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CASE REPORT

Is there any association between celiac disease, myelodysplastic symdrome and primary sclerosing cholangitis?: A rare case report

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Abstract

Celiac disease (CD) is an autoimmune disease characterized by a specific serological and histological profile. Hematological findings are one of the most common presentations and can sometimes be the only manifestation of the disease. In patients with unexplained isolated hematological abnormalities, a high index of suspicion for CD is necessary. A 33-year-old woman was admitted to the Department of Gastroenterology and Hepatology because of abdominal pain and fatigue. She was diagnosed with myelodysplastic syndrome. After many investigations, it is explained that she has CD. It is important to consider myelodysplastic syndrome as a hematological manifestation of CD. All patients with myelodysplasia should be investigated for CD and related conditions such as primary sclerosing cholangitis.

Introduction

Celiac disease (CD) is an autoimmune condition characterized by a specific serological and histological profile triggered by gluten ingestion in genetically predisposed individuals.[1]

The extraintestinal features of CD include a wide range of rheumatologic, neurologic, hematologic, endocrine, metabolic, and dermatologic manifestations.[2,3] Among them, hematologic findings are one of the most frequent presentations, and sometimes, they can represent the sole manifestation of the disease.[4]

A high index of suspicion for CD is needed in patients with unexplained, isolated hematological abnormalities, and this depends on better awareness among physicians of general medicine-related specialties.[5]

The hematological features of CD include a variety of conditions—anemia, platelet alterations (thrombocytopenia/thrombocytosis), hemorrhagic or thrombotic events, IgA deficiency, hyposplenism, and the fearful lymphoma.[6]

Primary sclerosing cholangitis (PSC) is a chronic and progressive cholestatic liver disorder of unknown etiology. Inflammation, fibrosis, and stricturing of intrahepatic and/or extrahepatic biliary ducts characterize PSC.[7]

The association of PSC with CD was first reported in 1988, strongly suggesting an immunological link between the two diseases.[8] We report a case of a 33-year-old female with abdominal bloating, abdominal pain, and fatigue to turn out later that she had CD associated with myelodysplastic syndrome (MDS) and PSC.

Case report

A 33-year-old female was admitted to the Department of Gastroenterology and Hepatology presenting with symptoms of abdominal bloating, abdominal pain, and fatigue. Notably, she had a history of smoking, with an estimated consumption of 10 packs per year. In addition to her smoking history, the patient had been diagnosed with MDS, a diagnosis confirmed through biopsy and laboratory tests. It is important to note that she had not undergone any chemotherapy treatment. Upon physical examination, the presence of splenomegaly was observed, a feature not commonly associated with MDS.

Abdominal ultrasound revealed pronounced hepatic heterogeneity, attributed to the presence of hypoechoic areas surrounding the branches of the portal vein. The subsequent Doppler ultrasound demonstrated dilation of both the splenic vein and the portal vein, as well as their respective branches within the liver, indicative of high portal vein tension. To further investigate the splenomegaly, hepatic heterogeneity, and portal hypertension, a series of serum viral liver tests were conducted. The results indicated negative findings for hepatitis B surface antigen (HBs Ag), hepatitis C antibody (HCV AB), and antinuclear antibody (ANA).

A peripheral blood smear exhibited evidence of hypochromic microcytic anemia, along with decreased white blood cell (WBC) and platelet count (40 000/mcl). Further laboratory investigations demonstrated the following values: B9 = 9.1 ng/mL, B12 = 200 pg./mL, transferrin saturation = 9, ferritin = 5 µg/L, Fe = 16 µg/dL, total iron-binding capacity (TIBC) = 377

mcg/dL, anti-tissue transglutaminase antibodies (anti-TTG IgA) = 34 AU/mL, anti-parietal cell = 140 units, anti-intrinsic factor = 25 AU/mL, alanine aminotransferase (ALT) = 15, and aspartate aminotransferase (AST) = 12 U/L. Electrophoresis findings indicated the presence of cirrhosis of the liver.

