Reviewer's report

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

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Reviewer: Avi Livneh

Level of interest: A paper whose findings are important to those with closely related research interests

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

Discretionary revisions

The authors present an interesting case of an FMF patient with nephrotic syndrome caused by fibrillary glomerulopathy (FGP), instead of amyloidosis, which should be expected in the context of FMF. The paper is badly written. The only thing in favor of it is that the association of FMF and FGP has not been reported previously.

Compulsory revisions

Major points

1. The paper includes superfluous information that is completely unrelated to their finding.
   a. The description of the genetics and pathogenesis of FMF should be omitted, unless the authors try to link it to FGP. In this case, it should be significantly shortened, and the anarchronistic speculations on pyrin as a transcription factor or as an inhibitor of C5a should be avoided.
   b. The large space devoted in this paper to amyloidosis should be reduced to a minimum.

2. In contrast, the paper lacks important information
   a. There is no mention of other non-amyloid kidney diseases associated with FMF, and how FGP is embraced into these entities.
   b. There is no description of the pathogenesis or the etiology of FGP and how these may explain the association with FMF.
   c. Alternatively, if the authors think that the association is fortuitous, which is probably the case, they should admit it and explain.

3. The case report does not provide enough data on the patient's kidney disease.
   a. Has it evolved gradually or abruptly?
   b. How much protein is excreted daily?
   c. What were the other urinary findings?
   d. What about serology findings, pertinent to nephritic syndrome in any context, such as ANA, anti
DNA, C/PANCA, anti GBM antibodies, complement.
What about serology tests relevant to FGP such as protein electrophoresis, Igs levels, Bence Jones protein, cryoglobulins, hepatitis C antibodies?
b. The Discussion should devote some room to the clinical features of FGP and how one may suspect, on clinical grounds, that the patient does not have amyloidosis.

Minor points
1. "RhoRet" should be RoRet (P.4, L.9)
2. To date, more than 40 mutations have been identified (P.4, L11)
3. PCR is part of gene analysis in at least 3 different methods. Indicate which was used (e.g., PCR and restriction enzyme analysis, etc.) (P.5, L11)
4. References 11 and 12 use different methods for FMF gene analysis. Which one was used? (P.5, L12)
5. The patient does not conform with the genetic diagnosis of FMF, which requires 2 mutations, one on each allele (P.5, L12)
6. There is no need for Tables 1 and 2. The information included should be briefly inserted in the text (P5., L11, 15)

Competing interests:

None declared.