Celiac Disease Associated With Autoimmune Myocarditis

Andrea Frustaci, MD; Lucio Cuoco, MD; Cristina Chimenti, MD; Maurizio Pieroni, MD; Giuseppina Fioravanti, CTER; Nicola Gentiloni, MD; Attilio Maseri, MD; Giovanni Gasbarrini, MD

Background—Both celiac disease (CD) and myocarditis can be associated with systemic autoimmune disorders; however, the coexistence of the 2 entities has never been investigated, although its identification may have a clinical impact.

Methods and Results—We screened the serum of 187 consecutive patients with myocarditis (118 males and 69 females, mean age 41.7±14.3 years) for the presence of cardiac autoantibodies, anti–tissue transglutaminase (IgA-tTG), and anti-endomysial antibodies (AEAs). IgA-tTG–positive and AEA-positive patients underwent duodenal endoscopy and biopsy and HLA analysis. Thirteen of the 187 patients were positive for IgA-tTG, and 9 (4.4%) of them were positive for AEA. These 9 patients had iron-deficient anemia and exhibited duodenal endoscopic and histological evidence of CD. CD was observed in 1 (0.3%) of 306 normal controls (P<0.003). In CD patients, myocarditis was associated with heart failure in 5 patients and with ventricular arrhythmias (Lown class III-IVa) in 4 patients. From histological examination, a lymphocytic infiltrate was determined to be present in 8 patients, and giant cell myocarditis was found in 1 patient; circulating cardiac autoantibodies were positive and myocardial viral genomes were negative in all patients. HLA of the patients with CD and myocarditis was DQ2-DR3 in 8 patients and DQ2-DR5(11)/DR7 in 1 patient. The 5 patients with myocarditis and heart failure received immunosuppression and a gluten-free diet, which elicited recovery of cardiac volumes and function. The 4 patients with arrhythmia, after being put on a gluten-free diet alone, showed improvement in the arrhythmia (Lown class I).

Conclusions—A common autoimmune process toward antigenic components of the myocardium and small bowel can be found in >4% of the patients with myocarditis. In these patients, immunosuppression and a gluten-free diet can be effective therapeutic options. (Circulation. 2002;105:2611-2618.)

Key Words: celiac disease ▪ myocarditis ▪ immune system

Myocarditis, particularly the giant cell type,1 can be associated with systemic autoimmune disorders that if unrecognized and untreated can prevent the recovery of or even worsen myocardial function. Celiac disease (CD) is a chronic inflammatory disease of the small bowel that is caused, in genetically susceptible individuals, by a permanent intolerance to dietary wheat gliadin and related protein, resulting in small bowel mucosal inflammation, villous atrophy, and crypt hyperplasia. It is characterized by a classic malabsorption syndrome (diarrhea, steatorrhea, and weight loss) or by minor or apparently unrelated symptoms, such as upper abdominal complaints, iron-deficiency anemia, osteopenic bone disease, amenorrhea, and infertility.2–4 Several studies have demonstrated a close association between CD and autoimmune disorders, such as insulin-dependent diabetes mellitus,5 thyroid disorders,6 Addison’s disease,7 and connective tissue disorders.8 An increased prevalence of CD (5.7%) has been recently recognized in patients with idiopathic dilated cardiomypathy,9,10 and an immunologic associative mechanism has been suggested.

The present study reports CD prevalence in a large cohort of patients with biopsy-proven myocarditis and the impact of a gluten-free diet, alone or in combination with immunosuppressive therapy, on cardiac arrhythmias and dysfunction.

Methods

Patient Selection

From January 1997 to January 2001 in our institution, 187 consecutive white Italian patients (118 males and 65 females, mean age 41.7±14.3 years) had a clinical and histological diagnosis of myocarditis. Among these, 110 (75 males and 35 females [60%]) were admitted because of heart failure and because the mean echocardiographic left ventricular ejection fraction (LVEF) and left ventricular end-diastolic diameter (LVEDD) were 31.1±9.2% and 62.5±8.3 mm, respectively. The remaining 77 patients were admitted because of cardiac arrhythmias (66 patients [36 males and 30 females]) with preserved left ventricular function (74%; LVEF 55.7±3.7%, LVEDD 48.2±4.6 mm) or mildly reduced left ventricular function (26%; LVEF 42.6±5.4%, LVEDD 57.4±7.4 mm) or because of a myocarditis mimicking a myocardial infarction (11 patients [7 males and 4 females]; LVEF 53.8±4.1%, LVEDD 50.1±3.8 mm).
No patient was diagnosed with a gastrointestinal, pancreatic, or hepatic disorder, but 13 of them exhibited a sideropenic anemia with a negative hemoccult test refractory to oral iron administration, suggesting the possibility of intestinal malabsorption.

