

EXTENSIVE PULMONARY THROMBOEMBOLISM AS FIRST SIGN OF A LUNG CANCER - CASE REPORT

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EXTENSIVE PULMONARY THROMBOEMBOLISM AS FIRST SIGN OF A LUNG CANCER - CASE REPORT (ABSTRACT): *Background:* The malignancies increase the risk for thromboembolic disease, which may be present as an additional clinical entity or as a first sign in a patient with occult neoplastic disease. *Case Report:* We present the case of a 45 years old man initially admitted in emergency due to dyspnea, hypoxemia and hemoptysis. The CT scan and ultrasound exam diagnosed a thromboembolism. The anticoagulant therapy was performed. After one month the patient was readmitted for the same symptoms and the CT scan revealed an atelectatic opacity in the base of the left lung and extension of the thromboembolic disease in the superior vena cava and right atrium. The bronchoscopy including ultrasound and biopsy revealed an adenocarcinoma and adenopathies (stage IIIB - T₂N₃M₀). Chemotherapy has been initiated and, after 3 cycles, partial regression of the tumor and significant regression of thromboembolic disease were revealed. However, both malignant and thromboembolic disease recurred within 6 months, despite optimum anticoagulation and completion of 6 chemotherapy cycles and the patient died 7 months after initial diagnosis. *Conclusions:* The present case demonstrates potential difficulties in the management of thromboembolic disease in patients with lung malignancies where the usual treatment with anticoagulants may fail. The management of the primary disease by chemotherapy may provide a transient regression of thromboembolic symptoms if malignancy regresses. However, definitive control of the disease is difficult to achieve in these cases.

KEY WORDS: THROMBOEMBOLISM, LUNG CANCER

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INTRODUCTION

Thromboembolic disease may be present either as an additional clinical entity in a patient with known lung cancer or as a novel clinical entity in a patient with occult disease [1]. It is demonstrated that malignancies increase the risk for thromboembolic disease [1,2]. The manifestation of thromboembolic disease may extend from simple deep vein thrombosis (DVT) to pulmonary embolism (PE) and disseminated intravascular coagulation (DIC) [1-3]. The presence of thromboembolic disease augments the risk of mortality in patients with cancer and treatment is necessary [1-3]. However, the management of thromboembolic events in this setting may be challenging for physicians. The present case reports our experience with a patient with severe thromboembolism and lung cancer.

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CASE REPORT

A 45-year-old man was admitted due to dyspnea, hypoxemia and hemoptysis. His medical history was unremarkable except for smoking (30 pack years). On admission his temperature was normal. Blood pressure was 125/70 mmHg and SpO₂ was 90% on air. Clinical examination revealed abnormal alveolar sounds in the base of the left lung, edema and pain in the inferior extremities. Cardiac examination showed tachycardia, hepatic-jugular reflux, and left basic chest pain.

Chest X-ray showed a left base lung opacity and mediastinal enlargement. ECG revealed no ischemic changes but sinus rhythm and an aspect S1Q3 characteristic for pulmonary embolism were present. Chest CT revealed pulmonary embolism in the left pulmonary arteries. Cardiac ultrasound showed FELV 50%, left ventricle (LV) and right ventricle (RV) were not dilated. Ultrasound revealed a thrombus 3.0 x 1.5 cm situated in the cavity of right atrium. Ultrasound of the lower extremities showed thrombus in both left and right vena saphena internal and external with bilateral iliac extension and thrombosis of the deep vein of the right and left tibia. Ultrasound of the upper extremities showed thrombosis in both right and left deep brachial veins. Thus, thromboembolism was diagnosed.

The patient was started on anticoagulants by heparin followed 7 days later by Sintrom[®]. An International Normalized Ratio (INR) between 2.5 and 3.5 was achieved and was subsequently checked on a weekly basis. Diagnostic test results indicated that the patient was negative for Leyden factor, anti-thrombin III levels were normal, anti-cardiolipines antibodies were negative, anti-antigen antibodies were absent, and Farr-test was negative.

Four weeks later, the patient was readmitted with symptoms of deep vein thrombosis and dyspnea. INR was 2.7. A new chest X-ray and CT demonstrated a non-specific opacity in the base of the left lung indicating infectious pneumopathy and atelectasia. Ultrasound of the lower extremities and upper extremities showed increased deep vein thrombosis with extension, especially on upper extremities deep veins. Based on CT findings, a bronchoscopy including ultrasound (EBUS) was performed to evaluate the possibility of lung malignancy. After switching from Sintrom[®] to low molecular weight heparin (LMWH), the patient underwent EBUS examination which revealed enlarged lymph nodes in the 4L, 7, and 4R stations and TBNA revealed lung adenocarcinoma.

