Reviewer's report

Title: The Familial Non-Syndromic Thoracic Aortic Aneurysms and Dissections maps to Marfan Disease Gene (Fibrillin 1) locus

Version: 2 Date: 14 May 2010

Reviewer: Joerg Schmidtke

Reviewer's report:

Major points

1. The affected members of this family have still not been evaluated according to Ghent criteria. It is not possible to exclude Marfan syndrome. The patients have not been evaluated for dural ectasia, lung symptoms, skin symptoms, and all necessary ophthalmic features. It is incorrect to assume that MFS could be excluded even if dural ectasia was present.

2. The authors state repeatedly that "no nonsynonymous mutation was identified". Synonymous or non-synonymous mutations are terms used for coding DNA, as it refers to codon changes resulting in identical or non-identical amino acids. Their use implies that the authors have found synonymous mutations. These need to be named. It needs to be shown that they are not, e.g., mutations affecting splicing. The same holds true for the intronic mutations. They also need to be named. What is the basis to exclude them from disease causing? Are they known polymorphisms?

3. p. 6: It is said that the daughter of the index case presented with TAAD. However, in the pedigree (fig. 3) the index case has no affected daughter.

4. What is the basis for the statement that skin biopsies of three patients showed "significantly lower FBN1 deposition"? How was it measured? There is no documentation.

5. What is the basis for sequencing MFAP1? It is about 5 cM away from FBN1, well outside the lod score peak.

6. Text, legend to figure 3, and figures 3 and 4 show many inconsistencies with respect to marker nomenclature.

7. Table 1 and Fig 3: Individual 16 shows no positive clinical symptoms in the Table but is marked as affected in the figure.

8. A linguistic revision was not performed. Not even the aforementioned "careers" were corrected to "carriers". The text contains numerous grammatical and other stylistic errors.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Not suitable for publication unless extensively edited
Statistical review: No, the manuscript does not need to be seen by a statistician.