

Early Involvement by Extra-Pulmonary Sarcoidosis Presenting with Epigastric Pain

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Abstract

Gastrointestinal sarcoidosis leads to the formation of non-caseating granulomas in any GI-related organ. Overt presentation is rare, with subclinical involvement of the GI tract estimated to be higher. The diagnosis of GI sarcoidosis depends on clinical manifestations of the disease, and when possible, histology demonstrating characteristic non-caseating granulomas. Diseases capable of producing a similar clinical and/or histological picture must be excluded. Herein, we report a case of a patient with pulmonary sarcoidosis in remission, presenting with mild epigastric pain, and subsequently diagnosed with biopsy-proven gastric sarcoidosis.

Index terms— sarcoidosis, GI sarcoidosis, extra-pulmonary sarcoidosis, gastrointestinal diseases.

1 I. Introduction

Sarcoidosis is a well-known multisystem disease characterized by non-caseating granulomas. 1 Of those with extra-pulmonary involvement, the heart, lymphatic system, eyes and skin are the most frequently affected organ systems. 2 While gastrointestinal (GI) involvement is extremely rare with an incidence of <1%, the stomach remains the most common site of involvement. 1,3 These cases of GI sarcoidosis are difficult to diagnose in that they are often clinically silent, and symptomatic in only 0.9% of patients. 3,4,11 II.

2 Case Report

A 41-year-old African American woman with known pulmonary sarcoidosis (in remission) presented to the ED complaining of epigastric pain for 5 days. She had previously been treated with prednisone, which was discontinued 8 years ago due to adverse side effects. She was doing well over the last several years off steroid treatment. However, over the last one-month prior to presentation, she did endorse a 10-lb weight loss, which she felt was "partly intentional," and ultimately presented due to the epigastric pain. She denies any nausea or vomiting.

On encounter, the patient had normal vitals, with physical exam notable for mild epigastric tenderness on deep palpation, along with erythema nodosum of the lower extremities. There was no evidence of hepatic or splenic enlargement. Laboratory findings were significant for creatinine of 2.17 mg/dL, calcium 10.2 mg/dL, amylase 1583 U/L, lipase 89 U/L, alkaline phosphatase 171 U/L, C-reactive protein (CRP) 4.9 mg/dL, and angiotensin converting enzyme (ACE) 72 U/L.

A computed tomography (CT) scan of the abdomen showed no evidence of pancreatitis or gastric malignancy but highlighted the presence of retroperitoneal lymphadenopathy. Abdominal ultrasound with doppler revealed hepatic steatosis with no dilation of the bile ducts or cholelithiasis. Esophagogastroduodenoscopy (EGD) demonstrated moderate gastritis in the gastric body, antrum, and fundus, with no evidence of any ulceration or mass (Figure 1).

Multiple biopsies were taken from the stomach and normal appearing duodenum, which ultimately revealed focal ill-formed granulomas and few giant cells with calcified material (Figure 2). These findings, per expert review, were consistent with early involvement by sarcoidosis.

During the hospital course, the patient was given IV hydration and a daily oral proton pump inhibitor (PPI), with gradual improvement of her epigastric pain. Within 3 days, her creatinine normalized, suggesting a pre-renal

cause of acute kidney injury, likely from poor appetite and dehydration. Given her overall improvement on a PPI and previous poor response to prednisone, the decision was made to hold off on steroid treatment. The patient's epigastric pain ultimately resolved and she was subsequently discharged on a PPI alone, with close follow up with gastroenterology.

3 III. Discussion

Sarcoidosis is an inflammatory condition characterized by the formation of non-caseating granulomas in response to an unknown trigger.⁵ It most commonly involves the pulmonary system, however, non-pulmonary systems such as cardiac, gastrointestinal, reticulo-endothelial, ophthalmic, skin, and others, are commonly involved as well.⁶⁻⁸ African American women are the most frequently affected population, and have a higher incidence and prevalence of extra-pulmonary disease.^{9, 10, 12.}

