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Evaluation of mandibular bone structure in sickle cell anemia patients

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ÖZET

Orak Hücreli Anemi Hastalarında Mandibular Kemik Yapının Değerlendirilmesi

Orak hücreli anemi (OHA) ailesel kaynaklı hemoglobinopatidir. OHA ve osteomiyelit başlangıcına dair birçok radyografik bulgu vardır. Retrospektif olarak Konik Işınlı Bilgisayarlı Tomografi (KIBT) ile 10 hasta değerlendirildi. KIBT ile elde edilen DICOM verileri OHA hastalarında mandibular kemik yapıdaki değişimleri değerlendirmek üzere üçüncü bir yazılıma transfer edildi. Hastalarda kemik dansitesi, trabeküler kalınlık, trabeküler ayrılma, trabeküler sayı, fraktal boyut, kapalı por sayısı, kapalı por hacmi, kapalı por yüzeyi, kapalı porozite, açık por hacmi, açık porozite, por boşluğunun total hacmi ve total porozite gibi kriterler değerlendirildi. Ortalama fd değeri sağlıklı bireylerden daha düşük bulundu. SCA hastaları ile sağlıklı bireylerin FD değerleri arasındaki fark istatistiksel olarak anlamlı olarak bulundu ($p<0,05$). Aynı zamanda, trabeküler kalınlık sağlıklı bireylerden daha fazla bulundu ($p<0,05$). Bulgularımıza gore, SCA da FD azalması olduğunu gösterdi ancak daha geniş hasta grubunda çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: Anatomi, Dijital Görüntü Analizi, Radyoloji, Orak Hücreli Anemi

SUMMARY

Sickle cell anemia (SCA) is a familial hemoglobinopathy. There are several radiographic findings regarding both SCA and onset of osteomyelitis. Cone Beam CT examinations of 10 patients were evaluated retrospectively. The DICOM data from CBCT examinations were transferred to a 3rd party software in order to evaluate the mandibular bone changes in SCA patients. Following parameters were evaluated; Bone surface density, Trabecular thickness, Trabecular separation, Trabecular number, Fractal dimension, Number of closed pores, Volume of closed pores, Surface of closed pores, Closed porosity, Volume of open pore space, Open porosity, Total volume of pore space, Total porosity. The mean of FD values was found to significantly lower than healthy individuals. Statistical analysis of FD values barely reached to significance between SCA patients and the healthy individuals ($p<0,05$). It was also found that trabecular thickness was also significantly higher than healthy patients ($p<0,05$). Our findings revealed decreased FD with SCA, further studies should be done with larger groups in order to define optimal parameters for SCA patients in mandible.

Key words: *Anatomy, Digital image analysis, Radiology, Sickle Cell Anemia*

Introduction

Sickle cell anaemia (SCA) is a familial hemoglobinopathy that is inherited through an autosomal recessive mutant gene that is present on chromosome II. It primarily affects the members of the black race; however, Afro-Caribbeans, Mediterranean, Middle Eastern, and East Indian people may also be at risk (1,2). There are several complications regarding SCA in the oromaxillofacial region; Osteomyelitis is an inflammatory condition of the bone, beginning in the medullar 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 (3,4).

There are several radiographic findings regarding both SCA and onset of osteomyelitis. Abnormal skull radiography findings in sickle cell anaemia are well documented. The patients X-rays show widening of the diplopic space, thinning of the outer table, vertical trabeculations (the classical hair-on-end), and granular appearance of the skull. Moreover, consequently, trabecular changes, bony expansion of the jaws, hyperplasia, and widening of bone marrow spaces and coarsening of the trabeculae are noticed (4,5). The radiographic findings in the mandible regarding the trabecular area, fractal dimension have not been studied intensively.

Knowledge of the normal changes with aging of bone marrow in jaws is important for accurate and early diagnosis of focal or diffuse bone marrow changes, including those of neoplastic, infectious etc. Hence, the aim of this study was to assess the properties of mandible with SCA patients and compare with that of healthy individuals.

Material And Methods

Cone Beam CT examinations (Newtom 3G machine, QR Verona, Italy) of 10 patients age range was 17-23, mean 18,7 years) were evaluated retrospectively. 5 healthy individuals and 5 SCA patients were included in this study. There was no other systemic disease apart from SCC in the patients. In order to have similar age groups for SCA (-) and SCA (+) patients. For a normal distribution, the agreement between age-related variation and normal distribution was tested using the Shapiro-Wilk test. The descriptive statistics of age-related variables are shown as medians [interquartile range (IQR)].

