Clinical and Experimental Rheumatology 2001; 19 (Suppl. 24): S59-S61.

Behcet's disease complicated by pylephlebitis and hepatic abscesses

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Received on May 24, 2000; accepted in revised form on November 7, 2000.

Key words: Behçet's disease, pylephlebitis, hepatic abscess, vasculitis.

Abstract

A 22 year old man presented with fever, abdominal pain, weight loss and diarrhea. Past medical history revealed recurrent aseptic meningitis, uveitis, and erythema nodosum. Further inquiry unveiled a prominent history of oral aphthous ulcers; all features of Behçet's disease. Imaging revealed mesenteric arteritis and pylephlebitis, septic thrombophlebitis of the portal vein, a previously unrecognized complication of Behçet's disease, with multiple intrahepatic abscesses. Portal venography demonstrated an extensively diseased, expanded, and obstructed portal venous system. Blood cultures and portal vein aspirate yielded polymicrobial flora. Percutaneous intraportal thrombolytic therapy and mechanical thrombectomy were attempted to restore flow to the portal venous system. This distinctly rare manifestation of Behçet's Disease, pylephlebitis, may result from ischemic injury and structural compromise of the bowel mucosa, resulting from underlying vasculitis.

Introduction

Behçet's disease is a multisystem inflammatory disorder characterized by oral aphthous ulcers, frequent genital ulceration, and the potential for severe visceral involvement. Inflammation may involve the ophthalmic, neurologic and gastrointestinal systems, which may manifest as uveitis, aseptic meningitis and colitis, respectively (1,2). Unusual among the rheumatic disorders is that Behçet's disease may result in both an arteritis as well as thrombophlebitis, even concomitantly. We present such a patient with extensive vascular disease and a previously unrecognized manifestation of this disorder.

Case description

A 22 year old African American man moved to Maryland to begin graduate work in chemistry. These studies were delayed by spiking fevers, severe diffuse abdominal pain, voluminous nonbloody diarrhea, and weight loss.

At age 13, he developed aseptic meningitis. One year later, bilateral uveitis followed. He remained well until admission at age 20, with fever, headache, abdominal pain, weight loss and arthralgias. Evaluation was remarkable for raised inflammatory markers. Cerebrospinal fluid examination showed pleocytosis of 420 wbc/mm^3 with 77% neutrophils, raised total protein of 242 mg/dl,and sterile cultures. Rheumatoid factor, antinuclear and antineutrophil cytoplasmic antibodies were negative. Computerized tomography of the abdomen was unremarkable. Prednisone 0.5 mg/kg/day was prescribed with improvement. However, he developed painful erythematous nodules over the shins; histology revealed lobular and septal panniculitis. Chest radiograph demonstrated no hilar adenopathy or parenchymal infiltrate; transbronchial biopsy was negative for granuloma. Steroids were weaned off over six months.

He remained well for 18 months until fever, abdominal pain, weight loss and diarrhea recurred. Prednisone 0.5 mg/kg/day was begun. Blood cultures were positive for *peptostreptococcus* and *clostridium perfringens*; a source was not identified. Abdominal ultrasound and computerized tomography were unremarkable. Modest improvement ensued. Following discharge, however, abdominal pain intensified. Visceral arteriography, four weeks later, revealed several branches off the superior mesenteric artery that were diminutive with alternating stenosis and dilatation (Fig. 1). Ultrasound, that same day, now showed extensive portal and splenic vein thromboses.

Referral for urgent inpatient rheumatology evaluation and management followed. Prior uveitis, recurrent aseptic meningitis, erythema nodosum, and abdominal pain suggested the diagnosis of Behçet's Disease. Further inquiry unveiled previous bouts of oral ulcers, requiring medical evaluation and treatment. There was no history of genital ulceration or pathergy. A quotidian fever reached 39.5 degrees. Examination revealed generalized abdominal tenderness without peritonism. Hematology showed normocytic normochromic anemia with hemoglobin 9.5 g/dl and neutrophilia of 24,000 WBC/mm^3. Liver function tests demonstrated AST of 43 IU/L and ALT 74 IU/L. Sed-

