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BRIEF ARTICLE

Celiac disease markers in patients with liver diseases: A single center large scale screening study

Pavel Drastich, Eva Honsová, Alena Lodererová, Marcela Jarešová, Aneta Pekáriková, Iva Hoffmanová, Ludmila Tučková, Helena Tlaskalová-Hogenová, Julius Špičák, Daniel Sánchez

Pavel Drastich, Julius Špičák, Department of Hepatogastroenterology, Institute for Clinical and Experimental Medicine, 14021 Prague, Czech Republic
Eva Honsová, Alena Lodererová, Department of Clinical and Transplant Pathology, Institute for Clinical and Experimental Medicine, 14021 Prague, Czech Republic
Marcela Jarešová, Department of Immunology, Institute for Clinical and Experimental Medicine, 14021 Prague, Czech Republic
Aneta Pekáriková, Ludmila Tučková, Helena Tlaskalová-Hogenová, Daniel Sánchez, Department of Immunology, Institute of Microbiology, Academy of Sciences of the Czech Republic, 14220 Prague, Czech Republic
Iva Hoffmanová, 2nd Department of Internal Medicine, 3rd Faculty of Medicine, Charles University, 10034 Prague, Czech Republic
Author contributions: Honsová E, Lodererová A, Jarešová M, Pekáriková A, Hoffmanová I, Tučková L and Tlaskalová-Hogenová H performed the research; Honcová E analyzed and interpreted liver histology; Špičák J analyzed the clinical data of patients; and Drastich P and Sánchez D designed the research and wrote the paper.
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Correspondence to: Pavel Drastich, MD, PhD, Department of Hepatogastroenterology, Institute for Clinical and Experimental Medicine, Vídeňská 1958/9, 14021 Prague, Czech Republic. drastich@hotmail.com
Telephone: +420-603-869913 Fax: +420-261-362697
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Abstract

AIM: To study the coincidence of celiac disease, we tested its serological markers in patients with various liver diseases.

METHODS: Large-scale screening of serum antibodies against tissue transglutaminase (tTG), and deamidated gliadin using enzyme-linked immunosorbent assay and serum antibodies against endomysium using immunohistochemistry, in patients with various liver diseases (n = 962) and patients who underwent liver transplantation (OLTx, n = 523) was performed. The expression of tTG in liver tissue samples of patients simultaneously suffering from celiac disease and from various liver diseases using immunohistochemistry was carried out. The final diagnosis of celiac disease was confirmed by histological analysis of small-intestinal biopsy.

RESULTS: We found that 29 of 962 patients (3%) with liver diseases and 5 of 523 patients (0.8%) who underwent OLTx were seropositive for IgA and IgG anti-tTG antibodies. However, celiac disease was biopsy-diagnosed in 16 patients: 4 with autoimmune hepatitis type Ⅰ, 3 with Wilson's disease, 3 with celiac hepatitis, 2 with primary sclerosing cholangitis, 1 with primary biliary cirrhosis, 1 with Budd-Chiari syndrome, 1 with toxic hepatitis, and 1 with non-alcoholic steatohepatitis. Unexpectedly, the highest prevalence of celiac disease was found in patients with Wilson's disease (9.7%), with which it is only rarely associated. On the other hand, no OLTx patients were diagnosed with celiac disease in our study. A pilot study of the expression of tTG in liver tissue using immunohistochemistry documented the overexpression of this molecule in endothelial cells and periportal hepatocytes of patients simultaneously suffering from celiac disease and toxic hepatitis, primary sclerosing cholangitis or autoimmune hepatitis type Ⅰ.

CONCLUSION: We suggest that screening for celiac disease may be beneficial not only in patients with associated liver diseases, but also in patients with Wilson's disease.

