A Case of Multiple Mandibular Molar Extractions for a Hemophilia a Patient

Aesa Alzaroug Jaber[1], Alshame M. J. Alshame[2], Prabhu Manickam Natarajan[3], Asok Mathew[4]

[1]Assistant Professor in Oral Surgery, College of Dentistry, University of Science and Technology of Fujairah, [2]Assistant Professor, Department of Oral Surgery, Sebha University, Libya, [3]Associate Professor in Periodontics, College of Dentistry, University of Science and Technology of Fujairah, UAE, [4]Clinical Assistant Professor in Oral Medicine, College of Dentistry, University of Science and Technology of Fujairah, UAE

Abstract

Hemophilia A is a genetic coagulation disorder associated with a deficiency of clotting factor VIII.

It can be inherited or acquired and have different levels of severity. The present case report describes a Libyan male patient with Factor VIII deficiency who underwent multiple remaining roots extraction.

The patient was a 26-year-old Libyan male with history of hemophilia A of mild type. The patient underwent blood tests and imaging to assess the severity of hemophilia and the condition of the surgical area. The blood examination revealed normal Bilirubin level (0.6), low levels of, RBC (4.55), HGB (10.9), PT (17.7) and slight changes in platelet count and Factor VIII level.

The treatment plan for the day of surgery was accordingly, the patient was administered Factor VIII 24 hours before the day of surgery. The patient underwent the multiple roots extraction of lower left first and second molar under local anesthesia using 2% Lidocaine with 1:80, 000 Adrenaline. The Injection technique was regional nerve block (inferior alveolar, Lingual, and long buccal nerve block).

After extraction, direct pressure on the area using a damp gauze swab, maintained for at least 30 min, a hemostat and multiple thread suture were applied. One hour after surgical removal of the roots again the patient administered Factor VIII.

There was no subsequent bleeding or complications at follow-up in the first three days. In the fourth day there was moderate bleeding at the extraction sockets continued for a day. At fifth day the patient was admitted at the Sebha Medical Centre. The bleeding stopped after 24 hours.

Treatment plan in the Medical Centre was administration of factor FVIII, tranexamic acid 500 mg three times a day and vitamin K once a day. All injections were given intravenously. Then the patient discharged from the Centre in the sixth day after bleeding controlled. The wound had healed completely without abnormalities.

Keywords: *Bleeding, extraction, Factor VIII, hemophilia A*

Introduction

Bleeding may occur at different sites in the body, including the oral cavity, in patients with bleeding disorders, and it may also occur during dental treatment; this may delay a dental surgical treatment and prolong the recovery after the surgical intervention in most cases. Hemophilia A is a genetic bleeding disorder associated with the deficiency of clotting factor VIII (FVIII) [1, 2,3].

It can be inherited or acquired and have different levels of severity [4,5]. It is broadly divided into hemophilia A (deficiency of factor VIII), hemophilia B or Christmas disease (deficiency of factor IX), and hemophilia C or Rosenthal syndrome (deficiency of factor XI). Other variants include parahemophilia (Owren's disease),

which occurs due to factor V deficiency, and acquired hemophilia.[19-20]

Complications in hemophiliacs include musculoskeletal complications such as chronic hemophilic arthropathy, synovitis, contractures, pseudotumor formation, development of inhibitors against factor VIII, and most importantly transfusion-related infections such as human immunodeficiency virus (HIV), hepatitis B virus (HBV), hepatitis C virus (HCV), hepatitis A virus.[21-22]

In this case report, we describe a patient with Factor VIII deficiency that presented with gingival bleeding around badly decayed mandibular left first and second molar.

Case Report

Chief complaint

A twenty-six year-old Libyan male with blood type A Rh – (negative) presented at the Balkis- Alshame private Dental clinic in Sebha City (Libya). The patient had been referred from the Algatroun General Hospital in South West of Libya. The chief complaint was mild pain and bleeding in the lower left mandibular first and second molars roots, and he requested for extraction of the remaining roots.

