

Acute Pulmonary Embolism and Occult Lung Adenocarcinoma: A Case Report of Trousseau's Syndrome

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In patients with underlying malignancy, systemic venous thromboembolism (VTE) is a common complication in the cancer-related hypercoagulable state. Under certain circumstances, systemic VTE may be the only presentation before cancer is diagnosed. Acute pulmonary embolism (PE) is a severe form of systemic VTE. Its symptoms manifest from asymptomatic state, dyspnea, chest pain, and syncope, to sudden circulatory collapse. Acute PE is a less common diagnostic entity in Asian countries than in Western countries. In addition, patients with acute PE seem to have a higher cancer occurrence than those with other mild VTE presentations. This population difference leads to an underestimation, and therefore, delays in the early detection of an occult cancer. Herein, we report a 54-year-old man who was admitted due to acute PE. He was finally diagnosed with lung adenocarcinoma with multiple liver and bony metastasis. However, he had symptoms related to acute PE only, and no cancer-related complaints were noted. Based on this unusual case experience, we suggest a detailed search for occult malignancy is crucial to prevent a delayed diagnosis in patients presenting with acute PE without a known etiology of thrombosis. (*Thorac Med* 2007; 22: 243-248)

Key words: acute pulmonary embolism, lung adenocarcinoma, Trousseau's syndrome

Introduction

Systemic venous thromboembolism (VTE) includes deep vein thrombosis (DVT) and acute pulmonary embolism (PE). Some risk factors are inherited, such as a deficiency of antithrombin III, protein C, or protein S; and acquired, for example, old age, smoking, obesity, oral contraceptive pill use, atherosclerosis, or malignancy [1]. The events increase sharply after the age of

60, and acute PE accounts for the majority of the increase. If all inherited and acquired causes are excluded, VTE is classified as idiopathic. More and more studies have revealed that idiopathic VTE is the sign of occult malignancy, no matter the tumor size or the clinical manifestations of DVT or acute PE. Acute PE is the most severe form of systemic venous thrombosis. It is interesting that there is far less incidence of acute PE in Asian populations than in Western populations.

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This population difference leads to an underestimation, and therefore, delays in the early detection of an occult cancer if the patient was treated only with thrombolytic therapy.

In this report, we describe a patient who was finally diagnosed with lung adenocarcinoma with liver and bony metastasis. However, he had the manifestations of acute PE only. We also discuss the studies of low-molecular weight heparins (LMWHs) in cancer patients with systemic VTE. In relatively small populations of acute PE patients among idiopathic VTE patients, clinicians should keep in mind the possibility of an occult malignancy.

Case Report

A 54-year-old man was admitted to this hospital because of fever, dyspnea, chest pain without radiation, and productive cough with blood-twisted sputum. The patient was a gardener in good health, without any underlying disease. He sometimes took Chinese herbal medications for his arthralgia. He had no previous smoking history, no drinking, and reported no allergies.

One month prior to this admission, he noticed that he had dyspnea on exertion and bilateral lower limbs edema, especially on the left side when walking. There was no improvement after he visited his family physician and received some medications. Because the fever, productive cough, and chest pain were aggravated, he visited the chest clinic in this hospital. A chest radiograph was taken and revealed consolidation in the left lower lung field (Figure 1); pneumonia was suspected. After a 1-week course of antibiotics therapy, he reported no improvement, but had cough with blood-twisted sputum in the following visit. Persistent dyspnea on exertion, bilateral lower limbs painful edema, and low oxygenation of

