

“Should Patients with Liver Disease be Screened for Celiac Disease?”

Janaína Luz Narciso-Schiavon*, Simone Aiko Hatanaka and Leonardo de Lucca Schiavon

Department of Internal Medicine, Division of Gastroenterology, Federal University of Santa Catarina, Santa Catarina, Brazil

Celiac disease was first described by Samuel Gee in 1887 as “a kind of chronic indigestion which is met with in persons of all ages” and could be cured through the diet [1,2]. In the 1950s, during World War II, wheat was identified as a toxic agent for children with celiac disease [2,3]. Today, celiac disease is known as an autoimmune disease of world wide distribution, affecting not only children but adults as well, with a varied clinical picture and symptoms ranging from diarrhea, anemia, and malnutrition to neurological symptoms and association with other autoimmune diseases [4].

Celiac disease is always remembered as a differential diagnosis for malabsorption syndrome or iron deficiency anemia [5]. However, when the clinician has a patient with liver disease, it rarely occurs to him that the patient may suffer from associated celiac disease.

Liver involvement in celiac disease has been widely described in case reports and case series. Abnormal liver tests found during diagnosis of celiac disease are commonly normalized with a gluten-free diet [6-14]. Celiac disease has been associated with primary biliary cirrhosis [15-24], primary sclerosing cholangitis, autoimmune hepatitis [25-27], hepatitis C [28-33], hepatitis B [34-37], non-alcoholic steatohepatitis, and even Wilson’s disease, cirrhosis, and portal hypertension [38-42].

Asymptomatic persistent elevation of aminotransferases unrelated to the usual causes of liver disease, such as non-alcoholic fat liver disease, alcohol abuse, viral infection, autoimmune hepatitis, or rare genetic and metabolic disorders, is relatively common among patients undergoing outpatient hepatology. Celiac disease is frequently found in this setting and should be considered in the differential diagnosis of altered alanine aminotransferase [43].

In autoimmune liver diseases, patients with primary sclerosing cholangitis [39,44,45], primary biliary cirrhosis, or autoimmune hepatitis should undergo celiac screening with tissue transglutaminase and endomysial antibody blood tests [46-48] because an association has been indicated. Patients with celiac disease do not always improve using a gluten-free diet [44,45,49]. However, early recognition and treatment of celiac disease is recommended; gluten restriction improves its symptoms and can also reduce the risk of complications (malabsorption, osteoporosis, and malignant neoplasms) [48,50-52].

In individuals with viral hepatitis, an increased number of celiac antibodies has been described, but the association is not clear and active screening for celiac disease is not recommended [30,53]. However, if the patient will undergo interferon-based therapy, screening is recommended, and if antibodies are present, a gluten-free diet should be established before initiating treatment to reduce the risk of triggering overt celiac disease that can lead to discontinuation of interferon [54].

In individuals with liver cirrhosis, screening for celiac disease during evaluation is recommended, even when another etiology for the cirrhosis has already been determined [42]. It is not clear, however, if celiac disease has a specific effect on the liver or is a coincidental finding [42].

Thus, the hepatologist needs to consider celiac disease during differential diagnosis of abnormal liver blood tests, autoimmune liver diseases, pre-interferon viral hepatitis, and cirrhosis of various etiologies.

