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CASE REPORT

CELIAC DISEASE WITH CONGENITAL HEPATIC FIBROSIS

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ABSTRACTS: BACKGROUND: Celiac disease and congenital hepatic fibrosis rare association. **CASE CHARACTERISTICS:** 8 year female diagnosed celiac disease, congenital hepatic fibrosis with portal hypertension. **INTERVENTION**: Gluten free diet, Endoscopic band ligation **OUTCOME**: Partial improvement. **MESSAGE**: Rare association but should keep in mind.
KEYWORDS: Celiac disease, Congenital hepatic fibrosis.

INTRODUCTION: Celiac Disease (CD) is characterized by mucosal inflammation and villous atrophy of small bowel, due to hypersensitivity to gluten, leading to features of mal absorption such as diarrhea, growth failure and signs of vitamin deficiency.

Congenital hepatic fibrosis (CHF) is a rare congenital, fibro polycystic disorder of liver and other organs. It is a histopathology diagnosis that refers to a developmental disorder of the portobiliary system characterized by Defective remodeling of the ductal plate (ductal plate malformation; DPM), Abnormal branching of the intrahepatic portal veins, Progressive fibrosis of the portal tracts and may be associated with cystic dilatation of the intra/extra hepatic biliary tree.

CASE REPORT: 8-year-old female, 2nd degree consanguineous from north-west India, had complains of loose motions, recurrent vomiting and irritability from the age of 6-7 months. She had complains of abdominal distension from the age of 2 years and hematemesis and melena 3 episodes at the age of 5, 6 and 7 years. No history of jaundice and seizure. She had taken multiple consultations before came to us. She was diagnosed as celiac disease at the age of 7 years on the basis of positive serology (IgA TTG-47), scalloping of duodenal folds on Endoscopy and marsh grade-3b features in duodenal biopsy. She partially responded to Gluten free diet in the form of weight and height gain (5kg and 4cm in 1 year) may be because of poor compliance of gluten free diet.

On physical examination she had revealed pallor, frontal bossing and hepatosplenomegaly. The liver was palpable 8 cm below the xiphisternum in the midline in epigastric region, firm, smooth and rounded borders. Her right lobe at mid clavicular line was just palpable. Her spleen was firm, 5 cm towards umbilicus from left costal margin.

Investigations showed Complete blood counts–Hemoglobin-7.3 g/dl, Total leucocyte counts-5990/mm^3, Platelet-141000/mm^3, Prothrombin time-16.6 and INR-1.27. Liver function test revealed Bilirubin Total/Direct-0.6/0.2 mg/dl, AST/ALT-51/72, albumin 3.8 gram/dL, globulin-2.8, alkaline phosphatase (528 U/L, normal: 38-155) and gammaglutamyl transpeptidase 74 U/L, normal: 7-32). Urea/Creatinine-22/0.6 mg/dl and electrolytes were normal. Viral hepatitis markers, HBsAg and HCV antibody- were negative and serum ceruloplasmine-35 (range-20-40).

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IgG level and other autoimmune markers (ANA, SMA, LKM) were within normal limit. Abdominal ultrasonography showed Hepatomegaly with coarse echotexture, splenomegaly and bilateral polycystic kidney disease. USG Doppler showed patent hepatic veins and inferior vena cava and with appropriate flows, ruled out Budd chiary syndrome. Her UGI endoscopy showed 2 large esophageal varices- grade-3 with features of portal hypertensive gastropathy. Liver biopsy revealed markedly expanded portal tracts due to fibrous tissue and large number of anatomizing billiary channels with bile casts in some ducts without any inflammatory reactions and steatosis consistent with congenital hepatic fibrosis.

She advised Strict Gluten free diet, Vitamin supplements. Her endoscopic band ligation was done successfully. She was explained regular follow up to look for progression of fibrosis and possibility of liver cirrhosis and liver transplantation in future.

DISCUSSION: Here we are describing a case of advanced liver disease, diagnosed as congenital hepatic fibrosis on the basis of clinical parameters and liver biopsy. She was also found to have celiac disease, diagnosed on the basis of symptomatology, serology and biopsy.