**Cardiac Studies**

All 187 patients underwent both noninvasive cardiac examinations (ECG, Holter monitoring, exercise stress testing, and 2D echocardiography) and invasive cardiac examinations (cardiac catheterization, biventricular and coronary angiography, biventricular endomyocardial biopsy, and electrophysiological study according to class I indication of American College of Cardiology/American Heart Association guidelines). Additional cardiac catheterization and biopsy were obtained at 1, 3, and 5 months of follow-up in those patients with active myocarditis who were undergoing immunosuppressive therapy. All invasive cardiac exams were performed after informed consent was given and were approved by the ethics committee of our institution.

Endomyocardial biopsies (3 or 4 per ventricular chamber) were performed in the septal-apical region of both ventricles. Four to 6 endomyocardial samples obtained from each patient were processed for histological and immunohistochemical studies. For histology, multiple 5-μm-thick sections were cut and stained with hematoxylin-eosin, Miller’s elastic van Gieson, Masson’s trichrome, and Ziehl-Neelsen stain. In all samples, immunohistochemical analysis for the characterization of inflammatory infiltrate was performed. Histological Dallas criteria were used for the diagnosis of myocarditis.

Polymerase chain reaction (PCR) and sequencing analysis were performed on frozen myocardial samples from all patients to detect RNA and DNA genomes of common cardiotropic viruses (adenovirus, enterovirus, influenza A and B viruses, cytomegalovirus, hepatitis C virus, herpes simplex viruses, and Epstein-Barr virus) as previously described. Viral types were identified when nucleotide comparisons revealed an identity of >95% with known type.

**Serological Studies**

Blood samples, collected at the time of endomyocardial biopsy, were divided into aliquots and stored at −80°C until use. Sera of all the 187 patients were screened for the presence of human IgA anti–tissue transglutaminase antibodies (IgA-tTGs), determined by an ELISA commercial kit (Eu-tTG, IgA Umana, Eurospital) and IgA antiendomysial antibodies (AEAs), detected by an indirect immunofluorescence technique on commercial sections of distal monkey esophagus (Antiendomysium, Eurospital). Samples were tested in duplicate, and results were evaluated according to the manufacturer’s instructions and cut-off points. Sera containing antibody at a titer of ≥1:5 were considered positive. Total serum IgA immunoglobulins (normal value 90 to 450 mg/dL) were tested in all patients to exclude selective IgA deficiency.

Patients’ sera were also tested to detect the presence of cardiac autoantibodies by standard indirect immunofluorescence. Patients positive for tissue transglutaminase (tTG) and AEAs and/or cardiac autoantibodies were also screened for other autoimmune disorders through the determination of organ-specific autoantibodies (anti-islet cells, anti-thyroglobulin, anti- thyroid peroxidase, anti-liver-kidney microsomes, and adrenal autoantibodies) and non–organ-specific autoantibodies (antinuclear, anti-DNA, antiphospholipid, anti sarcosomal, antinucleosomal, and antineutrophil cytoplasm antibodies).

As a control population, we enrolled 306 healthy blood donors (212 males and 94 females, mean age 37.0 years [range 21 to 54 years]).

**Gastrointestinal Studies**

Patients positive to tTG or AEAs or to both and patients who exhibited iron-deficiency anemia underwent upper gastrointestinal endoscopy with multiple biopsies in the descending duodenum, and duodenal juice samples were obtained by sterile tube for bacteriological and parasitological analysis (direct microscopic examination and culture). Biopsy specimens were formalin-fixed, paraffin-embedded, and hematoxylin-eosin–stained for histological evaluation. Patients with subtotal/total villous atrophy (Marsh stage II or III) were considered to have CD, as were patients with intraepithelial lymphocytic infiltration (Marsh stage I, intraepithelial lymphocytic infiltration >40/100 enterocytes), and they were started on a gluten-free diet. After 6 to 8 months, the CD patients were reevaluated for compliance to the gluten-free diet by means of clinical examination, by evaluation of iron metabolism improvement, and by AEA and tTG assessment.

**HLA Analysis**

Determination of HLA was performed in patients who were affected by CD. Lymphotype plates for serological determination of HLA phenotype were purchased from Biotest AG and One Lambda, Inc.