References

1. Dowd B, Walker-Smith J (1974) Samuel Gee, Aretaeus, and the coeliac affection. *Br Med J* 2: 45-47.
2. Paveley WF (1988) From Aretaeus to Crosby: a history of coeliac disease. *BMJ* 297: 1646-1649.
3. Ciclitira PJ, King AL, Fraser JS (2001) AGA technical review on Celiac Sprue. *American Gastroenterological Association. Gastroenterology* 120: 1526-1540.
4. Green PH, Jabri B (2003) Coeliac disease. *Lancet* 362: 383-391.
5. Di Sabatino A, Corazza GR (2009) Coeliac disease. *Lancet* 373: 1480-1493.
6. Thatcher N, Stephens AD, Besser GM (1973) Turner's syndrome with coeliac disease, thin bones and abnormal liver function tests. *Postgrad Med J* 49: 738-741.
7. Lance P, Gazzard BG (1983) Ulcerative enteritis and liver disease in a patient with coeliac disease. *Gut* 24: 433-437.
8. Mitchison HC, Record CO, Bateson MC, Cobden I (1989) Hepatic abnormalities in coeliac disease: three cases of delayed diagnosis. *Postgrad Med J* 65: 920-922.
9. Bardella MT, Fraquelli M, Quatrini M, Molteni N, Bianchi P, et al. (1995) Prevalence of hypertransaminasemia in adult celiac patients and effect of gluten-free diet. *Hepatology* 22: 833-836.
10. Volta U, De Franceschi L, Lari F, Molinaro N, Zoli M, et al. (1998) Coeliac disease hidden by cryptogenic hypertransaminasaemia. *Lancet* 352: 26-29.
11. González-Abraldes J, Sánchez-Fueyo A, Bessa X, Moitinho E, Feu F, et al. (1999) Persistent hypertransaminasemia as the presenting feature of celiac disease. *Am J Gastroenterol* 94: 1095-1097.
12. Bardella MT, Vecchi M, Conte D, Del Ninno E, Fraquelli M, et al. (1999) Chronic unexplained hypertransaminasemia may be caused by occult celiac disease. *Hepatology* 29: 654-657.
13. Volta U, Granito A, Franceschi LD, Petrolini N, Bianchi FB (2001) Anti tissue transglutaminase antibodies as predictors of silent coeliac disease in patients with hyper transaminasaemia of unknown origin. *Digestive and liver disease : official journal of the Italian Society of Gastroenterology and the Italian Association for the Study of the Liver* 33: 420-425.
14. Zanini B, Baschè R, Ferraresi A, Pigozzi MG, Ricci C, et al. (2014) Factors that contribute to hypertransaminasemia in patients with celiac disease or functional gastrointestinal syndromes. *Clin Gastroenterol Hepatol* 12: 804-810.
15. Logan RF, Ferguson A, Finlayson ND, Weir DG (1978) Primary biliary cirrhosis and coeliac disease: an association? *Lancet* 1: 230-233.
16. Ginn P, Workman RD (1992) Primary biliary cirrhosis and adult celiac disease. *West J Med* 156: 547-549.
17. DiBaise JK, Paustian FF (1998) Steatorrhea and weight loss in a 72-year-old man: primary biliary cirrhosis? Celiac disease? Bacterial overgrowth? What else? *Am J Gastroenterol* 93: 2226-2230.

*Corresponding author: Narciso-Schiavon JL, Hospital Universitário - UFSC, Departamento de Clínica Médica Rua Professora Maria Flora Pausewang, s/no, 3o andar- Trindade - Florianópolis (SC) - Brazil - 88040-900, Tel: 55-48-3721-9149; E-mail: janaina.narciso@uol.com.br

Received October 1, 2014; Accepted October 14, 2014; Published November 06, 2014

Citation: Narciso-Schiavon JL, Hatanaka SA, Schiavon LDL (2014) “Should Patients with Liver Disease be Screened for Celiac Disease?”. *J Res Development* 2: 116. doi: [10.4172/2311-3278.1000116](https://doi.org/10.4172/2311-3278.1000116)

Copyright: © 2014 Narciso-Schiavon JL, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

