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CASE STUDY

Dental extraction in congenital factor VII deficiency with inhibitor – a case report

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Background: Hereditary factor VII (FVII) deficiency is a rare bleeding disorder with autosomal recessive inheritance, and FVII deficiency with an inhibitor is extremely rare. There is sparse information in the literature on the management of tooth extraction in patients with FVII deficiency and an inhibitor. **Case description:** We report the case of a five-year-old child with FVII deficiency and an inhibitor who underwent dental extraction. The child had had multiple bleeding episodes including intracranial haemorrhage and had a history of severe allergic reaction to the infusion of recombinant FVII. The tooth was extracted using lignocaine gel and the antifibrinolytic agent oral tranexamic acid. **Conclusion:** The extraction of a deciduous tooth in a patient with FVII deficiency and an inhibitor was undertaken without bleeding complications. There are currently no guidelines regarding management of this type of case. Further studies and evidence are required so that management can be standardised.

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A rare case of extraction of a deciduous tooth in a child with factor VII deficiency and an inhibitor calls for standardised guidelines for the management of such patients.

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Hereditary factor VII (FVII) deficiency or Alexander's disease is a rare bleeding disorder with autosomal recessive inheritance , and causes both spontaneous bleeding and excessive or prolonged bleeding after injury or trauma [1]. It is commonly seen in births following consanguineous marriage with family who have FVII deficiency.

FVII (labile factor or proconvertin) is one of the vitamin K dependent coagulation factors synthesised in the liver. Acquired deficiency can occur in liver disease, vitamin K deficiency and in those taking oral anticoagulants. Acquired conditions have to be excluded before diagnosing hereditary FVII deficiency. The first case of FVII deficiency was reported in 1951. The incidence is around 1 per 300,000–500,000 population and there is no gender difference. FVII has the shortest half-life (3–4 hours) among the coagulation factors. The normal FVII activity is 50–150%. Patients may present with a wide variation in clinical symptoms, ranging from asymptomatic to life-threatening bleeding. One third of individuals with FVII deficiency may never have any bleeding problems. FVII deficiency can cause epistasis, bleeding of the gums, easy bruising, prolonged or excessive bleeding following surgery or physical injury, haemarthrosis, haematuria, menorrhagia and rarely intracranial hemorrhage. Rarely FVII deficiency can cause thrombotic events like ischaemic stroke which may be difficult to manage [2]. FVII deficiency is classified as severe (FVII activity of less than 10% with risk of spontaneous major bleeding), moderate (FVII activity of 10–20% with risk of triggered bleeding) or mild (FVII activity of 20–50% where the patient is mostly asymptomatic). Diagnosis of FVII deficiency is based on discordance between a prolonged prothrombin time (PT), elevated international normalised ratio (INR) and normal activated partial thromboplastin time (APTT) in presence of normal platelet count. Diagnosis is confirmed by FVII assay. Acquired causes of FVII deficiency have to be ruled out. Genetic testing is not routinely required although, if available, may identify heterozygous or homozygous gene mutation [2].

Patients with congenital FVII deficiency who require surgery can be treated efficiently and safely using recombinant activated FVII (rFVIIa) and antifibrinolytic agents [3]. The recommended dose of rFVIIa is 15–30mcg/kg and must be given at intervals of four to six hours until coagulation parameters become normal [4]. Other treatment alternatives include fresh frozen plasma (FFP) and prothrombin complex concentrate containing factors II, VII, IX and X. Maintaining a FVII level of at least 15–25% provides an adequate haemostatic level for most surgical procedures [5]. Studies show the administration of rFVIIa in spine surgery reduces the total perioperative blood loss and the total volume of intraoperative blood transfusion compared with tranexamic acid, with no evidence of adverse effects [6].

Antibodies against FVII are extremely rare and very few cases are reported in the literature [7,8]. These antibodies cause increased clearance of FVII or neutralise its activity. The inhibitor activity can occur in patients with severe FVII deficiency who have previously received plasma FVII-containing concentrates or rFVIIa for the treatment of various bleeding episodes. Monitoring of ELISA-detectable antibodies against FVIIa in FVII-deficient patients undergoing treatment with rFVIIa can identify seropositive cases [9]. A study conducted in Iran to assess the prevalence of FVII inhibitors in 50 patients with congenital FVII deficiency under on-demand or prophylaxis treatment with rFVIIa showed two patients (4%) developed an inhibitor [10]. Treatment with immunosuppressive therapy consisting of corticosteroids and cyclophosphamide may result in normalisation of FVII levels and resolution of bleeding symptoms in acquired FVII deficiency and should be considered as first-line management for patients with this condition [11].

As FVII deficiency with an inhibitor is extremely rare there are not many reported cases in the literature, or guidelines on managing dental extractions in such cases. Against this backdrop we report a case of extraction of a deciduous tooth in a child with FVII deficiency with an inhibitor.

