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Managing the dental patient with sickle cell anemia: a review of the literature

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Introduction

In 1910, a black West Indian student was found by JB Herrick to have strange sickle-shaped cells within his bloodstream (Barnhart et al. 1979). In 1929, a similar observation was documented in a white individual (Benjamin and Gootenberg 1987). However, it was not until 1949 that Linus Pauling actually identified hemoglobin S as the abnormal hemoglobin associated with sickle cell anemia (SCA; Barnhart et al. 1979).

Sickle cell anemia is a genetic disease that primarily affects the black population. This anemia is due to a homozygous state of the abnormal hemoglobin S (Rose and Kaye 1983). An alteration occurs on the DNA molecule involving the substitution of the amino acid valine for glutamic acid at the sixth position on the beta polypeptide chain (Rose and Kaye 1983). This biochemical variation on the DNA molecule creates a physiological change that causes sickle-shaped red blood cells to be produced. The sickle-shaped cells are the result of the hemoglobin S being deoxygenated. With a decrease in affinity of oxygen to an abnormal hemoglobin, deoxygenation will occur, again producing more sickle-shaped cells. This leads to obstruction or microvasculature erythrostasis, causing vasocclusion and extensive organ damage (Rose and Kaye 1983). It is a cyclic process .

Sickle cell anemia may be diagnosed in the sixteenth week of gestation, but manifestations normally do not appear until the sixth month after birth. Newer techniques for hemoglobin electrophoresis can be used to diagnose the abnormal hemoglobin at birth. Painful episodes or "crises" characteristic of this disease are vasocclusion, sequestration, aplastic, and to a lesser degree, hyperhemolysis.

The vasocclusive or infarctive type crisis most commonly is associated with excrutiating pain (Rose and Kaye 1983). Barnhart et al. (1979) have reported that infection, dehydration, acidosis, exposure to cold, some forms of stress, rigorous exercise, or an emotional disorder may be precipitating factors for a crisis. Symptoms may include increased breathing, abnormal heart rate, jaundice, fever, or abdominal tenderness (Rose and Kaye 1983). An early indication of SCA in infancy is the symmetrical hand-foot syndrome (sickle-cell dactylitis), which is described as the swelling of the hands and feet due to vasocclusion of the microvasculature in the small bones. Sickle cell dactylitis frequently occurs around two years of age; however, it may be diagnosed as early as six months of age (Barnhart et al. 1979).

Sequestration crises occur mainly in the young child. One symptom is the sudden enlargement of the liver and spleen caused by massive accumulation of blood in these organs. The enlarged liver leads to an increase in unconjugated bilirubin, and eventually is associated with jaundice and scleral icterus in SCA patients (Barnhart et al. 1979). Gallstones may be detected in SCA patients in the first and second decades of their lives, and are common in the third decade. A palpable spleen is common in children. After age six, however, the spleen decreases in size because of fibrosis and the presence of scar tissue resulting from the frequent occurrence of infarctions. The reduction in size or loss of the spleen may be a contributing factor to the likelihood of widespread bacterial infections, especially in infants and young children who have not developed adequate immunity to certain bacterial pathogens (Barnhart et al. 1979).

Rose and Kaye (1983) report that aplastic crisis results from the nonproductive function of bone marrow, which leads to severe anemic conditions. The less common type of crisis, hyperhemolytic, is sometimes associated with glucose-6-phosphatase (G-6-PD) deficiency. This deficiency can cause lactic acidosis which could precipitate a crisis for the SCA patient (Behrman and Vaughan 1987). Painful crises are common with the SCA patient and affect the entire body; moreover, changes are seen in the renal, central nervous (CNS), cardiovascular (CVS), and pulmonary systems. Evidence of renal lesions indicates that sickle-shaped cells

in the vasa recta of the medulla eventually lead to the development of a "sickle cell nephropathy" (Barnhart et al. 1979).

CNS infarctions may occur anywhere in the body due to occlusion of the vessels; however, 5-10% of patients reportedly suffer from "strokes" (Barnhart et al. 1979). The timing mechanism for the occurrence of these "strokes" is still under investigation, but some neurological problems that SCA patients experience include headaches, convulsions, aphasia, and hemiparesis (Barnhart et al. 1979).

