Orofacial Manifestations in Patients With Sickle Cell Disease

Fawad Javed, PhD, Fernanda O’Bello Correa, PhD, Nasser Nooh, MSc, Khalid Almas, FICD, Georgios E. Romanos, PhD and Khalid Al-Hezaimi, MSc

Abstract: Background: The aim of this study was to review the orofacial manifestations in patients with sickle cell disease (SCD). Methods: Indexed databases were explored using various combinations of the following keywords: “sickle cell anemia,” “sickle cell disease,” “oral health status” and “dental inflammation.” Results: Hypoxia has been associated with osteomyelitis of the jaws, particularly the mandible in patients with SCD. Bone marrow hyperplasia in these patients causes depression of nasal bridge, midfacial overgrowth and malocclusion. Mental nerve neuropathy due to osteomyelitis of the mandible causes numbness in the lower lip and chin. A diminished blood supply to teeth causes necrosis of the dental pulp in patients with SCD. Dental caries is a common manifestation in patients with SCD, particularly in those with underprivileged living standards. The association between SCD and periodontal inflammatory conditions remains unclear. Conclusions: Oral health problems in patients with SCD are rare and occur mainly as a result of the poor oral hygiene maintenance.


The detrimental effects of systemic disorders on oral health have been reported. Several studies have shown that patients with medical illnesses such as poorly controlled diabetes, impaired glucose tolerance, cardiovascular anomalies, renal disorders, rheumatoid arthritis and acquired immune deficiency syndrome are more susceptible to develop oral inflammatory conditions as compared with their medically healthy counterparts. Likewise, studies have also shown that patients with hematologic disorders are more susceptible to develop periodontal inflammatory conditions, oral mucositis, tooth morphological disorders such as agenesis and microdontia, and developmental defects in the enamel and dentin as compared with their medically healthy counterparts. Although hematologic therapeutic regimes (such as stem cell transplant, chemotherapy, radiotherapy and surgery) may improve the overall health status of the affected individuals, they may concurrently trigger side effects that may in turn jeopardize other areas of the body including the oral cavity.

Sickle Cell Disease—Etiology and Epidemiology
Sickle cell disease (SCD) is a group of inherited hematologic disorders (including sickle cell anemia [SCA], sickle cell hemoglobin disease and beta-thalassemia) in which an abnormal form of hemoglobin (hemoglobin S) polymerizes under low oxygen tension thereby giving a sickle shape to red blood cells and reducing their normal elasticity. SCA is the most common form of SCD, which if left untreated may result in early childhood death.

Most of the patients with SCD and carriers of its trait belong to African, Asian, Arabian and Mediterranean origins; however, worldwide population migration has made SCD a global issue. Across equatorial Africa, the prevalence of healthy SCD trait carriers ranges between 10% and 40% as compared with North and South Africa where the prevalences of SCD are between 1% and 2% and <1%, respectively. In West African countries, such as Ghana and Nigeria, the frequency of sickle cell trait carriers ranges between 15% and 30%, whereas East African countries, such as Uganda and Tanzania, show wide variations of up to 45%. In Nigeria, approximately 20 out of every 1000 births are estimated to be affected by SCD, which corresponds to nearly 150,000 children with SCD born annually in the country. In Saudi Arabia, the prevalence of SCD varies significantly in different parts of the country, with the highest prevalence in the eastern province, followed by the southwestern provinces. The prevalence for sickle cell trait in Saudi Arabia ranges from 2% to 27%, and up to 2.6% will have SCD in some areas. In the United States, at least 70,000 individuals have SCD and nearly 2 million people are carriers of the SCD trait.

Clinical Features and Complications of SCD
The clinical manifestations of SCD vary depending upon the phenotype of the disease. In the hemolysis-associated phenotype, anemia, leg ulcers and pulmonary hypertension are salient features whereas the vaso-occlusion phenotype is characterized by acute chest pain, stroke and avascular necrosis of joints. A number of orofacial manifestations have also been reported in patients with SCD, such as midfacial overgrowth, anesthesia of mandibular nerve, asymptomatic pulpal necrosis and gingival enlargement. A number of orofacial manifestations such as asymptomatic pulpal necrosis, anesthesia of mandibular nerve, gingival enlargement, midfacial overgrowth and osteomyelitis of the mandible have also been reported in patients with SCD. Because oral health status may be jeopardized in patients with SCD, the aim of the present study was to review the orofacial manifestations in subjects with SCD.

MATERIALS AND METHODS

Eligibility Criteria
The following eligibility criteria were imposed: (1) clinical studies and case reports, (2) retrospective studies, (3) control group: individuals without SCD (healthy controls), (4) reference list of potentially relevant original and review articles.
oral health status of patients with sickle cell disease (SCD) and (6) articles published only in English. Letters to the editor, historic reviews and unpublished data were excluded.