**Statistical Analysis**

Data were analyzed by using the χ² test.

**Results**

According to the patients’ clinical histories, no family member with myocarditis or with a recent pregnancy or history of alcohol abuse was reported. By 2D echocardiogram, no pericardial effusion was observed, even for those patients with myocarditis mimicking a myocardial infarction. Exercise stress tests failed to induce ST-T changes suggestive of myocardial ischemia. Ventricular arrhythmias were suppressed by exercise and reappeared on recovery. Coronary angiography was normal for all patients.

At histological examination, diffuse or focal inflammatory lymphomononuclear infiltrates associated with necrosis of adjacent myocytes were observed in all patients meeting the Dallas criteria for myocarditis. Two patients had giant cell myocarditis. Different degrees of interstitial and/or replacement fibrosis were also evident by Masson’s trichrome and Miller’s elastic van Gieson staining. Ziehl-Neelsen staining was negative for acid fast bacteria in all patients. Immunophenotypical characterization of the inflammatory cells showed the presence of activated T lymphocytes (CD45RO+), including a moderate amount of cytotoxic lymphocytes (CD8+). Giant cells were stained for the macrophage marker CD68 but not for the muscle markers actin and desmin, suggesting the macrophage origin of the giant cells. PCR analysis showed the presence of viral genomes in 86 (46%) of 187 patients. Among these, 26 had enterovirus (30%), 21 had adenoovirus (24%), 16 had Epstein-Barr virus (19%), 8 had hepatitis C virus (9.5%), 8 had cytomegalovirus (9.3%), 5 had influenza A virus (6%), and 2 had influenza B virus (2.4%). Sequencing analysis of enterovirus and adenoovirus PCR amplimers showed a high homology with coxsackievirus B3 and B4, rhinovirus 14, and adenoovirus 2 and 5. Comparison of influenza A virus and Epstein-Barr virus showed high homology with human viral sequences. Hepatitis C virus–positive cases showed high homology for genotype 1b.

Positivity for organ-specific anti-heart autoantibodies with diffuse cytoplasmic staining was evident in 53 (28%) of the patients.

No patient showed selective IgA deficiency. Thirteen of 187 patients were positive for IgA-tTG antibodies, and all showed iron deficiency anemia refractory to oral iron replace-
Among tTG-positive patients, 9 showed positivity for AEA. Endoscopy was performed in all the IgA-tTG–positive and AEA-positive patients. We found a normal endoscopic pattern in 4 patients, a reduction of number or a loss of duodenal folds (Figure 1A) in 7 patients, and an appearance as “scalloped valvulae” (Figure 1B) in the 2 remaining patients. Histological examination of bioptic specimens was consistent with a diagnosis of CD in the 9 AEA-positive patients with abnormal endoscopic patterns (4.4%): 5 showed subtotal villous atrophy and crypt hyperplasia (Marsh stage II), and the other 4 patients showed total villous atrophy, crypt hyperplasia, and lymphoplasmacellular infiltrate of the lamina propria (Marsh stage III) (Figure 2). Among the remaining 4 patients submitted to a duodenal biopsy, none showed histological findings of CD; 3 had eosinophilic infiltrate of the lamina propria of intestinal mucosa without changes in intestinal villi and crypts and without an increase of intraepithelial lymphocytes, and the remaining patient showed normal intestinal mucosa. For 2 of these patients, the final diagnosis was Giardia lamblia infestation, and in the remaining 2 patients, duodenal diverticula with massive bacterial overgrowth were detected by coculture of the duodenal juice.

The prevalence of CD in our myocarditis population was 4.4%. In the control population, 2 (0.6%) of 306 individuals showed IgA-tTG positivity, but only 1 (0.3%) was AEA positive and showed intestinal histology consistent with a diagnosis of CD. The results were statistically significant (P<0.003).

Patients With CD and Autoimmune Myocarditis

Clinical and histological data of the 9 CD patients with autoimmune myocarditis are summarized in Table 1. None of the CD patients had a history of recurrent abdominal pain, chronic diarrhea, or weight loss, but all had iron-deficiency anemia refractory to oral iron replacement. PCR analysis on frozen myocardial tissue was negative, but all 9 patients were positive for anti-heart autoantibodies in the serum. As a result of organ-specific autoantibody screening, no additional autoimmune disorder was found in the CD patients. Positive antinuclear antibodies with a diffuse homogeneous pattern were found in 5 of 9 patients, including 1 patient with giant cell myocarditis. HLA analysis showed a combination of DQ2-DR3 haplotypes in 8 patients and the presence of DQ2-DR5(11)/DR7 in 1 patient (Table 2).