Barnhart et al. (1979) describe cardiovascular symptoms in sickle cell patients which may result from the following: 1) chronic anemia, 2) pulmonary arterial occlusion, and 3) myocardial damage from infarctions and iron deposition. These authors also have documented that children experience cardiac abnormalities such as tachycardia and cardiomegaly; older patients often suffer congestive heart failure. Precordial murmurs have been detected as a result of increased pulmonary blood flow and can be heard over any part of the cavity that surrounds the heart. A systolic type murmur probably is an indication of tricuspid or mitral valve stenosis (Barnhart et al. 1979). Recurrent episodes of pneumonia are probably the most common pulmonary manifestation of SCA; *Streptococcus pneumoniae* frequently is the organism involved (Barnhart et al. 1979). The hypoxic state of pneumonia increases the sickling process of red blood cells, thereby decreasing the oxygen affinity for the abnormal hemoglobin. This results in further complications from increasing viscosity, stasis, and ischemia (Barnhart et al. 1979). Research has shown that adminstering the pneumococcal vaccine to children over the age of two may be helpful in decreasing these episodes of pneumococcal infection (Behrman and Vaughan 1987).

Incidence

Approximately one of every 500 black children in the United States has SCA (Barnhart et al. 1979). The homozygous state of this chronic hemolytic anemia typifies the most devastating effect. Persons with the sickle cell trait occasionally may show manifestations of the disease in hypoxic states caused by exposure to high altitudes or shock. These patients are usually without symptoms; however, it has been reported that systemic diseases, dehydration, infection, and hypoxia can cause a crisis in the patient with the sickle cell trait (Smith and Gelbman 1986). Eight to 10% of the US black population possesses the trait (Behrman and Vaughan 1987).

Diagnosis of Sickle Cell Anemia

Aside from clinical manifestations of SCA, laboratory data must be documented to reach a conclusive diagnosis. The sickle cell preparation test is performed to identify the presence of hemoglobin S. A blood sample is collected, then the red blood cells are exposed to a deoxygenating agent such as sodium metabisulfate (Barnhart et al. 1979). Sickling of the cells will occur if the patient has the disease or trait, but a patient homozygous for SCA will have a rapid rate of sickling, with almost all of the red blood cells involved (Barnhart et al. 1979). Solubility tests are appropriate for detection of hemoglobin S, but a definitive diagnosis is not conclusive until an electrophoretic examination is performed (Barnhart et al. 1979).

Behrman and Vaughan (1987) report that hemoglobin values for patients with SCA fall in range between 5-9 g/dl compared with a normal range of 12-17 g/dl depending on the gender of the patient (University of Alabama at Birmingham Hospital 1987). Usually the white blood cell count is increased with counts ranging from 12,000–20,000/mm^3 (Behrman and Vaughan 1987) as opposed to normal values of 400-11,000/mm^3 (University of Alabama at Birmingham 1987).

Morbidity and Mortality

The life expectancy of patients with SCA is variable because these patients are plagued with infections and chronic anemia, and suffer decreased nutritional health and frequent blood transfusions. Three common causes of death for the SCA patient are massive bacterial infections, decreased splenic activity, and infarction of the CNS (central nervous system, Barnhart et al. 1979); however, in infants and young children, the major cause of morbidity and mortality is bacterial infection. Pneumococcal infection is the most common type of septicemia that affects the patient with SCA.

Powars and Overturf (1987) feel children are at the highest risk for pneumococcal septicemia before age three. Studies have shown that regular compliance with antibiotic therapy has decreased the number of infections. The length of time to continue the type of therapy is debatable; however, the objective is to continue treatment until the child can develop protective antibodies (Powars and Overturf 1987). A seven-year study on penicillin therapy conducted at the Children's Medical Center of Dallas showed favorable results using oral penicillin prophylaxis and vaccination with the 23 polyvalent pneumococcal vaccine which became available in 1983 (Buchanan and Smith 1986). Six cases (7.0%) of pneumococcal septicemia developed in the SCA patients, even though all had received the first vaccine before 24 months of age. An adequate documented history of oral penicillin compliance was not obtained; however, the study provided positive research data for improving controlled penicillin treatment (Buchanan and Smith 1986). When the vaccine is administered to

children older than two, results have been favorable, especially in those with splenic dysfunction (Behrman and Vaughan 1987). Future research on prophylactic antibiotic coverage will continue to focus on a way to minimize septicemia in these patients.

Medical Management of SCA

Presently, there is no cure for SCA and no program to prevent a crisis. However, analgesics and other medicines have been used to decrease pain. Regular narcotic use to relieve painful episodes should be avoided, to prevent drug addiction. A daily regimen of folic acid may be given to children to minimize the severity of the anemia (Rose and Kaye 1983). Antibiotic therapy is recommended for bacterial infections, and all efforts to prevent dehydration and acidosis should be employed (Behrman and Vaughan 1987). Palliative efforts that can maintain the SCA patient in a relatively healthy state have prolonged the lives of many. Because of the seriousness of SCA, dentists should perform a thorough medical history before initiating treatment.

