

Bone Marrow Suppression Associated With Celiac Disease in a 4-Year-Old Boy

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ABSTRACT

Celiac disease is an immune-mediated process against gluten, resulting in inflammation and villous atrophy of the duodenum. Symptoms of malabsorption characterize the classic presentation; however, abdominal pain, constipation, and nutritional deficiencies can also be seen. We present a case of a 4-year-old boy who was found to have celiac disease after presenting with diarrhea, abdominal pain, weight loss, and new-onset pancytopenia. Symptoms resolved, and laboratory values normalized after the initiation of a gluten-free diet, indicating the bone marrow suppression was due to celiac disease, which needs to be considered when hematologic abnormalities are present, even in the absence of gastrointestinal symptoms.

INTRODUCTION

Celiac disease (CD) is an immune-mediated disease against gluten that is characterized by inflammation and villous atrophy of the duodenum. Prevalence is approximately 1%, and many risk factors including genetics, geographic location, ethnicity, and microbiome impact development of disease.¹ The presentation of CD varies widely. Classical CD presents with symptoms of malabsorption (diarrhea, steatorrhea, or weight loss); nonclassical CD presents without malabsorption but potentially with abdominal pain, constipation, or iron deficiency. CD can also be asymptomatic.² Extraintestinal manifestations typically include dermatitis herpetiformis, osteoporosis, short stature, failure to thrive, and delayed puberty.³ Impaired absorption of essential nutrients such as iron, folate, and vitamin B12 often causes hypoproliferative anemia.^{4,5} We present a case of severe bone marrow suppression occurring in a pediatric patient with newly-diagnosed celiac disease and no associated nutritional deficiencies.

CASE REPORT

A 4-year-old boy presented to his pediatrician's office with a 6-month history of diarrhea and intermittent abdominal pain. He had a 1-month history of fatigue and night sweats. He denied hematochezia, melena, or steatorrhea. Review of systems was negative for fevers, cough, congestion, rhinorrhea, emesis, change in appetite, joint pain, or rashes. There was no significant medical or surgical history. His family history included a maternal uncle with recurrent idiopathic thrombocytopenic purpura, but no history of inflammatory bowel disease, rheumatologic disorders, or CD. He attended daycare, but his parents denied any known sick contacts.

A workup revealed hemocult positive stools with no visible hematochezia or melena. Stool studies were negative for enteric infection, and multiple repeat complete blood counts demonstrated a slow decline in all cell lineages over a 1-month period. On follow-up, his absolute neutrophil count was found to be 100, hemoglobin 8.4 g/dL with mean corpuscular volume of 82 fL, reticulocyte percentage 0.1%, and platelets 140,000/ μ L (150,000–450,000/ μ L). Erythrocyte sedimentation rate was 63 (0–10 mm), C-reactive protein was 4.4 (0–1.0 mg/dL), and albumin was 2.8 g/dL (3.8–5.4 g/dL). The remainder of his laboratory values were within normal limits. A tissue transglutaminase (TTG) immunoglobulin A (IgA) antibody was obtained at this time also.

