Bleeding from endometrial and vaginal malignant tumors treated with activated recombinant factor VII

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Summary

The authors report two cases of successful employment of human recombinant activated factor VII in gynecological oncological patients (endometrial cancer and vaginal sarcoma) without pre-existing coagulopathy. They conclude that recombinant factor VIIa may be an important and effective drug in severe bleeding in gynecological oncology.

Key words: Recombinant factor VIIa; Coagulation; Hemorrhage; Cancer of endometrium; Vaginal sarcoma.

Introduction

The authors report two cases of successful employment of human activated recombinant factor VII (FVIIa) NovoSeven®, Novo Nordisk, in gynecological oncology. To the best of their knowledge, these are the first cases ever reported on such usage of recombinant FVIIa in gynecology in patients without pre-existing coagulation factor deficiency.

Case Report

Case 1

A 67-year-old female was admitted to the Division of Gynecological Surgery, with severe bleeding from the genital organs on April 7, 2001. She had a history of endometrial adenocarcinoma confirmed by hysteroscopy in 1997. There was also a history of severe cardiac insufficiency (IV° NYHA), hypertension and NIDDM. She had a large umbilical hernia and was obese (96kg/161cm - BMI=37). In 1997, following the analysis of surgical risks and benefits, a decision not to operate was reached by the attending team and the patient herself. Complete irradiation therapy was followed by hormonal treatment. The patient had no personal or family history suggestive of a bleeding disorder. The gynecological examination revealed severe bleeding from the enlarged, fixed uterus. The laboratory findings showed RBC of 4.41T/l; HGB of 8.5mmol/l; HCT of 0.40l/l and PLT of 149G/l.

Etamsylate (0.5g i.v. per 8 hours), tranexamic acid (0.5g i.v per 8 hours) and aminocapronic acid (5g p.o. per 8 hours) were administered and also a vaginal tampon was inserted. The bleeding slowly decreased. On the sixth day of treatment her laboratory values were RBC - 3.14T/l; HGB - 5.6mmol/l; HCT - 0.28l/l and PLT - 119G/l) and one unit of blood was transfused.

Suddenly, on the tenth day of hospitalization, the bleeding increased again and was heavier than at admission. Since the conventional therapy had failed and the bleeding was life-threatening, the authors decided after to administer human activated recombinant factor VII (FVIIa) having obtained the informed consent from the patient. She received NovoSeven® at a dose of 21 μg/kg iv. The first indication of NovoSeven® efficacy was observed after 20 minutes and during the first two hours her bleeding continuously decreased. After 24 hours another dose of factor VIIa in the same amount was administered. Within 20 minutes the bleeding subsided. Her recovery was fast and lasting. She was discharged on the 12th day after admission, in good condition and without bleeding.

Case 2

A 42-year-old female was admitted to our department with severe bleeding from the genital organs on May 4, 2001. She had a history of vaginal sarcoma. In 1997, tumor excision and radiotherapy had been performed. After three years, a recurrent tumor was noted. Chemotherapy according to the CyVADic protocol was employed. Subsequently, the vaginal tumor was excised along with a metastatic lesion situated in the mandibular region. Except for that, her past history did not reveal anything specific. She had no personal or family history suggestive of a bleeding disorder.

On admission she reported a six-hour history of severe bleeding from the vagina. Her weight was 71kg. The gynecological examination revealed a tender, necrotic and bleeding tumor in the vagina. The laboratory findings showed RBC of3.08T/l; HGB of 6.7mmol/l; HCT of 0.31l/l and PLT of 181G/l. Etamsylate (0.5g I.V. per 12 hours) and tranexamic acid (0.5g I.V per 6 hours) were administered and three units of blood were transfused. During the subsequent four hours the bleeding was constant and heavy enough to be life-threatening. Having obtained the informed consent of the patient, the authors decided to administer human recombinant FVIIa at a dose of 10 μg/kg I.V. The first indication of its effectiveness was noted after 20 minutes and over the subsequent 30 minutes the bleeding was controlled. In consequence, the authors decided against giving the patient the second dose of FVIIa. She was discharged on the fourth day in good condition and without bleeding.

Discussion

The cases reported here are quite unique with respect to standard employment of human activated recombinant factor VII, but these situations were dramatic and life-threatening. The effectiveness of FVIIa was spectacular, prompt and lasting. The majority of reports on the use of

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FVIIa describe patients with coagulation factor deficiency – VIII or IX, especially with inhibitors. [1-6].

Reports have also been published on employing FVIIa in patients without pre-existing coagulopathy in neurosurgery, traumatology, gastrological – and cardiac surgery [7, 8, 9]

We can not exclude the possibility that the previously administered conventional therapy contributed to the cessation of bleeding, but after the administration of FVIIa the effects were prompt and lasting [8].

We hypothesize that in our patients the successfulness of FVIIa may be associated with a supra-physiological level of factor VIIa after its exogenous administration [8]. It can accelerate or even facilitate hemostasis in large bleeding areas in tissues after malignant transformation.

Conclusion

Recombinant factor VIIa may be an important and effective drug in severe bleeding in gynecological oncology, especially when conventional therapy fails.

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