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Key words: Tissue transglutaminase; Anti-tissue transglutaminase antibodies; Autoimmune liver diseases; Wilson's disease; Celiac disease; Liver transplantation

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INTRODUCTION

Celiac disease (CLD) is a frequent, lifelong, primarily small intestinal enteropathy with an incidence of more than 1:250 which is induced in genetically susceptible individuals after ingestion of wheat gluten. The duodenal and jejunal mucosa of patients with active CLD is infiltrated by leukocytes and structurally remodeled. Villous flattening and crypt hyperplasia develop in the mucosa of these patients and cause malabsorption syndrome, diarrhea, abdominal pain, and weight loss. However, these symptoms predominate in pediatric patients (accompanied by growth retardation), whereas latent and silent forms of CLD occur more often in adult patients[1-3].

Interestingly, a growing proportion of new cases of CLD are being diagnosed in adults and in patients with extraintestinal manifestations. CLD may affect several organs including kidney, skin, heart, and the nervous, endocrine and reproductive systems, however, liver injury is one of the most frequent extraintestinal manifestations of the disease. Although the spectrum of liver manifestations associated with CLD is particularly wide, two main forms of liver damage, namely cryptogenic and autoimmune, appear to be strictly related to this disease. The most frequent finding documenting liver damage in CLD is a cryptogenic hypertransaminasemia, observed in approximately 15%-55% of untreated patients, as an expression of mild liver dysfunction with a histological picture of nonspecific reactive hepatitis ("celiac hepatitis"). However, in a few cases a more severe liver injury, characterized by a cryptogenic chronic hepatitis or liver cirrhosis requiring liver transplantation, is present. A close association is known to exist between CLD and autoimmune liver diseases such as primary biliary cirrhosis with a prevalence of 3%-7%, autoimmune hepatitis (3%-6%), and primary sclerosing cholangitis (2%-3%). This is probably related to an association between CLD and the human leukocyte antigen (HLA)-DQ heterodimer DQA1/0501/DQB1/0201 on antigen-presenting cells. In CLD, the number of gliadin-specific HLA-DQ2- or HLA-DR4-restricted T-lymphocytes expands and high titers of antibodies against gliadin and various autologous antigens are generated, which can affect the functions of many organs[3-7].

The therapy of CLD is still based on the withdrawal of gluten and its related proteins from the diet of patients [gluten-free diet (GFD)]. After 6-12 mo on a GFD, most CLD patients experience a clinical improvement accompanied by restoration of the intestinal mucosa and a reduction in the number of gliadin and autoantigen-restricted lymphocytes. The serum concentrations of anti-gliadin antibodies and antibodies against autologous antigens are also reduced. Interestingly, mild liver dysfunction with a histological picture of nonspecific reactive hepatitis (celiac hepatitis) may improve after institution of a GFD[8-11]. Although the withdrawal of gluten from the patients' diet improves celiac hepatitis, its influence on autoimmune hepatitis is controversial and in childhood, in which the diagnosis and the introduction of GFD are not usually delayed, it seems ineffective. However, the diet may reduce the risk of CLD complications and development of the most severe refractory CLD[12-15].

The diagnosis of CLD is based on the histological analysis of a duodenal/jejunal biopsy and the testing of serum antibodies against gliadin and autoantibodies against endomysium or tissue transglutaminase (tTG).

This study focused on serological screening for CLD in patients with liver diseases and those who underwent liver transplantation, i.e., patients with a known higher risk of developing CLD. Moreover, we also analyzed the tissue expression and distribution of tTG in the liver of patients with various liver diseases, especially those simultaneously suffering from CLD and compared these to morphologically unaltered liver tissue.

MATERIALS AND METHODS

Patients and controls

The study enrolled patients treated in the Department of Hepatogastroenterology, Institute for Clinical and Experimental Medicine, Prague, in 2009-2010. Sera from a total of 1485 patients were tested. The tested cohorts included 962 patients with diagnosed liver diseases (mean age 55 years, range: 21-76 years) and 523 patients (mean age 49 years, range: 18-66 years) who underwent liver transplantation during 1994-2010 as a consequence of end stage of liver disease. Table 1 summarizes the baseline clinical characteristics of the patients and healthy controls included in our study. The cohort of healthy controls (n = 300, mean age 23 years, range: 18-45 years) was selected from the Institute of Hematology and Blood Transfusion (Prague, Czech Republic).

