CASE REPORT

Dental Management of Factor XIII Deficiency Patients: A Case Series

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Abstract

Aim: To create awareness about rare clotting disorders in children and to highlight the different dental treatment approaches that can be used while planning the management in such cases.

Background: A prerequisite for successful wound healing is achieving good hemostasis by effective vascular spasm, platelet plug formation, and finally blood coagulation. In the general population, postoperative bleeding after dental treatment is self-limiting. However, a certain segment of the population does suffer from inherited bleeding and clotting disorders, wherein standard invasive dental procedures can trigger bleeding episodes, which could be life-threatening in absence of the requisite precautionary measures being followed.

Case description: One such condition is congenital factor XIII deficiency, a rare autosomal recessive disease usually associated with early onset of serious or life-threatening bleeding episodes, such as, intracranial hemorrhage or umbilical cord bleeding. This case series details the complete dental management of three children suffering from factor XIII deficiency.

Conclusion: Factor XIII is a rare coagulation cascade, and by this case series, complete dental treatment varying from noninvasive to be kept under observation to invasive dental extraction and fracture reduction was carried out with the hematologists consultations.

Clinical significance: This case series creates awareness about this rare condition and the need for a multidisciplinary approach involving dentists and hematologists in the effective management of such patients.

Keywords: Case series, Children, Dental management, Factor XIII deficiency, Intracranial hemorrhage, Umbilical bleeding.

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Introduction

Factor XIII is also known as Laki–Lorand factor after the scientists who first proposed its existence in 1948.[1] It is the final enzyme in the coagulation cascade and is essential for normal hemostasis by increasing clot strength and resistance to fibrinolysis. It circulates in plasma as a tetramer with two catalytic A subunits and two carrier B subunits. The A subunits are synthesized in bone marrow and placenta, while the B subunits are synthesized in the liver.[2]

Congenital factor XIII deficiency originally recognized by Duckert in 1960 is a rare autosomal recessive disease, which can cause life-threatening bleeds in the form of intracranial hemorrhage in children.[3] It is a disorder with the incidence of about 1 per 2–5 million with male to female ratio of 1:1.[4] It is due to mutations in the 'A' subunit, located on chromosome 6, many of which are missense mutations (6p24–p25).[5] The acquired variant is due to hepatic failure, inflammatory bowel disease, and myeloid leukemia.

Common symptoms include bleeding diathesis like bleeding from the umbilical cord stump at birth/within the first few days, which is a characteristic sign in 80% of affected individuals,[6] hemarthrosis, epistaxis, and bleeding in the central nervous system (brain and spinal cord) and mouth (particularly after dental surgery or tooth extraction and soft tissues). Other common symptoms also include easy bruising with poor wound healing and abnormal scar formation.[7]

There is a paucity of data regarding this factor deficiency, especially in the pediatric population. Only about 200 cases have been reported in the world and very few of those are from dental literature.[2] This case series thus aims to create awareness about this rare deficiency among dental professionals and to highlight the different treatment approaches that can be used in such cases based on the underlying dental complaint of the patient.

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Case Description

Case 1

A 3-year-old male patient reported to the department of dental surgery, 24 hours post suffering a fall at home. The patient complained of bleeding in the upper anterior deciduous incisor region post trauma and the bleeding had not ceased since then (Fig. 1).

Elicitation of the past medical history from the parents revealed that the patient was diagnosed with factor XIII deficiency due to prolonged umbilical bleeding, 5 days post birth. No other suggestive history in relation to the present trauma was given by the patient regarding factors, such as, loss of consciousness, epistaxis, and vomiting, etc.

The patient had also been transfused with one unit of cryoprecipitate just prior the dental procedure. On dental

examination, mild bruises on the chin and intraoral bleeding between the upper deciduous incisors was noted. The region was first debrided for better visualization, on which it was noted a stable clot had been formed. A pressure pack using a local hemostatic agent, aminocaproic acid was applied for an hour to protect the formed clot. The patient was advised to maintain a soft diet and was kept under observation. No active treatment was planned.

At the 24-hour follow-up visit, no bleeding was noted and the wound healing was satisfactory at 7 days (Fig. 2). No other dental treatment needs were needed then.

