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CASE reports

Dental treatment of a patient with congenital afibrinogenemia — complications of supportive care

Mark L. Helpin, DMD
Francis S. Morrison, MD

Abstract

A seven-year-old black girl with congenital afibrinogenemia received replacement blood products in order for dental treatment to be performed. During the post-treatment period the patient developed serious systemic complications. These included pulmonary manifestations, refractoriness to infused fibrinogen, and breakdown of healing gingival tissues. The relationship of these complications to her underlying disease and supportive care is considered.

Introduction

In the past twelve years there have been no reports in the dental or medical literature which related to dental management of patients with congenital afibrinogenemia. In addition, the authors of standard medical texts and journals who do not mention this disorder, fail to consider oral manifestations or problems beyond the fact that gingival bleeding may occur.[1,2,5,8,9,10]

Congenital afibrinogenemia is a rare inherited hematologic disorder characterized by an inability to synthesize fibrinogen. The mode of inheritance is generally considered to be autosomal recessive. Heterozygotes usually go undetected despite their subnormal level of fibrinogen.[1,4,5,7,8] The bleeding history is similar to that of a mild hemophiliac, in that the patient is unlikely to bleed spontaneously but may experience severe hemorrhage when injured or subjected to surgery. Hematologic laboratory evaluation reveals a markedly prolonged clotting time, partial thromboplastin time (PTT), prothrombin time (PT) and thrombin time (TT). There is essentially no clot formation. The bleeding time is usually normal.[1,2,5,6] By way of comparison, the PT and TT are characteristically normal in hemophilia.

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Hemmorrhagic episodes are usually controlled by the administration of cryoprecipate, which is a rich source of fibrinogen and is less likely to be associated with hepatitis than fibrinogen prepared commercially from pooled plasma. Volume considerations usually preclude the use of plasma or whole blood as a source for fibrinogen replacement. The two major complications related to fibrinogen replacement therapy are, as in the case of factor VIII replacement in classic hemophilia, hepatitis and the development of antibodies to the infused foreign protein.

In reviewing twenty reported patients with afibrinogenemia, Frick and McQuarrie[6] found that eight of these died by 22 years of age as a result of bleeding. The oldest of the 12 surviving patients was 19. They also pointed out that while fibrinogen is an essential factor in hemostasis, it also plays a role in the healing process. This role has never been well defined.

Our report describes a patient with afibrinogenemia who experienced an unusual response to supportive replacement therapy which was administered for dental treatment.

Case Report

A seven-year-old black girl with the diagnosis of congenital afibrinogenemia was referred for dental evaluation from the Division of Pediatric Hematology to the Pediatric Dental Clinic. The diagnosis of afibrinogenemia had originally been established as the result of diagnostic work-up for prolonged umbilical stump bleeding, cephalhematomas, and prolonged bleeding from a minor laceration. Laboratory assays revealed no detectable fibrinogen. Although immunologic determination of fibrinogen antigen was not done, the diagnosis of afibrinogenemia was based on; a) the absence of clottable protein in the patient, b) the total absence of any family history of a bleeding

disorder, and c) the presence of a reduced quantity of clottable protein in her mother's plasma with no history of bleeding. Patients with dysfibrinogenemia usually have some clottable protein, but may not, and therefore, the total lack of bleeding in the family history is important. The congenital dysfibrinogenemias are inherited as autosomomal dominant traits and should provide a positive history.

Minor bleeding episodes following superficial wounds in this patient regularly responded to topical fibrinogen; however, two episodes which required the administration of plasma were associated with a systemic reaction. On one occasion the patient simply experienced uticaria. At thirteen months of age, however, administration of fibrinogen was followed by vomiting, shock and acrocyanosis. These symptoms resolved after treatment with epinephrine and corticosteroids.

Oral examination at the time of referral revealed normal facial symmetry with a convex facial profile; lip lengths were adequate. No lymphadenopathy was present. Marginal gingivitis associated with the patient's poor oral hygiene was noted throughout the mouth. The buccal mucosa, hard and soft palate, tongue, floor of the mouth, and frena were all within normal limits. Moderate to severe caries were present throughout the child's mixed dentition. Except for some mandibular anterior crowding, the patient's occlusion was within normal limits.

Oral hygiene and dietary education was instituted with patient and family and the extreme importance of these measures were emphasized. Prophylaxis and topical fluoride application were then completed. Because of the patient's known hematologic disorder, and the potential therapeutic ramifications, the child was admitted to the hospital for treatment in the ambulatory dental clinic. Because of the patient's severe apprehension in the dental setting, she was sedated with oral Demeraol (55mg.) and Atarax (100mg.), the patient's weight being 21kg. Hematologic preparation consisted of eight units of cryoprecipitate given 30 to 60 minutes before each scheduled treatment. Since 30-50% of the available fibrinogen is usually precipitated in the cryoprecipation process, it was estimated without assay that this dosage represented approximately 1½ grams of fibrinogen. This was considered adequate replacement according to standard recommendations.[10] Measurements of PT, PTT, and TT normalized after infusion of the cryoprecipitate. This therapy was continued throughout the four days of dental treatment.

Two class I, four class II, and two class V amalgam restorations, four stainless steel crowns, four pulpotomies, three indirect pulp caps, and one extraction were completed over the four-day period. After extraction of the mandibular left second primary molar, interrupted sutures were used to approximate friable tissue. Infiltration anesthesia was administered at each appointment. Good homostasis was apparent at the end of each session. The duration of dental visits varied from one half to one and a half hours. Six units of cryoprecipitate were given on each of the two days immediately following completion of dental treatment and four units were given each day for the next two days. There had been no evidence of any bleeding problem, but the staff planned for replacement therapy to continue until the sutures were removed. This extremely conservative approach was selected in order to minimize any risk of complications should the patient's hematological status change.

