Dermatomyositis associated with celiac disease: Response to a gluten-free diet

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The association between dermatomyositis and celiac disease in children has been well documented. In the adult population, however, the association has not been clearly established. A rare case of concomitant dermatomyositis and celiac disease in a 40-year-old woman is presented. After having been diagnosed with dermatomyositis and iron deficiency anemia, this patient was referred to the gastroenterology clinic to exclude a gastrointestinal malignancy. Blood tests revealed various vitamin deficiencies consistent with malabsorption. The results of gastroscopy with duodenal biopsy were consistent with celiac disease. After she was put on a strict gluten-free diet, both nutritional deficiencies and the dermatomyositis resolved. The patient's human leukocyte antigen haplotype study was positive for DR3 and DQ2, which have been shown to be associated with both juvenile dermatomyositis and celiac disease. It is suggested that patients with newly diagnosed dermatomyositis be investigated for concomitant celiac disease even in the absence of gastrointestinal symptoms.

Key Words: *Celiac disease; Dermatomyositis; Gluten*

Dermatomyositis is a rare clinical entity characterized by symmetric proximal muscle weakness and distinctive skin manifestations (1). Although most cases are idiopathic, the disease commonly presents in association with another connective tissue disorder. It may also present as a paraneoplastic syndrome associated with, for example, ovarian or gastrointestinal malignancies.

Celiac disease is a malabsorption syndrome resulting from a small-bowel enteropathy related to the intake of dietary gluten in susceptible individuals (2-4). Gluten is thought to cause both direct and immune-mediated toxicity. Although most cases are discovered in early childhood, the diagnosis of celiac disease in adults is not uncommon. The clinical presentation of celiac disease in the adult population is more variable, however, with a tendency toward atypical features. Moreover, celiac disease has been associated with other autoimmune disorders including thyroiditis, autoimmune hepatitis, Addison's disease, and pernicious anemia (5,6). There is also a strong association between celiac disease and type I diabetes, and dermatitis herpetiformis.

There have been numerous reports suggesting an association between polymyositis and celiac disease (7,8). An association between juvenile dermatomyositis and celiac

La dermatomyosite associée à la maladie cœliaque : La réponse à un régime sans gluten

L'association entre la dermatomyosite et la maladie cœliaque est bien documentée chez les enfants. Au sein de la population adulte, cependant, cette association n'est pas clairement établie. Un rare cas de dermatomyosite concomitante à une maladie cœliaque est présenté chez une femme de 40 ans. Après un diagnostic de dermatomyosite et d'anémie ferriprive, la patiente a été aiguillée vers une clinique de gastroentérologie pour exclure le risque de malignité gastro-intestinale. Les analyses sanguines ont révélé diverses carences vitaminiques compatibles avec une malabsorption. Les résultats de la gastroscopie avec biopsie duodénale suggéraient une maladie cœliaque. Après avoir entrepris un régime sans gluten strict, tant les carences nutritionnelles que la dermatomyosite ont disparu. L'étude d'haplotypes HLA était positive au DR3 et au DQ2, dont l'association avec la dermatomyosite juvénile et la maladie cœliaque est démontrée. On suggère que les patients atteints d'une dermatomyosite nouvellement diagnostiquée fassent l'objet d'explorations pour déceler une maladie cœliaque concomitante, même en l'absence de symptômes gastro-intestinaux.

disease has also been reported (9-11). To our knowledge, only two cases of concomitant dermatomyositis and adult celiac disease have been reported (12,13). Herein, we report a case of unsuspected celiac disease diagnosed following the clinical presentation of dermatomyositis in an adult female patient. We describe the complete resolution of the dermatomyositis while she was on a gluten-free diet.

CASE PRESENTATION

A 40-year-old woman of Irish descent presented with the gradual onset of a diffuse skin eruption associated with easy fatigability of the upper arms and a 20 kg weight loss. She denied any gastrointestinal symptoms other than occasional heartburn and rare abdominal cramps. There was no family history of connective tissue disorder or neuromuscular disease, but there was a family history of colon cancer on her mother's side. Physical examination revealed erythematous and violaceous patches involving the forehead, cheeks, nose, upper back and arms as well as the elbows, knees, and extensor surfaces of the forearms and hands. There was marked periungual erythema, and flat-topped, violaceous (Gottron's) papules present over the knuckles. These cutaneous findings were present on the face and body, despite

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TABLE 1
Patients with concomitant celiac disease and dermatomyositis