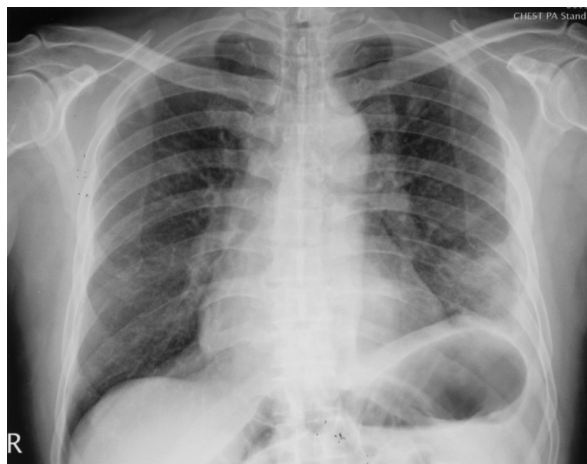


Fig. 1. A chest radiograph showing consolidation in the left lower lung field

about 90~95% in the pulse oxymeter, were noted in the clinic. The blood test for D-dimer revealed a 3561 ug/L level. With the impression of acute pulmonary embolism, the patient was admitted.

Blood levels of electrolytes and serum levels of urea nitrogen, creatinine, aspartate aminotransferase, alanine aminotransferase, and glucose were normal. His white-cell count was 15,800 per cubic meter with 3% band forms and 71% segment forms. Lung perfusion scan on the second hospital day revealed a multiple ventilation-perfusion mismatch (Figure 2). On the third day, his chest computed tomographic (CT) scan with contrast showed multiple filling defects, mainly within the segmental branches of the pulmonary arteries and more severe on the right side, compatible with the pulmonary embolism diagnosis (Figure 3). The lower limbs color duplex showed DVT of both femoral and popliteal veins. In addition, multiple subaortic tumor growth and liver nodules were also noted on the chest CT scan. Bone scan confirmed multiple bony metastasis. The cytology of left-side pleural effusion revealed adenocarcinoma. The lung and liver tumors were proved to be adenocarcinoma in the

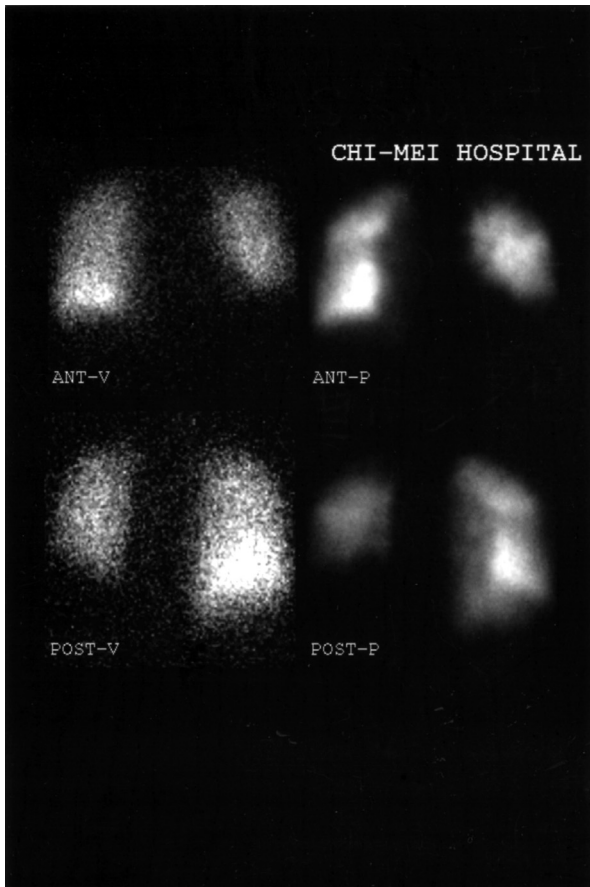


Fig. 2. Lung perfusion scan revealing a multiple ventilation-perfusion mismatch

ultrasonographic-guided lung and liver biopsy.

The final diagnosis was adenocarcinoma of the lung with malignant pleural effusion, and multiple bony and liver metastasis. He was treated with heparin and oral warfarin for acute PE and DVT. Chemotherapy with gemcitabine and cisplatin was prescribed. Local palliative radiotherapy was also administered for multiple bony metastases. The patient was discharged in a stable condition, and was followed up at the chest clinic.