Case 2

A 9-year-old boy reported to the department of dental surgery with a chief complaint of dull and radiating pain in the right mandibular posterior tooth region along with the presence of multiple carious teeth.

The child's past medical history was significant in revealing prolonged umbilical bleeding, 12 days after birth, and an episode of intracerebral bleed leading to medial deviation of left eye at 8 months of age. The family history of the patient revealed a nonconsanguineous marriage between the patient's parents.

Intraoral dental examination revealed a deep carious lesion which with respect to 84. Dentinal carious lesions in the permanent molars - 26, 36, and 46 and deciduous molars - 64, 74, 75, 83, and 85 were seen. An orthopantomograph was advised and it revealed a coronal radiolucency involving pulp and distal root resorption periapically with respect to 84 (Fig. 3).

Infusion of 2 units of cryoprecipitate along with antibiotics and antifibrinolytics was advised just prior to the procedure as a prophylactic measure. Caries was excavated and resin-reinforced glass ionomer cement restorations were placed with respect to 26, 36, 46, and the following deciduous teeth - 64, 74, 75, 83, and 85 (Figs 4 and 5).

Eighty-four was then extracted by administering 2% lignocaine with adrenaline under infiltration for pain control, and complete hemostasis was achieved using local application of aminocaproic acid gauze plug.

Follow-ups were done after 24 hours and 7 days (Fig. 5). The postoperative healing was uneventful.

Case 3

A 13-year-old male child reported to the department of dental surgery with a complaint of severe bleeding from the lower right anterior region. Patient gave history of a fall one day back, after which there was severe bleeding from 41 to 42 regions.

