Author's response to reviews

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

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PDF covering letter
AUTHORS COMMENTS

Familial Mediterranean Fever, Inflammation and Nephrotic Syndrome: Fibrillary Glomerulopathy and the M680I Missense Mutation.
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Dear Sir/Madam:

We would like to respond to the comments that were kindly made by the reviewers point by point.

Reviewer #1
Avi Livneh

Major points

1. a. The description of the genetics and pathogenesis of FMF was further clarified to include details that present an understanding of inflammation in relation to FMF and the underlying role of inflammation in relation to fibrillary glomerulonephritis. Furthermore, regarding pyrin, (sentence three, paragraph two) of the Introduction was omitted per your recommendation.

b. The content regarding amyloidosis was reduced.

2. a. Non-amyloid kidney diseases associated with FMF have been added to the text. Characteristics distinguishing Fibrillary glomerulopathy from other entities specified are also discussed in more detail.

b. The etiology of fibrillary glomerulonephritis is unknown and is mentioned in the text. The pathogenesis of fibrillary glomerulopathy was expanded in detail and added to the text as recommended.

c. The association of FMF and fibrillary glomerulonephritis (FGN) may be fortuitous, however, there are striking similarities between the pathogenesis of FGN (now classified as one etiology under the entity known as immunotactoid glomerulonephropathy) and other inflammatory diseases with renal involvement
such as cryoglobulinemia, monoclonal gammopathy, as well as amyloidosis (AA variant). We believe we have further clarified this in the text.

3.

a. Details regarding the specific data in this patient were added in the text under Case Report.

b. Clinical features of amyloidosis and fibrillary glomerulopathy were elaborated on, and added to the text as recommended.

Minor Points

1. The correct spelling of RoRet was included.
2. The number of MEFV mutations currently identified has been updated to “40”.
3. Reference number 12 was omitted and reference number 11 (now reference #13) was not omitted, as this is the correct reference for the technique used in our patient.
4. See Minor Point #3
5. Your statement regarding the genetic diagnosis of FMF is correct. The appropriate definition in our patient was inserted in the text. It now reads: “The results demonstrated the presence of an MEFV missense mutation (M680I) on one allele.”
6. We prefer to keep table 1 in the manuscript. Table 2 has been omitted, as recommended. The pertinent results were added to the text.

REVEIWER #2
Fatos Yalcinkaya

Compulsory Revisions:

1. The diagnostic criteria for FMF were further clarified in the text as recommended. Furthermore, our patient meets the definition of clinical FMF using the accepted “Tel-Hashomer criteria”. This was added to the text with the appropriate reference.
2. The number of identified MEFV missense mutations was updated to “40”.
3. The following sentence was added to the Introduction: “However, individuals with mutations other than M694V are known to develop amyloidosis with renal involvement [11].”
4. We agree with your concerns regarding the nephrologic documentation in our patient. We have included the pertinent findings in the text.
5. The observations of non-amyloid renal diseases in this population were discussed in detail and added to the text with appropriate references per your recommendations

Discretionary Revisions:

1. The discussion of Pyrin was shortened.
Thank you very much for your time and consideration of our manuscript for publication in your journal. Please feel free to contact with any questions or concerns.

Sincerely,

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