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Association of familial Mediterranean fever and celiac disease in a 14-year-old girl with recurrent arthritis

Sirs,

Celiac disease (CD) is an immune-mediated enteropathy associated with some autoimmune and inflammatory diseases (1). Familial Mediterranean fever (FMF) is a genetic inflammatory disease presenting with recurrent self-limiting attacks of joint, chest and abdominal pain associated with fever (2). FMF is also associated with several inflammatory diseases and vasculitides (2, 3). Herein we report a case of CD in association with FMF.

A 10-year-old girl was admited with a 4-year history of recurrent monoarthritis, failure to thrive, refractory iron deficiency anemia (IDA), and intermittant elevation of acute phase reactants. Her family history was unremarkable. Physical examination revealed paleness and failure to thrive. She had IDA. Fecal occult blood was negative. Investigations for recurrent arthritis (immunglobulins G, A and M, complements C3 and C4, prothrombin and partial thromboplastine times, anti-streptolysin O titer, rheumotoid factor, antinuclear antibody, anti-double strain DNA, antineutrophilic cytoplasmic antibody, serological tests for viral or bacterial infections, ocular examination, ankle and chest x-rays, electrocardiogram and echocardiogram) were normal. IgA anti-endomysial (EMA) antibody was positive. Duodenal biopsy revealed type III CD. She had HLA DQ2. With the diagnosis of CD, a gluten-free diet (GFD) was started, her EMA disappeared, and anemia improved within 9 months.

One year later, the child was admitted with arthritis of the right ankle, chest pain, and dyspnea without fever. Acute phase reactants were elevated, while routine tests, chest x-rays, electrocardiogram, echocardiogram and repeated investigations for any possible causes of arthritis were normal. EMA IgA was negative. The arthritis improved within 5 days. The patient was suspected to have FMF because of her ethnic origin, and clinical and laboratory findings that revealed a homozygous M694V mutation. A diagnosis of FMF was made and colchicine was started. Her acute phase reactants normalized, physical development returned to normal within 2 years, and she has had no complaints for 2 years.

Although CD may occur together with other immune-mediated disorders, its coexistence with FMF has never been described before. Our patient met all the diagnostic criteria of both CD and FMF. Initially we thought that her arthropathy was an extra-intestinal finding of CD. Although rare, arthropathy may be the first and even the only symptom of CD, which takes the form of non-erosive oligoarthritis or polyarthritis affecting primarily the knees and ankles, resolves on GFD, and generally does not relapse (4).

Arthritis in FMF is recurrent and transient, as was seen in our patient, and irreversible joint destruction is rare (5). FMF is associated with several inflammatory diseases and vasculitides including inflammatory bowel disease, polyarteritis nodosa, Henoch-Schönlein purpura, and Behçet's disease (2, 3). The factors underlying these associations are not completely understood. The FMF gene (MEFV) has been suggested to act as a modifier affecting the expression of other inflammatory diseases (3). MEFV encodes pyrin, which probably normally assists in controlling inflammation by deactivating the immune response. Defective pyrin results in uncontrolled inflammation (3). In FMF patients increased transcription of the proinflammatory cytokines (TNF-α, IL-6 and IL-8) has been reported (6). Cytokines also play role in the pathogenesis of CD by stimulating intestinal mucosal immune cells, leading to inflammation that induces the intestinal lesion (7, 8). Inflammation induced by FMF may trigger potentially pathogenic intra-epithelial lymphocytes, and in genetically susceptible individuals this may turn into persistent pathogenic signalling. Although the underlying mechanism is unclear, we hypothesize that interactions between immunological and genetic factors may play a key role in the association of these two disorders.

In Turkey, the prevalence of CD and FMF is 0.09% and 2.8/10,000, respectively (9, 10). The theoretical prevalence of both diseases in a single individual would be 0.25/100,000. This report is the first description of CD and FMF found in a child patient, but studies with larger populations are needed to investigate whether this coexistence is coincidental or whether a relationship between the two diseases actually exists.

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