Gastrointestinal disease is seen in only 0.9-1.1% of patients with sarcoidosis.^{1,3} The small bowel is the least common GI site affected by sarcoidosis, while the stomach remains the most common site of GI-tract involvement.^{3,11,13,14} These cases of gastrointestinal sarcoidosis are often clinically silent. In those who are symptomatic, typical presentations include epigastric discomfort, and rarely, upper GI bleeding can be the presenting complaint.^{6,11,13,15,16} These findings were confirmed by Chinitz et al., in a review of 20 biopsyproven cases of symptomatic gastric sarcoidosis.¹⁷ The most prominent symptom in these patients included epigastric pain in 75% and GI tract bleeding in 25%.¹⁷ Less common but well described presentation includes ulcers, polyps, or local/diffuse inflammation.¹⁸ They can also result in catastrophic outcomes, such as fibrosis leading to pyloric obstruction or the development of a neoplasm. ^{7,13,15,19} Diagnosis of gastric sarcoidosis is based upon the histologic evidence of non-caseating granulomas along with a compatible clinical history. The gastric mucosa on endoscopy can oftentimes appear normal; hence, multiple biopsies and microscopic examination, has become essential for diagnosis. ⁷ The microscopic appearance of gastric sarcoidosis varies from small aggregations of epithelial histiocytes with or without multinucleate giant cells to large nodular or polypoid aggregates of granulomas.¹⁹ Caution is necessary while arriving at a diagnosis of GI sarcoidosis solely on the basis of microscopic exam, as a collection of epithelioid cells may form as a reaction to non-specific agents.²⁰ Additionally, other granulomatous diseases, including Crohn's disease, Whipple's disease, reaction to malignancy, tuberculosis, histoplasmosis, and syphilis, need to be excluded as well.

Compared to sarcoidosis of the heart, nervous system and eye, where there is a clear role for corticosteroid use, the role of steroids in treating gastric sarcoid is less apparent. ^{1,3,21} The decision to treat with steroids is largely based upon the severity of symptoms. In symptomatic patients steroids are the first line treatment of choice, and anti-acid therapy can be used as an alternative in less severe cases.^{13,18} Most patients respond well to steroids, and disease-modifying anti-rheumatic drugs are used for steroid refractory patients.⁷ Further studies are needed to fully assess the efficacy of corticosteroids in treating patients with GI sarcoidosis.

Given our patient's previous poor response to steroids, and her improvement in GI symptoms while on a PPI, we discharged our patient on a PPI alone. Whether she will need other immunosuppressive or surgical treatment will be based on the evolution of her symptoms on follow up.

Our case underscores the importance of considering gastrointestinal involvement of sarcoid in patients with a known history of sarcoidosis presenting with typical or unusual GI complaints. Individuals with organ-specific sarcoidosis, whether active or in remission, are still at risk for other organ manifestations of the disease. Clinical manifestations together with endoscopic biopsies remain pivotal for establishing a diagnosis, and allowing for appropriate directed management. Further studies are necessary to dictate standard treatment modalities for these patients with rare gastric manifestations of sarcoidosis.

