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Panoramic Radiographic Features of Patients with Acute Leukemia and Lymphoma who Are Candidates for Hematopoietic Stem Cell Transplantation

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Abstract

Background and Aim: Hematopoietic malignancies like leukemia and lymphoma may present several complications. This study aimed to evaluate the panoramic radiographic features of patients with acute leukemia and lymphoma who are candidates for hematopoietic stem cell transplantation (HSCT).

Materials and Methods: In this cross-sectional study, 63 panoramic radiographs of HSCT candidates (25 females, 38 males, between 16-75 years) and 62 healthy individuals (25 females, 37 males, between 16-73 years) were evaluated in Shiraz, Iran. Osteoporosis, pathological radiolucencies, pathological calcifications, cortical bone thickness, periodontal disease, condylar degeneration, and other alveolar bone findings were recorded. Data were analyzed by the Chi-square, Fisher's exact, and Mann-Whitney U tests (alpha=0.05).

Results: The thickness of nasal floor cortical bone, mandibular inferior cortex, and mandibular canal cortex was significantly lower in the patient group than the healthy group ($P<0.05$). Other abnormalities such as changes in periodontal ligament width, lamina dura thickness, and condylar degeneration were also more prevalent in HSCT patients compared to healthy controls ($P\leq0.05$).

Conclusion: It appears that panoramic views provide reliable information for detection of osteopenia and osteoporosis in HSCT patients. This may reduce the use of expensive and invasive diagnostic workups with radiation exposure to detect low bone density in this group of compromised patients.

Key Words: Jaw Abnormalities; Radiography, Panoramic; Hematopoietic Stem Cell Transplantation

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Introduction

As announced by the World Health Organization, malignancies are currently the second leading cause of death [1]. Blood cell malignancies comprise about 9% of all cancer cases which are confirmed annually [2]. Leukemia and lymphoma are the most prevalent hematopoietic malignancies which may present

with pallor, petechia, and ecchymosis of the skin and mucous membranes. Proliferation of hematopoietic cells within the growing skeleton makes the bone marrow a suitable site for proliferation of malignant cells; therefore, during the disease course, tenderness and multiple areas of bone destruction may be observed [3]. Although presence of bony lesions may not exacerbate the disease prognosis, they may appear earlier than other clinical manifestations. Many radiographic findings such as generalized reduction in bone density and lytic lesions would mimic benign or malignant intra-osseous lesions [3-5]. There is probably a multifactorial mechanism behind these complications; the nature of the disease, radiotherapy, and pharmacotherapy which are performed to control the disease, insufficient micronutrient intake by patients, and also diminished daily movement may lead to such complications [6, 7].

Treatment of hematological aplasia includes chemotherapy, radiotherapy, or a combination of both [8]. Salvage chemotherapy followed by hematopoietic stem cell transplantation (HSCT) remains the standard modality for recurrent lymphoma [9]; also, it has become a common therapy for treatment of benign and malignant hematological diseases [10]. This procedure involves the transplantation of multiple specialized hematopoietic stem cells normally obtained from the bone marrow, peripheral blood, or human cord blood [10].

Maxillofacial infections must be resolved prior to the ablative chemo-radiotherapy phase of HSCT to prevent possible infection transmission in donors with impaired immunity [11]. The need to provide dental care for HSCT candidates and recipients is growing every year [12]. In order to detect any occult or hidden lesion, infected teeth, or semi-erupted teeth, all HSCT candidates undergo screening examinations, including clinical examinations of the jawbone, teeth, gingiva, and oral mucosa. They also undergo radiographic examinations such as panoramic radiography and periapical radiography for clinically questionable teeth [13]. With a comparatively negligible exposure, panoramic radiography is low-cost, generally used, and comfortably carried out [14]. This imaging modality provides an acceptable view of the maxilla and mandible and related anatomical structures in one cliche. Considering the relatively low dose of radiation, its affordable price, and popularity among dental practitioners and patients, panoramic radiography is an appropriate choice for pre-transplantation dental screening [15]. Moreover, analysis of anatomical structures on a panoramic view of the head has been suggested as a substitute to dual-energy X-ray absorptiometry for detection and analysis of diminished bone mineral content and osteoporosis [16], and its application has been suggested for estimation of bone density level [17, 18].

