

Case Report

A case of sagittal splitting ramus osteotomy and genioplasty in a patient with congenital factor VII deficiency

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Blood coagulation factor VII is involved in the extrinsic clotting system, and congenital defects or deficiencies affecting blood coagulation factor VII are rare. We report the case of a patient who was diagnosed with factor VII deficiency based on a preoperative examination and then underwent factor VII replacement therapy and orthognathic surgery, together with a brief discussion of the literature.

The patient was a 25-year-old woman. She presented to our hospital after being diagnosed with jaw deformity and underwent sagittal splitting ramus osteotomy and genioplasty under general anesthesia. Preoperative tests revealed an abnormally short prothrombin time. Blood tests detected very low coagulation factor VII activity (33%), and so the patient was diagnosed with factor VII deficiency.

We conducted preoperative factor VII replacement therapy to inhibit bleeding, and then the abovementioned surgical procedure was performed safely. The operative time was 1 hour 30 minutes, and little intraoperative blood loss occurred. The patient's postoperative course was good, e.g., no abnormal bleeding occurred, and she was discharged on postoperative day 7.

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Introduction

Congenital factor VII deficiency is a hemorrhagic disease that was first reported by Alexander et al. in 1951. It is characterized by a prolonged prothrombin time (PT; 1-step method) and a normal partial thromboplastin time. It presents with an autosomal recessive inheritance pattern, and bleeding tendencies of varying severity are also seen. In addition, some reports have suggested that it can have serious adverse

outcomes. The incidence of the condition is 1 in 500,000 people, and about 280 cases from around the world, including 40 involving patients from Japan, had been registered in the FVII Mutation Database (The Haemostasis Research Group, Medical Research Council Clinical Sciences Centre, London UK) as of 2004.

We report the case of a patient with congenital factor VII deficiency, which was diagnosed during preoperative blood tests for orthognathic surgery. The patient safely underwent

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the orthognathic surgery after the administration of factor VII replacement therapy.

Case

A 25-year-old woman visited an orthodontic doctor for corrective mandibular treatment. She exhibited mandibular protrusion, edge-to-edge occlusion, deviation of the mandible to the right, and an anterior crossbite. Cephalometric radiographs showed mandibular prognathism due to lateral hypogrowth of the maxilla and anteroinferior hypergrowth of the mandible. After preoperative orthodontic treatment, a sagittal splitting ramus osteotomy and genioplasty under general anesthesia were planned. Preoperative hematological tests detected a PT of 40% (in-hospital reference value: 80–120%), an activated partial thromboplastin time (APTT) of 33.2 sec (in-hospital reference value: 28.0–45.0 sec), and a PT-international normalized ratio (PT-INR) of 1.58. The patient was therefore referred to our hematology department for further evaluation.

Abnormalities in extrinsic clotting factors were suspected, and additional blood tests revealed factor VII deficiency and decreased factor VII activity (33%, in-hospital reference value: 75–140%) (Table 1). The patient had not suffered any

prior episodes of spontaneous bleeding. To avoid bleeding during surgery, the patient was preoperatively supplemented with recombinant activated factor VII eptacog alpha (Novo-Seven HI®; Novo Nordisk Pharma, Denmark). Additional factor VII and blood transfusions were prepared in case massive bleeding occurred. Autologous blood preservation was not performed because the stored blood also exhibited factor VII deficiency.

On the day of surgery, the factor VII eptacog alpha preparation was administered at a dose of 30 $\mu\text{g}/\text{kg}$ without adverse effects. As a result, the patient's PT reached $\geq 200\%$ and her PT-INR had improved to 0.80 after 20 minutes, confirming that her bleeding tendency had been suppressed. Sagittal splitting ramus osteotomy and genioplasty were performed without causing abnormal bleeding. The operative time was 1 hour 30 minutes, and little intraoperative blood loss occurred.

A computed tomography scan performed on postoperative day 1 did not detect any signs of bleeding. During the first 2 days after the operation, the right and left continuous suction drains removed 131 ml and 100 ml of blood, respectively. No additional factor VII preparations were administered, and the continuous suction drains were removed. Blood tests performed on postoperative day 7 showed a PT of 39% and

Table 1. Blood test results

	initial examination	hematology department	In-hospital reference value
WBC (/ μl)	7620	-	3,500-9,000
RBC (/ μl)	426	-	380-480
Hb (/dl)	13.6	-	11.3-15.2
Platelets (/ μl)	293000	-	130000-400000
Total protein (g/dl)	7.3	-	6.3-8.3
AST (IU/L)	20	-	13-33
ALT (IU/L)	18	-	6-27
APTT (sec)	33.2	32	28.0-45.0
PT (%)	40	47	80-120
PT-INR	1.58	1.43	-
Fib (mg/dl)	-	259	200-400
Factor VII (%)	-	33	75-140