The diagnostic criteria for primary biliary cirrhosis included clinical symptoms, clinical chemistry, exclusion of infection with hepatitis viruses and evidence of anti-

Table 1 Patients with liver disease and patients who underwent liver transplantation

Disease	Diagnosis	*n* (M/F)
Liver disease	Alcoholic liver cirrhosis	152 (94/58)
	Autoimmune hepatitis type I	77 (27/50)
	Viral hepatitis B	117 (67/50)
	Viral hepatitis C	147 (82/65)
	Wilson's disease	31 (13/18)
	Primary biliary cirrhosis	32 (4/28)
	Primary sclerosing cholangitis	59 (40/19)
	Nonalcoholic steatohepatitis	23 (10/12)
	Liver steatosis	132 (77/55)
	Budd-Chiari syndrome	14 (5/9)
	Polycystic liver	10 (1/9)
	Others[1]	168 (74/94)
OLTx	Alcoholic liver cirrhosis	164 (131/33)
	Autoimmune hepatitis type I	33 (11/22)
	Viral hepatitis B	33 (20/13)
	Viral hepatitis C	79 (56/23)
	Wilson's disease	29 (12/17)
	Primary biliary cirrhosis	40 (5/35)
	Primary sclerosing cholangitis	64 (47/17)
	Cryptogenic liver cirrhosis	28 (16/12)
	Budd-Chiari syndrome	6 (2/4)
	Polycystic liver	14 (3/11)
	Others[2]	33 (16/17)

[1]Drug-induced hepatitis, cryptogenic liver cirrhosis, hepatitis A, hepatocellular carcinoma, focal nodular hyperplasia, mild liver test abnormalities, *etc.*; [2]Cryptogenic liver cirrhosis, hepatocellular carcinoma, hematochromatosis, alpha-1-antitrypsin deficiency, *etc.* M/F: Male/female; OLTx: Patients who underwent liver transplantation.

mitochondrial antibodies type M2. The diagnosis of autoimmune hepatitis was based on the scoring system devised by the International Autoimmune Hepatitis Group and International Association for the Study of the Liver[16]. The main diagnostic criteria for alcoholic liver cirrhosis were the patient's medical history, liver histology, and exclusion of other causes of liver cirrhosis. Diagnosis of Wilson's disease was based on the recommendation of Kodama *et al*[17], and Budd-Chiari syndrome in accordance with the concept of Fox *et al*[18]. Patients who underwent liver transplantation were treated with standard immunosuppressive therapy following appropriate guidelines. The study was approved by the local Ethics Committee.

Serology

Diagnostics and markers for screening of CLD: All serum samples were tested for immunoglobulin (Ig) A and IgG antibodies against tTG. Individuals seropositive for IgA or IgG anti-tTG antibodies were tested for IgA or IgG (in the case of patients with IgA immunodeficiency) isotypes of antibodies against deamidated gliadin (IgA and IgG) and anti-endomysium (IgA or IgG). The final diagnosis of CLD, in individuals seropositive for these IgA or IgG antibodies, was performed by duodenal/jejunal biopsy.

Serological assays used for CLD screening: All tests were performed in the immunological laboratory of the Institute for Clinical and Experimental Medicine according to the manufacturer's instructions. The BIN-DAZYME™ Anti-Tissue Transglutaminase EIA kit (the Binding Site, Birmingham, United Kingdom) and ORG 540A and ORG 540G Anti-Tissue-Transglutaminase ELISA kit (ORGENTEC Diagnostika GmbH, Mainz, Germany) were simultaneously used to test for IgA or IgG anti-tTG antibodies, IgA or IgG anti-gliadin antibodies were tested using QUANTA Lite Gliadin IgA or QUANTA Lite Gliadin IgG (INOVA Diagnostic Inc., San Diego, CA, United States), and by ELISA kits ANTI GLIADIN MGP IgA and ANTI GLIADIN MGP IgG (Binding Site). The results of the serological testing were expressed as a percentage of antibody-positive patients within individual groups. To exclude immunoglobulin deficiency, total IgA and IgG blood levels were analyzed using a routine method in all tested patients.

