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CONFLUENCE OF CELIAC DISEASE WITH IDIOPATHIC PORTAL HYPERTENSION: A RARE CASE REPORT

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Abstract – *Background:* Celiac disease (CD) is a chronic autoimmune disorder triggered by the consumption of a gluten-rich diet. It has been linked to other extra-intestinal manifestations, such as liver cirrhosis and portal hypertension. Idiopathic Portal hypertension (IPH) is a disorder of unknown etiology and presents with elevated liver enzymes and variceal bleeding.
Case Report: Here, we present an interesting case of idiopathic portal hypertension associated with celiac disease in a 22-year-old woman. The patient was initiated on nutritional supplementation and strict gluten free diet (GFD). Significant improvement was observed over the next 2 months.
Conclusions: This case underscores the occurrence of portal hypertension in individuals with celiac disease and emphasizes the importance of a multidisciplinary approach in managing such patients.

Keywords: Chronic autoimmune disease, Idiopathic non-cirrhotic portal hypertension, Gluten-free diet, Extra-intestinal celiac disease, Celiac disease.

INTRODUCTION

Celiac disease (CD) is a chronic immune-mediated disorder associated with HLADR3-DQ2 and HLA DR4-DQ8. It damages the small intestine, causing erosion and flattening of villi projections, leading to a decreased surface area for absorption. It is precipitated by dietary exposure to proline and glutamine-rich proteins contained in wheat, rye, and barley[1]. The growing focus is on understanding the connection between celiac disease and other liver-related pathologies.

Idiopathic Portal Hypertension (IPH) is a rare disorder leading to increased portal pressure without any recognizable cause. It presents with signs of portal hypertension, splenomegaly, and pancytopenia. It is one of the most important causes of esophageal variceal bleeding, commonly encountered in the Indian subcontinent[2]. Several pieces of evidence have mapped IPH to various autoimmune conditions, such as SLE, systemic sclerosis, and mixed connective tissue disease[3].

Literature seldom documents an association between celiac disease manifesting with idiopathic portal hypertension. Here, we report on a patient displaying a similar association observed at our healthcare center.

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CASE PRESENTATION

This case report describes a 22-year-old female who presented to the emergency room of Adesh Hospital with multiple episodes of painless hematemesis associated with generalized body weakness.

The patient presented with deranged vitals on arrival and management was initiated for correction of hypovolemic shock.

The patient's medical history included multiple intravenous blood transfusions over the past three years for correction of severe anemia.

On general physical examination, the patient was found to have gross pallor with discoloration of the palpebral conjunctiva and grade 3 palmar pallor. Abdominal examination revealed splenomegaly. Auscultation showed normal cardiac and respiratory findings.

Hematology reports revealed pancytopenia with dimorphic anemia characterized by severe hypo-chromic microcytic and macrocytic cells. Liver function tests revealed reduced albumin and total proteins (Table 1).

Ultrasound coupled with Hepatic Doppler showed evidence of heterogeneous echotexture of the liver with a dilated portal vein measuring 15.2 mm at the portal and showing normal centripetal flow with a main portal vein peak systolic velocity (PSV) of 24.89 cm/sec. There was no evidence of any vascular occlusion. The spleen was found to be enlarged, measuring 17.5 cm.

Esophagogastroduodenoscopy (EGD) showed a single column of grade 1 lower esophageal varix, multiple small gastric varices in the stomach fundus, and significant scalloping folds of the duodenal mucosa (Figure 1). Following EGD, an endoscopic biopsy of the duodenum was advised. Sections examined showed tissue lined by intestinal lining epithelium with focal flattening. This lining epithelium exhibited an increase in intraepithelial lymphocytes along with focal crypt hyperplasia and marked villous atrophy in places (Figure 2). The acquired impression of histological features suggested celiac disease (Modified Marsh Grade 3C).

As one of the differentials directed towards celiac disease, serology tests were ordered, which came out positive for serum Anti-tissue Trans-glutaminase antibodies (Anti-tTG).

Investigations for serological viral markers for HCV, HIV, and HBsAg were non-reactive. Autoimmune serological markers were not consistent with autoimmune hepatitis, with antinuclear antibodies (ANA), anti-Smith smooth muscle antibody (ASMA), and serum electrophoresis reported negative/normal.

