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Trousseau's Syndrome: A Case Report

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Abstract

Venous thromboembolism is a common complication of oncological disease and antineoplastic therapy and an important cause of morbidity and mortality. Trousseau's syndrome consists in thromboembolic events that precede or accompany the diagnosis of cancer. The treatment consists of anticoagulation and, most importantly, in the treatment of the underlying oncological disease. This syndrome generally translates as an advanced tumour, with a more aggressive behaviour and lower survival.

Keywords

Trousseau's syndrome; Recurrent venous thrombosis; Heparin; Malignancy; Lung adenocarcinoma

Core Tip

This case describes a patient with metastatic lung cancer who had several thromboembolic events accompanying the diagnosis of cancer and during the first cycle of chemotherapy. Some of the thromboembolic events occurred under anticoagulation, which suggests that this is a case of Trousseau's syndrome.

Introduction

Venous thromboembolism is a common complication of oncological disease and antineoplastic therapy and an important cause of morbidity and mortality [1]. Trousseau's syndrome (TS), described for the first time by the French physician Armand Trousseau in 1865, consists in thromboembolic events that precede or accompany the diagnosis of cancer [2]. This syndrome is characterized by recurrent and migratory venous thrombosis, arterial embolism, disseminated intravascular coagulation, microangiopathic haemolytic anaemia and non-bacterial endocarditis [2]. Although it may be associated with any kind of malignancy, it is most often related to pancreatic, lung, prostate, gastric, colorectal, ovarian and breast cancer [2,3].

Physiopathology of TS is complex and not yet well understood, reflecting the multiplicity of overlapping and interacting mechanisms that were described to explain the increased incidence of thrombosis in patients with malignancies [4,5]. Explanations of the aetiology of TS include hypercoagulability promoted by tumour cells which produce and release various products that induce platelet aggregation and promote coagulation. Changes in antithrombotic and prothrombotic proteins, cytokine activation are also proposed mechanisms [6]. Vessel wall damage and vessel stasis from direct compression of the tumour are other possible causes [1,4]. These alterations can eventually lead to chronic disseminated intravascular coagulation [6].

The treatment consists of anticoagulation and, most importantly, in the treatment of the underlying oncological disease [1,2].

Case Report

A 52-year-old man, ECOG performance status 1, former smoker, with a history of hypertension and obesity (BMI 32.95), started complaining of dyspnoea, cough, occasionally with scarce haemoptysis, and chest pain in August 2017. Two months later, a chest radiography revealed a suspicious pulmonary nodule in the right lower lobe. A thoracic CT scan was performed and showed a solid and nodular lesion in the right lower lobe with 50 x 38 mm and an adjacent cavitated nodule compatible with metastasis; mediastinal and hilar adenopathies and a lytic lesion in the D9 vertebral body (Figure 1). On the same day, a superficial vein thrombosis of the right internal saphenous vein was diagnosed in the context of swelling and pain in the right leg, therefore the patient was started on enoxaparin 60 mg, once daily. A thoracic biopsy of the lung lesion revealed a lung adenocarcinoma. The tumour was stage IV with metastasis in lung, lymph nodes, bone and right adrenal gland. The *ALK* rearrangement was negative and the tumour stained strongly positive for PD-L1. As the amount of tissue was insufficient for determining the *EGFR* mutation, the patient was highly symptomatic and pembrolizumab required a special authorization, it

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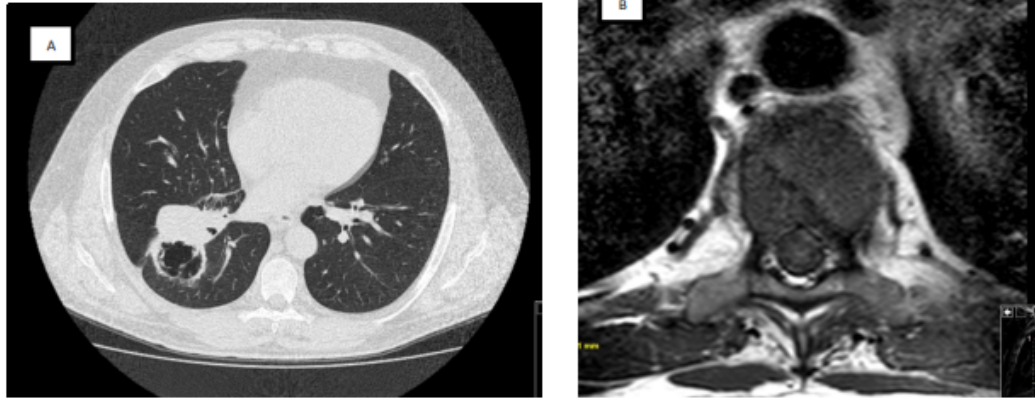


Figure 1: Chest computed tomography (axial view) showing right upper lobe mass at diagnosis (A); lytic lesion in D9 vertebral body detected by magnetic resonance imaging of the spine (B).

