

# Concurrent chronic recurrent multifocal osteomyelitis and familial Mediterranean fever. A case report

Sirs,

Familial Mediterranean fever (FMF) is the best-characterised monogenic autoinflammatory condition (1). Typically inherited in an autosomal recessive pattern, FMF occurs due to mutations in the *MEFV* gene, which codes for the pyrin protein. FMF is characterised by recurrent short-lived fever episodes with serositis, arthritis, and/or cutaneous findings (2).

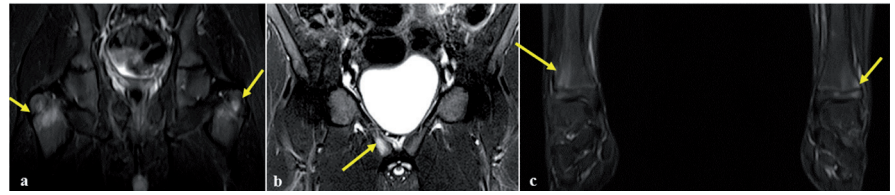
Chronic recurrent multifocal osteomyelitis (CRMO) is a condition that results in sterile inflammatory bone lesions with a relapsing and remitting course (3). CRMO is thought to be due to innate immune system dysregulation, but no monogenic cause has been consistently found. The aetiological basis of CRMO is thought to be due to an interaction of multiple alleles and environmental influence (4, 5).

The development of two autoinflammatory diseases in a single patient is an uncommon finding. Here, we report a case of a patient with a concurrent diagnosis of FMF and CRMO.

A 16-year-old male was diagnosed at the age of six with FMF after recurrent episodes of short-lived fevers, abdominal pain and vomiting. He is from a non-consanguineous family of Sephardic Jewish and Ashkenazi Jewish descent. The family medical history is pertinent for psoriatic arthritis in a maternal aunt and FMF in a distant maternal cousin. Genetic testing showed heterozygous mutations in V726A and M694V of the *MEFV* gene, both of which are pathogenic mutations.

Six years from his FMF diagnosis, our patient developed insidious bilateral thigh and groin pain. His hip MRI revealed multiple foci of abnormal high STIR signal in the left iliac bone, right pubis, right ischium, greater trochanters bilaterally, and distal tibial metaphyses bilaterally (Fig. 1). Given the multifocal involvement and distribution, the lesions were felt to be consistent with CRMO and no bone biopsy was required. His blood work was consistent with low-grade inflammation and his HLA-B27 was negative.

Our patient was treated with a non-steroidal anti-inflammatory drug (naproxen) for his CRMO and colchicine for his FMF. He has not had any clinical evidence of FMF attacks while on colchicine, but our patient continues to show low-grade inflammation characterised by elevated C-reactive protein and serum amyloid A levels. It remains difficult to tell if the elevated inflamma-



**Fig. 1.** Coronal STIR images demonstrating foci of bone marrow oedema involving the greater trochanteric apophyses bilaterally (a), and the right pubic bone (b). Increased STIR signal in bilateral distal tibial metaphyses and epiphyses (c).

tory indices are secondary to his FMF or CRMO, particularly in the context of poor medication adherence. During his 10 years of FMF disease course, he has had no renal complications. Furthermore, he has not developed any CRMO associated conditions such as psoriasis, inflammatory bowel disease, palmoplantar pustulosis, or ankylosing spondylitis.

To our knowledge, this is only the second documented case of concurrent CRMO and FMF in one patient. Daia *et al.* (6) previously reported a case of a paediatric female with FMF (heterozygous M694V mutation) who developed multiple bone lesions and palmoplantar pustulosis. Unlike our patient, this previously reported patient had persistent arthritis and vertebral involvement.

Sterile bone inflammation and lesions have not been consistently reported in FMF patients although M694V mutations (which is one of the mutations seen in our patient) may be associated with increased musculoskeletal phenotype expression (7). Theoretical possibilities for this association may be that the osteitis is a unique variant expression of the FMF phenotype, epigenetics may mediate the expression of both FMF and CRMO (8), or that the *MEFV* gene may modify the genes that are involved in the expression of CRMO (9).

In summary, we report a second unique case of CRMO in a paediatric patient with FMF. The precise mechanism for this association remains unclear. Rheumatologists should be alerted of this rare but possible association.

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