Pulpal necrosis with sickle cell anaemia

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Abstract

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Aim To investigate radiographic manifestations of sickle cell anaemia (SCA) and whether or not a pulpal necrosis may develop without a pathological history.

Methodology Thirty-six patients with homozygous SCA were evaluated, and a further 36 individuals without SCA were included in the study as a control group. All 72 patients participating in the study ranged between the ages of 16 and 40 years. General and dental histories of the individuals were recorded. Electrical pulp test, percussion and thermal tests were applied to all the teeth having no restorations. Orthopantomograms of all the subjects were taken. Data obtained from questionnaires, sensitivity tests and radiographic examinations were evaluated by chi-square and Fischer's exact test.

Results Fifty-one (6%) of the teeth having no restorations or history of trauma were determined as being nonvital in the SCA group. In 30 (83%) of these patients orofacial and dental pain with no obvious cause was detected and in 24 (67%) of the patients the quality of the bone tissue as examined radiologically had deteriorated. In eight (22%) of the patients cortical thinning and irregularity in the mandible was noted. A statistically significant difference between the SCA and control groups ($P < 0.05$) was found in terms of pulpal sensitivity and radiological findings.

Conclusion SCA is a genetic and systemic disease which may cause pulp necrosis without necessarily having an identifiable aetiology. SCA causes radiographically observable differences in jaw structure especially in the mandible.

Keywords: dental pulp, mandible, sickle cell anaemia.

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Introduction

Sickle cell anaemia (SCA) is one of the familiar haemoglobinopathies inherited through an autosomal recessive mutant gene. The term 'haemoglobinopath' is usually restricted to the inherited disorders of the structure and synthesis of globin. Since the first description of sickle cell haemoglobin by Pauling *et al.* (1949) more than 500 structurally different human haemoglobin variants have been discovered.

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SCA is caused by the presence of the autosomal recessive sickle haemoglobin gene which is present on chromosome II (Bishop *et al.* 1995). If only one of the pair of chromosomes is affected, sickle cell trait develops whilst SCA reflects the involvement of both chromosomes (Cherry-Peppers 1992). The gene defect causes an amino acid substitution in the β-haemoglobin chain in the red blood cells (RBCs). The abnormal haemoglobin S (HgS) is less soluble than normal haemoglobin and this results in the distortion of the RBC during periods of low oxygenation. This distortion gives rise to the classic 'sickle-shape' appearance of the cell (Bishop *et al.* 1995).

SCA primarily affects members of the black race. It is estimated that 8–10% of American blacks are heterozygous and 0.2% are homozygous. Although Afro-Caribbeans are predominantly affected, Mediter-

ranean, middle Eastern and East Indian people may also be at risk.

The most important health problem in Turkey (especially in the southern provinces) related to haemoglobin variants is SCA (Arcasoy 1992). There are various ethnic groups living in this area, in particular, Turkish, Arabic and Kurdish populations. Because of this characteristic ethnic distribution, haemoglobinopathies are found in this region, in particular, HgS (Koçak *et al.* 1995).

The high prevalence of sickle cell trait in these areas of the world, where malaria is common, has suggested that individual with sickle trait have a selective advantage over normal individuals when they contact this disease (Arcasoy 1992).

The clinical problems associated with SCA are attributed directly to the defective RBCs. The deformed cells are recognized as abnormal by the reticuloendothelial system and are destroyed. If this deformation is faster than the production of new cells, a haemolytic anaemia develops (Kelleher *et al.* 1996). Hyperplasia and widening of bone marrow spaces may occur as the body increases haematopoiesis in an attempt to maintain the number of blood cells (Andrews *et al.* 1983). The patient may also be more prone to infection as macrophages are involved in phagocytosis of the defective RBCs and may not be available for destroying bacteria (Patton *et al.* 1990). The distorted cells may also occlude the microvasculature and impede blood flow to an area. This can cause tissue anoxia, infarcts, necrosis and pain (Shroyer *et al.* 1991). Clinically, the anoxia results in a sickle cell crisis (SCC).

