

A Case of Cerebral Venous Thrombosis and Deep Venous Thrombosis Due to Hyperthyroidism with Increased Factor VIII Activity

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A 48-year-old woman was admitted to our hospital because of headache and fever. She was diagnosed with aseptic meningitis. Five days later, she had a seizure and developed left hemiparesis. Magnetic resonance imaging showed hyperintensity in the right parietal area on fluid attenuated inversion recovery imaging. She was diagnosed as having cerebral venous thrombosis (CVT) because the suprasagittal sinus was invisible on the venographic studies. Moreover, deep venous thrombosis (DVT) was detected in her left lower extremity. Laboratory findings showed hyperthyroidism and markedly increased factor VIII activity. This is a rare case of concomitant CVT and DVT induced by high factor VIII activity due to hyperthyroidism under the presence of meningitis, an additional risk factor for thrombosis.

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A 48-year-old woman was admitted with a 10-day history of persistent fever and headache. On neurological examination, she had no neurological deficits except for slight drowsiness and neck stiffness. Laboratory studies showed a white blood cell count of 7000/ μ L with neutrophil predominance and normal chemistry profiles, including C-reactive protein. Coagulation tests showed D-dimer of 3.3 μ g/mL. Cerebrospinal fluid examination showed elevated opening pressure (28 cm H₂O), mononuclear cell counts (155/ μ L) and protein levels (68 mg/dL). The

findings of head computed tomography and magnetic resonance imaging (fluid attenuated inversion recovery image, diffusion-weighted image, T1-weighted image, and T2-weighted image) were unremarkable. She was diagnosed as having aseptic meningitis and treated with acyclovir. Five days later, she developed a seizure and left hemiparesis. D-dimer level elevated to 8 μ g/mL. Follow-up magnetic resonance imaging showed hyperintensity in the right parietal area on fluid-attenuated inversion recovery imaging (Fig 1, A). She was diagnosed as having cerebral venous thrombosis (CVT) because the suprasagittal sinus was invisible on MR venography and cerebral angiography (Fig 1, B and C). Moreover, deep venous thrombosis (DVT) was detected in her left lower extremity by ultrasonography and contrast-enhanced computed tomography (Fig 1, D and E). The etiology of CVT and DVT was investigated by comprehensive assessment of coagulation function. She had not been taking oral contraceptives. Protein C and S levels were within normal ranges, and lupus anticoagulant, anticardiolipin antibody, and anticardiolipin- β 2GP1 complex antibodies were negative, but factor VIII activity was markedly increased (301.3%, normal range: 78.0%-165.0%). Further investigation of hormonal

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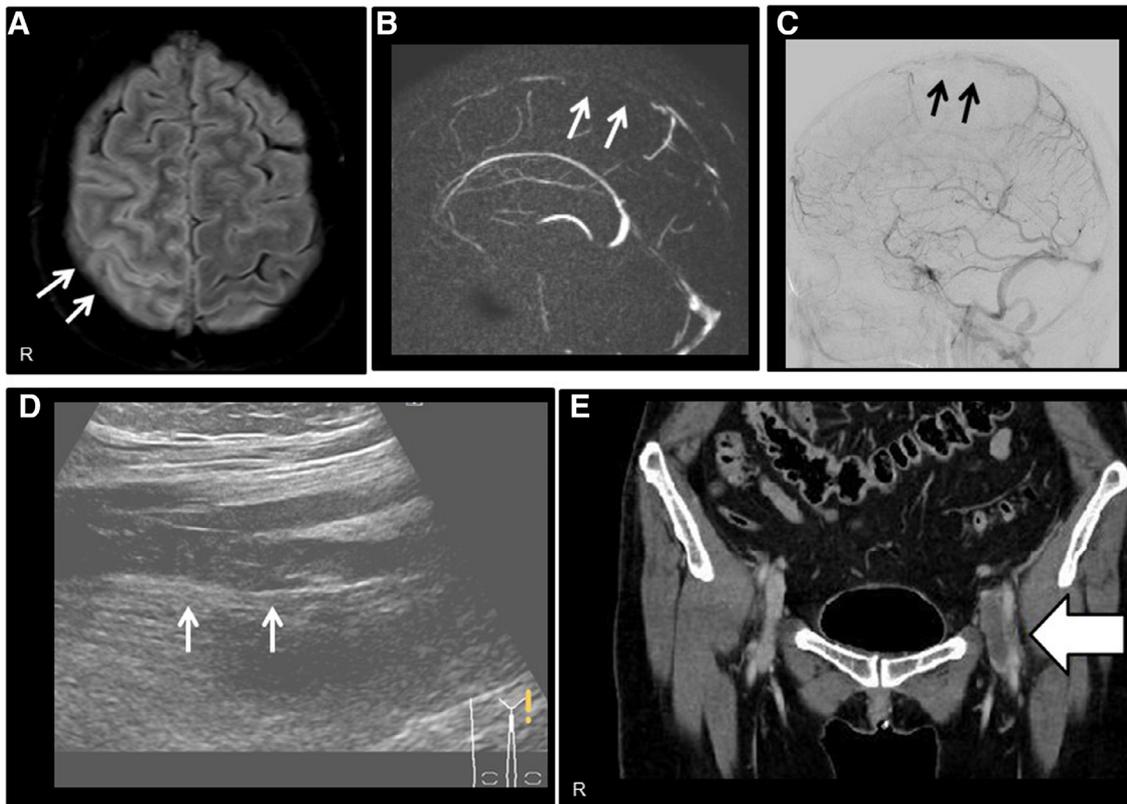