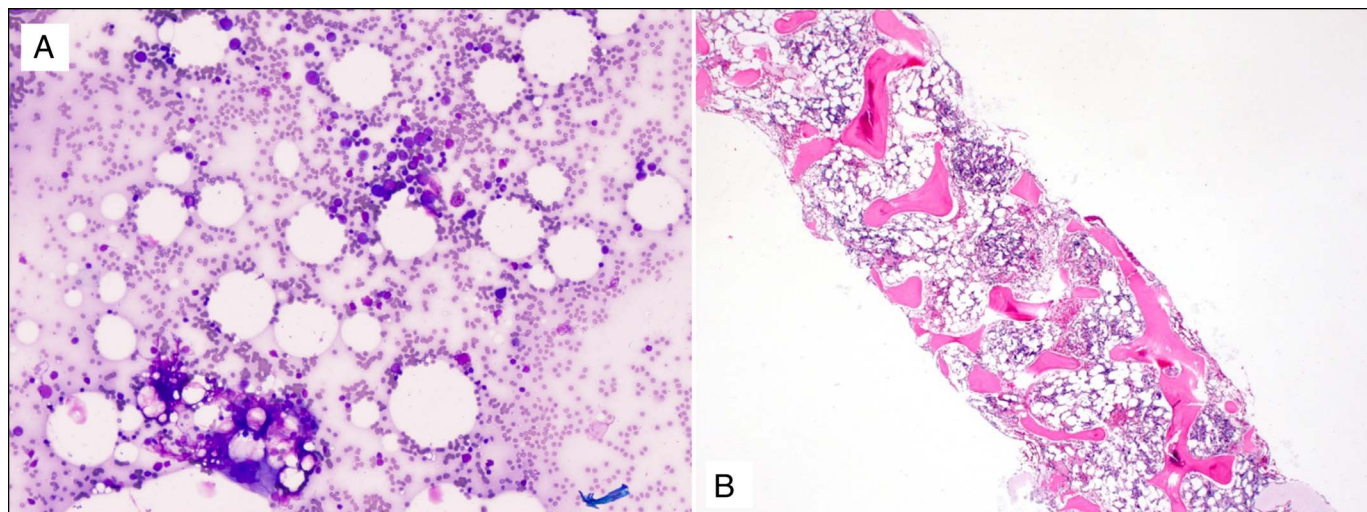


Figure 1. Photomicrographs of the bone marrow (a) aspirate and (b) biopsy that demonstrate hypocellular marrow with decreased myeloid and markedly decreased to absent erythroid elements. a: Wright-Giemsa, 100× magnification. b: Hematoxylin and eosin stain, 20× magnification.

Given the severe neutropenia, the patient was directly admitted to Children's Wisconsin on request of the pediatrician. He was tachycardic, had generalized pallor, and had bilateral cervical lymphadenopathy with a 1.5×1 cm right submandibular node. His abdominal examination was without tenderness, masses, or organomegaly. Perianal examination was normal. His growth curve revealed a weight Z-score decrease from 0.6 to -0.03 over the past 6 months.

At this time, the differential diagnosis was broad but focused on hematologic malignancy, very early onset inflammatory bowel disease (VEO-IBD), given the presence of gastrointestinal symptoms and other systemic inflammatory processes that would result in bone marrow suppression. A computed tomography scan of the abdomen was obtained and suggested mild terminal ileal inflammation. He underwent simultaneous esophagogastroduodenoscopy, colonoscopy, and bone marrow biopsy. Bone marrow demonstrated hypocellular marrow without megaloblasts, evidence of malignancy, or parvovirus inclusion bodies (Figure 1). Esophagogastroduodenoscopy

and colonoscopy demonstrated mucosal congestion and edema in the duodenum with normal terminal ileum and colon. Serum iron, ferritin, B12, folate, homocysteine, methylmalonic acid, copper, and zinc levels were normal. Immunoglobulin A, M, and G levels were also within normal limits (Figure 2). Histologic examination of the endoscopic biopsies revealed pathologic changes only in the duodenum showing chronic duodenitis with flattened villi and increased intraepithelial lymphocytes, classified as Marsh 3c (Figure 3). Mature plasma cells were appropriately present in the lamina propria. At this point, his previously obtained TTG IgA returned as positive (>128 U/mL), and the diagnosis of celiac disease was established.

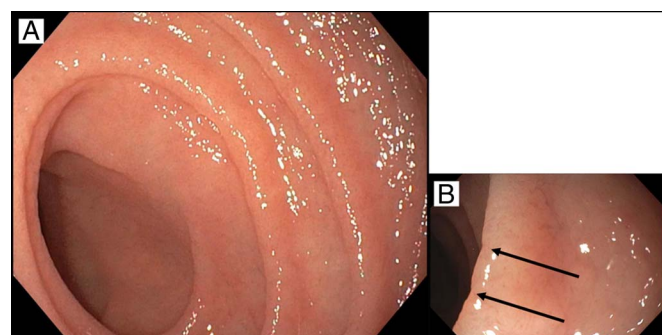


Figure 2. (A and B): Photographs of the duodenum taken during esophagogastroduodenoscopy. The mucosa appears edematous with less prominent villi and notching (black arrows).

