CASE REPORT: A case of dental surgery intervention for a hemophilia A patient

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Case Report

A case of dental surgery intervention for a hemophilia A patient

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Abstract

Hemophilia A is a genetic coagulation disorder associated with a deficiency of clotting factor VIII (FVIII). It can be inherited or acquired and have different levels of severity. The present case report describes a male patient with FVIII deficiency who underwent dental surgical treatment. The patient was a 70-year-old male with a prosthetic mechanical aortic valve who had undergone ascending aortic replacement surgery and coronary artery bypass surgery. He also had a history of cerebral infarction with right paraplegia. Therefore, he visited our hospital for surgical dental treatment. The patient underwent blood tests and imaging to assess the severity of hemophilia and the condition of the surgical area. The treatment plan for the day of surgery was to ensure that markers for bleeding tests would not be increased and prolongation of the partial thromboplastin time (PTT) would remain mild; accordingly, the patient was administered FVIII before the surgical treatment under local anesthesia. The blood examination revealed a mild prolonged PTT and slight changes in platelet count and FVIII level. There was no subsequent bleeding or complications at follow-up, and the wound had healed completely without abnormalities.

Keywords: Bleeding, dental surgery, Factor VIII, hemophilia A

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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).[1-3] It can be inherited or acquired and have different levels of severity.[4,5]

In this case report, we describe a patient with FVIII deficiency that presented with gingival bleeding.

CASE REPORT

Chief complaint before hospitalization

A 70-year-old male with blood type A Rh + presented at the Department of Dentistry Oral and Maxillofacial Surgery of the Osaka City University Hospital (after getting the consent agreement from the patient). The first visit was on January 31, 2018; he had been referred from the Yao Tokushukai General Hospital in Osaka. The chief complaint was mild pain in the lower left 7th molar root,

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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%. The patient had a prosthetic mechanical aortic valve. He had undergone ascending aortic replacement surgery and coronary artery bypass surgery in February 2012, and he was started on warfarin.

He had a history of cerebral infarction with right paraplegia, and he was also started on aspirin (Bayaspirin, Bayer Group, Ltd., Japan) (100 mg) on February 2, 2012; he was still using aspirin on presentation.

Medical history

The patient was diagnosed with femoral hernia when he was around 11 years; during his treatment, he was also diagnosed with appendicitis and underwent an appendectomy. It took 3 months to recover. The patient underwent a hernia repair when he was 12 years.

The patient underwent a lower left third molar tooth extraction when he was 30 years; he continued bleeding for 3 days after the tooth extraction and was admitted at the Nippon Dental University Niigata Hospital. The bleeding stopped after 10 days. He also underwent laser treatment for the left eye retinal detachment when he was 60 years. The patient was treated for ascending aortic aneurysm, coronary artery disease, and aortic valve stenosis when he was 65 years. During this time, he was being followed up for hemophilia with observation only. The patient underwent curative colorectal polyp resection and was started on treatment for cerebral infarction when he was 68 years.

He reported no family history of hemorrhagic disease.

Allergies

The patient was allergic to some elastic cotton bandage (Eco-hota, Hakujuji Co., Ltd.). He developed allergic complications, such as angioedema rash and itching, 15 min after using it.

Present condition

General examination findings

The patient was slightly thin, with a height of 166.2 cm and a weight of 64.8 kg; he was mildly malnourished.

Intraoral and imaging findings

Horizontal bone resorption was observed in all jaws on panoramic radiographs; the resorption was especially prominent in the lower left side around the lower left 6th and 7th molars and around the remaining root of the lower left 7th molar.

Blood test results

The blood test results showed a low platelet count (17.5 × 10^4/uL) and a low FVIII concentration in plasma (14%); the hemoglobin (Hb) level and hematocrit were within the reference ranges.

In addition, the results of blood tests revealed a prolonged prothrombin time (PT: 24.2 s) (reference range: 11.5–14.5 s), increased International Normalized Ratio (INR: 1.90) (standard value: 1.0 ± 0.1), and prolonged activated partial thromboplastin time (APTT: 57.8 s) (reference range: 25–40 s).

Clinical diagnosis

Acute apical periodontitis of the lower left 7th molar area with mild hemophilia A disorder.

TREATMENT COURSE

The patient was admitted on February 5, 2018, and the condition of the remaining root of the left lower 7th molar was assessed [Figure 1]. A blood test was performed to assess the severity of the hemophilia by evaluating the FVIII level. A complete blood count (CBC) with a differential count of the white blood cells was also performed. Levels of reticulocytes, urea nitrogen, creatinine, uric acid sodium, potassium, chloride, total protein, albumin, total bilirubin, direct bilirubin, aspartate aminotransferase, aspartate aminotransferase, lactate dehydrogenase, PT, APTT, fasting blood glucose, fibrin degradation products, blood sugar, and C-reactive protein were measured. The results showed he had a mild hemophilia A; FVIII activity was about 15%–20%. There was a slight increase in PT, PT-INR, and APTT [Figure 2]. These findings were consistent with the medical history of the patient. The extraction of the lower left tooth roots was postponed until February 8.

