Kidney Stone Surgery in a Patient with Factor VII Deficiency: Case Report

Faktör VII Eksikliği Olan Bir Hastada Böbrek Taşı Cerrahisi

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ABSTRACT Factor VII (FVII) deficiency is a rare hereditary bleeding disorder. Recently, the use of rFVIIa as a replacement therapy in the management of bleeding in congenital factor FVII deficiency has been reported. In this article, we present the first case with congenital FVII deficiency that has been operated for kidney stones in which rFVIIa was used as replacement therapy to prevent intra and postoperative bleeding. The operation involved a high risk for operative bleeding complication as a result of moderate FVII deficiency. The operation was performed by administering a dose of 2.4 mg 30 minutes before and 2 hours after the operation. Thereafter, a bolus infusion of rFVIIa 1.2 mg (19 μg/ kg) was administered every 4 hours, then 1.2 mg every 8 hours on the third day and the same dosage every 12 hours on the fourth and fifth days after the operation. No bleeding or thrombotic complication was observed.

Key Words: Recombinant FVIIa; kidney calculi; hemophilia A

ÖZET Fakör VII (FVII) eksikliği nadir görülen herediter bir kan hastalığıdır. Son yıllarda kalıtsal FVII eksikliğine bağlı kanamalarda rFVIIa kullanımı bildirilmektedir. Bu makalede, literatürde kalıtsal FVII eksikliği bulunan, böbrek taşı nedeni ile opere edilen ve operasyon sırasında ve sonrasında oluşabilecek kanamaları azaltmak için rFVIIa kullanılan bir olgu sunulmaktadır. Olguda, orta düzeydeki faktör eksikliği nedeni ile yüksek riskli kanama olasılığı bulunuyordu. Operasyondan 30 dakika ve iki saat sonra 2.4 mg daha sonra ilk 24 saatte 4 saatte bir 1.2 mg, ikinci ve üçüncü günlerde 6-8 saatte bir 1.2 mg, 4. ve 5. günlerde 12 saatte bir 1.2 mg rFVIIa uygulandı. rFVII dozu kanama takibi ve protrombin değerlerine göre ayarlandı. Hastada kanama ve trombotik komplikasyon izlenmedi.

Anahtar Kelimeler: Rekombinan FVIIa; böbrek taşları; hemofili A

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Factor VII (FVII) deficiency is a rare autosomal recessive bleeding disorder affecting approximately one in 500.000 in the general population.[1] Findings on bleeding disorder are highly variable in affected patients. However, patients with FVII activities of less than 1% have the tendency to be under the risk of hemarthroses, postoperative bleeding, epistaxis, and menorrhagia. Patients with activities ranging from 1% to 5% are moderately affected. Patients may have bleeding after surgical interventions and trauma.[2] FVII functions have a pivotal role in the initiation of coagulation cascade. Binding of FVII to tissue factor (TF) in damaged tissue results in conversion of FVII to the activated factor VII (FVIIa) by proteases. FVIIa plays a role of in the activation of factor X (FX) and factor IX

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(FIX), which play a key role in the intrinsic and extrinsic coagulation pathway.[3] Previous treatment options or prophylaxis used to prevent bleeding in FVII-deficient patients included use of fresh frozen plasma (FFP), prothrombin complex concentrates (PCC), or plasma derived FVII concentrates are associated with risk of infection, volume overload with FFP, and thrombotic complications with PCC.[4]

A recombinant form of activated FVII was approved as a second-generation bypassing agent and for the treatment of bleeding in patients with hemophilia A and B, who have inhibitors to factor VIII and factor IX.[5] More recently, the use of rFVIIa as a replacement therapy in the management of bleeding in congenital factor FVII deficiency has been anecdotally reported.[6] We present the first case with congenital FVII deficiency, who has been operated for kidney stones in which rFVIIa was used as replacement therapy to prevent intra operative and postoperative bleeding.

CASE REPORT

A 24-year-old man with renal colic pain was admitted to our hospital. He had experienced various bleeding complications during his life including epistaxis, bleeding more than expected during circumcision procedure, and gingival bleeding. History of petechia and ecchymosis was found. On physical examination, there was tenderness on left costal vertebral localization. At preoperative kidney-ureter-bladder radiography, we found a few stones, which were 20 x 30 mm in diameter, and local calyceal dilatation was seen in the left kidney (Figure 1). On intravenous urogram, we found a renal pelvic stone leading to obstruction and, thus, delayed left kidney function. The hemoglobin, platelet count, and white blood cells were in the normal range. Biochemical parameters and hepatitis markers showed no specificity. The prothrombin time (PT) (n= 11-14.2 s), activated partial thromboplastin time (PTT) (n= 26-37.2 s), and international normalized ratio (INR) were measured as 25.8 s, 31.9 s, and 2.37, respectively. FVII activity was 4% (n= 70-130). With these findings, we decided to perform pyelolithotomy for kidney stone. Operation was performed under general anesthesia. During the operation, all kidney stones located in the renal pelvis and lower pole calyces were removed, and a JJ stent was placed. Surgery was completed without the occurrence of any bleeding complication. The postoperative kidney-ureter-bladder radiography proved that the patient was stone-free (Figure 2).

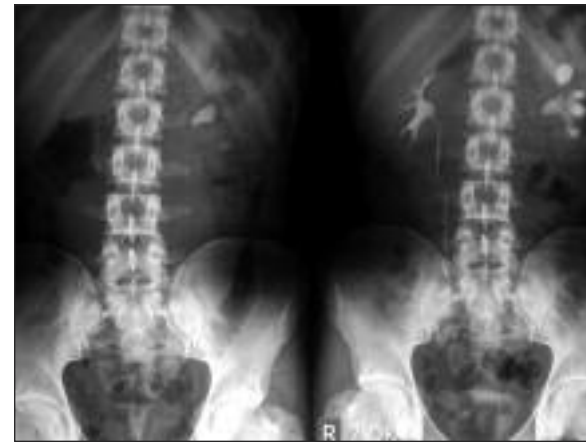

FIGURE 1: Preoperative kidney-ureter-bladder radiogram and intravenous urogram.