Previous studies about HSCT candidates mainly focused on oral soft tissue complications caused by chemotherapy; however, jawbone manifestations, which can be featured on panoramic views, have not yet been exclusively analyzed, and there is no information regarding low bone density in HSCT candidates detected on panoramic radiographs. Accordingly, different jaw lesions and abnormalities on panoramic views of patients screened for receiving HSCT were assessed in the present study, and compared with systemically healthy individuals to assess the hard tissue changes of the maxilla and mandible in such patients.

Materials and Methods

This study was carried out according to the Declaration of Helsinki. Written informed consent was obtained from all participants. This study was approved by the Ethics Committee of Shiraz University of Medical Sciences (IR.SUMS.RCC.1397.519).

This analytical cross-sectional study was carried out on 63 panoramic radiographs of patients who were candidates for HSCT (25

females, 38 males, aged 16-75 years) and 62 healthy controls (25 females, 37 males, aged 16-73 years). All participants were recruited among those presenting to the Oral Medicine Department of Shiraz Dental School (Shiraz, Iran) for routine dental check-up and screening prior to hospitalization for the transplantation procedure. A control group was also randomly chosen from healthy individuals visited for routine dental examination at the same department between December 2017 and July 2018. The control group matched the patient group in terms of age and gender. Written informed consent was obtained from all participants.

Dentate patients who had panoramic radiographs with a standard resolution, had been diagnosed with lymphoma or acute leukemia, and were waiting for HSCT were assigned to the case group. Edentulous patients, patients suffering from other systemic and metabolic bone diseases and also substance abusers and smokers were excluded from the study. Demographic information of patients including their gender, age, and duration of disease was recorded.

Panoramic radiographs had been taken with a Planmeca XC Proline panoramic machine (Helsinki, Finland) with Agfa PSP receptors (Germany). The exposure parameters were adjusted individually according to the weight and age of patients (57-85 kVp, 10 mA). The images were viewed on a Barco monitor (China) in a semi-dark room. All radiographs were observed by both an oral and maxillofacial radiologist and also an oral medicine specialist. Osteoporosis and abnormalities such as degenerative changes of the condyle, pathological radiolucencies, calcifications, tonsillitis, and other findings in the jawbone and temporomandibular joint were recorded. On panoramic radiographs, osteoporosis is characterized by diminished bone mass and bone micro-structural changes and rarefaction, thinning of the cortex, and absence of lamina dura [19].

Temporomandibular disorders were characterized by degenerative changes of the articular bone and presence of osteophytes on panoramic radiographs [20].

Idiopathic osteosclerosis or dense bone island in response to increased bone regeneration was diagnosed according to the presence of well-defined, circular, elliptical, or irregular radiopaque areas [21].

Panoramic radiographs were evaluated for presence of radiolucent jaw lesions of both odontogenic and non-odontogenic origin with different etiologies (reactive, benign, and malignant) [19] (Figure 1).

Figure 1. Thinning of the cortex, fading of lamina dura, and decreased bone density on the panoramic radiograph of a patient with leukemia

Statistical analysis:

Data were analyzed using SPSS version 18 (SPSS Inc., Chicago, IL, USA). The Chi-square test was utilized to compare the findings between the case and control groups. The Fisher's exact and Mann-Whitney-U tests were further used to compare the results. Level of statistical significance was set at 0.05.

Results

A total of 63 panoramic radiographs of patients (38 males, 25 females, with a mean age of 45.08 years) who were candidates for HSCT and 62 age- and sex-matched healthy controls (37 males, 25 females, with a mean age of 44.65 years) were evaluated. The patients' age ranged from 16 to 74 years. Among the patients, 36 had

leukemia (24 males, 12 females, with a mean age of 43.69 years) and 27 had lymphoma (14 males, 13 females, with a mean age of 46.48 years).

Statistical analysis showed a significant difference between the patient and control groups regarding the thickness of the nasal cortical bone (P≤0.05), mandibular inferior cortical bone (P≤0.05), mandibular canal cortex (P<0.05), and cortical bone lining of the maxillary sinus (P≤0.05). The cortical bone thickness in these locations was significantly lower in the HSCT candidates compared with healthy controls. Thinning of the sino-nasal cortical bone was more frequently observed in males who were candidates for HSCT in comparison to healthy males (P≤0.05). The sinus cortex appeared healthier in females than males in the HSCT group (P≤0.05). Females in the HSCT group had thinner mandibular canal cortex compared to healthy females (P≤0.05).