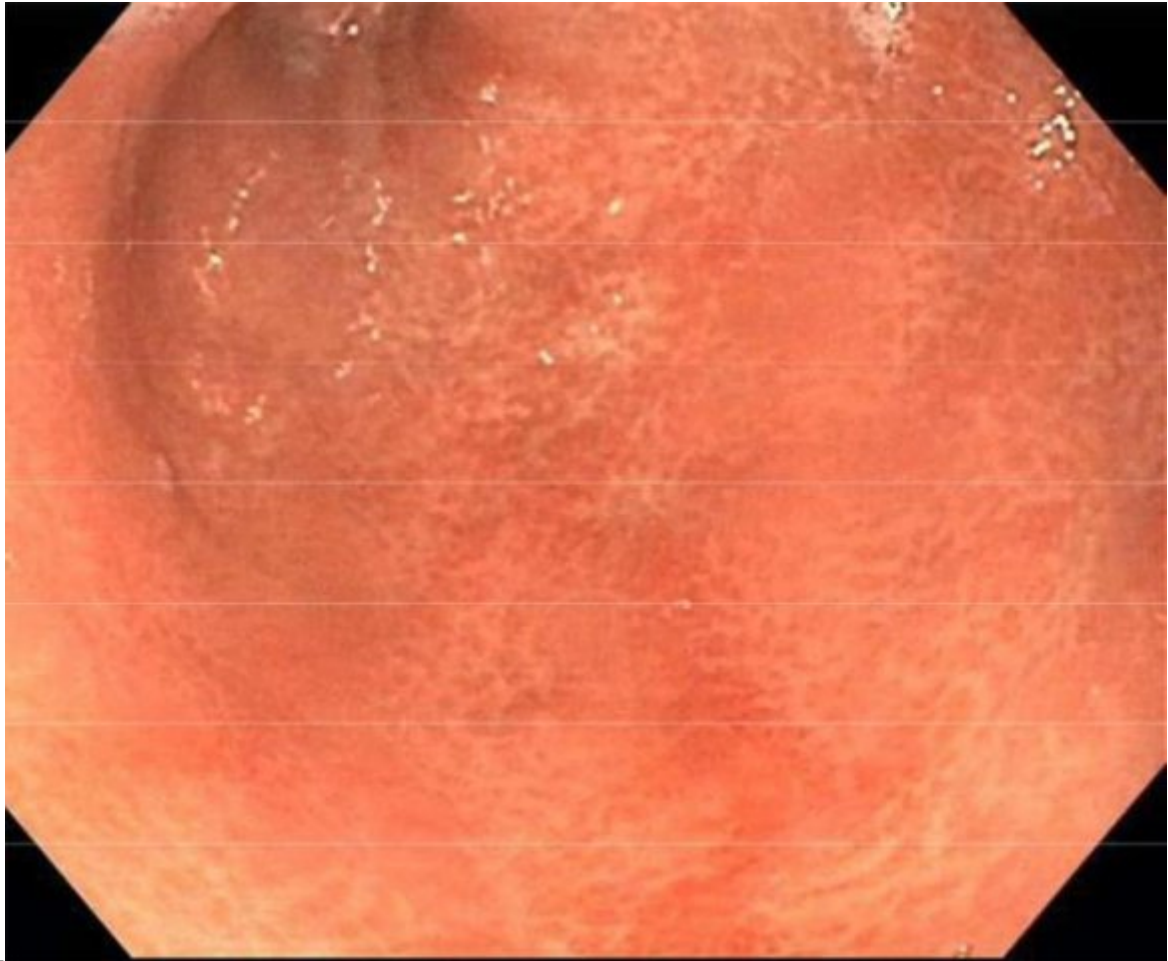


Figure 1: Figure 1 :

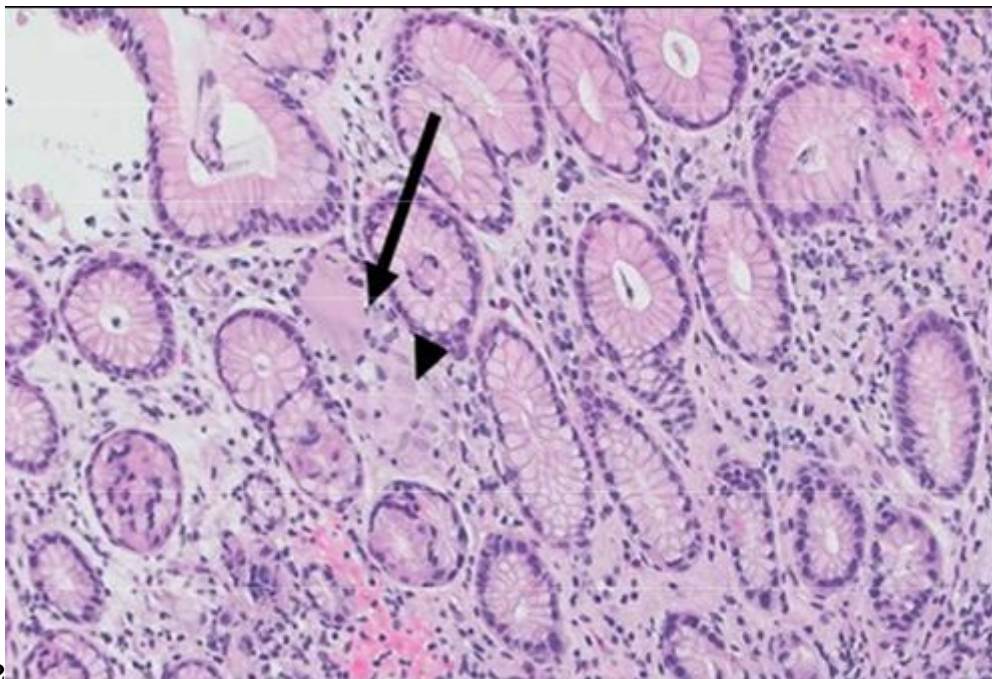


Figure 2: Figure 2 :

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