All images were recorded at 120 kVP and 3-5 mA using a 9-inch field of view, an axial slice thickness of 0.3 mm and isotropic voxels in order to include mandible bone. All CBCT images were evaluated retrospectively by a single observer

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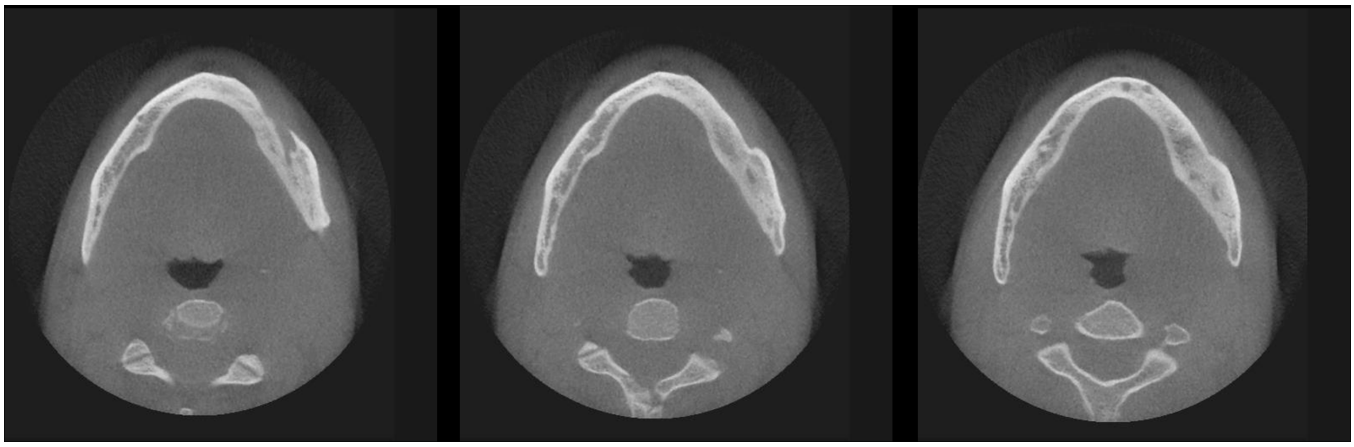

Figure 1. CBCT images showing mandibular bone structures in a Sickle cell anaemia patients with osteomyelitis

The DICOM data from CBCT examinations were transferred to a 3rd party software (CTAn, v 1.12, Brüker Skyscan, Kontig, Belgium) in order to evaluate the mandibular bone changes in SCA patients.

ROIs were then selected within each image by using CTAn software selected as a fixed elliptic size ROI for each patient that located between the first molar and second premolar teeth of the each (right/left) mandibular segment which were outlined manually in each radiograph (Fig. 2). The ROIs were selected as apically as possible in order to prevent the influence of transient alterations within the alveolar crestal bone on the fractal dimension (FD) measurements. Lamina dura, periodontal ligament and related regions, and root apices were not included within ROI. All digital manipulations and measurements were made within the ROIs rather than of the entire axial CBCT image. Following parameters were evaluated for both healthy and SCA patients; Bone surface density, Trabecular thickness, Trabecular separation, Trabecular pattern factor, Structural model index, Trabecular number, Fractal dimension, Number of closed pores, Area of closed pores, Surface of closed pores, Closed porosity (percent), Area of open pore space, Open porosity (percent), Total area of pore space, Total porosity (percent).

Statistical methods

Statistical analyses were carried out using SPSS 12.0.1 (SPSS, Chicago, IL, USA) software program. Pearson Chi square test also used to test the relationship between both gender and side and each variables ($p<0.05$).

