The coexistence of neurofibromatosis type I and celiac disease in a child

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Dear Editor,

A 12-year-old girl who had neurofibromatosis type 1 (NF1) for 6 years presented to a pediatric gastroenterology clinic with the complaint of short stature. She was the third child of non-consanguineous parents. Her older brother had been also diagnosed with NF1. Her physical examination revealed that her weight was 33 kg (3-10 percentile) and that her height was 139 cm (<3 percentile, Z score: -2.2). There were multiple cafe au lait spots on her skin; the largest one was 5×5 cm in diameter. Her ophthalmological examination revealed the presence of Lisch nodules on her iris. There were no pathological findings found in her brain and on performing orbital magnetic resonance imaging and abdominal ultrasonography. While her complete blood count; liver and kidney function test results; and electrolyte, basal growth hormone, free thyroxine (T4), free triiodothyronine (T3), thyrotropin-stimulating hormone, serum ferritin, folate, and total IgA levels were normal, her vitamin B12 and vitamin D3 levels were low. After positive serum anti-endomysial IgA level, upper gastrointestinal endoscopy was performed. A mosaic pattern was observed at the second portion of the duodenum, and her histopathological examination results were compatible with Marsh 3B. The patient with positive human leucocyte antigen (HLA) DQ2 was diagnosed as having celiac disease (CD), and a gluten-free diet (GFD) was introduced. At the 9th month of introducing the GFD, negative anti- endomysial IgA levels were observed, with a significant increase in the patient's height and weight.

NF1 is autosomal dominantly inherited neurocutaneous disease. Mutations in the NF1 gene (17q11.2) cause the formation of cutaneous and internal neurofibromas (1). Gastrointestinal submucosal neurofibromas have been observed in 25% of patients (2). Although usually asymptomatic, gastrointestinal neurofibromas may cause abdominal pain, bleeding, or malabsorption symptoms such as diarrhea or fatty stools (2). Growth retardation can also be frequently seen in NF1 patients.

The formation of neurofibromas causes the suppression of Fas-ligand expression and protection from the apoptosis of CD4+T cells in NF1 patients. This causes predisposition to autoimmune diseases (3). An association has been demonstrated between NF1 and autoimmune diseases such as systemic lupus erythematosus, multiple sclerosis, membranous glomerulonephritis, juvenile arthritis, autoimmune hemolytic anemia, vitiligo, autoimmune thyroiditis, and type 1 diabetes mellitus.

Celiac disease, which is an immune-mediated chronic inflammatory disease of the small intestine, is characterized by permanent susceptibility against gluten in genetically sensitive individuals. Immunological factors play a role in the pathogenesis of CD. It has been demonstrated that gluten is presented to CD4+T cells by HLA-DQ2 and/or HLA-DQ8 (4). Malabsorption disorders and associated classical symptoms of CD, such as growth retardation, diarrhea, abdominal distention, and fatty stools, can be seen in patients due to intestinal mucosal damage.

In our case, although normal growth hormone levels were seen and appropriate nutritional support was provided, there was growth retardation. Therefore, we made the diagnosis of CD. To date, there has been no study investigating the association between CD and NF1. Few cases of NF1 combined with CD have been reported in the literature (5). Although abdominal pain and chronic diarrhea are the main complaints in these cases, our patient presented with the complaint of short stature. This indicates the incidental togetherness of these two dis-

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eases. However, the presence of genetic understructure of these two diseases and the increment in the number of such cases indicate an association further than incidentally. Detailed genetic evaluation of such cases may lead to improvement in the diagnosis and management of such patients.

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