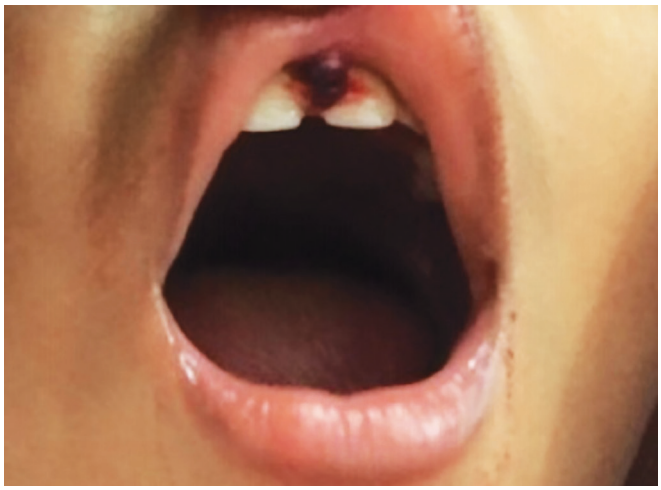

Fig. 1: Case 1—bleeding noted between the maxillary deciduous incisors

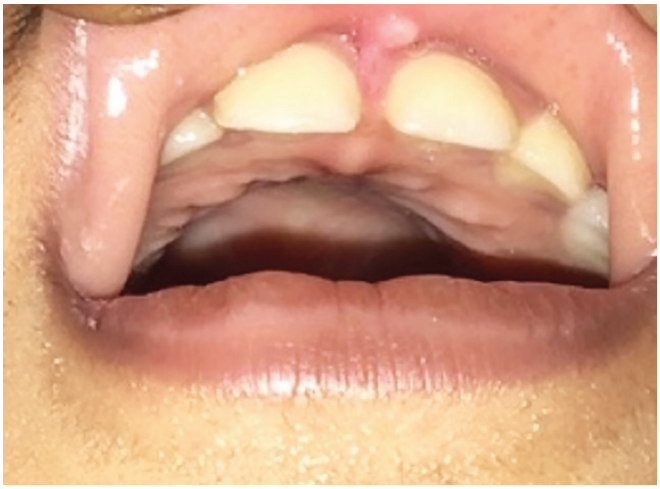

Fig. 2: Case 1—follow-up healing at 7 days

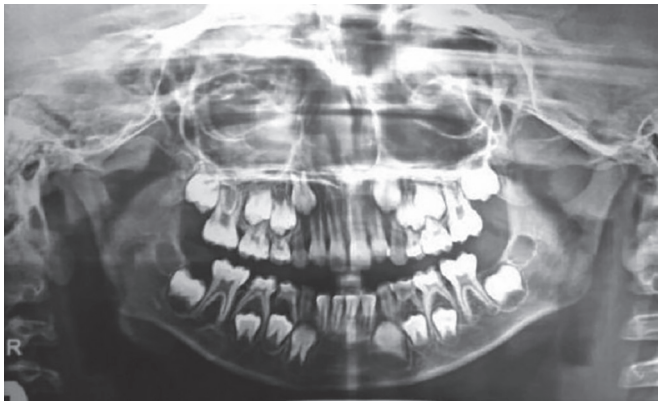

Fig. 3: Case 2—orthopantomograph showing multiple carious teeth

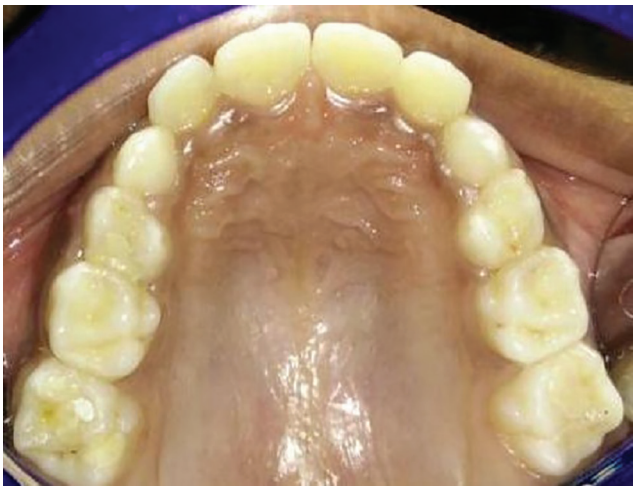

Fig. 4: Case 2—resin-modified glass ionomer restorations in the maxillary arch

The child's past medical history revealed no other symptoms except prolonged bleeding post injury at 2 years of age and a family history of consanguineous marriage.

Intraoral examination revealed a clot on the lingual aspect of the lower right anteriors and ecchymosis on the floor of the mouth with buccally displaced 41, 31, and 32 (Fig. 6). The posterior occlusion appeared stable. An orthopantomograph revealed a radiolucent line running between 41 and 42 leading to a diagnosis of dentoalveolar fracture of the right anterior mandible.

The dentoalveolar fracture was planned to be stabilized using a splint made of Erich's Arch Bar. After consulting the hematologist, the patient was transfused with 3 units of cryoprecipitate prior to the procedure. The arch bar was fixed from 43 to 34 regions using 26-gauge arch wire (Fig. 7). The fragment was stabilized and hemostasis was achieved. The patient was advised dietary restrictions preferably semisolid for a period of 2 months.

A follow-up orthopantomograph after eight weeks (Fig. 8 says that…) showed good healing of fracture, after which a second procedure for arch bar removal was planned. Three units of cryoprecipitate were transfused post which the arch wire was removed and oral prophylaxis was performed (Fig. 9). No significant bleeding was noted during this procedure.

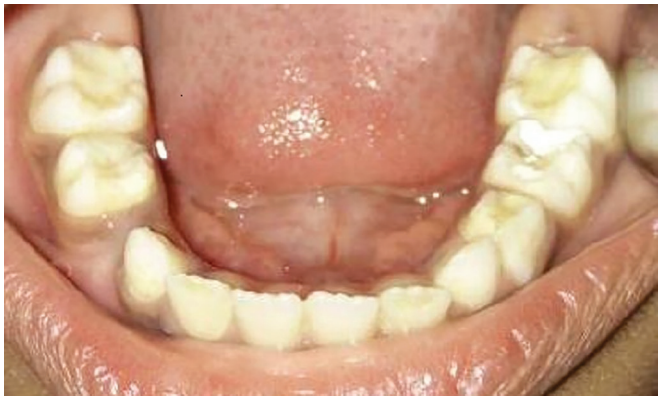

Fig. 5: Case 2—postoperative healing at 7 days after extraction of #84 and resin-modified glass ionomer restorations

