Familial Mediterranean fever diagnosed in an elderly patient

Sirs,

Familial Mediterranean Fever (FMF) is an autosomal recessive disease caused by mutations in the *MEFV* gene, which encodes the pyrin protein, and is characterised by recurrent attacks of fever with serositis, synovitis and skin involvement (1). Attacks of FMF last from 1 to 3 days and are typically characterized by colchicine responsiveness (2, 3). The diagnosis of FMF is based on clinical criteria, and the demonstration of *MEFV* mutations confirms the diagnosis in suspected patients (4).

Onset of FMF occurs before age 30 in 98% of patients, and before age 50 in the remaining 2% (5). Onset in a 53-year-old patient has recently been reported (6).

In January 2008, a 67-year-old Caucasian female (Southern Italian ethnicity) was admitted to our Institution for recurrent fever episodes (T >38°C), diffuse arthralgias and myalgias, erythematous skin rash mainly involving lower limbs during fever episodes and thoracic pain over the past 2 years. The duration of fever attacks was 2 to 3 days, and the patient reported more than 10 attacks over the past 12 months.

Her past medical history was relevant for chronic Hepatitis C (HCV) virus infection over the past twenty years. Laboratory analysis showed elevated C-reactive protein 1.98 (vn <0.5) and SAA levels 76 mg/L (vn <10). Antinuclear antibodies and cryoglobulins were negative. Kidney function and urine sediment were normal. HCV viral load performed upon admission was $1.3x10^5$ IU/mL. The patient underwent detailed investigations in order to exclude infectious diseases and underlying malignancies. Due to the short recurrent fever episodes over the past 2 years, although autoimmune disorders related to the HCV infection were initially suspected, the patient's DNA was analysed for mutations in the *MEFV* gene (exons 2, 3, 5, 10) and two low-penetrance P369S /R408Q heterozygous mutations were found in exon 3.

The patient was diagnosed with FMF and treatment with colchicine 1 mg/daily was started. Colchicine promptly brought about a complete resolution of fever episodes and at 12-month follow-up the patient did not show any sign of disease relapse, thus confirming the diagnosis.

More than 60% of FMF patients have onset of the disease before age 10 and 98% of FMF patients have disease onset before the age of 30 (5). One case of onset over age 50 has been recently reported (6). Yamane describes a 63-year-old patient who had an unusual disease onset at the age of 53. That patient carried a heterozygous M694I mutation in *MEFV,* and colchicine responsiveness confirmed the diagnosis of FMF. Patients carrying heterozygous *MEFV* mutations may present clinical symptoms (7). To date, no patients have been reported as having onset of FMF after age 60, as was the case with our patient. The cause of the late onset of FMF is still unclear, although heterozygosity and low-penetrant mutations may play a relevant role. Our report confirms, as Yamane *et al*. suggested, that patients in their fifties and sixties presenting with a medical history relevant for recurrent fever episodes and presenting clinical symptoms characteristic of FMF should be investigated for *MEFV* mutations. Responsiveness to colchicine treatment, as in our patient, may be further confirmation of the diagnosis of FMF.

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Competing interests: none declared.

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