TABLE 1. TABLE SHOWING LABORATORY VALUES.

Investigations	Values	Biological Ref. Interval
Hemoglobin (g/dL)	3.1	13.0-17.0
RBC Count (10^6/µL)	1.84	4.50-5.50
Packed Cell Volume (%)	11.5	40.0-50.0
MCV (fL)	62.8	83.0-101.0
MCH (pg)	17.0	27.0-32.0
MCHC (g/dL)	27.1	31.50-34.50
Red cell distribution width (%)	22.4	11.6-14
Platelet count (lakhs/cmm^3)	0.48	1.5-4.1
Serum Ferritin (ng/ml)	8.67	24-336
Serum Iron (mcg/dL)	42.6	60-160
TIBC (mcg/dL)	441.0	250-450
Anti-tTG (U/ml)	>200.0	<15.0
Total Proteins (g/dL)	5.8	6.6-8.8
Albumin (g/dL)	3.1	3.5-5.2

Mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), total iron binding capacity (TIBC), Anti-tissue Transglutaminase antibodies (Anti-tTG).

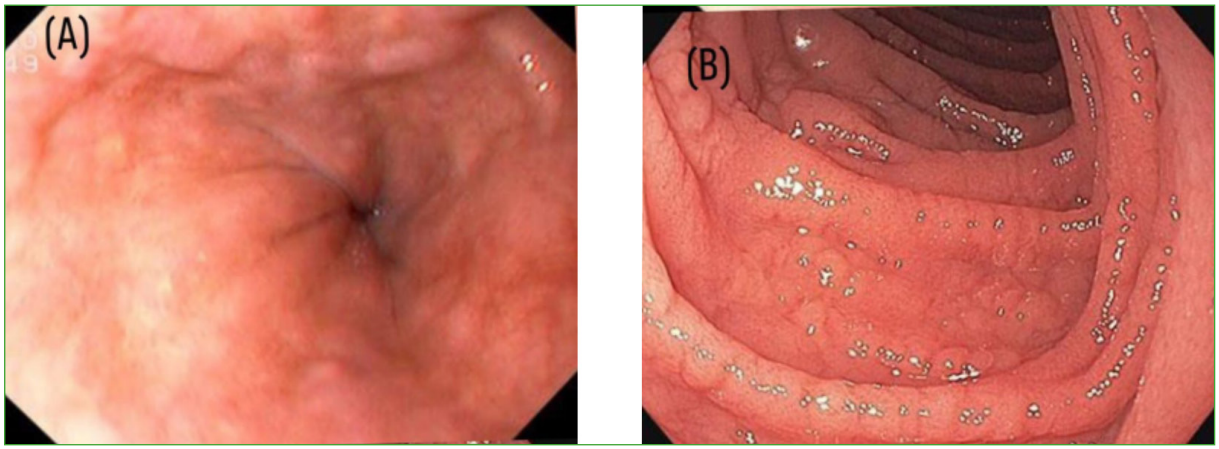

Figure 1. Esophagogastroduodenoscopy (EGD) shows a single column of grade 1 lower esophageal varix (**A**) and scalloping folds of the duodenal mucosa (**B**).

Treatment

The treatment approach involved a comprehensive multidisciplinary approach addressing pathologies observed in the patient. Intravenous therapy with Inj. Pantop, Inj. Emeset, Inj. Optineuron, and Inj. Ceftriaxone was administered, followed by Oesophageal Variceal Band Ligation (EVBL) as per the protocol for emergency management of hematemesis.

In addition to the treatment for the primary pathology, the patient was closely monitored and managed for correction of anemia and other nutritional deficiencies. Blood transfusion consisting of two Packed Cell Volumes (PCV) were initiated following observation of severe anemia and low hemoglobin levels. The nutritional deficiencies were addressed through supplementation of Vitamin D, Vitamin B12, Folate, Zinc and Calcium, primarily through dietary adjustments. Tab. Livogen-Z was prescribed for a duration of three months to help regulate red blood cell (RBC) production and restore normal levels of hemoglobin along with Tab. Neurobion for normal nerve function. The patient was advised to adhere to a lifelong strict gluten-free diet, which has contributed to enhance quality of life and prevent further damage to lining of small intestine.

