Reviewer's report

Title: A Neonatal Presentation Of Factor V Deficiency: A Case Report

Version: 2 Date: 20 September 2006

Reviewer: Paula Bolton-Maggs

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General
Thank you for asking me to review this manuscript. Case reports should only be published if there is some important message, or if a case is very rare. This report is of a very rare disorder where there is a paucity of information on the practical management. There is therefore benefit in publication to add to the overall data on treatment. This report can be improved in a number of ways (the English is poor in places and would benefit from some editing – there are several places where sentences could be shortened and improved). In particular it would be very useful for the authors to make a table summarizing all the cases reported in the literature comparing their clinical manifestations and complications (there are few) and perhaps even to list the other rare disorders which are in the differential diagnosis with their frequency including the important message that in FXIII deficiency the coagulation tests are normal.

Specific comments:

1. Rather than focusing on the nipple bleeding, it might be better to indicate that any unusual bleeding in an infant should prompt a coagulation screen, and particularly where there is consanguinity. The differential diagnosis of nipple bleeding must be discussed. The picture of the nipple bleeding is unnecessary.

2. A key message is for neonatologists to be alert to the risk of a severe (homozygous) rare bleeding disorder in children of consanguineous parents, so the conclusion should be revised to reflect this rather than focusing on FV deficiency alone.

3. In the ‘background’ section I do not understand what the authors mean where a comparison is made between heterozygous FV deficiency and haemophilia. This is an odd statement as heterozygous FV deficiency is not associated with bleeding symptoms (definition of a recessive disorder). The sentence should be deleted.

4. Factor V is a pivotal factor in the coagulation pathway having anticoagulant functions as well as procoagulant activity.

5. I do not believe it correct to use the word ‘heralded’ for the ICH. Severe FV deficiency is a recognized cause of ICH and need not be ‘heralded’ by anything, and there is no link between the two in terms of cause and effect, which for me the word ‘herald’ implies. Head ultrasound may not be sufficient to rule out ICH but was a reasonable investigation in the absence of symptoms.

6. The parents’ results are given for FV but there is no description of the method, and more importantly no record of the normal range for this laboratory. Presumably the siblings have been screened? The mutation analysis has been done, but there is no acknowledgement of the laboratory that performed this. Please add.

7. The child had several treatments with FFP. Was this virally inactivated (I presume yes, because that is national policy)? If so, this should be stated. What level of FV was considered to be haemostatic, and what level of FV was achieved, particularly once the ICH was diagnosed? This information is important as the authors have a significant paragraph about this in the conclusion which is not justified in the absence of any data in this report. Platelet transfusion represents an additional blood product exposure. Was it necessary? What was the evidence that rVIIa was also required? A logical approach would be to check the FV response to FFP to ensure adequate dose rather than unlicensed use of rVIIa. The subsequent discussion about the planned regimen should include information about the half life of FV. The data concerning a trough level being unrecordable is worrying. The interval was presumably 48 h but this is not explicit and should be clarified. What steps did the authors take to ensure there was no evidence of an inhibitor?

8. In the conclusions you state that early recognition of severe FV deficiency can enable prevention of ICH.
This child was not put on prophylaxis, which is particularly difficult in this disorder. Is that what the authors are advocating for a complication which occurs in 10% of patients? This estimate might be wrong as there is likely to be biased reporting of patients with more severe bleeding manifestations.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

Discretionary Revisions (which the author can choose to ignore)