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CASE REPORT | INFLAMMATORY BOWEL DISEASE

Incidental Hepatic Granulomata as the Initial Presentation of Crohn's Disease in a Pediatric Patient

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ABSTRACT

We describe a 9-year-old girl who presented with abdominal pain, found incidentally to have multiple liver granulomata. Extensive autoimmune and infectious workup was negative. The patient had esophagogastroduodenoscopy and colonoscopy, confirming the diagnosis of Crohn's disease. Hepatic granulomata are a rare complication of Crohn's disease and are often secondary to pharmacotherapy or infection in immunosuppressed patients. This case, to our knowledge, is the first reported case of a pediatric patient diagnosed with Crohn's disease after initially presenting with hepatic granulomata as an extraintestinal manifestation of the disease.

INTRODUCTION

Crohn's disease, a form of inflammatory bowel disease (IBD), is characterized by chronic or recurring inflammation of the gastrointestinal tract and often presents with abdominal pain, diarrhea, fatigue, gastrointestinal bleeding, and weight loss. Extraintestinal manifestations (EIM) of IBD are broad, involving ocular, dermatologic, musculoskeletal, hepatopancreatobiliary, and/or pulmonary systems.

CASE REPORT

A 9-year-old immunized girl with a history of migraines and anxiety presented with right flank/upper quadrant pain for 2-3 weeks. She additionally had weight loss over the previous 3 months, dropping from a mid-70th weight percentile to the 14th percentile (z score −1.04). She denied fevers/chills, nausea, vomiting, constipation, diarrhea, or hematochezia during this time.

Initial evaluation included complete blood count, erythrocyte sedimentation rate (ESR), complete metabolic and liver panel, antitissue transglutaminase IgA, total IgA, and complete urinalysis, notable only for elevated ESR (41 mm/hr). The patient underwent abdominal ultrasound, which showed normal kidneys and urinary bladder as well as 2 ill-defined, hypoechoic right hepatic lesions, prompting gastroenterology referral (Figure 1).

Magnetic resonance imaging demonstrated 5 T1 hypointense and T2 intense lesions in the posterior right hepatic lobe ranging between 1.0 and 2.6 cm in diameter (Figure 1). The patient underwent an ultrasound-guided needle biopsy of the hepatic masses, identified as necrotizing granulomata with chronic periportal and lobular inflammation (Figure 1). The biopsies were negative for steatosis, cholestasis, or other features suggestive of focal nodular hyperplasia or hepatic adenoma. Acid-fast bacillus and Grocott methenamine silver stains were negative for mycobacterial or fungal organisms, respectively. The differential diagnosis for the granulomata initially included infectious, adverse drug reaction, autoimmune, and idiopathic etiologies. The patient's only medication, topiramate, was weaned.

