Olgu Sunumu

Use of Recombinant Factor VIIa for Femoral Surgery in a Patient with Factor VII Deficiency: A Case Report

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Abstract

First identified in 1951, congenital deficiency of factor VII (FVII) is an autosomal recessive hemorrhagic diathesis leading to hemorrhagic disorder related to level of factor. Its half-life has been reported as 2.5 to 3 hours. Today, hemorrhage control is achieved with factor VII in the individuals with deficiency of FVII. Here we present a case with congenital FVII deficiency who was hospitalized with diagnosis of supracondylar femoral fracture. As long-term response was obtained following single dose of rFVIIa in the challenge test performed to the patient, we achieved post-traumatic and perioperative control of hemorrhage at replacement dose of 25 µg/kg/6 hours.

Key words: Factor VII deficiency, femoral surgery, rFVIIa

Introduction

Congenital coagulation disorders are usually due to decreased or defective production of one of the coagulation factors. Von Willebrand disease, hemophilia A and hemophilia B are the most common hereditary hemorrhagic diatheses. Deficiencies of the other coagulation factors are seen rarer, show autosomal recessive inheritance and named rare bleeding disorders (RBD) (1, 2).

Although it is a rare condition, deficiency of factor VII (FVII) is the most common in RBD. After first identification in 1951, about 200 cases of true FVII deficiency have been reported so far (3). Its prevalence is equal in men and women and is about 1:500.000 (4).

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For the patients with deficiency of FVII, risk of hemorrhagic complication varies depending on the level of the factor. Treatment of FVII deficiency is based on replacement of the plasma derived FVII or recombinant FVIIa (rFVIIa) (5). We present here a patient with congenital deficiency of FVII who presented with distal femoral fracture and in whom we used (rFVIIa) in order to prevent post-traumatic and peri-operative hemorrhagic complications.

Case Report

A 21 year-old male was admitted to the emergency service room of our hospital with complaint of fall. The patient had been diagnosed as having deficiency of FVII eight years ago. His history revealed that he had developed spontaneous hemorrhage of knee for 7 times and of wrist joint for one time and 3 uncontrollable hemorrhage of gum and that he had had septoplasty operation under local anesthesia. His family history was normal. On his physical examination, he had swelling and tenderness on his left knee and supracondylar area. Other system examinations were normal. His laboratory findings in the emergency service room were as follows; prothrombin time (PT): 44.6 second, international normalized ratio (INR):4.53, activated partial thromboplastin time (aPTT):34.3 second, hemoglobin (Hb): 13.7 g/dL; platelets

Table 1. Coagulation Profile Following Single Dose of Recombinant Factor VIIa

	Hour 0	Minute 30	Hour 2	Hour 4	Hour 6	Hour 8
INR	5,86	0,87	0,77	0,77	0,78	0,78
PT	54,7	12	10,8	10,8	10,9	10,9
Factor VII Level (%)	3	507	139	131	109	65

Abbreviations: PT, prothrombin time; INR, international normalized ratio.

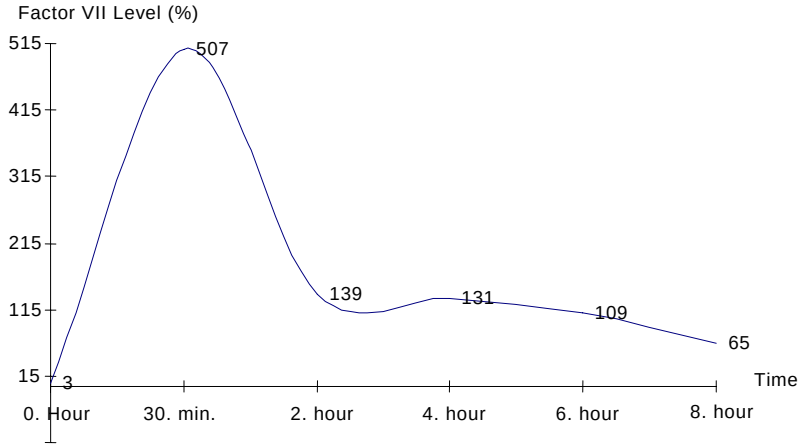
(PLT): 240x10^6/L. Left supracondylar femoral fracture was detected on the plain radiography**.** The patient was hospitalized in the orthopedics ward. He was given rFVIIa at dose of 25 µg / kg once every 8 hours. Control PT and INR values following administration of rFVIIa were 12.8 second and 0.94, respectively. In the patient with continuing complaints of pain and local swelling, rFVIIa was continued at dose of 25 µg /kg given once every 8 hours on the second day of hospitalization. PT and INR values following administration of rFVIIa were 12 second and 0.87, respectively. The patient underwent a "challenge test" on the third day of admission. He was given a single dose of rFVIIa at a dose of 25 µg /kg in the morning and levels of PT, INR and FVII were monitored by 2-hour intervals (Table 1). We observed that the FVII level was maintained at hemostatic level until the 8th hour following a single dose of rFVIIa at a dose of 25 µg/kg. However, in spite of the possibility of any surgical complication, operation was considered with a dose of 25 µg / kg that would be given once every 6 hours. The patient was operated in the morning of the fourth day of hospitalization. Before the operation, he was given rFVIIa at a dose of 25 µg/kg.