The sickled erythrocyte is more adherent than are normal red cells to the vascular endothelium, which suggests an additional mechanism for vascular obstruction (Barnkart *et al.* 1979). The first and most commonly involved organ is the spleen. By adulthood, the SCA patient has only a small remnant of fibrous tissue where the spleen once was; this phenomenon is termed 'autosplectomy'. Other organs commonly affected by recurrent episodes of vaso-occlusion are the joints of the extremities, the brain, kidneys, bones including the mandible, lungs, retina, and skin, especially on the distal lower extremities (Embury 1986, Iwu 1989, Fabry & Kaul 1991). Of patients with SCA approximately 50% die before they are 20 years old and most die before they are 40 years old (Barnkart *et al.* 1979).

Oral problems have been described, but these are not as common as other complications (Ryan 1971, Friendlander *et al.* 1980, Andrews *et al.* 1983, Patton *et al.* 1990, Shroyer *et al.* 1991, Gregory & Olujohungbe 1994, Kelleher *et al.* 1996). Those that have been recorded include: mandibular osteomyelitis, anaesthesia of the mandibular nerve and asymptomatic pulpal necrosis.

Sickle cell osteomyelitis is more common in long bones; it can also affect facial bones (Kelleher *et al.* 1996). The mandible is particularly at risk because of a relatively poor blood supply (Andrews *et al.* 1983, Patton *et al.* 1990). Intravascular sickling is thought to lead to an ischaemic infarction and necrosis of bone that creates a favourable environment for bacterial growth. After an SCA crisis, permanent neuropathies affecting the inferior dental nerve and resulting in persistent anaesthesia for up to 24 months have been reported (Friendlander *et al.* 1980, Gregory & Olujohungbe 1994).

The loss of sensation is thought to be caused by an infarction of the microvascular blood supply to the inferior dental nerve or its branches. The inferior dental nerve may be particularly vulnerable because it passes through a narrow bony canal (Ryan 1971).

The sickle cells are suspected of compromising the microcirculation of the pulp (Ingle & Taintor 1985). Andrews *et al.* (1983) observed asymptomatic pulpal necrosis in healthy teeth of patients with SCA. They reported that this was more common in patients with SCA and suggested that the sickled cell caused a blockage of the blood vessels supplying the pulp, which resulted in necrosis. Sickle cells have also been identified in teeth with a history of repeated episodes of pulpal pain (Andrews *et al.* 1983).

O'Rourke & Hawley (1998) have stated that patients with sickle cell disease (SCD) had been suffering from orofacial and dental pain without exhibiting dental pathology.

The purpose of this study was to determine a population of known homozygous sickle cell patients for possible radiographic manifestations of the disease and whether or not a pulpal necrosis develops without having any pathological history.

Materials and methods

This study was carried out at Çukurova University located in an area that has a high prevalence of heterozygote patients with SCA. Diagnoses of the individuals forming the study and the control groups were made by the haemoglobin electrophoresis test. Thirty-six individuals diagnosed with homozygous SCA in the Haematology Department of Çukurova University were evaluated as a patient group. These patient

had not experienced any sickling crises for at least 1 month during the present study and had not reported mandibular paraesthesia. A further 36 individuals without SCA living in the same area were included as a control group. The control group consisted of accompanying siblings and parents whose haemoglobin genotype was known to be free of SCA. After recording the general histories of the cohorts that were between the ages of 16 and 40 years, detailed dental histories were taken. The questionnaire developed by O'Rourke & Mitropoulos (1990) was used to determine the orofacial and dental pain endured by the individuals forming the study and control groups. The teeth and the restorations in the mouths of the subjects were determined by using a questionnaire (WHO Oral Health Assessment form), and to all the teeth having no restorations were subject pulp sensitivity tests (Digitest; Parkell, Farmingdale, NY, USA). A percussion, thermal tests were carried out by one individual.

Endodontic access cavities were prepared in the teeth that had no restorations and gave no response; local anaesthesia was not used.

Orthopantomographs of the subjects were obtained using a panoramic X-ray unit (Planmeca PM 2002 CC proline, Helsinki, Finland), with a 2.5 mm Al equivalent total filtration Lanex medium screen cassette (Kodak Co., Rochester, NY, USA) and Trimex 3M films (15 × 30 cm; 3M, Ferrania, Italy) at 70 kV, 10 mA, for 18 min. The films were processed in fresh solutions (Hacettepe, Ankara, Turkey) in an automatic processor (DÜrr XR 24, Bietigheim-Bissingen, Germany) at 28 °C for 4.3 min. Periapical radiographs were taken using Kodak ultraspeed films (58 × 76; Eastman Kodak Co., Rochester, NY, USA) exposed at 70 kV and 10 mA for 0.64 s with a dental X-ray unit that had 2.5 mm of Al equivalent filtration (Trophy, Vincennes, France). Radiographs were studied blindly by three radiologists, each of whom had at least 15 years expertise. Only cases where they agreed on the interpretation were included in the study.

