

An 18-month-old Child with Seizures and Bloody Diarrhea

To the Editor:

An 18 month-old infant with stupor status was admitted to the local hospital in April 2002. Three months earlier, he had presented with occasional mucus and fresh blood in his stool. One week prior to hospital admission, he begun to experience progressively worsening paleness, fatigue, and bloody diarrhea with mucus, and had an episode of tonic-clonic fits of the right arm lasting a few seconds. On hospital admission, a blood analysis revealed the following: hemoglobin concentration, 3.6 mg/dL; platelet count, 748,000/mm³; and C-reactive protein concentration, 2.9 mg/dL. A lumbar puncture was performed, revealing normal cerebral spinal fluid. During a blood transfusion, the child experienced a generalized seizure with loss of consciousness and upward deviation of his eyesight. Computerized axial tomography, magnetic resonance (MR) imaging, and MR angiography scans of the brain revealed bilateral hemorrhagic infarctions of the basal ganglia, and thrombosis of the internal cerebral veins, Galeno's vein, rectum, and left transverse sinus (Fig. 1). Blood flow was preserved in the superior sagittal sinus and the right transverse sinus.

The child was then transferred to the pediatric intensive care unit of our hospital where a physical examination revealed a suffering, pale, dehydrated child, who was in opisthotonus without signs of meningism. Some type of encephalitis was initially suspected, and therapy with antibiotics, steroids, acyclovir, aspirin, and phenobarbitone was started. Because of intestinal bleeding, anticoagulants were not administered. As soon as his clinical condition was stabilized, he was transferred to our ward. His neurologic condition improved, but bloody diarrhea with mucus was still present up to 7 to 10 times a day. Prothrom-

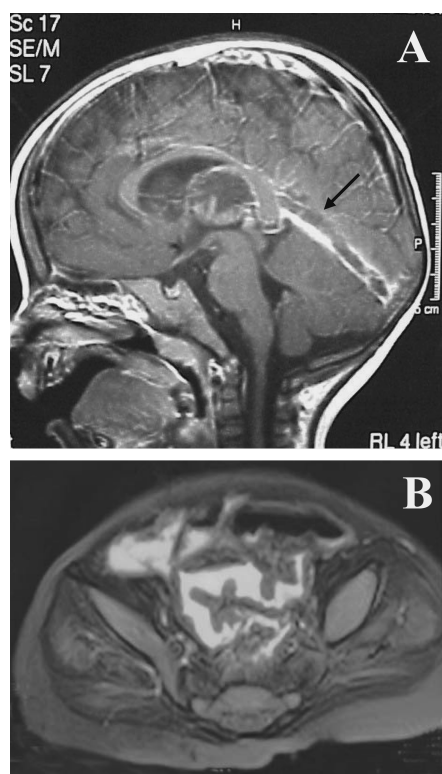


Figure 1. MR imaging scan of the brain (A) and colon (B). A T1-weighted image of the brain showing thrombosis (arrow) of the rectum sinus (A). A T2-expressed sequence showing the irregular shapes of the sigmoid colon and rectum (B).

bin time, partial thromboplastin time, plasma levels of protein C and protein S, and resistance to activated protein C and antithrombin III were compatible with endothelial distress. The Leyden factor V mutation and the G20210A mutation of factor II were absent, although the patient was heterozygous for the methyltetrahydrofolate reductase (C677T) mutation. The plasma concentrations of homocysteine, vitamin B12, and folate were normal. The results of immunologic tests, such as those for anticardiolipin antibodies and lupus anticoagulants, were normal, but test results for antineutrophil cytoplasmic antibodies with a perinuclear pattern were positive. The findings of a rectosigmoidoscopy with biopsy and histopathologic examination were consistent with the diagnosis of ulcerative colitis (UC). The patient was started on a

treatment regimen of broad-spectrum intravenous antibiotics, intravenous methylprednisolone, and total parenteral nutrition. After 9 days of treatment, he was still presenting with bloody diarrhea, and a blood transfusion was required. For this reason, intravenous cyclosporine (3 mg/kg/d) was added to therapy, and then continued orally (7 mg/kg/d) with 6 mercaptopurine. At this stage, an MR imaging scan of the brain and abdomen was performed, and it revealed the complete recanalization of the cerebral vessels, although irregular appearances of the sigmoid colon and rectum were detected (Fig. 1).

Despite such intensive medical treatment, the child continued to have bloody diarrhea with slowly declining hemoglobin levels, which required a blood transfusion. Therefore, a total colectomy with ileoanastomosis and protective ileostomy was performed 3 months after hospital admission. The macroscopic and histologic appearance of the colon confirmed the diagnosis of UC. During the postoperative course, the patient initially required therapy for severe electrolyte disturbance. His clinical condition then improved, and consequently oral feeding was reintroduced and total parenteral nutrition was stopped. The ileostomy was closed after 1 year. At the 2-year follow-up, the child was growing well. From a neurologic perspective, however, ambulation and speech deficits were present, and he developed postischemic epilepsy.

