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Recombinant activated factor VII administration in a patient with congenital lack of factor VII undergoing laparoscopic hysterectomy: A case report

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ABSTRACT

INTRODUCTION AND IMPORTANCE: Case report of patient with congenital lack of factor VII, suffering from recurrent hematomas and massive menstrual bleedings resulting in severe anemia and multiple hospitalization.
CASE PRESENTATION: Patient was diagnosed with endometrial hyperplasia and not responding to hormonal treatment and substitution with recombinant factor VII was not effective to reduce the bleedings. This case describes successful laparoscopic technique of using bipolar coagulation and non-absorbable clips.
CLINICAL DISCUSSION: We describe premedication and post-surgical management – which we had to modify from this found in very scarce literature. Despite previous vaginal deliveries without any complications during the puerperium, 20 days after the surgery patient presented with intraperitoneal bleeding after stopping rFVIIa therapy. It was treated medically without the need for re-laparoscopy.
CONCLUSION: Laparoscopic surgery is possible in patients with lack and deficiency of FVIIa, but they need close post-operative surveillance and prolonged supplementation with recombinant FVIIa.

1. Introduction

Congenital factor VII deficiency is rare hematological disorder leading both to serious deterioration of quality of life- and life-threatening medical complications. Due to rarity of this disease most publications describe single case experiences and only few larger studies can be found [1,2]. During our cross-reference search we have found only 68 publications from years 1965 to 2018 dedicated to women's health mostly concerning treatment of perinatal hemorrhage. Recent review of 94 deliveries have shown serious postpartum bleeding in 10–13% of cases, comparing to 3.9% in general population [3]. From known data menorrhagia is leading symptom occurring in approximately 50% female patients with FVII deficiency. There is still no consensus concerning treatment of abnormal vaginal bleeding in those patients as all of them bear dreadful risks – there are reports of serious thrombotic events in patients during replacement therapy with prothrombin complex concentrates or plasma derived FVII concentrates [4] or after surgical procedures [1]. Despite high frequency of gynecological manifestations to our best knowledge only three cases of hysterectomy were published up to date [4–6]. When analyzing indications for hysterectomy in that group of women non-hematological reasons for excessive bleeding such as uterine fibroids, endometrial hyperplasia and polyps, and endometriosis have to be considered [7].

2. Case report

The patient was a 37-year-old woman (gravida 2, para 2, 166 cm, 66 kg). She had no significant past medical history and had two uneventful vaginal deliveries conveyed in prophylaxis with recombinant activated factor VIIa (rFVIIa) administration. Her family history was unremarkable. She had had regular hematological examinations and her FVII activity was constantly below 1%. Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request. This report has been prepared according to The SCARE 2020 Guideline [8].

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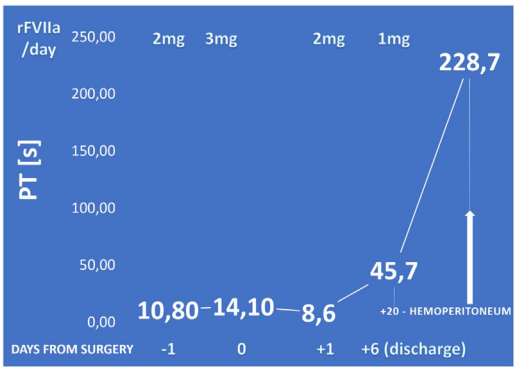

Fig. 1. The mode of pre-surgical prophylaxis with rFVIIa according to PT.

Since menarche she was experiencing excessive menstrual bleeding treated sub-effectively with rFVIIa, tranexamic acid, oral contraceptive and progesterone replacing therapy. In past years she was frequently hospitalized due to severe anemia (with hemoglobin drops to 7,2 g/dl) leading to multiple blood, plasma, and thrombocyte transfusions. For years, her cytology was normal and endometrial biopsy was normal. Two months prior admission she suffered massive menstrual bleeding needing surgical curettage of uterus – she was diagnosed with simple endometrial hyperplasia.

We discussed treatment options with the patient and planned to perform the simple laparoscopic hysterectomy and bilateral salpingectomy. We agreed to leave the ovaries intact as no pathology was detected during ultrasound and computed tomography screening. Leaving the ovaries and maintaining their hormonal function reduces patient's life-long risk of osteoporosis and cardiovascular diseases.

During presurgical preparation patient were consulted by anesthesiologist and hematologist. Her blood tests have shown anemia, which was not responding to previously implemented iron supplementation with hemoglobin level 9.5 g/dl and red blood count 3.64 10*6/uL. Despite weekly administered rFVIIa (Novoseven 1 mg i.v.) the prothrombin time (PT) was 14.6 s (reference range, 9.0–12.5 s) the INR was 1.36 and activated partial thromboplastin time (aPTT) was 31.9 s (reference range, 25.0–35.0 s). Other blood test results, including those for liver, thyroid and renal function were within normal range. Patient was tested negative for hepatitis B and C and HIV virus. Despite increasing dosage of rFVIIa to 1 mg daily and adding tranexamic acid at dose of 3 g daily patient was still suffering from vaginal spotting and spontaneous bleedings. After literature search and reconsultation with hematologist we decided to transfuse 3 units of concentrated red blood cells (problematic due to patient blood phenotype 0 Rh+ D+ Cw- C+ c+ E- e+ K-) and 3 units of fresh frozen plasma. Before the surgery we managed to diminish level of vaginal bleeding and achieve hemoglobin level of 11.5 g/dl, RBC 4.29 10*6/uL, PT 14.1 s, INR 0.9, aPTT 26.9 s.

