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Reply

Sirs,

We thank Cantarini *et al*. for their report on another instance of mutations in *MEFV* and *TNFRSF1A* occurring together in a single patient. In their case, concerning a 17-year-old female of presumed Italian origins, the presentation was typical of familial Mediterranean fever (FMF) with recurrent attacks of fever, diffuse abdominal and thoracic pain, arthritis of the knee, onset of symptoms before the age of 20 years, and duration of flares less than 5 days. Moreover, the fever attacks were responsive to colchicines but were steroid-resistant. In their observation, no clinical signs could have evoked the diagnosis of tumor necrosis factor [TNF-receptor associated periodic syndrome (TRAPS)], contrary to our case report in which the symptoms responded poorly to colchicines but regressed with steroids (1).

In the patient described by Cantarini *et al*., genetic analysis revealed M694I and V726R mutations in *MEFV* – both classic mutations observed in Italian patients (2) – associated with a low penetrance heterozygous R92Q mutation in *TNFRSF1A*. In fact, their observation really raises the question of the role of R92Q mutation in *TNFRSF1A*: Could it represent a modifying genetic factor for FMF, as suggested for the SAA1 loci (3)? At present it is impossible to answer this question. To better understand the role of the R92Q mutation in *TNFRSF1A* in FMF, this mutation should be analyzed not only in FMF patients with an atypical presentation and a poor response to colchicines, or with only one *MEFV* mutation, but – as suggested by the case reported by Cantarini *et al*. – it should also be screened in typical FMF patients. Until large-scale studies are undertaken, the publication of isolated case reports is welcome.

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