WHEN THE BLEEDING WON'T STOP:

A CASE REPORT ON A PATIENT WITH HEMOPHILIA

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ABSTRACT

A 39-year-old male developed severely prolonged bleeding after periodontal surgery because of a previously undetected clotting Factor XI deficiency (Hemophilia C). Diagnosis and treatment of this bleeding disorder are discussed.

Prolonged postsurgical bleeding poses a serious health hazard to patients. Most hereditary bleeding disorders are discovered in childhood after an injury or minor surgical procedure. A patient with a hereditary bleeding disorder who reaches adulthood without a history of prior excessive bleeding is rare. Therefore, the medical and dental histories must obtain such information so the dentist can observe the necessary precautions.

This paper reports the case of a 39-year-old patient with previously undiagnosed and unmanifested Factor XI deficiency. The deficiency was discovered after prolonged bleeding followed a gingival graft procedure. Diagnostic and therapeutic aspects of the disorder are also discussed.

CASE REPORT

The patient, a 39-year-old white Jewish male, was referred by his family dentist for a gingival graft in the mandibular incisor region. His medical history was normal, and showed no prior incidents of excessive bleeding. Local anesthesia was used (lidocaine 2 percent with epinephrine 1:100,000). An autogenous gingival graft[1] was placed near the mandibular left central and lateral incisors.

The graft was secured with 5-0 plain gut sutures (Figure 1). The donor site was the maxillary left palate. Analgesics (ibuprofen 800 mg and oxycodone 5 mg with acetaminophen 500 mg) were prescribed. The patient was instructed to return for a follow-up visit in one week.

On the fifth postoperative day, the patient returned because of bleeding from the palatal donor site. After anesthesia and hemostasis were achieved, a 4-0 silk suture was placed to ligate the lesser palatine artery.

On the eighth postoperative day, the patient again returned with bleeding from the palatal donor site. After local anesthesia, three additional palatal sutures were placed. The patient reported that he might be rubbing his tongue against the palatal wound, and that this might be partly responsible for the bleeding.

On the 10th postoperative day, the patient returned with bleeding from the palatal area and three more sutures were placed. Two days later, the patient reported that bleeding had resumed. He was immediately referred to the emergency room of a nearby community hospital for blood tests to rule out a bleeding or clotting disorder.

Test results indicated that the partial thromboplastin time was severely elevated. The patient was then evaluated by a hematologist. After additional laboratory tests, Factor XI deficiency was diagnosed. The patient's plasma level of Factor XI activity was only one-tenth of the normal level.

The patient first received three units of fresh frozen plasma which did not improve his condition. He was then hospitalized for two days. He received transfusions of 11 units of fresh frozen plasma to raise the Factor XI level to near normal. Partial thromboplastin times were checked after the initial and second four units, and after the 11th unit. After a

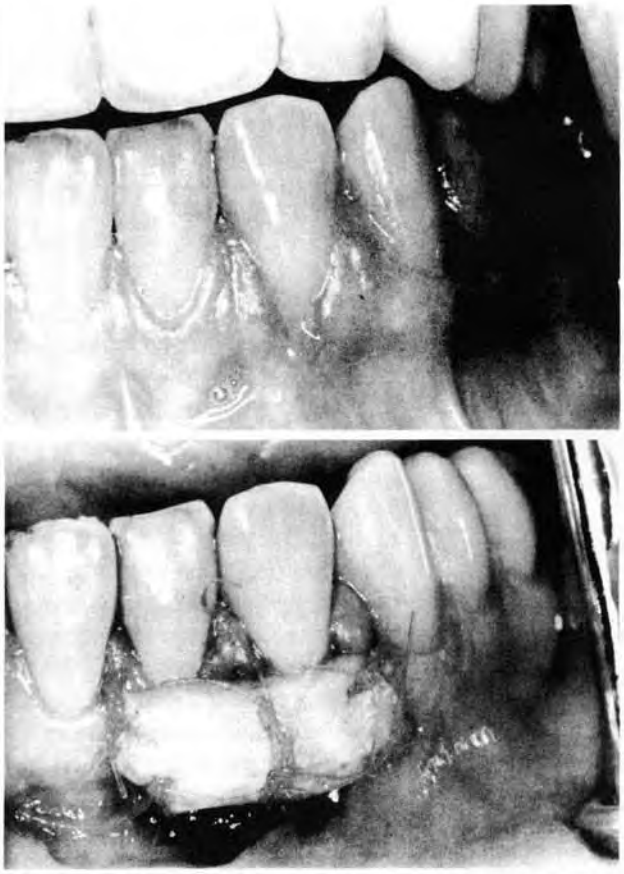

Figure 1. Photos taken the day of surgery. Top: Pre-surgical view of gingival recession, mandibular left lateral incisor. Bottom: Sutured gingival graft.

