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Case Report

A case of anticoagulant treatment-resistant Trousseau syndrome controlled by treatment of the underlying lung adenocarcinoma: Utility of monitoring D-dimer levels

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ABSTRACT

We report herein a 70-year-old woman, with repeated thromboembolic events, including three cerebral embolisms and two venous thromboembolisms, despite adequate anticoagulant therapy. Trousseau syndrome was suspected, and she was diagnosed as having lung adenocarcinoma. Chemoradiotherapy was started, achieving improvements in the lung cancer, and thrombosis was also brought under control. Ten months later, the lung cancer relapsed, and second-line chemotherapy was performed. D-dimer levels, which had normalized after the first-line therapy, increased together with the relapse, but became negative again following the chemotherapy. In general, the prognosis of Trousseau syndrome is diverse. However, in this case, the course was good following the second lung cancer therapy: D-dimer levels did not increase, and there were no recurrences of thromboembolism. This experience reminds us the prognosis is most affected by whether the underlying disease is being effectively treated, and suggests that for Trousseau syndrome, despite adequate anticoagulant therapy, elevation of D-dimer levels should consider the recurrent cancer.

<**Learning objective:** We report herein a case with repeated thromboembolic events as a result of Trousseau syndrome due to lung cancer. Chemotherapy achieved improvements, but the cancer relapsed and second-line chemotherapy was done. D-dimer levels, which had normalized, increased with the relapse before again becoming negative. This experience reminds us that prognosis is affected by treating underlying disease and suggests that elevation of D-dimer levels should consider the cancer recurrence.>

Introduction

Malignant tumors are often accompanied by complications such as thromboembolism, caused by a hypercoagulable state of the blood, termed Trousseau syndrome. In 1865, Armand Trousseau first reported a comprehensive association between thrombosis and malignancy. He also suggested the importance of screening for malignancy when recurrent or idiopathic thromboembolic disease is encountered [1,2]. We report herein our experience in treating a patient who had repeated episodes of cerebral embolism and venous thromboembolism (VTE) of the lower extremities despite adequate anticoagulant therapy, and who was ascertained to have Trousseau syndrome as a complication of lung cancer. Treatment of the underlying lung cancer also

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resulted in long-term control of the refractory thrombosis, with no recurrent events.

Case report

The patient was a 70-year-old woman. She had been previously treated for hypertension, dyslipidemia, and rheumatoid arthritis. She had no family history of thromboembolism, and no history of smoking. In July 14, 2012, she experienced sudden speech difficulty and was examined by the neurosurgery department of a local hospital. Brain magnetic resonance imaging (MRI) showed infarct lesions scattered throughout the right inferior frontal gyrus, left frontal lobe, and right occipital lobe (first cerebral embolism). She was referred to the department of cardiology of another hospital from that neurosurgeon for complete cardiac examination. None of electrocardiography (ECG) or Holter ECG in that hospital yielded any findings of arrhythmia, such as paroxysmal atrial fibrillation, which may lead to cardiogenic embolism. Other systemic examinations of the patient were not performed. However, because of this shower of emboli, the possibility of a cardiac origin was considered, and the patient was started on dabigatran at 220 mg/day. On October 18, 2012, the patient experienced sudden weakness of the left arm. She was examined by the same hospital, and brain MRI showed fresh cerebral infarction in the right frontal lobe and left occipital lobe. Recurrence of cerebral embolism was diagnosed (second cerebral embolism), and the dose of dabigatran was therefore increased to 300 mg/day. On October 26, she was examined at the hospital because of onset of left homonymous hemianopia, and MRI indicated recurrence due to a fresh cerebral infarction in the right occipital lobe (third cerebral embolism). The patient was hospitalized, and dabigatran was replaced by warfarin. At discharge, prothrombin time-international normalized ratio (PT-INR) was 2.14 and activated partial thromboplastin time (APTT) was 46.4 s.

On December 4, 2012, she came to our hospital for consultation for cardiovascular disease, complaining of left lower-limb edema. PT-INR was 2.07, and D-dimer level was 27.6 μg/mL. Ultrasonography revealed fresh thrombus in the left popliteal vein, and she was hospitalized with a diagnosis of VTE. Continuous drip infusion of heparin and an increased dosage of warfarin brought the D-dimer level down to 7.2 μg/mL. Ultrasonography confirmed regression of the thrombus. At discharge, PT-INR was 3.28.

