

Dental management of idiopathic aplastic anemia: report of a case

James E. Jones, DMD, MS

Thomas D. Coates, MD

Charles Poland, DDS

Abstract

Aplastic anemia is a serious and often fatal hematological disorder characterized by hypoplastic bone marrow and peripheral pancytopenia. Epistaxis, oral lesions and gingival hemorrhage often necessitates multiple platelet transfusions in these patients. The use of aminocaproic acid to control hemorrhagic episodes has been especially beneficial in patients with bone marrow hypoplasia as they often become refractory to repeated transfusions. In this case presentation, a 15-year-old black female with idiopathic aplastic anemia was treated with a combination of modalities including initial platelet transfusion, oral hygiene instruction, dental prophylaxis and systemic aminocaproic acid. The health of the oral tissues greatly improved following this regimen.

Introduction

Aplastic anemia is a serious and often fatal hematologic disorder characterized by hypoplastic bone marrow and peripheral pancytopenia. Recently, the use of systemic aminocaproic acid^a in these patients has demonstrated positive results in the control of oral hemorrhagic episodes, thus reducing the need for multiple platelet transfusions.¹ In this case presentation, a 15-year-old black female with severe idiopathic aplastic anemia was treated with a combination of modalities, including initial platelet transfusion, oral hygiene instruction, dental prophylaxis and systemic aminocaproic acid. The oral tissues appeared clinically healthy following this regimen.

Literature Review

Aplastic anemia was first described in 1888 by Ehrlich as a rapidly fatal hematologic disease seen in young adults between the ages of 15 and 30.² Today, the concept of aplastic anemia has been broadened

since the disease has been known to occur at any age. Usually, the onset is gradual, but acute fulminating cases have been reported.^{3,4} The mortality in severe cases is more than 50 percent during the first year and may be greater than 70 percent at five years.⁵ Aplastic anemia is normochromic and normocytic, and manifests itself as a pancytopenia. The bone marrow is devoid of megakaryocytes, myeloid and erythroid precursors.⁶

Clinical signs and symptoms include: 1) severe weakness and dyspnea even after mild physical exertion, 2) pallor of the skin, 3) numbness and tingling of the extremities, 4) decreased resistance to infection, and 5) petechiae of the skin and mucous membranes.⁷ These clinical manifestations are caused by the inability of the hematopoietic system to deliver enough red cells, white cells and platelets to the peripheral circulation. The specific clinical picture varies according to the cell line predominantly affected. Oral signs include: 1) spontaneous bleeding from the mucous membranes, 2) petechiae, 3) purpuric spots, and 4) frank hematomas of the mucosa, pharynx and gingiva.

Aplastic anemia is generally recognized in two forms: idiopathic and secondary. Idiopathic aplastic anemia affects young adults, progresses rapidly and is usually fatal. This form accounts for approximately 60 percent of the reported cases.⁸ Secondary aplastic anemia is of known etiology and can affect individuals at any age. The prognosis, once again, is poor even if the causative agent is identified. Among the agents associated with secondary aplastic anemia are: ionizing radiation,⁹ Atabrine,¹⁰ chloramphenicol,^{11,12} benzene,^{13,14} gold compounds,¹⁵ viral hepatitis, and miliary tuberculosis.^{4,8} Secondary aplastic anemia accounts for approximately 40 percent of reported cases.⁸

Report of Case

A 15-year-old black female was referred to the James Whitcomb Riley Hospital for Children in

Accepted: December 29, 1980

^aNon-proprietary name and trademarks of drug: aminocaproic acid — Amicar, Cuprocid.



Figure 1. Initial intraoral view demonstrating gingivitis and spontaneous gingival hemorrhage.

March, 1979, with complaints of malaise and prolonged epistaxis. The patient denied any episodes of jaundice or hematuria. The family history was negative for sickle cell anemia or Fanconi's anemia. The patient had been transfused with 5 units of random donor platelets and packed cells prior to arrival at Riley Hospital.

Physical examination revealed a well-developed black female in no acute distress. Heart rate was 80, respiratory rate 18, weight 38.1 Kg. The examination was unremarkable with the exception of mucosal and petechial hemorrhage. Specifically, there was no hepatosplenomegaly or lymphadenopathy. No abnormality of the digits was noted. The patient was admitted to the hospital for evaluation. Admission laboratory data were as follows: Hemoglobin 7.6 gr.%, hematocrit 24%, white cell count 2,400/cu mm, platelets 10,000/cu mm, PT 11.5 seconds, PTT 23.0 seconds, SGOT 20, SPGT 19, and Alkaline Phosphatase 91. Antinuclear antibody was negative.