Interestingly liver disease had apparent symptoms compatible with celiac disease, suggesting that the celiac disease related liver involvement was not necessarily a complication of malabsorption. Rather, it may well be a gluten-dependent immunologically induced extra intestinal manifestation of celiac disease. Recently, Ventura et al.[1] showed that prolonged exposure to gluten in patients with celiac disease contributes to the development of other autoimmune diseases such as diabetes mellitus, autoimmune thyroid and liver disorders. Celiac disease is associated with various autoimmune conditions.[2] Common associations are:

- Type 1 Diabetes Mellitus: 2.4-16.4%
- Multiple Sclerosis (MS): 11%
- Hashimoto's thyroiditis: 4-6%
- Autoimmune hepatitis: 6-15%
- Addison disease: 6%
- Arthritis: 1.5-7.5%
- Sjögren's syndrome: 2-15%
- Idiopathic dilated cardiomyopathy: 5.7%
- IgA nephropathy: 3.6%

Celiac disease has been found in 0%–7% of patients with primary biliary cirrhosis[3] and 3.4% of patients with autoimmune hepatitis.[4] There are some case reports on an association between celiac disease and primary sclerosing cholangitis.[5]

In a study Kaukinen et al.,[6] Out of 4 patients with severe liver disease and celiac disease, 1 had congenital liver fibrosis, 1 had massive hepatic steatosis, and 2 had progressive hepatitis without apparent origin. Hepatic dysfunction reversed in all cases when a gluten-free diet was adopted.

CHF has usually autosomal recessive inheritance and presents between ranges 1.8-14 years. Renal involvement is seen with < 10% tubules being affected. Development of bile ducts and hepatic vasculature are closely related. The ductal plate malformation has been shown to be

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associated with a "pollard willow" malformation of the portal vein, which results in too many small and closely branched portal veins. The usual presentation of CHF is with abdominal distension, hematemesis or melena, failure to thrive, jaundice, and hepatosplenomegaly.[7] Our patient had presented with hematemasis due to esophageal varices thrice and splenomegaly suggestive of portal hypertension.

Hallmark of diagnosis is liver biopsy which shows bands of fibrous tissues. There is diffuse portal and perilobular fibrosis varying in thickness but it does not distort lobular structures. The limiting plate is intact and parenchyma is separated by islands of fibrosis. There are no inflammatory changes and regenerative nodules. The management and prognosis of CHF is dependent on alimentary bleeding secondary to PH. Prognosis may be improved by shunt surgery and antifibrotic agents eg- Pirfenidone [8] and in advanced stage liver transplantation.

It may be hypothesized that ingestion of gluten sometimes results in liver damage in patients with celiac disease. Such hepatic involvement is usually considered to be mild, but our findings suggest that in some cases it may eventually lead to chronic liver disease and further leads to end-stage liver disorder. There is one earlier anecdotal report in which a gluten-free diet was shown to reverse severe liver failure in 2 patients with celiac disease and primary biliary cirrhosis.[7]

CONCLUSION: Although, CD is commonly reported to be associated with various liver diseases in children or even mildly raised liver enzymes only. Celiac disease also be found with various chronic liver diseases. Congenital hepatic fibrosis is one of them. Though it is a rare entity but it should be considered among the differential diagnosis of various liver disorders associated with celiac disease.

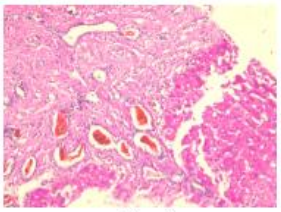


Fig. 1

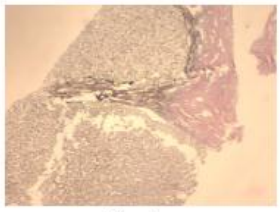
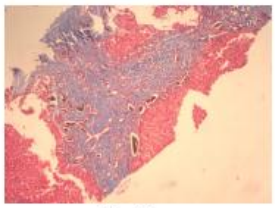


Fig. 2



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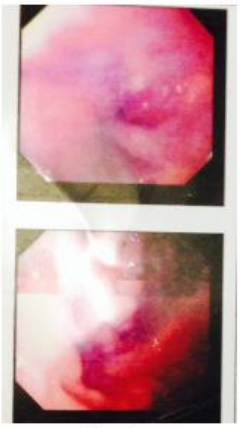

