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ORIGINAL ARTICLE

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Dental and maxillofacial outcomes in childhood head and neck cancer survivors: a retrospective study and dental care considerations

Abstract

Cancer treatment during childhood, including head and neck radiotherapy and chemotherapy, can cause persistent dental and maxillofacial changes, which may lead to long-term complications in dental care and oral rehabilitation. **Objective:** The aim of this study was to evaluate dental and maxillofacial alterations resulting from childhood head and neck cancer treatment and discuss considerations regarding dental care for these patients. **Methods:** This retrospective study utilized a Cancer Center database, including patients referred to the Stomatology Department from 2004 to 2018. **Results:** The sample comprised 12 patients (7 males and 5 females) with a mean age of 5 years at diagnosis, who underwent oncological treatment in the head and neck region. Half exhibited facial bone hypoplasia, predominantly mandibular (33.33%) over maxillary (16.67%). Nearly all patients showed dental abnormalities, including agenesis (50%), supernumerary teeth (16.67%), and root formation anomalies (66%). **Conclusion:** This study underscores the importance of understanding these treatment-related alterations to ensure appropriate dental care for these patients. The involvement of a dental surgeon is crucial to providing comprehensive care and effectively monitoring any dental and maxillofacial complications.

Keywords: Cancer Survivors, Long-Term; Radiotherapy; Chemotherapy; Maxillofacial Abnormalities.

INTRODUCTION

Childhood cancer aggregates a group of diseases that present the uncontrolled proliferation of cells with alterations in their DNA, affecting cells of the blood system and supporting tissues. Unlike tumors in adults, their occurrence is not directly associated with lifestyle and environmental factors. Although cancer incidence is gradually rising in many countries, the survival rates for childhood malignancies have improved markedly. The number of childhood cancer survivors is increasing due to the improvement of available treatment options, 5-year survival rates now range from 68% to 98%, depending on the type of malignancy[1]. In the head and neck region, the most prevalent tumors in childhood are rhabdomyosarcomas, non-Hodgkin's lymphomas, and undifferentiated carcinomas, followed by retinoblastomas and squamous cell carcinomas. The most affected sites are the nasopharynx (40% of undifferentiated carcinomas and 30% of rhabdomyosarcomas), the oropharynx, and the oral cavity[2,3].

Clinical relevance statement
The findings of this study highlight the high prevalence of dental abnormalities and bone hypoplasia in childhood head and neck cancer survivors, underscoring the importance of specialized dental follow-up to properly monitor and treat these complications, ensuring effective oral rehabilitation and improved quality of life.

The treatments of choice used in pediatric oncology include surgery, radiotherapy, and chemotherapy. Both radiotherapy and chemotherapy demonstrate a number of long-term side effects such as damage to soft tissues and bones, endocrine deficiencies, and deformities. These alterations impact the patient's

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quality of life, causing infertility, physical and sensory disability, and difficulty in social relationships. Dental and craniofacial anomalies are also recognized as sequels of long-term cancer treatment, especially in head and neck tumors[3,4]. The impact of chemotherapy (cytotoxic agents) and radiation on tooth-forming cells can lead to sublethal or lethal damage, which is particularly concerning because, unlike other bone structures, teeth do not undergo remodeling. The side effects of radiation on bones, soft tissue, and blood vessels are dose-dependent and are increased in children who are developing (up to 6 years of age and during puberty)[4].

In head and neck, other potential consequences of radiotherapy to the oral cavity are fibrosis around the muscles of mastication, leading to trismus and irreversible damage to the salivary glands, causing hyposalivation. Furthermore, bones exposed to high levels of radiation undergo irreversible physiologic changes including narrowing of the vascular channels (endarteritis), which diminishes blood flow to the area and loss of osteocytes. The bone essentially becomes nonvital, which leads to limited remodeling of the bone and limited healing potential[5]. The most common dentition and facial changes resulting from head and neck radiotherapy and chemotherapy in developing patients (up to 6 years of age) include root agenesis, hypodontia, microdontia, maxillary and mandibular hypoplasia, enamel hypoplasia, enamel hypomineralization, malocclusion, and decreased temporomandibular joint mobility[4,6].