The patient had a mild hemophilia A. The blood test results showed that the factor VIII activity was about 15%–20%. He had no history of underlying systemic conditions.

Medical history

The patient was diagnosed with history of hemophilia, and he had blood transfusion since 3 years back, no history of diabetes. The patient had no history of previous complications of tooth extraction. He reported no family history of hemorrhagic disease.

Allergies

The patient has no history of allergic reaction.

General examination findings

The patient was conscious oriented, not Dyspnia, no tachycardia, pallor, no external bleeding, and no jaundice, slightly thin, and with a height of approximately 160 cm.

Intraoral and imaging findings

Clinical oral examination showed that the patient has a bad oral hygiene, presence of dental calculus, gingivitis and multiple remaining roots, and impacted lower third molars.Figure 1.

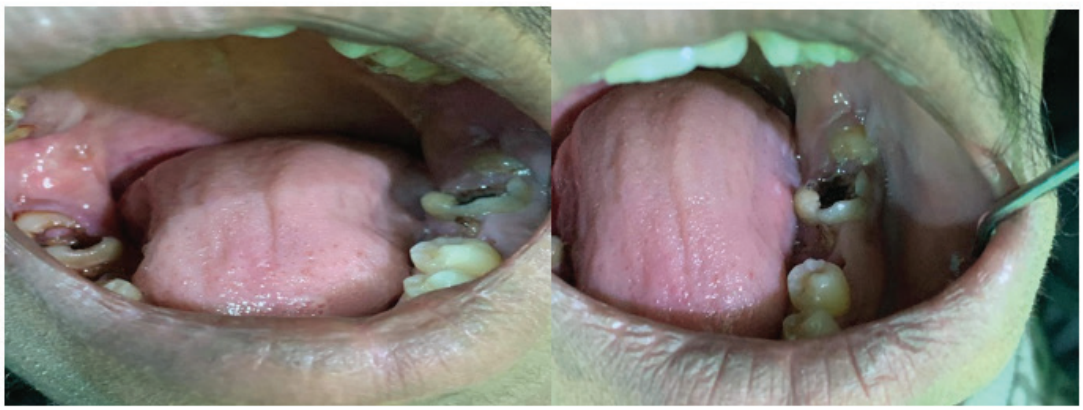


Figure 1: Preoperative intraoral view

Bone resorption was observed on panoramic radiographs; the resorption was especially prominent in the lower left side around roots of the first and second molars and around the remaining root of the lower right molars. Moreover, panoramic view revealed horizontally impacted lower right and left third molars, Figure 2.