Fig. 4

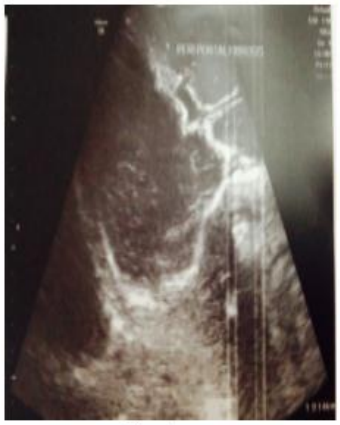

Fig. 5

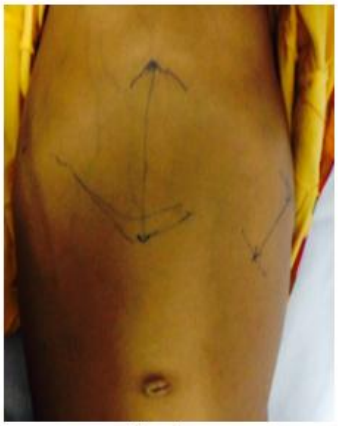

Fig. 6

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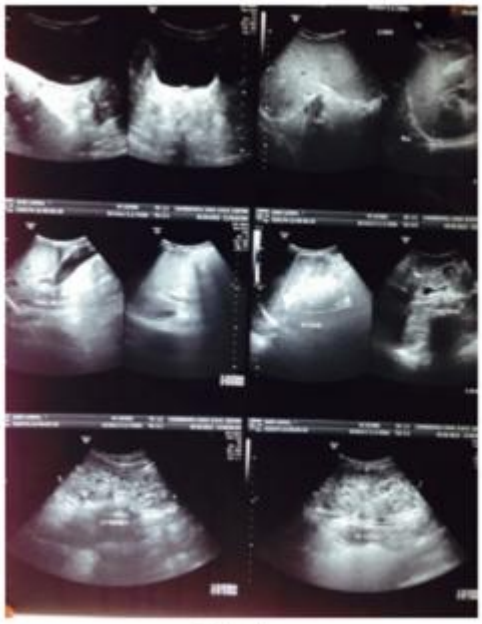

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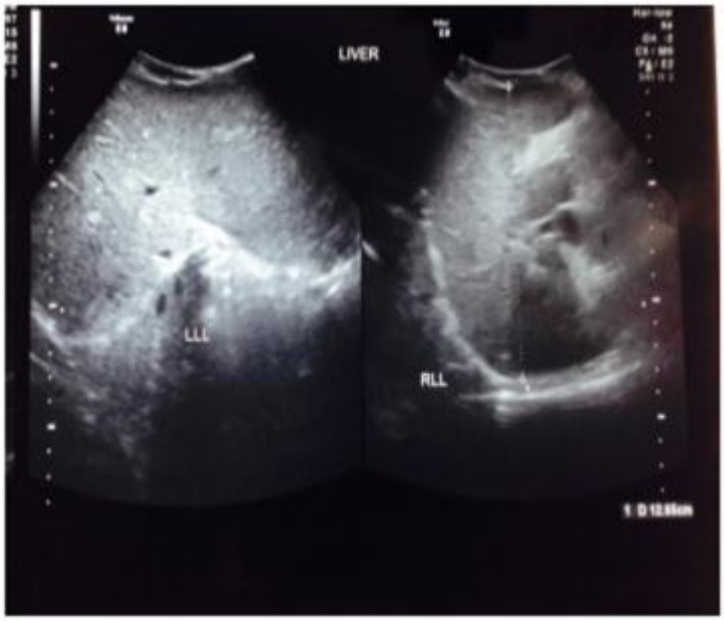

Fig. 8

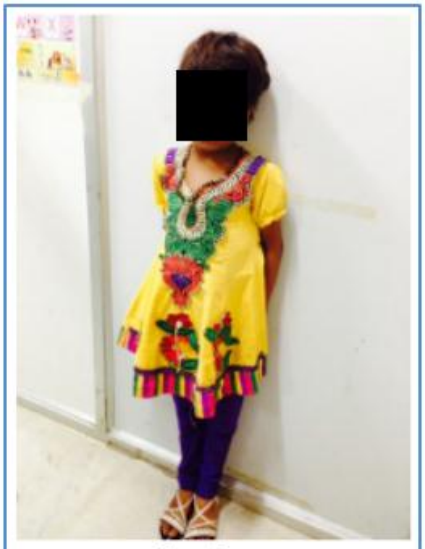

Fig. 9

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