The patient was transfused with packed red cells, whole blood and five units of random donor platelets shortly after admission. A repeat hemoglobin was 9.1 gr.%. A bone aspiration and biopsy were performed. These demonstrated a marked decrease in precursors of all cell lines. Prominent mast cells and plasma cells were noted. There were no megaloblastic changes

noted. Subsequent normal B₁₂ and folate levels were documented. A sucrose hemolysis test proved negative. In the absence of historical evidence for marrow toxins and the fact that the physical findings were not consistent with familial aplastic anemia, the diagnosis of idiopathic aplastic anemia was made. A histocompatible donor was unavailable for marrow transplantation. The patient was discharged from the hospital to her parents five days after admission. Subsequent attempts at treatment with high dose corticosteroids and antithymocyte globulin were unsuccessful.

At the request of the hematology service, the patient was seen in the dental clinic of Riley Hospital on October 18, 1979 for evaluation of gingival hemorrhage and oral lesions. Her oral temperature was 38.9° C, hematocrit 20%, and a platelet count of 1,000 cu mm.

Oral and Radiographic Examination

Oral examination demonstrated generalized gingivitis with spontaneous gingival hemorrhage (Figure 1). Periodontal examination demonstrated no pocket formation greater than three millimeters. Multiple round, raised lesions approximately 3 mm in diameter were present on the anterior half of the tongue (Figure 2). Bilateral lesions approximately 1 cm in diameter were distal to the second permanent molars on the buccal mucosa (Figure 3). There was no history of oral trauma. Radiographic examination, including panorex, bite-wing and two maxillary anterior periapical radiographs were negative for pathology.

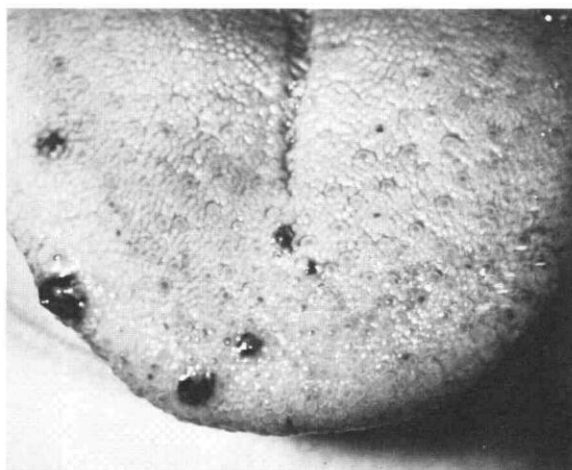
The patient reported severe pain during toothbrushing and had not been practicing regular oral hygiene in the past. At this time the patient was readmitted to the hospital for dental evaluation and treatment of the oral condition.

Initial Dental Treatment

The patient received two transfusions of 10 units each of platelets. The platelets were matched by major blood groups only. This brought her platelet

Figure 2. Multiple round, raised lesions on the anterior half of the tongue (left).

Figure 3. Intraoral view of lesion on patient's left buccal mucosa (right).



count to 190,000/cu mm. At this time, definitive dental treatment was initiated. Oral hygiene instructions were given to the patient and her parents. The need for daily oral care was stressed and the patient demonstrated that she could remove plaque from all surfaces of her teeth using a toothbrush and dental floss. A thorough debridement of the gingiva and a prophylaxis of the teeth were completed. Nitrous oxide-oxygen analgesia was used to reduce the patient's anxiety concerning dental treatment. The patient was seen daily in the dental clinic for the remainder of her admission for evaluation and reinforcement of her oral hygiene. Upon her release from the hospital, five days after initial dental treatment, the gingivitis had been reduced, although some spontaneous gingival hemorrhage continued and the oral lesions remained essentially unchanged. This was thought to be secondary to her thrombocytopenia.

The patient was evaluated in the dental clinic on November 26, 1979. She was again admitted to the hospital for severe, prolonged epistaxis and gingival hemorrhage. Her hematocrit was 30% and her platelet count was 2,000/cu mm. She received 10 units of platelets. The patient complained of moderate intraoral pain and was given two Tylenol #3^b tablets one hour before dental treatment, which consisted of reinforcing oral hygiene, gingival debridement and prophylaxis. Due to her anxiety concerning dental treatment, these procedures were accomplished using nitrous oxide-oxygen analgesia. On the following day, the procedure was repeated without the use of Tylenol #3. She was discharged later that same day after the gingival hemorrhage had been controlled.