Childhood cancer survivors face an elevated risk of oral and dental complications because of disruptions to dental developmental networks, particularly when treatment occurs at a younger age. Managing dental care and dental rehabilitation for these patients poses a significant challenge in clinical practice. Moreover, while extensive and well-designed systematic reviews evaluate the late effects of childhood cancer treatment on dental structures, studies assessing facial deformities and dental alterations in patients who underwent exclusively head and neck oncological treatment, and discussing the challenges of rehabilitation and dental care for these patients are less common[4,6,7]. Understanding the dental and maxillofacial alterations and their progression is crucial for effective dental treatment planning and counseling for patients and their caretakers to enhance their quality of life. Therefore, this study aims to evaluate the bone and dental side effects in patients who underwent head and neck oncological treatment during childhood, as well as to discuss considerations regarding dental care for this population.

MATERIAL AND METHODS

This is a retrospective, observational, and longitudinal study that evaluated 12 patients who were referred to the Stomatology Department of a Cancer Center from 2004 to 2018. The study was approved by the Hospital Research Ethics Committee (no. 5.099.339). The inclusion criteria were patients who were submitted to head and neck cancer treatment during childhood (aged between 0 and 10 years) and who were referred to the Stomatology Department for follow-up. All information was collected from the department's database, such as oncological diagnosis, treatment modalities, age at diagnosis, and gender. The presence of maxillofacial alterations, jaw bone, and dental changes were acquired from photographic records and panoramic radiographs. To assess the stage of root formation, the Nolla classification was adopted[8]. Patients with incomplete data in the database, such as those without clinical photographs and panoramic radiographs, were excluded. Data were collected and inserted into Excel spreadsheets (Microsoft Office) and, subsequently, tabulated and submitted for descriptive analysis.

RESULTS

A total of 12 patients (7 males and 5 females) with a mean age of 5 years (ranging from 4 months to 10 years) were evaluated. All patients underwent chemotherapy, five received the combination of chemotherapy and radiotherapy and another five received the combination of chemotherapy, radiotherapy, and brachytherapy (Table 1). In the study, six patients (50%) exhibited some form of facial bone hypoplasia, with mandibular hypoplasia (four patients – 33.33%) more prevalent than maxillary hypoplasia (two patients – 16.67%) (Figure 1). All patients presented dental alterations, whether coronal or radicular. Agenesis was observed in six patients (50%), most commonly affecting ≤3 teeth (41.67%). Supernumerary teeth were found in two patients (16.67%), affecting ≤3 teeth. Microdontia and taurodontism were present in one patient (8.33%), affecting ≤3 teeth each. Additionally, seven patients (66%) exhibited abnormalities in root formation, with Nolla's stages ranging from 4 to 8, with stage 8 being the most frequent (25 teeth in this stage), followed by stages 7 and 5 (22 teeth each) (Table 2; Figures 2 and 3). Regarding the presence of recurrences, four patients (33.33%) had at least one recurrence, and three (25%) patients had a new primary tumor, being the only one considered radio-induced (Table 3).

Table 1. Clinical and treatment data.

Case	Tumor	Site	Gender	Age at diagnosis (y.o)	Treatment modality			
					Chemotherapy	Radiotherapy		Brachytherapy
						≤40 Gy	≥40 Gy	
1	Rhabdomyosarcoma	Maxillary sinus	F	06	X		X	
2	Rhabdomyosarcoma	Maxillary sinus	M	09	X	X		X
3	Rhabdomyosarcoma	Parameningeal	M	04	X		X	X
4	Rhabdomyosarcoma	Maxillary sinus	M	05	X		X	X
5	Lymphoepithelioma	Rhinopharynx	F	10	X		X	X
6	Lymphoepithelioma	Rhinopharynx	F	09	X		X	
7	Retinoblastoma	Ocular	F	02	X		X	X
8	Retinoblastoma	Ocular	M	04	X		X	
9	Undifferentiated carcinoma	Nasal cavity	F	06	X		X	
10	Ewing sarcoma	Mandible	M	07	X			
11	Langerhans cell histiocytosis	Mandible	M	08	X			
12	Pleomorphic sarcoma	Maxillary sinus	M	07	X	X		