Detection of anti-endomysial antibodies

Anti-endomysial antibodies were routinely tested by an indirect immunofluorescence method using human umbilical cord tissue cryostat sections. The test serum samples were diluted 1:20 and 1:50. Slides were examined using a Nikon Eclipse E600 immunofluorescence microscope (Nikon, Japan). A positive result was recorded if the connective tissue surrounding the muscle cells was brightly fluorescent, forming a honeycomb pattern.

Immunohistochemistry

Analysis of tTG expression in liver tissue: The expression and distribution of tTG in the liver biopsy samples from 25 patients were analyzed and compared. Eight patients suffered from CLD simultaneously with liver diseases (2 patients with primary sclerosing cholangitis, 1 with autoimmune hepatitis type I , 1 with toxic hepatitis, 1 with Budd-Chiari syndrome, 3 with celiac hepatitis), 8 patients with liver diseases (3 with primary sclerosing cholangitis, 2 with autoimmune hepatitis type I , 1 patient with steatosis, 1 with Budd-Chiari syndrome and 1 patient with primary biliary cirrhosis), and 9 patients with liver metastasis from colorectal carcinoma where tTG expression was analyzed on histologically confirmed unaltered liver tissue at least 3 cm away from the metastasis. The patients with liver disease simultaneously suffering from CLD were seropositive for IgA antibodies against tTG, endomysium and gliadin. MARSH IIIb-c stage of jejunal mucosa was present in these patients. On the other hand, the patients suffering from liver diseases, but not from CLD, included in the analysis of tTG expression in liver were seronegative for all of the mentioned antibodies. Therefore, there was no reason to perform a small intestinal biopsy in these patients.

The tTG detection in liver tissue was performed using the immunoperoxidase staining technique, N-Histofine® Simple Stain MAX PO (MULTI, Nichirei, Japan). Detection was performed on 4 μm thick paraffin sections. Tissue sections were deparaffinated, rehydrated, and antigen retrieval was performed using heat-induced

Table 2 Immunoglobulin A anti-tissue transglutaminase seropositivity in patients with liver disease and patients who underwent liver transplantation

IgA anti-tTG seropositivity	Diagnosis	M/F	*n* (%)
Liver disease	Wilson's disease	1/3	4 (12.9)
	Autoimmune hepatitis type Ⅰ	1/4	5 (6.5)
	Primary biliary cirrhosis	0/1	1 (3.1)
	Budd-Chiari syndrome	0/1	1 (7.1)
	Mild hepatic liver tests abnormalities	5/2	7 (20)
	Liver steatosis	3/1	4 (3.3)
	Viral hepatitis B	1/0	1 (0.9)
	Toxic hepatitis	1/0	1 (4.8)
	Nonalcoholic steatohepatitis	0/2	2 (8.7)
	Primary sclerosing cholangitis	1/1	2 (3.4)
	Polycystic liver	0/1	1 (10)
OLTx	Wilson's disease	1/1	2 (6.9)
	Autoimmune hepatitis type Ⅰ	0/2	2 (6.1)
	Alcoholic liver cirrhosis	1/0	1 (0.6)

IgA: Immunoglobulin A; tTG: Tissue transglutaminase; OLTx: Patients who underwent liver transplantation; M/F: Male/female.

epitope restoration in an EDTA buffer of pH 8.0. Endogenous peroxidase was inactivated with 0.3% H_2O_2 in 70% methanol for 30 min at room temperature. The sections were then incubated for 2 h with anti-tTG antibody CUB 7402 (Acris, Germany), diluted at 1:1200 in antibody diluent, Dako Real (Dako, Glostrup, Denmark). After a washing step, Histofine Simple Stain Max PO was added for 30 min. Tissue staining was visualized with a 3,3'-diaminobenzidine substrate chromogen solution (Dako). Slides were counterstained with hematoxylin, dehydrated, and mounted. A negative control was included by omitting the anti-tTG antibody. An isotype control was included using a nonspecific mouse IgG1 instead of specific anti-tTG antibody.