CASE REPORT

A five-year-old male child weighing 17kg reported at the dental outpatient department for extraction of his deciduous mobile right lower central incisor. The permanent tooth had begun to erupt, and the child's mother was concerned that severe bleeding would occur if the tooth came out at home. The child was a known case of FVII deficiency with an inhibitor and was born by full term normal delivery to non-consanguineous parents. Neither of his parents had a history of similar bleeding disorders in their family. The first bleeding episode in the child was reported in the right ankle joint at the age of three months and resolved spontaneously. The second bleeding episode occurred during the ninth month in the right ankle and right shoulder, which led to the diagnosis of FVII deficiency (prolonged INR with normal APTT and platelets, FVII activity was 0.6 BU/ml). The inhibitor level gradually diminished and by the age of three years had reached zero.

The child experienced multiple episodes of joint swelling which were managed locally with rest and cold compression. Treatment with FVII infusion was avoided because of the previous severe allergic

reaction. In January 2018 the child fell and developed a subdural haemorrhage. Since there was no deterioration in the Glasgow Coma Score (GCS) of the child and no midline shift in the MRI, he was managed conservatively in the intensive care unit (ICU) with intravenous tranexamic acid.

The child was admitted to the haemophilia ward at the Government District Hospital, Aluva, Kerala, India, for dental extraction and was started on oral tranexamic acid 250mg six-hourly. Extraction was undertaken on the following day after applying lignocaine gel as local anaesthetic. Post-extraction, a cotton pack soaked with tranexamic acid was placed on the extraction socket and oral tranexamic acid continued for the next three days. The child was observed for one more day as an inpatient and discharged after ensuring haemostasis. Post-discharge the child was followed up at the haemophilia treatment centre and there was no further bleeding from the extraction site.

DISCUSSION

The management of dental extraction in a person with a bleeding disorder includes the use of haemostatic agents and prophylactic treatment with the deficient factor [12]. There are few reports of managing dental extraction in patients with severe FVII deficiency. A case report by Weinstock et al. concluded that the degree of FVII deficiency poorly correlates with bleeding risk [13]. This is supported by the findings of Kim et al. in patients with congenital factor VII deficiency who underwent surgery including dental extraction [3]. There are no proper guidelines for the management of dental extractions in patients with FVII deficiency with an inhibitor. A study by Shams et al. found that two of their 50 patients with congenital FVII deficiency developed inhibitor activity [10]. Success in managing patients with inhibitors varied. One 14-year-old boy who was diagnosed in the neonatal period with FVII deficiency and had been managed with rFVIIa developed a high titre inhibitor and was managed with on-demand therapy with FEIBA (factor VIII inhibitor bypass activity). The second patient, a 70-year-old man diagnosed with inhibitor activity at the age of 66 years, was treated several times with rFVIIa but there was no change in his inhibitor activity.

In the case of our child, after developing a severe allergic reaction to infusion of FVII, all further bleeding episodes were managed conservatively with rest, cold compression and tranexamic acid without using FVII infusion. Dental extraction in this patient might have led to profuse bleeding, and hence was deemed difficult. Due to his previous severe allergic reaction to rFVIIa infusion, severe bleeding during extraction could have been catastrophic. Tranexamic acid, a synthetic analogue of amino acid lysine, reversibly binds to the lysine receptor sites of plasminogen and prevents conversion to plasmin thus preventing fibrinolysis. Tranexamic acid has also been shown to have direct inhibition of plasmin activity. Studies show replacement therapy with recombinant and plasma-derived FVIII and IX in combination with tranexamic acid produces excellent haemostasis in patients with haemophilia A and B [14], though we could not find similar studies in FVII deficiency with an inhibitor.

In the present case oral tranexamic acid was used for effective haemostasis. Local anaesthetic injection was avoided and instead lignocaine gel was used. As the extraction was of a deciduous tooth, the wound was not sutured and a cotton pack soaked with tranexamic acid was placed over the socket. There was no bleeding and the patient was discharged the next day with advice to report in case of bleeding. Another local haemostatic agent that warrants further research in cases of dental extraction in patients with FVII-deficiency is the Ankaferd Blood Stopper (ABS). This has been evaluated for the control of bleeding following tooth extraction in patients with haemophilia A, with the conclusion that it can be considered as an alternative and effective local haemostatic agent and can help reduce the use of clotting factor concentrates in this type of surgery [15].

CONCLUSION

This case report shows the concerns in the extraction of a deciduous tooth in a case of FVII deficiency with an inhibitor. The case was managed successfully through prophylactic administration of oral tranexamic acid and local application of lignocaine gel for the extraction, and the use of a cotton pack soaked with tranexamic acid for haemostasis in the post-extraction period. FVII deficiency with inhibitors may present either with acute haemorrhage or with an elective procedure where haemorrhagic complications may need to be dealt with. Considering the anecdotal nature of this report, we feel that further studies and evidence are needed so that a standardised regimen may be formulated for the management of these patients.

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