18. Kingham JG, Parker DR (1998) The association between primary biliary cirrhosis and coeliac disease: a study of relative prevalences. *Gut* 42: 120-122.
19. Sorensen HT, Thulstrup AM, Blomqvist P, Nørgaard B, Fonager K, et al. (1999) Risk of primary biliary liver cirrhosis in patients with coeliac disease: Danish and Swedish cohort data. *Gut* 44: 736-738.
20. Fracchia M, Galatola G, Corradi F, Dall'Omo AM, Rovera L, et al. (2004) Coeliac disease associated with Sjogren's syndrome, renal tubular acidosis, primary biliary cirrhosis and autoimmune hyperthyroidism. *Digestive and liver disease: official journal of the Italian Society of Gastroenterology and the Italian Association for the Study of the Liver* 36: 489-491.
21. Bizzaro N, Tampoia M, Villalta D, Platzgummer S, Liguori M, et al. (2006) Low specificity of anti-tissue transglutaminase antibodies in patients with primary biliary cirrhosis. *Journal of clinical laboratory analysis* 20: 184-189.
22. Gillett HR, Cauch-Dudek K, Jenny E, Heathcote EJ, Freeman HJ (2000) Prevalence of IgA antibodies to endomysium and tissue transglutaminase in primary biliary cirrhosis. *Can J Gastroenterol* 14: 672-675.
23. Habiore A, Lewartowska A, Orłowska J, Zych W, Sankowska M, et al. (2003) Association of coeliac disease with primary biliary cirrhosis in Poland. *Eur J Gastroenterol Hepatol* 15: 159-164.
24. Sedlack RE, Smyrk TC, Czaja AJ, Talwalkar JA (2002) Celiac disease-associated autoimmune cholangitis. *Am J Gastroenterol* 97: 3196-3198.
25. Sima H, Hekmatdoost A, Ghaziani T, Alavian SM, Mashayekh A, et al. (2010) The prevalence of celiac autoantibodies in hepatitis patients. *Iran J Allergy Asthma Immunol* 9: 157-162.
26. Vajro P, Paoletta G, Pisano P, Maggiore G (2012) Hypertransaminasemia and coeliac disease. *Aliment Pharmacol Ther* 35: 202-203.
27. Mounajjed T, Oxentenko A, Shmidt E, Smyrk T (2011) The liver in celiac disease: clinical manifestations, histologic features, and response to gluten-free diet in 30 patients. *Am J Clin Pathol* 136: 128-137.
28. Plot L, Amital H (2009) Infectious associations of Celiac disease. *Autoimmun Rev* 8: 316-319.
29. Ruggeri C, La Masa AT, Rudi S, Squadrito G, Di Pasquale G, et al. (2008) Celiac disease and non-organ-specific autoantibodies in patients with chronic hepatitis C virus infection. *Dig Dis Sci* 53: 2151-2155.
30. Hernandez L, Johnson TC, Naiyer AJ, Kryszak D, Ciaccio EJ, et al. (2008) Chronic hepatitis C virus and celiac disease, is there an association? *Dig Dis Sci* 53: 256-261.
31. Fine KD, Ogunji F, Saloum Y, Beharry S, Crippin J, et al. (2001) Celiac sprue: another autoimmune syndrome associated with hepatitis C. *Am J Gastroenterol* 96: 138-145.
32. Nadir A, Van Thiel DH (2003) Celiac disease in patients with HCV genotype 1A. *Am J Gastroenterol* 98: 940-941.
33. Marconcini ML, Fayad L, Shiozawa MB, Dantas-Correa EB, Lucca Schiavon Ld, et al. (2013) Autoantibody profile in individuals with chronic hepatitis C. *Rev Soc Bras Med Trop* 46: 147-153.
34. Nau AL, Fayad L, Lazzarotto C, Shiozawa MB, Dantas-Corrêa EB, et al. (2013) Prevalence and clinical features of celiac disease in patients with hepatitis B virus infection in Southern Brazil. *Rev Soc Bras Med Trop* 46: 397-402.
35. Leonardi S, La Rosa M (2010) Are hepatitis B virus and celiac disease linked? *Hepat Mon* 10: 173-175.
36. Soto Iglesias S, Vázquez Rodríguez S, Ulla Rocha JL, Baltar Arias R, DíazSaá W, et al. (2010) [Onset of celiac disease after acute hepatitis B infection]. *Gastroenterol Hepatol* 33: 17-20.