Overall, the patient's condition improved significantly following three months of prescribed medications with adherence to gluten-free diet. The patient's general health and body composition enhanced with a recorded weight gain of 12 kgs post first visitation.

Figure 2. Duodenal biopsy showing villi flattening with villous atrophy (**A**) and focal crypt hyperplasia (**B**).

DISCUSSION

Idiopathic Portal Hypertension (IPH) is a diagnosis of exclusion, as it is identified after ruling out more common causes of portal hypertension like liver cirrhosis, non-cirrhotic portal fibrosis, schistosomiasis, and other extra hepatic venous occlusive disorders[2]. The exact pathophysiology of IPH remains largely unknown. Studies suggest potential triggers, such as autoimmune reactions, immunological threats, intra-abdominal infections, or vascular genetic disorders leading to portal thrombosis, though substantial evidence is lacking in the literature[4]. As portal hypertension progresses, collateral vessel formation occurs, with the left gastric vein backing up into the esophageal vein, causing dilatation and increased blood flow to the portal circulation. This can lead to hyperdynamic circulatory syndrome, potentially resulting in esophageal varices or ascites, and chronic internal bleeding may cause asymptomatic iron deficiency anemia.

Celiac disease (CD) presents with distinct clinical features, such as malabsorption syndrome with extra-intestinal manifestations, including anemia, renal failure, polyneuropathy, arthritis, and gluten-induced cognitive impairment (brain fog)[5]. Hepatic involvement in CD often presents as isolated hypertransaminasemia with mild or nonspecific histologic changes in liver biopsy, referred to as “celiac hepatitis”. The gut-liver axis is a complex network involving the intestinal barrier, gut microbiota, bile, shared lymphocyte homing, and hepatic receptors, such as PRRs, FXR, TGR5, and FGFR4. Disruption of this system can activate the liver’s innate immune response, potentially causing liver injury or exacerbating existing liver damage. Industrial food additives like gluten, microbial transglutaminase, glucose, salt, emulsifiers, and organic solvents, commonly used in dough, may compromise the intestinal mucosal wall barrier’s function[6].

In CD, the presence of celiac antibodies can hinder the activity of tissue transglutaminase-2 (TTG2) enzymes, potentially reducing the availability of active transforming growth factor (TGF)-β[7]. IgA antibodies directed against TTG2, found in liver biopsy samples from CD patients with elevated liver transaminase levels, suggest that inhibition by anti-TTG2 antibodies may contribute to extra-intestinal manifestations of CD, including liver damage[8].

While there are documented cases linking CD to Budd Chiari syndrome[9,10] and idiopathic non-cirrhotic intra-hepatic portal hypertension (NCIPH)[2], reports on the correlation between CD and portal hypertension are meager in the existing literature.

CONCLUSIONS

This case report highlights an uncommon affair of idiopathic non-cirrhotic intra-hepatic portal hypertension (NCIPH) with celiac disease. On incidental findings, idiopathic portal hypertension was diagnosed which further pointed out towards celiac disease. The discussion takes into account the immunological predispositions and its correlated liver pathologies with a shift to gluten free diet for a lifetime. Extra-intestinal manifestations of celiac disease are well established, however, the association between celiac disease and portal hypertension is sparsely accounted in literature. This case report highlights judicial and quick diagnosis and intervention towards patients with celiac disease to account for least complications in the future.

The cornerstone for preventing even the rarest associated complications lies in the early diagnosis and adoption of gluten free diet in celiac disease. Untreated CD could potentially trigger IPH, amongst other complications. Also, it is crucial to investigate patients with IPH for CD promptly to ensure best possible outcome for affected individuals.

Ethics Approval

The research was carried out following approval from the institute’s Research and Ethics Committee. Informed consent was also obtained from the patient whenever necessary, in accordance with ethical guidelines.

Conflict of Interest

The author declares no conflict of interest.

AI Disclosure

Author hereby declares that no generative AI technologies, such as Large Language Models and text-to-image generators have been used during writing or editing of this manuscript.

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