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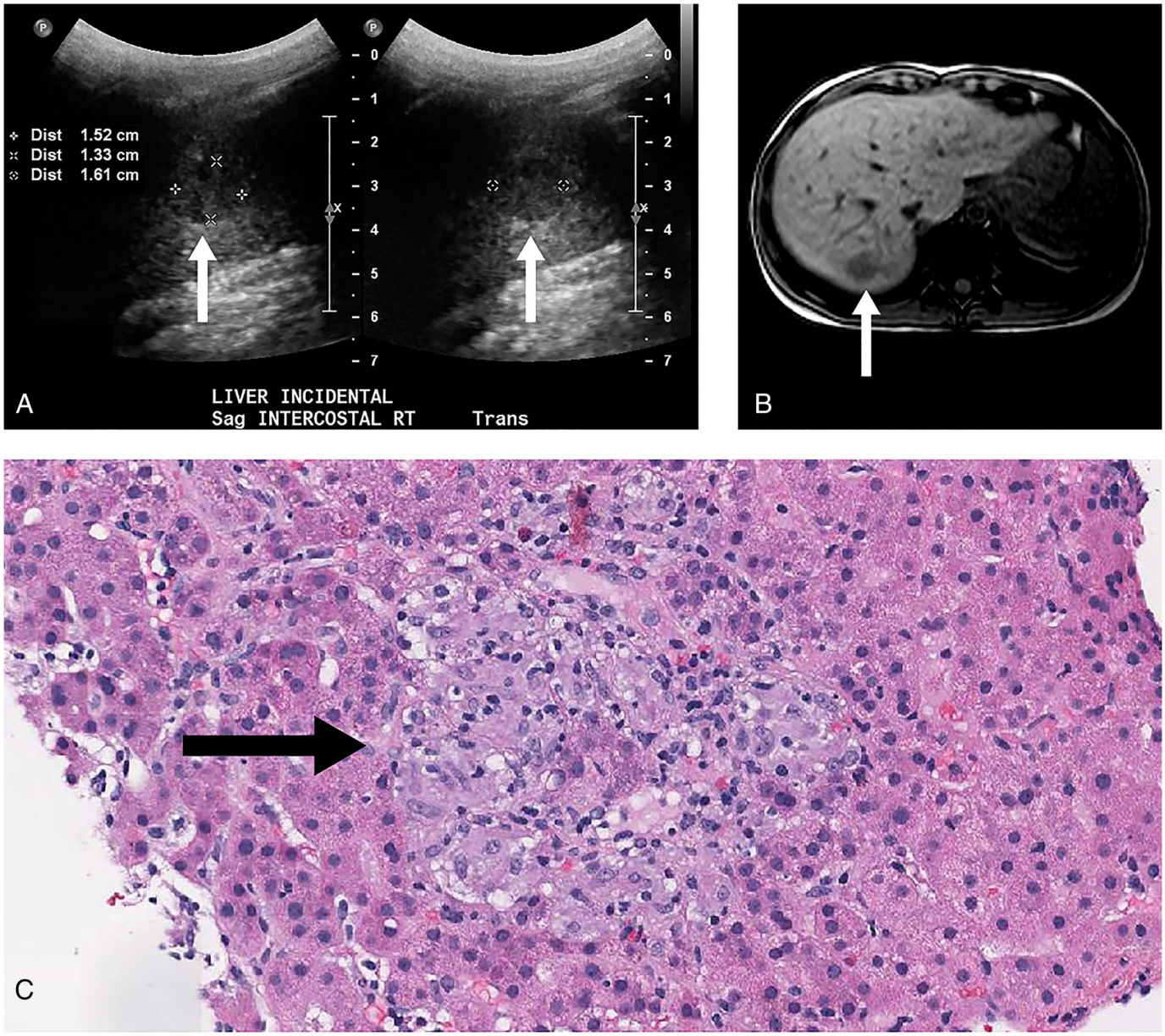

Figure 1. Ultrasound demonstrating (A) 1 of 2 identified nonspecific hypoechoic lesions; MRI demonstrating (B) 1 of the 5 identified T1-hypointense lesions; liver biopsy demonstrating (C) necrotizing granulomata at 20× magnification.

The patient had no family history of immunodeficiency, vasculitides, or gastrointestinal diseases. She had no significant environmental risk factors. Further evaluation was notable for normal C-reactive protein, angiotensin-converting enzyme level, total immunoglobulins, and neutrophil oxidative burst. ESR remained mildly elevated (38 mm/hr). Testing for tuberculosis, Bartonella, and HIV were negative. Epstein-Barr virus serologies were positive, suggestive of previous but not acute infection. Chest radiographs did not demonstrate evidence of sarcoidosis. The patient had normal neutrophil oxidative burst, effectively ruling out chronic granulomatous disease. No clear explanation for the development of necrotizing granulomata in this patient was identified in this workup.