RESULTS

CLD seropositivity and final diagnosis in patients with severe liver disease

In our study, 29 of 962 adult patients with various liver diseases (3%) were seropositive for IgA anti-tTG antibodies. A summary of the data on seropositive patients is given in Table 2. Seropositivity for anti-tTG antibodies-detected by employing two different diagnostic kits-was found in five patients with autoimmune hepatitis type Ⅰ, four patients with liver steatosis, four with Wilson's disease, two with primary sclerosing cholangitis, two with non-alcoholic steatohepatitis, and one each with polycystic liver disease, Budd-Chiari syndrome, primary biliary cirrhosis, toxic hepatitis, and hepatitis B. Seven patients with mild liver test abnormalities were also seropositive for anti-tTG.

Sixteen of 29 patients, i.e., those who were positive for IgA anti-tTG antibodies, were also seropositive for IgA anti-gliadin and anti-endomysial antibodies. This cohort included patients with autoimmune hepatitis type Ⅰ (4), Wilson's disease (3), celiac hepatitis (3, recruited from the group of anti-tTG seropositive patients with mild liver test abnormalities), primary sclerosing cholangitis (2), primary biliary cirrhosis (1), Budd-Chiari syndrome (1), toxic hepatitis (1), and non-alcoholic steatohepatitis (1). Histological analysis of duodenal or jejunal specimens confirmed the diagnosis of CLD in these 16 patients according to European Society for Paediatric Gastroenterology, Hepatology, and Nutrition criteria. MARSH Ⅲa-c stages of gut mucosa were observed in all 16 patients. The clinical data of these newly diagnosed patients are summarized in Table 3. After 6 mo of adhesion to the GFD, all tested antibodies decreased to values occurring in healthy individuals and staging of mucosal lesions improved substantially (MARSH 0- Ⅰ) in these patients. Four of these 16 patients (three with celiac hepatitis, one with non-alcoholic steatohepatitis) showed normalization of liver tests. However, no substantial clinical and laboratory improvements were observed in the other patients adequately treated for liver disease and adhering to a GFD.

Ten of the 16 newly diagnosed patients showed some non-specific symptoms of CLD (weight loss, diarrhea, abdominal pain), while 6 patients were asymptomatic for CLD.

Serum samples from the blood donors were negative for IgA anti-tTG antibodies.

CLD seropositivity in patients who underwent liver transplantation

Of the 523 patients who underwent liver transplantation, five (0.8%) were positive for IgA anti-tTG antibodies. A summary of the data on seropositive patients is given in Table 2. Anti-tTG antibody seropositivity occurred in 2 patients transplanted for autoimmune hepatitis type Ⅰ, two for Wilson's disease and one transplanted for alcoholic liver cirrhosis. However, none of these patients was seropositive for IgA anti-endomysial antibodies or for IgA and IgG anti-gliadin antibodies. CLD symptoms were not observed in five patients who were seropositive for IgA anti-tTG. For that reason, small intestinal biopsy was not performed in these patients.

TTG expression in liver tissue

In liver diseases, tTG is closely related with tissue repair, fibrogenesis and inflammation[19]. For this reason, we analyzed tTG expression in the liver tissue of twenty five patients simultaneously suffering from active CLD and liver disease, patients suffering from liver disease, but not from CLD, and patients with metastatic colorectal carcinoma.

In this pilot study, we found overexpression of tTG in the liver tissue of patients suffering from liver diseases in contrast to morphologically unaltered tissues. However, individual variability in tTG expression in the liver tissue of these patients was detected. Despite this, the overexpression of tTG was predominantly localized in endothelial cells and periportal hepatocytes and was more pronounced in the liver tissue of all patients suf-

