Cerebral venous sinus thrombosis as presenting feature of ulcerative colitis

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Abstract

Thrombosis is a well recognized complication of inflammatory bowel disease that occurs in 1.3 to 6.4% of patients, however, cerebral vascular involvement is unusual. We present the case of a 16-year-old female in whom cerebral venous thrombosis was the presenting symptom of an active ulcerative pancolitis. Thrombophilia screen (plasma levels of proteins C and S, antithrombin, antibeta2-glycoprotein, lupus anticoagulant and anticardiolipin antibodies, activated protein C resistance, homocystein level antinuclear antibodies) was negative. The patient was successfully treated with anticoagulant therapy, phenobarbital and sulfasalazine. Cerebral venous thrombosis is an exceptional presenting feature of ulcerative colitis. Disease activity may play a major role in the occurrence of thrombosis. (Acta gastroenterol. belg., **2009**, 72, **350-353**).

Key-words : cerebral venous thrombosis, ulcerative colitis.

Introduction

Thromboembolism is a serious and potentially life threatening event in patients with inflammatory bowel disease (IBD) (1). Thrombotic events occur prevalently as deep vein thrombosis and pulmonary embolism, whereas involvement of the central nervous system is rare (2-4). We report the case of a young patient in whom cerebral venous sinus thrombosis was the presenting symptom of ulcerative colitis (UC).

Case-report

A 16-year-old female was admitted to our department with complaints of severe left sided headache and blurred vision for the past 3 days. Upon questioning, she revealed that she has been passing 4-5 loose stools every day for the last 18 months, with occasional blood in the stool. She belonged to a low socio-economic stratum and did not consult any doctor before. She was not on any medication, including oral contraceptives.

Upon examination, she was confused, thin, poorly nourished and pale. Her body temperature was 38°. Neurological examination revealed no paralysis and sensory motor disturbances. Other systemic examination did not reveal any abnormality.

Laboratory data showed elevated C reactive protein level at 27.4 mg/L (normal range (nr) < 8.2 mg/L), erythrocyte sedimentation rate at 50 mm in the first hour, mild thrombocytosis (504,000/mm^3) and iron deficiency anemia with a haemoglobin value of 6 g/dL. Serum electrolytes and creatinine were all within normal limits.

Few hours after admission, she presented a tonic-clonic seizure. A computed tomographic (CT) scan and magnetic resonance (MR) of the head showed left lateral and sigmoid sinus thrombosis with left temporal infarction (Figs. 1 and 2).

She was immediately started on heparin and phenobarbital. Her symptoms improved over 3 days, she has had no recurrence of tonic-clonic seizure. Heparin was switched over to warfarin.

Before starting anticoagulant therapy, thrombophilia screen was performed. Plasma levels of proteins C and S as well as antithrombin were all within normal limits : 106% (nr : 70-130%), 78% (nr : 60-140%) and 115% (nr : 80-120%), respectively. Screening for anti-beta 2-glycoprotein, lupus anticoagulant and anticardiolipin antibodies was negative. Activated protein C resistance was not detected and homocystein level was normal. Antinuclear antibodies were absent.

The blood and stool cultures obtained on the first day of admission did not yield any pathogens. Colonoscopy revealed diffusely edematous, hyperhemic mucosa and patchy ulcers, ileoscopy was normal. Biopsy was taken, histology showed an abundant infiltration of lymphocytes and plasma cells and cryptitis in some areas of colic mucosa, tallying with features of UC. Ileal mucosa was normal as were intestinal barium study and gastroduodenoscopy.

Based on these findings, the patient was diagnosed with mild to moderate active ulcerative pancolitis complicated with cerebral venous sinus thrombosis. She was started on 4 g of sulfasalazine therapy. The frequency of her stools decreased and there was no associated blood in them. Her international normalized ratio was maintained at 2.5 on a usual dose of warfarin and she was discharged.

After 3 months of follow-up, the patient is still on maintenance therapy with sulfasalazine, phenobarbital and warfarin. Colitis is in remission and neurological recovery is complete.