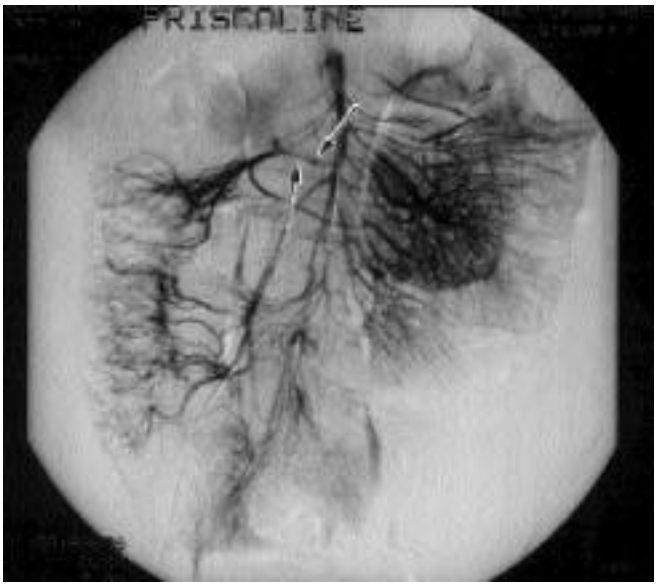

Fig. 1. Arterial phase from a superior mesenteric arteriogram following the administration of priscoline, demonstrating multiple areas of alternating stenoses and dilatation (**arrow**) consistent with a vasculitis process.

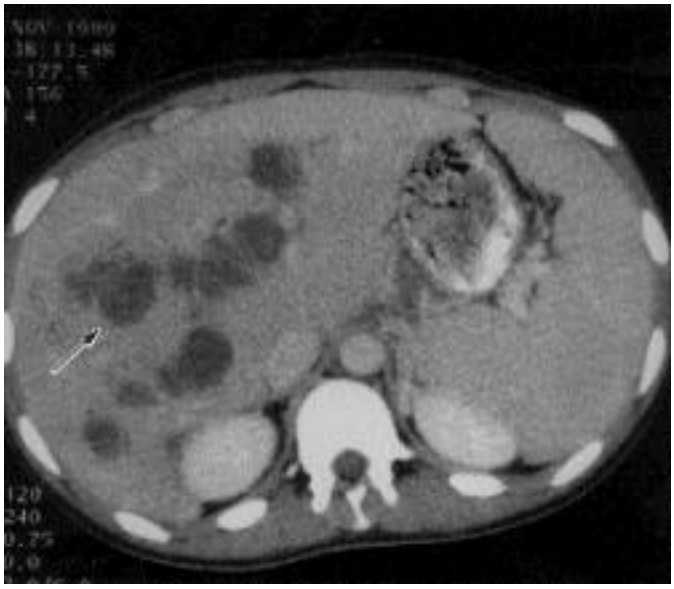

Fig. 2. Contrast-enhanced abdominal CT scan demonstrating multiple areas of low-attenuation within the liver suggestive of intrahepatic abscesses (**arrow**).

imentation rate exceeded 100 mm/hr. Ultrasonography revealed thrombus extending into the splenic and superior mesenteric veins. The portal vein was dilated with cavernous transformation. Computerized tomography revealed extensive portal vein thrombosis with marked distention, suggesting septic thrombophlebitis (pylephlebitis) (Fig. 2). Multiple low attenuation areas were identified in the liver consistent with intrahepatic abscesses.

Ultrasound-guided, percutaneous aspiration of the portal vein yielded pus which cultured *Escherichia coli.* Thereafter, antibiotic therapy with intravenous metronidazole and cefotaxime led to a dramatic resolution of fever and gastrointestinal symptoms.

In an attempt to restore blood flow within the portal venous system, catheter-directed thrombolysis was performed. Portal venography revealed an extensively diseased, expanded, and obstructed portal venous system that was aneurysmal and saccular (Fig. 3). Over a 72-hour period percutaneous thrombolysis was performed with direct infusion of tissue plasminogen activator (tPA) into the portal and superior mesenteric veins at 0.02 mg/kg/hr. The clot burden was not significantly reduced. The dose of tPA was increased to 0.04 mg/kg/hr without effect. Mechanical thrombectomy was attempted as a last resort but was unsuccessful.

