Non Invasive Management of Refractory Hemorrhage after Renal Surgery with Factor VIIa: Report of 3 Cases

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INTRODUCTION

Recombinant activated factor VII (rFVIIa) is a vitamin K-dependent glycoprotein consisting of 406 amino acid residues (molecular weight 50 K Dalton). It is structurally similar to human plasma-derived factor VIIa. Over the last few years, rFVIIa has been used “off-label” in patients with uncontrolled bleeding due to occult hemostatic abnormality caused by trauma and/or massive blood loss, thrombocytopenia, platelet dysfunction or liver dysfunction and many other situations characterized by critical bleeding. We present our experience of the successful use of rFVIIa to treat life threatening hemorrhage in 3 patients who had refractory hemorrhage following surgical procedures on the kidney.

CASE REPORT

Three previously healthy males, without pre-existing coagulopathy, presented with staghorn calculus (n = 2) and a large renal pelvic calculus (n = 1). Two patients were subjected to per-
cutaneous nephrolithotomy (PCNL) and one had open pyelolithotomy. In one case during PCNL, there was pneumothorax and retroperitoneal bleeding up to day 5 after the procedure. In the other case of PCNL, uncontrollable hemorrhage occurred on day 13 following removal of PCNL tube. Profuse bleeding started on day 5 in the patient with pyelolithotomy. All 3 patients were initially managed by blood transfusions. When hemorrhage persisted despite blood transfusions and the patients became hemodynamically unstable, rFVIIa was given at a dose of 60-90 µg/kg. The clinical characteristics and treatment response of all the 3 cases are shown in Table 1. Blood products usage and change in coagulation profile before and 24 hours after administration of rFVIIa is summarized in Table 2.

**DISCUSSION**

The Tissue Factor is exposed and forms a complex with rFVIIa following injury to the vessel wall. This complex activates factor X which leads to conversion of prothrombin to thrombin, and activation of platelets, greatly enhanced thrombin generation, and activation of thrombin activated fibrinolysis inhibitor (TAFI). rFVIIa is used to treat patients with hemophilia A and B, also for the treatment of life threatening hemorrhage in the setting of coagulopathy disorders, blunt and penetrating trauma and surgical bleeding. rFVIIa, can minimize blood loss and need for blood transfusion prior to retroperitoneal prostatectomy or in patients on platelet aggregation inhibitors, prior to renal transplantation. As shown on Table 1, our study demonstrated the effectiveness of intravenous (IV) administration of rFVIIa in late onset bleeding after renal surgery. In all 3 cases, hemorrhage subsided after rFVIIa administration. It is possible for bleeding to occur again in a patient that has shown response to initial administration of rFVIIa. From our third patient, it would appear that future responses to IV administration of rFVIIa can be expected with repeated dosing. Table 2 shows the possible mechanism of action of IV rFVIIa usage. In all 3 patients the hemoglobin remained stable and there was an improvement in prothrombin time (PT), partial thromboplastin time (PTT) and international normalized ratio (INR) after IV rFVIIa administration. Angiography with embolization of any bleeding vessels is the standard method of dealing with significant hemorrhage from the kidney after renal surgery. However, in some cases, the bleeding vessels may be difficult to identify. What is more, when bleeding is from other sources like lumbar vessels and etc., as an adjuvant prior to embolization, IV administration of rFVIIa is worth a trial. The advantage of IV rFVIIa administration over angiography and embolism is that, it does not require any expertise to administer and it is easier and quicker to use than angi-embolization. Furthermore, in patients in extremis, IV rFVIIa can be used easily. None of our patients experienced any further episodes of bleeding after a mean follow up of about 6 months. Similarly, there was no loss of renal function from the affected kidneys. When there is any clinical or laboratory signs of presence of thrombosis, the rFVIIa dosage should be reduced or stopped, depending on the patient’s symptoms.

**CONCLUSION**

This study revealed that administration of rFVIIa is a promising treatment option for patients undergoing renal surgery.

### Table 1. Clinical and imaging features of the series.

<table>
<thead>
<tr>
<th>Case</th>
<th>Age, years/sex</th>
<th>Primary Diagnosis</th>
<th>Coagulopathy</th>
<th>Dosage (µg/kg)</th>
<th>Clinical Efficacy*</th>
<th>Complications</th>
<th>Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>43/Male</td>
<td>Partial right stage horn stone</td>
<td>No</td>
<td>90</td>
<td>Yes</td>
<td>None</td>
<td>No</td>
</tr>
<tr>
<td>2</td>
<td>39/Male</td>
<td>Right renal pelvic stone</td>
<td>No</td>
<td>60</td>
<td>Yes</td>
<td>None</td>
<td>No</td>
</tr>
<tr>
<td>3</td>
<td>51/Male</td>
<td>Left lower calyceal stone</td>
<td>No</td>
<td>60*</td>
<td>Yes</td>
<td>None</td>
<td>No</td>
</tr>
</tbody>
</table>

*Defined as marked reduction or cessation of post-operative hemorrhage.

**Key:** rFVIIa, recombinant activated factor VII.

a Multiple doses administered.
complicated with life-threatening hemorrhage. It seems to be both effective and safe. However, further research is required to extend the approval of this product in urologic procedures while assessing potential complications.

CONFLICT OF INTEREST
None declared.

REFERENCES