Pathological jaw radiolucencies were more prevalent in healthy controls than the HSCT group (P≤0.05).

According to the Chi-square test, there was a significant difference between lymphoma cases and healthy controls concerning the presence of condylar thinning (P≤0.05).

Thinned and reduced lamina dura were more frequently detected in the HSCT group in comparison with healthy controls (P≤0.05). Also, periodontal ligament size was significantly smaller in the patient group (P≤0.05).

The two groups did not have a significant difference regarding radiographic pathological and non-pathological opacities (dense bone island, idiopathic osteosclerosis, tonsiloliths, sialoliths, and stylohyoid ligament elongation) (P>0.05). However, such opacities had a higher frequency in the HSCT males (P≤0.05) compared with healthy males. Furthermore, presence of periodontal disease did not demonstrate a significant difference between the two groups (P>0.05). Medial sigmoid depression was seen in four healthy women and none of the patients (P>0.05) (Table 1).

Discussion

HSCT is defined as the use of healthy hematopoietic stem cells in patients with insufficient or diseased bone marrow. This procedure regulates the action of bone marrow and depending on the type of abnormality being treated, it may either eradicate the tumor cells or produce normal cells to substitute the abnormal cells in cases with immune deficiency syndromes, hemoglobinopathies, and other diseases [22]. For this reason, the number of patients receiving this type of therapy has increased over the recent years [23]. Before, during, and immediately after HSCT, patients may present a variety of symptoms, of which bone degeneration is one of the most frequent and debilitating conditions [24].

Table 1. Prevalence of oral panoramic radiographic findings in HSCT patients and healthy controls

Radiographic findings	Leukemia	Lymphoma	Control	P value
Thin nasal floor cortical bone	40%	37%	4.8%	≤0.001
Thin sinus cortical bone	22.9%	29.6%	12.9%	0.039
Thin mandibular canal cortical bone	51.4%	74.1%	42.6%	0.024
Thin mandibular cortical bone	40.0%	37.0%	4.8%	≤0.001
Radiopaque lesions	58.3%	37%	33.9%	0.052
Periapical radiolucency	11.1%	14.8%	40.3%	0.002
Medial sigmoid depression	0%	0%	6.5%	0.058
Condylar degeneration	81.1%	61.1%	14.3%	0.010
Periodontal disease	72.7%	67%	60%	0.061
Thin lamina dura	48.5%	47.8%	28.3%	0.029
Reduced periodontal ligament thickness	39.4%	39.1%	8.3%	≤0.001

Boney changes, particularly jaw manifestations, have been rarely mentioned in HSCT candidates [1]. In the present study, radiographic findings were evaluated, and a wide variety of panoramic findings were observed in the HSCT group. The main finding of the present study was that jaw osteoporosis was the most common abnormality detected on panoramic radiographs.

Currently, cone-beam computed tomography is the most accurate method for examination of bony structures and is superior to panoramic radiography in accurate evaluation of subtle changes in bone structure. However, in the present study, digital panoramic radiographs were evaluated because panoramic radiography is more affordable, has lower radiation exposure, and is routinely used for pre-transplantation dental screening [25]. Furthermore, according to the literature, the efficacy of panoramic radiography and cone beam computed tomography in detection of anatomical structures is the same [26]. Universally, intraoral radiographs are preferred for detection of dental problems; however, they are not preferred for general assessment of bony structures [27]. Bone resorptions and calcifications could be detected on a panoramic cliché, and panoramic indices such as the mandibular cortical thickness and thickness of lamina dura can be used to predict osteoporosis [27]. In the current study, osteoporosis was assessed based on the cortical thickness of a number of anatomical landmarks and thickness of lamina dura on panoramic radiographs. According to the results, the majority of such indices, particularly mandibular and nasal floor cortical bone density and width, were significantly lower in the patient group than the control group. In agreement with this finding, a previous study evaluated the panoramic radiographs of 214 patients with acute leukemia and noted leukemia-related loss of bony crypts of the tooth buds of permanent teeth and loss or rarefaction of lamina dura of erupted teeth. Osseous changes of the jaws were reported in 62.9% of the children with active leukemia in a previous study [28]. Another study reported bone loss in an adult with acute myeloid leukemia and described discrete "punched-out" lesions resembling multiple myeloma in the maxilla and mandible of a 58-year-old man with chronic lymphocytic leukemia [29]. Ghapanchi et al. [18] used panoramic radiography to assess the radiographic features of patients with chronic liver failure in their pre-transplantation period. They recorded valuable findings on panoramic views including jaw osteoporosis, pathological radiolucency, pathological calcifications, tonsilloliths, and condylar degeneration.

