally. Three days later, he came to the emergency room with the chief complaint of fever, productive cough, and right flank pain. The chest film showed a huge mass shadow with air bubbles (Figure 2). Abdominal computed tomography (CT) revealed right lower lobe (RLL) lung abscess around 10.6 × 7 × 2.3 cm in size and right psoas muscle abscess from the T12 to the L2 level, around 3.1 × 4.5 cm in diameter (Figure 3).

Hematological findings were as follows: white blood cell count 15700/ul with a differential of 85.2% neutrophils, 6.9% lymphocytes and 6.2% monocytes, hemoglobin of 10.8 g/dL, and a platelet count of 529000/ul. Plasma biochemistry values were as follows: sodium 135 mEq/l; potassium 4.1 mEq/l; blood urine nitrogen 17 mg/dl; creatinine 1.1 mg/dl; alanine

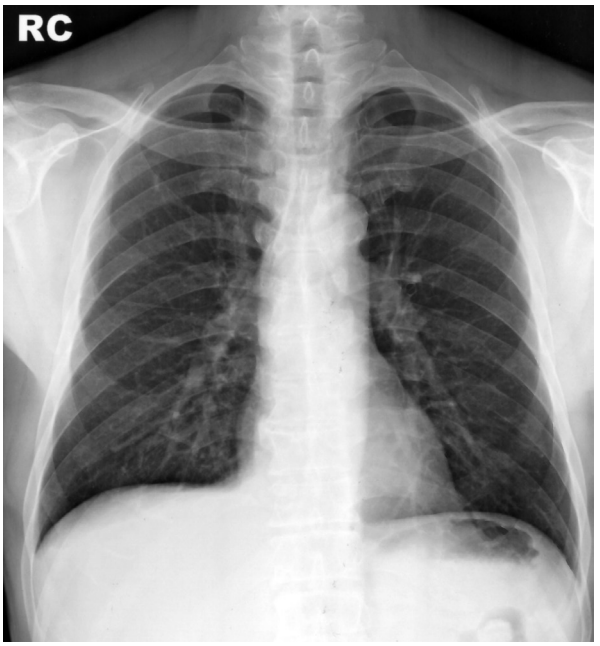


**Fig. 1.** The initial CXR film (3 days before admission)

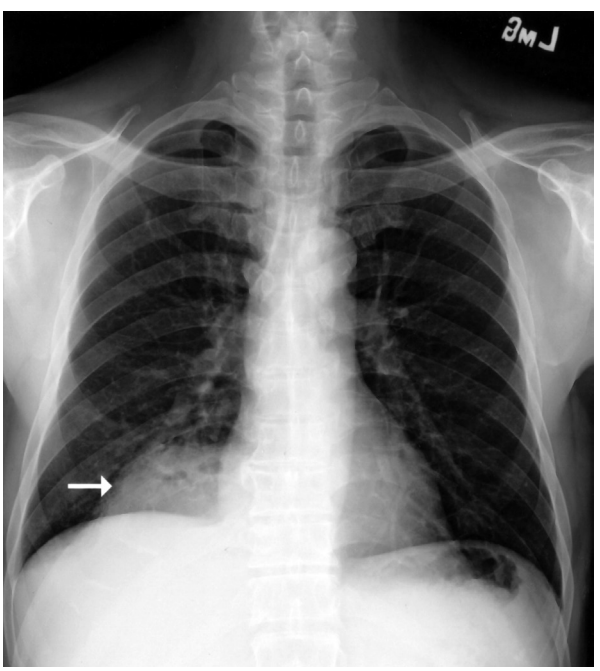

**Fig. 2.** CXR film showing a huge ground glass shadow with an air bubble (arrow) on the 1st day of admission

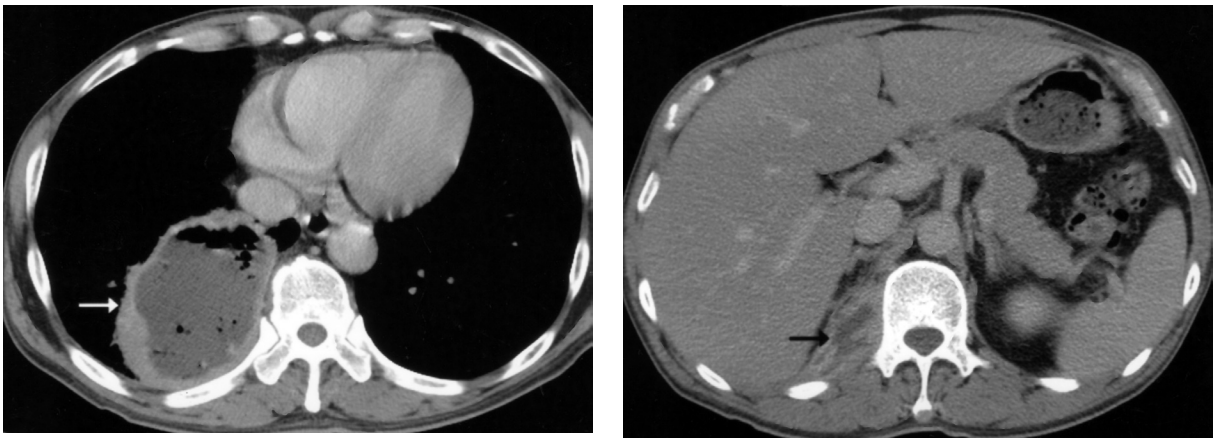

**Fig. 3.** Abdominal CT showing RLL lung abscess (white arrow) and right psoas muscle abscess (black arrow) on the 1st day of admission

aminotransferase 34 U/l; lactate dehydrogenase 104 U/l; C-reactive protein 22.52 mg/dl and lactate 8.1 mg/dL.

Lung aspiration yielded a pus-like, malodorous fluid. Empiric antibiotic treatment with Flomoxef 2g iv Q8H was administered for 7 days. The sputum Gram stain showed few Gram-negative bacilli and culture showed normal mixed flora. The blood culture, sputum fungal culture, sputum acid-fast stain, and serum latex test for *Cryptococcus* antigen were all negative. Culture of the lung aspiration yielded *Fusobacterium nucleatum* which was later susceptible to beta-lactam/beta-lactamase inhibitor. No malignant cells, no fungi, and no *Mycobacterium* were found in the lung aspiration. The antibiotic treatment was shifted to amoxicillin/clavulanic acid 1.2g iv q8h for 14 days. During antibiotic treatment, the C-reactive protein and leukocytosis with a left shift improved gradually. The CXR revealed cavity formation with an air-fluid level on the 5$^{th}$ day (Figure 4). Chest CT scan revealed improvements in resolution of the lung abscess and psoas muscle abscess on the 25$^{th}$ day (Figure 5). The patient was discharged with a prescription for oral amoxicillin/clavulanic acid 1g po Q12H.

## Discussion

The bacterial etiology of community-acquired lung abscess (CALA) has changed in Taiwan in recent years. Currently, *Klebsiella pneumoniae* is the most commonly isolated pathogen in CALA, followed by *Streptococci milleri* and then *Peptostreptococcus* [5]. Of the anaerobes, *Peptostreptococcus*, *Prevotella*, and *Bacteroides* are predominant [5]. In psoas muscle abscess, *Staphylococcus aureus* is the most common pathogen, followed by *Escherichia coli* [6]. In Taiwan, *Klebsiella pneumoniae* has also became an important pathogen in psoas muscle abscess, especially in immunocompromised cases such as those with diabetes mellitus or undergoing renal replacement therapy [7].

Combined pulmonary and psoas muscle nocardiosis was reported in a patient with lupus nephritis under prednisolone treatment [8]. The main predisposing factor of nocardiosis infection is an immunocompromised status. Combined pulmonary or miliary tuberculosis with tuberculous spondylitis and psoas abscess

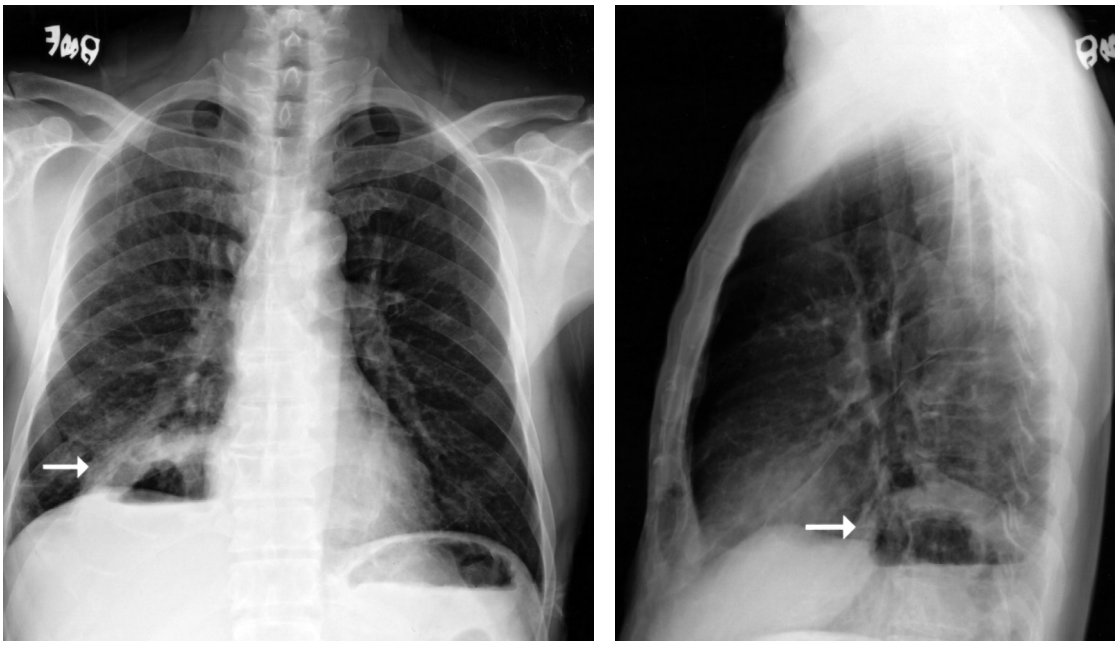

**Fig. 4.** CXR film showing a cavity lesion with an air-fluid level (arrow) on the 5th day of admission

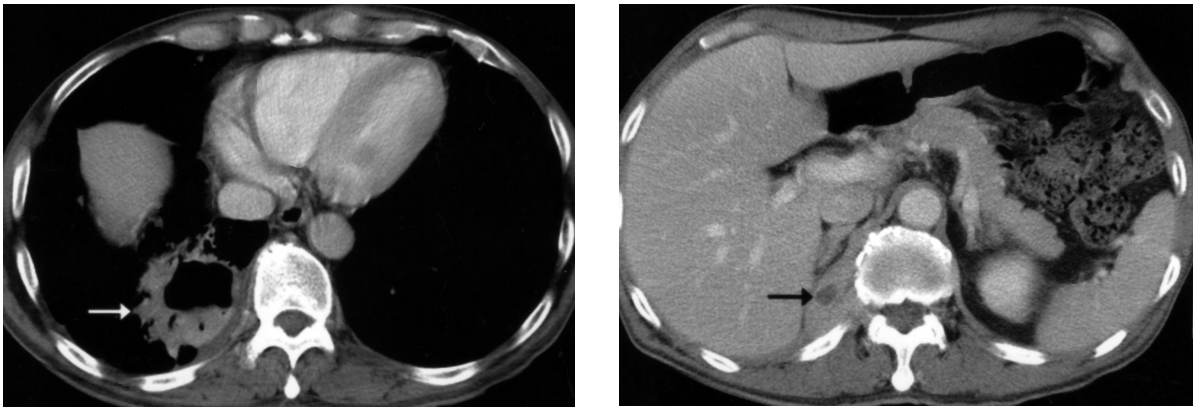

**Fig. 5.** Chest CT showing improvements in RLL lung abscess (white arrow) and right psoas muscle abscess (black arrow) 25 days later

[8-10], and, primary psoas muscle abscess due to *Fusobacterium nucleatum* have also been reported [11-12]. However, to the best of the authors' knowledge, the present case study is the first to report a combined lung abscess and psoas muscle abscess with monomicrobial *Fusobacterium nucleatum*.

The insidious onset and occult features of psoas muscle abscess usually delay its diagnosis and facilitate complications, such as septic shock or deep vein thrombosis [13]. Up to 76% of cases have localized and/or radiating pain [14]. Therefore, in lung abscess patients with an immunocompromised status and back or flank pain, it is prudent to exclude psoas muscle abscess by CT [15].

Necrotizing pneumonia and lung abscess occur 8-14 days after the initial aspiration event [1]. Jugular vein suppurative thrombophlebitis, bacteremia with *Fusobacterium* species, and septic emboli may also result in lung abscess. A purely anaerobic lung abscess is more likely to have a subacute or chronic presentation (with >30 days of presenting symptoms before diagnosis) than aerobic or mixed lung abscess (72% vs. 43%) [5]. Anaerobes are slow-growing and may be present in mixed culture with more rapidly growing aerobic bacteria.

*Fusobacterium nucleatum* is an anaerobic, non-spore-forming Gram-negative bacillus. The most common entry sources for *Fusobacterium nucleatum* are the lower respiratory tract, gastrointestinal tract, genitourinary tract, skin and soft tissue [16]. In 1 study, respiratory tract infection was the predominant identified source, especially for pneumonia, followed by intra-abdominal sites [17]. Jugular vein thrombophlebitis, bacteremia and septic emboli might induce disseminated *Fusobacterium* infection. Pneumonia has been shown to have high rates of respiratory failure (88.2%) and mortality (64.7%). Meanwhile, bacteremia has been associated with high mortality (41.5%), especially in patients with renal insufficiency, heart failure, or malignancy [18].

