

Double trouble – primary biliary cholangitis and coeliac disease in a young female: a case report

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Abstract

In this case report, we describe a patient who was diagnosed with both Primary Biliary Cholangitis and Coeliac Disease, presenting with symptoms and signs of severe malabsorption and portal hypertension. Extensive workup was done including duodenal and liver biopsies and our patient was ultimately found to have both autoimmune diseases. An association between the two diseases has been reported multiple times during the past four decades with current guidelines recommending screening patients with primary biliary cholangitis for coeliac disease.

Keywords: Celiac Disease, Primary Biliary Cholangitis, Malabsorption, Portal Hypertension.

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Introduction

Primary Biliary Cholangitis (PBC) and Coeliac Disease (CD) are both autoimmune diseases with distinctively defined aetiopathogenesis involving the hepatobiliary system and the upper gastrointestinal tract respectively. Interestingly, both of them are associated with a malabsorption syndrome. An association between the two entities has been explored variably in literature and a number of cases have been detailed¹ with some reports indicating a higher than normal prevalence of CD in patients with PBC.^{2,3} Reciprocal testing has been recommended for both diseases especially PBC as earlier intervention may lead to improved outcomes.⁴ A literature review reveals that no such case of PBC and CD occurring in the same patient has been reported from Pakistan yet.

Case Report

A 20-year-old girl presented to the Outpatients Department of Khyber Teaching Hospital with the

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complaints of disabling fatigue, abdominal distension and bilateral pedal oedema for the past one month. She had been unwell for the past four years. Over that period, she changed from being an active, healthy girl who helped her mother with household chores to a chronically tired person who was unable to do anything. She reportedly lost a lot of weight and had intermittent episodes of diarrhoea, steatorrhea and abdominal pain. Three months back, her mother noticed that she was unable to see after nightfall and kept bumping into objects. Her clinical condition came to a head after which she presented to us, however, at the time of presentation, she had no diarrhoea, abdominal pain or steatorrhea.

Past medical history was significant for one admission in January 2018 after an episode of profuse diarrhoea and steatorrhea, though she was discharged home later on without a definitive diagnosis. She had no history of surgery. She was not taking any regular medications and reported no drug or food allergies. There was a remote history of tuberculosis in relatives but none in her own family.

On examination, she was in no apparent distress and was vitally stable. Her BMI was 18 kg/m². She had conjunctival pallor but no jaundice or lymphadenopathy. Respiratory and cardiovascular examination was normal. Abdominal examination revealed flank fullness with mild hepatosplenomegaly. Shifting dullness was present. There was no tenderness or guarding. She had moderate pitting ankle oedema.

A synopsis of her initial lab workup is as follows. CBC showed pancytopenia with a haemoglobin of 9 g/dl (11-13 g/dl) with an MCV of 85 fl (79-100 fl), white cells of 3000 per microlitre (4500 – 11,000 per microlitre) and platelet count of 138,000 per microliter (150,000 – 300,000 per microliter). Renal function and electrolytes including calcium, magnesium and phosphorous were normal. Prothrombin time and activated partial thromboplastin time were both prolonged. PT was 24 seconds (12-16 seconds) with and INR of 1.7 (0.9 – 1.1) and aPTT 40 seconds (26- 30 seconds). Serum bilirubin and ALT were normal. Alkaline phosphatase was mildly elevated at 125 mg/dL (normal=110 mg/dL). Serum albumin levels were low at 2.5 mg/dL (3.5 – 5.5 mg/dL).

Her Vitamin D levels were very low at 12 ng/mL (40-80 ng/mL) and Vitamin B12 levels were also below normal at 180 pg/mL (200 – 1100 pg/mL). A serum ferritin was also done which was mildly elevated 400 micrograms/L (11-300 micrograms/L). A posteroanterior Chest Radiograph was reported normal. USG abdomen revealed coarse liver echotexture with hypertrophy of the caudate lobe and multiple nodules suggestive of regenerative nodules. It also showed splenomegaly and moderate ascites. Ascitic fluid routine examination was significant for an albumin level of 1.1 mg/dL. Consequently, the Serum Ascites Albumin gradient was 1.4 (≥ 1.1). Cells in the fluid were 80 with predominant lymphocytes.

