Dural Sinus Thrombosis in a Patient with Protein S Deficiency
—Case Report—

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Abstract

A 23-year-old female presented with dural sinus thrombosis caused by protein S deficiency. She suffered superior sagittal sinus thrombosis 6 days after delivering her first child. Past history showed deep vein thrombosis at the age of 20. While conservative management was initiated because of the potential risk of increasing intracranial hemorrhage, several hours later she deteriorated rapidly because of severe brain swelling with massive hemorrhage. The patient died despite surgical decompression. Autopsy disclosed organized thrombus in the superior sagittal and transverse sinuses. Although the total concentration of protein S was normal, the free protein S concentration and protein S activity were decreased. Protein S deficiency is a rare cause of dural sinus thrombosis, but is associated with a high mortality rate, so accurate diagnosis and urgent intervention are required.

Key words: cerebral sinus thrombosis, protein S, delivery, intracranial hemorrhage, brain swelling

Introduction

Protein S is a plasma protein that functions as a cofactor for the anticoagulant activity of activated protein C. Deficiency of protein S may result in recurrent episodes of superficial and deep venous thrombosis and pulmonary emboli. Protein S deficiency is an established risk factor for venous thrombosis, most commonly involving the deep vein of the leg and pelvis veins. Cerebral venous thrombosis is a rare complication of protein S deficiency, with only 18 previous cases of dural sinus thrombosis. We describe the occurrence of superior sagittal sinus (SSS) thrombosis in a patient with protein S deficiency, causing a rapid decline in clinical condition.

Case Report

A 23-year-old female developed severe headache, nausea, and vomiting 6 days after completion of an uneventful first pregnancy, labor, and delivery. She was uneventful in the postpartum period without infection or disseminated intravascular coagulation. She was admitted to our hospital with convulsions and loss of consciousness. She had received warfarin treatment for deep vein thrombosis at age 20 years, but had received no anticoagulant medication during the following 2 years. No oral contraceptive medication was taken.

Neurological examination found she was drowsy with left hemiparesis. Computed tomography (CT) revealed a patchy distribution of hemorrhage in the right parietal lobe accompanied by mild brain swelling (Fig. 1). Angiography showed occlusion of the SSS (Fig. 2). Conservative management was initiated with administration of glycerol, but she deteriorated rapidly over 7 hours to a Glasgow Coma Scale score of 4 as a result of massive hematoma in the right parietal lobe (Fig. 3). External decompression was performed emergently, but she died 4 days later. Autopsy of brain disclosed organized thrombi in the SSS and the transverse sinus. Other venous thrombosis was not disclosed because whole body autopsy was not performed.

Laboratory data at admission were as follows: Prothrombin time was 11.9 seconds (normal range 10.4 to 12.4), partial thromboplastin time was 30.7 seconds (26 to 31), platelet count was $275 \times 10^9/l$,
bleeding time was 3 minutes and 30 seconds, total protein S level was 91% (65% to 130%), free protein S level was 34% (60% to 150%), protein S functional activity was 24% (60% to 150%). Anticardiolipin antibody was not present. Protein C and antithrombin III levels were not measured. Clinical deterioration was so rapid that laboratory data could not influence on planning of treatments.

Discussion

Protein S is a vitamin K-dependent plasma protein which inhibits blood clotting by serving as a cofactor for activated protein C. Activated protein C binds to protein S attached to the phospholipids of platelets or the vascular endothelial surface. This protein C-S complex inhibits the clotting cascade by enzymatic inactivation of factors Va and VIIIa and also promotes fibrinolysis by dissociating tissue plasminogen activator from plasminogen activator inhibitor. The functional activity of protein S depends on the free form, which normally represents up to 40% of total protein S. The remaining protein is bound to a complement cofactor, C4-binding protein.

Protein S deficiency may be caused by congenital or secondary etiologies. Secondary deficiency is caused by liver disease, vitamin K deficiency, warfarin exposure, and nephrotic syndrome. Our patient had received warfarin for deep vein thrombosis, but not during the 2 years preceding sinus thrombosis. Also, she had an uneventful postpartum course. Therefore, a secondary protein S deficiency is unlikely in our case. Hemostatic imbalance could have caused predisposition to development of stroke by permitting thrombi to form in response to stimuli that would normally be insufficient to cause thrombus formation. In a series of 71 patients with
protein S deficiency, 39 patients (55%) had had thrombotic events and only one had sinus thrombosis. Eighteen cases of sinus thrombosis due to protein S deficiency have been reported previously. These cases showed no specific CT findings or neurological symptoms, like sinus thrombosis due to other etiologies. Only three cases had hemorrhage on initial CT. Although hemorrhage increased the day after administration of heparin in one patient, none died of intracranial hemorrhage.

Mortality for sinus thrombosis is 5.5% to 30%. One of 18 patients with protein S deficiency died due to pulmonary embolism. In our case, no specific features were found among the neuroradiological findings and neurological symptoms, but the rapid increase in hematoma resulted in the catastrophic outcome. Most patients were treated by administration of heparin following oral anticoagulant. In the previous series, 77% of patients had recurrence events, but no recurrence was seen in patients receiving adequate anticoagulant treatment, suggesting that oral anticoagulation is an effective way to prevent thrombosis in patients with protein S deficiency. However, the therapy for patients with hemorrhage is controversial. Systemic anticoagulation and even use of microcatheter techniques to directly infuse urokinase into the dural sinuses have been advocated even in the presence of intracerebral hemorrhage.

References


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