Thereafter on the day of operation and on the post-operative second day, he was given rFVIIa at a dose of 25 µg/kg once every 6 hours; once every 8 hours on the post-operative third day; and once every 12 hours on the post-operative fourth and fifth days. Developing no postoperative hemorrhagic complication, deep vein thrombosis and wound site infection, the patient was discharged on the post-operative sixth day with recommendation for taking rFVIIa at a dose of 25 µg/kg once every 12 hours for the next 4 days.

Discussion

Deficiency of FVII is a hemorrhagic disorder with a rare autosomal recessive hereditary pattern. In such patients, risk of hemorrhagic complication is related with level of FVII. Spontaneous ecchymosis, menorrhage, oral cavity bleedings, hemarthrosis and postoperative hemorrhages develop when activity of FVII is below 1% (6, 7). The patients with factor level between 1% and 5% are affected moderately and those with factor level above 5% are affected mildly (8). In the patient presented here, level of FVII was below 1% and he had developed spontaneous bleeding of joints and gum. Previously used options for treatment of FVII deficiency or bleeding prophylaxis were fresh frozen plasma and concentrates of vitamin K-dependent prothrombin complexes. But they had potential complications such as volume overload associated with fresh frozen plasma and thrombotic events associated with prothrombin complexes (5). Today, FVII deficiency is mostly treated with rFVIIa preparations first approved

Table 2. Timetable for Logarithmic Decrease Between the Factor Level and Time



for the patients developing inhibitors against factor VIII and factor IX, in hemophilia A and hemophilia B. FVII is the coagulation protein with shortest known half-life. Its half-life is 2.5 to 3 hours. There are, however, different reports in the literature that give its in vivo half-life as 4 hours, less than 4 hours, and as 5.3 hours (9-11). In the patient presented here, the factor level was monitored by 2-hour intervals following a single dose of rFVIIa of 25 µg/kg that we administered one day before the operation. It was observed that the level of the factor peaked at 30th minute and it maintained at a level to provide hemostasis until hour 8 (Table 2).

Case reports have been reported on the use of rFVIIa in orthopedic operations such as synovectomy and total hip arthroplasty (12, 13). In a study by Gopalan et al. in 2007, a patient with deficiency of FVII who underwent total hip surgery was given rFVIIa with continuous infusion every 5 hours at dose of 38 µg/ kg for the first day and at dose of 25 µg/ kg /6 hours for the next 5 days (14). We achieved hemorrhage control in our patient at a lower dose and with intermittent treatment. In conclusion, there is no predetermined standard procedure for the replacement treatment that will be administered during major surgery in patients with deficiency of FVII. We believe that in such patients, challenge test has a major role in determining the amount of the factor required for hemostasis and that rFVIIa at a dose of 25 µg/ kg /6 hours provides hemostasis during perioperative period in orthopedic surgery.

Factor VII eksikliği olan hastada femoral cerrahide rekombinant faktör VIIa kullanımı: Bir olgu sunumu

Özet

İlk olarak 1951 yılında tanımlanmış olan konjenital faktör VII eksikliği, faktör düzeyi ile ilişkili olarak hemostaz bozukluklarına neden olan, otozomal resesif bir kanama diatezidir. Faktör VII'nin yarılanma ömrü 2.5-3 saat olarak bildirilmektedir. Kanama kontrolü günümüzde faktör VII replasmanı ile sağlanmaktadır. Burada suprakondiler femur fraktürü tanısıyla yatırılan, konjenital faktör VII eksikliği tanılı bir olgu sunuldu. Hastaya yaptığımız chellenge testi'nde tek doz sonrası rekombinant FVIIa'ya aldığımız uzun süreli cevap nedeni ile 25 µg/kg/6 saat dozunda replasman ile post travmatik ve perioperatif kanama kontrolü sağladık.

Anahtar kelimeler: Faktör eksikliği, femoral cerrahi, rFVIIa

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