Cerebral Sinus Thrombosis Associated with Severe Active Ulcerative Colitis

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Abstract

A 19-year-old man with severe active ulcerative colitis was admitted to our hospital where he was prescribed 80 mg prednisolone and underwent leukocytapheresis (LCAP). Two weeks after initiating therapy, his symptoms had not recovered. We administered cyclosporin via continuous intravenous infusion for 12 days. Although his clinical symptoms improved, he complains of severe headache. Immediate plain computed tomography (CT) and magnetic resonance imaging angiography (MRA) revealed extensive thrombosis in the superior sagittal sinus and right transverse sinus. We report an occurrence of cerebral sinus thrombosis accompanying ulcerative colitis, where active anticoagulant therapy was useful.

Case Report

A 19-year-old man was admitted because of the recurrence of ulcerative colitis which had been diagnosed 2 years previously with severe active and total colitis based upon colonoscopy, air-contrast radiography, and histopathological findings. On admission, he was thin and poorly nourished. A total of 15 to 20 bowel motions with blood and mucous, and severe abdominal pain were observed.

A physical examination revealed body temperature of 37.6°C, blood pressure of 130/88 mmHg and pulse of 96 beats/minute. A complete blood cell count (CBC) revealed that his white blood cell (WBC) count had increased to 11,200/μl. The hemoglobin concentration was 10.4 g/dl and platelet count was 413,000/μl. The level of C-reactive protein (CRP) was 2.3 mg/dl and erythrocyte sedimentation rate was 37 mm/h. The prothrombin time was 13.1 seconds (normal, 10.5–12.5 seconds), the fibrinogen level was 561 mg/dl (normal, 200–400 mg/dl), and the thrombin anti-thrombin III complex (TAT) was 10.7 ng/ml (normal, <3.0 ng/ml), factor VIII was above 200% (normal, 50–150%). These data indicated increased activity of the coagulation systems. The colonoscopy revealed diffuse ulceration and edema in his sigmoid colon and rectum (Fig. 1). Therapy with 80 mg of prednisolone and LCAP for two weeks did not improve his symptoms, so he was continuously infused with 4 mg/kg/day cyclosporin i.v. for 12 days. Although this strategy improved the clinical UC symptoms, he complained of severe headache and profound fatigue.

A post contrast computed tomographic (CT) scan showed an area of high density from the dorsal superior sagittal sinus to the right transverse sinus (Fig. 2A and B). A phase contrast MRA image demonstrated that the venous flow of the superior sagittal and right transverse sinuses was blocked (Fig. 3A). A trial of 15,000 U heparin/24 hour was administered according to the American Heart Association (AHA) Scientific Statement (1). This is equivalent to a ratio (pa-
tient/control aPTT) of 1.5 to 2.5. The headache was improved and the phase contrast MRA image of the superior sagittal sinus and right transverse sinus became almost normal (Fig. 3B). Prednisolone (30 mg) and azathioprine (50 mg) controlled the ulcerative colitis, which remained quiescent (Fig. 4).

**Discussion**

Thromboembolism is a recognized but uncommon complication of IBD that occurs in 1.3–6.4% of all such patients (2, 3) and in up to 39% of autopsies (4). Although thromboembolic complications are rare in UC, they are important because of their high mortality. The incidence of UC is low in Japan, and cerebral thromboembolism associated with it has been found only in six patients (5–8). The reason for this low association in Japan is unknown. The pathogenesis of thromboembolism in UC remains unclear. Reports have indicated that the hypercoagulability associated with UC predisposes patients to arterial and venous thrombosis (9, 10). The hypercoagulability is induced by high-dose corticosteroid therapy, and its inhibition of reactive fibrinolysis. Coagulation abnormalities have been associated with IBD (11–14), but whether they play a pathological role in clinical thrombotic complications is not known. The coagulation abnormalities associated with active inflammatory bowel disease include elevated levels of factors V and VIII and fibrinogen, decreased levels of antithrombin III (13), as well as both quantitative and qualitative platelet disorders.
Figure 3. (A) Magnetic resonance imaging angiography (T2-weighted) showing the absence of blood flow to the superior sagittal and right transverse sinuses (arrow). (B) Virtually normalized venous flow after intensive anticoagulant therapy (arrow).

Figure 4. Clinical course of the patient. CT: computed tomography, MRI: magnetic resonance imaging.
The increased levels of clotting factors and thrombocytosis may simply reflect an increased activity of inflammation and an active clinical state of IBD, because they return to normal after the underlying disease is treated (13).

Cyclosporin is an effective treatment for patients with severe active UC who are unresponsive to steroids (16). Among patients with severe UC who are unresponsive to conventional medical therapy 73% can avoid colectomy if administered with cyclosporin and after 5–6 months after the maintenance treatment, the response rate is 60% (17, 18). These findings suggest that cyclosporin together with anticoagulant therapy could be an effective therapeutic approach to treating steroid resistant UC with complicating sinus thrombosis.

In conclusion, we described a patient with UC and complicating sinus thrombosis, whose symptoms were improved after treatment with cyclosporin and anticoagulant therapy.

References