Search Strategy

The authors explored the PubMed/MEDLINE (National Library of Medicine, Washington, DC) and Google Scholar databases for appropriate articles addressing the focused question—“What is the oral health status of patients with SCD?” Databases were searched from 1957 up to and including June 2012 using the following terms in different combinations: “dental inflammation,” “oral health status,” “sickle cell disease” and “sickle cell anemia.” Full text of the articles judged by title and abstract to be relevant were read and evaluated with reference to the eligibility criteria. The next step was to hand-search the reference lists of original and review studies that were found to be relevant in the first step, and any disagreement among the authors regarding the eligibility of included studies was resolved via discussion. Because only a limited number of original studies addressed our focused question, the pattern of the present review study was customized to chiefly summarize the pertinent information.

RESULTS AND DISCUSSION

Osteomyelitis of the Jaws

Osteomyelitis is an inflammatory condition of the bone, beginning in the medullary cavity and extending to involve the periosteum of the affected area. It is more common in the long bones. Osteomyelitis of the jaws secondary to SCD is rare; however, when it occurs, the mandible is the most commonly affected facial bone because of its relatively poor blood supply.31,32 Osteomyelitic lesions of the mandible usually occur in the third decade of life, whereas those of the maxilla mainly occur in patients in the first decade of life.33 In a case report,32 a 25-year-old woman reported to a health care center with complaints of pain and swelling over the right maxilla. Upon intraoral examination, maxillary congestion with suppuration and exposure of alveolar bone from the third molar region was observed. Radiological evaluation of the maxilla showed a large sequestrum of bone extending from the right maxillary first premolar to the maxillary tuberosity. The second premolar had exfoliated and the socket did not display any evidence of healing.32 The medical history revealed that the patient suffered from SCA and had sickle cell crisis 24 months earlier. Hematologic investigations confirmed that the patient’s hemoglobin level was 6 g/100 mL, sickling of red blood cells was positive on a smear and electrophoresis showed the presence of hemoglobin SS type.32 Similar clinical and hematologic features were observed in another case report.33

Various explanations have been posed regarding the pathophysiology of osteomyelitis. Because of the sickled cells, sludging occurs in the microvasculature that causes obstructed blood flow and leads to tissue ischemia and hence osteomyelitis can be established.34 Persistent ischemia may induce bone necrosis and invite secondary infection to the site. In long bones, secondary infection is caused by strains of various microorganisms such as Salmonella typhimurium, S enteritidis, S choleraesuis and S paratyphi B, followed by Staphylococcus aureus and gram-negative enteric bacilli.34 However, in jawbones, staphylococci and Escherichia coli are commonly cultured from such lesions.32,35

There is a risk of sickle cell crisis during surgical management of osteomyelitis under general anesthesia. Therefore, preoperative correction of hemoglobin deficiency, preoperative and postoperative antibiotic cover and prevention of hypoxia, avoidance of surgery during a crisis and a thorough postoperative care are essential.

Facial Overgrowth

It has been reported that SCD affects growth because of its chronic effects on bones.36,37 According to Gupta,36 children with SCD develop characteristic facial appearances that include frontal bossing and protrusion of the maxilla (which exposes their teeth, depresses the nasal bridge and causes malocclusion). This facial profile has been reported to be more prominent among children with SCD in the age-group of 11 to 14 years as compared with medically healthy children of the same age-group.37 Facial overgrowth is relatively uncommon in patients with SCD because of the small amount of marrow space within the maxillofacial bones. However, orbital wall infarction may occur in youths because there is more marrow space in the orbital bone in children than in adults.37 Likewise, maxillary overgrowth and consequent malocclusion in young patients with SCD has also been associated with bone marrow hyperplasia in these patients.38

Numb Chin Syndrome (Mental Nerve Neuropathy)

Numb chin syndrome (NCS), also called mental nerve neuropathy, is a sensory neuropathy characterized by numbness involving the distribution of the mental nerve.39 Odontogenic etiologies of NCS include jaw osteomyelitis, dental abscess, facial trauma and dental anesthesia, whereas systemic conditions such as SCD, diabetes mellitus and acquired immune deficiency syndrome have also been associated with the development of NCS.39 Isolated numbness in the lower lip and chin are classic symptoms of NCS. In some instances, teeth may also exhibit loss of sensation (in case other branches of the inferior alveolar nerve are involved) and patients may bite their lip unintentionally causing painless ulcers.40 Symptoms are usually unilateral but up to a third may have bilateral symptoms.41–44 Sickle cell crisis causes a painful mental neuropathy due to vaso-occlusive disease and/or osteomyelitis of the mandible because of its relatively low blood flow as compared with other bones. A vaso-occlusive crisis in the mandible may cause permanent neuropathies affecting the inferior alveolar nerve that may cause persistent anesthesia for up to 24 months.43 This may be an explanation for studies41–43 that reported a significantly higher prevalence of mental nerve neuropathy in patients with SCD as compared with medically healthy controls.

