

Dental Management of a Patient with Factor X Deficiency

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ABSTRACT

Factor X deficiency (also known as Stuart-Prower factor deficiency) is an extremely rare hereditary hematologic disorder, affecting 1 person in 2 million. The gene causing this condition is autosomal recessive; thus, only those inheriting from both parents exhibit clinical symptoms, such as moderate bleeding, easy bruising and subcutaneous bleeding from mucous membranes. Patients with marked deficiency may have severe post-traumatic or spontaneous internal or external bleeding, leading to such complications as hemarthrosis or hemorrhagic strokes. This case report describes the dental management of a patient with severe factor X deficiency whose development was delayed due to multiple episodes of intracranial hemorrhage in early childhood. It also highlights the importance of timely interdisciplinary communication and consultation to promote a successful outcome.

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Factor X deficiency is a coagulation disorder reported in the mid-1950s by workers who were studying patients with a hemorrhagic disease resembling factor VII deficiency. It was named after the first male and female patients (Stuart and Prower) in whom it was recognized. Factor X is a vitamin K-dependent clotting factor synthesized in the liver and found in plasma at a concentration of about 1 mg/dL.¹ As the first member of the final common pathway, it plays an important role in the coagulation cascade system.

Dental extractions or other surgical procedures are often associated with postoperative bleeding, which in most instances is minor and inconsequential. However, patients with known bleeding or clotting problems can present a significant challenge for the dental practitioner, as excessive bleeding may not only be stressful for the patient and his or her family but also potentially life threatening.

Case Report

A 17-year-old presented to the pediatric dental department of the University of Florida with the chief complaint of toothache. His medical history indicated severe factor X deficiency, intracranial bleeding episodes and right-side hemiparesis resulting from a cerebrovascular accident (stroke) at age 5 years. Wolff-Parkinson-White syndrome with a heart murmur, partial seizures, speech delay, and cognitive and learning difficulties were also reported. Current medications included factor IX complex concentrate, carbamazepine and sertraline. An indwelling catheter was being used to administer prophylactic anticoagulant medication. At 8 and 12 years of age, he had received dental care under general anesthesia.

Intraoral examination revealed full permanent dentition, poor oral hygiene, multiple carious lesions and severe crowding in the mandibular arch. The patient's extreme level

of anxiety made a comprehensive oral examination difficult and radiography impossible. In view of his medical history and the extent of treatment required, a decision was made to carry out comprehensive dental treatment under general anesthesia.

The preoperative plan involved a discussion among the pediatric dentist, the patient's guardian, the pediatrician and the hematologist to review important dental, medical and hematologic issues. To assure effective communication between the family and the health care providers, a family care coordinator (who was an experienced hematology nurse) was also involved as liaison.

Preoperative recommendations by the hematologist included a full clotting profile and administration of 2100 U of intravenous factor IX complex concentrate (approximately 44 U/kg) half an hour before the procedure. Because of the long half-life of factor X, a second dose of 1200 U factor IX complex concentrate was recommended 24 hours after the procedure and on alternate days for 1 week. Local hemostatic measures included injection of thrombin or cellulose gel into extraction sites and, for postoperative clot stabilization, tranexamic acid or aminocaproic acid was recommended every 6 hours for 1 week. Patient admission was arranged by the hematology team who would also administer factor replacement therapy and monitor bleeding postoperatively. The anesthesiologist and hospital pharmacist were informed of the procedure in advance to allow them to make appropriate preparations and ensure the availability of an adequate amount of factor IX complex.

On the day of dental surgery, the patient was admitted without incident. His preoperative regime included 15 mg oral midazolam for anxiety, 2 g intravenous ampicillin for prophylaxis through the indwelling catheter and slow intravenous infusion of 2100 U of factor IX complex over 30 minutes. The patient was intubated orally to prevent perioperative epistaxis. Following tooth cleaning with prophylactic paste, clinical examination and radiography, comprehensive treatment was carried out.