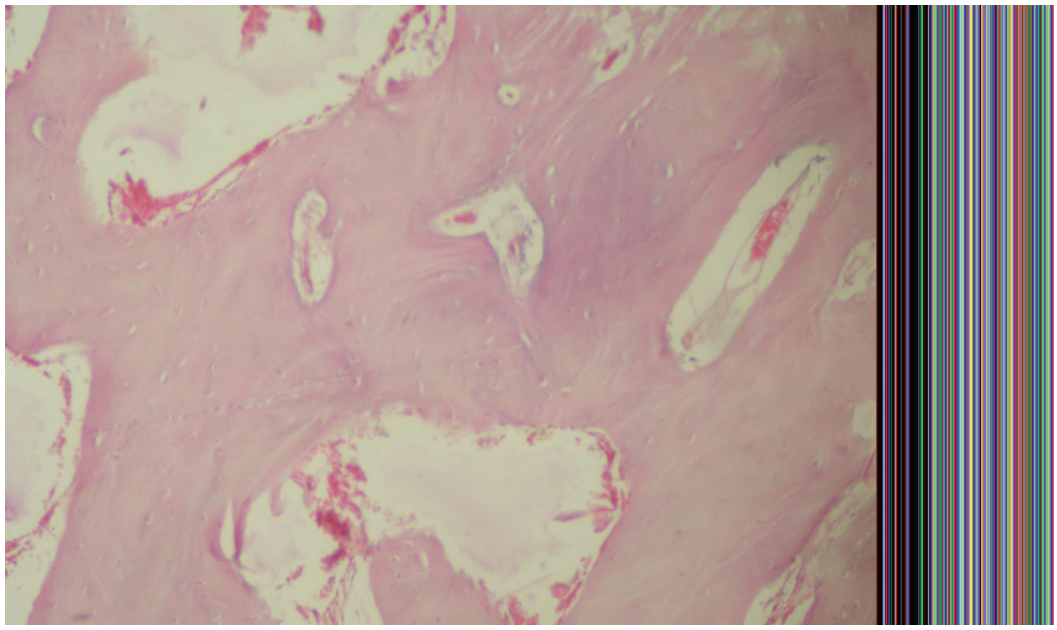


Figure 2: Shows preoperative radiographic condition of the teeth and alveolar bone in both jaws.

Blood Test Results

The blood test results showed a low platelet count (17.5 × 104/uL) and a low Factor VIII concentration in plasma (15%); the hemoglobin (HGB) level was (10.9 g/dl) [Table 1].

In addition, the results of blood tests revealed a prolonged prothrombin time (PT: 17.7 Sec), reference range: 11.0–15.0 Sec), increased International Normalized Ratio (INR: 1.5) standard value: 1.0 -1.3.

Total Bilirubin (0.6 mg/dl), Direct Bilirubin (0.3 mg/dl), liver function Test, Alanine aminotransferase (GPT: 6 U/L), aspartate aminotransferase (GOT 23U/L), kidney function Test, creatinine (0.98), urea (22 mg/dl). Glucose fasting (74mg/dl, Na^+ (139.7 mmol/l) , K+ (3.8 mmol/l), Ca+ (1.08 mmol/l) [Table 1].

Clinical diagnosis

Acute apical periodontitis of the lower left first and second molar area with mild hemophilia A disorder.

Treatment Course

The patient was admitted to Sebha Medical Centre, after the condition of the remaining root of the left lower first and second molars were assessed.

A blood test was made to assess the severity of the hemophilia by evaluating the Factor VIII level.

A Complete Blood Count (CBC) was also performed, Red Blood Cells (RBC), White Blood Cells (WBC), Platelets count(PLT) and Hemoglobin (HGB). Levels, of urea nitrogen, creatinine, sodium, potassium, calcium, total bilirubin, direct bilirubin, Alanine aminotransferase, aspartate aminotransferase, Prothrombin time, platelets account, hemoglobin, fasting blood glucose and blood sugar were measured. The results showed he had a mild hemophilia A; Factor VIII activity was about 15%–20%. There was a slight increase in PT, INR, [Table 1]. These findings were consistent with the medical history of the patient. The extraction of the lower left first and second molars roots was done after the patient administered Factor VIII 24 hours before dental extraction.

Table 1: shows different blood investigations

No	Tests	Test results
1	Red Blood Cells (RBCs)	4.5 10*12/L
2	White Blood Cells (WBCs)	4.3 10*g/L
3	Platelet Count	(17.5 × 104/uL)
2	Factor VIII concentration in plasma	(15%)
3	Hemoglobin (HGB)	(10.9 g/dl)
4	Prolonged prothrombin time(PT)	(17.7 Sec)
5	International Normalized Ratio (INR)	(1.5)
6	Total Bilirubin	(0.6 mg/dl)
7	Direct Bilirubin	(0.3 mg/dl)
8	Alanine aminotransferase (GPT)	(6 U/L)
9	Aspartate aminotransferase (GOT)	(23U/L)
10	Creatinine (0.98)	(0.98 mg/dl)
11	Urea	(22 mg/dl)
12	Fasting Blood Sugar (FBS)	(74mg/dl)
13	Sodium (Na+) (139.7 mmol/l)	(mmol/l)
14	Potassium (K+)	(3.8 mmol/l),
15	Calcium (Ca+)	(1.08 mmol/l)

The treatment plan for the day of surgery was to ensure that INR would not be increased, and prolongation of PT would remain mild. The patient was administered FVIII (Nuwiq (500 IU) Simoctocog alfa (recombinant human coagulation factor VIII, Octapharma AB, Sweden) intravenously 24 hours before the surgical the treatment Figure 3.