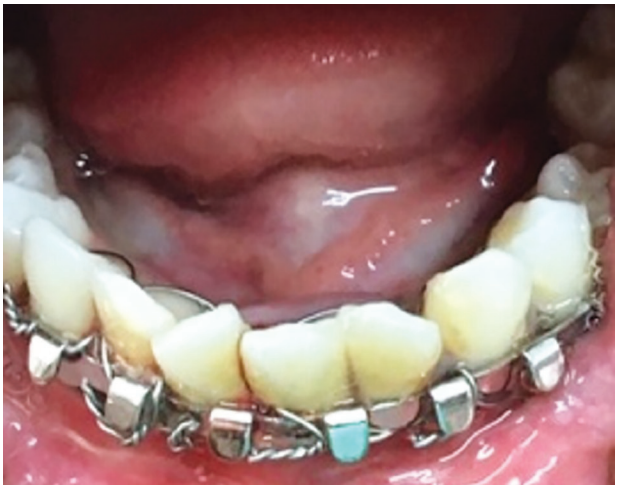

Fig. 7: Case 3—arch bar fixed from 43 to 34 regions

Discussion

Factor XIII is a plasma transglutaminase that catalyzes the final step in the coagulation cascade, cross-linking the loose fibrin polymer into a highly organized structure.[8] In addition, factor XIII covalently binds fibronectin a2-plasma inhibitor and collagen to the fibrin plug, thus enhancing adherence to the wound site, increasing resistance to fibrinolysis, and facilitating better wound healing by providing a scaffold for fibroblasts migration and proliferation. Hence, its deficiency is associated with severe bleeding and poor wound healing.

Incidence of intracranial hemorrhage is higher with factor XIII deficiency[7] and can pose a significant threat to life as was evidenced in the past medical history of the second patient. The patient suffered from an episode of intracerebral bleed due to a traumatic fall at 8 months of age due to which he developed medial deviation of the left eye (VIth nerve palsy). The first and third cases reported in this series had reported to the department after suffering from dental trauma, and hence, a thorough medical examination was done prior to the dental checkup to rule out such severe complications.

The diagnosis can be delayed since standard hemostasis assay including prothrombin time, activated partial thromboplastin time, fibrinogen level, platelet count, and platelet function testing are normal as factor XIII acts when fibrin has already formed.[9] Hence, none of these tests are capable of detecting a deficiency in factor XIII.[7]

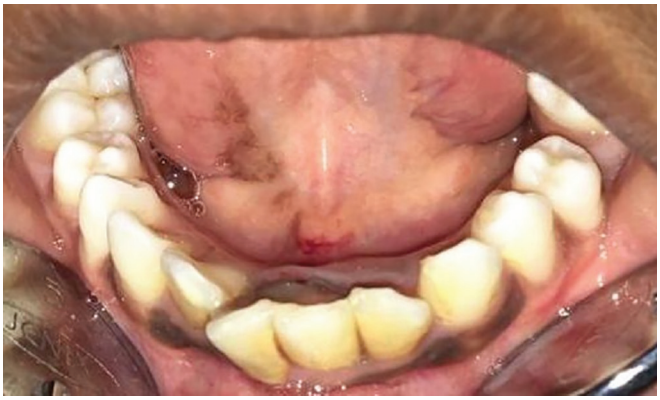

Fig. 6: Case 3—buccal displacement and lingual clot with respect to 41, 31, and 32

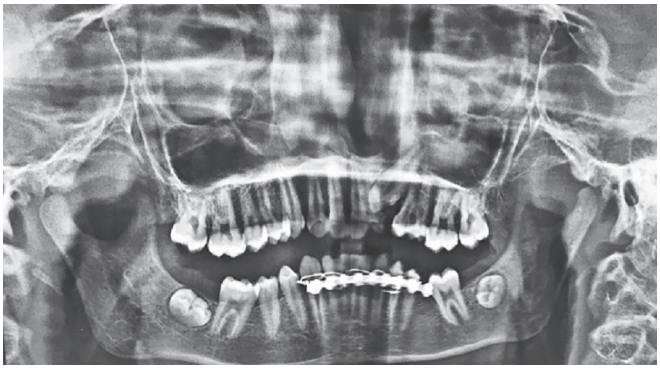

Fig. 8: Case 3—follow-up orthopantomograph at the end of 8 weeks and prior to removal of arch bar