Species of *Fusobacteria* are reported to be capable of producing β-lactamases with an incidence rate of up to 41.1% [19]. *Fusobacterium nucleatum* is the most common species of *Fusobacteria*. Anaerobes from lung abscess have shown an increase in resistance rates to penicillin (15%) and clindamycin (5%) in Taiwan [5]. But monotherapy with clindamycin as empirical treatment for lung abscess is unsuitable because of the high rate of resistance of *Streptococci milleri* to clindamycin (20%) and the lack of activity against Gram-negative bacilli [5]. A β-lactam/β-lactamase inhibitor or 2$^{nd}$ to 3$^{rd}$-generation cephalosporin plus clindamycin or metronidazole as empirical therapy for lung abscess is recommended.

In this case, we used Flomoxef, a broad-spectrum 3$^{rd}$-generation cephalosporin that covers anaerobes, Gram-positive cocci, and Gram-negative bacilli, including extended-spectrum beta-lactamase (ESBL)-producing species. Then we shifted the antibiotics to amoxicillin/clavulanic acid based on a drug sensitivity test of lung aspirate and as an empirical therapy for psoas muscle abscess. Effective treatment for psoas muscle abscess should include appropriate antibiotic therapy and drainage of the abscess. However, successful treatment with antibiotics alone has also been reported [14,20-21]. Abscesses smaller than 3 cm in size may be treated with antibiotics alone; surgery can be reserved for complicated recurrences [20].

In conclusion, we demonstrated the presence of *Fusobacterium nucleatum*, an anaerobic pathogen, simultaneously in lung abscess and psoas muscle abscess. Periodontal disease is a risk factor for anaerobic lung abscess. Immunocompromised status may have been the underlying cause of both the lung abscess and psoas muscle abscess in the reported patient. β-lactam/β-lactamase inhibitor or 2$^{nd}$ to 3$^{rd}$-generation cephalosporin plus clindamycin or metronidazole is recommended for treatment of combined lung and psoas muscle abscesses caused by *Fusobacterium nucleatum*.

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# 腰肌膿瘍合併快速生長的梭桿菌肺膿瘍－病例報告

黃漢笙　沈光漢　許正園

肺膿瘍通常起因於吸入性肺炎後導致肺實質壞死。口咽部厭氧菌是最常見的吸入性病原菌，然而在台灣，社區感染的肺膿瘍其細菌種類並不相同，克雷伯氏肺炎桿菌已成為最常見的細菌。我們報導一個59歲男性一開始以下背痛六個月為表現，胸腔X光和腹部電腦斷層顯示三日內快速擴大的肺膿瘍和腰肌膿瘍。肺部抽吸培養結果為具核梭桿菌，符合病人牙周病的病史，但並非腰肌膿瘍常見的病原菌。此病人並無機械性吞嚥缺陷或免疫功能不全的情況。我們一開始使用靜脈注射Flomoxef作為經驗性抗生素，並依據藥敏試驗以靜脈注射Amoxicillin/Clavulanic acid接替使用。以胸腔X光和胸腔電腦斷層追蹤，顯示肺膿瘍和腰肌膿瘍皆有改善，病人於開立口服Amoxicillin/Clavulanic acid後出院繼續藥物治療，門診胸腔X光追蹤顯示肺膿瘍完全消退。*( 胸腔醫學 **2013; 28: 215-221**)*

關鍵詞：肺膿瘍，腰肌膿瘍，厭氧菌，牙周病，具核梭桿菌

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# A Case of Disseminated (3 organs) and Complicated Tuberculosis Infection with Multiple Endocrine Disturbances

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We reported the case of a 22-year-old female presenting with disseminated and complicated tuberculosis (TB) infection with multiple endocrine disturbances. The patient had miliary pulmonary TB, TB meningitis with tuberculoma, and tuberculous enteritis. She also had multiple endocrine disturbances, including hypothyroidism, hypogonadism, and growth hormone deficiency. After 5 months of thyroxin supplement, all the endocrine disturbances, especially of the thyroid, had returned to normal under effective anti-tuberculous drug treatment. To now the best of our knowledge, there has been no published report such as ours of a case of disseminated and complicated TB with endocrine disturbances. ***(Thorac Med 2013; 28: 222-227)***

Key words: disseminated tuberculosis, hypogonadism, hypothyroidism, hypopituitarism

## Introduction

According to the statistical data of the Centers for Disease Control in Taiwan, 12,589 people were infected with mycobacterium tuberculosis (TB) in 2011. In the United States, extrapulmonary TB accounts for roughly 15% of TB cases among immunocompetent hosts [1], and in Taiwan, cases of new extrapulmonary TB amounted to around 4% of all TB cases in 2009 [2]. Lymphatic TB was the most common of the extrapulmonary TB cases, followed by bone and joint TB; involvement of the endocrine system was very rare [3]. In the published literature, involvement of the hypothalamopituitary axis, in the form of TB meningitis, is also uncommon, and is 1 of the most severe forms of extrapulmonary TB, resulting in high morbidity and mortality [4].

We report a rare case of disseminated TB complicated with multiple organ involvement, including the lung, brain, and intestine. Acute respiratory distress syndrome (ARDS) developed 3 days after hospitalization, although TB is a rare cause of ARDS [5]. There were also multiple endocrine disturbances, including hypothy-

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roidism, hypogonadism, and growth hormone deficiency. After successful anti-tuberculous treatment, the multiple endocrine disturbances returned to normal. To the best of our knowledge, this is the first published case of diffuse TB infection with multiple endocrine dysfunctions.

## Case Report

This 22-year-old female had no history of systemic medical problems. Her body height was 162 cm, and body weight was 42.9 kg. She had experienced chill/fever, lethargy, and general weakness for several weeks, and went to local medical doctors who diagnosed her as having upper respiratory tract infection. With progression of the symptoms, she was sent to our emergency department, where she reported burst headaches and lethargy. The brain MRI revealed multiple small, target-like enhancing nodules (Figure 1). The chest X-ray (CXR) also revealed diffuse and tinny lung lesions, compatible with miliary TB (Figure 2). The chest CT also revealed diffuse peribronchial infiltration, a tree-in-bud appearance and patchy consolidations in the bilateral lungs (Figure 3). She was then given anti-tuberculous drugs, including isoniazid, rifampicin, pyrazinamide, and ethambutol, and was admitted to the intensive care unit under the impression of disseminated TB infection.

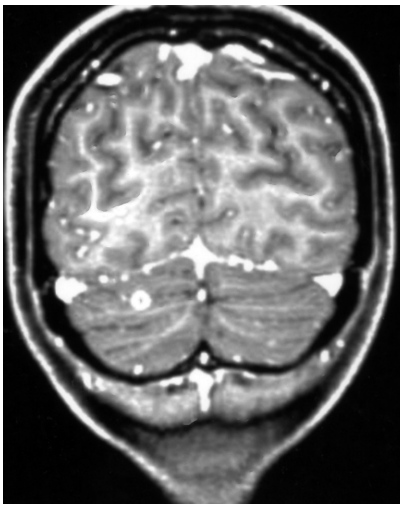

**Fig. 1.** Brain MRI revealed multiple small, target-like enhancing nodules.

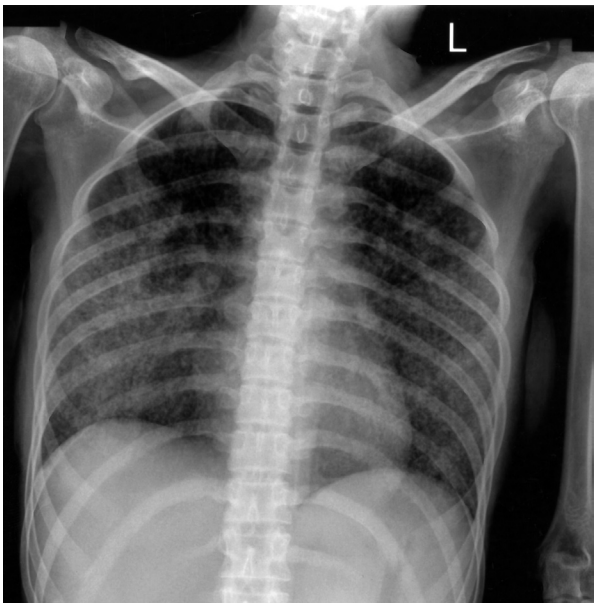


**Fig. 2.** CXR revealed diffuse tiny nodules in the bilateral lung fields (the 1st admission day).

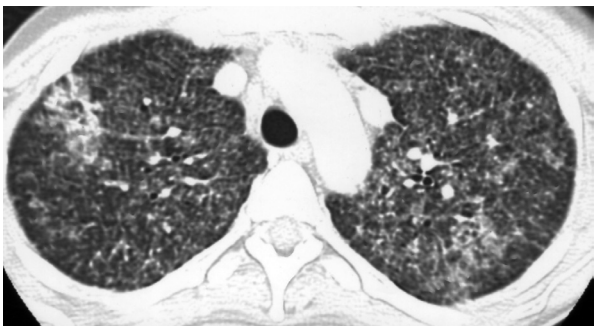

**Fig. 3.** Chest CT also revealed diffuse peribronchial infiltration, a tree-in-bud appearance, and patchy consolidations in bilateral lungs.

She received a lumbar puncture with low glucose and elevated protein levels in the cere-

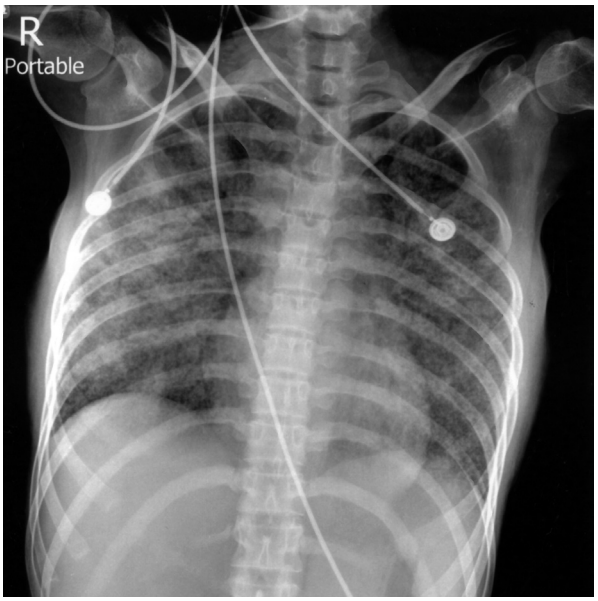


**Fig. 4.** CXR revealed diffuse tiny nodules and infiltration in the bilateral lung fields (the 2nd admission day).

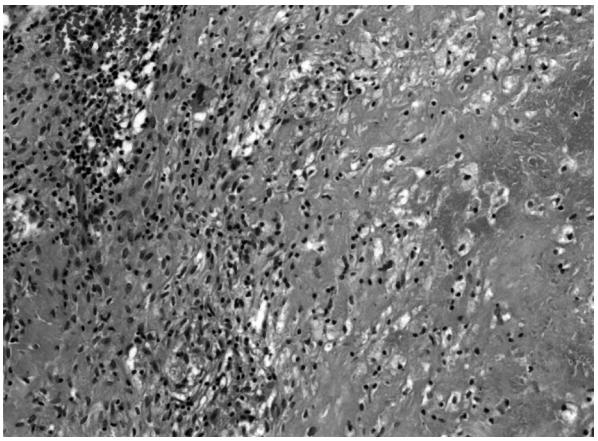

**Fig. 5.** Caseating granulomatous inflammation in the small intestine serosa.

brospinal fluid (CSF) and a positive TB polymerase chain reaction (PCR) finding. Under the impression of TB meningitis, dexamethasone (5 mg) 1 amp ivd q6h was thus prescribed for 8 days. Three days later, she developed ARDS (Figure 4). The sputum acid-fast bacilli stain was positive, and the acid-fast bacilli culture of sputum later revealed mycobacterium TB and was sensitive to all anti-tuberculous drugs. Due to disease severity, streptomycin and moxifloxacin were later added to the anti-tuberculous treatment. After endotracheal tube extubation and successful general medical control, she was transferred to a general isolation ward.

On the 21st admission day, she developed intestinal obstruction, and on the 28th day, underwent exploratory laparotomy with operative findings of severe adhesion status post-adhesiolysis and decompression. The pathology report of the small intestine serosa was fibrous adhesion band with caseating granulomatous inflammation (Figure 5). The TB PCR test of ascites was positive.

On 47th admission day, the CXR incidentally revealed right pneumothorax (Figure 6), which was poorly resolved, so she accepted video-assisted thoracoscopic surgery (VATS) 2 weeks later. After she had attained a stable condition,

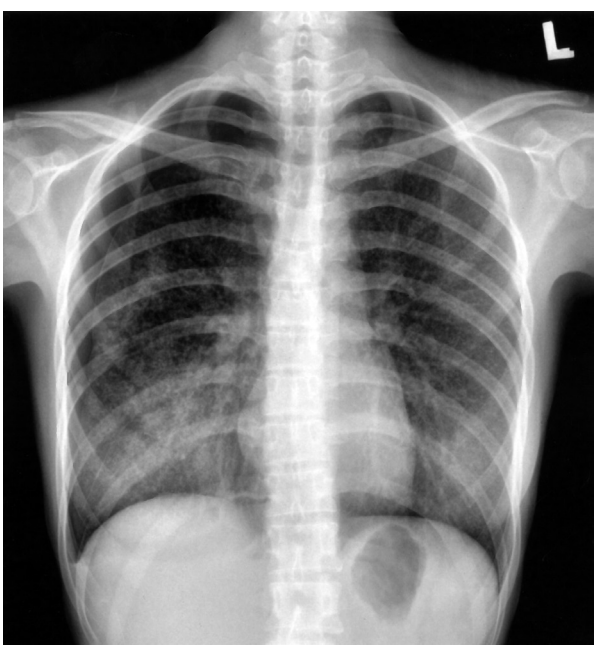


**Fig. 6.** CXR revealed right pneumothorax (the 47th admission day).

she was discharged with outpatient department follow-up.