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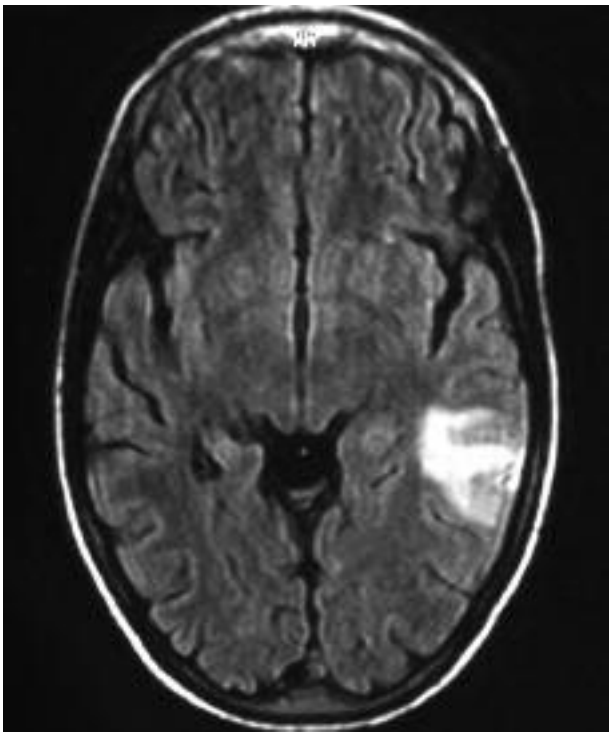

Fig. 1. — Cerebral magnetic resonance imaging (T2-weighted) showing one hyperintense left temporal lesion consistent with infarction.

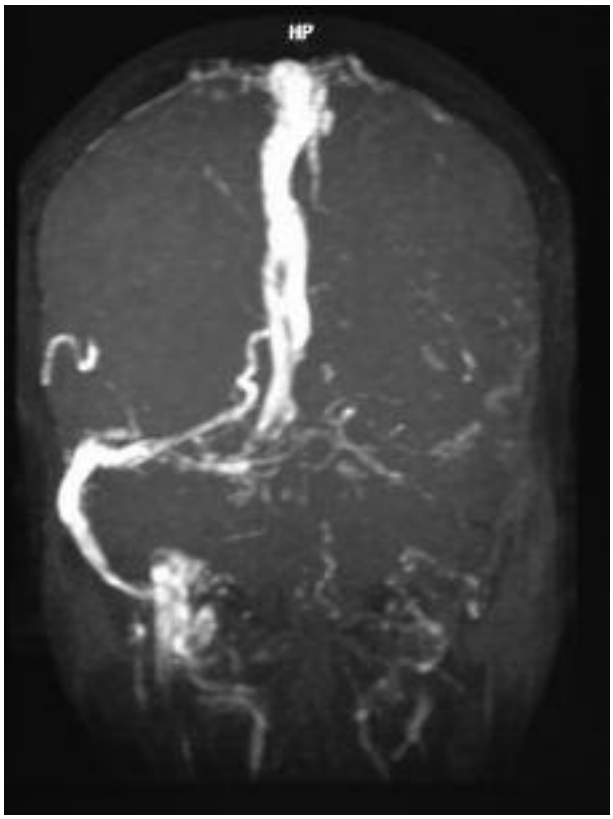

Fig. 2. — Cerebral magnetic resonance venography showing signal drop out in left lateral and sigmoid sinus.

Discussion

Thrombosis is a well-recognized but uncommon complication of IBD that occurs in 1.3 to 6.4% of all such patients and in up to 39% in autopsies (5). It has been shown that IBD patients have a three to four fold increased risk of thromboembolism (1).