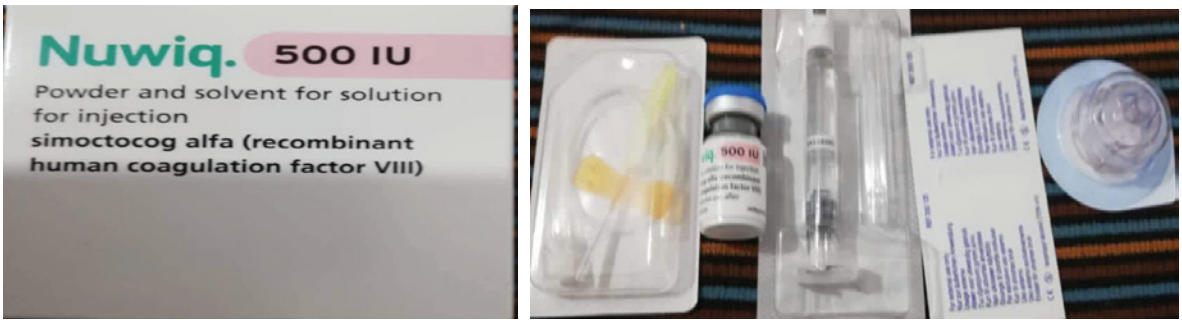


Figure 3: Shows a Huma coagulation factor VIII that given to the patient.

The patient underwent the multiple roots extraction of lower left first and second molar under local anesthesia using 2% Lidocaine with 1:80, 000 Adrenaline. The Injection technique was regional nerve block (inferior alveolar, Lingual, and long buccal nerve block). After extraction, direct pressure on the area using a damp gauze swab, maintained for at least 30 min, a hemostat and multiple thread suture were applied. Figure 4.

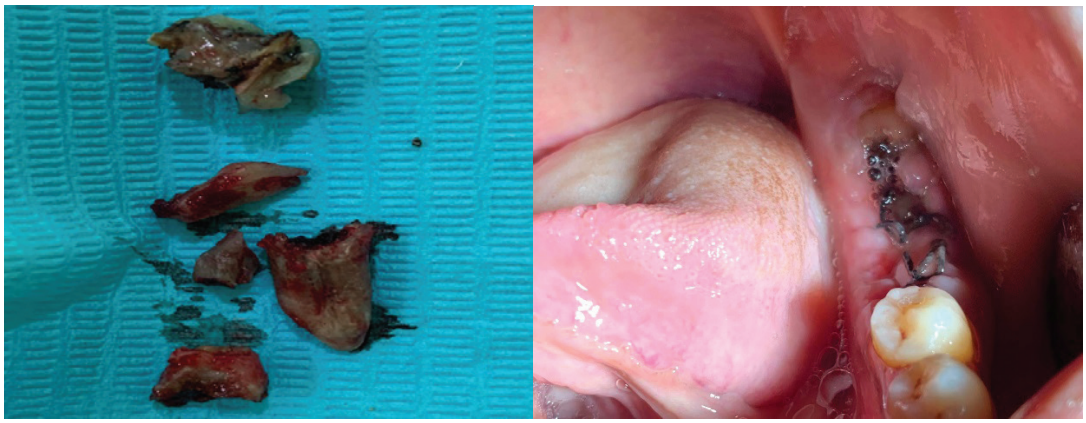


Figure 4: Shows multiple extracted roots and the multiple threads suture in place.

There was no subsequent bleeding or other complications on the first three days after extraction.

In the fourth day there was moderate bleeding at the extraction socket continued for a day.

