Recombinant activated factor VIIa in case of pregnancy with acute hepatic failure and massive blood loss

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All the points brought out in the LETTER TO THE EDITOR by Sqn Ldr VK Jha, Col G Shenoy and Maj PJ Borpujari pertaining to the article 'Recombinant activated factor VIIa in case of pregnancy with acute hepatic failure and massive blood loss. MJAFI 2012;68:96', published in the January 2012 issue of MJAFI had not been responded to owing to some glitch in the website. Only the first three points were forwarded to the corresponding author by the journal. The error was detected after publication of the issue.

The complete reply to the LETTER TO THE EDITOR on 'Recombinant activated factor VIIa in case of pregnancy with acute hepatic failure and massive blood loss. MJAFI 2011;67:390–393' by Col Shivinder Singh, Associate Professor, Department of Anaesthesiology, AFMC, Pune – 40, is published herewith along with the earlier published version of the LETTER TO THE EDITOR.

LETTER TO THE EDITOR MJAFI 2012;68:96

Dear Editor,

The case report 'Recombinant activated factor VIIa in case of pregnancy with acute hepatic failure and massive blood loss' published in MJAFI in October 2011 (MJAFI 2011;67:390–393) was interesting and we would like clarification on some points and offer these comments.

1. Recombinant activated factor VIIa (rFVIIa) is thought to act locally at site of tissue injury and vascular wall disruption by binding to exposed tissue factor, generating small amounts of thrombin that are sufficient to activate platelets.¹
2. The activated platelet surface can then form a template on which rFVIIa directly or indirectly mediates further activation of coagulation ultimately generating much more thrombin and leading to the conversion of fibrinogen to fibrin.²
3. Therefore adequate platelet count is must before administering rFVIIa. Here platelet count was just 40,000/mm³.
4. Anasarca in a case of acute hepatic failure cannot be explained. Serum albumin level and renal parameters are not given in this case.
5. Acute hepatic failure in ultrasonography should reveal shrunken liver, not a normal liver span.
6. Aetiology of acute hepatic failure not clearly mentioned.
7. Was it HELLP (Haemolysis Elevated Liver Low Platelet)? The HELLP syndrome can explain all the clinical features of the index patient and the only definitive treatment for HELLP is delivery. Most laboratory values normalise in 48 hours. For patients with ongoing or newly developing postpartum symptoms of HELLP, modalities as antithrombotic agents, plasmapheresis, and dialysis may be employed. Disseminated intravenous coagulopathy may be the only manifestation in HELLP as in this case with raised bilirubin, lactate dehydrogenase, fibrin degradation products, and D-dimer.

8. Was this patient not an ideal candidate for liver transplantation?
9. Many case reports and case series have examined the use of rFVIIa in patients with excessive or life-threatening blood loss occurring in array of clinical settings.³ However, no randomised controlled clinical have been completed, which is not surprising, given the difficulty of performing meaningful studies in such heterogeneous situations. Many reports claim that the use of rFVIIa resulted in rapid reduction of blood loss or a decrease in transfusion requirements after other therapeutic measures have failed. Although many of these reports appear to be compelling, it is difficult to assess the usefulness of rFVIIa properly since publication bias in case reports and series is likely.

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REPLY

The authors are grateful for the comments. Few clarifications are as under. The patient had a platelet count of 40,000 prior to six units of fresh frozen plasma, five packed cells, and one unit of single donor platelets being transfused as has been mentioned in the text of the article. The patient was extremely unstable and after confirming the absence of acidosis or hypothermia, rFVIIa was administered for the first time immediately after the single donor platelets were infused as she was thrombocytopenic. One single donor platelet pack is expected to increase the platelet count by 30,000 to 35,000 therefore the expected platelet count prior to the administration of rFVIIa was expected to be in the range of around 70,000 which was considered adequate. Platelet count and coagulation profile was not sent immediately prior to administration of rFVIIa and therefore in the table it seems that counts prior to its administration were 40,000.

The aim of highlighting the case was to bring out the role of rFVIIa in massive blood loss and thus the focus was directed at this. The case report was crossing the word limits and hence some of the details were removed during the review process.

The patient was extensively worked up for the aetiology of the hepatic failure, viral markers were negative, and workup for Wilson's disease was negative too. A hepatic biopsy was advised once the patient improved for confirmation of the diagnosis; however, the patient did not give consent for the same. From the clinical setting and the course in hospital it was considered that acute fatty liver of pregnancy was the cause of the fulminant hepatic failure. Though, a subset of these patients do have the HELLP syndrome it is associated with pre-eclampsia which was absent in our patient.

Anasarca may be present in patients with acute fatty liver of pregnancy due to the endothelial activation and capillary leakage. This patient in the case study also had hypoproteinaemia (total proteins 5.5 g/dL, albumin 2.9 g/dL, globulin 2.6 g/dL. The urea and creatinine were 45 mg/dL and 1 mg/dL and remained normal throughout). Various liver imaging techniques have been used to confirm the diagnosis; however, none are particularly reliable with sonography showing poor sensitivity.¹ Hepatic dysfunction usually resolves in up to a week time (not 48 hours) and these patients require intensive care support during this time as seen in our patient.¹

This patient obviously did not meet the criterion for liver transplant (LT) and was therefore never considered at any time for this modality of treatment. Potential candidates for LT are children and adults who, in the absence of contraindications, suffer from severe, irreversible liver disease for which alternative medical or surgical treatments have been exhausted or are unavailable.² The fact that this patient did not require a LT is amply borne out by the fact that she made a complete recovery.

We totally agree with the comment that 'although many of these reports appear to be compelling, it is difficult to assess the usefulness of rFVIIa properly since publication bias in case reports and series is likely'. However, there are now a number of controlled studies especially in patients of massive blood loss following trauma where the usefulness of rFVIIa has been clearly brought out.³⁻⁷

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