Table 3 Patients with liver disease newly diagnosed with celiac disease

No.	Age	Gender	Diagnosis	Liver histology
1	34	F	PSC	Portal tracts with ductular reaction and minimal inflammation, features of chronic cholestasis
2	37	M	PSC	Florid ductular reaction with accompanying mild mixed inflammation and focal dark-brown granules of copper-associated protein (in orcein stain) in periportal hepatocytes
3	33	M	Wilson's d.	Macrovesicular steatosis, periportal fibrosis and periportal hepatocytes with glycogenated nuclei
4	35	F	Wilson's d.	Focal steatosis, periportal and septal fibrosis
5	36	F	Wilson's d.	Mild nonspecific hepatocellular injury with spotty hepatocyte necrosis and mononuclear portal inflammatory infiltrate, scattered apoptotic bodies and mild steatosis
6	29	M	AIH type I	Portal and lobular inflammation, periportal fibrosis
7	33	F	AIH type I	Portal and periportal inflammation, spotty necrosis
8	33	F	AIH type I	Chronic hepatitis pattern of injury with portal-based inflammation and fibrosis
9	40	F	AIH type I	Periportal interface activity and scattered hepatocyte necrosis
10	35	F	PBC	Bile duct injury with epithelioid granuloma, portal inflammation
11	32	M	Toxic hepatitis	Portal inflammation with scattered eosinophils, spotty necrosis
12	50	F	Budd-Chiari s.	Extensive centrilobular necrosis of hepatocytes
13	22	M	Celiac hepatitis	Non-specific reactive hepatitis with mild portal inflammation
14	27	M	Celiac hepatitis	Mild lobular inflammation with apoptotic bodies and hepatocyte necrosis
15	50	F	Celiac hepatitis	Mild periportal fibrosis with mild portal inflammation and focal interface activity
16	40	F	NASH	Ballooned hepatocytes, macrovesicular steatosis accentuated in zone 3 without significant liver injury

No.: Number; F: Female; M: Male; d.: Disease; PBC: Primary biliary cirrhosis; s.: Syndrome; NASH: Non–alcoholic steatohepatitis; PSC: Primary sclerosing cholangitis; AIH: Autoimmune hepatitis.

fering simultaneously from both liver diseases and active CLD in contrast to patients suffering only from liver disease. Figure 1 shows more pronounced tTG staining in the liver specimens of patients simultaneously suffering from active CLD and primary sclerosing cholangitis, toxic hepatitis, and autoimmune hepatitis type I compared to patients suffering only from primary sclerosing cholangitis and steatosis.

DISCUSSION

CLD is frequently associated with various autoimmune liver diseases such as autoimmune hepatitis, primary biliary cirrhosis and primary sclerosing cholangitis, all of which may be indications for liver transplantation. On the other hand, a controversial association exists between hepatitis B and C virus and CLD. Chronic untreated CLD of long duration may also lead to liver damage severe enough to require liver transplantation[4,6,20-24]. Consistent with the above, reversal of hepatic failure has been described in CLD patients simultaneously suffering from liver disorders who followed a GFD[25]. On the other hand, GFD did not always lead to complete resolution of liver damage in all patients with CLD associated with liver disease[26-28].

This study on the occurrence of CLD and its serological markers in patients with various hepatic disorders and in those who underwent liver transplantation in the Czech Republic complements the serological screening for CLD in the general population (blood donors) and high-risk patients groups e.g., patients with osteoporosis, female infertility and some autoimmune diseases including systemic lupus erythematosus, Sjögren's syndrome and patients with connective tissue disorders in the Czech population performed by Vanciková *et al*[29]. In the present study, we estimated, for the first time, the coincidence of CLD and liver diseases and the relationship between CLD and liver transplantation in the Czech population. Surprisingly, our results documented the highest incidence of CLD in patients with Wilson's disease (9.7%), followed by autoimmune hepatitis (3.9%), primary biliary cirrhosis (3.0%), and primary sclerosing cholangitis (3.4%). While a higher incidence of CLD with primary biliary cirrhosis, primary sclerosing cholangitis and autoimmune hepatitis has been well described[26,28], the association between CLD and Wilson's disease is rare[30-32]. The coincidence of Wilson's disease and CLD was high compared with the coincidence of CLD and osteoporosis (0.98%), female infertility (1.13%) and systemic lupus erythematosus (approximately 2.7%) in the Czech population[29]. Our findings of a higher incidence of CLD in adult patients could be associated with the underestimation of CLD diagnosis described in the elderly[33].