During admission, she presented a series of endocrine problems, as follows:

***Hypothyroidism***

The TSH was 0.491 uIU/ml (normal range: 0.27~4.20), free T4 was 0.741 ng/dl (normal range: 0.93~1.71), and triiodothyronine (T3) was 84.05 ng/dl (normal range: 70~200), so central hypothyroidism was diagnosed, but she did not accept a thyroxin supplement for 3 months. The following TSH was 1.74 uIU/ml, free T4 was 0.765 ng/dl, and T3 was 130.6 ng/dl, so she then accepted thyroxine 0.05 mg po qd for 3 months following 0.1 mg qd po for 2 months. After cessation of thyroxine, the follow-up free T4 and TSH levels were within a normal range.

***Hypogonadism***

No menstruation had occurred for months, so she underwent a series of studies. In the mid-follicular phase, the follicle-stimulating hormone (FSH) level was 6.88 mIU/ml (normal range: 3.85~8.78), the luteinizing hormone (LH) level was 1.00 mIU/ml (normal range: 2.12~10.89), and the estrodiol level was less than 20 pg/ml (normal range: 27~122). Central hypogonadism was then diagnosed. She received 7 days of medroxyprogesterone and estradiol for the missed menstrual periods, but with little effect. After effective anti-TB treatment for 6 months, normal menstruation returned.

***Growth hormone deficiency***

The insulin-like growth factor 1 (IGF-1) level was 96.1 ng/ml (normal range: 116~358), but growth hormone therapy was not added. Two months later, after effective TB treatment, the IGF1 level returned to 369 ng/ml.

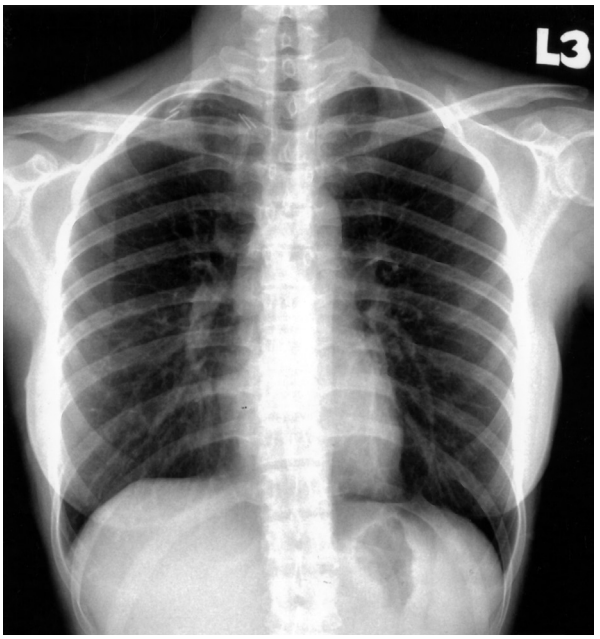


**Fig. 7.** CXR after anti-TB treatment revealed much improvement (the 11th month).

The clinical picture and CXR (Figure 7) showed much improvement after the successful treatment.

## Discussion

In Taiwan, the mortality rate of patients with active pulmonary TB requiring mechanical ventilation is very high [6]. According to the Science Citation Index (SCI) of published papers till now, the most commonly involved endocrine organ in TB is the adrenal gland [7]. This is the first reported case of disseminated and complicated TB infection with multiple endocrine system disturbances. Hypothalamic pituitary axis dysfunction, including hypothyroidism, hypogonadism, and growth hormone deficiency, was suspected to be central nervous system (CNS)-related TB infection. Thus the treatment was focused on the underlying

disease [8-9]. It was not surprising that the hypothalamic-pituitary axis dysfunction of the patient fully recovered after effective anti-TB treatment.

Hypomenorrhea and amenorrhea in patients with pulmonary TB may result from dysfunction of the CNS, premature ovarian failure, or organic lesions in the uterine endometrium. Amenorrhea due to TB is caused mostly by a functional or organic disorder in the hypothalamic-pituitary-ovarian axis [8-9]. As for growth hormone deficiency, the indication is mainly focused on Turner's syndrome, idiopathic short stature, and other factors [10], so growth hormone was not given to the patient during hospitalization.

The case number of patients with disseminated TB with multiple organ involvement is very low. We may perform an endocrine study under clinical suspicion, especially when the CNS is involved. If the patient receives treatment as soon as possible, there may still be a good prognosis.

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# 瀰漫性結核病感染併發多重內分泌失調－病例報告

林百揚　林俊佃*　余明治　白冠壬　林賢君　張哲華

我們報告一名22歲女姓同時有瀰漫性結核菌感染併發多重內分泌失調的病例。病人有粟粒性肺結核、結核性腦膜炎及結核腫、以及腸結核。病人同時有多重內分泌失調，包含甲狀腺功能低下，性腺功能低下，以及生長激素不足。在投與有效的抗結核病藥物的治療以及5個月甲狀腺素補充後，所有內分泌失調的問題，特別是甲狀腺功能都已回復到正常的範圍。在目前已發表的病例報告中，並沒有關於瀰漫性結核菌感染併發多重內分泌失調的病例，本篇論文係首篇探討此類案例之文獻。*( 胸腔醫學 **2013; 28: 222-227**)*

關鍵詞：瀰漫性結核病，性腺功能低下，甲狀腺功能低下，腦下腺功能低下

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# *Mycobacterium tuberculosis* Complicated with Acute Respiratory Distress Syndrome – A Case Report

Yu-Mu Chen*, Hsu-Ching Kao*, Po-An Chou*, Wen-Feng Fang*,
Chin-Chou Wang*,**, Chia-Cheng Tseng*

Tuberculosis (TB) that is caused by *M. tuberculosis* complex accounts for approximately 2.5% of all deaths in the world. The TB infection rate has increased as well with the rapid growth of the human immunodeficiency virus (HIV)-infected population in HIV endemic areas. The mortality rate of patients with TB-related acute respiratory distress syndrome (ARDS) ranges from 33% to 100%, which is higher than the ARDS mortality rate due to other causes. Early recognition and prescription of anti-TB medication is very difficult, which also explains the higher mortality rate of TB -related ARDS.

Herein, we reported a 60-year-old man who presented with non-responding community-acquired pneumonia. The final diagnosis was TB-related ARDS, which was confirmed by clinical evidence and positive TB polymerase chain reaction (PCR) testing. A literature review is also included. ***(Thorac Med 2013; 28: 228-234)***

Key words: pulmonary tuberculosis, acute respiratory distress syndrome (ARDS), polymerase chain reaction

## Introduction

Tuberculosis (TB) is caused by *Mycobacterium tuberculosis* (*M. tuberculosis*) complex infection. It is an important infectious disease associated with high mortality and morbidity, and accounts for 2.5% of all deaths in the world [1]. In TB endemic areas, *M. tuberculosis* accounted for about 2% of community-acquired pneumonia (CAP), but is easily misdiagnosed [2]. The TB infection rate has increased as well with the rapid growth of the human immunodeficiency virus (HIV)-infected population in HIV endemic areas [3].

Acute respiratory distress syndrome (ARDS) is a common disorder in critical care medicine. It is characterized by non-cardiogenic pulmonary edema, lung inflammation, hypoxemia, and decreased lung compliance, and is associated with high mortality and morbidity. The common etiologies include sepsis, aspiration of gastric contents, and multiple blood trans-

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fusions (>15 units/24 hr in 1 study) [1]. Most patients with TB infection have insidious onset symptoms, but ARDS as an initial presentation is a rare circumstance in previous case reports [4].

## Case Report

A 60-year-old male farmer with a history of type II diabetes mellitus suffered from intermittent fever up to 39°C for 10 days. The fever was associated with cough, scanty sputum and mild exertional dyspnea. The patient denied dysuria, a travel history, or a recent animal contact history. When the patient was admitted to the emergency department on 06 Jan 2011, the laboratory data showed no leukocytosis (WBC: 7.5 $10^3$/uL), but neutrophils were predominant in the differential count (segments: 91%). Biochemistry tests revealed normal renal function and a normal brain natriuretic peptide (BNP) level. Liver function impairment (AST: 131 U/L ALT: 60 U/L) and elevated procalcitonin (1.98 ng/mL) were noted. Chest radiographs revealed bilateral lung field infiltration with right costophrenic angle blunting (Figure 1), with consolidation and an interstitial pattern. Urinalysis results were within the normal range.

Moxifloxacin was administrated initially due to a suspicion of CAP. The antibiotic was shifted to imipenem combined with clarithromycin 48 hours later because of deterioration. The patient's sputum samples were sent for common aerobic culture and acid-fast bacillus stain. Nasal swab was also performed for possible influenza infection. Urine Legionella antigen (Ag), serum Cryptococcus Ag, and mycoplasma antibodies were also evaluated but all showed negative findings.

However, the patient was intubated on day 6 after admission for acute respiratory failure and ARDS status ($PaO_2/FiO_2$: 54). CXR revealed progression of the consolidation (Fig-

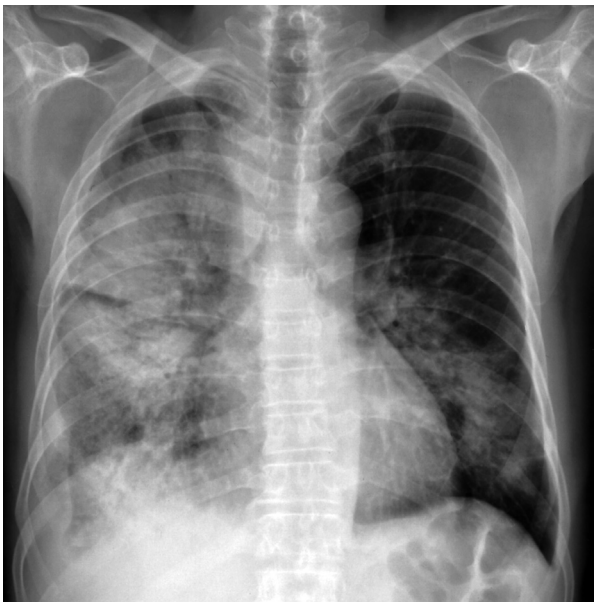

**Fig. 1.** The initial chest X-ray obtained on 06 Jan 2011 revealed bilateral lung consolidation.

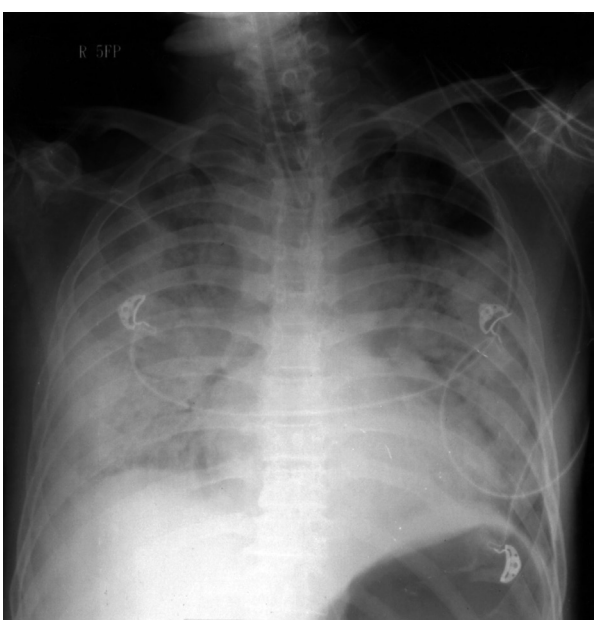

**Fig. 2.** Follow-up chest X-ray revealed progression of the bilateral lung consolidation.

ure 2). Chest computed tomography disclosed bilateral diffuse lung consolidation (Figure 3). Bronchoscopy revealed no endobronchial lesion, but some purulent secretion. Bronchial washing was performed from the right upper lobe and yielded a negative acid-fast stain result but a positive TB-polymerase chain reaction (PCR) finding. First-line anti-TB medication, with Rifater [rifampin (RMP) 120 mg, isoniazid (INH) 80 mg, and pyrazinamide 250 mg], 5 tablets and ethambutol 400 mg 3 tablets once daily, were then administrated since day 9 after admission. Hydrocortisone 300 mg per day and furosemide 120 mg per day in divided doses were also prescribed for ARDS. Although the AST level was elevated up to 3 times the upper limit before starting anti-TB medication, the patient had no symptoms of nausea, vomiting, or abdominal pain. He also denied a history of hepatitis B or C infection.

After appropriate anti-TB therapy, the chest radiograph (Figure 4) revealed rapid resolution and the patient was extubated on day 12 after admission. His liver function later improved. He was discharged on day 21, his respiratory condition was quite stable, and he was not in need of any respiratory support device. Positive culture with *M. tuberculosis* complex was confirmed 3 weeks later.