The patient was seen every two weeks in the dental clinic for observation of oral health and reinforcement of oral hygiene. She consistently demonstrated meticulous oral home care, although gingival hemorrhage and oral lesions were still present. This was primarily due to her thrombocytopenia. From her initial diagnosis of idiopathic aplastic anemia in March, 1979 to January, 1980, she had received approximately 190 units of random donor platelets (approximately 17 units per month) during 10 hospital admissions and numerous out-patient visits for epistaxis and gingival hemorrhage secondary to her thrombocytopenia.

Systemic Use of Aminocaproic Acid

Due to the frequency and severity of epistaxis, chronic gingival hemorrhage and the subsequent need of multiple platelet transfusions, the hematology service elected to start the patient on oral aminocaproic acid. The initial dosage was 6 gm per day (1.5 gm q.i.d.) The maximal recommended dosage of aminocaproic acid is 30 gm per day. Epistaxis and gingival hemorrhage ceased within 24 hours. Only 15 units of platelets were given over the next three months due to

persistent, severe thrombocytopenia (2,000/cu mm), and periodic epistaxis. The need for platelets had been reduced to approximately 5 units per month. Gingival inflammation and oral lesions decreased within two weeks. The patient did experience a mild candidosis during a three-day period (Figure 4-6). The patient maintained meticulous oral hygiene and was followed regularly in the dental clinic for observation and recall examinations. During the fourth month of aminocaproic acid therapy, the patient experienced significant episodes of nasopharyngeal hemorrhage requiring hospitalization. This was controlled by adjusting the dosage of aminocaproic acid to 20 gm/day (5.0 gm q.i.d.), nasal packing and platelet transfusions. She is being maintained at this dosage.

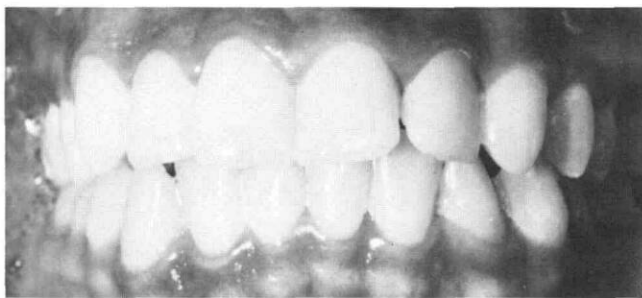


Figure 4. Intraoral view of gingival health approximately two weeks after aminocaproic acid therapy was initiated.

Discussion

Aminocaproic acid is a monoaminocarboxylic acid which inhibits fibrinolysis. The beneficial effects appear to be principally via inhibition of the plasminogen activator substances and through antiplasmin activity, although the exact mechanism is not known.^{1,16,17} The drug is absorbed rapidly following oral administration. In dentistry, aminocaproic acid has been especially useful to control patients with classic hemophilia A.¹⁸ Some patients experience orthostatic hypotension while undergoing aminocaproic acid therapy,¹ although this patient reports no such experience. Aminocaproic acid is also contraindicated in patients with hematuria.

The use of aminocaproic acid in the management of amegakaryocytic thrombocytopenia has been especially beneficial by reducing the need for multiple transfusions to control hemorrhagic episodes.¹ This is particularly important since patients with bone marrow hypoplasia often become refractory to repeated transfusions. It has been reported that aminocaproic acid therapy be discontinued when the platelet count consistently exceeds 20,000/cu mm.¹ In this patient, whose platelet count consistently remains 2,000/cu mm, the need for platelet transfusion to control epistaxis and gingival bleeding was reduced from approximately 17 units of platelets per month prior to aminocaproic acid therapy to approximately 5 units of platelets per month following aminocaproic therapy.

^bMcNeil Laboratories, Fort Washington, Pennsylvania 19034.

Figure 5. Clinical appearance of the tongue approximately two weeks after aminocaproic acid therapy was initiated. Note absence of lesions.



Figure 6. Intraoral view of patient's left buccal mucosa approximately two weeks after aminocaproic acid therapy was initiated. Note the healing of the lesion.



Summary

In this case presentation, a 15-year-old black female with idiopathic aplastic anemia was treated with a combination of modalities including initial platelet transfusion, oral hygiene instruction, dental prophylaxis and systemic aminocaproic acid. The health of the oral tissue greatly improved. Previous studies have demonstrated the positive results of meticulous oral hygiene in these patients.^{6,19,20} Although this patient consistently demonstrated meticulous oral hygiene, gingival bleeding and oral lesions were still evident during treatment. This suggests that in patients with severe thrombocytopenia (2,000/cu mm), meticulous oral hygiene can improve the oral environment but direct hematologic measures are essential for treatment. At this time, the patient remains stable and is continuing a relatively normal adolescence. She reports that her improved oral health has enhanced her sense of well-being.