While planning the surgery we were very concerned about the ability to uphold hemostasis. First, we discarded laparotomy as very invasive method resulting in risk of additional bleeding. Patient was lean and has not had previous surgery, so she was suitable for laparoscopy. Despite much experience in bipolar coagulation and harmonic knife we were not certain about efficiency of vessel sealing devices in this patient. We decided to use combined technique of bipolar coagulation with bipolar device (BiClamp Lap Forceps, Erbe, Tübingen, Germany) and hemostatic, non-absorbable clips (CLICK'AV PLUS, Grena, Bendford, UK). Patient received last dosage of rFVIIa 30 min before surgery, the mode of subsequent prophylaxis is described in Fig. 1. The surgery was done by two experienced operators, with experience of >100 laparoscopic hysterectomies/year each, it took 100 min and was uncomplicated.

Table 1
Selected laboratory results in perioperative period.

DAY	Hemoglobin	Platelets [*10^3]	PT
−1	11,5 mg%	299	10,8 s
Surgery	10,4 mg%	253	14,1 s
1	9,8 mg%	296	8,6 s
Discharge	10,9 mg%	457	45,7 s

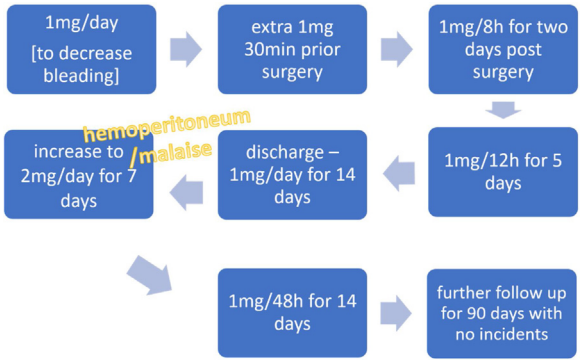

Fig. 2. Mode of treatment with rFVIIa.

The only unusual finding was massive sub-peritoneal hematomas visible on the abdominal surface (Video 1). Each step of surgical preparation consisted of bipolar coagulation, clipping, and then cutting the tissues. Uterine arteries and each visible vessel were secured with double clips. Vaginal cuff was sealed with double layer laparoscopic suture (STRATAFIX^{TM} Symmetric PDS^{TM} Plus Knotless Tissue Control Device – Dyed, Ethicon, USA). Blood loss was minimal, and drainage was removed the next day with total blood loss below 200 mL. Her postoperative blood tests were within normal range (Table 1) and patient was discharged home on day 6 with recommendation of iron supplementation and rFVIIa replacement therapy at dose of 1 mg for 7 days. Abdominal stiches were removed on day 12 post operatively – patient reported no vaginal bleeding and transvaginal ultrasound revealed no free fluid in minor pelvis. Post-operative pathological report was consistent with previous findings, describing endometrial polyps, simple endometrial hyperplasia and adenomyosis and hematomas in uterine muscle.

Surprisingly, patient came back to us on day 20, complaining with abdominal pain and malaise. During ultrasound we revealed free fluid reservoir in pelvis and hemoglobin drop to 8.5 mg%. Replacement therapy was reintroduced at dose of 2 mg of rFVIIa daily for 5 days. There was no need for additional blood transfusion nor surgical intervention. For the next 2 weeks 1 mg of rVIIa was given every 48 h with excellent effect. 90 days post-surgery patient is in good general condition, returned to sexual and social life and remains without any signs of internal bleeding, fatigue nor pain. The follow up was initially carried out weekly in hospital out-patient clinic for first 6 weeks, and later continued in local out-patient setting with bimonthly frequency. Currently patient came back to general screening in hers gynecological clinic. The mode of treatment with rFVIIa is described in Fig. 2.

3. Discussion

Gynecological problems of patients with congenital FVIIa deficiency is usually considered in connection to pregnancy and delivery [3,7,9]. The reports of surgical treatment in those patients are extremely scarce [2,4], and point out high complication rate. Our report describes new mode of treatment of concomitant intensive replacement therapy as proposed earlier [5] with modern approach to combined surgical techniques.

4. Conclusion

Laparoscopic surgery is safe option even for patients with severe FVIIa deficiency provided proper preparation with rFVIIa, surgery by experienced surgeon with access to modern instrumentation, however, prolonged rFVIIa replacement therapy is required to maintain hemostasis and prevent late postoperative bleeding.

Declaration of Competing Interest

Nothing to declare.

Funding

Nothing to declare; the treatment was covered by public health insurance.

Ethical approval

This case report is an exemption from the ethics committee approval – as it merely describes results of treatment of single patient, suffering from rare disease. The patient was fully informed about plans to publish the case and gave full consent to prepare manuscript for professional use only.

Consent

The consent has been given and we omitted any identifying details. Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Author's contribution

Filip Dabrowski (1) the conception and design of the study, acquisition of data, analysis and interpretation of data, (2) drafting the article or revising it critically for important intellectual content, (3) final approval of the version to be submitted.

Nikodem Sadlik (1).

Krzysztof Nowosielski (1), (2), (3).

Registration of research studies

Not applicable.

Guarantor

Filip Dabrowski, Krzysztof Nowosielski.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at https://doi.org/10.1016/j.ijscr.2020.12.093.

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