Psychosocial Aspects

Psychosocial aspects of SCA should be part of the evaluation of the patient. Shnorhokian et al. (1984) reported that children with SCA have short, thin body statures and less-than-normal body weight. Whitten and Fischhoff (1974) reported that these children are unable to keep up physically with their peers due to their inability to control the onset, frequency, or duration of crises that may be initiated by childhood games. The authors also believe that SCA patients develop a low self-esteem. Whitten and Fischhoff (1974) suggested that because of frequent crises and hospitalizations, children with SCA are often absent from school and fall behind in their academic performance. Floyd (1979) stated that SCA children score lower on intellectual exams than normal children of the same age, sex, and socioeconomic status. It is very important for these children to receive strong family support to build their self-confidence.

Dental Findings Associated With SCA

The dental implications of SCA must be understood fully to successfully treat SCA patients. Treatment should begin only after a thorough investigation has been performed on the patient's background. Mucosal pallor, delayed eruption, dental hypoplasia, and radiographic changes are common oral findings associated with the disease (Cox and Soni 1984). A study by Sears et al. (1981) found no significant difference in dental age between SCA patients and normal patients, and no significant difference between the chronologic and dental ages of sickle cell patients. Soni (1966) reports in his microradiographic study that interruption of the mineralization process occurs in dental tissues of the SCA patient. This study shows developmental problems occurring in the enamel and dentin, such as enamel hypomineralization, accentuated incremental lines, and interglobular dentin. Soni (1966) also reports peculiar foreign particles in the dentinal tubules, indicated by the presence of infectious agents in the canals of these tubules. The presence of denticle-like hardened bodies as a result of calcification in the pulp suggest the evidence of blood vessel thrombosis. Hypercementosis also has been observed in SCA patients (Soni 1966). These findings are not pathognomonic for SCA, but the sickling state has an effect on the aforementioned changes (Soni 1966).

The intrinsic opacity of enamel, malocclusion, (including overjet and overbite), dental caries, and diastemata are other dental observations found in SCA patients (Okafor et al. 1986). These authors also report a decrease in dental caries among SCA patients, compared with patients having normal hemoglobin A.

Some radiographic studies of the SCA patient show: 1) an increased radiolucency of the jaws due to the decreased number of trabeculae, 2) a thin inferior border of the mandible, 3) a coarse trabecular bone pattern, 4) generalized osteoporosis commonly caused by salmonella infections, 5) distinct areas of radiopacities, and 6) the step ladder effect created in the interdental alveolar bone by horizontal rows of trabeculation (Cox and Soni 1984). Cephalometric analyses of the SCA patient indicate that these patients exhibit a tendency for a protrusive maxilla, forward advancement of the mandible, and retroclined maxillary and mandibular incisors—presumably due to the lip pressure from the protrusion of the maxilla (Shnorhokian et al. 1984). Brown and Sebes (1986) have reported that maxillary protrusion can be evaluated radiographically by assessing the palato-alveolar ridge angle with respect to the length of the hard palate. These authors report that such growth of the maxilla is due to marrow hyperplasia. Angle measurements greater than 120° indicate notable deformation of the maxillofacial component (Brown and Sebes 1986). Radiographic evaluation is important in assessing gnathological developments or noting trabeculation patterns, although some radiolucencies are associated with pathological changes of the pulp.

In a study by Cox and Soni (1984), the presence of sickle-shaped cells was revealed in the pulpal vasculature after viewing tooth sections from SCA patients two to three days after an acute crisis. This tissue infarction may produce pulpal pain or create a necrotic condition which could lead to a periapical disease (Andrews et al. 1983). An obvious radiolucency involving the apices of the teeth should be evaluated by thermal, electrical, and

percussion methods. A definitive diagnosis of pulpal necrosis is a negative response to the test cavity method (Andrews et al. 1983). A study by Andrews et al. (1983) on SCA patients evaluated suspected radiolucencies associated with teeth; approximately 38.1% periapical radiolucent areas were reported. A four-year follow-up indicated healing of the lesions, suggesting thrombosis as the etiology of these necrotic pulps, in accordance with SCA. Usually SCA patients are asymptomatic for pulpal changes (Andrews et al. 1983).