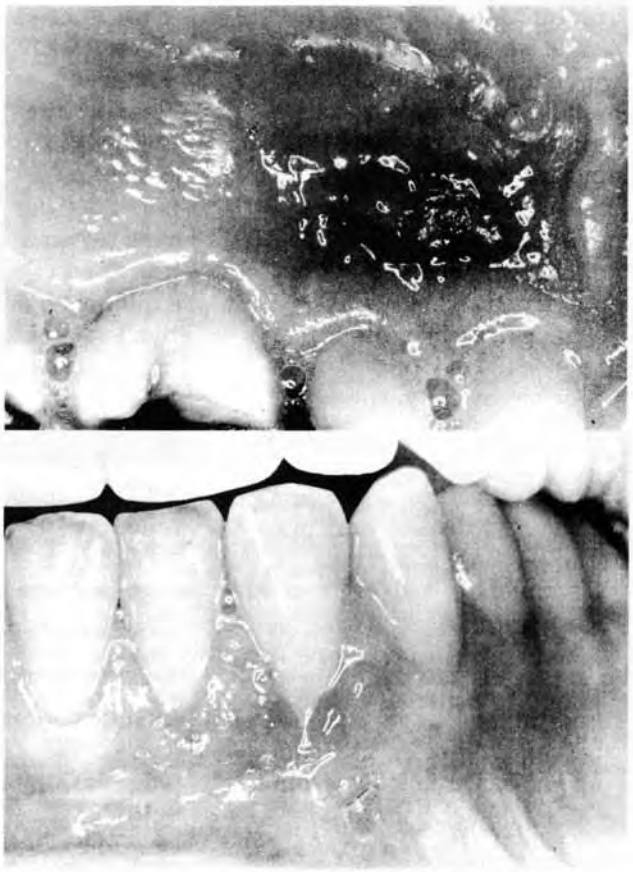

Figure 2. Three weeks after surgery. Top: Palatal donor site. Bottom: Recipient site. Severely delayed healing is noted.

clinically normal level of Factor XI was reached, bleeding stopped and healing progressed normally. The patient returned for removal of sutures on the 17th postoperative day, and healing progressed normally (Figure 3).

The patient returned to the hematologist for follow-up laboratory tests and medical counseling about his condition. No excessive bleeding occurred.

DISCUSSION

Factor XI deficiency, also called Hemophilia C, is an incomplete autosomal recessive trait. Factor XI deficiency is not gender specific, though it seems to have a preference for Jews of European descent.[3-5] Factor XI deficiency was first reported in 1953 by Rosenthal and others[6] who described three members of the same family with a mild hemorrhagic disease that differed from classic hemophilia. The patients showed slightly prolonged clotting time, but no history of spontaneous bleeding. The newly identified clotting factor, designated plasma thromboplastin antecedent, was severely deficient in these patients.

Factor XI deficiency is a rare clotting disorder of the intrinsic clotting pathway comprising only 7 percent of all hereditary bleeding disorders.[6] Two types of Factor XI deficiency are generally thought to occur. Major Factor XI deficiency appears in the homozygous patient with the level of Factor XI of less than 20 percent. Minor Factor XI deficiency (heterozygous patients) have levels of Factor XI ranging from 20 to 63 percent. Patients with factor levels higher than 63 percent are not considered to have a genuine Factor XI deficiency.

The patient described in this report was a 39-year-old Jewish male with no history of excessive bleeding. In fact, he had donated blood only five weeks earlier without incident. Bleeding after the gingival graft procedure originated from the palatal donor site, but not from the mandibular recipient site. This supports the fact that the

exposed vascular bed of the palate was an overwhelming challenge to the patient's impaired clotting system.

Rappaport[7] reported that among more than 60 surgical procedures undergone by patients with major Factor XI deficiency about half did not experience any serious postsurgical bleeding. Rimon and others[8] reported on a 22-year-old patient with major Factor XI deficiency (3 percent Factor XI activity). The patient had never bled or bruised abnormally despite multiple injuries: scalp laceration requiring four sutures, a broken nose while playing basketball, a broken nose a second time in a surfing accident, repeated minor injuries including cuts of his tongue from karate, cuts and bruises on his legs from a motorcycle accident and an accident in which a grinding wheel scraped his face causing extensive abrasion to his upper lip and cheek.