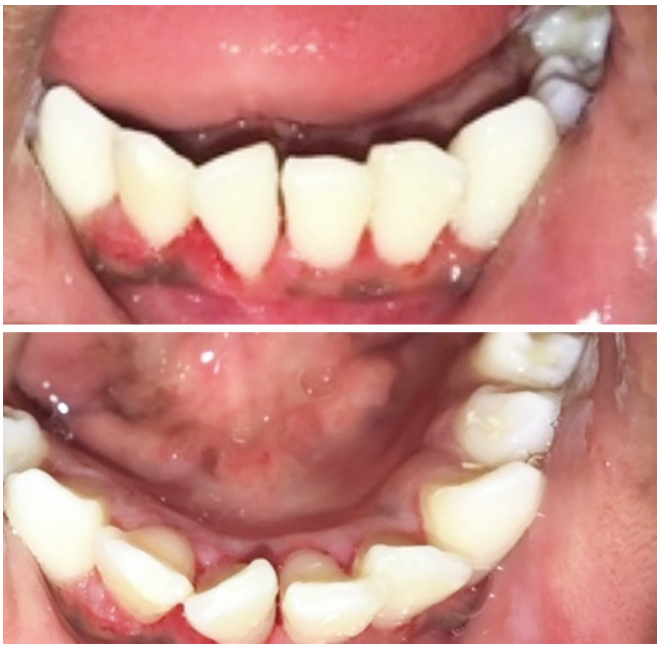

Fig. 9: Case 3—immediate postoperative picture after arch bar removal and oral prophylaxis

Assessment of clot stability is a diagnostic screening test for this deficiency. Dissolution of a clot in 5 mol/L urea, 2% acetic acid, or 1% monochloro acetic acid is indicative of factor XIII deficiency. All the above-mentioned cases were diagnosed using urea clot lysis test.

Plasma-derived sources of factor XIII, namely, whole blood, fresh frozen plasma, and cryoprecipitate have been widely used to treat this deficiency due to the ease of availability. Factor XIII concentrate from plasma is the treatment of choice for long-term prophylaxis as it contains adequate and reliable concentrations of factor XIII in optimal volume with fewer contaminations and is virally inactivated.[10] Due to unavailability of factor XIII concentrate in India, the patients were transfused with plasma derivatives.

Factor replacements (1 unit cryoprecipitate per kg weight) along with antifibrinolytic agents like tranexamic acid (25 mg/kg twice a day for 3–5 days starting prior procedure) and antibiotic prophylaxis (20–40 mg/kg divided over twice or thrice a day) must be given to such patients prior to dental procedures. However, at the same time, each case should be assessed individually keeping in mind the treatment needs of the patient, whether active dental intervention is needed. Antifibrinolytic agents like epsilon aminocaproic acid can be used postoperatively to protect the formed clot.[11]

Factor XIII deficiency is one of the few coagulation disorders where greater emphasis is placed on primary prophylaxis. Prophylactic treatment (10/20 U kg factor XIII every 4–6 weeks) is recommended for all patients diagnosed with severe factor XIII deficiency to prevent life-threatening bleeds.[12] A new prophylactic therapy is FXIIIA-subunit recombinant (rFXIIIA-subunit) injections 35 IU/kg monthly.

Conclusion

Factor XIII is a rare inherited disorder of the coagulation cascade, which may affect limited sections of the population. Prophylactic factor replacement therapy is now significant in maintaining the general health status of the child and avoiding complications. It is rare for a dental professional to come across such cases and be involved in their management along with medical professionals. Factor replacement therapy along with antifibrinolytics prior to dental procedures must be advised depending on the invasiveness of the procedure.

Clinical Significance

Treating these cases poses a challenge which may be successfully overcome by adopting a multidisciplinary approach in conjunction with the child's hematologist and adhering to requisite prophylactic measures recommended by the hematologist.

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