In order to determine the status of trabecular bone, the panoramic radiographs and periapical films were evaluated. During visual examination of the radiographs, those thought to have a change in trabecular pattern were evaluated on a second occasion. In this second evaluation, further radiographs of the patients were obtained at a reduced exposure to establish the presence of an expected but sparse trabeculation that was overexposed and burned out in the initial projection, this method was suggested by Goaz & White (1987).

In order to establish the thickness of the cortical bone, the method used by Horner & Devlin (1998) was applied. Normal cortical bone was scored as 1, and those showing porosities within the cortical bone structure were scored as 2.

Data obtained from both questionnaires, the sensitivity tests and the radiographic examinations were evaluated statistically using chi-square and Fischer's exact tests to determine difference between the SCA and control groups.

Results

The results are summarized in Table 1. Statistical analyses of the clinical and radiological findings of all subjects revealed that the number of nonvital teeth, the number of individuals with orofacial and dental pain, the ratio of 'stepladder' appearance in the radiographs, increase in bone density, cortical thinness and irregularity were significantly different in the SCA patient group when compared with those in the control group ($P < 0.05$). Pulp sensitivity tests were applied to the 878 teeth with no restorations in the 36 patients monitored in the study. Overall, 50 (6%) of the those teeth were nonresponsive to sensitivity tests. Endodontic access cavities were created without giving anaesthesia to all the teeth that had not responded to the sensitivity tests (Table 2). Contrary to this no nonvital tooth was encountered in the control group.

In 30 (83%) patients with SCA oral and dental pain without any obvious cause was recorded. However, it was found that five (14%) patients in the control group had complaints of orofacial pain whose aetiology could not be identified.

Table 1 Summary of the findings in 72 subjects

	Patient	Control
Number of the patients examined	36	36
Total number of teeth examined	827	1084
Number of teeth with crown	11	37
Number of nonvital teeth	51[a] (5.8)	–
Patients with orofacial and dental pain (excluding the sickling crises periods)	30 (83.3)	5 (13.9)
Patients with 'step ladder' pattern	10 (27.8)	–
Patients with decreased amount of trabecular bone	24 (66.7)	–
Patients with cortical bony thinning and irregularity	8 (22.2)	–

[a]Teeth having some restoration present were not been taken into consideration. Values in parentheses are in percentage.

Table 2 Distribution of 51 teeth found to have necrotic pulp

Molar		Premolar		Anterior teeth	
Maxilla	Mandible	Maxilla	Mandible	Maxilla	Mandible
3	12	12	20	2	2

Evaluation of radiographs revealed that significant changes, especially in the mandibular bone tissue of the patients with SCA; no extraordinary manifestation were noted on the control group.

In 24 (67%) of the patients the quality of the bone tissue in the mandible had deteriorated significantly, the trabecular bone density had decreased, and the bone marrow spaces were enlarged and had become locular (Fig. 1). A 'stepladder' trabecular pattern was observed in 10 patients (28%) (Fig. 2). As well as the changes in the trabecular tissue of the mandible of the patients, significant changes in the cortical bone were also observed. Thus, in eight (22%) of the SCA patients cortical thinning and irregularity in the mandible was observed (Fig. 2).

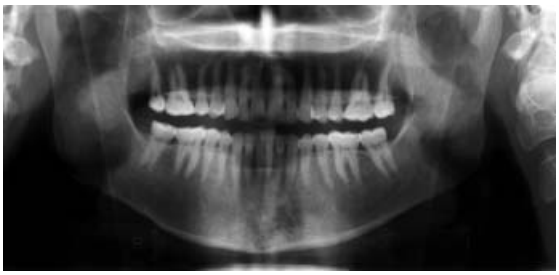

Figure 1 Orthopantomogram shows that the trabecular bone density had decreased, and the bone marrow spaces were enlarged and had become locular (age 33).