Based on the wide variability of bleeding experiences in patients with Factor XI deficiency, there may be an alternative pathway for blood coagulation which bypasses the need for Factor XI.[9] In most cases, tooth extraction or tonsillectomy aggravate the bleeding disorder.[8,10] Tooth extractions and tonsillectomies leave open surfaces in the mouth where there are high levels of plasminogen activity.[11]

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However, many of these patients have undergone major surgical procedures with less bleeding risk than with tooth extraction or tonsillectomy. This reduced risk may be explained by the fact that major surgical procedures require transfused blood or plasma that may have adequately high levels of Factor XI. Also, most tooth extractions and tonsillectomies leave open wounds. Major surgical procedures are usually sutured.

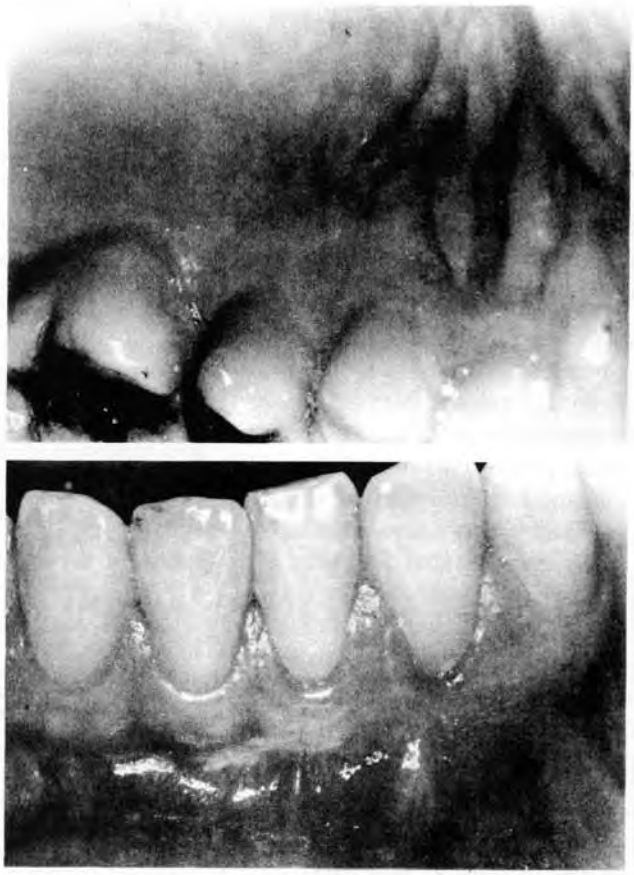

Figure 3. Nine weeks after surgery. Top: Donor site. Bottom: Recipient site. Healing has progressed normally.

In Factor XI deficiency, the blood platelet count, bleeding time and prothrombin time are usually normal. Partial thromboplastin time is severely prolonged. The definitive diagnosis of Factor XI deficiency is determined by plasma level Factor XI analysis. Dental extractions are usually performed on an out-patient basis without presurgical blood tests. Most cases reported in the literature have been diagnosed because of persistent bleeding after a tooth extraction.[12-15]

Conditions of patients hospitalized for extractions usually are diagnosed before surgery so appropriate precautions can be taken.[16,17] Evian and others[8] described a patient with undiagnosed Factor XI deficiency who developed serious bleeding complications after periodontal flap surgery. Sciullo and others[9] reported on bleeding after apicoectomy.

Treating Factor XI deficiency involves raising the plasma level of Factor XI to about 20 to 30 percent of the normal serum content.[20] Because banked blood loses 80 percent of its Factor XI content during the first week of storage,[21] fresh whole blood or plasma or fresh frozen plasma must be used for transfusions.

The half-life of infused Factor XI is 60 to 80 hours.[22] Transfusion of fresh frozen plasma is used for both preoperative and postoperative treatment of Factor XI deficiency.[8,10,14] Monitoring can be done with partial

thromboplastin time analysis and plasma Factor XI assays. Since spontaneous bleeding is not usually a feature of Factor XI deficiency, maintenance therapy is not needed.

CONCLUSIONS

Factor XI deficiency shows an unusually wide variation of bleeding tendencies, from complete absence of symptoms to injury-related bleeding that requires massive transfusions. Also, there is no correlation between the severity of bleeding and the plasma levels of circulating Factor XI.[8] Most often, because of little or no symptoms, patients with Factor XI deficiency go unrecognized until excessive postsurgical bleeding occurs.