On January 23, 2013, we again examined the patient due to renewed exacerbation of the lower-limb edema. Ultrasonography showed occlusion due to an extensive fresh thrombus in the left superficial femoral vein (Fig. 1a), and the right popliteal vein (Fig. 1b). In addition, T2-weighted brain MRI showed areas of cystic degeneration and atrophic changes (Fig. 1c and d), thought to be associated with past cerebral infarctions. Since chest X-rays had shown a nodular shadow in the right middle lung field (Fig. 2a), chest contrast-enhanced computed tomography (CT) was performed and revealed a nodular shadow, 18 mm in diameter with an irregular margin in segment 3 of the right lung, leading to

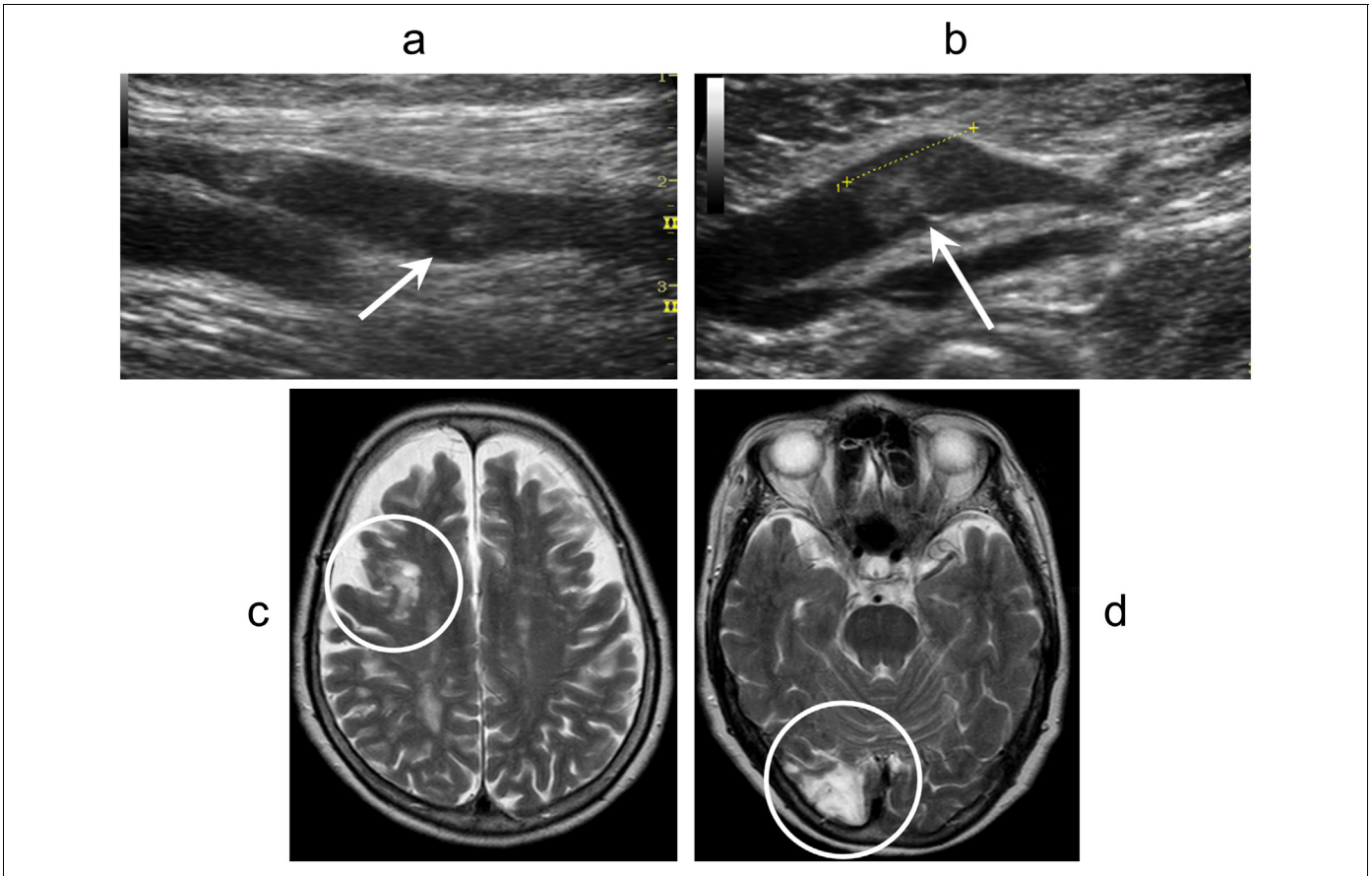

Fig. 1. Images of repeated thromboembolic events. Venous ultrasonography of lower extremities indicates an extensive fresh thrombus in the middle portion of the left superficial femoral vein (a) and a 13-mm thrombotic occlusion in the right popliteal vein (b). T2-weighted brain magnetic resonance imaging shows areas of cystic degeneration and atrophic changes are seen in the right frontal lobe (c) and right occipital lobe (d). These were thought to be associated with old cerebral infarctions.

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