Results

The SCA (-) patients' mean age was 18.2 (IQR=9.0) years, while SCA (+) had a mean age of 19.2 (IQR=8.0) years; this age difference was not significant ($Z=1.560$, $p=0.119$). The patients age was found to be normally distributed ($W=0.946$, $p<0.001$). The mean of FD values were found to significantly lower than healthy individuals. Statistical analysis of FD values showed significance between SCA patients and the healthy individuals (mean FD SCA (+) 1.51; mean FD controls; 1.80 ($p<0,05$). It was also found that trabecular thickness (mean 7.73/mm) was also significantly lower than healthy patients (5.49/mm) ($p<0,05$). (Table I). Moreover, a significant decreased bone density, trabecular number, trabecular pattern factor, number of closed pores and structural model index were found for SCA (+) ($p<0,05$). A significant increase was also found for "area of open pore space" and "total area of pore space" in SCA (+) patients ($p<0,05$). No significant difference was found

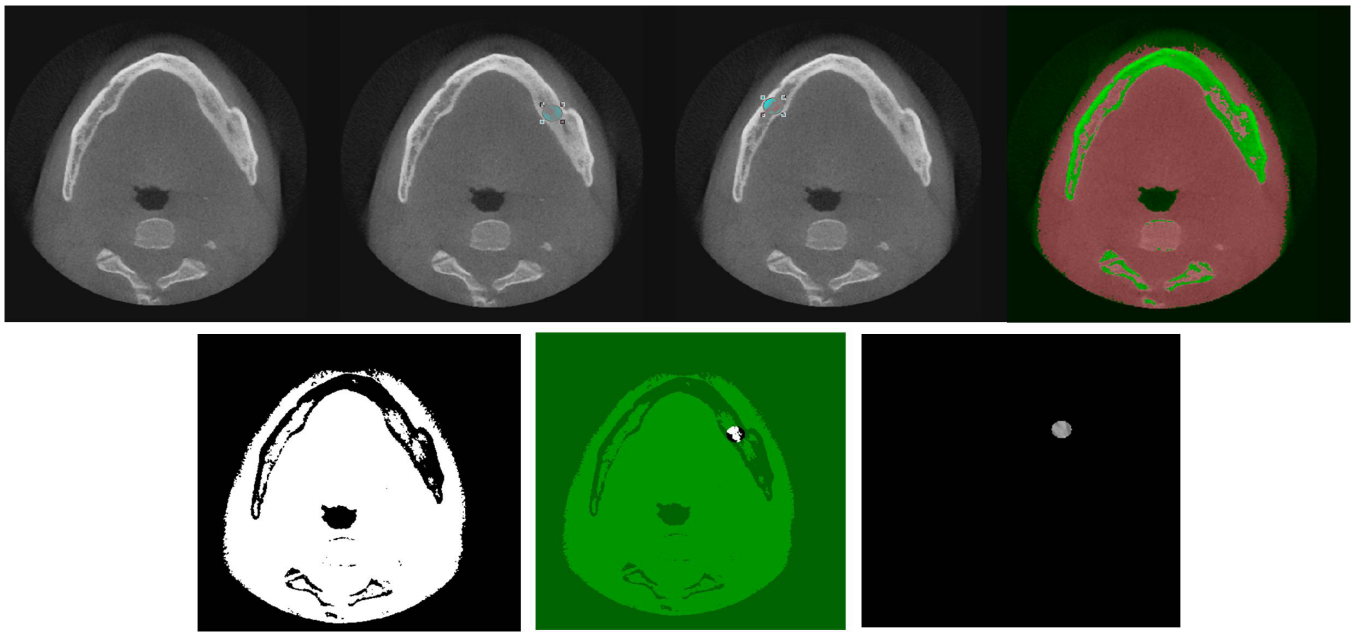

Figure 2. The evaluation of bone parameters in CTAn software (v 1.12, Brüker Skyscan, Kontig, Belgium)

for right/left sites both for SCC(-) and SCC (+) (p>0,05).

Discussion

Numerous studies have investigated the bone and its marrow changes of the vertebrae, femur, pelvis, and knee in the settings of hematological malignancy, chronic anemia and osteomyelitis using different kinds of radiographical techniques techniques (6-11). Recent studies on mandible are more focused on TMJ have focused on bone marrow alterations (edema, osteonecrosis) in the mandibular bone marrow alterations. Most of them stated that bone marrow edema is closely related to internal derangement, osteoarthrosis and effusion. They also reported that edema may be a precursor for osteonecrosis in the mandibular condyle, and suggested that osteonecrosis might be a separate entity and primarily a bone marrow disease (12-17). The osteonecrosis has proved to be a painful condition in the femoral head, knee, clivus, vertebrae and it was proved that the bone marrow edema can result irreversible osteonecrotic lesions. The etiology for this kind of edema pattern in these joints can be transient osteoporosis, stress fracture, major or minor trauma, and chronic anemia (sickle cell disease) (18-22).