The patient continued to have abdominal pain, prompting further evaluation, including fecal calprotectin which was borderline elevated (230 mcg/g). Esophagogastroduodenoscopy (EGD) was notable for few superficial ulcers in the stomach antrum but was otherwise unremarkable. Colonoscopy was notable for erosions, erythema, friability, inflammation, and ulceration in the terminal ileum, concerning for Crohn's disease (Figure 2). Pathology confirmed active Crohn's disease in the stomach and in the terminal ileum. The patient was started on a prednisone taper with improvement in symptoms. The patient subsequently transitioned to infliximab 5 mg/kg every 8 weeks as maintenance therapy, although she required dose escalation to 15 mg/kg every 4 weeks.

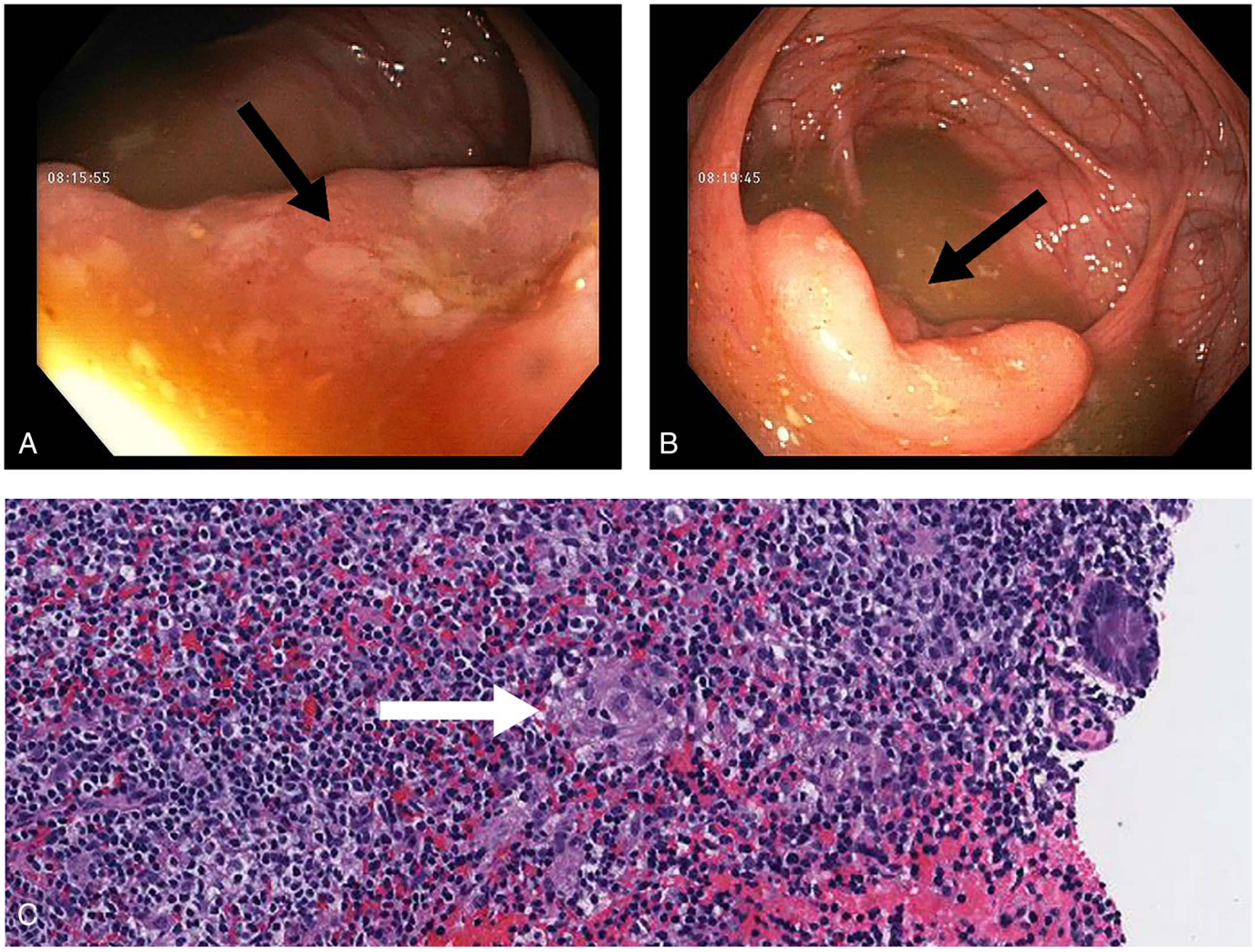

Figure 2. Colonoscopy demonstrating (A) erosion, erythema, friability, inflammation, and ulceration in the terminal ileum and (B) inflammation of the ileocecal valve. Biopsies from initial colonoscopy demonstrating (C) loose histiocytic aggregate (granuloma) in the lamina propria of the ileum.