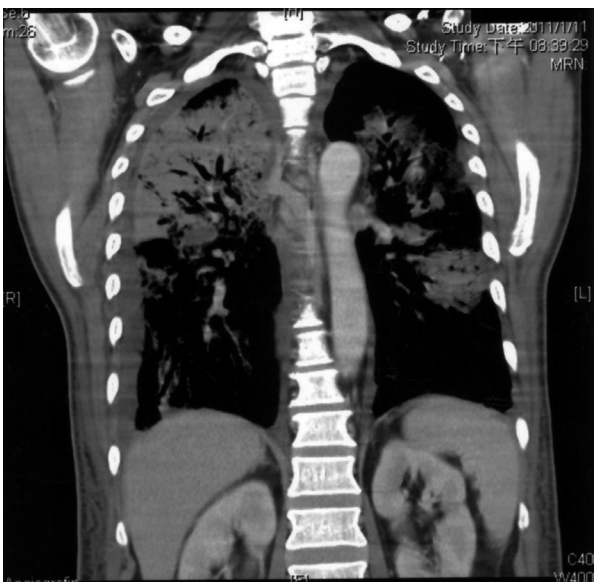


**Fig. 3.** Chest computed tomography revealed bilateral diffuse lung consolidation.

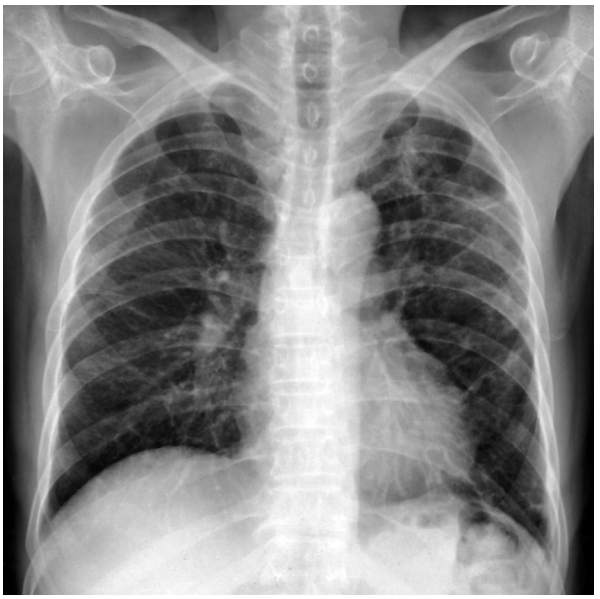

**Fig. 4.** CXR revealed much resolution of the lung consolidation after initiation of anti-TB therapies.

## Discussion

Identification of the primary cause of respiratory distress is vital for the initiation of appropriate therapy. Active pulmonary TB is a rare primary cause of ARDS and is associated with very high mortality [5]. TB occurs initially as an acute and rapidly progressive pneumonia. This is unusual because tubercle bacilli multiply only once every 18 to 24 hours as opposed to most pathogenic bacteria, which can multiply every 20 to 30 minutes. It is suggested that for this to occur, either a massive number of tubercle bacilli or, more likely tuberculoprotein

must be aspirated causing an acute exudative hypersensitivity reaction into new areas of the lung [6].

Acute tuberculous pneumonia is characterized by fever, productive cough, and high temperature with signs of severe toxicity and consolidation, the presence of large confluent dense shadows on chest X-ray film involving at least 1 lobe, and tubercle bacilli in the sputum [7]. The rapidly progressive course of acute tuberculous pneumonia can mimic that of bacterial pneumonia. However, the longer duration of symptoms before admission is the most important factor differentiating TB from other infectious etiologies [8]. In acute tuberculous pneumonia, symptoms are usually less than 1 month in duration [9].

ARDS is more common in miliary TB than in tuberculous bronchopneumonia, and also has a worse prognosis [10]. ARDS caused by miliary TB is associated with a high fatality rate [11]. The mortality rate in patients with pulmonary TB requiring mechanical ventilation is very high, with the presence of multiple organ failure and consolidation on chest radiograph [12].

Treatment has been considered to be an important factor affecting patient outcome [13-15]. Higher mortality is present in patients who do not receive optimal treatment with a triple combination that includes INH and RMP. Impaired liver function is a major reason to withdraw the INH and RMP, but other causes have also been described [16]. With anti-TB treatment, diffusing capacities may improve rapidly, and oxygenation may function well. Thus, mortality may be improved by resolving the ARDS status.

Early recognition and prescription of anti-TB medication is very difficult and is the reason why ARDS caused by TB has a higher mortality rate than ARDS due to other etiologies [17-20]. This patient was a non-responder to empirical therapies for CAP [21]. The possible reasons for the non-response to CAP therapies include unusual microbial etiologies that were not covered by the empirical therapeutic regimens. Based on previous research, *Pseudomona aeruginosa* causes about 10% of non-responding CAP cases [22]. Another study revealed that methicillin-resistant *Staphylococcus aureus* was the primary causative agent of non-responding CAP [23-24].

Other less common microorganisms responsible for non-responding CAP include mycobacteria, fungi, *Pneumocystis jirovecii*, *Nocardia*, and anaerobes that are not covered by antibiotics recommended in the CAP or HAP guidelines [25].

For non-responders to CAP treatment, it is important to completely reevaluate the history and physical examination, and review risk factors, environmental factors, professional factors and recent travel or animal contact histories [21]. Tests should be performed, such as chest X-ray, which can detect cavitation and effusion, antigen tests for detection of *Legionella pneumophila* and cytomegalovirus, and acid-fast stain for Mycobacterium spp. and Nocardia spp.

After the initial empirical antibiotics therapies had failed, our patient followed up with a chest radiograph that revealed bilateral pulmonary infiltration. As suggested in the study above, urine Legionella Ag, Cryptococcus Ag and sputum acid-fast stain were checked, but all revealed negative results. Bronchoscopy was arranged for further evaluation and revealed positive TB PCR results [26] and negative common aerobic and anaerobic cultures.

An interesting question is whether TB caused ARDS to occur in this patient or he was

just a man who had TB combined with ARDS due to another cause. Such a debate is reasonable since only 40-50% of CAP pathogens can be isolated under extensive diagnostic procedures [27-28]. The negative acid-fast stain results in both the sputum culture and bronchial washing of this patient meant he had a low burden of mycobacteria bacilli. Can such a low burden of mycobacteria bacilli cause TB-ARDS? In a previous study, the positive acid-fast stain rate was 44% in sputum and 48% in tracheal aspiration among TB-ARDS patients (4). With such a low burden of mycobacteria bacilli, the ARDS pattern caused by hypersensitivity reacted to tuberculoprotein rather than direct invasion by the *M. tuberculosis* organism (6). This may also be the reason why the patient improved so quickly. This patient had progressive disease even with 4 days of broad spectrum antibiotics [25,29-30], but achieved rapid improvement after taking anti-TB medication. Thus, TB was the most likely cause of this ARDS event.

## Conclusion

Identification of the primary cause of respiratory distress is vital for the initiation of appropriate therapy. Active pulmonary TB is a rare primary cause of ARDS and is associated with very high mortality. Acute pneumonia probably represents an exudative hypersensitivity reaction to tuberculoprotein, rather than actual inflammation caused by the *M. tuberculosis* organism. These infiltrates can appear within a matter of days and can clinically simulate acute bacterial pneumonia. TB should be considered in the differential diagnosis of acute pneumonic infiltrates with respiratory failure; rapid diagnosis and treatment may rescue the patient from possible mortality.

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# 社區型肺炎對經驗性抗生素無效－肺結核併發急性呼吸窘迫症候群個案報告

陳友木 * 高旭卿 * 周柏安 * 方文豐 * 王金洲 *,** 曾嘉成 *

肺結核是由結核桿菌感染所造成肺結核造成之急性呼吸窘迫症候群臨床上並不常見，也因為診斷上的困難，死亡率較其他原因造成之急性呼吸窘迫症候群高出許多。近年來由於愛滋病患者增加，肺結核感染個案節節上升，使的防疫工作更加困難。

我們提出的個案為一位中年男性表現為對經驗性療法無效之社區型肺炎。病人血液，痰液培養，肺炎雙球菌抗原，退伍軍人症肺炎抗原，新型隱球菌抗原，以及肺炎黴漿菌抗體試驗皆陰性。該病患之後演變為呼吸窘迫症候群併發呼吸衰竭，經由支氣管沖洗液中結核菌聚合酶連鎖反應陽性而確診為肺結核。且病人在給予肺結核藥物後得到臨床上的改善。*( 胸腔醫學 **2013; 28: 228-234**)*

關鍵詞：結核菌，急性呼吸窘迫症候群，聚合酶連鎖反應

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# Video-assisted Thoracoscopic Excision of Double Para-esophageal Bronchogenic Cysts, One Intramural and the Other Extramural: A Case Report

Ying-Yuan Chen, Wei-Li Huang, Yau-Lin Tseng

Bronchogenic cysts, which are congenital bronchopulmonary malformations, are frequently solitary and are located in the superior and middle mediastinum and in the lung parenchyma. Para-esophageal and especially intramural esophageal bronchogenic cysts are very rare. We report an unusual case of a middle-aged woman with double para-esophageal bronchogenic cysts: 1 was intramural and the other was extramural. Video-assisted thoracoscopic excision of both cysts was performed successfully and the patient was discharged after a very short duration of hospitalization. ***(Thorac Med 2013; 28: 235-240)***

Key words: bronchogenic cyst, esophageal, video-assisted thoracoscopic, surgery

## Introduction

Bronchogenic cysts result from abnormal budding of the primitive ventral foregut [1]. The most common locations of bronchogenic cysts are the mediastinum and lung parenchyma. Para-esophageal, and especially intramural bronchogenic cysts are rare; the majority of intramural cysts are esophageal or enterogenous cysts [2]. The tumor location and composition in imaging studies can assist in the differential diagnosis, but surgical resection is inevitably recommended for the definite diagnosis, symptom relief, and prevention of complications and malignant transformation [2-3]. Herein, we report the case of a middle-aged woman with double para-esophageal bronchogenic cysts who successfully underwent video-assisted thoracoscopic excision of both cysts.

## Case Report

The patient was a 51-year-old housewife with a normal health status who denied dysphagia, odynophagia or weight loss. At the time of the report, she had no history of smoking or drinking. A retrocardiac paraspinal mass, about 3 cm in size, was noted incidentally in routine chest radiography (Figure 1A). Chest computed tomography (CT) showed 2 ovoid, homogenously hypodense, mediastinal masses; 1 was about 3.8 × 2.6 cm at the T3-4 level, and

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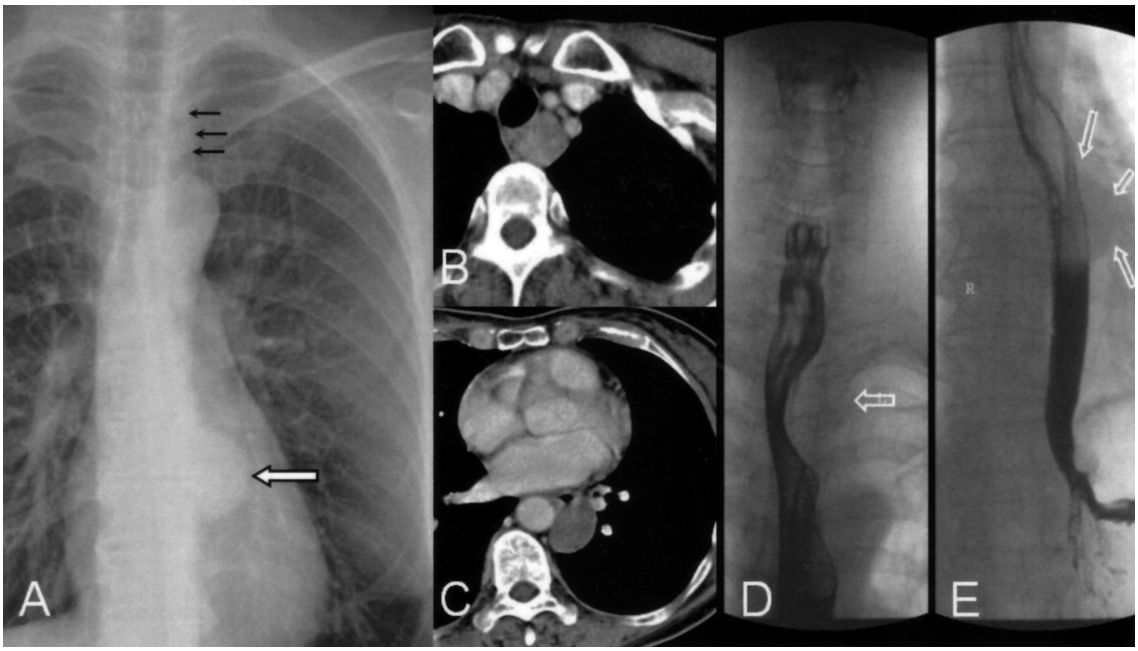


**Fig. 1.** Imaging studies of this case; A: Chest X-ray (PA view) showed 2 mediastinal tumors; 1 at the left upper mediastinum (black arrows) and the other at the left lower mediastinum (hollow arrow); B: CT showed an ovoid hypodense mediastinal mass to the left of the upper esophagus; C: CT showed an ovoid hypodense mediastinal mass posterior to the lower esophagus; D: Esophagography showed an external indentation of the esophagus at the T2-4 level (hollow arrow); E: Esophagography showed a paraesophageal mass superimposed on the lower esophagus at the T9 level (hollow arrows).

the other was 3.2 × 2.3 cm at the T9-T10 level (Figures 1B, 1C). Both masses were without contrast-enhancement, and the borders between the masses and esophagus were unclear. Esophagography showed that there was an extrinsic indentation at the T2-4 level, and a para-esophageal mass superimposed at the lower esophagus at the T9 level (Figures 1D, 1E). There was no communication between the masses and the esophagus. The differential diagnosis included enteric or bronchogenic cysts, leiomyoma, and gastrointestinal stromal tumor. There were no other notable findings in physical and laboratory examinations.