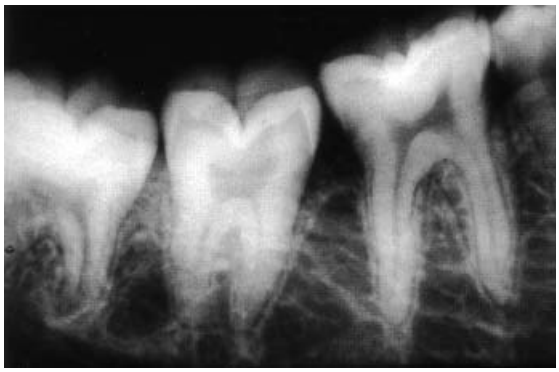

Figure 2 'Stepladder' in periapical radiograph of right posterior mandible (age 19).

Discussion

Sickle cell anaemia is the most important health problem related to haemoglobin in Turkey, especially in the southern provinces (Arcasoy 1992). There are various ethnic groups living in this area, especially, those of Turkish, Arabic and Kurdish origin. Because of this characteristic ethnic distribution, haemoglobinopathies are found in this region, in particular, HgS (Koçak *et al.* 1995).

The frequency of HgS found by the use of sickling test was 4% in the entire group. In the villages where Arabic was spoken, the rate was 10%, in the villages inhabited mainly by Turks the rate was 3%, this difference has been found to be statistically significant (Koçak *et al.* 1995).

Permanent neuropathies affecting the inferior dental nerve following an SCC have also been reported, and similarly, resulted in anaesthesia that persisted for up to 24 months (Friendlander *et al.* 1980, Gregory & Olujohungbe 1994). The loss of sensation is thought to be caused by an infarction of the microvascular blood supply to the inferior dental nerve or its branches. The inferior dental nerve may be particularly vulnerable as it passes through a narrow bony canal (Friendlander *et al.* 1980, Gregory & Olujohungbe 1994). Disruption of the sensory nerve supply means that conventional sensitivity tests are of little value and, as a result, such methods could not be used to confirm the radiographic or clinical findings (Rowe & Pitt-Ford 1990). Paraesthesia development in the mandible of patients with SCD is reported in the literature and it has been stated that the loss of sensation might affect the results of sensitivity tests (Terezhalmy & Moore 2003). To be able to eliminate this probability, in this study patients exhibiting no symptoms of paraesthesia were evaluated.

In previous studies pulpal necrosis without an aetiological factor has been reported (Andrews *et al.* 1983, Rowe & Pitt-Ford 1990, Bishop *et al.* 1995). Of the 36 individuals with SCA on whose 827 teeth the sensitivity tests were applied, pulp necrosis occurred with pathoses in 6%. This finding indicates that not only the mandibular bone structure is affected by the sickling crises, but also the tooth pulps are influenced.

Furthermore, it has been suggested that amongst the individuals with aetiologically undetermined nonvital teeth radiographic changes were determined (Smith *et al.* 1987, Bishop *et al.* 1995). Andrews *et al.* (1983) reported that 23% of the SCA patient group had been radiographically different. Smith *et al.* (1987) found

maxillary and mandibular changes in the 79–100% of patients with SCA. In this study, the prevalence of rarefaction was 67% in the mandible of the SCA patient group.

In patients with SCA the marrow spaces occur most commonly as radiolucent areas between the apices of the teeth and the inferior border of the mandible. Because of the characteristic horizontal trabecular arrangement, the pattern is referred to as a 'stepladder' (Sanger & McTigue 1978, Rose & Kaye 1983). This appearance in the bone tissues of patients with SCA has been reported previously (Andrews *et al.* 1983, Gregory & Olujohungbe 1994, Terezhalmy & Moore 2003). In 22% of the SCA patients cortical thinning of the mandible occurred. This indicates that the more compact cortical bone in the mandibular bone tissue had been affected by the sickling crises.

O'Rourke & Hawley (1998) reported pain without dental problems in 68% of the patients with SCA. The orofacial and dental pain of no reason in the 83% of patients in this study is rather higher than the control group.

Conclusion

SCA, a genetic and systemic disease, causes pulp necrosis. As SCA affects pulpal microcirculation, pulpal necrosis occurs without any other aetiological factor.

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