Clinical and Experimental Rheumatology 2001; 19: 201-203.

An uncommon association: Celiac disease and dermatomyositis in adults

I. Marie, F. Lecomte, E. Hachulla[1], M. Antonietti[2], A. François[3], H. Levesque, H. Courtois

Department of Internal Medicine, Centre Hospitalier Universitaire de Rouen-Boisguillaume, Rouen; [1]Department of Internal Medicine, Centre Hospitalier Universitaire de Lille, Lille; [2]Department of Gastroenterology, [3]Department of Pathology and Cytology, Centre Hospitalier Universitaire de Rouen, Rouen, France.

Isabelle Marie, MD, PhD; Frédéric Lecomte, MD; Eric Hachulla, MD, PhD; Michel Antonietti, MD; Arnaud François, MD; Hervé Levesque, MD, PhD; Hubert Courtois, MD, PhD.

Please address correspondence and reprint requests to: Dr. Isabelle Marie, 16 rue Arthur Duval, 76300 Sotteville-lès-Rouen, France.

Received on August 18, 2000; accepted in revised form on November 7, 2000.

Key words: Celiac disease, gastrointestinal involvement, malignancy, dermatomyositis, polymyositis.

ABSTRACT

We describe the case of a patient with a two-year history of adult dermatomyositis (DM) who developed malabsorption revealing celiac disease. Our observation raises the question of an association between DM and celiac disease as part of a continuum, suggesting that celiac disease may be included within the spectrum of the gastrointestinal manifestations of DM and polymyositis (PM). From a practical point of view, our data indicate that the diagnosis of celiac disease should be suspected in PM/DM patients exhibiting malabsorption syndrome. Based on our findings, we further emphasize that an evaluation for celiac disease, including anti-gliadin antibodies, anti-endomysium antibody and tissue transglutaminase antibodies should be considered in PM/DM patients presenting with unusual and unexplained gastrointestinal features. This could lead to the early management of such patients, resulting in decreased morbidity (i.e., malnutrition and malignancy) related to misdiagnosed celiac disease.

Introduction

Polymyositis (PM) and dermatomyositis (DM) are systemic inflammatory disorders affecting skeletal muscles and other organs, especially the digestive tract (1). Esophageal motor abnormalities predominate, and involvement of the gastrointestinal tract is considered to be less frequent in PM/DM patients, although it may lead to life-threatening complications, i.e., dramatic hemorrhage, perforation, pseudo-obstruction or pneumatosis cystoides intestinalis (1-4). Recently, a few cases of patients with both PM/DM and celiac disease have been reported, principally juvenile DM occurring after the onset of celiac disease (5-9).

We observed a case of particular interest, where a patient with a 2-year history of adult DM developed malabsorption related to celiac disease.

Case report

A 63-year-old woman was diagnosed with DM in January 1998 based on the criteria of Bohan and Peter (10, 11). The first criteria was symmetric muscle weakness. Muscle power was gauged for 8 proximal muscles (neck flexors, trapezius, deltoid, biceps, psoas, maximus and medius gluteus, and quadriceps) by a modification of the British Medical Research Council Grading system (1), with a theoretical maximum score of 88 points. The muscle power of the patient was 71 points. Other criteria were increased serum muscle enzymes; myopathic changes on electromyography; muscle damage on histological examination; and characteristic dermatologic manifestations, i.e., heliotrope rash and periungual erythema.

Autoantibody screening was positive for antinuclear antibodies (ANA) with a value of 1:160. Investigations, including pulmonary function tests, computerized tomography (CT) scan of the lungs, and echocardiography were within normal limits. Other tests were performed to exclude an underlying malignancy: abdominal ultrasound and colonoscopy were normal.

Treatment with prednisone was initiated at a dose of 1 mg/kg daily (i.e., 55 mg per day for 2 months), which resulted in rapid improvement of muscle strength and clearance of dermatologic signs. Prednisone was decreased gradually to 5 mg every 15 days. At one year follow-up, the patient remained free of both clinical muscle and cutaneous features, and serum muscle enzymes were normal, taking oral steroid at a dose of 15 mg daily.

In August 1999, the patient presented with a one-month history of asthenia and a 3 kg weight loss. She received prednisone therapy 9 mg daily. Physical examination was normal, in particular hepatosplenomegaly and peripheral lymphadenopathy were absent; muscle power was 86 points. Laboratory findings were as follows: erythrocyte sedimentation rate 20 mm/hour, C-reactive protein 10 mg/l, hemoglobin 10 g/dL, mean corpuscular volume 88 μm^3, reticulocytes 50 x 10^9/l, white blood cell count 6,500/mm^3, platelet count 170,000/mm^3, creatine kinase 52 IU/l and aldolase 1.3 IU/l. Renal and liver function tests, serum lactic dehydrogenase, $_2$ microglobulin, blood protein immunoelectrophoresis, and quantita-

tive immunoglobulins were within normal limits. Total protein was 57 g/L and albumin was 27 g/L.

