Sarcoidosis: an Extremely Rare Cause of Granulomatous Enterocolitis

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**Abstract**

Clinically recognizable gastrointestinal (GI) system involvement with sarcoidosis is extremely rare. We present a case of a 51-year-old Caucasian male who was evaluated for abdominal pain, elevated liver enzymes, leukopenia, thrombocytopenia, severe peripheral arthralgias, and chronic watery diarrhea. He had a history of mediastinal and periaortic lymphadenopathy. Extensive laboratory workup for liver diseases, infections, malabsorption and a bone marrow biopsy was essentially unremarkable. Esophagogastroduodenoscopy was unremarkable. Colonoscopy showed scattered right colon ulcerations and erythema. The terminal ileum appeared normal. Biopsies from the duodenum, terminal ileum, and colon showed intramucosal non-caseating granulomas with focal multinucleate giant cell formation in a background of chronic active duodenitis, ileitis, and colitis. Liver biopsy showed moderate non-specific chronic hepatitis with non-caseating granulomas present within portal and lobular parenchyma. The clinical presentations, along with biopsy results were suggestive of sarcoidosis. The patient was started on prednisone and had a significant improvement in his symptoms including diarrhea.

**Key words**


**Introduction**

Sarcoidosis is a systemic granulomatous disease of unknown etiology, characterized by the formation of noncaseating granulomas. Clinically recognizable gastrointestinal (GI) system involvement is extremely rare. The stomach is the most commonly involved portion of the GI tract, but sarcoidosis of the esophagus, liver, small intestine, appendix, colon, rectum, pancreas, and peritoneum has also been described [1]. Small intestine sarcoidosis is the rarest.

Some autopsy studies did not find any GI involvement [2-3]. Another autopsy study reported intestinal and gastric disease in 3.4% and 2.5% of cases, respectively [4]. However, in the frequency of involvement, liver follows the lymph nodes and the lung. Around 50–79% of liver biopsies and 67–70% of autopsies demonstrate liver involvement [3, 5–7].

**Case report**

A 51-year-old Caucasian male patient was followed in the gastroenterology clinic for complaints of abdominal pain, diarrhea and weight loss of 60 pounds over 4 months. The diarrhea was watery, up to 12 times a day with nocturnal fecal incontinence. His abdominal pain was in the left and upper quadrants. He has a history of hypertension, diabetes, previous heavy alcohol drinking and mediastinal lymphadenopathy found incidentally on chest x-ray and CT scan. The lymphadenopathy was followed up by serial CT scans for 15 months and remained stable.

His initial labs showed white blood cells 2900/mcL, hemoglobin 11.1 g/dL, platelets 104,000/mcL, total bilirubin 1.7 mg/dL, AST 164 U/L, ALT 81 U/L, ALP 185 U/L and LDH 282 U/L. Fecal leukocytes and FOBT were positive. Ultrasound of the abdomen showed mildly echogenic liver suggestive of fatty liver, dilated portal vein measuring 1.6 cm, enlarged spleen measuring 16.1 cm and gallstones. The rest of his lab work was negative (or normal) including albumin, INR, viral hepatitis panel, urine histoplasma antigen, HIV Ab, H. pylori Ab, PPD, urine legionella antigen, anti-gliadin antibodies, carcinoembryonic antigen, urine 5-hydroxyindoleacetic acid (5-HIAA), ACE level, RPR and brucella IgM and IgG, anti-mitochondrial antibody, CMV IgG and IgM, Monospot test, ANA, smooth muscle antibody,
ceruloplasmin level, anti-smooth muscle antibody, alpha 1-antitrypsin, HFE C282Y and HFE H63D.

Stool studies were negative for ova, parasites, culture, gram stain, giardia antigen, clostridium difficile, shigella, salmonella and cryptosporidium antigen. CT scan of the abdomen and pelvis showed multiple enlarged periaortic lymph nodes. Bone marrow biopsy showed only slightly hypercellular marrow with normoblastic trilineage hematopoiesis.

