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CASE REPORT | LIVER

Sarcoidosis Presenting as Necrotizing Sarcoid Granulomatosis of the Liver, Sclerosing Cholangitis, and Gastric Ulcer

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Abstract

Sarcoidosis is a multisystem granulomatous disease. The liver is affected in up to 50–90% of cases. Sarcoidosis typically presents as non-necrotizing epithelioid granuloma. The occurrence of non-infective necrotizing sarcoid granuloma (NSG) is infrequent, and the finding of NSG in the liver is rare. We report a case of NSG of the liver and lymph nodes, granulomatous gastric ulcer, and secondary cholangitis coexisting in a patient. We discuss the clinical features of the case and briefly review NSG. There is only 1 previously reported case of NSG of the liver in literature.

Introduction

Sarcoidosis is a multisystem granulomatous disease that has a prevalence of approximately 3–5 per 100,000. The incidence is highest among young adults aged 25–40 years old. The immunopathologic basis is complex and involves interplay between genetic predisposition, sarcoid antigen, and immune cells. The liver is affected in to 50–90% of cases. Sarcoidosis typically presents as non-necrotizing epithelioid granuloma, and presentation as non-infective necrotizing sarcoid granuloma (NSG) is infrequent. The finding of NSG in the liver is rare.

Case Report

A 26-year-old African-American male was referred for epigastric and right upper quadrant (RUQ) abdominal pain and pruritus for 1 year, with associated nausea and intermittent vomiting. He denied nonsteroidal anti-inflammatory use. Physical exam revealed scleral icterus, generalized lymphadenopathy, and tender hepatosplenomegaly. To evaluate his symptoms, an esophagogastroduodenoscopy (EGD) was done and showed esophageal varices and a gastric ulcer. Gastric ulcer biopsy showed chronic active gastritis and acute inflammation with focal granuloma, with stains negative for *Helicobacter pylori*. RUQ ultrasound showed gallbladder wall thickening and a cholecystectomy was planned; during the operation, the gallbladder was noted to be adherent to the liver and could not be dissected. The liver appeared nodular, so a wedge biopsy was performed, which demonstrated granulomatous inflammation with areas of necrotizing granulomata and portal triads that were difficult to locate.

Laboratory tests showed cholestatic liver pattern (Table 1). He had normal lipase, with negative tests for viral hepatitis and HIV. Ferritin, cerruloplasmin, and alpha-1 antitrypsin serum levels were normal. Cytoplasmic anti-neutrophil cytoplasmic antibodies (C-ANCA), perinuclear anti-neutrophil cytoplasmic antibodies (P-ANCA), anti-nuclear, anti-mitochondrial, anti-smooth muscle, and anti-liver kidney antibodies were negative. Tests for *Toxoplasma gondii*, *Bartonella*, *Brucella*, *Treponema pallidum*, and *Histoplasma* were negative. Purified protein derivative (PPD) skin test was non-reactive. Chest computed tomography (CT) showed hilar and mediastinal lymphadenopathy. Abdominal CT showed hepatomegaly with asymmetric left lobe enlargement, splenomegaly,

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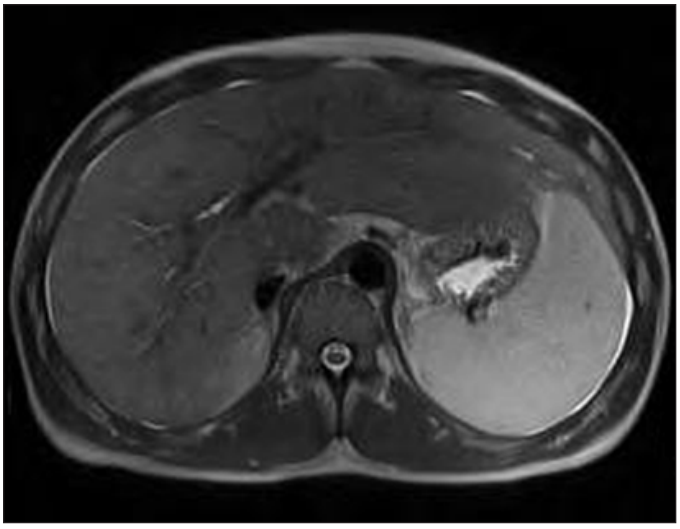

Figure 1. Magnetic resonance cholangiogram of the liver showing hepatomegaly and sclerosing cholangitis.

and retroperitoneal and periportal lymphadenopathy. A magnetic resonance cholangiogram showed sclerosing cholangitis (Figure 1). An endoscopic retrograde cholangiogram (ERCP) was done to evaluate for extrahepatic biliary obstruction and showed a normal common bile duct, though the left hepatic duct showed diffuse rarefaction and the right hepatic duct did not opacify. To confirm that the lymphadenopathy was part of the same disease process, a right cervical lymph node biopsy was done, which showed necrotizing and non-necrotizing granulomatous inflammation (Figure 2). Gram stains, acid fast bacilli (AFB), and Warthin-Starry stains were negative for microorganisms. Cultures for AFB, anaerobic, and fungal organisms were negative. Given these findings, the patient was diagnosed with sarcoidosis.

The patient was started on 40 mg of prednisone. He showed an improvement in abdominal pain and a decrease in total bilirubin. He was discharged with a plan for outpatient management. His total bilirubin decreased (Table 1) and he continued to require prednisone therapy.

