

# Recombinant Factor VIIa after surgery for uterine fibroids complicated by pregnancy of unknown location

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## Abstract

The role of Recombinant Factor VIIa (rFVIIa) in arresting intractable bleeding has been reviewed extensively in literature. However its use in gynecology and obstetrics still remains limited. This case highlights, that judicious use of rFVIIa may reduce morbidity and save diminishing blood pools.

## CASE REPORT

Mrs S.K. was on the waiting list for a total abdominal hysterectomy for massive uterine fibroids (36 weeks gestation size) causing menorrhagia and iron deficiency anaemia. She had been unable to conceive because of the uterine fibroids despite an attempted open myomectomy 5 years back.

A month after receiving her first dose of injection for pituitary down-regulation, she presented to the accident and emergency department with abdominal pain and a positive pregnancy test.

Initially a diagnosis of an early pregnancy was made due to doubling of serum  $\beta$  HCG levels in 48 hours (210 iu/ml to 564 iu/ml). She presented 10 days later with acute abdominal pain not responding to opiates, falling haemoglobin levels, episodes of fainting and very high levels of serum  $\beta$  HCG (10,800 iu/ml) with no ultrasonographic evidence of an intrauterine pregnancy.

A laparotomy was decided based on a strong suspicion of an ectopic pregnancy.

A total abdominal hysterectomy with removal of the massive right broad ligament fibroid was undertaken with some difficulty. The right fallopian tube was enlarged and engorged. The left adnexae was normal and was preserved.

A total blood loss of 5 litres was measured at the primary operation, requiring 8 units of blood transfusion intraoperatively. A 28 French gauge Robinsons tube drain

was inserted into the pelvis and a 10 French gauge high vacuum wound drain was placed in the sub rectus sheath. The patient was transferred to intensive care unit (ITU) for postoperative monitoring and support.

Later that night, observation of the drains showed continued intra-abdominal bleeding. The abdomen was explored as an emergency. Generalised ooze from the pelvic sidewall and the pouch of Douglas was seen with no specific site of bleeding. No definitive surgical procedure could be made. The coagulation parameters were checked which revealed a prolonged APTT and PT along with reduced platelet count. The pelvis was packed and the patient returned to ITU. Conventional measures to correct her deranged clotting parameters included blood products and tranexamic acid. Even after transfusion with 75 units of blood, 40 units of cryoprecipitate, 25 units of fresh frozen plasma and 20 units of platelets, she still continued to bleed.

In view of the deteriorating condition of the woman, the intensivists and haematologists decided to infuse Recombinant factor VIIa (rFVIIa) before proceeding for the third laparotomy. There was a dramatic improvement in the operating conditions. It was possible to ligate the internal iliac arteries on both sides and complete haemostasis was achieved with considerable ease. She remained in the ITU for 48 hours after which she was returned to the general ward from where she was discharged 10 days later with full recovery.

## DISCUSSION

The two issues that get highlighted from this case are the

difficulties in management that can be encountered when pregnancies occur in the presence of fibroids and the important use of rFVIIa to arrest intractable bleeding during pelvic surgery.

Pregnancy of unknown location (PUL) continues to pose a significant management dilemma. Use of ultrasound, levels of serum HCG and clinical symptoms help in formulating a plan of management. In our case it was difficult to locate the pregnancy due to the severe distortion of the endometrial cavity with the fibroid. The histology report confirmed an intrauterine pregnancy which was lodged at the base of a polyp in the cornual region of the uterus. The decision to perform a laparotomy was based on a diagnosis of PUL, the deteriorating clinical condition and the presence of massive uterine fibroids extending up to the xiphisternum.

Surgery was technically very difficult. The generalised ooze at the time of laparotomies could not be arrested until the infusion of rFVIIa in this case.

Recombinant FVIIa is a genetically engineered product that was first introduced in 1988 for the treatment of patients with haemophilia A and B with high inhibitory antibody titres to factors VIII and IX (1). The mode of action of activated recombinant factor VII is not completely clear. It is thought to form a complex by binding tissue factor at the site of vascular damage and this activates the intracellular mechanism of coagulation within the platelets (2)

Several case reports have been published which demonstrate a beneficial role of rFVIIa as an adjunctive haemostatic agent in cases of severe intractable bleeding of any cause, where other conventional measures to stop the bleeding have failed (3,4). There is no controversy in the use of rFVIIa in cardiac surgery or surgery in patients with haemophilia. Consideration needs to be given for its use to arrest intractable bleeding during gynaecological surgery,

especially in exceptional situations including Jehovah's Witness with life threatening or massive bleeding. Interestingly there has been a study which showed that last-ditch rFVIIa therapy in patients resistant to conventional treatment did not rescue these patients or significantly alter outcomes (5). Although rFVIIa is expensive, it would be appear to be cost effective when compared with the combined cost of large amounts of blood and blood products. Moreover, the risks of transfusion e.g. incompatibility, infection etc cannot be ignored. The earlier use of rFVIIa may also help to conserve the already diminishing blood pool and stores. The main side effect associated with its use is thrombosis and thrombosis related complications. Studies have shown less than 1% incidence of thrombosis and related complications with the use of Factor VII (6).

In conclusion, the judicious use of rFVIIa may help to reduce the morbidity in patients with intractable bleeding at the time of pelvic surgery.

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