At fifth day the patient was admitted at the Sebha Medical Centre. The bleeding stopped after 24 hours. A Complete Blood Count (CBC) was also performed. Red Blood Cells (RBCs: 3.41), White Blood Cells (WBCs: 8.1), and Hemoglobin (HGB: 7.7). There was significant decrease in number of red blood cells and hemoglobin level [Table 2].

Table 2: Shows blood test results (RBC, WBC, and HGB) following moderate bleeding from extraction sockets for one day.

No	Tests	Tests result
1	Red Blood Cells (RBC:)	(3.41 10^12/L)
2	White Blood Cells (WBC)	(8.1 10^9/L)
3	Hemoglobin (HGB)	(7.7 gd/L).

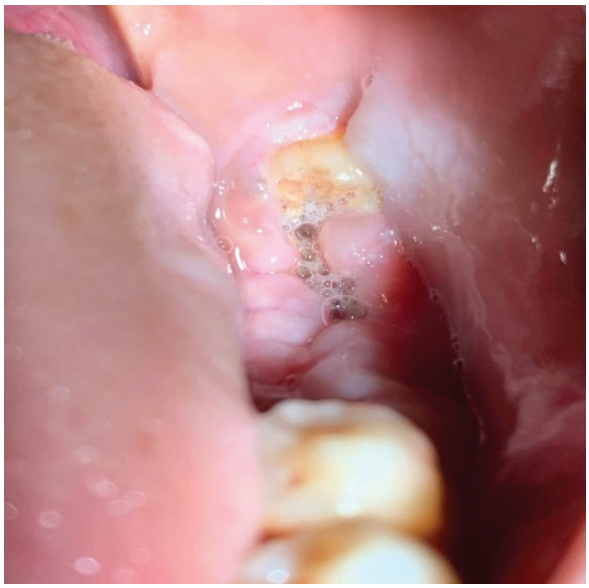
Treatment protocol in the Medical Centre was administering of factor FVIII (500 IU), tranexamic acid 500 mg three times daily and vitamin K once a day injection intravenously. Then the patient discharged from the Centre in the sixth day after bleeding controlled.

Ten days postoperatively, suture was removed at the extraction sockets and the wound had healed completely without abnormalities.

Figure 5: A photograph showing the condition of the extraction area after the 10 days postoperatively. There was no feature of bleeding, swelling and redness in and around the extraction sockets.

With regard to this article, there is no conflict of interest to disclose.

Figure 5: shows the condition of extraction area 10 days post operatively



Discussion

Factor VIII or antihemophilic factor present at the intersection of the intrinsic and the extrinsic coagulation pathways and an essential blood-clotting protein. It is encoded by the F8 gene and plays a major role in the fundamental pathway of blood coagulation.[6]

Hemophilia A causes prolonged bleeding and usually affects males more than females. The bleeding can be internal, inside joints and muscles, or external, such as following minor injuries, dental procedures, trauma, or accidents[2,6]. In hemophilia A, the Complete Blood Count(CBC) including the platelet count and PT are usually normal. However, sometimes, the hemoglobin (HGB) level and the Red Blood Cells count(RBCs) can be low, especially if the patient has heavy or prolonged bleeding[7,8].

In the preset case the similar figures of blood screening were reported after complete blood count was performed. Factor VIII is considered a cofactor for Factor IX which converts Factor X to the activated form of Factor X (Xa) to form blood clots in the blood coagulation mechanism, in the presence of Ca++ and phospholipids[9]. Its mechanism of action is unknown, but its major effect is to increase the rate of the reaction. The defects in Factor VIII gene and the genetic deficiency in Factor VIII result in hemophilia (a common X-linked recessive coagulation disorder)[9]. The normal Factor VIII activity is 80%–140%, and symptoms correlate with Factor VIII activity. However, only 25% of FVIII activity is required for the normal hemostasis[10]. Prothrombin Time is also prolonged in patients who are receiving Vitamin K antagonists and anticoagulants, such as warfarin[11,12]. Hemophilia A is usually treated mainly with infusion of recombinant Factor VIII; this treatment is currently widely preferred due to its greater safety[13,14]. However, in some cases, this treatment be used only as needed[15]. Some cases with a mild can often be managed with drugs that release stored Factor VIII from blood vessel walls. Moreover, current studies have indicated using gene therapy in hemophilia A treatment[16].

