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Duodenal Ulcer, Hepatic Abscesses, and Fatal Hemobilia with Behcet's Syndrome: A Case Report

Armin E. Good, M.D., Milton G. Mutchnick, M.D., and Lee Weatherbee, M.D.

Department of Internal Medicine (AEG, MGM) and Department of Pathology (LW), Veterans Administration Medical Center and University of Michigan Medical School, Ann Arbor, Michigan

A 43-yr-old man with longstanding Behcet's syndrome had fatal massive hemobilia and multiple hepatic abscesses stemming from a penetrating ulcer at the ampulla of Vater obstructing the biliary tract. Although classic features are lacking, the evidence suggests that the ulcer was a manifestation of Behcet's syndrome and not merely incidental peptic ulcer disease.

INTRODUCTION

No longer regarded merely as a symptom triad of aphthous stomatitis, genital ulcerations, and eye involvement, Behcet's syndrome (BS) can evolve into a catastrophic multifaceted disease. Recent newly reported manifestations include pancreatitis (1), peripheral neuropathy (1), renal involvement (2), perforation of the palate (3), diffuse myositis (4), and ventricular aneurysm (5). Involvement of the intestines, CNS, and vascular system can occur, each with a frequency of about 10%. These complications account for most of the mortality (6).

We report a patient with fatal spontaneous hemobilia as an unusual complication of BS. Other noteworthy features in our case are splenomegaly and autopsy demonstration of unsuspected pancreatitis and myocarditis.

CASE REPORT

A black man first experienced intermittent pain and swelling of his right elbow at the age of 35 yr. He developed paresthesias in his forearm and fingers and painful recurrent ulcers on the shaft of his penis 5 yr later. This was followed by the onset of headaches, episodes of partial memory loss, and recurrent painful buccal and pharyngeal ulcers. He was admitted to a hospital with low grade fever, persistent stomatitis, pustules on his legs, and weight loss of 50 lb. Positive laboratory studies included multiple urinalyses showing 20–30 white cells per high powered field; peripheral blood white cell counts of between 4000 and 5000/ml^3, and moderate elevations of the serum glutamic-oxaloacetic transaminase and lactic dehydrogenase. The results of the following tests or procedures were normal or negative: rheumatoid factor; lupus erythematosus cell test; urine cultures; Hb electrophoresis; lymphangiograms; x-rays of the chest, sinuses and kidneys; and biopsies of the liver, bone marrow, and inguinal nodes. The patient subsequently developed splenomegaly, keratitis, and large ulcers in his nares, anus, and inguinal region. The various symptoms did not respond to a 4-month course of prednisone, 20 mg/day.

The patient's first admission to the Ann Arbor Veterans Administration Medical Center occurred 7 yr after onset of symptoms. He had multiple small punched out buccal ulcers with gray erythematous bases and similar ulcers of the glans penis and scrotum. The liver edge was palpable 1 cm below the costal margin. The splenic tip was also palpable. Synovial swelling was present at the ankles, right wrist, and right elbow. Positive studies included multiple urinalyses showing moderate numbers of white and red cells per high power field; mild to moderate elevations of alkaline phosphatase, lactic dehydrogenase, serum glutamic-oxaloacetic transaminase, creatine phosphokinase, and aldolase; a serum protein electrophoresis showing polyclonal increase of the γ globulin with a total protein of 8.5 g/dl and a γ globulin of 2.8 g/dl; and an electrocardiogram showing ST and T wave abnormalities suggesting myocardial changes. A synovial biopsy of an ankle showed changes of nonspecific chronic synovitis and was sterile on culture. Normal or negative studies included the Hb; white blood cell count; urine cultures and cytology; serum bilirubin, creatinine, urea, antinuclear antibodies, rheumatoid factor; Hb electrophoresis; x-rays of the chest, lumbosacral spine, sacroiliac joints, and peripheral joints; an intravenous pyelogram and upper gastrointestinal series; and muscle biopsies. Prednisone was discontinued without obvious change in the course, and the oral ulcers healed with a tetracycline mouthwash. Other medications consisted of buffered aspirin, indomethacin, and antacids.

When readmitted 6 months later, the patient complained of fever, weakness, muscle aches, and nasal discharge. He also had experienced recurrent vague epigastic pain which was not relieved by food or antacids. His wife observed that he spoke irrationally at times and occasionally appeared quite confused. Nonspecific nasal mucous membrane ulcerations were evident. There was

blunting to pin testing over the lower extremities. Spinal fluid dynamics, protein, sugar, and cell count were normal. X-rays of the sinuses showed chronic sinusitis involving the frontal, ethmoid, and maxillary sinuses. A barium contrast study again showed no intrinsic disease of the stomach, duodenum, or small bowel. An electromyogram showed motor units of short duration and normal amplitude. A right scalene node biopsy and a left deltoid muscle biopsy were normal. Although the nasal discharge decreased with ampicillin therapy, persistent fever to 39.2°C remained a problem.

