Case report

Unusual presentation of celiac disease in a child

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SUMMARY

Celiac disease is a genetic, immunologically mediated small bowel enteropathy that causes malabsorption. The immune inflammatory response to gluten frequently causes damage to many other tissues of the body. We report the association of celiac disease and alopecia areata in a girl. The alopecia developed after 11 years nonadherence to a gluten-free diet; the patient had HLA phenotype DR3/DQW2. Our patient had IgA class endomysial antibodies, IgA and IgG antigliadin antibodies and subtotal villous atrophy on jejunal biopsy. Administration of a gluten-free diet resulted complete hair growth.

Key words: celiac disease, alopecia areata

INTRODUCTION

Celiac disease (CD) is a gluten enteropathy occurring in both children and adults. The condition is characterized by a permanent sensitivity to gluten that results in inflammation and atrophy of the mucosa of the small intestine. Clinical manifestations include malabsorption with symptoms of diarrhea, steatorrhea and nutritional and vitamin deficiencies. CD has been reported in association with many other conditions, particularly those of autoimmune origin. Secondary immunologic illnesses may be the primary presentation[1,2].

Alopecia areata (AA) is a common, unpredictable, non-scarring form of hair loss. This disorder affects all age groups, with a higher prevalence in children and adolescents. The etiology of AA is as of yet unclear, but is presumed to be due to an autoimmune reaction. Consistent evidence of autoantibodies directed against anagen stage hair follicle structures are found both in affected humans and in mouse models[3,4].

We describe one patient with AA and CD:

CASE REPORT

A 13-year-old girl was referred to the Pediatric Department because of failure to thrive and anemia. Physical examination showed malnutrition (her weight was < -3 SD), marked abdominal distention, dry and pale skin and four vast areas of patchy AA on her scalp that appeared in 1997. Her personal and family history was negative for gastrointestinal disease and she never complained of diarrhea. Her parents had consulted various specialists in addition to dermatologists for their daughters hair loss. Previous treatments included systemic steroids and psoralen plus UVA, without achieving hair regrowth. Laboratory studies revealed serum hemoglobin: 6.5 mmol/L (normal: 8-9.9 mmol/L), hypochromia and microcytosis, iron: 7.3 μmol/L (normal: 9-26.9μmol/L), albumin: 30 g/L (normal: 35-50 g/L). Values of thyroid stimulating hormone (TSH) and thyroid hormone (T3, T4) were normal and autoantibodies for thyroid disease (antithyroid and antimicrosomal) were absent. Her HLA

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Abbreviations:

CD: Celiac Disease

AA: Alopecia Areata

EMAs: Endomysial Antibodies

AGAs: Antigliadin Antibodies

HLA: Human Leucocyte Antigen

phenotype was DR3/DQW2 and class IgA endomysial antibodies (EMAs) and antigliadin antibodies (AGAs) IgG and IgA were positive. Multiple endoscopic biopsy specimens were therefore taken at the distal duodenum, showing subtotal villous atrophy. After a year of gluten-free diet, a second duodenal biopsy was performed and findings were normalized. There was complete regrowth of hair; she had gained 5 kg in weight and the hematochemical parameters returned to normal values. The patient continues to be under observation, while still on a gluten-free diet, and the situation remains unchanged.

DISCUSSION

An association between AA and CD has recently been reported[5]. Both CD and AA are thought to have an immunologic basis and, more specifically, a T-cell-immune dysregulation[6]. A frequent association of both conditions with many other autoimmune disorders has been described[7,8]; however, the association of these two conditions in the same patient is extremely rare.

In a prospective screening, 254 consecutive outpatients with alopecia areata were tested, using antigliadin and antiendomysial antibodies. Results were positive in three patients and, despite a lack of gastrointestinal symptoms, these patients underwent intestinal biopsy. All three were found to have celiac disease, and treatment with a gluten-free diet was initiated. Thus the observed frequency of association between these 2 entities is much greater than can be expected by chance[5].

Celiac disease is a genetic, immunologically mediated, small intestine enteropathy in which mucosal villi are destroyed by cellular and humoral-mediated immunologic reactions to gliadin protein[9]. The diagnosis of celiac disease does not require further confirmation if the initial diagnosis is based firstly on the appearance of flat small intestinal mucosa with the histological features of hyperplastic villous atrophy while the patient is eating adequate amounts of gluten, and secondly on unequivocal and full clinical remission after withdrawing gluten from the diet. The finding of circulating antibodies (IgA gliadin, antireticulin, and antiendomysium) at time of diagnosis and their disappearance when the patient is on a gluten-free diet add weight to the diagnosis[10]. EMA screening was superior to that for either IgA AGA or IgG AGA in identifying untreated cases of celiac disease, and it had specificity comparable with that of IgA AGA[11].

Studies of patients with CD using molecular techniques demonstrate a strong association with specific HLA class II genotypes. Approximately 95% of patients with CD have a particular type of HLA DQ alpha and beta chain encoded by two genes, HLA-DQA1 0501 and HLA-DQB1 0201[12]. Our patient has HLA phenotype DR3/DQW2. If people genetically predisposed to CD do not ingest gluten, they do not manifest illness. Delaying ingestion of gluten products through breast feeding or dietary habits may change or delay the onset of disease[13]. Viral exposures may trigger an immunologic response in persons genetically susceptible to CD; this occurs with adenovirus 12, which shares a sequence of 8 to 12 amino acids with the toxic fraction[14].

AA is an autoimmune disease, though autoantibodies are postulated to play an integral role in the disease process, current research implicates a cell-mediated autoimmune mechanism as the underlying pathogenic etiology[15]. Supporting this theory is that activated CD4 and CD8 T lymphocytes have been found in a characteristic peri- and intrafollicular inflammatory infiltration of anagen hair follicles of affected individuals[16-18]. AA, similar to many other autoimmune diseases, is linked with certain HLA-Class II alleles. The HLA antigen DQ3 (DQB1*03) has been identified as a general susceptibility marker for AA[19-20]. AA has also been linked with a number of autoimmune disease[21,22].

It is not clear why the association with alopecia is so rare in CD compared with other autoimmune disease. Alopecia may precede the clinical manifestations of intestinal disease and the gliadin antigens are the primary event leading to the alopecia. This may occur as a general immune response to the antigens or to a specific, shared antigenic mimicry between the gliadin and elements in the hair bulb[23].

New data have determined that CD is more common than was previously thought. The diverse secondary clinical manifestations make it easy to miss. A high index of suspicion is required to diagnose CD in a patient with a confounding presentation. Studies with more patients may disclose the factors involved in these rare cases of CD associated with AA.

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