The treatment plan for the day of surgery was to ensure that INR would not be increased, and prolongation of APTT

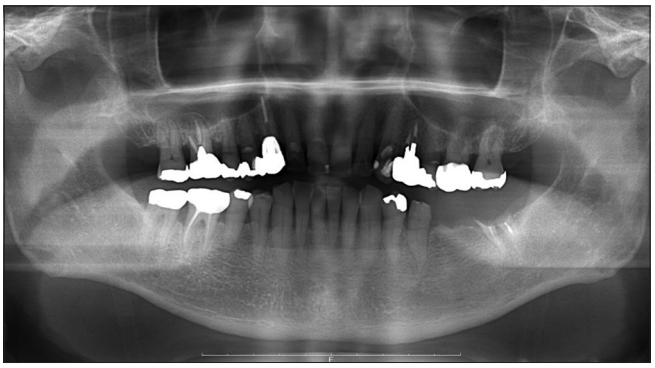

Figure 1: A panoramic X-ray at the first visit shows full bone resorption in the horizontal plane and the area around the roots of the lower left 7th molar

would remain mild. The patient was administered FVIII (Advate, Shire Pharmaceuticals Limited, Japan) (1500 units) intravenously before the surgical treatment.

Oral tranexamic acid (Transamin, Daiichi Sankyo, Japan) (250 mg) was started 4 days before February 8.

In the unlikely event that bleeding would be difficult to control, it was planned that FVIII would be added while monitoring INR, APTT, and levels of FVIII. It was also planned that menatetrenone (Vitamin K2) (Keitsu N, Eisai Co., Ltd., Japan) (10 mg) would be administered intravenously as a warfarin antagonist.

Aspirin was stopped before and resumed after the root extraction.

On February 8, the patient underwent the root extraction under 2% xylocaine local anesthesia. After the extraction, a surgical gauze and one thread suture were applied.

Tranexamic acid (250 mg) three times a day, after each meal, was prescribed for 4 days. There was no subsequent bleeding on follow-up, and the patient was discharged from the hospital on February 15, 2018. He continued with the follow-up as an outpatient.

On February 22, 2018, results of blood tests showed a slight change in platelet count, INR, APTT, and FVIII levels. Clinically, there were no complications, and the wound had healed slightly without abnormalities [Figure 3]. Teeth cleaning were performed at this time.

The patient came back to the hospital on March 14, 2018, for a follow-up, and the wound was completely healed. Results of blood tests showed a slight change in platelet count, INR, APTT, and FVIII levels; however, INR was within the reference range.

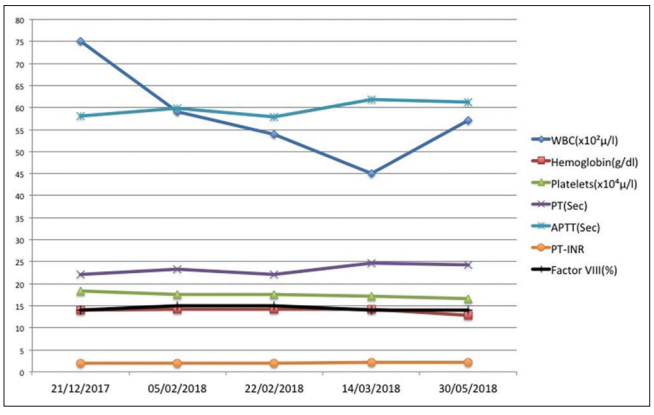

Figure 2: A line graph shows the progression of the coagulation tests during the treatment course

At the beginning of May, the patient had started working in his garden; however, 2–3 weeks later, he developed a swelling of the right lower limb, which was associated with pain and subcutaneous bleeding. On May 29, the patient stopped taking aspirin in the morning and started taking oral tranexamic acid (250 mg) at night. The patient underwent a blood test, and it showed slight mild abnormalities of platelet count, INR, APTT, and FVIII level. Clinically, he had a swelling (++) of the right lower limb and subcutaneous bleeding (+), but no bleeding in any other sites.

INR was within the control range, and the patient had mild anemia.

The treatment plan was to stop aspirin immediately and to restart it within 2 weeks. Tranexamic acid (250 mg) was also prescribed. The patient would be re-examined if there would be no improvement in the lower limb swelling.