Condylar degeneration was another significant finding on radiographs of patients in the present study. As shown in the literature, osteoporosis can affect the mandibular condyle which is probably a reliable marker as a preliminary indicator of osteoporosis on panoramic views [30]. The fibrocartilage of the temporomandibular joint is placed over the mandibular condyle which makes the mandibular condyle more susceptible to immunological problems and is also a valuable marker for detection of any alteration in the articular structure. Moreover, serum levels of biomarkers of inflammation such as epithelial neutrophil-activating peptide, matrix metalloproteinase-3, plasminogen activator inhibitor-1, vascular endothelial cadherin, vascular endothelial growth factor, and granulocyte-macrophage colony-stimulating factor were found to be associated with bone degeneration in this area [31]. These findings are all supportive of the effect of systemic changes on condylar morphology. Based on the literature, emotional pressure also affects temporomandibular disorders; there was an up-regulation in cytokines such as tumor necrosis factor-α and interleukin-1ß in the mandibular condylar cartilage following stressful situations, possibly leading to temporomandibular disorders [32].

Furthermore, pathological intra-osseous defects or abnormalities were more prevalent in healthy controls than the HSCT group. These lesions are mainly due to dental caries and pulp necrosis. The significant difference between the two groups in this regard can be justified by the fact that the HSCT patients had received oral hygiene instructions for several months to prevent dental infections. On the other hand, these patients are usually under the supervision of a dentist for a long time from the onset of their disease. Thus, sources of oral and dental infections are more rapidly identified and treated in them.

Other skeletal changes such as radiopaque lesions were also more prevalent, although not significantly, in the HSCT group compared to the control group. Idiopathic osteosclerosis is defined as localized bone growth with no detectable cause [33]. This asymptomatic lesion needs no treatment, but it has to be distinguished from other causes of bone opacity resulting from inflammatory causes and systemic diseases [34]. Tonsilloliths may appear incidentally on panoramic radiographs as multiple and small radiopacities superimposed on the mandible and the surrounding soft tissue. They cause discomfort, halitosis, bad taste, and otalgia and can be a cause of glossopharyngeal neuralgia [35].

Another panoramic finding which was more prevalent in the HSCT patient group was periodontal disease in the present study. Overholser et al. [36] studied acute leukemia other than the lymphocytic subtypes for detection of periodontal disease at the time of hospital admission for acute exacerbations during myelosuppressive chemotherapy. They reported periodontal disease in more than half of the patients and all patients had asymptomatic periodontal disease at the time of admission. However, in the present study, the difference between the case group and the control group was not significant in this regard. This could be attributed to the high prevalence of periodontal disease in the control group (60%), or the type of study which was only based on radiographic findings and did not evaluate clinical signs and symptoms of patients. Given the importance of these changes and the role of such indicators in preventing post-transplantation or dental infections, further research is required regarding the frequency and etiology of these lesions in the HSCT patients.

Small sample size and poor quality of some radiographs were among the limitations of this study.

Conclusion

Panoramic radiography is a valuable modality for detection of osteopenia and osteoporosis in HSCT patients. Bone density analysis can be planned for individuals to estimate the overall risk of bone fracture after finding diminished bone density or osseous rarefaction on routine panoramic radiographs taken for dental assessment prior to transplantation surgery. This can reduce the need for expensive and invasive diagnostic workups with radiation exposure to detect low bone density in this group of compromised patients.

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Conflict of Interest

The authors alone are responsible for the content and writing of the paper and declare no conflict of interests.

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