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SHORT REPORT

Celiac disease suspected at endoscopy in patients with chronic liver disease

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Abstract Endoscopic findings of celiac disease have high specificity and sensitivity. We evaluated records of 137 consecutive patients who had endotherapy for variceal hemorrhage, and who had features of celiac disease at endoscopy; patients who had such markers at endoscopy had undergone duodenal histology and serology. Thirty-one patients had changes of portal hypertensive vasculopathy in the duodenum, 8 had scalloping, and 6 had mosaic pattern; 3 patients also had decreased fold height or sparse folds in the descending duodenum. Six of these 8 patients had positive serology and histology suggestive of celiac disease. Endoscopic evaluation resulted in diagnosis of CD in 4.37% patients of chronic liver disease undergoing endotherapy.

Keywords Celiac sprue · Cirrhosis · Gluten enteropathy

Introduction

Celiac disease (CD) in adults often manifests with atypical features [1]. Asymptomatic elevation of transaminases may be the only manifestation of liver disease associated with CD [2–5]. Other liver abnormalities linked to CD include primary biliary cirrhosis (PBC) [6, 7], autoimmune hepatitis (AIH) [2, 8] and primary sclerosing cholangitis (PSC) [9, 10]. The association between CD and liver diseases is being increasingly recognized with one Swedish study showing a greater risk of liver failure in patients with CD [11]. While endoscopic markers of CD are said to have high specificity and sensitivity, and have been used to pick up undetected or unsuspected CD in open access endoscopy [12, 13], there are no studies on the same issue in patients with chronic liver disease (CLD). We report our experience on use of endoscopic markers to detect CD in consecutive patients of portal hypertensive bleeding in northern India where there is a high prevalence (1 in 300) of CD [14].

Methods

One hundred and thirty-seven consecutive patients of portal hypertension (alcoholic cirrhosis 50, chronic hepatitis B related cirrhosis 38, chronic hepatitis C related cirrhosis 23, Budd-Chiari syndrome 6, autoimmune liver disease 5, non-alcoholic statohepatitis (NASH) 8, PBC 1, cryptogenic cirrhosis 6) enrolled for secondary prophylaxis of variceal bleeding with band ligation or sclerotherapy between January 2005 and June 2008 were studied for endoscopic markers of CD. Patients with portal hypertension had been investigated for the etiology of liver disease; tests for hepatitis B and hepatitis C, and liver biopsy were done wherever indicated. At each endoscopy session, findings noted included esophageal and gastric varices, changes of portal hypertensive gastropathy and duodenal changes of portal hypertension (portal hypertensive vasculopathy) in the form of varices, ectasias, hyperemia and edema [15]. In

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Table 1 Characteristics of six patients with celiac disease and variceal bleeding

Age/Sex	Diagnosis	Duration of liver disease (y)	Endoscopy[a]	tTG (IU/mL) (N <15 IU/mL)	Other features	Follow up	Response
55/F	PBC	2	Mosaic pattern	88	Osteoporosis	15 month	Liver functions and bone mineral density improved
21/F	NCPF	1	Mosaic pattern	96.3	Childhood diarrhea, primary infertility	18 month	Hemoglobin improved, delivered normal baby
19/M	BCS	1.5	Decreased fold height, mosaic pattern	>300	–	15 month	Stable, off diuretics
69/F	AIH	1	Decreased fold height, mosaic pattern	112	–	14 month	Stable
40/M	AIH	1.5	Scalloping	>300	Childhood diarrhea	10 month	Improved
38/F	CC	1	Mosaic pattern	100	–	16 month	Stable

[a] All patients had scalloping of duodenal folds. All patients were negative for HBsAg, anti-HCVand had a normal serum cerruloplasmin and iron profile

VH variceal hemorrhage; *NCPF* non cirrhotic portal fibrosis; *AMA* antimitochondrial antibodies; *BCS* Budd-Chiari syndrome; *MR* magnetic resonance; *PBC* primary biliary cirrhosis; *tTG* anti tissue-transglutaminase antibodies; *AIH* autoimmune hepatitis; *CD* celiac disease; *CC* cryptogenic cirrhosis

addition, a note was made of endoscopic markers of CD in the descending duodenum (scalloping, mosaic pattern, and decrease in number or height of duodenal folds) [16]. Two senior endoscopists (RK, UD) confirmed the abnormal findings in each patient and only those findings with consensus between the two were recorded.

Three biopsies were obtained from the descending duodenum for histological examination, and blood samples were sent for anti-tissue transglutaminase antibodies (anti-tTG; ELISA, Celikey, Germany) and antiendomysial antibodies (EMA; immunoflourescence, Purimmun, Germany) in patients with endoscopic markers of CD. For the purpose of this study, patients with positive serology (both anti-tTG and anti-EMA), histological evidence of CD (villous atrophy, crypt hyperplasia, increased intraepithelial lymphocytes) and response to gluten free diet (as per ESPGHAN criteria) [17] were labeled as 'cases'.

Clinical details of the cases were recorded and patients advised gluten free diet, and vitamin and calcium supplements. They were also given specific treatment for the underlying liver disease. All cases were followed up for at least 6 months. The Institute's ethics committee had approved the study and an informed consent was taken from each patient included in the study.