On the fourth day after completion of dental work, the patient complained of headache and pain around the umbilicus. Her temperature was 100°, pulse 100, and respirations 28. The lungs were clear and no focus of infection was identified. On the fifth post-treatment day the oral mucosa was noted to be in good condition and the extraction site was healing well. Sutures were removed, but the child was kept in the hospital for further observation.

Over the next four days the patient's condition deteriorated. She developed fever of 102°, generalized abdominal pain, and a severe sore throat with tonsillar and pharyngeal erythema. On two occasions she vomited blood. The superficial attached and unattached gingiva throughout the mouth began to break down and slough. This was associated with generalized gingival oozing of blood. There was wide involvement of the buccal and lingual gingiva, even in areas where no specific dental treatment had been done. Chest x-rays showed infiltrates opacifying most of the left and some of the right lung fields. In addition to pneumonia or allergic penumonitis, the possibility of pulmonary hemmorrhage was suggested by the radiologist.

Clotting studies revealed a markedly prolonged PT, PTT, and TT, and there was essentially no clot formation, despite the continued daily administration of cryoprecipitate. The platelet count was 465,000 and there was no evidence of hemolysis or suggestion of cryoangiopathy in the blood smear. Further testing on subsequent days consistently showed the PT, PTT, and TT to be prolonged. The platelet count remained normal. Fibrinogen assay demonstrated a level of 100mg. % of fibrinogen one hour after administration of eight units of cryoprecipitate. This dropped to 76mg. % four hours after the cryoprecipitate administration and to 40mg. % at six hours, immediately preceding the next dosage.

Bleeding was controlled by increasing cryoprecipitate dosage to 6-8 units every six hours. Additional medical treatment during this time consisted of supportive oxygen therapy and broad antibiotic coverage, despite failure to culture a pathogenic organism. The only dental treatment during this time period was the application of Stomahesive®* to the extraction site.

The sixth day following onset of deterioration, ten days after dental treatment had been completed, the patient began to improve. She became afebrile. The lungs sounded clearer with good air movement on both sides. The tonsils and pharynx looked better, and the oral tissues began to heal. Coagulation studies normalized prior to administration of her cryoprecipitate dosage. Fibrinogen was 204 mg. %. The administration of cryoprecipitate was continued for another week. The chest x-ray gradually improved and was entirely normal by the end of the week, and the patient was discharged in good condition to be followed by her referring physician.

Sequelae

Follow-up eleven months later revealed no further bleeding episodes, sequelae to her treatment, or complication. One year after that visit, however, the patient experienced delayed bleeding following suturing of a foot laceration. At that time she was given six days of cryoprecipitate replacement therapy. This therapy achieved good control of bleeding and there was no complication.

Discussion

The hospital course of a patient with congenital afibrinogenemia who received dental treatment has been described. The dental procedures were routinely accomplished with adequate replacement therapy provided in a standard manner using cryoprecipitate. During the post-treatment period, however, the patient developed major medical complications. These included severe pulmonary infiltration, pharyngitis, delayed healing of an extraction site, and generalized breakdown and sloughing of superficial gingival tissue.

While respiratory complications of plasma infusion in this disease have been described in the literature,[3,11] the oropharynegeal problems encountered have not been previously reported. Because fibrinogen is known to be vital to the integrity of soft tissues and to the healing process, the question of relationship of fibrinogen deficiency to the several oral lesions must be related.

The administration of eight units of cryoprecipitate, to a 21 kilogram patient certainly should have been adequate replacement fibrinogen if given every two or three days. The actual half-life of an initial dose of transfused fibrinogen has been established to be approximately one day because of equilibration in the extravascular compartment; subsequent to the initial dose, however, the biological half-life can be demonstrated to be approximately three days.[10] Because of this, discontinuation of replacement therapy upon completion of treatment should have resulted in a sufficient level of fibrinogen for three to five days. In this case cryoprecipitate was administered for four days after the surgery to assure good hemostasis for a longer period.

Occurrence of generalized bleeding during administration of the missing plasma factor, associated with a reaction to the infused blood product, suggested immunologic destruction of infused fibrinogen. The findings were also consistent with accelerated consumption secondary to an infection, but no pathogenic organism was found and, more importantly, the platelet count remained in the 300,000/cmm range with no evidence of hemolysis or microangiopathy.

Sequential assays demonstrated very rapid destruction of all infused fibrinogen. The fact that the destructive mechanism could be overcome by massive infusion of fibrinogen on a regular basis supports the likelihood of a fibrinogen antibody in this patient. This type of antibody has been reported in 1954 by Broman[11] and again in 1961 by de Vries.[3]

The fact that healing was finally sufficient to discontinue fibrinogen infusion does not negate the possible persistence of a very high antifibrinogen titer, since prior to surgery the level of fibrinogen was approximately 0, and the presence of a very strong inhibitor could only effect a similar level. The cause of the gingival break-down and sloughing, including areas where no dental treatment had been given, remains enigmatic. This is especially true considering the fact that these patients characteristically do not bleed without severe trauma or laceration.

Conclusion

Complications following dental treatment for a patient with congenital afibrinogenemia have been described and the possible role of inhibitors to replacement blood products and the comprised host have been discussed.

Dr. Helpin is associate professor, department of pediatric dentistry, University of Mississippi Medical Center, Jackson, Mississippi 39216. Dr. Morrison is professor of medicine and chief, division of hematology, at the same address. Requests for reprints should be sent to Dr. Helpin at that address.

*Stomahesive® Squibb

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