Approximately 16 months later, the patient underwent repeat EGD and colonoscopy to evaluate for mucosal healing. EGD was unremarkable. Colonoscopy again demonstrated edema, erythema, and friability of the terminal ileum, consistent with active disease. Biopsy from the terminal ileum was notable for chronic ileitis with granulomata in the lamina propria (Figure 2). Repeat calprotectin was improved (56 mcg/g). Repeat abdominal ultrasound showed 2 superior right hepatic lobe hypoechoic lesions similar to previous imaging, although slightly decreased in size.

Overall, the patient demonstrated clinical and biochemical improvement with infliximab, although she continues to have evidence of mild active disease. The hepatic granulomata are thought to be an extraintestinal manifestation of her Crohn's disease, given the extensive and largely negative work up to date. At this time, the patient plans to continue maintenance infliximab.

DISCUSSION

EIM are thought to be present in 6%–47% of patients with IBD.[1] The most common forms of EIM are arthritis, aphthous stomatitis, uveitis, erythema nodosum, pyoderma gangrenosum, and primary sclerosing cholangitis.[2] A recent study found nearly 30% of patients with IBD had at least 1 EIM, with 1 quarter of these patients presenting with an EIM before the diagnosis of IBD itself.[3]

The presence of histological granulomata in the liver is frequently referred to as granulomatous hepatitis.[4] Despite this name, patients are often asymptomatic without elevation in transaminases. Granulomatous hepatitis exists as a spectrum, with more severe forms including recurrent fever, myalgias, fatigue, and laboratory abnormalities.[5] The formation for hepatic granulomata can occur as an extraintestinal manifestation of IBD or as a complication associated with the treatment for the condition. Although the cause of granulomata formation is

unknown, it is thought to be a result of abnormal inflammation secondary to microbacterial dysbiosis.[6–8]

Granulomatous hepatitis occurs in <1% of patients with IBD.[9] Conversely, <2% of patients with hepatic granulomas have been found to have Crohn's disease.[10] Granulomas have diagnostic value in IBD because they are a key feature of Crohn's disease and are absent in ulcerative colitis.[11] The development of hepatic granulomata in patients without IBD is thought to be relatively benign if not considering the initial workup; however, the presence of hepatic granulomata in IBD constitute an EIM, of which having 2 or more systems involved raises concerns for a more aggressive IBD phenotype complicated by frequent flares requiring hospitalization, need for surgery, and poor response to current pharmacotherapy.[12] The formation of hepatic granuloma is more often secondary to pharmacotherapy (ie, mesalamine and sulfasalazine) or infection in immunosuppressed Crohn's patients (ie, histoplasma capsulatum).[9] In the case above, the patient had no evidence of infection on extensive workup and was not taking medications associated with granuloma formation.

To our knowledge, this is the first reported case in which a pediatric patient was diagnosed with Crohn's disease after the incidental finding of hepatic granulomata, an extraintestinal manifestation of the disease. This case clearly demonstrates the importance of keeping EIM of IBD in mind when evaluating patients because such symptoms may be their initial presentation of the disease.

DISCLOSURES

Author contributions: M. Mostafavi wrote the manuscript. W. Sayej and B. Hirsch provided the endoscopy images. B. Hansen provided the radiology images. A. Cretara and J. Mueller provided the pathology images. All authors revised the manuscript for intellectual content and approved the final manuscript. W. Sayej is the article guarantor.

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