No abnormalities of serum proteins or plasma electrolytes were observed in these patients.

In 5 patients, the clinical manifestation of cardiac disease was progressive heart failure (Figure 3A) that failed to improve after conventional supportive therapy administered for >6 months and including digitalis (0.25 mg daily), diuretics (furosemide 25 to 50 mg daily), ACE inhibitors (enalapril 25 mg twice daily), and carvedilol (25 to 50 mg daily); no inotropic agent was additionally provided. In the remaining 4 patients, myocarditis plus ventricular arrhythmias (Lown class III-IVa) were associated with normal cardiac volume and function and normal intracavity pres-
sures. Ventricular arrhythmias were abolished during the cardiac stress test. Because of the positivity of cardiac autoantibodies (with the absence of cardiotropic viruses at PCR analysis suggesting an autoimmune myocarditis) and because of the progressive heart failure refractory to conventional therapy, the 5 patients with heart failure were treated with immunosuppression (azathioprine 1 mg/kg daily for 6 months and prednisone 1.25 mg/kg daily for 4 weeks, tapered off to 0.33 mg/kg daily for 5 months) and a gluten-free diet in addition to the current supportive treatment. All patients demonstrated an improvement in cardiac volume and function (Figure 3B) that was maintained at 12 months of follow-up. At control biopsy, lymphocytic and giant cell myocarditis had progressed to a healed phase (Figure 4A and 4B). The 4 arrhythmic patients received a gluten-free diet alone and were followed by 2D echo and Holter monitoring.

<table>
<thead>
<tr>
<th>No.</th>
<th>Age/Sex</th>
<th>Clinical Presentation</th>
<th>Myocardial Histology</th>
<th>Duodenal Endoscopy</th>
<th>Duodenal Histology</th>
<th>Treatment</th>
<th>Follow-Up (overall 12 months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>24/F</td>
<td>CHF (NYHA III; LVEF 32%) + IDA</td>
<td>ALM</td>
<td>Scalloped valvulae</td>
<td>SVA/CH</td>
<td>GFD + I</td>
<td>Improved (NYHA I; LVEF 54%)</td>
</tr>
<tr>
<td>2</td>
<td>22/F</td>
<td>CHF (NYHA IV; LVEF 21%) + IDA</td>
<td>GCM</td>
<td>Reduction of duodenal folds</td>
<td>TVA/CH</td>
<td>GFD + I</td>
<td>Improved (NYHA I; LVEF 56%)</td>
</tr>
<tr>
<td>3</td>
<td>35/F</td>
<td>VEB (Lown Class IVa) + IDA</td>
<td>ALM</td>
<td>Loss of duodenal folds</td>
<td>TVA/CH</td>
<td>GFD</td>
<td>Improved (Lown Class I)</td>
</tr>
<tr>
<td>4</td>
<td>16/F</td>
<td>VEB (Lown Class III) + IDA</td>
<td>ALM</td>
<td>Reduction of duodenal folds</td>
<td>SVA/CH</td>
<td>GFD</td>
<td>Improved (Lown Class I)</td>
</tr>
<tr>
<td>5</td>
<td>32/M</td>
<td>CHF (NYHA IV; LVEF 17%) + IDA</td>
<td>ALM</td>
<td>Scalloped valvulae</td>
<td>SVA/CH</td>
<td>GFD + I</td>
<td>Improved (NYHA II; LVEF 46%)</td>
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<td>6</td>
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<td>ALM</td>
<td>Loss of duodenal folds</td>
<td>TVA/CH</td>
<td>GFD</td>
<td>Improved (Lown Class I)</td>
</tr>
<tr>
<td>7</td>
<td>16/F</td>
<td>CHF (NYHA II; LVEF 36%) + IDA</td>
<td>ALM</td>
<td>Loss of duodenal folds</td>
<td>SVA/CH</td>
<td>GFD + I</td>
<td>Improved (NYHA I; LVEF 54%)</td>
</tr>
<tr>
<td>8</td>
<td>36/M</td>
<td>CHF (NYHA III; LVEF 27%) + IDA</td>
<td>ALM</td>
<td>Loss of duodenal folds</td>
<td>TVA/CH</td>
<td>GFD</td>
<td>Improved (NYHA I; LVEF 48%)</td>
</tr>
<tr>
<td>9</td>
<td>14/F</td>
<td>VEB (Lown Class III) + IDA</td>
<td>ALM</td>
<td>Reduction of duodenal folds</td>
<td>SVA/CH</td>
<td>GFD</td>
<td>Improved (Lown Class I)</td>
</tr>
</tbody>
</table>