Following intraoral local anesthetic infiltration with 1.2 mL 2% xylocaine with adrenaline 1:100 000 (Septodont USA, New Castle, Del.), tooth 17 and tooth 32 were extracted. The extractions were carried out initially to allow sufficient time for application of local measures to maintain adequate hemostasis. This included injection of thrombin gel into the extraction sockets, placement of 3/0 vicryl sutures and a gauze pressure pack. Hemostasis was achieved, and the remaining carious permanent teeth were restored using resin-modified glass ionomer cement (Fuji II LC, GC America, Alsip, Ill.) and resin-based composite material (TPH, Dentsply International, Milford, Del.). A stainless steel crown (3M ESPE, St. Paul, Minn.) was cemented on tooth 46 using glass ionomer luting cement (Fuji I, GC America).

Box 1 Signs and symptoms of factor X deficiency

Clinical signs and symptoms

- Epistaxis
- Hemarthrosis
- Gastrointestinal bleeding
- Umbilical cord bleeding
- Prolonged menorrhagia
- Hematuria
- Intracranial bleeding
- Postpartum hemorrhage

Blood test findings

- Normal bleeding time
- Normal thrombin time
- Prolonged prothrombin time
- Prolonged activated partial thromboplastin time

The patient's immediate recovery from general anesthesia was uncomplicated and he was admitted by the hematology team for observation as planned. He received 1200 U factor IX complex intravenously and 70 mg/kg of aminocaproic acid within 24 hours after surgery and remained hemodynamically stable throughout his hospital stay. He was discharged from hospital after 36 hours with a prescription for 10 mL of aminocaproic acid mouth-rinses every 6 hours for 7 days, Peridex oral rinse (chlorhexidine gluconate 0.12%; 3M ESPE) 10 mL, 3 times a day for a week and meticulous oral hygiene instructions. The family was instructed to administer 1200 U of the factor X complex concentrate once daily on alternate days for the first week and resume his usual anticoagulant therapy of twice weekly from the second week onwards.

The patient returned to the pediatric dental clinic one week postoperatively, reporting no complications. Because of his high risk for caries, the patient was placed on a regular 3-month recall schedule and has shown promise regarding compliance with dental appointments and preventive dental recommendations.

Discussion

Along with factors II, VII and IX, factor X requires vitamin K for its synthesis. It is activated to form factor Xa by factor IXa (with its cofactor, factor VIIIa) and factor VIIa with its cofactor, tissue factor. Its half-life is 40–45 hours.

In humans, the factor X gene is located on the 13th chromosome (13q34). Factor X deficiency is a clotting

Table 1 Comparison of features of fresh frozen plasma and prothrombin complex concentrate

Feature	Fresh frozen plasma	Prothrombin complex concentrate
Content	Contains all coagulation factors and proteins	Combination of clotting factors II, VII, IX and X and inhibitor proteins C and S (may also contain a small amount of heparin)
Uses	Factor II, V, VII, IX, X and XI deficiencies Antithrombin III deficiency	Congenital factor II, IX and X deficiencies and hemophilia A with inhibitors
Availability	Readily available	Not readily available (preoperative planning required)
Cost	Inexpensive	Expensive
Volume	Larger volume needed for replacement therapy	Lower volume needed for replacement therapy
Side effects	Risk of volume overload Viral contamination and infection Anaphylactic reaction	Lower risk of volume overload Thromboembolic episode Disseminated intravascular coagulopathy Anaphylactic reaction Generation of clotting factor or inhibitor antibodies Transmission of infectious disease

disorder, in which both amount and activity of the antigen are decreased (type I deficiency) or antigen level is normal or near normal, but activity is low (type II).² Factor X deficiency may present as epistaxis, hemarthrosis or gastrointestinal bleeding and is characterized by prolongation of prothrombin time and activated partial thromboplastin time, with normal bleeding and thrombin times.³ A summary list of the signs and symptoms of factor X deficiency is presented in **Box 1**.