Characteristics	Song et al (present study)	Marie et al (12)	Iannone and Lapadula (13)
Patient's age	40 years	63 years	48 years
Ethnicity	Irish	Not identified	Not identified
First diagnosis	Dermatomyositis	Dermatomyositis	Celiac disease
Length of time between diagnoses	10 months	2 years	3 years
Duodenal biopsy	Yes	Yes	Yes
Antidendymal antibodies	Negative	Negative	Positive
SBFT	Yes, consistent with celiac disease	No	No
HLA typing	DR3, DQ2	Not available	Not available
Treatment	Gluten restriction Methylprednisolone (2 doses)	Steroid (2 years) Gluten restriction	Gluten restriction Methyl- prednisolone (2 weeks) Daily prednisone, taken orally Daily cyclosporin A

HLA Human leukocyte antigen; SBFT Small-bowel follow-through

treatment with mild and potent topical steroids, as well as photoprotection. The skin biopsy was consistent with dermatomyositis. Neurological examinations demonstrated reduced power in the proximal upper extremities. There was no muscle tenderness although repetitive activity provoked aching in the deltoids.

Initial laboratory data showed a mild normocytic anemia (hemoglobin concentration 119 g/L) with elevated red cell distribution width (20.7%). Leukocyte and platelet counts were normal. Serum creatine kinase activity was normal. Serum alkaline phosphatase was elevated at 249 U/L (bone fraction 226.7 U/L, liver fraction 22.3 U/L); serum total bilirubin, gamma glutamyl transferase and alanine aminotransferase levels were normal. Antinuclear antibody was positive with a titre of 1:40, speckled pattern. Other autoimmune markers were negative including anti-DNA antibody, anti-Smith, anti-Ro, anti-La, anti-RNP and anti-Scl 70. Anti-Jo-1 antibody was also negative but an electromyogram of the left deltoid revealed abnormalities consistent with dermatomyositis. This diagnosis was subsequently confirmed by the muscle biopsy, which showed interstitial inflammation with prominence of the capillary endothelial cells, and small regions in the muscle where capillarity was reduced.

The patient was referred to the gastroenterology clinic to rule out an underlying gastrointestinal malignancy, a routine measure in adult dermatomyositis. Meanwhile, therapy with intravenous pulse methylprednisolone (500 mg) was initiated. In total, the patient received only two steroid doses. The clinical course was complicated by severe hypocalcemia (serum calcium level 1.16 mmol/L) with carpopedal spasm following the ingestion of oral fleet phosphosoda in preparation for colonoscopy. This episode required brief admission to the intensive care unit, where she was treated with intravenous calcium. Subsequent laboratory testing revealed worsening anemia

(hemoglobin concentration 101 g/L) with evidence of combined deficiencies of iron (serum iron level 4 µmol/L, total iron binding capacity 78.9 µmol/L and serum ferritin 5 µg/L) and folate (serum folate 3 nmol/L, red blood cell folate 14 nmol/L); vitamin B₁₂ levels were normal. In addition, there were deficiencies in some fat-soluble vitamins (serum vitamin E level 6 µmol/L, carotene less than 2 µmol/L). The international normalized ratio was elevated at 1.46, reflecting a lack of vitamin K. Serum protein and albumin levels were low (64 g/L and 33 g/L, respectively). Laboratory workup further demonstrated secondary hyperparathyroidism with a parathyroid hormone level of 505 pg/mL (normal 10 pg/mL to 45 pg/mL); serum 1-25 vitamin D was greater than 100 pg/mL (normal 15 pg/mL to 45 pg/mL).

The patient underwent upper gastrointestinal endoscopy with a small-bowel biopsy. Pathology revealed severe villous atrophy, crypt hyperplasia, and moderate chronic inflammation in the lamina propria, mild intraepithelial lymphocytosis, mild degenerative change in surface epithelium and focal acute inflammation in the lamina propria. Small-bowel follow-through revealed dilation and segmentation of the jejunum, consistent with celiac disease. Antidendymal antibody was negative. Serum human leukocyte antigen typing yielded the following association: A1/A2, B8/B15, C3, DR3/DR4 and DQ2/DQ8.

The patient was placed on a gluten-free diet, along with supplemental iron, folate and calcium. With strict dietary adherence, she showed remarkable improvement as demonstrated by an approximately 11 kg weight gain, restoration of full power and complete resolution of the skin lesions within six to nine months. In addition, all laboratory findings normalized and there was a reversal of all muscle weakness. A repeat small-bowel biopsy, seven months after the dietary modification, remained abnormal but showed clear improvement.

