Frequency of Non-cirrhotic Portal Fibrosis in Patients with Celiac Disease: A Single Center Experience From Northern India

To the editor,

Portal hypertension is well known in patients with celiac disease (CeD). However, only a few patients with non-cirrhotic portal fibrosis (NCPF) are reported in patients with CeD.[1] The association between NCPF and CeD is uncommon, and the data on this issue are sparse. Accordingly, we undertook a study to know the frequency of NCPF among patients with CeD. The present study included 150 patients with CeD whose data were prospectively maintained on a questionnaire including demographic, clinical, biochemical, and histological parameters during a five-year period (2016–2021) in the Department of Gastroenterology at Sanjay Gandhi Postgraduate Institute of Medical Sciences. All patients underwent necessary tests to look for the presence of portal hypertension. Patients with portal hypertension, who had normal liver ultrasonography, patent splenoportal axis, and low liver stiffness value (<10 kPa), underwent liver biopsies and hepatic venous pressure gradient (HVPG) measurement. Asia Pacific Association for the Study of the Liver (APSAL) criteria were used to diagnose NCPF.[2] Among 150 patients, three (2%) had NCPF. Their clinical, biochemical, and histological features are described here (Table 1). On examination, all of them had clinically palpable splenomegaly. Liver biopsies revealed periportal fibrosis in two patients and normal in one, suggesting the diagnosis of NCPF. Following a gluten-free diet (GFD), their symptoms improved.

NCPF has been now classified as porto-sinusoidal vascular disease (PSVD).[3] PSVD encompasses a group of disorders that is characterized by lesions involving small vasculature of the liver or sinusoids because of underlying immune disorders, infections, or thrombophilia. A liver biopsy is mandatory to diagnose PSVD.[3] Non-specific duodenal biopsies findings are common in patients with portal hypertension, and false positive celiac serology is also reported in patients with cirrhosis.[4] But the combination of high anti-TTG, villous atrophy, and response to gluten therapy point toward the diagnosis of CeD.

In our study, 2% of patients with CeD had NCPF. Similar results were found in a study from India. A study by Nijhawan *et al.* showed that of 363 patients with CeD, 12 (3.3%) had NCPF.[5] Other reports from India have shown similar presentations.[6] Following GFD, symptomatic improvement was noted; however, the improvement of portal hypertension was not documented in most of the studies. The prevalence of autoimmune liver diseases like autoimmune hepatitis (AIH), primary biliary cholangitis (PBC), and primary sclerosing cholangitis is high among patients with CeD (4–11%).[7,8] The association between CeD and autoimmune liver diseases can be explained by underlying genetic predisposition and immunogenic mechanisms.[9,10] Interestingly, patients with CeD and other autoimmune liver diseases share common HLA which was shown by Kaukinen *et al.*.[9] In that study, 39% of patients with PBC with CeD and 58% of patients with PSC and CeD shared HLA DR3 DQ2 or DR4-DQ8. Hence, a GFD can reverse liver dysfunction in CeD which has been reported in earlier studies.[9] NCPF is uncommonly associated with CeD, and the presence of

Abbreviations: CeD: Celiac disease; GFD: Gluten-free diet; HVPG: Hepatic venous pressure gradient; HLA: Human leukocyte antigen; LSM: Liver stiffness measurement; NCPF: Non-cirrhotic portal fibrosis; PSVD: Porto-sinusoidal vascular disease; TTG: Tissue transglutaminase

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Table 1 Clinical, Biochemical, and Histological Profile of All the Patients with Non-cirrhotic Portal Fibrosis (NCPF).

Patient characteristics	Patient 1	Patient 2	Patient 3
Age (years)	27	33	19
Sex	Female	Female	Female
Presenting complaints	Easy fatigability and recurrent iron deficiency anemia	Easy fatigability and left hypochondrium pain	Chronic diarrhea
Clinically palpable splenomegaly	++	++	+++
Hemoglobin (g/dL; normal12–16 g/dL)	7.6	8.5	10.2
Total leukocyte count (4500–11000/mm^3)	3500	2450	4100
Platelet count (1.5–4.5/mm^3)	80,000	1.41	76,000
Bilirubin mg/dL (total/conjugated)	1.4/0.7	2.3/1.3	1.2/0.4
SGOT/SGOT (U/L)	40/35	18/32	34/24
Alkaline phosphatase (U/L)	254	115	59
Albumin (g/dL)	3.7	3.4	4.0
INR	1.62	1.43	1.63
Anti-TTG (normal <3 Unit/mL)	>100	78	112
Concomitant autoimmune disease	Hypothyroidism	Nil	Subclinical hypothyroidism
LSM (kPa)	11	9.1	9.8
HVPG (mm of Hg) (normal < 5)	9	8	7.5
Varices	Small esophageal varices	Small esophageal varices	Small esophageal varices
Spleen size (7.6–13 cm)	22	25	20
PV diameter (<13 mm)	16	15	18
Liver biopsy	Inconspicuous portal tract with fibrosis	Normal liver biopsy	Peri-portal tract fibrosis
Response to GFD	Died of intestinal perforation after eight months of diagnosis after transient response	Yes Gained weight, anemia improved	Yes Diarrhea improved

AMA: anti-mitochondrial antibody; ANA: antinuclear antibody; HVPG: hepatic venous pressure gradient; INR: international normalized ratio; kPa: kilo-pascal; LKM1: liver kidney microsomal antibody 1; SGOT: serum glutamic-oxalacetic transaminase; SGPT: serum glutamic-pyruvic transaminase; TTG: tissue transglutaminase; U/L: unit per liter.
The normal values are given within brackets.

splenomegaly should prompt a physician to look for portal hypertension.

CREDIT AUTHORSHIP CONTRIBUTION STATEMENT

SM and UCG have been involved in conceptualizing the study. SM, UCG, AM, PM, and AK have cared for and managed the patients. UCG has been the supervisor. PR and NK were involved in the pathology reporting.

CONFLICTS OF INTEREST

None of the other authors has any conflict of interest to declare concerning this paper.

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