CHF indicates congestive heart failure; NYHA, New York Heart Association class; IDA, iron deficiency anemia; LVEF, left ventricular ejection fraction; VEB, ventricular ectopic beats; ALM, active lymphocytic myocarditis; GCM, giant-cell myocarditis; SVA, subtotal villous atrophy; TVA, total villous atrophy; CH, crypt hyperplasia; GFD, gluten-free diet; and I, immunosuppression.

### TABLE 2. Serological and HLA Profile of Patients With Autoimmune Myocarditis and Celiac Disease

<table>
<thead>
<tr>
<th>Patients</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
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<tr>
<td>AEA (IgA)</td>
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<td>+</td>
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<tr>
<td>Anti-heart</td>
<td>+</td>
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<tr>
<td>HLA pattern</td>
<td>DQ2-DR3</td>
<td>DQ2-DR5(1)-DR7</td>
<td>DQ2-DR3</td>
<td>DQ2-DR3</td>
<td>DQ2-DR3</td>
<td>DQ2-DR3</td>
<td>DQ2-DR3</td>
<td>DQ2-DR3</td>
<td>DQ2-DR3</td>
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<tr>
<td>ANA</td>
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<td>+</td>
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<tr>
<td>ANCA</td>
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<td>Anti-DNA</td>
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<td>Anticardiolipin</td>
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<td>Antisarcocolemmal</td>
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<tr>
<td>Antimyolemmal</td>
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<td>Adrenal autoantibodies</td>
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<tr>
<td>Anti-islet cells</td>
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<tr>
<td>Anti liver-kidney microsomes</td>
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<tr>
<td>Anti-thyroglobulin, anti-thyroid peroxidase</td>
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<tr>
<td>FT3, FT4, TSH</td>
<td>Normal</td>
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</tbody>
</table>

AEA indicates Anti-endomysial antibodies; ANA, Antinuclear antibodies; and ANCA, Anti-neutrophils-cytoplasm antibodies.
every 4 to 6 weeks. At 12 months of follow-up, cardiac arrhythmias improved from Lown class III-IVa to class I (Figure 5A and 5B), and the cardiac 2D echo parameters remained normal. All CD patients experienced a disappearance of the CD-specific autoantibodies 8 months after gluten withdrawal, with a normalization of iron metabolism.

Discussion

A reciprocal negative interaction between the heart and small intestine is known to occur whenever either organ is severely compromised. Less recognized is the possibility of simultaneous damage of the 2 organs due to a common pathogenetic mechanism. The present study showed the presence of an intestinal inflammatory disease in 4.4% of a large population of patients with myocarditis, with a prevalence that was 14 times higher than that in normal control subjects. This amount appears to be rather reliable, because for both AEA and tTG antibodies, a high sensitivity (95% and 100%, respectively) and specificity (90% and 100%, respectively) have been found.16

The presenting symptom of intestinal malabsorption was in our series a sideropenic anemia that was refractory to oral iron supplementation, whereas a diagnosis of CD was obtained by both positivity of AEA and identification of the characteristic duodenal endoscopic and histological findings. In fact, a combination of villous atrophy with lymphocytic infiltration of the small bowel mucosa was documented in all of our 9 patients. In these patients, clinical manifestation of myocarditis was, in 5 cases, heart failure that markedly improved after a combination of gluten-free diet and immunosuppressive therapy. The latter was prompted because of the severity of cardiac dysfunction (which was unresponsive to full conventional supportive therapy), histological evidence of active lymphocytic or giant cell myocarditis, negative serology and PCR on frozen endomyocardial biopsies for the most common cardiotropic viruses, and, finally, the presence of circulating cardiac autoantibodies.

It can be argued that cardiac improvement cannot be attributed with certainty to the therapeutic regimen adopted because a spontaneous resolution has been observed in up to 40% of the patients with myocarditis.17 However, this kind of improvement is mainly attributed to patients with acute lymphocytic myocarditis, whereas our patients had chronic heart failure and failed to respond to supportive treatment administered for >6 months. Moreover, 1 of our patients had giant cell myocarditis, which is known as a progressive disease, and had a poor prognosis unless treatment with a strong immunosuppressive regimen was implemented or heart transplantation was performed.1,15

In the 4 patients with ventricular arrhythmias, only the gluten-free diet was instituted, and cardiac contractility was preserved, and no sustained ventricular tachycardia or synco-
pal event was observed. Arrhythmic patients seemed to benefit from diet, because at sequential Holter monitoring, the arrhythmias markedly improved (from Lown class III-IVa to class I).