Deep venous thrombosis with or without pulmonary embolism remains the most common vascular event whereas involvement of the central nervous system is rare (2-4,6). In a study of 7199 IBD patients, only 9 of the 92 patients suffering from thrombotic complications had cerebral vessel involvement (7). Cerebral venous thrombosis associated with IBD is rare and occur more often in patients with UC than in those with Crohn's disease (4,8). However, only anecdotal case reports of cerebral venous embolism associated with UC have been reported in the world literature (3-5,8-32). In our investigation, cerebral venous embolism associated with UC has previously been reported in 36 patients with a mean age of 25 (extremes : 7-53 years) (3-5,8-32). Clinical features are summarized in Table 1. In 86% of these cases, cerebral venous embolism occurred in patients with diagnosed UC, with a mean duration time of 4 years (3-5,8-32). In our patient, cerebral thrombotic manifestations were concomitant with UC diagnosis.

The pathogenesis of thromboembolism in UC remains unclear. The coagulation cascade, as well as fibrinolysis and platelet functions are altered, resulting in a generalized prothrombotic state (33).

Prothrombotic risk factors in IBD patients could be distinguished as inherited, such as factor V mutation, prothrombin gene mutation, methylenetetrahydrofolate reductase (MTHFR) gene mutation, protein C, S and antithrombin deficiencies ; or acquired, such as active inflammation, immobility, surgery, steroid therapy, and use of central venous catheters (2,8).

Several trials have been performed on the prevalence of resistance to activated protein C and factor V Leiden, factor II polymorphism and deficiencies of protein C, S and antithrombin among IBD patients (1,34). None of these studies was able to prove a specific role for one of these disorders in IBD. Although IBD patients were shown to have higher level of homocystein, no increased incidence of mutation in the MTHFR gene has been established (6). These data suggest that prothrombotic mutations play a minor role in inducing thrombotic complications in IBD, and acquired risk factors may play a major role.

Among all acquired risk factors, disease activity appears to be the most likely. In the study of Mishler *et al.*, 60% of thromboembolism in IBD occurred during

Table 1. — **Clinical features of ulcerative colitis patients with cerebral venous thrombosis reported in the literature** (3-5,8-32)

	n patients/ n total	*Percentage*
Gender		
Male	17/36	47%
Female	15/36	42%
NR	4/36	11%
UC diagnosis		
Concomittant	5/36	14%
Known previously	31/36	86%
UC activity		
Active	20/36	55%
Remission	9/36	25%
NR	7/36	20%
Involved cerebral vein		
Sinus	28/36	78%
Cortical	2/36	5.5%
Sinus and cortical	4/36	11%
NR	2/36	5.5%
Coagulopathy	8/36	22%
Outcome		
Remission	20/36	55.5%
Residual	7/36	19.5%
Death	7/36	19.5%
NR	2/36	5.5%

n : number, NR : not reported, UC : ulcerative colitis.

disease activity or in the presence of complications such as stricture, abscess or fistulisation (1). Solem et al, showed that 79% of the 37 UC and 80% of the 31 Crohn's disease patients with venous thromboembolism had active disease at the time of clot diagnosis, whereas thrombophilia was present only in 33% of the 40 patients tested (35). In the same study, UC extent was pancolonic in 76% of cases, as in our patient, implying that the extent of colonic disease may also correlate with thromboembolic risk.

In the cases of UC with cerebral venous thrombosis reported in literature, thromboses occur in approximately 55% of cases in the setting of a flare up colitis whereas only one fourth of patients have some coagulation abnormalities such as factor V Leiden mutation, hyperhomocysteinemia, positive anticardiolipin antibodies, protein S deficiency, active protein C resistance and prothrombin gene mutation (3-5,8-32).

In our patient no inherited thrombophilia was identified, suggesting that the activity and the extent of the disease was the main risk factor of thrombosis. We estimate that we could have foreseen the thrombotic complication if UC was diagnosed and treated before.

Conclusion

Cerebral venous thrombosis is a rare complication of UC and exceptionally the presenting feature. Whereas the exact pathogenesis of thrombosis is still conjectural, our case suggests that disease activity might play a major role in its occurrence. The thrombotic complication might partially be prevented by optimal management of the underlying condition.

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