Dental Caries

Dental caries is a disease of the mineralized tissues of teeth (namely enamel, dentin and cementum) caused by the action of cariogenic bacteria (chiefly Streptococcus mutans) on fermentable carbohydrates leading to the demineralization of these mineral portions and (if left untreated) disintegration of their organic matrix. In a study on African American adults, Laurence et al46 investigated the association between SCD and dental caries. In this study,46 102 African American adult patients with SCD and 103 age-matched and sex-matched controls (individuals without SCD) were included. All participants underwent a standardized oral examination and interview to ascertain risk factors for dental caries including socioeconomic status (SES), dietary habits, age, sex and frequency of toothbrushing. The results demonstrated that individuals with SCD having a household income of <15,000 dollars had 6 times as many decayed teeth as compared with those without SCD, with no significant differences in dietary habits and frequency of toothbrushing between the groups (individuals with and without SCD).48 Similar
results were reported by Luna et al. An underprivileged SES among patients with SCD may have prevented them from receiving appropriate treatment for dental caries. It is also possible that patients with SCD focus on the treatment of their hematologic disorder and management of dental caries may be a secondary issue for these individuals. In another study, Laurence et al. showed decayed tooth surfaces to be higher in children with SCA as compared with those without SCA; however, there was no statistically significant difference between the groups. In the study by Okafor et al., prevalence of dental caries was higher in subjects without SCA (54%) as compared with those with SCA (35.13%). These results may be explained by another study in which the authors showed that long-term antibiotic therapy in patients with SCA reduces the acquisition of S mutans, thereby significantly reducing the caries rate in these patients. However, recently, Passos et al. reported that the risk factors known to cause dental caries are associated with oral health maintenance than with SCD.

Dental Pulp Necrosis

Toothaches are more frequent in patients with SCA as compared with healthy controls, which may possibly be due to abnormal blood flow to the dental pulp. In the study by Cox and Soni, dental pulps of tooth sections of patients with SCA were analyzed. Sickle-shaped cells in the dental pulp vasculature were visible from patients with SCA 2 to 3 days after an acute crisis. Infarction/thrombosis of dental pulp vessels may expose the vital pulp to hypoxia, thereby mimicking pulp pain. Persistent hypoxia in the pulp chamber may cause pulp necrosis that may radiologically appear as a periapical lesion. In the study by Andrews et al. nearly 38% periapical lesions were reported around teeth of patients with SCD. A 4-year follow-up indicated healing of the periapical lesions, suggesting thrombosis as the main factor associated with dental pulp necrosis in patients with SCD. It has been reported that some patients with SCD may remain asymptomatic to pulp changes, which may make them unaware of the ongoing dental pulp tissue damage.

Periodontal Disease

It has been reported that the severity of periodontal disease and inflammatory conditions in patients with SCD are associated with oral hygiene maintenance rather than the hematologic disorder itself. In a prospective comparative study, the association between SCA and periodontal disease was assessed using 50 adolescents (11–19 years) with SCA and 50 age-matched controls. The results showed no significant differences in the mean gingival and plaque indices. The periodontal status of the adolescent boys with SCA was similar to that of their female counterparts, whereas the adolescent boys in the control group had poorer oral statuses as compared with the adolescent girls in the same group. This study concluded that SCA does not lead to increased severity in periodontal disease. In the study by Guzeldemir et al., gingival and plaque indices were higher in patients with SCD as compared with their medically healthy counterparts; however, no clinical periodontal disease or attachment loss was detected in patients with SCD.

There are isolated reports, where SCD has been associated with periodontal inflammation. Scipio et al. presented a case report of a 14-year-old Afro-Trinidadian boy, who was diagnosed with SCA at the age of 6 years. The patient presented with enlarged mandibular gingivae, which were firm on the buccal and lingual aspects. There was no evidence of dental caries on clinical and radiological grounds. Gingival biopsies were obtained, and the results showed extensive areas of hemorrhage and a densely fibrotic lamina propria with some inflammatory cells. In this case report, the authors suggested that the repeated episodes of hemorrhage with fibrous tissue repair were associated with gingival enlargement.

CONCLUSIONS AND RECOMMENDATION

SCD is a rare disease with special oral health findings for importance for the clinician. Although the prevalence of the disease seems to have geographic and genetic epidemiological characteristics, the oral health problems are mainly caused by the poor oral hygiene maintenance among patients with SCD. Also, a deprived SES may compel these patients to neglect oral health maintenance and focus more on achieving the basic standards of survival. Because of the significant clinical and possibly emergency events in these patients, the oral health provider is responsible to contribute in the diagnosis and treatment of the oral and perioral infections and to control orofacial pain to help these patients with SCD.

It is recommended that periodic oral/dental health screening should be provided as part of the general physical examination in subjects with SCD. Furthermore, the significance of oral health maintenance should be emphasized through oral health promotion programs in patients with SCD and in the community. Routine dental checkups and regular oral hygiene maintenance may help minimize (if not prevent) oral health-related complications in patients with SCD.

REFERENCES