She underwent video-assisted thoracoscopic excision of the mediastinal masses through the left hemithorax. The upper mass was totally encompassed within the superior mediastinum above the aortic arch, but it was located outside the esophageal wall and was excised without interfering with the esophagus (Figure 2A). In contrast, the lower mass was an exophytic tumor protruding from the lower esophagus and originating beneath the muscular layer of the esophagus. This tumor was enucleated from the esophageal submucosal layer with partial myectomy (Figure 2B). An esophagoscope was introduced to ensure mucosal integrity while dissecting the tumor from the esophageal submucosa. The edge of the esophageal muscle was closed after tumor excision. Both tumors were cyst-like masses, but the content of the upper mass was serous fluid and that of the lower mass was yellow-whitish mucus (Figure 2C).

The patient was allowed to eat a soft diet after the operation, and her postoperative course

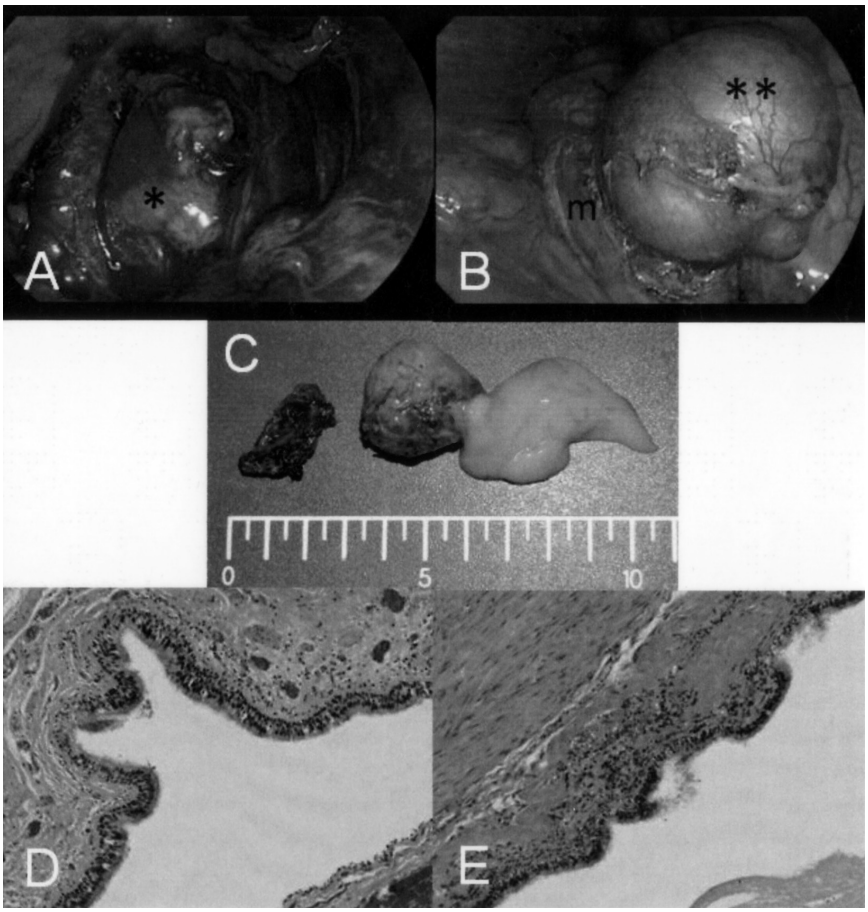


**Fig. 2.** A and B: Intraoperative images of the 2 cysts. The upper cyst (*) was within the upper mediastinum (A). The lower cyst (**) originated beneath the esophageal muscle (m) (B). C: The gross picture of these 2 bronchogenic cysts. The upper cyst (left) contained serous fluid and was ruptured during dissection; the lower cyst (right) contained mucus-like material; D and E: The microscopic view of the upper cyst (D) and the lower cyst (E). Both showed respiratory epithelial lining with bronchial-type glands, smooth muscle bundles and hyaline cartilage in the cyst wall (H&E, 100x).

was uneventful. She was discharged on postoperative day 3. The microscopic findings of these 2 masses showed pictures of bronchogenic cysts lined with respiratory epithelium. The cyst wall contained bronchial-type glands, smooth muscle bundles and hyaline cartilage (Figures 2D, 2E). No evidence of malignancy was seen.

## Discussion

Bronchogenic cysts, a type of bronchopulmonary malformation, result from abnormal budding of the primitive ventral foregut between the 3rd and 6th week of gestation [1]. The true incidence of bronchogenic cysts is unknown and is believed to be underestimated because many cases are asymptomatic [4]. The location of bronchogenic cysts depends on when

the abnormal budding of the primitive ventral foregut occurs. Mediastinal bronchogenic cysts occur in the early stages of gestation, and intrapulmonary cysts occur at a later stage of gestation [1]. Approximately 2/3 of bronchogenic cysts develop in the mediastinum and 1/3 in the lung parenchyma; very few bronchogenic cysts are reported in unusual locations along the route of foregut development, such as the neck, subdiaphragm and retroperitoneum [2-3]. In cases of mediastinal bronchogenic cysts, the common locations are hilar, subcarinal and paratracheal; those in the para-esophageal region are uncommon, and those totally within the esophageal wall are rare [5]. Most bronchogenic cysts are solitary. There have been 4 reports of double bronchogenic cysts, and only 1 case report discussing double intramural esophageal bronchogenic cysts [6].

Dysphagia is infrequently presented in mediastinal and intrapulmonary bronchogenic cysts, but it is the most common symptom in esophageal bronchogenic cysts [5]. The other common symptoms of esophageal bronchogenic cysts are chest pain and chest discomfort. Although the upper cystic lesion of this patient showed external compression of the esophagus on esophagography, she did not develop symptoms. This must have been due to the fact that the pressure derived from the serous content of this cyst was low.

There are many diagnostic modalities that can be used to distinguish a mediastinal cystic lesion from other space-occupying lesions and assist in preoperative diagnosis. These tools include chest radiography, CT, magnetic resonance imaging (MRI), esophagography, endoscopy, and endoscopic ultrasound (EUS); chest radiography and CT are the 2 most common diagnostic methods. However, the accuracy of preoperative diagnosis based on radiologic images is only 10-40%, and none of the above techniques can indicate the exact nature of a cyst [7]. Moreover, it is usually difficult to distinguish whether a para-esophageal cystic lesion is located inside or outside the esophageal wall [8]. The esophagography findings in this study suggested the upper cyst was possibly inside the esophagus and the lower cyst was outside the esophagus. This was incompatible with the operative findings of the locations of these 2 cystic lesions. Although its content was serous fluid, the upper cyst was located in the thoracic inlet, which was a relatively narrow space; thus, an esophageal indentation was seen. On the other hand, the cyst with jelly-like content originating beneath the muscle layer of the esophagus showed no compression of the esophagus, because it protruded into the free pleural cavity. Endoscopic ultrasound might play a role in preoperatively defining the relationship between a tumor and the esophageal wall, but we did not perform this examination.

The majority of intramural esophageal cysts are esophageal or enterogenous cysts; intramural esophageal bronchogenic cysts are extremely rare [2]. Bronchogenic cysts are usually filled with white milky material, are lined with pseudo-stratified columnar epithelium and sometimes contain foci of smooth muscle, hyaline cartilage and seromucous glands. On the other hand, esophageal cysts contain green mucoid material and are lined with intestinal or gastric epithelium [9]. In our case, the materials within these 2 cysts were different, the reason for which is unclear.

Surgical resection of bronchogenic cysts provides a definite diagnosis and also prevention of complications, such as intracystic hemorrhage, infection, inflammation, ulceration,

and rupture, and potentially malignant changes [2-3]. Excision of mediastinal bronchogenic cysts by thoracotomy is the conventional standard. With the development of video-assisted thoracoscopic surgery, thoracoscopic excision of these lesions has been reported to be safe and have the many benefits of minimally invasive surgery [4,7]. Although excision by thoracotomy is still favored by most surgeons when an intramural esophageal cystic lesion is encountered, these cysts actually can be enucleated from the esophageal mucosa using thoracoscopic surgery, with acceptable complication rates [5,10]. In addition, video-assisted thoracoscopic surgery can be used as a diagnostic tool for defining the locations of the cysts before a definite procedure is performed, if the preoperative diagnosis is vague. We agree that esophagoscopic monitoring during thoracoscopic excision of a mass, as in thoracotomy surgery, is very useful in terms of controlling the integrity of the esophageal mucosa [11]. If the adhesion between the cyst wall and the peripheral structure is too severe, rendering submucosal dissection unsafe or resulting in other situations that lead to abandoning thoracoscopic surgery as an option, conversion to the thoracotomy approach should be undertaken, without a doubt, to prevent possibly disastrous complications.

In conclusion, bronchogenic cysts should be taken into account during the differential diagnosis of a paraesophageal cystic lesion, and it should be noted that esophageal bronchogenic cysts can be multiple. The degree of esophageal luminal compression does not imply the layer from which the cystic lesion is derived. Video-assisted thoracoscopic surgery could have diagnostic and therapeutic benefits for excision of para-esophageal bronchogenic cysts with both a safe and improved recovery course.

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# 以胸腔鏡手術切除雙顆胸腔內食道旁支氣管源性囊腫，一肌肉層外，一肌肉層內：病例報告

陳盈元　黃維立　曾堯麟

支氣管源性囊腫（Bronchogenic cyst）是一種不常見的先天性支氣管肺部畸型，一般多為單顆發生。常見的發生位置在上縱膈腔、中縱膈腔及肺實質內部。發生在食道旁，特別是食道肌肉層內的支氣管源性囊腫是很罕見的。此篇的病例報告是一中年女性，於例行的健康檢查中發現兩顆位於食道旁的囊腫。經過一系列的檢查之後成功接受胸腔鏡囊腫切除手術。於術中發現上方的囊腫位於食道肌肉層外且內容物為澄清液體，而下方的囊腫則在食道肌肉層內，內容物為黃白黏液狀。病理檢查發現兩顆囊腫皆含呼吸上皮，壁內有呼吸腺體、平滑肌及透明軟骨，證實皆為支氣管源性囊腫。病人術後恢復良好，並在很短的時間內即出院。*( 胸腔醫學* ***2013; 28: 235-240)***

關鍵詞：支氣管源性囊腫，食道，胸腔鏡手術

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# Endobronchial Hamartoma Removed by Flexible Bronchoscopy via Electrocautery – A Case Report

Wen-Ming Lee*, Chih-Yen Tu*,**, Wei-Chih Liao*, Chia-Hung Chen*, Chuen-Ming Shih*, Wu-Huei Hsu*

Primary tumors of the trachea are usually malignant (90%). Only 10% of them are benign, and include fibroma, schwannoma, leiomyoma and hamartoma. About 1.4-20% of hamartomas has an endobronchial location and can be symptomatic due to airway obstruction. Surgical resection has been considered traditionally as the standard of care for endobronchial hamartoma. However, endoscopic resection has a therapeutic efficacy comparable to surgical resection, but spares a major operation. Herein, we report a 56-year-old female with an endobronchial chondroid hamartoma complicated with obstructive pneumonia in the right middle lobe and the right lower lobe that was diagnosed and definitively treated with bronchoscopic techniques. Endobronchial treatment was performed using a flexible bronchoscope with electrosurgery. This approach resulted in complete resolution of the patient's symptoms. Follow-up bronchoscopic examinations 1 year after the bronchoplasty procedure excluded residual or recurrent disease. Minimally invasive bronchoscopic resection for endobronchial harmatoma is a safe, effective method with a low complication rate. ***(Thorac Med 2013; 28: 241-246)***

Key words: endobronchial harmatoma, interventional bronchoscopy, electrocautery

## Introduction

Pulmonary hamartoma is a very rare form of benign neoplasm of the lung [1]. In 1934, Goldsworthy applied this term to benign tumors located in the lung that were composed predominantly of a combination of fat and cartilage [2]. These tumors occur in parenchymal and endobronchial locations, the latter representing 10-20% of the total number of pulmonary hamartomas [3-5]. Even though endobronchial hamartomas are considered benign in nature, they are generally broad-based lobulated nodules that grow slowly, resulting in symptoms of airway obstruction including cough, hemoptysis, dyspnea, or obstructive pneumonia, and have the potential of fatal complications [6]. Therefore, surgical resection has been considered the standard of care for endobronchial hamartoma. In this report, we describe a 56-year-old woman

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who presented with obstructive pneumonia due to endobronchial tumor. The endobronchial hamartoma was diagnosed and successfully resected using flexible fiberoptic bronchoscopy with electrocautery, sparing a surgical intervention.

## Case Report

This 56-year-old female non-smoker with a history of asthma presented with a primary complaint of intermittent fever, dyspnea and productive cough for several weeks. The physical examination was unremarkable. Her chest x-ray (CXR) in May 2011 revealed bilobar pneumonia in the right middle lobe (RML) and right lower lobe (RLL) (Figure 1). She was treated with empirical antibiotics without any improvement in the CXR image. An endobronchial lesion with airway obstruction was suspected because of her unresolved pneumonia. Chest CT (Figure 2) scans revealed an irregular lesion of low attenuation, which totally obstructed the right intermediate bronchus. We then performed bronchoscopy for the endobronchial tumor, which had a non-friable, smooth surface (Figure 3A). The tumor was totally resected endoscopically by electrocautery mechanical debridement (Figure 3B) at the same time, because it had caused RML and RLL collapse related to her dyspnea. After the bronchoplasty procedure, the follow-up CXR revealed her obstructive pneumonia had recovered (Figure 4). The histological examination of the endobronchial tumor was compatible with hamartoma (Figure 5). Follow-up bronchoscopic examination of the patient 1 year after the interventional bronchoscopic procedure excluded residual or recurrent disease.