We administered rFVIIa 2.4 mg (39 μg/kg) as a bolus infusion 30 minutes before and 2 hours after the operation. Thereafter, bolus infusion of rFVIIa 1.2 mg (19 μg/kg) was administered every 4 hours in six doses in the first 24 hours. On postoperative second and third days, rFVIIa was administered at a dose of 1.2 mg every 6-8 hours and 1.2 mg every 12 hours on the fourth and fifth days. Ultrasonographic examination of the kidney was performed everyday after the operation for follow-up of bleeding. There were no signs of postoperative hematoma or excessive bleeding than expected. The PT and INR were in the normal reference range during and after the operation. Decision of rFVIIa dosing was made according to clinical evaluation of bleeding and INR. Recombinant FVIIa was well tolerated, and there were no signs of postoperative thrombosis. The patient was discharged on the postoperative fifth day.

DISCUSSION

Recombinant FVIIa has been used successfully to prevent bleeding in congenital and acquired FVII-deficient patient. Based on the review of the litera-

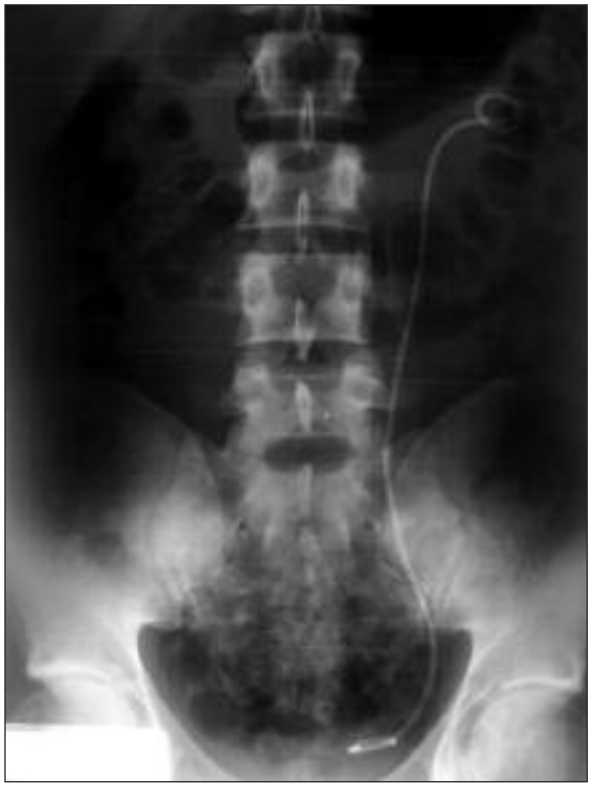

FIGURE 2: Postoperative kidney-ureter-bladder radiogram.

ture, there are some reports regarding orthopedic operations performed in some hemophilia patients with inhibitors, total hip arthroplasty in severe congenital FVII deficiency, laparoscopic gynecologic surgery, childbirth, caesarian section, and circumcision operation in which rVIIa was used.[7,8] One of the longest single case studies to date that provided convincing evidence for the use of rFVIIa as a replacement therapy and for prevention of bleeding in patients with FVII deficiency was performed in 30 patients in different clinical settings, which were associated with elective and emergency surgery, parturition, and trauma.[6]

In this case report, we described the use of rFVIIa as a replacement therapy in patients with moderate congenital FVII deficiency undergoing kidney stone surgery. The operation involved a high risk for operative bleeding complication as the result of moderate FVII deficiency. We chose open surgery rather than percutaneous nephrolitotomy because the risk of uncontrolled bleeding may occur during percutaneous access. The operation was performed by administering a dose of 2.4 mg (39 μg/kg) before and after the operation. Thereafter, a bolus infusion of rFVIIa 1.2 mg (19 μg/kg) was administered every 4 hours at a total of 6 dosages in the first 24 hours, then 1.2 mg every 8 hours on the third day and the same dosage every 12 hours on the fourth and fifth days after the operation. In the literature, dose regimens vary depending on the clinical setting. In a case report, rFVIIa was used at a dose of 17-19 μg/kg as a prophylactic agent every 6 hours for up to13 days in two patients with FVII deficiency undergoing elective surgery.[9] Similarly, a report published by Mariani et al. assessed 17 patients with congenital FVII deficiency were treated with rFVIIa at doses ranging between 8.1 and 70.5 μg/kg. The recommended dosage of rFVIIa is 15-30 μg/kg every 4-6 hours for FVII deficiency; compared with 90 μg/kg for both hemophilia and Glanzmann's thrombasthenia.[6,10] We administered 39 μg/kg as an initial dosage before and two hours after the operation. This dosage is slightly higher than recommended. There was no study on patients who have kidney stones with FVII deficiency in the literature. Therefore, to control undesirable bleeding during and after the operation, in our patient, we administered a dosage slightly higher than the suggested. After the second dosages, the administered dosages (19 μg/kg) were consistent with surgical cases published in the literature.

We successfully administered rFVIIa perioperatively and postoperatively for kidney stone operation in a patient with FVII deficiency. No bleeding and thrombotic complication was observed. On the basis of successful administration of rFVIIa in a FVII-deficient patient, we recommend the use of rFVIIa during renal operation in FVII-deficient patients.

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