Results

Thirty-seven (27.4%) of the 137 patients had abnormal duodenal findings at endoscopy. These included 31 with portal hypertensive vasculopathy (varices 4, hyperemia 10), ectasia 16 or edema 8) and 8 with markers of CD (scalloping 8, mosaic pattern 6, sparse folds or decrease in fold height 3). Table 1 gives the details of endoscopic findings, serology and histological features of these 6 patients. The diagnosis of liver disease in these 6 patients was autoimmune hepatitis in 2, and PBC, Budd-Chiari syndrome, non-cirrhotic portal fibrosis and cryptogenic cirrhosis in one each. All the 6 patients had successful eradication of varices and had no rebleeding during the follow up. Two of the 8 patients with endoscopic markers of CD did not have positive serology or any other histological changes of CD. Both had alcoholic cirrhosis.

Table 2 gives the comparison between 6 patients with CD and 131 patients without CD. Follow up of the 6

Table 2 Clinical parameters in patients with and without celiac disease

	Celiac PHT	Non-celiac PHT
Mean age (range) years	40.50 (19–69)	52.5 (22–72)
Gender (M:F)	3:3	106:25
Child's status		
A	1	23
B	1	84
C	4	24
Etiology		
Alcohol	0	50
Hepatitis B	0	38
Hepatitis C	0	23
NASH	0	8
Budd-Chiari syndrome	1	5
Cryptogenic cirrhosis	1	4
Autoimmune hepatitis	2	3
Primary biliary cirrhosis	1	0
NCPF	1	0

PHT portal hypertension; *NASH* non-alcoholic steatohepatitis; *NCPF* non cirrhotic portal fibrosis

patients with CD ranged from 6–21 months. The two patients with autoimmune hepatitis were started on prednisolone and azathioprine, and the one with PBC was given ursodeoxycholic acid. The patient with Budd-Chiari syndrome had protein C and protein S deficiency and was started on oral anticoagulation; this case has been reported previously [18]. Five patients have remained well on follow up with no decompensation, while the patient with PBC (case 1) died of ischemic heart disease 15 months after the diagnosis.

Discussion

Widespread use of serological testing and increase in awareness of CD have led to a shift in its presentation with more cases being diagnosed with atypical features [19]. Diarrhea is reported in less than 50% of patients at presentation, and weight loss is an uncommon feature [19]. Endoscopy has been rarely reported to give the first clue to the diagnosis of CD [20–22]. In our study 6 (4.3%) patients with variceal bleed due to portal hypertension were detected to have CD on the basis of endoscopic markers and further confirmatory tests.

Endoscopic findings in CD are loss of duodenal folds, scalloping of folds, and mucosal mosaic pattern, and visualization of underlying vessels in the second part of duodenum [16, 20]. Less common findings are a visible vascular pattern and micronodularity in the duodenal bulb [19]. Awareness of these endoscopic findings may alert the endoscopist to the presence of CD and the need for duodenal biopsy in patients undergoing endoscopy due to symptoms unrelated to the disease.

We studied duodenal changes in patients with portal hypertension who had no obvious clinical suspicion of CD. Two patients had history of childhood diarrhea. This history was obtained retrospectively after serological testing for CD had been done. One patient, with PBC, had osteoporosis with history of fracture of neck femur, which had been attributed to cholestatic liver disease.

There are few studies on endoscopic markers of CD in patients in whom the diagnosis of CD was not suspected. Dickey [12] found that 10 out of 500 patients undergoing open access endoscopy had one or more markers of CD and 8 of them had villous atrophy. Bardella et al. [21] studied 517 dyspeptic subjects for endoscopic markers of CD. At least one endoscopic finding of CD was present in 5 patients, 3 of whom had villous atrophy histologically. Dickey and Hughes [22] assessed 150 patients of upper gastrointestinal symptoms or iron deficiency anemia for markers of CD. At least one marker of CD was present in 7 (5%) patients all of whom had villous atrophy.

In our study, of the 8 patients with endoscopic markers of CD, 6 (75%) had CD. The other two, who had alcoholic cirrhosis, had scalloping but no histological changes of CD. We obtained duodenal biopsies only from patients who had endoscopic markers of CD, and only these patients were subjected to serological testing. Thus we may have underestimated the prevalence of CD in our patient cohort. CD has also been implicated in liver function derangements ranging from elevated liver enzymes [2, 5] to liver failure [11]. A Swedish study suggested that CD is associated with 2–3 fold increased risk for hepatocellular cancer and 7–8 fold increased risk for death from liver cirrhosis [11]. Despite these statistics, surveillance for CD is not recommended in patients of chronic liver disease.

Limitations of our study are that it was a retrospective analysis of data and neither celiac serology nor duodenal biopsies was done in the whole cohort; only IgA anti-tTG antibodies were tested. Moreover 3 of the 6 cases with CD among the portal hypertension cohort had liver pathology with a known association with CD. Among the rest of the 131 patients only 3 had autoimmune hepatitis and none had PBC.