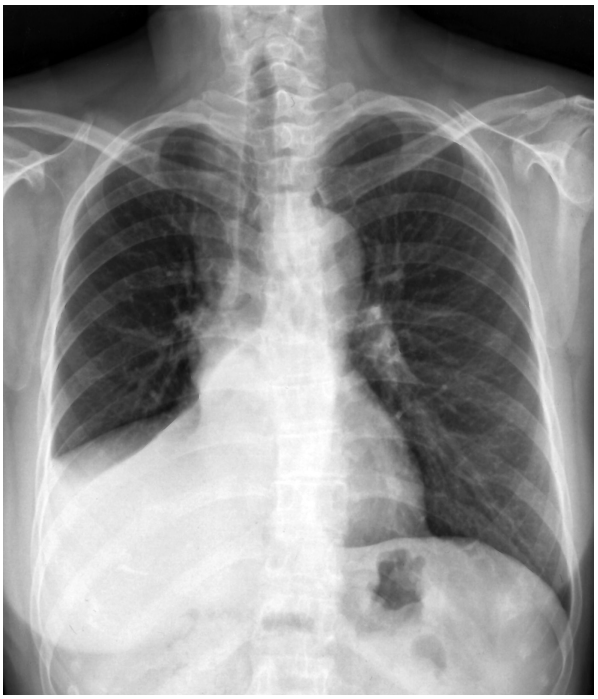

**Fig. 1.** Chest radiograph revealed bilobar collapse in the RLL and RML.

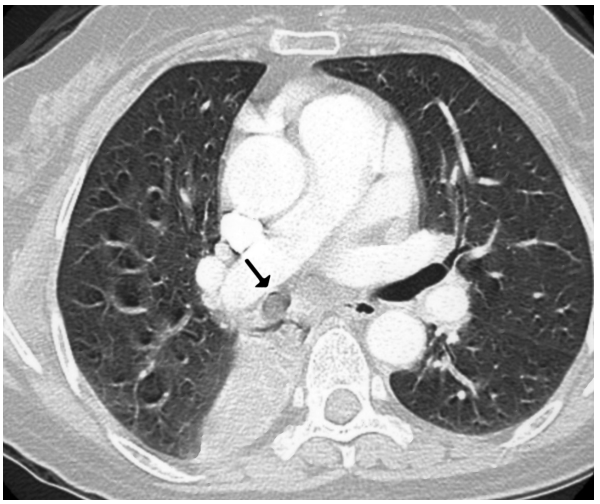

**Fig. 2.** The tumor (arrow) located in the bronchus intermedius is seen in the CT section.

## Discussion

Pulmonary hamartomas are benign lesions that consist of pulmonary and bronchial elements, which are usually combined with car-

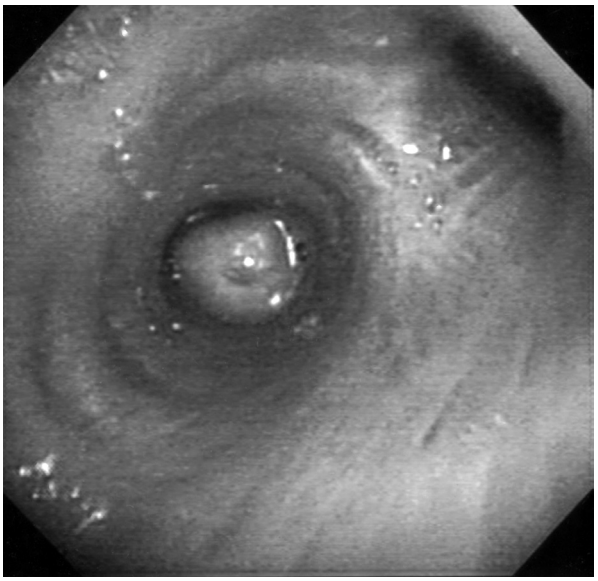

**Fig. 3A.** Bronchoscopic view of the endobronchial tumor in the bronchus intermedius.

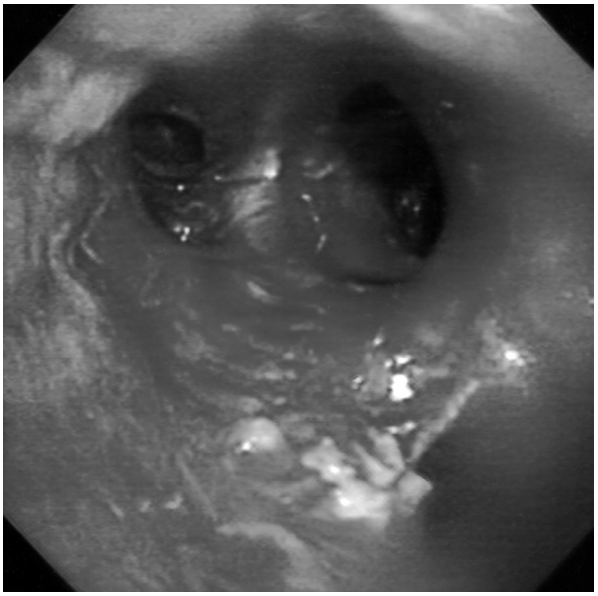

**Fig. 3B.** Bronchoscopic view after the endobronchial tumor was resected by electrocautery.

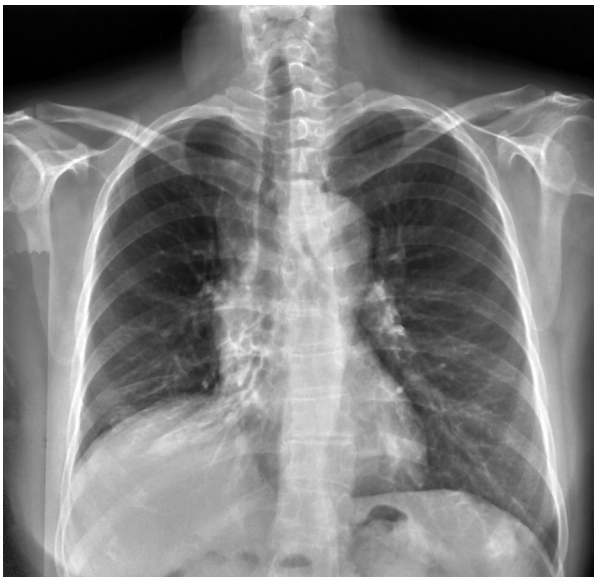

**Fig. 4.** Follow-up chest radiograph after electrocautery revealed that the RML and RLL had expanded.

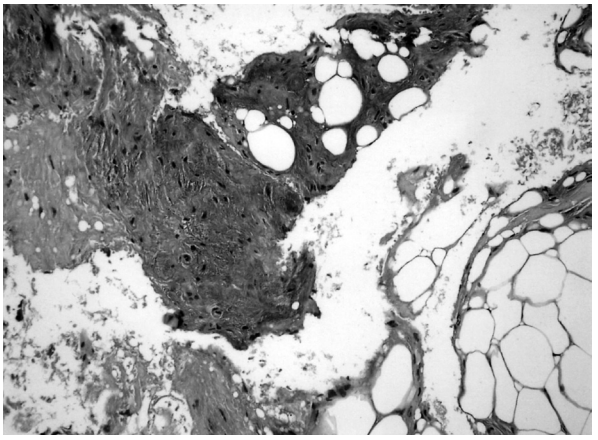

**Fig. 5.** Microscopic feature: section stained with hematoxylin and eosin (× 200). Structures that are part of the condroid and seromucinous glands were found in lipomatose areas.

tilaginous tissue, fat, and smooth muscle [2]. Although hamartomas are the most common benign lung tumors, they are still rare, with an incidence of only 0.025% to 0.96% in different studies [7-8]. The peak age of incidence is between 40 and 60 years, with a male preponderance [9]. Most pulmonary hamartomas appear as solitary peripheral lesions and are asymptomatic. However, endobronchial hamartomas are frequently present, with symptoms caused by endobronchial obstruction. It is very hard to establish the diagnosis of endobronchial ham-

artoma based on radiographic images if there is no distal parenchymal change of the lung such as atelectasis, obstructive pneumonia, or abscess formation.

Bronchoscopy and biopsy should be performed for any patients with pulmonary symptoms such as cough, repeated pulmonary infection, and hemoptysis [5]. Endoscopic examination typically reveals a lesion with a smooth, regular, soft surface that is non-friable to the touch of the device [7,9]. Although these features suggest a benign lesion, on some occasions, distinguishing between the tumors and malignant lesions based on macroscopic findings alone might be difficult; therefore, biopsy should be performed routinely in all patients presenting with such lesions. An adequate tissue sample for diagnosis is hard to obtain from an endobronchial hamartoma covered with normal epithelium, and the diagnosis is easily missed in the differential diagnoses due to its rarity. Only 15% of endobronchial hamartomas are diagnosed preoperatively. As a result, lobectomy or pneumonectomy is performed in 47% of endobronchial hamartomas, even though the tumor is benign [10].

Endobronchial tumor-related lung collapse requires interventional bronchoscopy for endobronchial tumor excision to relieve the patient's symptoms, such as dyspnea or obstructive pneumonia. The technique employed for the resection of endobronchial hamartomas depends on the tumor location, the presence of lung parenchymal disease reaching the distal airways, the presence of extrabronchial growth, and eventual symptoms. The management of such tumors should be individualized according to the characteristics of each patient and the lesion. The traditional treatment is thoracotomy with bronchostomy, lobectomy, or lung resection [7]. Due to the benign nature of these lesions, endoscopic resection has become a popular technique for their resection, because it provides satisfactory results without the risks associated with thoracotomy [11-12]. Rigid bronchoscopic treatment provides excellent outcomes, control of symptoms, and avoids the risks of surgical intervention [13-14]. However, the advantages of the use of flexible bronchoscopy in the management of these tumors include less invasiveness, lesser need for general anesthesia, quicker bronchial opening, shorter hospital stays, and lower costs. The various methods for resecting endobronchial lesions include the use of laser, electrocautery, cryotherapy, and argon plasma coagulation. Complete excision of the tumor and treatment of the tumor base reduces the chance for local recurrence and maintains the patency of the affected bronchus. Therapeutic bronchoscopy with electrocautery was reported recently to be a safe and effective choice of treatment [15-17]. Although endobronchial electrocautery is usually safe, complications such as tracheal fires [15], bleeding [18], and aspiration pneumonia post-procedure [16] may occur and have been reported.

In conclusion, endobronchial hamartoma is a rare benign tumor of the tracheo-bronchial tree, and diagnosis of these lesions can be challenging. Moreover, endoscopic removal, performed by an experienced bronchoscopist, is a safe and effective alternative to surgical resection for these endobronchial hamartomas.

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# 支氣管內過誤瘤藉由支氣管鏡電燒灼術切除

李文銘 * 涂智彥 *,** 廖偉志 * 陳家弘 * 施純明 * 徐武輝 *

氣管的原發性腫瘤通常為惡性居多（90%），大約只有 10% 左右是良性的。在這些良性腫瘤中，纖維瘤，神經鞘瘤（許旺氏細胞瘤），平滑肌瘤，以及過誤瘤都有可能被發現。大約 1.4-20% 的過誤瘤會位於氣管內，且因為氣道的阻塞而造成症狀。傳統的觀念中，外科手術切除被認為是支氣管內過誤瘤的標準治療。然而，內視鏡切除的治療效果與外科手術治療是相當的，還可以減少動大手術之需要。我們在此報告一位 56 歲女性病患因支氣管內過誤瘤而導致右中肺及右下肺阻塞性肺炎的病例，藉由支氣管鏡的介入性處置獲得到明確的診斷及充分的治療。支氣管內治療是藉由可曲式支氣管鏡加上電燒灼術的方式進行。如此的處置方式可以完全緩解病患的症狀。而在此氣管內治療後，我們追蹤此病患長達一年，並未發現有殘餘或復發性病灶的發生。微侵入性支氣管鏡切除術對於支氣管內過誤瘤而言，是一項安全、有效，且產生併發症機率低的治療方式。*( 胸腔醫學 **2013; 28: 241-246**)*

關鍵詞：支氣管內過誤瘤，介入性支氣管鏡治療，電燒灼術

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# Non-renal Microscopic Polyangiitis with Acute Pulmonary Hemorrhage: A Case Report

Chin-Liang Chuang, Wann-Cherng Perng*, Chin-Feng Giian*, Chuan-Chou Tu, Deng-Ho Yang**, Shou-Cheng Wang

Microscopic polyangiitis (MPA) is a systemic small-vessel necrotizing vasculitis associated with antineutrophil cytoplasmic antibodies, similar to granulomatosis with polyangiitis (GPA), but without granuloma. The pathogenesis of MPA may be endothelial damage and vasculitic lesions. The manifestations often include renal or pulmonary involvement; however, other systemic lesions might also be observed. Over 90% of MPA patients exhibit renal involvement with extra-renal vasculitis at varying sites. Cases of non-renal MPA are clinically uncommon. We report the case of a 46-year-old male with pulmonary fibrosis, which had persisted for 10 years before the diagnosis of non-renal MPA. The patient also had acute pulmonary hemorrhage due to an infection-induced flare-up of vasculitis, which occurred 2 years after the diagnosis of non-renal MPA. ***(Thorac Med 2013; 28: 247-252)***

Key words: microscopic polyangiitis, pulmonary fibrosis, pulmonary hemorrhage

## Introduction

Microscopic polyangiitis (MPA) is a small-vessel necrotizing vasculitis associated with antineutrophil cytoplasmic antibodies (P-ANCA). It affects men more often than women and usually begins after the age of 50. The 2 organs usually involved — and often defining the prognosis — are the kidneys and lungs [1]. MPA commonly involves the kidney with a variable course of renal disease; 25-45% of patients progress to dialysis [2-3]. In contrast, pulmonary involvement occurs in a smaller proportion of patients (10-30%) [4]. Diffuse alveolar hemorrhage is the most serious form of lung involvement in MPA and has been reported in 12-29% of patients in several series [2,5]. An alternative presentation of lung involvement is pulmonary fibrosis (PF), which is observed in 36% of patients at the time of diagnosis [6]. PF has a poor prognosis and may precede other disease manifestations by a variable length of time. We report the case of a 46-year-old man with PF for 10 years prior to the diagnosis of non-renal MPA, and acute alveolar hemorrhage, which occurred 2 years after the diagnosis of

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non-renal MPA.

