Reviewer's report

Title: Anti-glomerular basement membrane glomerulonephritis and thrombotic microangiopathy in first degree relatives; a case report

Version: 1 Date: 20 May 2012

Reviewer: Kostas Stylianou

Reviewer’s report:

This is an interesting paper regarding two cases, a mother with anti-glomerular basement membrane glomerulonephritis and her daughter who presented with thrombotic microangiopathy 14 years earlier. The authors tried to connect the two cases by seeking a common genetic defect, focusing on the complement proteins. The daughter was found to be heterozygous carrier of the CFI G261D mutation, yet the mother was not. They also found a common polymorphism of the complement factor H which is associated with increase susceptibility for aHUS but not for anti-GBMGN. The manuscript is well written but there are some major concerns.

1) The authors state that the G261D mutation has no functional effect on complement regulation. A citation is needed for this statement. I suspect they mean that the mutation does not affect the plasma CFI levels as happened with the two cases with CFI mutation reported by Servais et al (ref 9). Did they measure CFI levels?

2) Servais et al (9) reported on two CFI mutations (A222G and G243D). I wonder whether the G243D mutation is the same with the present G261D mutation.

3) It would be interesting to look at other family members (e.g. the father) for haematuria or history of kidney disease. Since the mother was not a carrier of the mutation, the father should at least be heterozygous. Therefore, if the father has some kind of kidney pathology (and especially C3 glomerulopathy) we could come up to the conclusion that the G261D mutation does have some impact. If he’s not affected, then it is indeed possible that the mutation has no functional effect.

4) The authors state the daughter’s renal biopsy did not show any deposits but only thrombotic microangiopathy lesions. Lack of C3 deposits makes complement dysregulation a less likely explanation for the pathogenesis of aHUS; even more so, if the G261D mutation has no functional effect. Please comment.

Minor Essential Revisions: Please improve quality and size of Figure 1.

In conclusion, although the concept is interesting, the pathogenetic linkage between the two pathologies and the G261D mutation or the CFH polymorphism cannot be safely supported.
Level of interest: An article of limited interest

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

No competing interests exist