

Protracted synovitis without systemic manifestations in familial Mediterranean fever (FMF)

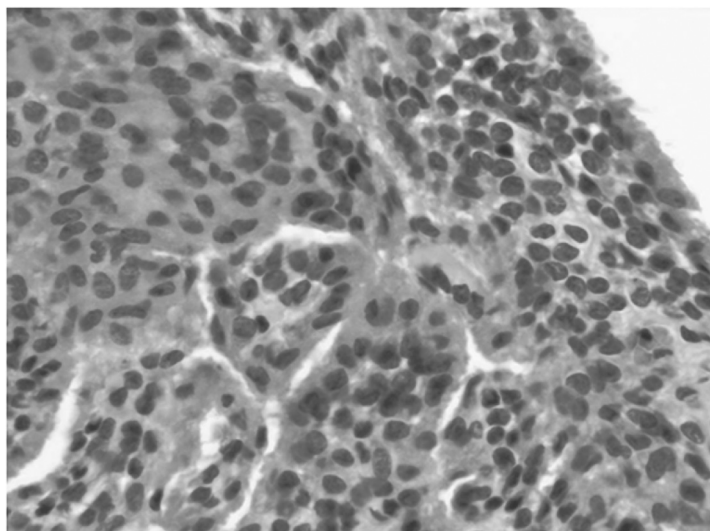
Sirs,

It is now being recognised that familial Mediterranean fever (FMF) also occurs in non-Mediterranean populations, including Japanese (1). The arthritis of FMF consists of acute attacks of pain and swelling of one articulation at a time, most frequently affecting the large joints of the lower extremities within 2-3 days duration (2). In some cases, however, protracted arthritis develops, mostly in the hips and knees (3). Furthermore, disabling joint damage, including joint replacement therapies, has been reported (4). We describe a patient with FMF with protracted arthritis without elevations of acute phase proteins.

A 17-year-old Japanese girl was hospitalised because of pain and swelling of her bilateral knee joints. She suffered from repeated massive bilateral knee joint effusions, for 2 years. Synovial fluid aspirated from the knee joint was clear and cultures for microorganisms were negative. The patient was referred to our hospital because of sustained knee joint pain and effusion. Review of the patient's medical history indicated that the knee joint pain or effusion were not associated with fever, chest or abdominal pain. Physical examination showed a temperature of 36.4°C; pulse 82 beats/min; blood pressure 110/72mmHg. The knees were swollen with marked effusions. Radiographic evaluation demonstrated no positive findings except soft tissue swelling. Laboratory data indicated no abnormal findings, including a lack of anti-nuclear antibody, rheumatoid factor, or anti-cyclic citrullinated peptide (CCP) Ab. There was no elevation of CRP (<0.30mg/dl), ESR (6mm/hr) or serum amyloid A protein (SAA, 3.8µg/ml). MRI imaging of the knee demonstrated the massive fluids and synovial hypertrophy. Arthroscopy showed synovial hypertrophy, which was characterised by heavy and villosity proliferative synovial tissues (Fig. 1). The histopathological findings of the biopsied synovial tissues showed severe synovial inflammation with infiltrations of plasma cells, lymphocytes and neutrophils (Fig. 2). We performed the sequencing of all 10 exons of the *MEFV* gene and detected a heterozygous mutation (GAG to AAG) in codon 84 of the exon 1 of the *MEFV* gene that resulted in a substitution of lysine for glutamic acid (E84K). We initiated daily colchicine treatment (1.0mg/day), the loss of joint effusions was confirmed and the bilateral knee joint pains disappeared.

The frequency of arthritis in FMF has been reported to be more than 70% (5). The arthritic episodes in FMF are usually asso-

Fig. 1. High-power of photograph of the biopsied synovial tissues. Note the infiltrations of inflammatory cells, including plasma cells lymphocytes and neutrophils, into the synovial tissues (Hematoxylin-Eosin; original magnification x200)



ciated with fever and affect the large joints of the lower extremities (6). The arthritis typically resolves spontaneously, over the course of a few days (6). However, about 5% of patients have recurrent attacks and develop chronic arthritis (7). Previous reports have estimated that only 10% patients with FMF experience arthritis as their sole manifestation (8).

We described a patient with FMF who developed long-standing, symmetrical knee joint arthritis with synovial hyperplasia. We speculate that this case is a distinct and rare clinical subtype of FMF arthritis without fever or elevations of acute phase proteins, which has not been described previously.

More recently, Tomiyama *et al.* reported a new *MEFV* mutation, E84K, in a Japanese FMF patient (9). We could not comment on linkage between the E84K genotype and the arthritis-dominant phenotype observed in our FMF case. The recent study indicated that colchicine was effective in non-typical cases of *MEFV*-associated diseases apart from FMF (10). Alternatively, we should reconsider the possibility of the additional *MEFV* gene mutation-associated syndromes. Future studies aimed to clarify the role of *MEFV* variants in the clinical manifestations of FMF are needed.

In conclusion, arthritis could present as the sole manifestation in FMF patients without systemic manifestations. The present case highlights the importance of FMF in the differential diagnosis of chronic symmetrical arthritis in young adults.

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