## Case Report

A 46-year-old man had a persistent dry cough and had been receiving symptomatic treatment in a local clinic for 13 years. PF and posterior mediastinal masses were noted at the age of 42. At the age of 44, the patient underwent surgery for the posterior mediastinal mass and an open lung biopsy. The posterior mediastinal mass was found to be a bronchogenic cyst. The open lung biopsy showed capillaritis with perivascular infiltration of inflammatory cells and subclinical alveolar hemorrhage. Palpable purpura appeared simultaneously on both lower limbs and the trunk. Laboratory data revealed positive results for myeloperoxidase (P-ANCA) and elevated levels of C-reactive protein (CRP), although renal function was within normal limits. Definite MPA was diagnosed on the basis of the presence of palpable purpura, open lung biopsy findings, positive results in the myeloperoxidase (P-ANCA) test, and elevated CRP levels. Since diagnosis, the patient had been receiving immunotherapy, including prednisolone and cyclophosphamide, in the rheumatology outpatient department. Two days before the current admission, a cough with intermittent bloody discharge was noted. In the emergency room, we observed massive hemoptysis, fever, dyspnea, and disturbances in consciousness. The physical examination revealed pale conjunctiva, and breathing with the sound of bilateral crackles. Laboratory data were as follows: white blood cell count, 13900/uL (normal 4,500 to 11,000); hemoglobin, 9.6 g/dL; C-reaction protein (CRP), 20.3 mg/dL (normal 0 to 0.5); BUN, 16 mg/dL (normal 6 to 20); creatinine, 0.8 mg/dL (normal 0.7 to 1.2). Arterial blood gas was: pH, 7.05 (normal 7.35 to 7.45); $PaCO_2$, 100.3 mmHg (normal 35 to 45); $PaO_2$, 140.2 mmHg (normal 75 to 100); $HCO_3^-$, 27.6 mEq/l; $O_2$ saturation, 97% (normal 92 to 98.5) under an $O_2$ mask (15 L/min). Chest x-rays revealed a bilateral alveolar filling pattern with extensive consolidation (Figure 1). Chest computed tomography showed areas of consolidation interspersed with areas of ground glass attenuation in the bilateral lung fields (Figure 2). Under the impression of MPA complicated with acute pulmonary hemorrhage, the patient was admitted to the intensive care unit. Chest radiography and polymerase chain reaction analysis of the sputum revealed *Pneumocystitis jiroveci* pneumonia; therefore, sulfamethoxazole/trimethoprim was administrated to treat the hypothesized lung infection. Methylprednisolone (1000 mg daily for 3 days) was administered intravenously to control the MPA flare-up, but a poor

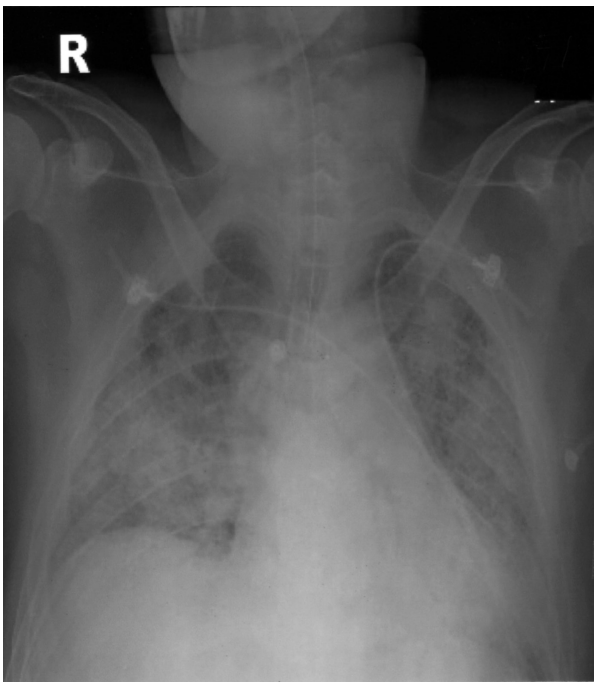


**Fig. 1.** Bilateral alveolar filling pattern with extensive consolidation, compatible with acute pulmonary hemorrhage in this case

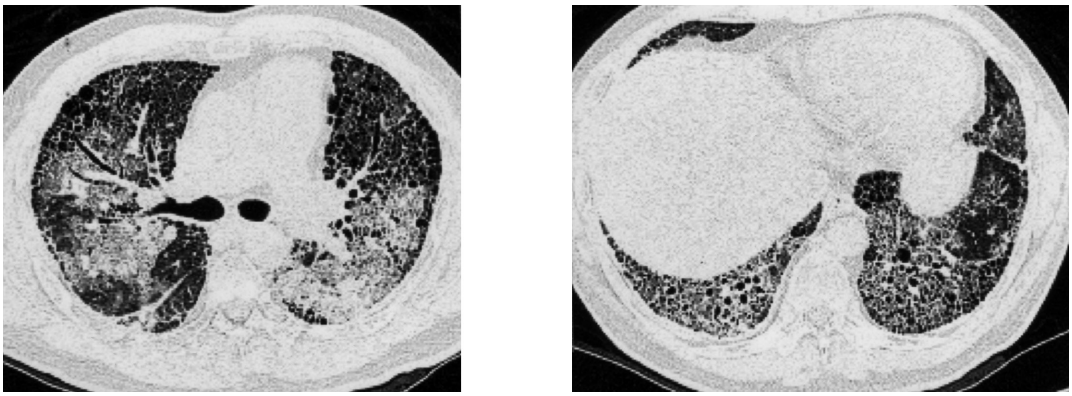

**Fig. 2.** Bronchiectastic change and areas of consolidation interspersed with areas of ground glass attenuation compatible with interstitial lung disease with acute pulmonary hemorrhage

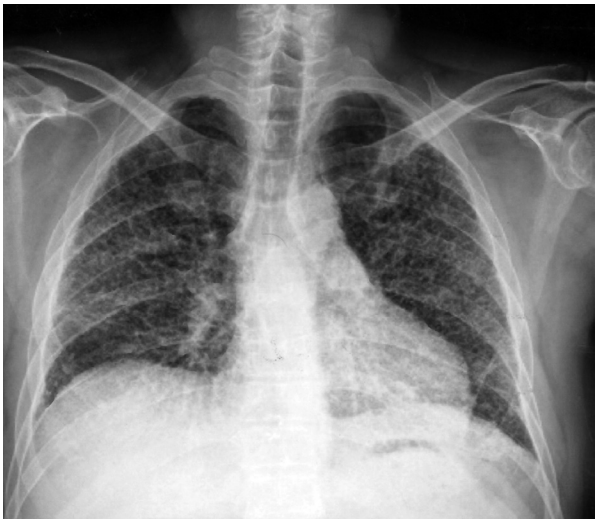

**Fig. 3.** Chest x-rays after adequate treatment

response was noted. Plasma exchange was performed subsequently, after which the patient's general condition and hemoptysis improved. He was successfully weaned from the ventilator on the 9$^{th}$ hospital day. The CRP levels, which were 10.5 mg/dL (normal level, 0-0.5 mg/dL), and the chest X-ray images suggested disease resolution (Figure 3).

## Discussion

ANCA can activate primed neutrophils to release reactive oxygen species and lyse endothelial cells. Moreover, neutrophils activate the alternative complement pathway to generate factors such as C5a and C3a, which amplify the intensity of ANCA-induced inflammation. Systemic or local infection can trigger and amplify this effect by stimulating the release of proinflammatory cytokines and chemokines, which upregulate the expression of endothelial adhesion molecules [7-8]. The main fluoroscopic staining ANCA patterns are the diffuse, granular cytoplasmic (C-ANCA) pattern, and the perinuclear (P-ANCA) pattern. C-ANCA is also known as PR3-ANCA due to the presence of autoantibodies targeting serine protease proteinase-3, while P-ANCA (known as MPO-ANCA) represents antibodies directed against many antigens, among which, myeloperoxidase is the most frequent in patients with ANCA-associated vasculitis [9-10]. Antigen specificity (PR3 or MPO) does not effectively differentiate among various types of ANCA-associated vasculitis. However, C-ANCA/PR3-ANCA are

mainly found in GPA, while P-ANCA/MPO-ANCA are more prevalent in MPA. Non-renal MPA is usually P-ANCA-negative, although 5% of renal MPA cases are also P-ANCA-negative. MPA involving the lung but not the kidney has been reported in 4 cases of alveolar capillaritis without detectable glomerulitis among 25 autopsy cases of MPA [11]. Non-renal MPA can be accompanied with PF at the time of diagnosis, more commonly in ethnic Chinese and Japanese patients; moreover, PF is less responsive to treatment than vasculitic manifestations [12]. In this case, PF was noted before the diagnosis of MPA; progressive pulmonary destruction and alveolar hemorrhage were observed 2 years after the diagnosis of MPA. One report described 3 elderly patients who had PF as an unusual clinical manifestation of MPA [13]. The theory of PF is currently based on fibroblastic foci. PF associated with MPA may be caused by subclinical alveolar hemorrhage, vasculitis, or other conditions [14-16]. The association between PF and ANCA-associated vasculitis is not accidental; the anti-myeloperoxidase antibody plays a direct role in the pathogenesis of PF, which is the major cause of death [17]. Diagnosis in such cases is typically delayed by at least 3 months, and there is a longer delay in the absence of extra-renal disease [18].

Interstitial lung disease is an underappreciated manifestation of MPA [13,19-21], and the age at which ANCA-associated vasculitis is diagnosed in patients with PF often seems higher than expected [16]. The diagnosis and classification of MPA are more difficult if renal vasculitis is absent, as in the present case, or if ANCA is absent. These factors often lead to a delay in the diagnosis and treatment of MPA. In our case, the gap between the initial detection of PF and the diagnosis of MPA was 10 years, i.e., the diagnosis was greatly delayed. Therefore, MPA should be considered in the differential diagnosis for PF of unknown etiology. The presence of ANCA will increase the risk of developing vasculitis in the future, and the monitoring of ANCA levels will allow for specific monitoring of at-risk patients. Infection could trigger a flare-up of the patient's vasculitis, which would in turn lead to alveolar hemorrhage. A *Pneumocystis jiroveci* pneumonia infection was found in our case. During the course of ANCA-associated vasculitis, bacterial, fungal, or viral infection can trigger a vasculitis flare-up. Therefore, infection in these patients should be avoided, and infected patients should be monitored closely for flare-up of vasculitis.

Patients with MPA complicated with diffuse alveolar hemorrhage are treated with plasmapheresis and immunotherapy, including high doses of prednisolone and cyclophosphamide [22]. We observed a poor response with the initial steroid therapy and a good response with plasma exchange in our patient. Plasma exchange might be useful in dialysis-dependent patients and in those with alveolar hemorrhage [23].

## Conclusion

PF can be the initial manifestation of non-renal MPA, which is relatively rare. Detecting PF and taking MPA into consideration in the differential diagnosis of PF can facilitate early diagnosis of MPA in such cases. Avoiding infections could decrease the incidence of vasculitis flare-ups and subsequent complications. Plasma exchange can be used as a rescue therapy in MPA with alveolar hemorrhage.

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# 無腎臟侵犯之顯微性多血管炎合併急性肺出血：病例報告

莊志亮　彭萬誠 *　簡志峰 *　涂川洲　楊登和 **　王守正

顯微性多血管炎是一種全身小血管壞死性血管炎與 antineutrophil cytoplasmic antibodies 有關，類似 granulomatosis with polyangiitis（GPA），但沒有肉芽腫產生。顯微性多血管炎的發病機制可能是由於血管內皮損傷和血管炎病變所導致。經常以腎臟或肺部侵犯來表現；然而，全身其他部位病變也可能見到。顯微性多血管炎的患者中，超過 90% 會表現出腎臟侵犯合併腎臟以外不同部位的血管炎。在顯微性多血管炎的病人中，在臨床上以沒有腎臟侵犯來表現是少見的。我們報告一個 46 歲的男性表現肺纖維化之後十年診斷無腎臟侵犯之顯微性多血管炎，確診之後二年發生由於感染引起血管炎急性惡化合併急性肺出血。
*( 胸腔醫學 **2013; 28: 247-252**)*

關鍵詞：顯微性多血管炎，肺纖維化，肺出血

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# Pulmonary Sequestration Presenting as Chronic Intermittent Hemoptysis

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Ya-Chun Chang*, Shih-Feng Liu*,***

We reported a 28-year-old female patient with no systemic illness who presented with chronic intermittent hemoptysis for 5 years. Chest computed tomography revealed pulmonary sequestration with 1 feeding artery originating from the celiac trunk. Right lower lung lobectomy with pulmonary sequestration resection was performed, after which, the hemoptysis resolved. By presenting this case we hope to emphasize the concept that pulmonary sequestration cannot be excluded by a normal chest x-ray, and that pulmonary sequestration alone can be the cause of chronic intermittent hemoptysis in an otherwise asymptomatic patient. A review of the literature on pulmonary sequestration is also presented. ***(Thorac Med 2013; 28: 253-259)***

Key words: pulmonary sequestration, chronic hemoptysis, bronchopulmonary sequestration

## Introduction

Bronchopulmonary sequestration (BPS), or pulmonary sequestration, is a congenital anomaly consisting of a nonfunctioning mass of lung tissue that lacks normal communication with the tracheobronchial tree. Instead of being normally supplied by pulmonary circulation, the sequestered lung receives part or all of its blood supply from systemic circulation [1]. Because of its various chest x-ray (CXR) presentations, sequestered lung could easily be overlooked if there is not enough alertness to the possibility of this disease. We report the case of 28-year-old woman with chronic intermittent hemoptysis. The initial CXR was nearly normal, but chest computed tomography (CT) revealed intralobar pulmonary sequestration (ILS). The hemoptysis resolved completely during the follow-up after resection of the pulmonary sequestration.

