Familial Mediterranean fever as a rare cause of recurrent monoarthritis

Sirs,

Common causes of recurrent episodic arthritis of the knee include: reactive arthritis, psoriasis crystal synovitis, Behçet's disease, sarcoidosis, and colitis arthritis.

Here we report the case of a 26-year-old Arab female who presented with a 6-year history of recurrent episodic arthritis of the right knee. Each attack would last around 2 weeks before resolving, and would recur few months later. However, the last attack lasted 4 months. No other joints were involved. Associated with each attack, the patient would have a fever (39°C) along with diffuse abdominal pain and diarrhoea. The patient also reported occasional oral ulcers, but not genital ulcers. Initially, no cause was found. There was no past history of psoriasis or uveitis.

On examination, there was a large effusion of the right knee (Fig. 1). She fully unfolded her lumbar lordosis and there were no skin rashes or mouth ulcers.

Her haemoglobin 9.6 mg/L, white cell count $8.0x10^9$/L (80% neutrophils), platelet count 280,000 HLA B27, C-reactive protein 38, antinuclear and CCP antibodies were negative. Inflammatory bowel disease was excluded by endoscopy. She had a partial response respond to oral corticosteroids, sulphasalazine, hydroxychloroquine and methotrexate. Genetic testing for the MEFV gene revealed M694V homozygosity. She eventually responded to oral corticosteroids and colchicine. After corticosteroids were stopped, she remained symptom free on 1.5 mg colchicine. No further recurrences occurred.

Familial Mediterranean fever (FMF) (OMIM #249100) is most prevalent in individuals of Arab, Armenian, Ashkenazi Jewish, non-Ashkenazi Jewish, Turkish, and Italian ancestry (1). FMF is characterised by brief and self-limiting febrile attacks of peritonitis, arthritis, pleurisy, or an erysipelas-like erythema (2). Arthritis occurs in approximately 70% of the patients with the hip, knee, and ankle joints being frequently affected. The most common articular attack is an acute, painful large joint monoarthritis which usually affects the knee or hip and lasts for a few days (1).

Protracted arthritis attacks lasting more than a month and even years have been reported in around 10% of FMF patients. The knee and, to a lesser extent, the hip joints are most commonly affected (3). Full recovery, with the exception of the hip, is a major feature of FMF-associated arthritis. Articular attacks occur at an early age, being of abrupt onset, usually accompanied by fever, redness, warmth, swelling, and tenderness of the affected joint (3). Inflammation usually subsides within two weeks, but synovial effusion lasts longer (4). Uthman *et al*. reviewed retrospectively 74 Lebanese FMF patients over an 18-year period, arthritis was the presenting symptom in 16.2% of the cases, and 31% of patients had definite arthritis during the course of their disease (5). The knee was the most frequently involved joint affected in 57% of patients. Among 83 Syrian FMF patients studied for *MEFV* gene mutations, 36 patients had arthritis (6).

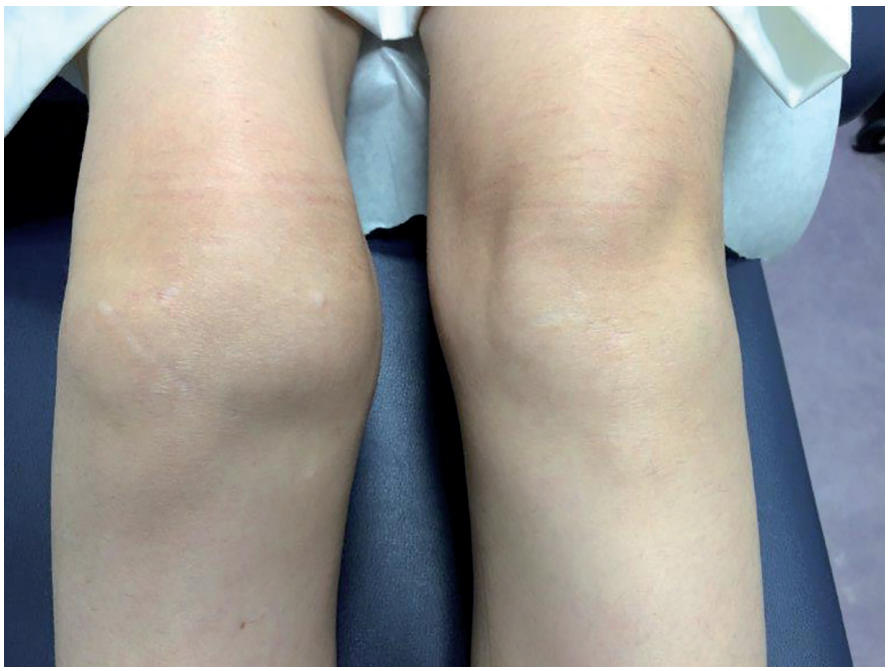

Fig. 1. A large right knee effusion on physical examination.

Mutations of the *MEFV* gene have been identified in most FMF patients. It includes four conservative missense mutations (M680I, M694V, M694I, V726A) clustered in exon 10 of chromosome 16 (7). Mattit *et al*. identified the distribution and the frequency of the *MEFV* gene mutations in Syrian FMF patients, and performed a genotype/phenotype correlation in the patients' cohort (6). They found that among 83 patients, 76 had a mutation in the *M694V* gene. 20 patients were homozygotes for the *M694V* gene mutation with 14 patients having arthritis.

Histological specimens from involved FMF joints have revealed non-specific synovitis with destruction of cartilage (8).

In conclusion, FMF should be considered in patients with recurrent episodes of a febrile illness associated with acute monoarthritis especially if the patient is young and of an appropriate ethnic origin. The diagnosis is confirmed by genetic testing and it usually responds to regular colchicine.

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References

1. SOHAR E, GAFNI J, PRAS M, HELLER H: Familial Mediterranean fever: A survey of 470 cases and review of the literature. *Am J Med* 1967; 43: 227-53.
2. BAKKALOGLU A: Familial Mediterranean fever. *Pediatr Nephrol Berl Ger* 2003; 18: 853-9.
3. INCE E, CAKAR N, TEKIN M *et al*.: Arthritis in children with familial Mediterranean fever. *Rheumatol Int* 2002; 21: 213-7.
4. GARCIA-GONZALEZ A, WEISMAN MH: The arthritis of familial Mediterranean fever. *Semin Arthritis Rheum* 1992; 22: 139-50.
5. UTHMAN I, HAJJ-ALI RA, ARAYSSI T, MASRI AF, NASR F: Arthritis in familial Mediterranean fever. *Rheumatol Int* 2001; 20: 145-8.
6. MATTIT H, JOMA M, AL-CHEIKH S *et al*.: Familial Mediterranean fever in the Syrian population: gene mutation frequencies, carrier rates and phenotype-genotype correlation. *Eur J Med Genet* 2006; 49: 481-6.
7. French FMF Consortium: A candidate gene for familial Mediterranean fever. *Nat Genet* 1997; 17: 25-31.
8. HERNESS D, MAKIN M: Articular damage in familial Mediterranean fever. Report of four cases. *J Bone Joint Surg Am* 1975; 57: 265-7.