The optimum level of factor X activity required for hemostasis is 10%.⁴ In the mild form of the deficiency, factor X activity level is about 6%–10% and the condition may be discovered incidentally following mild bruising or menorrhagia. The moderate form (activity level 1%–5%) may present with bleeding following a hemostatic challenge, such as surgery or trauma, and the severe form (activity level < 1%) is usually diagnosed in the neonatal period with umbilical cord bleeding, subcutaneous deep tissue bleeding or bleeding into body cavities shortly after injury.

Most reports of factor X deficiency discuss the recessive mode of its inheritance in Asia⁵ and in communities where consanguineous marriages are prevalent.^{6,7} Sinha and others³ report the perioperative management of a 20-year-old woman with isolated factor X deficiency. The patient presented in this report is a Caucasian male with no family history of consanguinity, although his mother and grandmother both carry the recessive gene.

Factor X is not commercially available as a concentrate, but is present in fresh frozen plasma (FFP) and prothrombin complex concentrate (PCC). The advantages of FFP include ready availability, low cost and a prolonged half-life of 20–40 hours.³ Our patient was receiving factor IX complex regularly as prophylaxis. Factor IX

complex, a PCC, is a combination of blood clotting factors II, VII, IX and X; it produces a rapid reversal of the anticoagulant effect of vitamin K antagonists such as warfarin. PCC requires a shorter administration period than FFP products and a much lower volume is needed for replacement therapy.⁸ It also results in a better clinical outcome, as well as avoidance of the volume overload associated with FFP (**Table 1**).

Patients with factor X deficiency have also been treated with a number of replacement therapies, using blood products or hemophilia concentrates. Mori and others⁵ suggest that PPSB-Nichiyaku (Nihon Pharmaceutical, Tokyo, Japan), the concentrate for hemophilia B, which contains prothrombin, proconvertin, Stuart factor and hemophilia B, is efficient as replacement therapy for factor X deficiency. In addition to recommended therapies, the application of aggressive local measures and administration of an antifibrinolytic agent, such as tranexamic acid or aminocaproic acid, are essential to stabilize localized clots in the extraction sockets by countering the fibrinolytic enzymes naturally present in saliva.

Aminocaproic acid (also called ϵ -aminocaproic acid or 6-aminohexanoic acid) is a derivative and analogue of the amino acid lysine. It works as an anti-fibrinolytic or anti-proteolytic agent and, as a lysine analogue, it binds reversibly to the kringle domain of the enzyme plasminogen and blocks binding of fibrin, which is normally activated to plasmin. Aminocaproic acid is used to treat excessive postoperative bleeding and it can be given orally or intravenously. Because aminocaproic acid and factor IX complex are prothrombotic agents, amino-caproic acid was not given to this patient with the initial high dose of factor IX complex to reduce the

likelihood of disseminated intravascular coagulopathy and thrombosis.

Factor X deficiency is so rare as to preclude both the development of a specific product for replacement and an organized clinical trial of any existing drug that could potentially be used for its treatment. In the United States, this results in a serious lack of access to appropriate therapy for those with factor X deficiency and other small but important subsets of patients with coagulation disorders.⁹

Treating patients with rare medical conditions can present such challenges as lack of available protocol for a perioperative plan. For dentists who have difficulty obtaining current information on patients with bleeding or coagulation disorders, a detailed handbook for patients and health care support personnel is available from the Canadian Hemophilia Society.¹⁰

Our patient had refused to attend past dental appointments because of anxiety. His family had also expressed difficulty in managing his oral hygiene, which worsened as he got older, and his noncompliance subsequently resulted in toothache and extensive dental disease. The complexity of this patient's condition required collaboration among a multidisciplinary team to implement an effective treatment plan. The team involved the patient's primary caregivers, his pediatrician, a pediatric hematologist, a hemophilia nurse practitioner, the pediatric dentist, the anesthesia team and the hospital pharmacist.

We highlight this case to raise awareness among dental professionals, especially pediatric and special care dentists, of issues in the management of a rare yet significant condition. Timely and efficient communication among all members of the team was crucial in achieving a successful outcome. ✦

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