Interestingly, the patient's twin sister, who was being investigated for hypocalcemia and vague abdominal complaints, was also diagnosed with celiac disease after a small-bowel biopsy, but there was no report of skeletal muscle weakness.

DISCUSSION

We describe a 40-year-old woman who presented with weight loss, skin lesions and muscle weakness attributed to dermatomyositis. She was referred for a gastrointestinal malignancy workup. She had no overt gastrointestinal complaints. Unlike in juvenile celiac disease, the clinical presentation of celiac disease in adults is more variable, with a tendency toward atypical features including unexplained iron deficiency anemia, dental enamel hypoplasia, epilepsy with cerebral calcifications, recurrent aphthous ulceration or metabolic bone disease (14).

An association between celiac disease and juvenile dermatomyositis (JDM) had been proposed by Buderus et al (9). They described an eight-year-old girl who had been diagnosed with both diseases and postulated a common genetic susceptibility and pathogenic mechanisms. Based on this earlier observation, Falcini et al (10) investigated the occurrence of celiac disease in a group of 14 children with JDM. They found a prevalence of one in 14 in their group, which was 20-fold higher than that estimated for the normal Italian population. Both groups recommended that endomysial antibody should be routinely investigated in children with JDM, even in the absence of gastrointestinal symptoms.

To our knowledge, the association between dermatomyositis and adult celiac disease has been reported only twice before (Table 1). The case reported by Marie et al (12) described a

63-year-old woman who was diagnosed with celiac disease after having been treated for dermatomyositis with oral prednisone for approximately two years. Iannone and Lapadula (13) described a 48-year-old woman who was diagnosed with dermatomyositis after being diagnosed with celiac disease and being on a gluten-free diet. The patient was treated with prednisone and cyclosporine for one month before symptoms improved.

In the case presented, it is unique that the patient did not have overt gastrointestinal symptoms and that both the dermatomyositis and celiac disease remitted in response to gluten withdrawal. Although our patient did receive two doses of pulse methylprednisolone when the diagnosis of dermatomyositis was first established, she was never placed on continuous steroid treatment. Furthermore, the gradual improvement in her symptoms occurred only after gluten restriction was initiated, and dermatomyositis remained in remission with a gluten-free diet. After dietary modification was instituted, a subsequent duodenal biopsy showed an improvement of both villous atrophy and crypt hyperplasia and also reduced inflammation in the lamina propria. Although the muscle biopsy was not repeated, the clinical picture suggested a resolution of myositis.

The antibody test for endomysial antibody was negative. The test has a 90% to 95% sensitivity and specificity and is routinely performed in patients with suspected celiac disease (15-17). A false negative may explain this result. The duodenal biopsy, the small-bowel follow-through, the family history of celiac disease, improvement and resolution of her nutritional and vitamin deficiencies and improvement of duodenal biopsies on the gluten-free diet consolidated the diagnosis of celiac disease. Before we had the opportunity to perform the more recently developed antitissue transglutaminase test, the patient had moved back to her native country.

Both celiac disease and JDM share common HLA associations, including most notably the DQA1*0501 allele (18-20). HLA typing in our patient revealed the presence of the class II major histocompatibility antigens DR3 and DQ2 – a heterodimer encoded for by the DQA1*0501 and DQB1*0201 alleles. This heterodimer is thought to present gliadin-derived peptides to helper T cells, which trigger the changes leading to the enteropathy. These antigens are found in 95% of northern Europeans with celiac disease. Similarly, genetic studies in JDM have shown increased frequency of B8, DR3 and the DQA1*0501 allele. The common HLA type in these two conditions suggests a related immune-based susceptibility. In addition, while genetically susceptible to both disorders, the concurrence of both entities in our patient over a short period of time may suggest a common antigenic stimulus, which may be gluten or a novel intrinsic antigenic stimulus.

CONCLUSION

Our report suggests an association between adult celiac disease and dermatomyositis. We recommend that patients with newly

diagnosed dermatomyositis be tested for celiac disease, given that the dermatomyositis may respond to a gluten-free diet. Further studies to determine the prevalence of celiac disease in patients with dermatomyositis, to find a potential common antigenic susceptibility gene or antigenic stimulus and to determine the effect of a gluten-free diet on dermatomyositis, seem indicated.

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