HLA analysis showed the presence of DQ2-DR3, which is commonly observed in patients with CD (DQ2 in up to 95% of the cases) and with systemic autoimmune disorders. Serological detection of AEA and cardiac autoantibodies, HLA profile, negative PCR studies for cardiotropic viruses, and responsiveness to a gluten-free diet and immunosuppressive therapy strongly suggest the existence in our patients of an autoimmune disorder directed toward antigenic components of both the myocardium and small bowel. Indeed, both myocarditis (particularly giant cell myocarditis) and CD are known to occur in association with systemic autoimmune disorders. The observation that these entities can be combined in the same patient is of clinical relevance.

In fact, CD is invariably associated with an increase of intestinal permeability, which could lead to the translocation of many intestinal luminal antigens (such as ingested food proteins, bacterial breakdown products, endotoxins, and active enzymes) that can exacerbate myocardial inflammation. Indeed, some other extraintestinal findings of CD, such as chronic unexplained hypertransaminasemia, are attributed to the mechanism of antigenic overload.

Furthermore, active CD is accompanied by consistent production of IgA autoantibodies to reticulin, a common constituent of the extracellular matrix; serum IgA antibodies of patients with untreated CD have been reported to strongly react against human brain–blood vessel structures, and this mechanism has been hypothesized to be involved in the abnormal nervous system manifestations frequently described in association with CD. Recent studies have demonstrated that anti-gliadin autoantibodies react with common epitopes on gliadin, calreticulin, and enterocytes and with a nuclear autoantigen expressed in intestinal endothelial cells and in fibroblasts. On the other hand, tTG, recognized as the target antigen of CD-specific autoantibodies, is an intracellular enzyme that is distributed in the cells of all organs. A possible link between tTG and cardiac damage and also an upregulation of mRNA for tTG in rat models of cardiac failure have been reported. These findings lead us to hypothesize that antigenic mimicry could be actually involved in the pathogenesis of CD-associated disorders. In our CD patients, we were able to detect an autoimmune process against cardiac antigens that could play a key role in the pathogenesis of inflammatory heart damage. The evidence that improvement of cardiac function and of ventricular arrhythmias was paralleled by the disappearance of AEAs and tTG in the serum supports this hypothesis. Nevertheless, other potential mechanisms, such as resumed absorption of proteins with an antioxidant or cardioprotective effect, cannot be excluded.

An interesting finding in the present study was the subclinical presentation of CD even in the presence, in some cases, of marked histopathological lesions. It has been clearly demonstrated that the risk of autoimmune disorders is significantly more elevated in untreated CD and that the prevalence of autoimmune disorders in CD patients is related to the duration of exposure to a gluten-containing diet; compared with healthy subjects, patients with early diagnosis of CD do not show an increased prevalence of autoimmune disorders. This observation suggests the need for early diagnosis, prompt instauration of a gluten-free diet, and strict compliance to gluten withdrawal. Finally, malabsorption can reduce the availability of cardiovascular drugs and essential nutrients that can, in turn, impair contractile and electrical cardiac function.

Clinical Implications

Patients with biopsy-proven myocarditis, especially in the presence of clinical findings of malabsorption, should be screened for CD.

In fact, if CD is associated with autoimmune myocarditis, a gluten-free diet alone or the diet in combination with immunosuppressive agents can significantly improve the clinical outcome.
Limitations of the Study
In our 5 patients with CD and autoimmune myocarditis presenting with heart failure, immunosuppressive treatment was administered together with a gluten-free diet because of the severe cardiac dysfunction and hemodynamic instability that were unresponsive to full conventional therapy. The efficacy of a gluten-free diet alone on recovery of cardiac function should be tested in patients with autoimmune myocarditis and CD who exhibit a myocardial compromise with a stable hemodynamic profile and less aggressive inflammatory disease. Such an investigation could definitively clarify the relationship between the 2 entities.

Acknowledgments
This study was supported by the “Myocarditis: therapeutic impact of etiological diagnosis based upon molecular and immunologic findings” (MURST) project and by “Fondazione per il cuore.”

References


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