Acknowledgments

The authors would like to thank Dr. David R. Avery, Dr. Kenneth D. Snawder, and Professor Paul Barton for their suggestions during the preparation of this manuscript.

Dr. Jones is in private practice at the Medical Arts Tower, 207 Sparks Avenue, Suite 204, Jeffersonville, Indiana, 47130. He is also clinical instructor, department of pedodontics, University of Louisville, School of Dentistry. Dr. Coates is senior fellow in pediatric hematology-oncology, and Dr. Poland is associate professor of pedodontics & oral-facial genetics, Indiana University School of Dentistry. Requests for reprints should be sent to Dr. Jones.

References

- Gardner, F. H. and Helmer, R. E.: Aminocaproic acid. Use in control of hemorrhage in patients with amegakaryocyte thrombocytopenia, *JAMA*, 243:1, 35-37, January 4, 1980.
- Ehrlich, P.: Uber einen fall von anaimie mit bemerkungen uber regentzrative veränderungen des knochenmarys, *Charite — Ann*, 13:300, 1888.
- Geary, C. G.: Blood and neoplastic disease: Acquired aplastic anemia, *Brit Med J*, 2:432-435, May 25, 1974.
- Moffitt, M. and Cooley, R. O.: Aplastic anemia: A case report, *J Dent Child*, Sept.-Oct., 379-381, 1970.
- Wintrobe, M. M.: *Clinical Hematology*, Ed. 7. Philadelphia: Lee and Febiger, 1974, pp 1749-1769.
- Stamps, J. T.: The role of oral hygiene in a patient with idiopathic aplastic anemia, *JADA*, 88:1025-1027, 1974.
- Shafer, W. G.; Hine, M. K.; and Levy, B. A.: *A Textbook of Oral Pathology*, Ed. 3, Philadelphia: W. B. Saunders Co., 1974, pp 669-671.
- Williams, W. J.: *Hematology*. New York: McGraw-Hill Book Company, Inc., 1972, pp 207-227.
- Davidson, S. (Sir): *The Principles and Practice of Medicine*, Ed. 3. Edinburgh and London: E. and S. Livingston, Ltd., p 648, 1956.
- Custer, R. P.: Aplastic anemia in soldiers treated with atabrine, *Am J M Sc*, 212:211, 1946.
- Smiley, R. K.; Cartwright, G. E.; and Wintrobe, M. M.: Fatal aplastic anemia following chloratiphenicol (chloromycetin) administration, *JAMA*, 149: 914, 1952.
- Scott, J. L.; Cartwright, G. E.; and Wintrobe, M. M.: Acquired aplastic anemia: An analysis of thirty-nine cases and review of the pertinent literature, *Medicine*, 38:119, 1959.
- Loge, J. P.: Aplastic anemia following exposure to benzene hexachloride (lindane), *JAMA*, 193:110, 1965.
- Powars, D.: Aplastic anemia secondary to glue sniffing, *N Engl J Med*, 273:700, 1965.
- Wintrobe, M. M.; Stowell, A.; and Roll, R. M.: Report of a case of aplastic anemia following gold injections in which recovery occurred, *Am J M Sc*, 197:698, 1939.
- Gaum, L. I.: Use of aminocaproic acid in oral surgery for haemophiliacs: Report of case, *J Can Dent Assoc*, 35:599-602, November, 1969.
- Nilsson, I. M.; Andersson, L.; and Bjoryman, S. E.: Epsilon aminocaproic acid (EACA) as a therapeutic agent: Based on five years' clinical experience, *Acta Med Scand*, suppl. 448, 17, 1966.
- Corrigan, Jr., J. J.: Oral bleeding in hemophilia: Treatment with epsilon aminocaproic and replacement therapy, *J Pediatr*, 80:124-128, January, 1972.
- Lasser, S. D.; Camitta, B. M.; and Needleman, H. L.: Dental management of patients undergoing bone marrow transplantation for aplastic anemia, *Oral Surg*, 43, 2:181-189, 1977.
- McIlwain, J. E.: Dental support of severe metabolic disease: Aplastic anemia, *J Dent Child*, 43:54-55, July-August, 1976.