Further assessment of the anemia involved both upper and lower gastrointestinal endoscopies, which revealed findings consistent with portal hypertensive gastropathy (PHG), characterized by a reddened and edematous appearance of the gastric mucosa, accompanied by a superimposed mosaic pattern of villous atrophy. Additionally, multiple esophageal varices were observed, two of which exhibited diameters exceeding 5 mm, indicating pre-disposition to potential bleeding. Duodenal endoscopy exhibited scalloped duodenal folds, grooves, and fissurations (Fig. 1a). A duodenal biopsy confirmed CD Marsh 3a, characterized by crypt hyperplasia, mild focal, and increased intraepithelial lymphocytes (IELs; Fig. 1b).

The liver ultrasound findings suggested the presence of PSC. Further confirmation of this diagnosis was pursued through magnetic resonance cholangiopancreatography (MRCP), which revealed severe splenic hypertrophy measuring approximately (7.6 × 16.7 × 27.7 cm), as well as a 17 mm diameter splenic vein, and a 16 mm diameter portal vein. Additionally, ill-defined areas within the liver exhibited slightly increased signal intensity in T2W1, thus confirming the diagnosis of PSC.

Given the confirmed diagnosis of CD, the patient has been put on a gluten-free diet and is receiving vitamin B12 and B9 supplementation. However, due to logistical constraints, the possibility of a bone marrow transplant in Syria is unfortunately precluded.

Discussion

The MDSs represent a collective of hematological disorders characterized by the presence of peripheral blood cytopenias and varying degrees of dysmyelopoiesis.[1]

Several medical conditions have been documented in relation to MDSs, including vasculitis, Sweet's syndrome, pyoderma gangrenosum, leukemia cutis, erythromelalgia, and opportunistic infections.[3]

We report the case of a female with MDS confirmed by bone marrow biopsy, in addition to iron and B12 deficiency proven by smear.

The presence of antibodies related to CD, during the investigation of the underlying cause of iron deficiency, prompted the performance of duodenoscopy and biopsy for confirmation of the diagnosis. Subsequently, the search for antibodies to both intrinsic factor and parietal cells was conducted, confirming the presence of a B12 deficiency. Although low serum levels of vitamin B12 and malabsorption of vitamin B12 are frequently observed in untreated CD, clinically significant vitamin B12 deficiency is uncommon.[8]

In the medical literature, there are few cases of splenomegaly associated with MDS, so the presence of hypersplenism, which is not commonly observed in cases of MDS, raised suspicions of an underlying pathological process that may be responsible for the splenomegaly.[9] In this article, the patient suffered from splenomegaly, which cannot be explained by MDS because it causes neither splenomegaly nor hepatomegaly.

The presence of cirrhosis-related manifestations in the patient, such as splenomegaly, portal vein hypertension, and esophageal varices seen with upper gastrointestinal endoscopy, despite normal liver function, led her to undergo a liver ultrasound, which revealed a sever liver heterogeneity, that prompted the referral to PSC.

Elevations in serum alkaline phosphatase (ALP) and gamma-glutamyl transferase values in a cholestatic pattern are the biochemical hallmark of PSC, though up to 30%–40% of patients have normal ALP at diagnosis or during the course of their disease,[10] as was reported in the case of our patient, while serum aspartate transaminase (AST) and alanine transaminase (ALT) levels are usually two to three times higher than the upper limit of normal,[9] in contrast to our case where ALP was normal.