Malabsorption was suspected and confirmed by fecal fats ranging from 3 to 5 g/day, low plasma folate 4 nmol/L and ferritin 30 µg/L. Both blood vitamin B_{12} and digestive alpha-1-antitrypsin levels were normal. A D-xylose test was abnormal. Stool cultures detected no bacteria, parasites or fungi. Duodenal biopsies showed marked mucosal abnormalities, associating subtotal villous atrophy, crypt hyperplasia and intra-epithelial inflammatory infiltrates composed of lymphocytes. Further investigations, including thoracic and abdominal CT-scan, were normal. Autoantibody screening was positive for ANA with a speckled pattern and IgG and IgA anti-gliadin antibodies, and was negative for IgA anti-endomysium antibody, rheumatoid factors, anticardiolipin and antiphospholipid antibodies, lupus-like anticoagulant, antineutrophil cytoplasmic antibodies and cryoglobulin.

The diagnosis of celiac disease was made. The patient was successfully treated with a gluten-free diet, resulting in: 1) correction of her malabsorption and weight gain; and 2) disappearance of both biochemical and histological duodenal abnormalities. In November 1999, steroid treatment was discontinued. To date, the patient remains free of DM and celiac disease features, continuing a gluten-free diet as the sole therapy.

Discussion

Celiac disease is a frequent enteropathy, which is characterized histologically by mucosal villous atrophy. Its prevalence has been estimated to be as high as 1:300 in the general population (12-14). Its diagnosis is often delayed or overlooked as both the presentation patterns and clinical manifestations are non-specific for the disease (14-16). Celiac disease is usually associated with various autoimmune disorders, including insulin-dependent diabetes, dermatitis herpetiformis, autoimmune thyroiditis, IgA nephropathy, primary biliary cirrhosis, autoimmune hepatitis and sclerosing cholangitis (12-14). In a series of 929 patients with celiac disease, Ventura *et al.* (17) found that 35% had an underlying autoimmune condition. However, only a few cases of patients with both PM/DM and celiac disease have been described, especially juvenile DM occurring during the course of celiac disease (5-9). In our cohort of 85 patients with adult PM/DM, only one patient experienced clinical digestive manifestations due to celiac disease (1.18%).

Our case is original in that the patient with a 2-year history of adult DM developed malabsorption revealing celiac disease, although the disease had probably been latent in the patient for many years. In this instance, the diagnosis could be made because the patient fulfilled all the criteria for celiac disease (12, 14), i.e.: 1) duodenal biopsy specimens demonstrated characteristic histological damage; 2) both the clinical features and histological duodenal abnormalities completely healed after institution of a gluten-free diet; and 3) serum IgG and IgA anti-gliadin antibodies were positive.

IgA anti-endomysium antibody was negative in our patient, although the sensitivity and specificity of this antibody have been noted to be as high as 70-100% and 95-100%, respectively, in celiac disease (13, 14, 16); negativity of IgA anti-endomysium antibody was probably due to DM therapy (i.e., prednisone). Tissue transglutaminase antibody has recently been identified as the autoantigen eliciting endomysium antibody, and has been reported to have a high sensitivity (92%) and specificity (98%) (18-21). It was not investigated in our patient because the test is not yet available in our hospital.

Our findings raise the question of an association between DM and celiac disease as part of a continuum, suggesting that celiac disease may be included within the spectrum of the gastrointestinal manifestations of PM/DM in adults. Celiac disease may be due to both immunologic and genetic dysfunction in patients with PM/DM. Our case report therefore confirms the findings of previous investigators, who reported evidence for a marked association between the HLA class II extended haplotypes (i.e., DR2-DQ2 and DR5/7-DQ2) and both PM/DM and celiac disease (5-7, 12, 13).

From a practical point of view, our data indicate that the diagnosis of celiac disease should be suspected in PM/DM patients presenting with malabsorption. Based on our findings, we further emphasize that an evaluation for celiac disease, including anti-gliadin antibodies, anti-endomysium antibody and tissue transglutaminase antibody, should be considered in PM/DM patients prsenting with unusual and unexplained gastrointestinal features. This could lead to the early, accurate diagnosis and management of PM/DM patients, resulting in decreased morbidity (i.e., malnutrition and malignancy) related to misdiagnosed celiac disease.