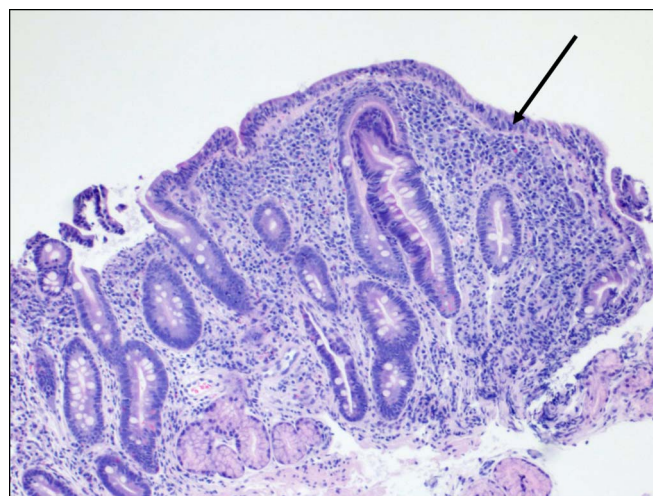


Figure 3. Photomicrograph of duodenal mucosa. The duodenal biopsy demonstrates cellular lamina propria, flattened villi, elongated crypts, and increased intraepithelial lymphocytes (demonstrated by arrow). Classified as Marsh 3c. Hematoxylin and eosin stain, 40× magnification.

No viral testing was performed because the patient was asymptomatic and the decline of all cell lines was slow in nature, rather than new and abrupt. He did not undergo imaging or biopsy of the enlarged submandibular lymph node. On follow-up, approximately 6 months after a gluten-free diet was initiated, he demonstrated weight gain with no further diarrhea or abdominal pain, and all laboratory values normalized, including TTG IgA, erythrocyte sedimentation rate, C-reactive protein, hemoglobin, ANC, and platelet count. Given the full resolution of symptoms, no further abdominal imaging was obtained.

DISCUSSION

The differential diagnosis for pancytopenia in pediatric patients is broad but can be split into 3 categories: bone marrow infiltration (includes malignant processes such as leukemia or metastatic cancer), bone marrow failure (encompasses immune suppression due to aplastic anemia, systemic inflammation, or autoimmune diseases; nutritional deficiencies due to vitamin B12, folate, zinc, or copper; and viral bone marrow suppression), or destruction/sequestration.⁵ All should be considered, with special attention based on clinical presentation.

In a pediatric patient with pancytopenia and gastrointestinal symptoms, it is important to specifically consider VEO-IBD, congenital autoimmune disorders (such as severe combined immunodeficiency and common variable immunodeficiency), nutritional deficiencies due to malabsorption, and CD. VEO-IBD can present with immunological manifestations including various cytopenias and autoimmune anemias.⁶ In addition to low immunoglobulin G and total immunoglobulin, combined immunodeficiency and common variable immunodeficiency may manifest as pancytopenia and lymphadenopathy along with symptoms of malabsorption due to duodenal villous atrophy.⁷ CD, which was not previously on the differential diagnosis, needs to be considered because this case demonstrates that the systemic inflammation caused by severe CD can result in bone marrow suppression that is responsive to a gluten-free diet.

Acquired aplastic anemia (AA) has been reported as being associated with CD and is postulated to be due to the fact that both involve the autoreactive T cell destruction of tissue; therefore, AA should still be considered even with a diagnosis of CD.⁸ On bone marrow aspirate, diagnostic criteria for AA includes hypocellular marrow with morphologically normal cells; however, the diagnosis of AA is made over time because the pancytopenias are pervasive and resolve only with initiation of immunosuppressive treatment.⁹

We present a 4-year-old boy with new-onset celiac disease associated with neutropenia, normocytic anemia, and thrombocytopenia, all of which resolved with initiation of a gluten-free diet. This case highlights the importance of considering celiac disease in patients who present with hematologic abnormalities, especially pancytopenia, with or without gastrointestinal symptoms.

DISCLOSURES

Author contributions: All authors contributed equally to this manuscript. A. Watson is the article guarantor.

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Previous presentation: This case was presented at the North American Society for Pediatric Gastroenterology Hepatology and Nutrition (NASPGHAN) Annual Meeting, October 17-19, 2019; Chicago Illinois.

Informed consent was obtained for this case report.

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