Thromboembolism (TE) is a potentially life-threatening event that is associated with inflammatory bowel disease (IBD). A population-based cohort study¹ has recently shown that IBD patients have a 3-fold increased risk of developing deep venous thrombosis and pulmonary embolism compared with the general population. IBD seems to be a specific risk factor for TE as neither rheumatoid arthritis, another chronic inflammatory conditions, nor celiac disease, another chronic bowel disease, carry an increased risk of TE.² IBD pa-

tients seem to experience venous thrombosis earlier in life than do non-IBD patients, as was found in a survey including a large population of patients.³ During the last several decades, the incidence of IBD in children has increased. The onset of IBD also has been described in very young children.⁴ In this age group, the disease can be very aggressive. TE in children is a rare event and, when associated with IBD, occurs most commonly in the central nervous system.⁵ The mean age at the time of the cerebral ischemic event in a literature review⁶ of 11 reported cases was 14 years (range, 12 to 18 years).

To our knowledge, our patient is the youngest ever reported, with the largest involvement of the cerebral vessels. The patient survived and partially regained his motor functions, probably because of the plasticity of his young cerebral nervous system. Elevated concentrations of plasma total homocysteine negatively correlated with plasma folate levels have been found recently in children with IBD without the association of an increased prevalence of homozygosity for the thermolabile variant of the methyltetrahydrofolate reductase *C677T* gene.⁷ The presence of genetic mutations that predispose patients to hypercoagulable states does not appear to correlate with the prevalence of IBD or thromboembolic events in children and adolescents with IBD.⁸ Our patient was negative for the genetic and metabolic risk factors for thrombosis that were investigated. The only risk factors known in our child were active UC and progressive anemia. One month after making the diagnosis, thrombosis spontaneously resolved despite the fact that anticoagulant therapy had not been administered and UC was still moderately active although the patient was receiving intensive medical treatment.

In a neurologically compromised child presenting with bloody diarrhea with mucus, the presence of a cerebrovascular accident associated with an active IBD should always be suspected.

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REFERENCES

1. Bernstein CN, Blanchard JF, Houston DS, et al. The incidence of deep venous thrombosis and pulmonary embolism among patients with inflammatory bowel disease: A population-based cohort study. *Thromb Haemost.* 2001; 85:430–434.
2. Miehsler W, Reinisch W, Valic E, et al. Is inflammatory bowel disease an independent and disease specific risk factor for thromboembolism? *Gut.* 2004;53:542–548.
3. Grip O, Svensson PJ, Lindgren S. Inflammatory bowel disease promotes venous thrombosis earlier in life. *Scand J Gastroenterol.* 2000; 35:619–623.
4. Mamula P, Telega GW, Markowitz JE, et al. Inflammatory bowel disease in children 5 years of age and younger. *Am J Gastroenterol.* 2002; 97:2005–2010.
5. Lloyd-Still JD, Tomasi L. Neurovascular and thromboembolic complications of inflammatory bowel disease in childhood. *J Pediatr Gastroenterol Nutr.* 1989;9:461–466.
6. Keene DL, Matzinger MA, Jacob PJ, et al. Cerebral vascular events associated with ulcerative colitis in children. *Pediatr Neurol.* 2001; 24:238–243.
7. Nakano E, Taylor CJ, Chada L, et al. Hyperhomocystinemia in children with inflammatory bowel disease. *J Pediatr Gastroenterol Nutr.* 2003;37:586–590.
8. Kader HA, Berman WF, Al-Serafi AS, et al. Prevalence of factor V G1691A (Leiden), prothrombin G20210A, and methylene tetrahydrofolate reductase C677T thrombophilic mutations in children with inflammatory bowel disease. *J Pediatr Gastroenterol Nutr.* 2002; 35:629–635.

Infliximab for the Treatment of Metastatic Hepatic and Pulmonary Crohn's Disease

To the Editor:

Metastatic Crohn's disease (MCD) is defined as granulomatous inflammation in an area that is not contiguous with

the gastrointestinal tract in a patient with Crohn's disease (CD). Although there have been rare case reports of isolated pulmonary and hepatic granulomas, there are no reports of simultaneous hepatic and pulmonary MCD. We report a case of a 20-year-old woman with CD who presented with concurrent hepatic and pulmonary lesions, which resolved with infliximab (INF) therapy.

The patient was a 20-year-old African American woman in whom CD had been diagnosed at the age of 11 years and whose condition had been maintained with INF for several years. She stopped therapy with INF secondary to the loss of medical care. Eight months later, she presented to our institution with a 2-month to 3-month history of loose stools, averaging 10 per day, a 10-lb weight loss, nausea, fatigue, and occasional bleeding from the rectum. She also noted occasional arthralgias but denied vomiting, abdominal pain, loss of appetite, fever or chills, tenesmus, rash, jaundice, or any eye symptoms. There was no family history of inflammatory bowel disease (IBD) or colon cancer. The patient smoked 3 cigarettes a day, drank occasional alcohol, and had smoked marijuana in the past. She denied any current recreational or intravenous drug use.

A physical examination was unremarkable. An abdominal examination demonstrated a soft, nontender abdomen, with bowel sounds present and without palpable masses. A rectal examination revealed no tags, fissures, or abscesses.

The patient was scheduled to resume INF therapy, and a colonoscopy was performed to restage her disease before infusion. The colonoscopy was notable for inflammation and edema with an associated stricture in the sigmoid colon, and a fistula or sinus tract in the descending colon that was consistent with active CD. Two weeks later, she developed severe abdominal pain and was admitted to the hospital. INF therapy was planned to control her CD exacerbation. An abdominal computed tomography (CT) scan was obtained to rule out any intraabdominal abscess or obstruction