After the percutaneous drains were placed, temperature spiked to 39.9 degrees, with blood cultures positive for *Escherichia coli.* When the indwelling tubing was removed, the catheter tip exposed pus and cultured group B and group D *streptococcus, Streptococcus viridans,* and *Escherichia coli.*

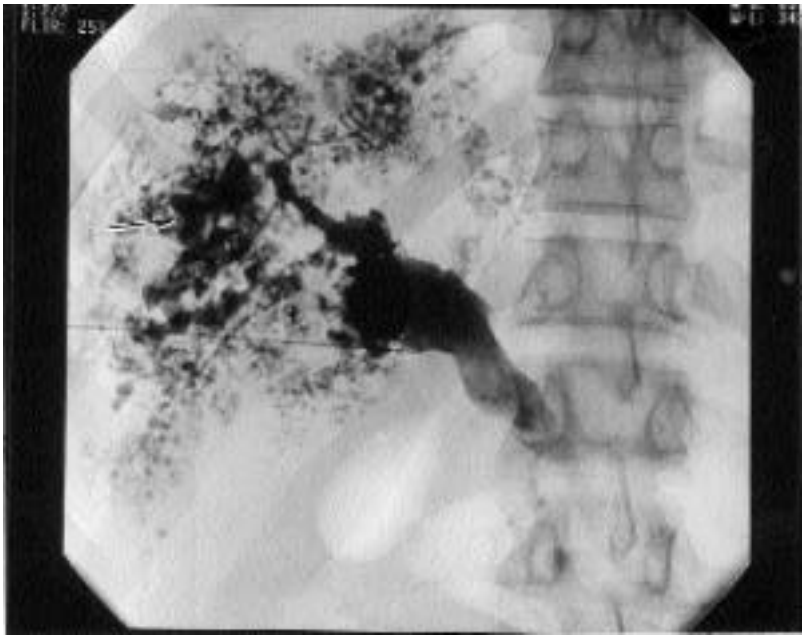

Fig. 3. Transhepatic portal venogram demonstrates a markedly diseased, expanded and obstructed portal vein with saccular dilatation of numerous intrahepatic portal venous branches (**arrow**).

Discussion

In addition to aphthous oral ulceration, many patients with Behçet's disease develop visceral manifestations, including uveitis, aseptic meningitis and vasculitis (1, 2). Vasculitis in Behçet's disease may result in both an arteritis and thrombophlebitis. We present such a patient with abdominal vasculitis involving both the arterial and venous systems. This case was complicated by pylephlebitis, septic thrombophlebitis

of the portal vein, a heretofore unrecognized manifestation of Behçet's disease, and resulted in hepatic abscesses. Among 844 patients with Behçet's disease evaluated over a 25 year period in Turkey, 66 (7%) had evidence of large vessel disease, either arterial or venous (3). Six (0.7%) developed cavernous transformation of the portal vein, observed in the present case. In a smaller series from Israel, 15 of 41 patients had thrombophlebitis; none had evidence of gastrointestinal involvement (4). Over a 10 year period, 10 (2.2%) of 450 patients with Behçet's disease in Tunisia manifested arterial occlusions and aneurysms (5). Of note, "angio-Behçet's syndrome" refers to patients with predominant vascular manifestations (5, 6).

In this report, Behçet's disease was complicated by hepatic abscesses. Such abscesses are frequently polymicrobial. Enteric gram-negative bacilli, predominantly *Escherichia coli*, are most often cultured (7). Anaerobes include gram-positive cocci and bacteroides species are frequently identified. Pyogenic liver infections may arise from the portal system, as from acute suppurative thrombophlebitis of the portal vein. This condition, pylephlebitis, was often ascribed to appendicitis and diverticulitis in the pre-antibiotic era (7,8). Precedence for pylephlebitis to result from an inflammatory gastrointestinal disorder exists in Crohn's disease (9,10). The present case of pylephlebitis in Behçet's disease, perhaps analogous to inflammatory bowel disease, may represent the sequelum of mesenteric vasculitis in which ischemic injury compromises the structural integrity of gastrointestinal mucosa and leads to seeding of intestinal flora.

In summary, we present a 22 year old man whose course included recurrent aseptic meningitis, uveitis, erythema nodosum and oral aphthous ulcers. Moreover, this case of Behçet's disease was complicated by the development of pylephlebitis, intrahepatic abscesses and mesenteric vasculitis. In addition to catheter-directed thrombolytic therapy, treatment included antibiotics, corticosteroids, cyclophosphamide and warfarin. At 6 months of follow-up, prednisone has been tapered to 5 mg daily. He is running 4 miles a day and has resumed his graduate studies.

Acknowledgment

We acknowledge the skilled and comprehensive medical care provided by Drs. Walter Dehority, Derek Fine, Moeen Abedin, and Hetty Carraway.

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