## Case Report

A 28-year-old woman without systemic dis-

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ease in the past presented to our chest outpatient department with a history of recurrent intermittent hemoptysis. Hemoptysis occurred with a frequency of 4 to 6 times every year, persisting for 5 years before she sought medical advice at our hospital.

The hemoptysis usually presented with spitting a mouthful of fresh blood. There was no predilection for morbidity timing or synchronicity with menstruation, but a few episodes of fever with copious sputum occurred around the time of the hemoptysis attack in the past. The patient had never experienced symptoms indicative of a bleeding tendency in the past, like gastrointestinal bleeding, easy bruising or gum bleeding.

The initial hemogram and coagulation profile in our hospital showed a normal platelet level, prothrombin time, and activated partial thromboplastin time. CXR imaging revealed bilateral clear lung fields, except mild infiltration in the right lower lung field, close to the right-side border of the heart (Figure 1). Some hemostatics were prescribed, with a partial response. Bronchoscopy was carried out for identification of the bleeder 3 days later. No blood streak or blood clot was noted during the procedure. The accessible bronchial mucosa was all smooth and intact.

High-resolution chest CT (Figures 2, 3) was arranged soon after the normal bronchoscopy result. A focal consolidation patch with emphysematous bordering was found in the medial inferior aspect of the right lower lung, and was supplied possibly by 2 aberrant arteries from the right side of the celiac trunk. Pulmonary sequestration of the posteromedial basal lung was suspected, due to the imaging findings.

Thoracoscopic wedge resection of the right lower lung pulmonary sequestration was carried out following the chest CT. During the operation, right basal lung consolidation with an obstructed bronchial lumen and frank pus

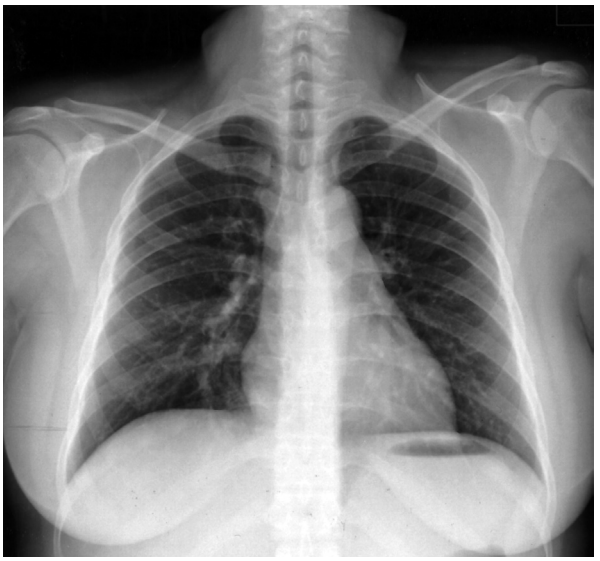

**Fig. 1.** The initial CXR obtained on 14 May 2012.

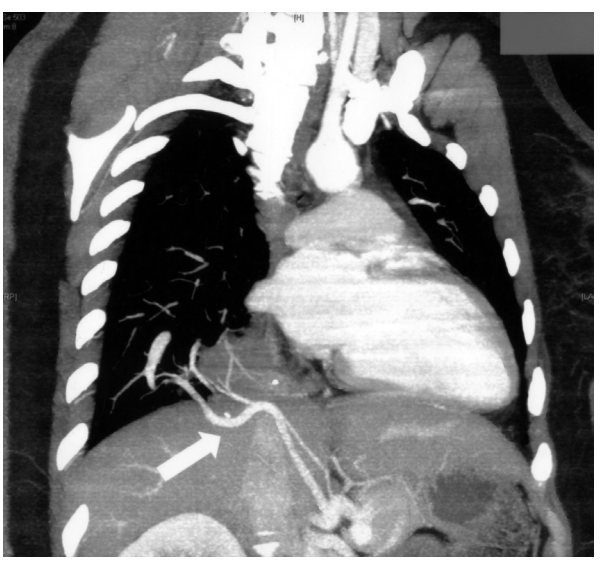

**Fig. 2.** Chest contrast-enhanced CT, parasagittal view, obtained on 25 June 2012. A mass lesion (3.3 × 2.6 cm in size) located at the right posteromedial basal lung. The supplying artery (marked by a white arrow) is clearly delineated with its origin at the celiac trunk.

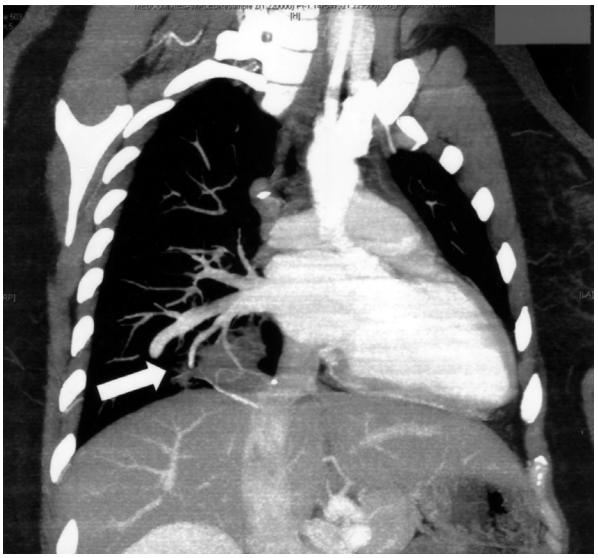

**Fig. 3.** Chest contrast-enhanced CT, parasagittal view, obtained on 25 June 2012. The venous drainage of the sequestered lung (marked by a white arrow) collected in the right atrium.

accumulation was noted. A feeding artery that originated from the paraesophageal side of the celiac artery was ligated. Pathology reported a whitish fibrotic pulmonary tissue, measuring 9.8 × 5.5 × 3.2 cm, and the microscopic evaluation was compatible with pulmonary sequestration. No malignant cells or evidence of congenital pulmonary airway malformation (CPAM) could be seen in the specimen. The operative findings and pathology report were compatible with ILS.

There was no recurrence of hemoptysis during the 2-month postoperative follow-up, and the patient did not experience copious sputum production as before. Medical control with hemostatics and antibiotics was no longer required.

## Discussion

Pulmonary sequestration is traditionally classified as ILS or extralobar pulmonary sequestration (ELS), based on its pleural investment. By definition, ILS is located within a normal lobe and lacks its own visceral pleura, and ELS is found outside the normal lung and has its own pleura. Some experts have proposed bronchopulmonary-foregut malformation as another variant when the sequestered lung is connected to the gastrointestinal tract [2].

Of the various congenital anomalies of the lung, BPS accounts for 0.15-6.4% of all malformations [3]. ILS is more common by far and comprises 75-90% of all BPS [3-4]. ILS affects males and females equally, but there is a significant male predominance in ELS [1-2].

The pathogenesis of pulmonary sequestration is still debated. Despite the obvious correlation of ELS with other congenital diseases, some cases of ILS seemed to be acquired after birth. This is based on the finding that there was a paucity of cases in a neonatal autopsy series [5], and the observation that pulmonary inflammation can stimulate collateral circulation to the lung [6]. In contrast, most of the cases with ELS were diagnosed within the first year of life, with or without the development of respiratory compromise [7]. ELS also has higher incidence of associated congenital anomalies than ILS. In a series of 28 cases among children and adults, associated malformations occurred in 43% of ELS and 17% of ILS cases [3].

The clinical features of pulmonary sequestrations vary, depending on the type of malformations, age at presentation and the size of the sequestered lung. On prenatal ultrasound, pulmonary sequestration commonly presents as an incidental finding of an echogenic thoracic mass that can be small or occupy most of the hemithorax [8-10]. Mediastinal shift is often seen in cases of large pulmonary sequestration. Hydrops may develop in a minority of patients, possibly due to vascular compression [8-9,11-

13]. There is no validated predictive factor currently to estimate the progression of pulmonary sequestration and the risk of developing hydrops.

ELS typically presents in symptomatic newborns with respiratory compromise. Recurrent pneumonia is less commonly reported, and most patients remain asymptomatic throughout the course. Most cases of postnatal ELS were identified during evaluation of an associated anomaly.

ILS is usually detected in adolescents with recurrent pneumonia or signs of airway infection, like fever and productive cough. It is rarely diagnosed in the perinatal period. When patients with ILS become older, hemoptysis and chest pain may occur. If the aberrant artery supplying a sequestered lung is large, heart failure can develop in rare cases as a result of high cardiac output [4,14].

Hemoptysis is generally considered the result of elevated perfusion pressure from systemic circulation. In a case series reported by Berna *et al*. [15], hemoptysis was present in 30% of patients, and is considered the most common symptom of adult-type ILS. Clinicians would usually use thoracic angiography or CT for the definite diagnosis in a patient with massive hemoptysis. However, there would be a long path to the diagnosis in a patient with mild symptoms, like our patient.

Congenital anomalies may be associated with pulmonary sequestration. Reported anomalies include congenital diaphragmatic hernia, vertebral anomalies, congenital heart disease, pulmonary hypoplasia, and colonic duplication [2,16]. The sequestered lung may occasionally be a mixed lesion with CPAM, which is a risk factor for pulmonary malignancy in the future. However, the incidence of malignant change is very low and is usually limited to cases of ILS in adults, probably due to an undetected mixed ILS and CPAM lesion.

There are many diagnostic tools that can be used for pulmonary sequestration. Prenatal diagnosis usually relies on sonography and occasionally on magnetic resonance imaging (MRI) for difficult cases [8,17]. However, we will focus more on the diagnosis of postnatal pulmonary sequestration in the following discussion.

CXR is necessary for initial evaluation when pulmonary sequestration is considered. Sequestrations typically appear as a uniformly dense mass in the lower lobes, especially the left lower lobe [2,16,18], but they can be found virtually anywhere in the lung parenchyma. In addition, cystic formation in the sequestered lung may occur with recurrent infection, and air-fluid levels can be found with the existence of bronchial communication. Some ELS were found as extrathoracic lesions in the subdiaphragmatic or retroperitoneal region. All of the above findings, however, are nonspecific to pulmonary sequestrations.

On sonography, pulmonary sequestrations are usually found as a homogenously echogenic mass [19], but cystic structure or complex formation can be seen in some cases. Doppler ultrasound can help identify the aberrant systemic blood supply and the venous drainage. The supplying arteries usually come from the aorta or its branches, with venous drainage returning to the left atrium. Venous return to the right atrium, as in this patient, is a less common finding.

CT is considered the tool of best resolution for lung parenchymal abnormalities associated with pulmonary sequestration. As with the findings on CXR, the appearance of sequestered lung can vary, including a solid mass, cystic formation, cavitary mass with air-fluid level

or a collection of multiple cysts [4,10,19-20]. Emphysematous changes at the margin of the lesion are common findings. With the wide application of contrast-enhanced or helical CT, visualization of small supplying arteries and venous drainage has become easier, making it the diagnostic procedure of choice. MRI usually is not involved in the diagnosis of pulmonary sequestration, but MR angiography can assist in identifying the vascular supply and its orientation in difficult cases [18,21-22].

The differential diagnosis includes CPAM, congenital diaphragmatic hernia, bronchogenic cyst, and congenital lobar emphysema. CPAM, in particular, should always be excluded because of the high incidence (around 50%) of hybrid lesion in ELS. Some cases of pathologically proved CPAM had a systemic supplying artery, which increased the uncertainty of radiological diagnosis in pulmonary sequestration.

Treatment of BPS consists of surgical excision, mainly lobectomy and resection of the sequestered lung. In symptomatic patients, surgical excision is curative and is associated with minimal morbidity [23-24]. As for asymptomatic cases, fetal intervention is usually not required because of the high ratio of spontaneous regression. Operation is often suggested for all postnatally diagnosed patients in order to prevent future risk of recurrent infection and other complications, like hemoptysis or malignant transformation of hybrid lesions with CPAM [3,25-26]. There are still some experts that advocate the performance of serial monitoring in asymptomatic ELS.

In summary, we reported the case of a young female with chronic recurrent hemoptysis and a nearly normal initial CXR. Being alert for recurrent pulmonary infection and hemoptysis, chest CT was arranged and revealed the sequestered lung. We can learn from this case that CXR is not conclusive in pulmonary sequestration and that a high degree of suspicion regarding abnormal presentations is key to the diagnosis. Also, in cases with recurrent hemoptysis with negative bronchoscopic findings, further thoracic imaging may help identify rare causes of airway bleeding, like pulmonary sequestration.

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# 游離肺合併慢性反覆咳血病例報告

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一位 28 歲女性病患，本身無重大疾病史，本次因慢性反覆咳血五年而入院。病患接受胸部電腦斷層發現疑似游離肺及源自腹腔動脈幹的供應血流，病患接受右下肺及游離肺切除手術後，咳血問題已完全緩解。經由該病例可知胸部 X 光呈顯異常並不能排除游離肺之可能性，而慢性反覆咳血的原因可能單獨源自未發現的游離肺。*( 胸腔醫學 **2013; 28: 253-259**)*

關鍵詞：游離肺，慢性咳血，支氣管肺葉隔離

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