Unexplained prolonged postsurgical bleeding should alert the practitioner to possible previously undiagnosed bleeding or a clotting disorder. Routine blood tests, including a complete blood count, bleeding time, prothrombin time and partial thromboplastin time, reveal such a disorder. Hemophilia-type bleeding disorders should be suspected if there is an abnormally high partial thromboplastin time. If a true bleeding disorder is suspected, the patient should be referred to a hematologist. ▪

The opinions expressed or implied are strictly those of the authors and do not necessarily reflect the opinion or official policies of the American Dental Association.

1. Miller PD Jr. Root coverage using a free soft tissue autograft following citric acid application. Int J Periodontics Restoration Dent 1982;2:65-70.

2. Lieba H, Ramot B, Many A. Hereditary and coagulation studies in ten families with factor xr (plasma thromboplastin antecedent) deficiency. Br J Haematol 1965;II:654-65.

3. Seligsohn U. High gene frequency of factor XI (PTA) deficiency in Ashkenazi Jews. Blood 1978;51(6):1223-8.

4. Asakai R, Chung DW, Davie EW, Seligsohn U. Factor XI deficiency in Ashkenazi Jews in Israel. N Engl J Med 1991;325(3):153-8.

5. Rosenthal RL, Dreskin OH, Rosenthal N. New hemophilia-like disease caused by deficiency of a third plasma thromboplastin factor. Proc Soc Exp Biol Med 1953;82:171-4.

6. Frick PG. The relative incidence of anti-hemophilic globulin (AHG), plasma thromboplastin component (PTC), and plasma thromboplastin antecedent (PTA) deficiency: a study of fifty-five cases. J Lab Clin Med 1954;43:860.

7. Rapaport SI, Proctor RR, Patch MJ, Yettra M. The mode of inheritance of PTA deficiency: evidence for the existence of major PTA deficiency and minor PTA deficiency. Blood 1961;18:149-65.

8. Rimon A, Schiffman S, Feinstein DI, Rapaport SI. Factor XI activity and factor XI antigen in homozygous and heterozygous factor XI deficiency. Blood 1976;48(2):165-74.

9. Osterud B, Rapaport SI. Activation of factor XI by the reaction product of tissue factor and factor VII: additional pathway for initiating blood coagulation. Proc Natl Acad Sci USA 1977;74(12):5260-4.

10. Rosenthal RL, Dreskin OH, Rosenthal N. Plasma thromboplastin antecedent (PTA) deficiency: clinical, coagulation, therapeutic and hereditary aspects of a new hemophilia-like disease. Blood 1955;10:120-31.

11. Megquier RJ. Fibrinolytic activity in human dental sockets after extractions. J Oral Surg 1971;29:321-8.

12. Williams JL. Plasma thromboplastin antecedent deficiency. Br J Oral Surg 1972;10:126-32.

13. Schwartz HC, Stone JD. Hereditary Factor XI deficiency. J Oral Surg 1976;34(5):453-5.

14. Gilmore WC, Doku HC. Factor XI deficiency resulting in severe postoperative hemorrhage after odontectomy. J Oral Surg 1979;37(12):885-7.

15. Poker ID, Reade PC, Cook RM. Factor XI deficiency disclosed following haemorrhage related to a dental extraction. Brief review and case report. Aust Dent J 1990;35(3):258-60.

16. Murphy JB, Robinson K, Segelman A. PTA deficiency (Factor XI deficiency). Oral Surg Oral Med Oral Pathol 1976;42(1):26-30.

17. Redding SE, Shaw AS. Factor XI deficiency (PTA deficiency): a case study. J Oral Med 1980;35(2):45-7.

18. Evian CI, Corn H, Guernsey LH, Rosenberg ES. Complications of severe bleeding in a patient with undiagnosed Factor XI deficiency. Oral Surg Oral Med Oral Pathol 1981;52(1):12-8.

19. Sciullo PA, Nacht ES, Tesone AR. Postsurgical complications in an undiagnosed hemophiliac: a case report. ASDC J Dent Child 1972;39(3):194-6.

20. Colman RW, Hirsh J, Marder VJ, Salzman EW. Hemostasis and thrombosis: basic principles and clinical practice. 2nd ed. Philadelphia: Lippincott;1987:25-7.

21. Horowitz HI, Fujimoto MM. Survival of factor XI in vitro and in vivo. Transfusion 1965;5:539-42.

22. Nossel HL, Niemetz J, Mibashan RS, Schulze WG. The measurement of factor XI (plasma thromboplastin antecedent). Br J Haematol 1966;12:133-44.