Esogastroduodenoscopy was grossly unremarkable. Colonoscopy showed scattered right colon ulcerations and erythema. Mucosal biopsies from the duodenum (Fig. 1), terminal ileum, and colon all shared common features. There was brisk granulomatous inflammation characterized by intramucosal non-caseating granulomas with focal multinucleate giant cell formation in a background of chronic active duodenitis, ileitis, and colitis. Schaumann bodies and asteroid bodies were not identified in any of the biopsy material. PAS fungal stains and fite stains performed on biopsy material from each mucosal site were negative for microorganisms. The liver biopsy (Fig. 2) showed moderate non-specific chronic hepatitis with non-caseating granulomas present within portal and lobular parenchyma. Within some granulomas there was focal multinucleate giant cell formation. A PAS fungal stain and a fite stain were negative for microorganisms. Schaumann bodies and asteroid bodies were not identified. The liver parenchyma surrounding the granulomas demonstrated a portal and lobular mononuclear inflammatory cell infiltrate with moderate fibrosis demonstrated by trichrome stain.

Sarcoidosis was favored over Crohn’s disease in light of the systemic lymphadenopathy and liver involvement with non-caseating granulomas. The patient was started on prednisone taper dose and a remarkable improvement in the diarrhea was observed within a few days. However, 6 weeks after starting the prednisone he was admitted to another hospital with chest pain and prednisone was stopped. As soon as prednisone was halted the diarrhea became worse. Eventually, prednisone was restarted and the patient had substantial improvement in his symptoms.

**Discussion**

The diagnosis of sarcoidosis in general is based on a consistent history, presence of granulomas in at least two different organs, absence of occupational or domestic exposure to toxins, negative staining and culture for acid fast bacilli and lack of drug-induced disease. ACE levels are elevated in 60% of the patients [8]. The presence of non-caseating granulomatous inflammation is the key for diagnosis. However, Crohn’s disease, Whipple’s disease, tuberculosis, fungal infections, syphilis, and foreign body reaction can have a similar pathological appearance.

Sarcoidosis of the small intestine was reported previously in only a few cases [9-14]. Symptoms include non-bloody diarrhea, abdominal pain, weight loss, anorexia, low-grade fever, and weakness. Complications might include folate deficiency or malabsorption of vitamin B12 with terminal ileal disease or achlorhydria. Sarcoidosis of the colon was reported previously in a few cases [12-26]. It might present as aphthous erosions, multiple nodules, polyps, obstructive lesions, stenosis, or small punctuate bleeding sites. Intestinal obstruction due to external compression by lymphadenopathy can also happen. Sarcoidosis of the colon and terminal ileum can resemble Crohn’s disease [27-29]. Moreover, sarcoidosis coexists rarely with Crohn’s disease or ulcerative colitis [30-33].

Histopathological features that can distinguish sarcoidosis from Crohn’s disease include the presence of calcium and protein inclusions within the cytoplasm of Langhans multinucleate giant cells (Schaumann bodies), intramucosal rather than submucosal granulomas, and the lack of fistulas. Crohn’s disease is not typically associated with elevated ACE level [34]. There is overall a lack of mucosal architectural distortion and acute inflammation in sarcoidosis. Sarcoidosis generally responds better to corticosteroid treatment than it does in Crohn’s disease, often with improvement after only a few days [18].

Up to 35% of patients with sarcoidosis have abnormal liver function tests [35-36]. Most patients with liver involvement are asymptomatic and have only biochemical abnormalities. Clinically apparent liver disease is uncommon even in patients who have numerous hepatic granulomas. Liver biopsy
typically shows non-caseating granulomas. The granulomas are often located in the portal tract. Schaumann bodies are diagnostic of sarcoid granulomas, but rarely seen in hepatic granulomas. Excluding other granulomatous liver disease with staining for mycobacteria and fungi is helpful. Rarely, clinical complications will lead to cirrhosis, cholestatic liver disease [37], and hepatic vein thrombosis [38].

The lymphadenopathy, hepatic non-caseating granulomas, intramucosal intestinal non-caseating granulomas, rapid response to prednisone and negative testing for other granulomatous diseases favored the diagnosis of sarcoidosis in our patient.

Conclusion

Gastrointestinal involvement in sarcoidosis is very rare. Our patient had diffuse involvement with sarcoidosis of the liver, small intestine and colon. Symptoms included abdominal pain and diarrhea. Sarcoidosis may resemble Crohn’s disease. Lymphadenopathy and liver involvement with non-caseating granulomas favor the diagnosis of sarcoidosis.

References

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