It appeared that this patient had a malabsorption syndrome (night blindness, pancytopenia, low levels of Vitamin D) alongside the evidence of portal hypertensive ascites and hypersplenism. An attempt was made to rule out Chronic Liver Disease in this patient. HBsAg, HBcAb (IgM, IgG), HCV Ab and HIV serology were negative. Tests for Wilsons disease and Autoimmune hepatitis were also negative. A triphasic Computed Tomography (CT) scan showed hypertrophied caudate lobe of the liver and splenomegaly. A liver biopsy was done. It was consistent with Primary Biliary Cholangitis. Meanwhile, an Upper GI endoscopy was performed which showed effaced duodenum. There was mild oesophagitis but no oesophageal varices. Duodenal biopsy showed partial to complete villous blunting with increased inflammation (Marsh type 3B).⁵ Serum IgM levels were elevated but Anti-mitochondrial antibodies (AMA) were negative. Coeliac serology including tissue transglutaminase IgA and IgG were also negative.

The patient was put on gluten-free diet and fat-soluble vitamins were replaced. She improved over the course of her stay in the hospital and has been followed up regularly. Ursodeoxycholic acid was also started for AMA negative Primary Biliary Cholangitis.

The spectrum of diseases in this patient warranted that further testing with anti-endomysial antibodies and HLA typing for CD and antimitochondrial antibodies via immunofluorescence should be done. However, cost-effectiveness was a major concern therefore HLA typing was not done.

Informed consent was taken from the patient for publishing her case for promotion of science.

Discussion

Among the autoimmune conditions affecting the gut and the hepatobiliary system, Coeliac Disease (CD) and Primary Biliary Cholangitis (PBC) are commonly known

diseases and while CD is quite prevalent, affecting about 1% of the world population,⁶ the prevalence of PBC varies globally with rates ranging from 19 to 492 per million inhabitants. PBC enjoys a significant female preponderance (Female: Male 10:1) as compared to Coeliac Disease where the ratio is not so high. (Female: Male 3:2)⁷

Coeliac disease is an inflammatory response to a genetically defined sensitivity to gluten or gluten containing products and even though it is centered on the gut, it has wide ranging manifestations in other organs such as the skin and liver. PBC is centered exclusively on the hepatobiliary system and is characterized by autoimmune granulomatous destruction of the intrahepatic bile ducts and seropositivity for anti-mitochondrial antibodies (AMA) in 95% of the patients.⁸

Although the pathophysiology differs, both PBC and CD lead to malabsorption and the spectrum of presentation for both conditions ranges from asymptomatic patients to gross manifestations. PBC can present with jaundice, fatigue, pruritis and right upper quadrant pain. Unchecked, it has a natural progression to liver cirrhosis.⁷

Coexistence of both the conditions has been variably reported, however, in an effort to formally document prevalence, a 12-year study was performed on a stable population of South Wales. Out of 143 patients with Coeliac Disease, 3% were found to have PBC and out of 67 patients with PBC, 6% were found to have Coeliac Disease.⁹ Another retrospective study sought to compare the prevalence of Coeliac disease in 51 patients with PBC and 348 patients with other liver diseases. The prevalence was 11.8 % in those with PBC and only 2.9 % in patients with other liver diseases.³ Similarly, an elevated prevalence of Coeliac disease was found in 57 Irish patients with PBC who did not have any gastrointestinal symptoms.¹⁰

Much progress has been made to elucidate the individual pathogenesis of Coeliac Disease and PBC, however a clear answer for the association is still elusive. There are a number of proposed theories. The gut-liver axis plays a comprehensive role. Primed T-lymphocytes from the gut in Coeliac disease may be home to the liver and cause immunologically driven hepatobiliary injury.⁴

Sensitive serological markers exist for both Coeliac Disease and PBC. IgA tissue Transglutaminase antibodies are highly sensitive for Coeliac disease in the general population as well as those with PBC. Similarly, anti-mitochondrial antibodies remain useful for screening of

PBC in patients with Coeliac Disease. If negative, the test should be repeated with Immunoblotting or Elisa, which are more specific.⁶

In patients with mild cholestatic liver injury that has not yet progressed to liver cirrhosis, the diagnosis of coeliac disease is prognostically significant. It allows for the initiation of a gluten free diet which along with bile acid treatment can potentially reverse the liver damage and prevent the need for an orthotopic liver transplant.¹¹

Conclusion

This case highlights the importance of considering screening patients with Primary Biliary Cholangitis for Coeliac Disease and vice versa. It also serves to raise awareness regarding the widely reported association between the two conditions among physicians who regularly see such patients. Case-control and Cohort studies should be undertaken to further explore this relationship.

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