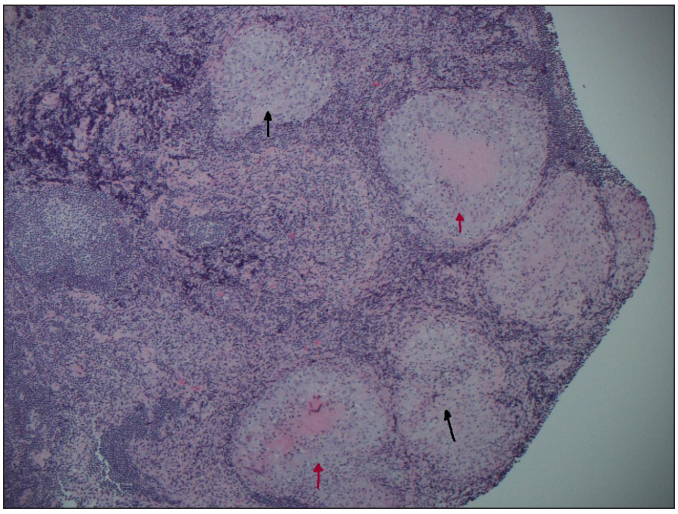

Figure 2. Lymph node biopsy showing both necrotizing granulomas (red arrows) and non-necrotizing granulomas (black arrows).

Table 1. Patient Laboratory Values at Baseline and After 1 Year Of Prednisone

	Baseline	After 1 Year of Prednisone
WBC, k/uL	3.4	4.3
Hemoglobin, g/dL	10.6	12.8
Hematocrit, g/dL	31.1	38.6
AST, U/L	162	96
ALT, U/L	151	117
ALP, U/L	993	288
GGT, U/L	344	NA
T. bilirubin, mg/dL	8.6	1.4
T. protein, g/dL	8.8	7.4
Albumin, g/dL	2.1	2.9
INR	1.1	1.1
ACE	70	10

ACE = angiotensin-converting enzyme; AST = aspartate aminotransferase; ALT = alanine transaminase; ALP = alkaline phosphatase; GGT = gamma glutamyl aminotransferase; INR = international normalized ratio; NA = not applicable; WBC = white blood cell

Discussion

Sarcoidosis is a multisystem disease. The liver is commonly affected, but hepatic presentations are usually mild.[1] Up to 3% of patients develop severe hepatic involvement with portal hypertension and esophageal varices.[2] Sarcoidosis rarely involves the luminal gastrointestinal tract and is usually asymptomatic. It is diagnosed on the basis of clinical presentation, biochemistry, radiology, and histopathology. The features depend on the affected organ. Hepatic sarcoidosis may present as fatigue, RUQ abdominal pain, pruritus, jaundice, weight loss, and fever.[3] Features of esophageal sarcoidosis include dysphagia from impaired motility, esophagitis, stricture, or extrinsic compression from paraesophageal nodes.[4] Gastric presentation includes epigastric pain, ulcers, gastric polyps/nodules, or linitis plastica-like lesions.[4] Ten percent of individuals with sarcoidosis have gastric involvement with normal appearing mucosa.[5] Involvement of the small bowel may clinically present with abdominal discomfort, malabsorption, protein losing enteropathy, gastrointestinal bleed, or intestinal obstruction. Colonic manifestations include colitis, polyposis, or a mass.[4]

Our patient had compelling features of sarcoidosis, including including anergy to PPD, elevated serum angiotensin-converting enzyme (ACE) levels, a cholestatic liver biochemistry, hilar and mediastinal lymphadenopathy, and histologic granulomas. The histology of sarcoidosis is typically described as non-necrotizing epithelioid granulomas, though necrotizing granuloma in the setting of sarcoidosis has been described.[6]

There are 3 histologic categories of hepatic sarcoidosis: cholestatic, necroinflammatory, and vascular patterns.[7] Our patient falls in to the necroinflammatory pattern, which has chronic portal inflammation and spotty necrosis.

Liebow first described non-infective necrotizing granulomas and coined the term necrotizing sarcoid granuloma (NSG) in 1973.[8] The majority of reported cases of NSG affect the lungs, but cases involving the skin, subcutaneous tissues, kidney, colon, and orbit have been reported. There is only 1 report of NSG involving the liver,[7] but the clinical presentation of the patient was not described. There is currently no consensus on whether NSG is a manifestation of sarcoidosis or a distinct vasculitic entity. Saldana et al believed that NSG was a different entity. Their patients with NSG lacked extra-thoracic involvement, had normal serum ACE levels, and only a few had hilar adenopathy.[9] Churg et al concluded that NSG was a histologic manifestation of nodular sarcoid.[10]

There is no confirmatory test for sarcoidosis. The diagnosis is based on excluding other causes of granulomatosis, such as primary biliary cirrhosis, Crohn's disease, tuberculosis, brucellosis, viral hepatitis, fungal infections, lymphoma, and drugs. The treatment of NSG is empiric. Oral prednisone 40–60 mg daily for 8 weeks with a slow taper based on clinical response has been recommended.[11] The unique features of this case are 2 rare manifestations of sarcoidosis—NSG and a gastric ulcer—in the same patient, which has not been previously reported.

Disclosures

Author contributions: N. Momah designed the study and revised and critically reviewed the manuscript for content. A. Otesile obtained and edited the images. R. Pawa critically reviewed the manuscript. S. Shedlofsky revised and critically reviewed the manuscript for content, and is the article guarantor.

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Informed consent was obtained for this case report.

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