Regarding to local anesthetic administration, there are no restrictions with respect to the type of local anesthesia used, those with vasoconstrictors may provide additional local hemostasis. Buccal infiltration is sufficient to anesthetize all the upper teeth and lower anterior and premolar teeth. Mandibular molar teeth are anesthetized using inferior alveolar nerve block after increasing the clotting factor levels by appropriate replacement therapy, as there is a risk of bleeding into the muscles along with potential airway compromise due to a hematoma in the retromolar or pterygoid space. In contrast, the intraligamental technique or interosseous technique should be considered as a potential alternative to the nerve blocks.[21-23] In the present case the inferior alveolar nerve block was given to anaesthetize the roots of the mandibular left first and second molars.

Regarding, the bleeding at the extraction socket or the soft tissues around, local treatments like direct pressure on the area using a damp gauze swab, maintained for at least 30 min should be considered. Suturing of the wound, application of local hemostatic agents, and use of tranexamic acid as a mouthwash can be administered[24].In the present case, the patient was treated with Factor VIII infusion and when the patient admitted to the medical three days post extraction due to moderate bleeding from the extraction sockets; the bleeding completely stopped gradually after 24 hours. Normally, the tooth extraction cavity is filled with clot within 1 day after tooth extraction; then, it is covered with a fibrin network.

In blood clots, new blood vessels and regenerated bone granulation tissue organically combine to form a callus bone. In contrast, in the gingival area, the vascular networks and the fibroblasts extend along the surface of the clot toward the center of the wound, and the epithelial

covering is completed in about 2 weeks.[17]It is important for safety reasons to administer factor VIII 24 hours before the extraction and one-hour post extraction. In addition, administration of tranexamic acid, or vitamin K[18].

In patients with persistent gingival hemorrhage or those with persistent bleeding after tooth extraction, it is important to consider the possibility of blood coagulation disorders and to measure blood coagulation factor levels. Moreover, the assessment by an internal medicine physician should be promptly arranged, and follow-up with hematologists should be scheduled during treatment.

Conclusion

Hemophilia should be suspected in patients with a history of easy bruising in early childhood, spontaneous bleeding, particularly into the joints, muscles, and soft tissues, or prolonged bleeding following trauma or surgery. Hemophilia runs in families; therefore, a family history of bleeding disorders should be carefully prompted. Hemophilic patients form a priority group for dental and oral health care, since bleeding after dental treatment may cause severe or even fatal complications.

In addition, oral hygiene maintenance and prevention of dental diseases is of great consequence to improve the quality of life and avoid the risks of surgery. The close cooperation between hematologists, oral surgeons, and general dentists will support to deliver greatest care and appropriate treatment for patients with hemophilia A, avoiding all undesirable consequences. Genetic counseling is an important part of hemophilia care to help people with hemophilia. Dentists can not only provide comprehensive oral care for hemophilia (A) patients but also contribute in the genetic counseling through wide range of tests for diagnostic and carrier detection, as well as individual counseling.