Finally, we also suggest that anti-gliadin antibodies, anti-endomysium antibody and tissue transglutaminase antibody should become an integral part of the initial immunologic evaluation of PM/ DM patients, particularly DM patients over age 65 years as: 1) elderly DM patients have an increased risk of developing malignancies, notably digestive cancers (22); and 2) the risk of small intestinal lymphoma has been estimated to be more than 50-100 fold greater in elderly patients with overlooked celiac disease compared to the general population) (12).

However, no definite conclusion can be drawn and our data warrant further prospective trials to evaluate the frequency of celiac disease in patients with adult PM/DM.

References

1. MARIE I, HACHULLA E,LEVESQUE H *et al*.: Intravenous immunoglobulins as treatment of life threatening esophageal involvement in polymyositis and dermatomyositis. *J Rheumatol* 1999; 26: 2706-9.
2. DOWNEY EC, WOOLLEY MM, HANSON V: Required surgical therapy in the pediatric patient with dermatomyositis. *Arch Surg* 1988; 123: 1117-20.
3. ESHRAGHI N, FARAHMAND M, MAERZ LL, CAMPBELL SM, DEVENEY CW, SHEPPARD BC: Adult-onset dermatomyositis with severe gastrointestinal manifestations: Case report and review of the literature. *Surgery* 1998; 123: 356-8.
4. PASQUIER E, WATTIAUX MJ, PEIGNEY N: First case of pneumatosis cystoides intestinalis in adult dermatomyositis. *J Rheumatol* 1993; 20: 499-503.

5. BUDERUS S, WAGNER N, LENTZE MJ: Concurrence of celiac disease and juvenile dermatomyositis: Result of a specific immunogenetic susceptibility ? *J Pediatr Gastroenterol Nutr* 1997; 25: 101-3.
6. EVRON E, ABARBANEL JM, BRANSKI D, STHOEGER ZM: Polymyositis, arthritis, and proteinuria in a patient with adult celiac disease. *J Rheumatol* 1996; 23: 782-3.
7. FALCINI F, PORFIRIO B, LIONETTI P: Juvenile dermatomyositis and celiac disease. *J Rheumatol* 1999; 26: 1419-20.
8. HENRIKSSON KG, HALLERT C, NORRBY K, WALAN A: Polymyositis and adult coeliac disease. *Acta Neurol Scand* 1982; 65:301-19.
9. HENRIKSSON KG, HALLERT C, WALAN A: Gluten-sensitive polymyositis and enteropathy. Lancet 1976; 2: 317.
10. BOHAN A, PETER JB: Polymyositis and dermatomyositis. *N Engl J Med* 1975;292:344-7.
11. BOHAN A, PETER JB: Polymyositis and dematomyositis. *N Engl J Med* 1975; 292: 403-7.
12. MÄKI M, COLLIN P: Coeliac disease. *Lancet* 1997; 349: 1755-9.
13. SCHUPPAN D: Current concepts of celiac disease pathogenesis. *Gastroenterology* 2000; 119: 234-42.
14. TRIER JS: Celiac sprue. *N Engl J Med* 1991; 325: 1709-19.
15. BARDELLA MT, MINOLI G, RAVIZZA D *et al*.: Increased prevalence of celiac disease in patients with dyspepsia. *Arch Intern Med* 2000; 160: 1489-91.
16. HIN H, BIRD G, FISHER P, MAHY N, JEWELL D: Coeliac disease in primary care:Case finding study. *Br Med J* 1999; 318: 164-7.
17. VENTURA A, MAGAZZU G, GRECO L, for the SIGEP Study Group for Autoimmune Disorders in Celiac Disease: Duration of exposure to gluten and risk for autoimmune disorders in patients with celiac disease. *Gastroenterology* 1999; 117: 297-303.
18. DIETERICH W, LAAG E, SCHÖPPER H *et al*.: Autoantibodies to tissue transglutaminase as predictors of celiac disease. *Gastroenterology* 1998; 115: 1317-21.
19. BIAGI F, ELLIS HJ, YIANNAKOU JY *et al*.: Tissue transglutaminase antibodies in celiac disease. *Am J Gastroenterol* 1999; 94: 2187-92.
20. SBLATTERO D, BERTI I, TREVISIOL C, *et al*.: Human recombinant tissue transglutaminase ELISA: An innovative diagnostic assay for celiac disease. *Am J Gastroenterol* 2000; 95: 1253-7.
21. SUGAI E, SELVAGGIO G, VAZQUEZ H *et al*.: Tissue transglutaminase antibodies in celiac disease:Assessment of a commercial kit. *Am J Gastroenterol* 2000; 95: 2318-22.
22. MARIE I, HATRON PY, LEVESQUE H *et al*.: Influence of age on characteristics of polymyositis and dermatomyositis in adults. *Medicine* 1999; 78: 139-47.