Despite the fact that Wilson's disease, which is characterized by accumulation of copper in tissue, is rarely associated with CLD[30-32], it has been reported that copper metabolism is also impaired in CLD. In CLD patients, copper uptake from the gut is significantly reduced and levels of copper in urine are higher than in healthy individuals[31,32].

In our study, anti-tTG seropositivity in patients who underwent liver transplantation was lower than that described in previous studies[6]. A possible explanation for this is the exclusion from screening of 5 patients who underwent liver transplantation for primary sclerosing cholangitis (2 men, 39 years and 40 years), autoimmune hepatitis type I (woman, 25 years), viral hepatitis B (woman, 51 years) and viral hepatitis C (woman, 56 years), in whom CLD was diagnosed before the beginning of this study. All five patients who underwent liver transplantation and were seropositive for IgA anti-tTG

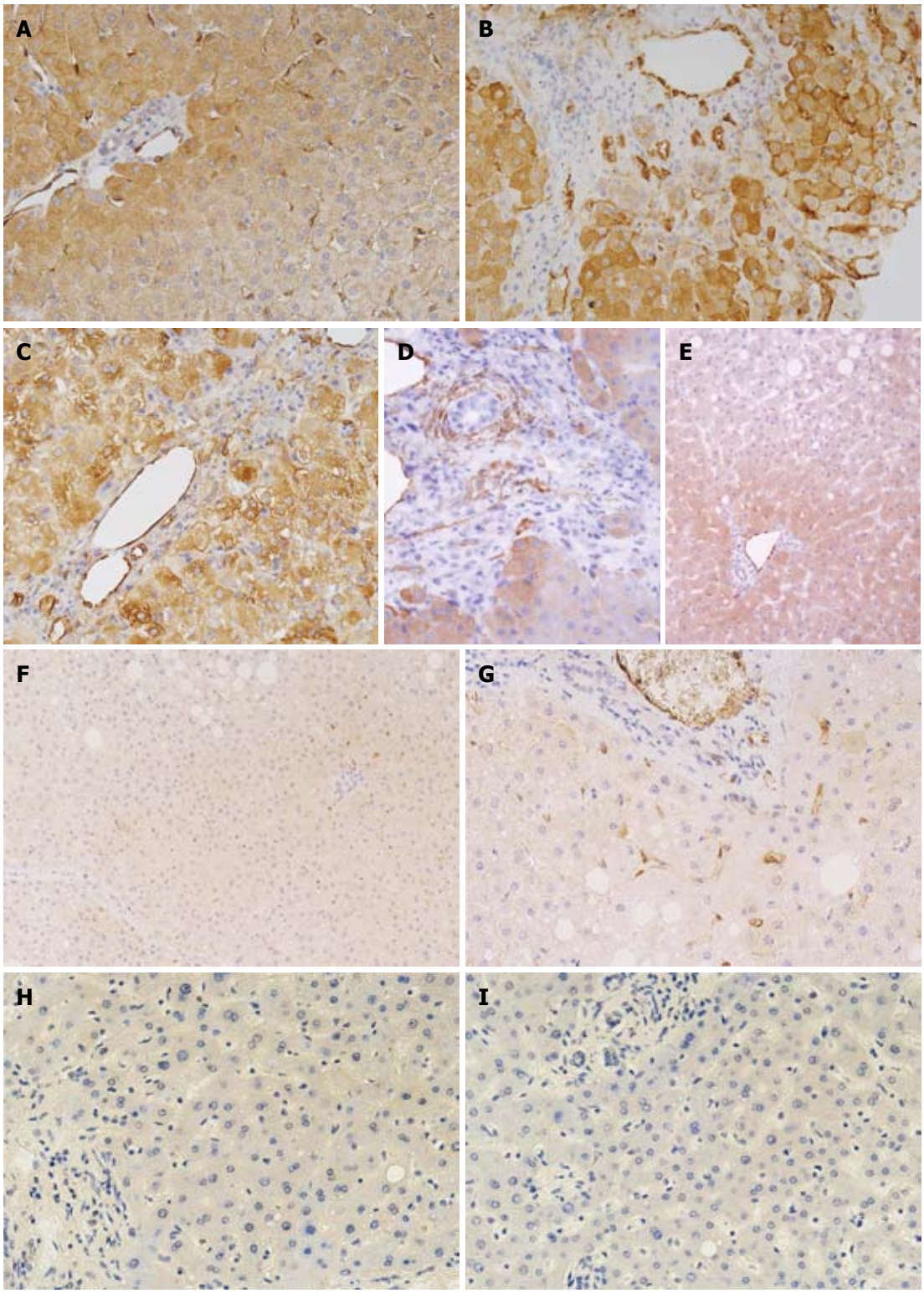

Figure 1 Tissue transglutaminase expression in liver tissue specimens from patients. A: Specimens from patients simultaneously suffering from active celiac disease and primary sclerosing cholangitis; B: Toxic hepatitis; C: Autoimmune hepatitis type Ⅰ; D: Patient with primary sclerosing cholangitis without celiac disease (CLD); E: Steatosis without CLD; F, G: The basal tissue transglutaminase (tTG) expression in morphologically unaltered liver tissue surrounding colorectal adenocarcinoma metastasis; H: Negative control (no anti-tTG antibody); I: Isotype control (nonspecific mouse Immunoglobulin G1 antibody).

antibodies were also seropositive for the IgG isotype of the antibodies, but seronegative for the remaining CLD markers - antibodies against deamidated gliadin and endomysium. The antibody levels, as well as histological changes in small intestine mucosa characteristic of CLD, could have been affected by immunosuppressive treatment complicating the diagnosis of CLD in those patients who underwent liver transplantation[34]. This could also be the reason for the difference in seropositivity between cohorts of patients suffering from liver dis-