Discussion

In 1861, Dr. Armand Trousseau reported a

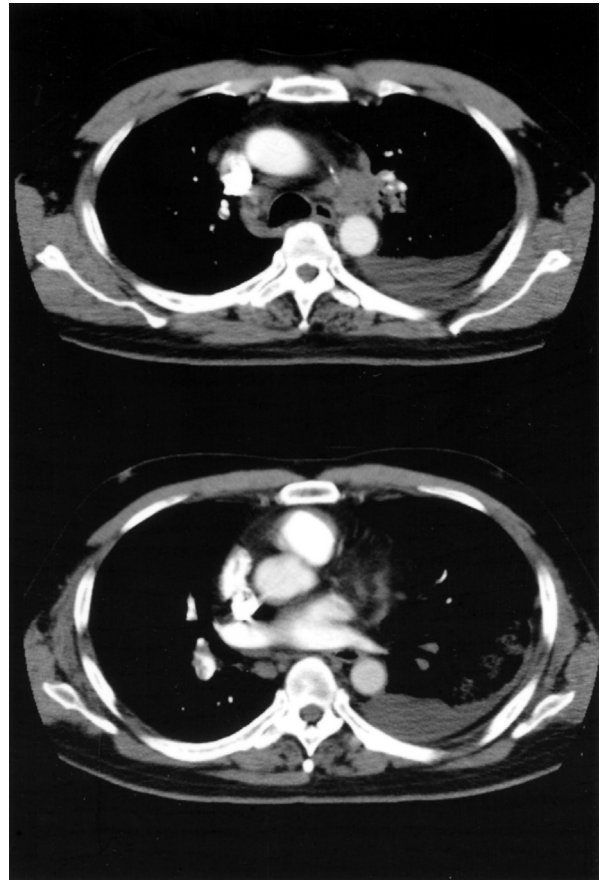


Fig. 3. Chest computed tomographic scan with contrast showing subaortic tumor growth and multiple filling defects within segmental branches of the right-side pulmonary arteries, compatible with the pulmonary embolism diagnosis.

patient with cancer and cancer cachexia who developed migratory thrombophlebitis [2]. In patients with underlying malignancy, the cancer-associated hypercoagulable states may cause spontaneous blood clotting in the deep veins of the extremities, or in superficial veins anywhere in the body. These hypercoagulable states result in recurrent deep venous thrombosis that can migrate anywhere in the body, and chronic disseminated intravascular coagulopathy [3]. This paraneoplastic syndrome was called Trousseau's syndrome. Trousseau's syndrome associates migratory thrombophlebitis with an underlying malignancy, such as lung, colon, pancreatic, or

gastric cancer. Ironically, Dr. Armand Trousseau was finally found to have gastric cancer when he observed that he himself had this sign [2]. In some studies, about 60% of patients with cancer manifest at least 1 episode of thrombophlebitis and migratory thrombophlebitis [4]. It is very clear that systemic VTE may occur in the form of mild migratory thrombophlebitis, as well as DVT, acute PE, or both, in patients with preexisting cancer.

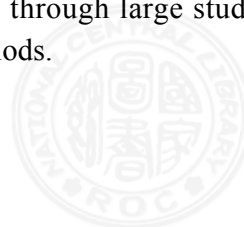
More and more studies have discovered that idiopathic VTE is the sign of occult cancer. Schulman *et al.* demonstrated the cancer incidence in patients with a first episode of systemic VTE without a preexisting malignancy diagnosis. In that study, a total of 111 patients were diagnosed with cancer during a mean follow-up of 8.1 years, accounting for 13.0 percent in 854 patients. There was a malignancy incidence of 3.4% in the first year of the VTE episode, and a 1.3~2.2% incidence in the following 5 years [5]. In elderly persons with idiopathic VTE, occult malignancy should be considered. In a large postmortem examination study, adenocarcinoma was the most common histopathologic type in thrombotic PE, followed by leukemia. The digestive and respiratory tracts were the top 2 involved systems [6].