Our study suggests that awareness of endoscopic markers of CD may help in diagnosing some hitherto undiagnosed cases especially in areas with high prevalence of CD. The implication of diagnosing CD in patients with CLD is a possible favorable impact on clinical outcome of such patients [23]. Untreated CD with altered permeability can possibly affect the liver disease adversely. While it is recommended that gluten withdrawal be instituted in patients having CD in association with PBC, AIH or PSC [2], data on impact of gluten free diet in such patients on liver functions or histology is lacking.

To conclude, 4.3% of 137 patients of CLD being treated for variceal bleed were detected to have CD. Endoscopic markers raised the first suspicion of CD in these patients. More data on this issue are needed to recommend screening for CD using endoscopic markers in patients with chronic liver disease.

References

1. Ciacci C, Cirillo M, Sollazzo R. Gender and clinical presentation in adult celiac disease. Scand J Gastroenterol. 1995;30:1077–81.
2. Rubio-Tapia A, Murray JA. The liver in celiac disease. Hepatology. 2007;46:1650–8.
3. Bardella MT, Franquelli M, Quatrini M, Molteni N, Bianchi P, Conte D. Prevalence of hypertransaminasemia in adult celiac patients and effect of gluten-free diet. Hepatology. 1995;22:833–6.
4. Volta U, De Franceschi L, Lari F, Molinaro N, Zoli M, Bianchi F. Celiac disease hidden by cryptogenic hypertransaminasemia. Lancet. 1998;353:26–9.
5. Bardella MT, Vecchi M, Contre D, et al. Chronic unexplained hypertransaminasemia may be caused by occult celiac disease. Hepatology. 1999;29:654–7.

6. Dickey W, McMillan S, Callender M. High prevalence of celiac sprue among patients with primary biliary cirrhosis. J Clin Gastroenterol. 1997;25:328–9.
7. Kingham JGC, Parker DR. The association between primary biliary cirrhosis and celiac disease: a study of relative prevalence. Gut. 1998;42:120–2.
8. Volta U, DeFranceschi L, Molinaro N, et al. Frequency and significance of anti-gliadin and anti-endomysial anti-bodies in autoimmune hepatitis. Dig Dis Sci. 1998;43:2190–5.
9. Hay JE, Wiesner RH, Shorter RG, La Russo NF, Baldus WP. Primary sclerosing cholangitis and celiac disease. A novel association. Ann Intern Med. 1988;109:713–7.
10. Fracassetti O, Delvecchio G, Tambini R, Loernzi N, Gavazzeni G. Primary sclerosing cholangitis with celiac sprue: four cases. J Clin Gastroenterol. 1996;22:71–2.
11. Ludvigsson JF, Elfstrom P, Broome U, Ekbom A, Montgomery SM. Celiac disease and risk of liver disease; a general population-based study. Clin Gastroenterol Hepatol. 2007;5:63–9.
12. Dickey W. Diagnosis of celiac disease at open-access endoscopy. Scand J Gastroenterol. 1998;33:612–5.
13. McIntyre AS, Ng DPK, Smith JA, et al. The endoscopic appearance of duodenal folds is predictive of untreated adult celiac disease. Gastrointest Endosc. 1992;38:148–51.
14. Sood A, Midha V, Sood N, Avasthi G, Sehgal A. Prevalence of celiac disease among school children in Punjab, North India. J Gastroenterol Hepatol. 2006;21:1622–5.
15. Figueredo P, Almeida N, Lerlas C, et al. Effect of portal hypertension in the small bowel: an endoscopic approach. Dig Dis Sci. 2008;53:2144–50.
16. Ravelli AM, Tobanelli P, Minelli L, Villanacci V, Cestari R. Endoscopic features of celiac disease in children. Gastrointest Endosc. 2001;54:736–42.
17. Oberhuber G, Granditsch G, Vogelsang H. The histopathology of coeliac disease: time for a standardized report scheme for pathologists. Eur J Gastroenterol Hepatol. 1999;11:1185–94.
18. Kochhar R, Masoodi I, Singhal M, et al. Celiac disease associated with Budd-Chiari syndrome: a case report with review of literature. Eur J Gastroenterol Hepatol. 2009;21:1092–4.
19. Lo W, Sano K, Lelswahe B, Diamond B, Green PHR. Changing presentation of adult celiac disease. Dig Dis Sci. 2003;48:395–8.
20. Olds G, McLoughlin R, O'Morian C, Sivak Jr MV. Celiac disease for the endoscopist. Gastrointest Endosc. 2002;57:407–15.
21. Bardella MT, Minoli G, Radaclli F, Quentrim M, Bianehi PA, Conte D. Reevaluation of duodenal endoscopic markers in the diagnosis of celiac disease. Gastrointest Endosc. 2000;51:714–6.
22. Dickey W, Hughes D. Prevalence of celiac disease and its endoscopic markers among patients having routine upper gastro-intestinal endoscopy. Am J Gastroenterol. 1999;94:2182–6.
23. Kaukinen K, Halme L, Collin P, et al. Celiac disease in patients with severe liver disease: gluten-free diet may reverse hepatic failure. Gastroenterology. 2002;122:881–8.