References

1. Acharya S, Rathore K, Mahapatra U, Sethi S, Sahu N. An unusual oral manifestation of hemophilia in a child. J Int Oral Health 2018; 10:314-6. [Doi: 10.4103/jioh.jioh 183 18].
2. Mansouritorghabeh H. Clinical and laboratory approaches to hemophilia A. Iran J Med Sci 2015;40:194-205.
3. Kisseih E, Yerrapotu N, Yadav D, February M. A case of hemophilia A presenting in a neonate and a review of the literature. Glob Pediatr Health 2017; 4:1-3.
4. Binet Q, Lambert C, Sacré L, Eeckhoudt S, Hermans C. Successful management of acquired hemophilia A associated with bullous pemphigoid: A case report and review of the literature. Case Rep Hematol 2017;2017.
5. Gale AJ. Continuing education course #2: Current understanding of hemostasis. Toxicol Pathol 2011; 39:273-80.
6. Van Cott EM. Evaluation of a prolonged prothrombin time: Commentary. Clin Chem 2008; 54:769.
7. Cocero N, Pucci F, Messina M, Pollio B, Mozzati M, Bergamasco L. Autologous plasma rich in growth factors in the prevention of severe bleeding after teeth extractions in patients with bleeding disorders: A controlled comparison with fibrin glue. Blood Transfus 2015; 13:287-94.
8. Mo L, Bao GC. Acquired factor VIII deficiency: Two case reports and a review of literature. Exp Hematol Oncol 2017; 6:8.
9. Lenting PJ, van Mourik JA, Mertens K. The life cycle of coagulation factor VIII in view of its structure and function. Blood 1998; 92:3983-96.
10. Butenas S, Parhami-Seren B, Undas A, Fass DN, Mann KG. The “normal” factor VIII concentration in plasma. Thromb Res 2010; 126:119-23.
11. Habib G, Nashashibi M, Khateeb A, Goichman S, Kogan A. Excessive prolongation of prothrombin time among patients treated with warfarin and admitted to the emergency room. Eur J Intern Med 2008; 19:129-34.
12. Nagarakanti S, Sappati H, Gunupati S, Ramesh Reddy BV, Chava VK. Dental management of a patient with incidentally detected hemophilia: Report of a clinical case. J Indian Soc Periodontol 2019; 23:281-3.
13. López-Villareal S, Rodríguez-Luis O, Cruz-Fierro N. Hemophilia A. Considerations in the dental management of pediatric patients. A case report. J Oral Res 2014; 3:173-7.
14. Ramos EA, Diamante M, Caruso D, Muiño JM, Baques A, Antonelli LB, et al. Outpatient minor oral surgery in patients with hemophilia: A case series of 23 patients. J Clin Exp Dent 2019;11:e395-9.

15. Liras A, Romeu L. Dental management of patients with haemophilia in the era of recombinant treatments: Increased efficacy and decreased clinical risk. BMJ Case Rep 2019;12. pii: e227974.
16. Nathwani AC, Davidoff AM, Tuddenham EGD. Gene Therapy for Hemophilia. Hematol Oncol Clin North Am 2017; 31:853-68.
17. Periayah MH, Halim AS, Mat Saad AZ. Mechanism action of platelets and crucial blood coagulation pathways in hemostasis. Int J Hematol Oncol Stem Cell Res 2017; 11:319-27.
18. Lin ZX, Woolf SK. Safety, efficacy, and cost-effectiveness of tranexamic acid in orthopedic surgery. Orthopedics 2016; 39:119-30.
19. Patton LL. Bleeding and clotting disorders. In: Greenberg MS, Glick M, Decker BC, editors. Burket's Oral Medicine: Diagnosis and Treatment. 10th ed. Hamilton, ON: BC Decker; 2003. pp. 454–77.
20. Rogaev EI, Grigorenko AP, Faskhutdinova G, Kittler EL, Moliaka YK. Genotype analysis identifies the cause of the "royal disease" Science. 2009;326:817.
21. Prabhu Manickam Natarajan et al. Hemorrhage control, infection prevention and application on anesthetics in exodontia of natal teeth. Acta Stomatologica Naissi, Vol 34, Issue 77, June 2018, 1813-1820.
22. Rodriguez-Merchan EC. Musculoskeletal complications of hemophilia. HSS J. 2010;6:37–42.
23. Nazif M. Local anesthesia for patients with hemophilia. ASDC J Dent Child. 1970;37:79–84.
24. Franchini M, Rossetti G, Tagliaferri A, Pattacini C, Pozzoli D, Lorenz C, et al. Dental procedures in adult patients with hereditary bleeding disorders: 10 years experience in three Italian Hemophilia Centers. Haemophilia. 2005;11:504–9.