DISCUSSION

FVIII 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] FVIII is considered a cofactor for FIX which converts FX to the activated form of FX (Xa) to form blood clots in the blood coagulation mechanism, in the presence of Ca++ and phospholipids.[7] Its mechanism of action is unknown, but its major effect is to increase the rate of the reaction. The defects in *F8* gene and the genetic deficiency in FVIII result in hemophilia A (a common X-linked recessive coagulation disorder).[7]

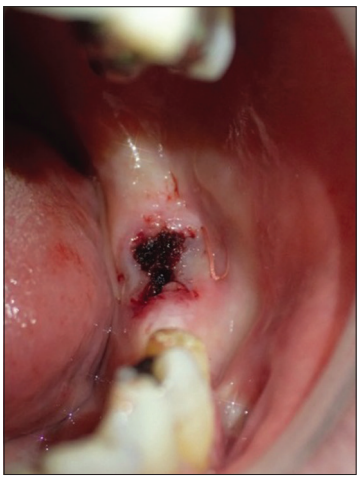

Figure 3: A photograph showing the condition of the extraction area after the treatment and the slightly healed wound without abnormalities. With regard to this article, there is no conflict of interest to disclose

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]

APTT and clotting time are usually prolonged in patients with the disease; therefore, these tests can be used as screening tests for hemophilia A.[8,9] The CBC (including the platelet count) and PT are usually normal. However, sometimes, the Hb level and the red blood cells count can be low, especially if the patient has heavy or prolonged bleeding.[10,11]

The reduction in FVIII activity was consistent with many other conditions; the patient had a prosthetic mechanical aortic valve, had a cerebral infarction with right paraplegia before, had undergone multiple surgical procedures, and was using aspirin and warfarin as well as other medications.

In this case, both PT and APTT were prolonged. This may have many explanations. The clotting mechanism has two pathways: the extrinsic and the intrinsic pathway. These two pathways then merge into a common pathway to complete the clotting mechanism.[6,10]

PT usually measures the clotting ability of factors I, II, V, VII, and X in the extrinsic and common pathways, whereas APTT measures the clotting ability of factors VIII, IX, XI, and XII in intrinsic and common pathways.[6,12] In addition, the complex formed by FIX and FVIII, which are in the intrinsic pathway, binds to FX, which is in the extrinsic pathway and activates it (converting it factor Xa).[1,13] Common symptoms of deficiency of extrinsic factors are purpura, nasal bleeding, gingival bleeding, excessive menstruation, and excessive bleeding after an operation; deficiency of intrinsic factors sometimes presents with severe bleeding, such as joint bleeding and intracranial hemorrhage.[4,6,7] This interrelation between the two pathways may explain why both test results were prolonged: it was due to a deficiency in any of these factors. In addition, PT is also prolonged in patients who are receiving Vitamin K antagonists and anticoagulants, such as warfarin.[14-16]

The normal FVIII activity is 80%–140%, and symptoms correlate with FVIII activity. However, only 25% of FVIII activity is required for the normal hemostasis.[7,17]

Hemophilia A is usually treated mainly with infusion of recombinant FVIII; this treatment is currently widely preferred due to its greater safety.[18,19] However, in some cases, this treatment be used only as needed.[20] Some cases with a mild can often be managed with drugs that release stored FVIII from blood vessel walls. In addition, recent studies have reported using gene therapy in hemophilia A treatment.[21]

In the current case, the patient was treated with FVIII infusion and during his hospitalization for 10 days after the dental procedure; the bleeding completely stopped gradually. Normally, the tooth extraction cavity is filled with clot within 1 day after tooth extraction; then, it is covered with a fibrin net.[4] In blood clots, new blood vessels and regenerated bone granulation tissue organically combine to form a callus bone.[4] On the other hand, in the gingival region, 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.[4,22]

It is important for safety reasons to administer tranexamic acid, or aminocaproic acid (which has an antagonistic effect on fibrinolytic enzymes contained in saliva and helps to maintain the blood clots) during invasive dental treatment, such as tooth extraction, some authors have suggested.[23] Although there was no abnormality in the number of platelets, primary hemostasis was achieved, fibrin nets and the clot were formed, and tranexamic acid was administered, it took about 10 days for the bleeding to completely stop during the hospitalization.

This suggests that FXIII activity should be in the treatment of disorders of hemostasis; it seems to be one of the necessary factors in achieving hemostasis. In the current case, there was a history of surgical operations; however, there was no problem in stopping the bleeding previously although the prolongation of PT and APTT had detected on blood tests. The cause of bleeding was investigated by the previous doctors. 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.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will

not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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