A relevant diagnostic algorithm was applied to categorize the malignancy and to reevaluate the thromboembolic disease. Lung carcinoma proved to be of IIIB grade (T₂N₃M₀) while there was evidence of extension of the thromboembolic disease: the known thrombus was evident in the superior vena cava and in the right atrium (Fig. 1).

Chemotherapy (Cisplatine - Alimta) was initiated while LMWH was continued with regular examination of AntiXa serum levels. After 3 curative chemotherapy cycles there was evidence of partial regression of mediastinal tumor lesions and significant regression of thromboembolic disease (Fig. 2).

However, both malignant and thromboembolic disease recurred within 6 months, despite optimum anticoagulation and completion of 6 chemotherapy cycles (Fig. 3).

A second chemotherapy regimen with taxanes was then introduced which resulted in stabilization of the malignancy and partial regression of the thromboembolic disease after 3 months (upon completion of 3 chemotherapy cycles).

However, both malignant and thromboembolic disease recurred with new right atrium thrombus complicated by right posterior cerebral arterial embolism. The patient died 7 months after initial diagnosis.

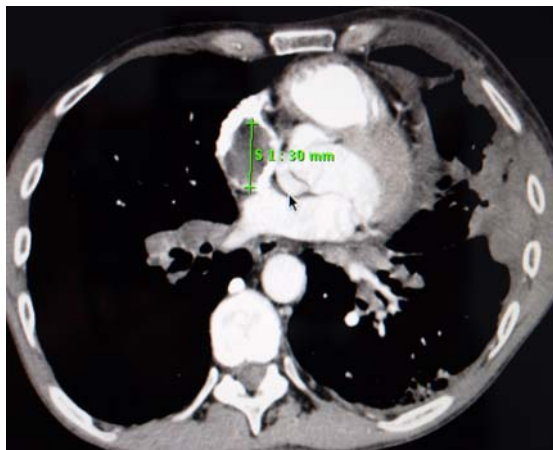


Fig. 1 Thoracic CT on second admission
Voluminous thrombus in the right atrium



Fig. 2 Thoracic CT after 3 chemotherapy cycles:
Good response of lung cancer to chemotherapy and disappearance of the right atrium thrombus and pulmonary embolus.



Fig. 3 Thoracic CT after 6 chemotherapy cycles
Disease progression and new pulmonary embolus

DISCUSSIONS

This report illustrates that the management of thromboembolic disease, which complicates lung malignancies, may pose additional clinical challenges. The course of thromboembolic disease correlates with the course of malignancy, despite optimum treatment with oral anticoagulants or LMWH.

The disease may regress during the period where lung cancer responds to chemotherapy but can occur in the absence of a treatment response.

It is well known that malignancies may increase the risk for thromboembolic disease which in turn may augment the risk of mortality in patients with cancer. Several mechanisms may contribute to the development of thromboembolism in malignancies such as neoangiogenesis, proteases activity, heparin-like glycosaminoglycane, and genetic factors [4,5]. The disease presentation may extend from simple DVT to PE and DIC. Thromboembolic disease may be present as a concomitant clinical entity in a patient with known lung cancer or as a dynamic feature in a patient with occult disease. In this case, thromboembolic disease was introduced as a result of occult disease. Thus, this case demonstrates that occult malignancy should always be considered in patients who present with thromboembolic disease without any other cause for thrombophilia, especially when they are young and have risk factors for malignancy (i.e., smokers).

Previous studies reported that LMWH may be effective in the treatment of thromboembolic disease and that it may be more advantageous than unfractionated heparin or oral agents [6]. LMWH may be easier to monitor and may be safer than unfractionated heparin or oral agents [6]. However, as this report demonstrates, the management of thromboembolic disease in the setting of malignancy is challenging. Thromboembolic disease may not respond well to anticoagulation treatment. On the other hand, more invasive measures, such as vena cava filter placement, may not always be effective and may introduce major complications when extensive thrombosis is already evident [7-9]. In addition, the management of thromboembolic disease may be affected by the course of the malignant disease. Stocking et al. [10] showed that progression of malignancy may facilitate the development of thromboembolic events. In this case, the disease appeared to respond to the treatment for cancer, such as chemotherapy. The most plausible explanation for this “anticoagulative effect” of chemotherapy may be common pathways which are involved in the pathogenesis of both malignant and thromboembolic disease. However, the exact mechanism has yet to be elucidated.

CONCLUSIONS

The present case demonstrates potential difficulties in the management of thromboembolic disease in patients with lung malignancies where the usual treatment with anticoagulants may fail. The management of the primary disease by chemotherapy may provide a transient regression of thromboembolic symptoms if malignancy regresses. However, definitive control of the disease is difficult to achieve under these conditions.

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