Dental Considerations

After a diagnosis has determined that dental treatment is required, anesthetic assessment must be considered. SCA patients are categorized as an ASA III anesthetic risk (Malamed 1985). A local anesthetic is the preferred method for treating these patients because it does not lower the oxygenation of blood (Smith et al. 1987). Research has yet to discover the "ideal" local anesthetic, with or without a vasoconstrictor. The type of dental procedure to be performed can determine the type of local anesthetic to be used (Smith et al. 1987). Lidocaine 2% with a vasoconstrictor is preferred if profound anesthesia is required, such as for extraction procedures (Smith et al. 1987). Nitrous oxide-oxygen, commonly used by the pediatric dentist, is not contraindicated in SCA patients as long as a 50% oxygen concentration is maintained along with a high flow rate and adequate ventilation (Smith et al. 1987). Oral sedation is an alternative to help decrease preoperative anxiety levels. Light doses should be employed; however, if moderate levels are needed, additional oxygen by nasal cannula is suggested (Malamed 1985). Cullen (1982) suggests chloral hydrate or Valium® (Roche Laboratories, Nutley, NJ) as a premedication for anxiety control. Before general anesthesia is induced in a patient with SCA, proper hemoglobin levels should be obtained through transfusions. This should be accomplished 10 to 15 days before the operation. For children, optimum hemoglobin levels obtained after blood transfusions should be in the range of 10-12 g/dl (Smith et al. 1987).

Most dental procedures produce some form of bacteremia. Therefore, the SCA patient's physician should be contacted before a proposed procedure to determine the recommended antibiotic regimen for that patient. Infectious states as well as surgical procedures invariably will require antibiotic coverage (Smith et al. 1987).

Preventive dental therapy is the ideal approach for treatment of the SCA patient. The goal of the pediatric dentist is to improve and maintain excellent oral health and to decrease the possibility of oral infections. Treatment should never be initiated during a crisis unless in an emergency situation, and then treatment should be designed only to decrease infection and discomfort (Rada et al. 1987). Rada et al. (1987) report that periodontal infections, if severe enough, may precipitate a sickle cell crisis. Treatment of pericoronitis and periodontal abscess in their study included antibiotic therapy, irrigation, and curettage respectively.

Orthodontic treatment for the SCA patient is strictly elective. These patients may have malocclusions or skeletal abnormalities, and their correction may improve the child's self-esteem. Certain forms of orthodontic therapy may, however, initiate bacterial infections. Basically, orthodontic treatment moves teeth through remodeled bone or varies growth patterns by repositioning the mandible. The disease process of SCA may compromise the outcome of the planned treatment (van Venrooy and Proffit 1985). Treatment must be monitored closely, especially during a crisis. Orthodontic appliances should be designed to prevent irritation of soft tissues (van Venrooy and Proffit 1985).

Oral surgical procedures have the highest probability of causing an oral infection. A definite protocol should be followed if any type of surgery is planned. Black patients should be screened routinely for sickle cell if a past medical history is unclear. Blood transfusions completed before the operation should result in 40% or less of the abnormal hemoglobin. During the procedure, sufficient oxygenation and body temperature should be maintained. Extubation should be completed after the patient becomes conscious and is breathing on his own, followed by oxygen administration (Kinsey et al. 1979). To prevent dehydration during the operation, copious amounts of IV normal saline should be given. Lactated Ringer's solution should be avoided because the lactate may cause lactic acidosis in these patients (Smith et al. 1987).

The main contraindication for dental treatment with the SCA patient is routine care during a crisis. Following are a few guidelines that may be helpful:

1. Schedule dental appointments during the morning with minimum treatment for a brief visit (Primley et al. 1982)
2. Prescribe CNS depressants judiciously (Primley et al. 1982)
3. Use acetaminophen for treatment of pain because salicylates may induce acidosis (Smith et al. 1987)
4. Avoid elective surgery, such as the removal of asymptomatic impacted teeth (Rouse and Hays 1979)
5. Incorporate home fluoride therapy and routine dental recall visits into the preventive dental treatment regimen (Rouse and Hays 1979).

Conclusion

This review was designed to present background information on SCA, describing the course of complica-

tions of this disease. The dentist's goal should be to treat the SCA patient with a thorough understanding and knowledge of the disease; ramifications of the disease must be considered carefully before dental treatment is initiated. One of the dentist's main goals should be to instill a positive attitude in the patient and parents toward maintaining good dental health. The dentist should monitor preventive dental care at routine follow-up visits. A three-month recall may be necessary in some cases. The dentist must be sure that SCA patients are receiving the latest preventive dental measures (e.g., sealants, fluorides, antimicrobial rinses, etc.) Finally, a team approach including the physician, dentist, and patient is vital to the successful dental management of the patient with sickle cell anemia.

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