At his final elective admission 1 month later, his chief complaints were bloody nasal discharge, abdominal pain, and mucous stools. He appeared weak and apprehensive with a temperature of 39°C, blood pressure 98/60, and a sinus tachycardia at a rate of 124. Pertinent findings included an erythematous nasal mucosa with yellow discharge, an aphthous ulcer of the lower lip, and corneal dystrophy with epithelial and endothelial deposits as well as an active chronic iritis bilaterally. The liver edge was palpable 2 cm below the right costal margin with a total hepatic span of 9 cm. The spleen was also palpable. Diffuse midabdominal tenderness was noted. There was tenderness over the ankles and temporomandibular joints without objective changes. He walked with an unsteady gait, apparently due to hip girdle pain and weakness. Neurological examination showed muscle atrophy, weakness of the hip flexors and abductors, hyperpathia at the feet bilaterally, and some diminution of sensibility to fine touch in a stocking distribution over the feet. The peripheral blood white cell count was 11,700/mm^3 with 88% polymorphonuclear cells. Total serum bilirubin was 1.9 mg/dl (0.85 direct). The serum glutamic oxalacetic transferase was normal. His medications were indomethacin, aspirin, and antacids.

A month after discharge from the hospital he passed a massive maroon-colored stool. On readmission his blood pressure was 70/40 with a pulse rate of 130, hematocrit 8%, and Hb 4 g/dl. While receiving blood replacement therapy the patient continued to pass large amounts of dark red stools with clots. Shortly thereafter blood appeared in his nasogastric tube. Emergency laporotomy and gastroduodenotomy disclosed blood in the small bowel and bright red blood welling up from the second portion of the duodenum. At the area of the ampulla of Vater blood was noted issuing forth from the base of a large penetrating ulcer. The gallbladder and common bile duct were enormously distended with bright red blood. A choledochotomy incision revealed active bleeding from the liver. When a finger was inserted into the common duct a large cavity was entered, interpreted as an abscess cavity near the hilum of the liver. A left hepatic lobectomy was undertaken, but during this procedure the patient suffered a cardiac arrest from which he was not successfully resuscitated.

AUTOPSY FINDINGS

Grossly the autopsy showed a 4 cm posterior deeply penetrating ulcer in the second portion of the duodenum distorted by multiple sutures in the area of the ulcer and ampulla of Vater. The surface of the pancreas seen in the base of the duodenal ulcer was hemorrhagic and edematous. Large and small abscesses were noted within the liver; the biliary tract was contiguous with a larger abscess. The spleen weighed 330 g. The stomach, brain, heart, and kidneys appeared normal. Postmortem cultures of the liver abscesses grew *Escherichia coli.*

Microscopically the duodenal ulcer showed necrosis and hemorrhage with lymphocytes and polymorphonuclear leukocytes around vessels and in the muscularis. The gallbladder showed striking acute purulent and chronic inflammation (Fig 1). There was diffuse necrotizing cholangitis with purulent exudate in the bile ducts (Fig 2). Multiple hepatic microabscesses were noted with bile stasis and centrilobular necrosis with hemorrhage (Fig 3). The pancreas showed fibrosis and some edema as well as focal fat necrosis (Fig 4). The myocardium