In Taiwan, 2 studies were designed to study the incidence of cancer in patients with a clinical diagnosis of DVT and acute PE respectively. Lee HC *et al.* retrospectively reviewed 245 patients with the diagnosis of DVT between 1989 and 1995. Among these patients, 40 (16.3%) had cancer. Adenocarcinoma was the most common type of malignancy (25 patients, 62.5%), and the gastrointestinal tract (16 patients, 40%) was the most frequently involved system [7]. Chen LK *et al.* published their study on the association of occult malignancy with acute PE. Forty-five patients with acute PE, from July 1993 to June

1998, were included in this study. The cancer incidence after or concomitant with acute PE was 47.37%, significantly higher than in previous reports [8]. Adenocarcinoma was the most common histological type. The occult cancer origins were mainly in the gastrointestinal tract, similar to reports from Western countries and Lee HC's study. In these studies, there seemed to be a higher cancer incidence in the more severe form of systemic VTE, that is to say, higher in patients with acute PE.

These study results imply a practical clinical guideline in the search for unknown malignancy in patients with acute PE. In addition to the serum level of D-dimer and the lung perfusion scan, chest CT with intravenous contrast has become a principal diagnostic tool in an integrated approach to the evaluation of patients with suspected PE. The chest CT is at least as accurate as invasive pulmonary angiography, even in the detection of pulmonary subsegmental embolization. Because the majority of occult cancers hide in the gastrointestinal tract [5-8], the CT scan may extend its scanning area to the abdomen in patients with acute PE to search for possible sites of unknown cancer.

Recent studies have shown that the hemostatic system plays a key role at different stages in the process of tumorigenesis [9-10]. In their studies, Schulman *et al.* also found a lower cancer incidence risk among patients treated with oral anticoagulants for 6 months than among those treated for 6 weeks [5]. It was supposed that vitamin K antagonists express an antineoplastic effect by influencing the pathway involving tissue factor and factor VIIa, which inhibit tumor invasion [9]. It will be important to clarify what mechanisms of antithrombotic agents exert a possible antineoplastic effect, through large studies with long follow-up periods.



In conclusion, acute PE is uncommonly seen in Asian populations and should be considered as a pre-cancer sign. This condition requires a detailed workup for an underlying malignancy. CT scan is the diagnostic tool of choice, and should be performed in not only the chest, but also the abdomen, whenever possible.

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急性肺栓塞和潛藏的肺腺癌：Trousseau 症候群之一病例報告

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因為癌症會造成高凝血狀態，所以全身靜脈血栓栓塞症在癌症病人身上是很常見的併發症。在特定情形下，全身靜脈血栓栓塞症可能是病人在最終被發現有癌症前唯一的臨床表現。急性肺栓塞是一種嚴重的全身靜脈血栓栓塞症，它臨床表現不一，從沒有症狀、呼吸喘、胸痛、昏厥、甚至到突然猝死都有。相較於西方，急性肺栓塞在東方是比較罕見的診斷。此外，對照於比較輕微的全身靜脈血栓栓塞症，在急性肺栓塞的病人似乎具有比較高的癌症發生率。這種東西方的人群差異讓本病比較少被診斷出來，因此可能會延後發現病人其實潛藏了未知癌症。在本篇文章中，我們報告一名 54 歲的男性病人因為急性肺栓塞住院，最後他被診斷出肺腺癌併多處轉移。然而，除了因為急性肺栓塞造成的臨床表現外，這個病人並沒有任何和癌症相關的不適症狀。基於這種罕見的病人經驗，我們建議在沒有明顯容易造成血栓症原因的病人，如果出現了急性肺栓塞，徹底地檢查體內是否藏有未知惡性腫瘤是相當重要的工作。(胸腔醫學 2007; 22: 243-248)

關鍵詞：急性肺栓塞，肺腺癌，Trousseau 症候群

