Reviewer's report

Title: Familial Mediterranean Fever, Inflammation and Nephrotic Syndrome: Fibrillary Glomerulopathy and the M680I Missense Mutation

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Reviewer: fats yalcinkaya

Level of interest: A paper of considerable general medical or scientific interest

Advice on publication: Unable to decide on acceptance or rejection until the authors have responded to the compulsory revisions

This is an interesting case report that describes an FMF patient who developed fibrillary glomerulonephritis. However, some key definitions need to be clarified and should be discussed according to the literature.

Over all, the case provide data on fibrillary glomerulonephritis in an FMF patient but the discussion of the role of certain mutations on the development of amyloidosis should be changed. In addition, glomeruler disease other than amyloidosis that were described in the literature should be included to the text as further detailed to the authors.

Compulsory revisions:

1. The paper describes a patient who has the clinical diagnosis of FMF and who bears only one of the studied mutations. The diagnostic criteria of the patient should be given in detail. So, one can imagine this is an FMF patient who seems to be heterozygote but could have one of the unstudied or unidentified mutation.

2. More than 20 mutations have been discovered in the MEFV gene (that can easily be found in the FMF mutations web site) that should be changed in the text.

3. M694V mutation might cause a risk factor for the development of amyloidosis in Jewish population. However, it was also shown that patients who bear mutations other than M694V can develop amyloidosis (N. Eng J Med 338:993-994,1998; Clin Genet 57:430-434,2000; QJM 93:681-684,2000). In addition, no association between the genotype and amyloidosis could be detected in Turkish patients with FMF (Amyloid 6:301-302,1999; Rheumatol 39:67-72,2000). So, particular mutations themselves do not appear to be sufficient to explain the development of amyloidosis. This should be specified in the abstract and in the text.

4. The nephrologic documentation of the patient is very important and should be added to the text. For example:
   - Did the patient have hematuria, hypertension or renal failure?
   - The levels of BUN, creatinine, total protein, albumin, complements etc. should be given.
5. The observations from different countries indicate that patients with FMF are prone to exhibit a variety of non-amyloid glomerular diseases such as Ig A nephropathy, Ig M nephropathy, rapidly progressive glomerulonephritis etc. (Kidney Int 41:414-419, 1992; NDT 14:21-23, 1999; NDT 14:475-479, 1999). The information about these reports should be given and discussed in the text.

Discretionary revisions:
1. The discussion on the role of pyrine in inflammation can be deleted or shortened

Competing interests:
None declared.