Sickle cell anaemia is a common inherited autosomal disease which is characterized by abnormally shaped red blood cells. However it can involve virtually any organ system (23, 24), but bone involvement is the most common clinical manifestation of SCA (3, 25). On the other hand, although bone involvement is the most common manifestation, it is rare in the maxillofacial bone and skull base because of the small amount of marrow. Royal et al. (26) reported that the most frequently location was the orbital wall, followed by the mandible and skull base in the head and neck area. According to Almeida and Roberts(3) bone changes should be classified as follows: radiopaque areas associated with previous vasoocclusive incidents, osteomyelitis due to infections, and regions with osteoporosis arising from bone marrow hyperplasia.

Abnormal skull radiography findings in sickle cell anemia are well documented. The patients X-rays show widening of the diplopic space, thinning of the outer table, vertical trabeculations (the classical hair-on-end), and granular appearance of the skull. These are non-specific findings that may be also seen in thalassemia major, hereditary spherocytosis, and iron deficiency (7-12). Although there are several reports (2-5, 23-29) which have been published evaluating the clinical and radiographic alterations in the oral and maxillofacial region, to the best of our knowledge, the differences in the radiographic changes of the jawbones of SCA have not been previously described by using CBCT.

Conventional radiographs were used for investigating sickle cell disease esp. applying fractal dimeanisonal analysis. Fractal dimension has been widely used in the field of image analysis. As a principle, Fractal analysis is a method for describing complex shapes and structural patterns. Fractal dimension on periapical radiographs has been accepted as a basic descriptor of bone structure by some authors (30,31). The use of FD on panoramic radiographs maybe useful but only if they are sensitive enough (32). Although both imaging modalities have some limitations on detection bone structure by using Fractal anaysis, Bollen et al. (32) obtained lower values of FD from panoramic compared with periapical radiographs. Demirbas et al. (5) found lower values of FD on panoramic images in SCA patients compared healthy individuals. To the best of our knowledge there is only a few authors who report FD on CBCT images (33). But there is no any other reports in SCA patients. According to our results, we also found lower values of FD in

Table I. Mean values observed in SCA (-) and SCA (+) patients, *indicates statistical significance

Parameters	SCA (-)	SCA (+)	p value
Bone surface density	1.2968E+004,mm^2	1.0468E+004,mm2	**p<0.05***
Trabecular thickness	7.7318E+000,mm	5.5918E+000,mm	**p<0.05***
Trabecular separation	3.0172E+000,mm	3.0474E+000,mm	p>0.05
Trabecular number	1.2303E-001,1/mm	1.0104E-001,1/mm	**p<0.05***
Fractal dimension	1.8032E+000	1.5162E+000	**p<0.05***
Number of closed pores	8,3214+000	6,2814+000	**p<0.05***
Area of closed pores	6.1140E+001,mm^2	6.0138E+001,mm^2	p>0.05
Bone surface / volume ratio (closed pores)	8.3169E-001,1/mm	7.9945E-001,1/mm	p>0.05
Closed porosity (percent)	9.2607E-001,%	9.1708E-001,%	p>0.05
Area of open pore space	5.6438E+002,mm^2	7.8437E+002,mm^2	**p<0.05***
Open porosity (percent)	1.9157E+001,%	1.9058E+001,%	p>0.05
Total area of open pore space	6.2552E+002,mm^2	8.6572E+002,mm^2	**p<0.05***
Total porosity (percent)	2.1565E+001,%	2.1465E+001,%	p>0.05
Trabecular pattern factor	2.1211E-001,1/mm	2.0011E-001,1/mm	**p<0.05***
Structure model index	2.6057E+000	2.3848E+000	**p<0.05***

SCA patients.

Although increased bone density in skull bones is known as a feature of SCA, low bone density and decreased trabecular thickness are general characteristic features of SCA. These features have been indicated in several reports in literature. According to these reports whole body bones included mandible are affected by low density (23,34-36). As we presented at Table I, our results were compatible with this feature.

In conclusion SCD is a rare disease with special oral health findings for importance for the clinician. Our findings revealed decreased; FD, bone density, trabecular number, trabecular pattern factor, number of closed pores and structural model index for SCA (+) patients. CBCT or µct Image Analysis can be useful in identifying the SCA patients in advance and also to understand the pattern of bone changes in mandible. Further studies should be done with larger groups in order to define optimal parameters for SCA patients in mandible.

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