Table 2. Test result trends after the administration of factor VII

	Before administration	After administration	1 week post surgery	2 weeks post surgery	2 months post surgery	In-hospital reference value
APTT (sec)	32	33.7	34.7	38.3	34.3	28.0-45.0
PT (%)	47	≥ 200	39	34	42	80-120
PT-INR	1.43	0.8	1.6	1.79	1.57	-
Factor VII (%)	33	-	-	16	26	75-140

a PT-INR of 1.60. The patient was discharged on postoperative day 7. On postoperative day 14, the patient displayed factor VII activity of 16%, a PT of 34%, and a PT-INR of 1.79. In the second month after surgery, she demonstrated factor VII activity of 26%, a PT of 42%, and a PT-INR of 1.57. The patient's subsequent course was uneventful (Table 2).

Discussion

Congenital factor VII deficiency is a form of bleeding diathesis caused by a quantitative deficiency or qualitative (functional) abnormality in factor VII resulting from a mutation in the blood coagulation factor VII gene. Factor VII is a vitamin K-dependent coagulation factor that is produced in the liver. Activated factor VII is central to the extrinsic coagulation activation mechanism and forms compounds with tissue factors and calcium ions on phospholipids and activates factor IX and factor X. Therefore, a characteristic of factor VII deficiency is that even though abnormalities are seen in the extrinsic coagulation system, the intrinsic coagulation system functions normally. Furthermore, patients with factor VII deficiency exhibit reduced factor VII activity in their blood and a prolonged PT, but their APTT, clotting time, and fibrinogen levels are normal.

The bleeding symptoms of factor VII deficiency vary widely, with the most typical being nosebleeds, gingival bleeding, and subcutaneous bleeding. In severe cases, complications such as intraarticular hemorrhaging, central nervous system hemorrhaging, and hypermenorrhea can occur. Intracranial bleeding is frequently reported in children, and neonatal intracranial hemorrhaging on delivery can have serious outcomes. In cases of frequent bleeding, maintaining a target factor VII level of around 20% is recommended, and Bauer found that hemostatic function is sufficiently maintained at 15–25%¹. However, the severity of bleeding does not necessarily correspond with factor VII activity in the blood². Thus, predicting the amount of bleeding is difficult. Fresh frozen plasma and prothrombin complex concentrate transfusions are used for replacement therapy, but some reports have suggested that they do not result in any improvement. The present report is the first to describe sagittal splitting ramus osteotomy and genioplasty in a patient with factor VII deficiency. Factor VII preparations have been demonstrated to improve the bleeding tendencies of patients with congenital factor VII deficiency in cases of massive blood loss during childbirth or other occasions³. In addition, in patients with severe factor VII deficiency factor VII preparations are widely used to prevent bleeding in cases of hemor-

rhaging, surgery, trauma, or invasive treatment⁴. In general, the administration of 15–30 $\mu\text{g}/\text{kg}$ of a factor VII preparation every 4–6 hours is recommended. In one reported case, a perioperative factor VII administration schedule was produced based on measurements of the rise in factor VII activity and its half-life before surgery⁵. Another study reported that there is no need to administer factor VII preparations in cases of minor surgery, even for patients with severe congenital factor VII deficiency². Currently, no established guidelines explaining the indications, dosage, administration frequency, or administration intervals for factor VII preparations exist³.

In the present case, PT-INR was used as an indicator of bleeding tendency. Preoperatively, the patient exhibited factor VII activity of 33% and a PT-INR of 1.58. Due to the possibility of marked blood loss occurring during the planned operation, a factor VII preparation was administered preoperatively to attempt to normalize the patient's PT-INR. To prevent intra- and postoperative coagulation disorders, additional recombinant activated factor VII preparations and blood transfusions were prepared. As a result, no abnormal bleeding occurred, and the additional administration of factor VII eptacog alpha was unnecessary.

Many reports have suggested that factor VII administration should be investigated in cases involving postoperative hemostasis. Patients with coagulation disorders who undergo major surgery are at increased risk of clot formation, disseminated intravascular coagulation, or exacerbation.

The procedure performed in the present case was considered to represent major surgery, and thus, a factor VII preparation was administered preoperatively.

The half-life of recombinant activated factor VII is 3–4 hours, which is shorter than those of all other coagulation factors. Thus, the frequent administration of factor VII is necessary to prevent bleeding. However, thrombosis and other side effects have been reported after the frequent administration of factor VII⁶. In the present case, the use of elastic stockings and early ambulation were performed after surgery. However, blood tests for parameters such as D-dimer were not performed. As no guidelines have been established regarding the timing, method, or dosage of recombinant activated factor VII administration, the establishment of indications for the use of VII preparations based on the accumulation of relevant cases is important.

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