ease and patients who underwent liver transplantation. The putative reason for the development of anti-tTG antibodies in patients who underwent liver transplantation could be overexpression of tTG in the graft during repair and healing processes. However, our findings concerning the expression of tTG in liver and induction of anti-tTG antibodies need further investigation. Nevertheless, the testing of CLD serological markers seems to be useful in patients considered for liver transplantation.

In conclusion, we suggest that screening for CLD may be beneficial not only in groups of patients with well-known associated diseases (autoimmune hepatitis, primary biliary cirrhosis, primary sclerosing cholangitis), but also in patients with Wilson's disease, where the relationship to CLD has not been fully analyzed.

COMMENTS

Background

Celiac disease (CLD) is a frequent, lifelong, primarily small intestinal enteropathy with an incidence of more than 1:250 which is induced in genetically susceptible individuals after ingestion of wheat gluten. A growing proportion of new cases of CLD are being diagnosed in adults and in patients with extraintestinal manifestations. CLD may affect several organs including kidney, skin, heart, and the nervous, endocrine and reproductive systems, however, liver injury is one of the most frequent extraintestinal manifestations of the disease.

Research frontiers

This study on the occurrence of CLD and its serological markers in patients with various hepatic disorders and in those who underwent liver transplantation in the Czech Republic complements the serological screening for CLD in the general population (blood donors) and high-risk patients groups.

Innovations and breakthroughs

The authors suggest that screening for CLD may be beneficial not only in groups of patients with well-known associated diseases (autoimmune hepatitis, primary biliary cirrhosis, primary sclerosing cholangitis), but also in patients with Wilson's disease, where the relationship to CLD has not been fully analyzed.

Applications

Their findings on the expression of tissue transglutaminase (tTG) in liver and induction of anti-tTG antibodies need further investigation. Nevertheless, the testing of CLD serological markers seems to be useful in patients considered for liver transplantation.

Peer review

The study is a large scale serological investigation on CLD in patients with liver disease. This study first time revealed a relation between Wilson's disease and CLD, and overexpression of tTG in liver tissue.

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