Figure 1. (A) MRI 14 days after onset of a seizure and left hemiparesis shows high intensity in the right parietal area on the FLAIR image (arrow). (B and C) MR venography (B) and cerebral angiography (C) 15 days after onset of symptoms show absence of flow in the suprasagittal sinus (arrow). (D and E) Echography (D) and contrast-enhanced CT (E) 25 days after onset of symptoms demonstrate deep venous thrombosis in her left common femoral vein (arrow).

activity possibly affecting the coagulation system showed hyperthyroidism with increased free triiodothyronine (6.16 pg/mL, normal range: 2.24-3.94 pg/mL) and free thyroxine (3.84 ng/dL, normal range: 0.77-1.59 ng/dL) and decreased thyroid-stimulating hormone (<0.01 μ IU/mL, normal 0.34-4.22 μ IU/mL). She was treated with inorganic iodide in addition to warfarin following intravenous heparin. Three weeks after administration of inorganic iodide, both thyroid function and factor VIII levels were normalized. She was discharged on day 63 with no neurological deficit.

Discussion

A highly significant increase in factor VIII activity is noted in hyperthyroid patients, and its normalization is accompanied by recovery to the euthyroid state,¹ which is compatible with the treatment outcome of the present patient. High factor VIII activity confers a strong risk of DVT and CVT.² However, only 3 (1.3%) of 155 patients with DVT showed hyperthyroidism,³ and in 624 patients with CVT, only 11 (1.7%) were reported to have thyroid disease.⁴ The mechanisms for a hypercoagulable state in thyroid disease include not only increased levels of factor VIII but also endothelial dysfunction and increased platelet adhesion.³ Therefore, CVT due to hyperthyroidism

with increased factor VIII levels could be much rarer,⁵⁻⁹ and the presence of additional risk factors might facilitate the onset of venous thrombosis. In fact, 50% of reported patients with CVT associated with hyperthyroidism and increased factor VIII levels were taking oral contraceptives, a well-known risk factor for CVT. In the present case not on oral contraceptives, the onset of CVT was presumably 15 days after the onset of aseptic meningitis (5 days after admission). The presence of infectious diseases including meningitis is also known as an important risk factor triggering CVT.¹⁰ Of note, the present patient had concomitant CVT and DVT. Although comorbidity of these 2 conditions is not surprising, no previous reports of hyperthyroidism-induced venous thrombosis are available. In cases of cerebral thrombosis, we re-emphasize the need for comprehensive risk factor investigations such as coagulation tests including factor VIII, thyroid evaluation, and signs of infection, as well as assessment of other venous thromboembolic events.

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