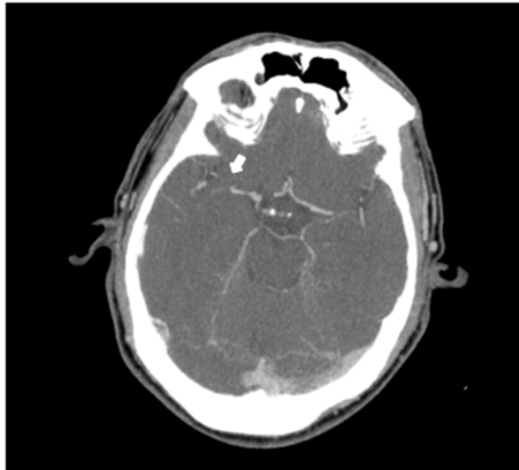


Figure 2: Head angiography CT showing an occlusive blood clot on the M2 segment of left middle cerebral artery with no signs of cerebral ischaemia.

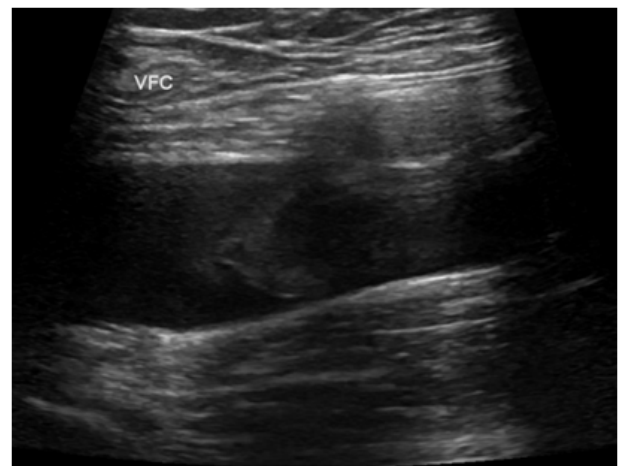


Figure 3: Left femoropopliteal vein thrombosis confirmed on doppler ultrasound after the patient started chemotherapy.

was decided to start chemotherapy. The case was discussed on the multidisciplinary tumour board and palliative systemic therapy was proposed. The patient initiated palliative chemotherapy with cisplatin 75 mg/m² and pemetrexed 500 mg/m² on day 1 of 21-day cycles. Three days after the first cycle, the patient felt acute pain and oedema on the left leg with a doppler ultrasound confirming a left femoropopliteal thrombosis and ipsilateral superficial femoral vein thrombosis (Figure 2). The dose of enoxaparin was adjusted to the therapeutic range of 1.5 mg/Kg/day (150 mg once daily). Fourteen days later, on D17 of cycle 1, the patient was admitted to the emergency department with dysarthria, labial commissure deviation and right hemiparesis. Head angiography CT showed an occlusive blood clot on the M2 segment of left middle cerebral artery with no signs of cerebral ischaemia (Figure 3). At the time of this event, unbeknownst to the oncology team, the patient's anticoagulation had been changed to rivaroxaban 20 mg daily. For those two reasons, a salvation thrombectomy was performed. This procedure was complicated with a small subaracnoideal haemorrhage. The patient had a total recovery of the neurological deficits 24 hours after the procedure. At discharge, enoxaparin was restarted with a lower dose, 60 mg twice daily, considering the recent bleeding episode.

Taking into account the absence of neurological sequelae after this cerebrovascular event and the advanced oncological disease, the

risks and benefits of continuing chemotherapy were discussed with the patient and his family and it was decided to continue treatment.

The patient tolerated well the following cycles of chemotherapy, with light asthenia, constipation controlled with purgatives and occasional nausea. After the fourth cycle, he had a partial response to the treatment (Figure 4) and a pemetrexed maintenance therapy was proposed. After the acute cerebrovascular event, no new thromboembolic events occurred. The patient continued maintenance therapy. The evolution of symptoms, thrombotic events and lung cancer diagnosis and treatment are summarized in the Figure 5.

Discussion

The diagnosis of an advanced oncological disease and the occurrence of several thromboembolic events, including some under anticoagulation, suggest that this is a case of Trousseau's syndrome. Proposed mechanisms for the development of this entity include changes in antithrombotic and prothrombotic proteins, cytokine activation, and endothelial dysfunction accompanying the neoplastic disease [6]. High degree of suspicion of this syndrome is essential to carry out the diagnostic investigation when an unexplained thrombotic event occurs. The prevalence of occult cancer in patients with idiopathic thromboembolism is about 4-10% [6].

TS generally translates as an advanced tumour, with a more aggressive behaviour and lower survival [7].



Figure 4: Chest computed tomography (axial view) showing tumour's response following 3 cycles of chemotherapy.

Conclusion

This report describes a case of TS associated with lung cancer diagnosed upon the investigation of a suspicious lung lesion. Our patient developed several venous thrombotic events in his lower limbs and an ischaemic cerebrovascular event. The presence of an undiagnosed, and later not yet treated, malignancy, and the anticoagulation undertreatment that ensued, may have triggered the thrombotic state, leading to an ischaemic stroke.

When facing such events, the implementation of effective anticoagulation therapy and treatment of the underlying neoplasm is the proper medical approach [8].

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