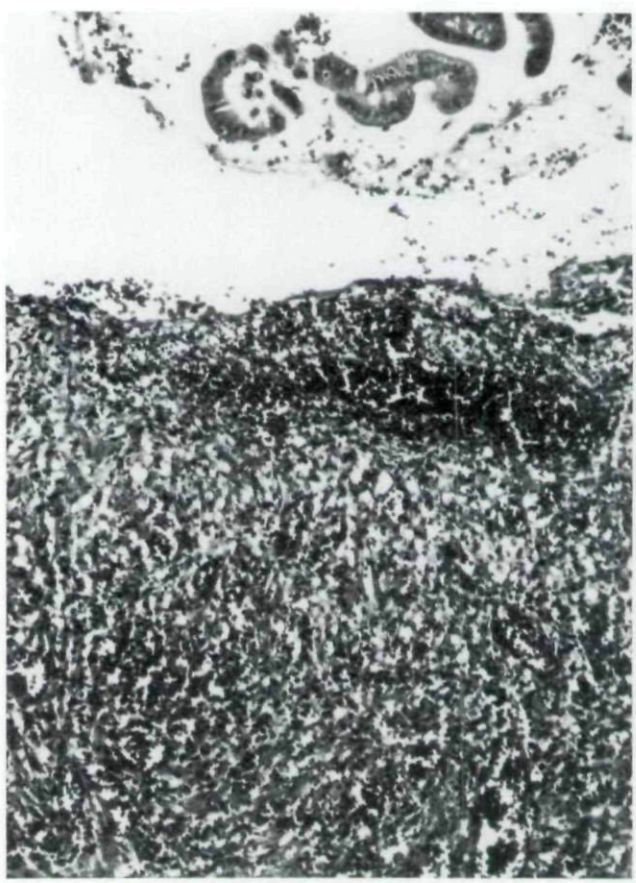

FIG. 1. The wall of the gallbladder resembles the hepatic abscess in that it is thickened, fibrotic, and contains an infiltrate of acute and chronic inflammatory cells. The epithelium is partially ulcerated with small foci of regeneration (hematoxylin and eosin stain, ×200 magnification).

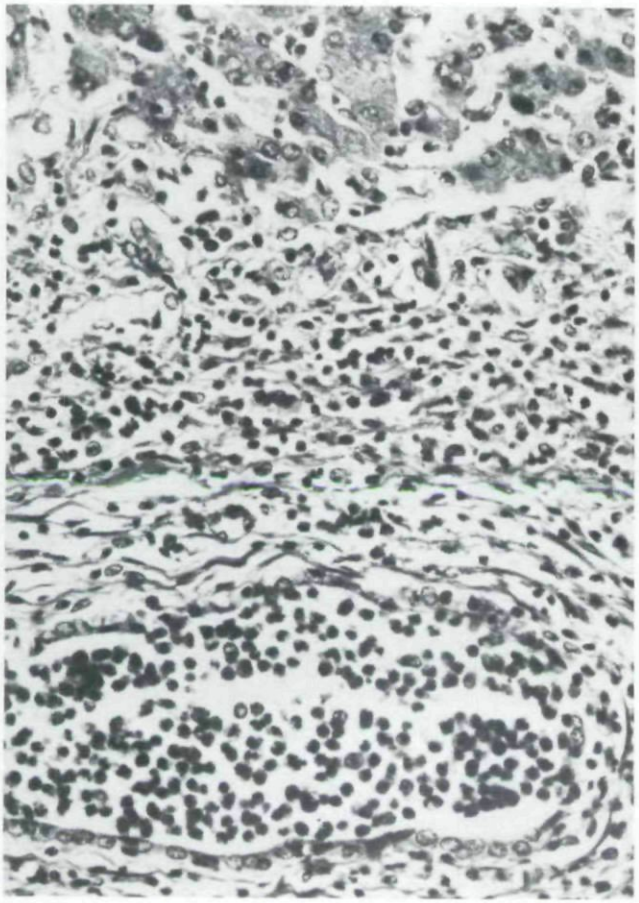

FIG. 2. In the liver in areas other than the abscess there is severe acute purulent cholangitis. Note the exudate in the bile duct (hematoxylin and eosin stain, ×500 magnification).

FIG. 3. The wall of the liver abscess is thickened and fibrotic with an infiltrate of acute and chronic inflammatory cells. The appearance is rather nonspecific (hematoxylin and eosin stain, ×80 magnification).

contained chronic inflammatory infiltrates that were mainly lymphocytes in small aggregates around arterioles or venules. There was no acute angiitis or fibrinoid change. The appearance was consistent with a focal chronic myocarditis. The kidneys were normal. Occasional perivascular lymphocytes were seen in various parts of the brain excluding the leptomeninges.

DISCUSSION

Our patient fulfilled the Mason-Barnes diagnostic schema (7) for complete BS with all four major criteria (oral ulcers, genital ulcers, eye lesions, skin lesions); in addition he presented several minor criteria (arthritis, neurological disease, gastrointestinal disease). We are aware of only one other report of a black patient with BS (4).

A salient feature of our report is the abdominal involvement beginning as nondescript pain 6 months antemortem and culminating as fatal hemobilia. The hemobilia most probably originated in large pyogenic abscesses associated with the severe cholangitis and multiple hepatic microabscesses (8). Presumably the cholangitis, in turn, was a consequence of the penetrating ulcer involving the ampulla of Vater that was ideally situated to obstruct the biliary tract.

The key question is whether the duodenal ulcer was a mucosal manifestation of BS or merely an incidental peptic duodenal ulcer. Although vasculitis has been associated with intestinal lesions in BS (6) and pulmonary arteritis purported to be the reason for massive hemoptysis (9), we found no evidence that arteritis was related to ulceration or hemorrhage in our case. The ulcer did not have the undermined edge that may be a feature of a Behcet's ulcer. However, the process was more diffuse than the classic appearance of peptic ulceration, showing a blend of polymorphous inflammatory cell infiltrates, necrosis of tissue, and hemorrhage. Finally, strong evidence against chronic peptic ulcer disease was provided by barium meals 8 months and 3 months before death that failed to show duodenal abnormality. Notwithstanding several years of moderate doses of aspirin and indomethacin, there were no gastric erosions.

