Familial Mediterranean fever and demyelinating plaques in the central nervous system

Metin Işık

To the Editor,

Familial Mediterranean fever (FMF) is an autosomal recessive hereditary disease, characterized by recurrent attacks of fever, polyserositis, and a marked tendency to develop secondary amyloidosis (1). FMF is mostly diagnosed in Jews, Armenians, Arabs, and Turks. The gene responsible for FMF was identified on chromosome 16p, named MEFV, and this gene product is a 781-amino-acid protein called ‘pyrin,’ or ‘marenostrin,’ which is thought to act as a down-regulator in inflammation (1). Although histopathological findings are rare, during an acute attack with abdominal pain, hyperemia and a neutrophilic exudate may be detected. Less frequently after recurrent attacks, fibrous adhesions may also be seen (2). In very rare cases with FMF, systemic vasculitis may also accompany, mostly mimicking Henoch-Schönlein purpura or polyarteritis nodosa (PAN) (3, 4). Neurological involvement, usually as aseptic meningitis, non-specific EEG abnormalities, pseudotumor cerebri, optic neuritis, and headaches in FMF are very rare findings (5, 6). But, in 1997, 3 cases with FMF and multiple sclerosis (MS) were reported, and soon after, other reports followed this first one (7). On the other hand, a prospective study evaluating neurological involvement among a small group of 17 patients with FMF, done by the researchers that originally described MS-like cases, reported no demyelination in the central nervous system (CNS) (8). Therefore, a relationship with demyelinating CNS disease and FMF is still a puzzle. A 24-year-old male patient was referred to our out-patient unit with recurrent abdominal pain and fever attacks. On the routine physical examination, there was no remarkable pathological finding, but the sedimentation rate, fibrinogen, and C-reactive protein (CRP) were all augmented during his acute bouts during the last 6 years. One of his brothers was diagnosed with FMF, and he had typical bouts; therefore, he was also diagnosed with FMF, and he had typical bouts; therefore, he was also diagnosed with FMF, and he was heterozygous for M694V. The patient was treated with colchicine with a daily dose of 1.5 mg. After a 3-month period, he applied to our out-patient clinics with autism and anorexia. The psychiatric evaluation and the laboratory tests were within normal limits; therefore, for further evaluation, cranial magnetic resonance imaging (MRI) was ordered. The cranial MRI revealed subacute edema at the medulla oblongata, at the left fifth nerve track, and also at the left cerebellar peduncle and acute edema at the periventricular area and also at the pericallosum. Furthermore, demyelinating plaques were seen (Figure 1), and a lumbar puncture was done to exclude infection. The first diagnosis was acute disseminated encephalomyelitis (ADEM), and methylprednisolone of 1 mg/kg was ordered with plasmapheresis. The patient did not benefit from this combination, and the number and size of the demyelinating plaques remained stable in the second MRI (Figure 2); moreover, on the cervical spinal MRI, there was a spinal lesion on the C4 segment, and clinically, paresthesia and gait problems occurred with an alternating pattern. Therefore, the second diagnosis was probable MS; and treatment with interferon beta-1a was ordered. After a 12-month-period on the interferon beta 1a treatment, he had no clinical recovery, and new neurologic findings, such as generalized tonic and clonic seizures, cerebellar ataxia, and bilateral dysdiadochokinesia, came out. The neurologic evaluation still goes on, but the clinical situation does not fit with any diagnosis.

Familial Mediterranean fever is known to be a multisystem disease, but the relationship between CNS and FMF is still not certain. Neurological complications in FMF patients are very rare, such as aseptic meningitis, nonspecific EEG abnormalities, pseudotumor cerebri, and headaches (5, 6). Hypercoagulability and subsequent stroke due to amyloidosis, vasculitis, and MS are the other neurological complications related to FMF (3, 4, 9, 10). Karabudak R et al. (8), in their prospective trial, evaluated 17 patients with FMF for neurologic complications but could not describe MS-like demyelinating plaques. Akman-Demir G et al. (7) stated that although the relation between FMF and MS is not clear, it is possible that MS might be associated with FMF, or an MS-like disease may be a feature of FMF that we are newly recognizing. They evaluated 2800 patients with MS and found 12 patients with FMF, 9 had MS, and 3 had other demyelinating diseases. The time
between the onset of neurologic disorders and FMF was nearly 20 years (7).

For our patient, the diagnosis was not clear. The primary diagnosis was ADEM, but the patient did not benefit from the treatment for ADEM or the treatment for MS, which was the secondary diagnosis. All of these diagnoses were clinical diagnoses, though the patient did not fit any of the diagnostic criteria for these two. This is also a point to consider if FMF may cause demyelinating plaques other than MS, as Akman-Demir G et al. have stated.

In conclusion, although it is not still clear, there may be a relation between MS or MS-like demyelinating diseases and FMF, or FMF may cause lesions resembling MS.

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References