37. Squintani G, Ferrari S, Caramaschi P, Cavallaro T, Refatti N, et al. (2009) Multineuropathy in a patient with HBV infection, polyarteritis nodosa and celiac disease. *Rheumatol Int* 29: 579-581.
38. Kaukinen K, Halme L, Collin P, Färkkilä M, Mäki M, et al. (2002) Celiac disease in patients with severe liver disease: gluten-free diet may reverse hepatic failure. *Gastroenterology* 122: 881-888.
39. Ludvigsson JF, Elfstrom P, Broome U, Ekblom A, Montgomery SM (2007) Celiac disease and risk of liver disease: A general population-based study. *Clin Gastroenterol Hepatol* 5: 63-69.
40. Singh P, Agnihotri A, Jindal G, Sharma PK, Sharma M, et al. (2013) Celiac disease and chronic liver disease: is there a relationship? *Indian J Gastroenterol* 32: 404-408.
41. Drastich P, Honsová E, Lodererová A, Jarešová M, Pekáriková A, et al. (2012) Celiac disease markers in patients with liver diseases: a single center large scale screening study. *World J Gastroenterol* 18: 6255-6262.
42. Wakim-Fleming J, Pagadala MR, McCullough AJ, Lopez R, Bennett AE, et al. (2014) Prevalence of celiac disease in cirrhosis and outcome of cirrhosis on a gluten free diet: a prospective study. *J Hepatol* 61: 558-563.
43. Lo Iacono O, Petta S, Venezia G, Di Marco V, Tarantino G, et al. (2005) Anti-tissue transglutaminase antibodies in patients with abnormal liver tests: is it always coeliac disease? *Am J Gastroenterol* 100: 2472-2477.
44. Hay JE, Wiesner RH, Shorter RG, LaRusso NF, Baldus WP (1988) Primary sclerosing cholangitis and celiac disease. A novel association. *Ann Intern Med* 109: 713-717.
45. Fracassetti O, Delvecchio G, Tambini R, Lorenzi N, Gavazzeni G (1996) Primary sclerosing cholangitis with celiac sprue: two cases. *J Clin Gastroenterol* 22: 71-72.
46. van der Windt DA, Jellema P, Mulder CJ, Kneepkens CM, van der Horst HE (2010) Diagnostic testing for celiac disease among patients with abdominal symptoms: a systematic review. *JAMA* 303: 1738-1746.
47. Abdulkarim AS, Murray JA (2003) Review article: The diagnosis of coeliac disease. *Aliment Pharmacol Ther* 17: 987-995.
48. Ludvigsson JF, Bai JC, Biagi F, Card TR, Ciacci C, et al. (2014) Diagnosis and management of adult coeliac disease: guidelines from the British Society of Gastroenterology. *Gut* 63: 1210-1228.
49. Dickey W, McMillan SA, Callender ME (1997) High prevalence of celiac sprue among patients with primary biliary cirrhosis. *J Clin Gastroenterol* 25: 328-329.
50. Murray JA, Watson T, Clearman B, Mitros F (2004) Effect of a gluten-free diet on gastrointestinal symptoms in celiac disease. *Am J Clin Nutr* 79: 669-673.
51. West J, Logan RF, Smith CJ, Hubbard RB, Card TR (2004) Malignancy and mortality in people with coeliac disease: population based cohort study. *BMJ* 329: 716-719.
52. Haines ML, Anderson RP, Gibson PR (2008) Systematic review: The evidence base for long-term management of coeliac disease. *Aliment Pharmacol Ther* 28: 1042-1066.
53. Silano M, Volta U, Vincentini O, Vincenzi MD (2009) Clinical features of chronic c virus hepatitis in patients with celiac disease. *European journal of clinical microbiology & infectious diseases* : official publication of the European Society of Clinical Microbiology 28: 1267-1269.
54. Durante-Mangoni E, Iardino P, Resse M, Cesaro G, Sica A, et al. (2004) Silent celiac disease in chronic hepatitis C: impact of interferon treatment on the disease onset and clinical outcome. *J Clin Gastroenterol* 38: 901-905.