LETTER TO THE EDITOR

The utility of genetic testing in the diagnosis of familial Mediterranean fever

Dear Editor,

In their otherwise excellent review of familial Mediterranean fever (FMF), Lidar and Livneh argue against testing for Mediterranean fever gene (MEFV) mutations both in their diagnostic algorithm and in their subsequent discussion of the case.[1] Although the clinical criteria for FMF are highly sensitive and specific, incorporation of genetic testing will not only confirm the diagnosis but adds valuable information about prognosis as the frequency of secondary amyloidosis varies between genotypes.[2]

Moreover, identifying the MEFV mutations in affected cases is crucial if genetic testing is to be offered to other family members. The FMF phenotype can show considerable intrafamilial variation and siblings of affected cases could be asymptomatic but still develop amyloidosis (type II FMF) which is potentially avoidable if treatment is instigated in a timely manner. Finally, mutation analysis for the common FMF mutations is inexpensive and readily available. For these reasons genetic testing should be an integral part of the diagnostic work-up of suspected cases, even when the clinical picture is obvious.

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1. Lidar M, Livneh A. Familial Mediterranean fever: clinical, molecular and management advancements. Neth J Med 2007;65:318-24.
2. Shohat M, Magal N, Shohat T, et al. Phenotype-genotype correlation in familial Mediterranean fever: evidence for an association between Met694Val and amyloidosis. Eur J Hum Genet 1999;7:287-92.

ANSWER TO LETTER TO THE EDITOR

Dear Editor,

We agree with Dr Tischkowitz's comment regarding the importance of MEFV mutation analysis in assessing the prognosis of a patient with FMF. The presence of the M694V genotype has indeed been associated with a phenotypically more severe disease as well as an increased risk of developing amyloidosis. We also affirm Dr Tischkowitz's contention that identification of this genotype should prompt screening of family members for the presence of asymptomatic amyloidosis (phenotype II). Our difference of opinion, therefore, is merely semantic.[1] While we do not routinely recommend MEFV mutation analysis in the diagnostic work-up of a patient, as the finding of one, two or null mutations will not add or distract from the clinical diagnosis when the patient fulfills the Tel-Hashomer criteria, we do propose genetic testing, *a priori*, in clinically equivocal cases in which identification of two MEFV mutations serves to confirm the diagnosis of FMF. We also believe that mutation analysis has an important role in the prognostic work-up of a clinically diagnosed patient, for the reasons mentioned above.

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1. Lidar M, Livneh A. Familial Mediterranean fever: clinical, molecular and management advancements. Neth J Med 2007;65:318-24.