Numerous reviews of BS have described nonspecific gastrointestinal signs and symptoms such as abdominal discomfort, distention, tenderness, nausea, eructation,

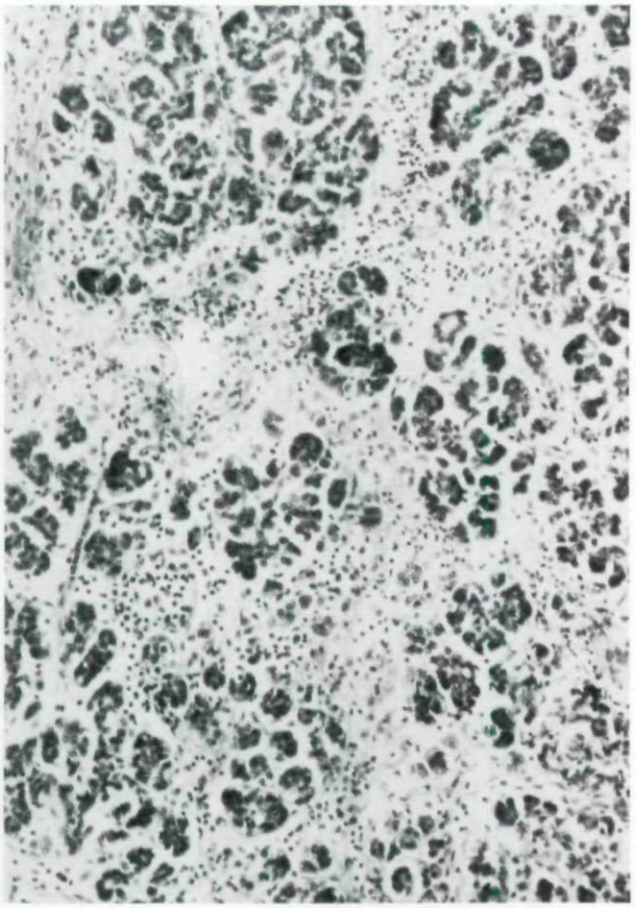

FIG. 4. Although there is focal fat necrosis, the most consistent pattern in pancreas is as above. There is a diffuse chronic inflammation throughout the interstitium (hematoxylin and eosin stain, ×200 magnification).

loss of appetite, and diarrhea. The incidence of these varies from high in Japan (6) to low in England (7) and Israel (10). Ulcerative hemorrhagic lesions have occurred in the esophagus, stomach, and small bowel, colon, and anus with a tendency to undermining and fissuring (6). Perforation, often at multiple sites, has been especially frequent in Japan, occurring in 41% of 61 cases with intestinal ulcers (6). None of the ulcers was located in the duodenum. In an English series (7), three patients with BS had duodenal ulcers visualized radiographically.

The mild chronic pancreatitis in our case, discovered unexpectedly at autopsy, did not contribute to biliary tract obstruction but possibly accounted for bouts of abdominal pain during earlier hospitalization. Serum amylase and lipase determinations were not done. Pancreatic involvement has been described once with BS as clinically acute pancreatitis (1). Another unusual feature in our case was mild splenomegaly characterized at necropsy as merely congestive. No vascular lesion was found to account for this. Splenomegaly was first reported with BS in 1946 (11) and reviewed in 1978, when two enlarged spleens also showed normal histology (12).

Liver involvement in BS has not been reported except for notation of abnormal bromsulphalein retention in a few patients during relapse (13). Palpable hepatomegaly has been mentioned rarely (14–16) and documented once with a Budd-Chiari syndrome from an associated venous thrombosis (17). In a patient with proven normal splenic and portal veins and with a firm enlarged liver, biopsy showed aggregates of inflammatory cells around the portal tracts (12). Liver biopsies in five patients reported in a Turkish series were normal (16).

Finally, at postmortem we looked carefully at the genito-urinary tract for pathology correlating with the several years of pyuria and hematuria in the presence of persistently normal renal function. A number of patients with BS have had prolonged benign hematuria or proteinuria without demonstration of a pathological substrate (13, 18). Despite the added feature of pyuria, our patient similarly showed normal renal histology devoid of focal glomerulitis or amyloidosis, the lesions hitherto related to BS (2). Similarly, the brain showed only occasional perivascular lymphocytes, a minor and nonspecific finding, despite the repeated occurrence of headache, confusion, and partial memory loss.

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Reprint requests: Armin E. Good, M.D., Veterans Administration Medical Center, 2215 Fuller Road, Ann Arbor, MI 48105.

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