This article highlights many questions about the hypotheses explaining the etiology of liver fibrosis. Is it CD, the role of which has been proven in many articles in the medical literature to cause liver cirrhosis, or is it PSC, which puts many question marks around this diagnosis, because the possibility of a chance

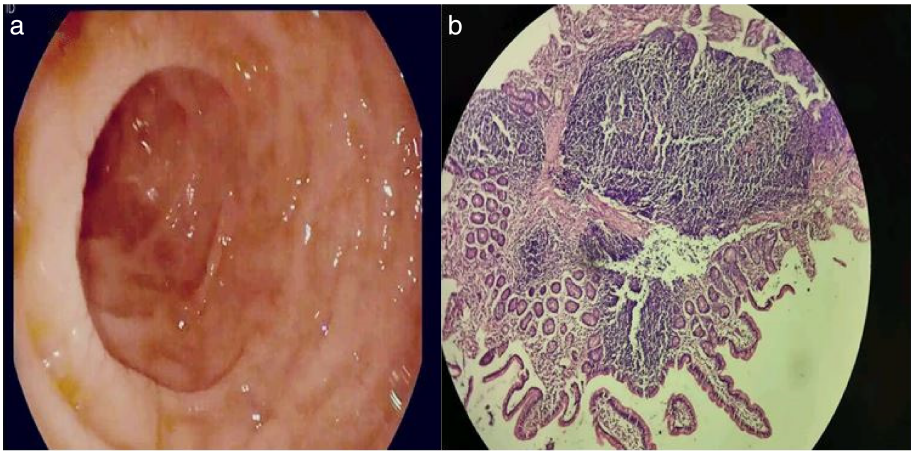

Figure 1 (a) Findings of duodenal endoscopy. (b) Findings of duodenal biobsy.

association of PSC and CD cannot be accurately assessed but seems unlikely given the rarity of both diseases. The relationship between the two diseases remains unknown, although an immunologic connection is suspected.[8]

This encourage more studies to establish the basic procedures for dealing with these rare cases. It is important to think of MDS as a hematological manifestation of CD; CD and its accompanying diseases, such as PSC, should be investigated in all patients with myelodysplasia.

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Ethics approval statement

Not applicable because all date belong to the authors of this article.

Patient consent statement

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request permission to reproduce material from other sources.

References

1 Fasano A, Catassi C. Celiac disease. *N. Engl. J. Med.* 2012; **367**: 2419–26.
2 Rodrigo L, Beteta-Gorriti V, Alvarez N *et al*. Cutaneous and Mucosal Manifestations Associated with Celiac Disease. *Nutrients*. 2018; **2110**: 7–800.
3 Dima A, Jurcut C, Jinga M. Rheumatologic manifestations in celiac disease: what should we remember? *Rom. J. Intern. Med.* 2019; **157**: 3–5.
4 Bala M, Radhakrishnan T, Kumar A, Mishra GP, Dobraia JR, Kirti PB. Erratum: Overexpression of a fusion defensin gene from radish and fenugreek improves resistance against leaf spot diseases caused by Cercospora arachidicola and Phaeoisariopsis personata in peanut. *Turk J. Biol*. 2019; **543**: 4–15.
5 Jinga M, Popp A, Balaban DV, Dima A, Jurcut C. Physicians' attitude and perception regarding celiac disease: A questionnaire-based study. *Turk. J. Gastroenterol.* 2018; **294**: 419–26.
6 Baydoun A, Maakaron JE, Halawi H, Abou Rahal J, Taher AT. Hematological manifestations of celiac disease. *Scand. J. Gastroenterol.* 2012; **47**: 1401–11.
7 Angulo P, Lindor KD. Primary sclerosing cholangitis. *Hepatology*. 1999; **30**: 325–32.
8 Hay JE, Wiesner RH, Shorter RG, LaRusso NF, Baldus WP. Primary sclerosing cholangitis and celiac disease. A novel association. *A Intern. Med.* 1988; **109**: 713–7.
9 Celiac disease in children: A review of the literature. *World J. Clin. Pediatr.* 2021; **10**: 53–71.
10 de Vries EM, Wang J, Leeflang MM *et al*. Alkaline phosphatase at diagnosis of primary sclerosing cholangitis and 1 year later: evaluation of prognostic value. *Liver Int.* 2016; **3612**: 1867–75.