Figure 1. Case 3: Clinical photographs taken at 11 years old—7 years after the end of cancer treatment. (A) Front view. (B) Side view. Asymmetry of the cervical and facial muscle is observed, due to the bone defect caused by the underdevelopment of the mandible.

DISCUSSION

This study emphasizes the side effects of head and neck cancer treatment in patients who underwent treatment during childhood. It highlights that these patients were referred to the department with complaints and needs for dental treatment and rehabilitation that deserve special considerations. In light of this study, we describe bone and dental alterations in order to facilitate early detection to optimize health and quality of life. In the head and neck region, the most prevalent tumors

Table 2. Bone and dental alterations.

Case	Facial bone hypoplasia	Dental alterations										
		Agenesis		Supernumerary	Microdontia		Taurodontism	Nolla's stage (number of teeth)				
		≤3 Teeth	≥3 Teeth	≤3 Teeth	≤3 Teeth	≥3 Teeth	≥3 Teeth	04	05	06	07	08
1	Maxillary sinus									01	02	
2	Maxillary sinus		X	X	X							
3	Mandible		X					10	16			
4	Mandible		X							02	05	
5	Mandible								04		04	
6	Mandible											
7			X			X		01	02	01	01	12
8		X										
9			X							02	06	04
10											03	05
11		X					X					
12											01	04

in childhood are rhabdomyosarcomas, non-Hodgkin's lymphomas, and undifferentiated carcinomas, followed by retinoblastomas and squamous cell carcinomas and the most affected sites in the head and neck region are nasopharynx (40% of undifferentiated carcinomas and 30% of rhabdomyosarcomas), facial sinuses, oropharynx, and oral cavity[3,9,10]. In this study, rhabdomyosarcoma was the most prevalent, followed by retinoblastoma, lymphoepithelioma, and facial sinuses, with the nasopharynx and oral cavity being the most affected sites.

Figure 2. Case 3: Panoramic radiograph performed 7 years after the end of cancer treatment. Bone and dental alterations are observed, such as mandibular hypoplasia, agenesis, and several dental elements with root malformation (Nolla stages 4 and 5).

Figure 3. Case 7: Panoramic radiograph performed 9 years after the initial diagnosis. Dental alterations are observed, such as agenesis, microdontia, and root malformation (ranging from 4 to 8 of the Nolla stage).

Çetiner et al.[11] evaluated the effects of cancer treatment (chemo- and radiotherapy) in long-term survivors and observed no changes in jaw bones in patients submitted only to chemotherapy. Meanwhile, radiation therapy has the ability to promote bone malformations but depends on the location of the irradiation, dose, and age of the patient. Radiation promotes a series of effects on the bone, such as the destruction of osteoblasts, vascular damage, and fibrosis by replacement in the medullary space. Children under 6 years of age and who received doses above 30 Gy present a 90% chance of developing skeletal changes in the irradiated area[2,12]. In our study, alterations in bone development were observed in half of the patients, and of these, 83% received a dose below 40 Gy.

Milgrom et al.[7,13] evaluated the relationship between head and neck radiation and the effects on tooth development and observed that risk factors include age at treatment and radiotherapy dose used (>20 Gy). Kang et al.[14] observed an association between radiation doses ≥40 Gy and the severity of dental disorders in younger patients; however, the same association with older patients was not statistically significant. A radiation dose of 10 Gy induced histological changes in the developing permanent tooth germ and higher doses of radiation result in cell death of ameloblasts and odontoblasts, regardless of their stage in the cell cycle[15]. According

Table 3. Recurrence and second primary cancer data.

Case	Tumor	Site	Second primary cancer			Recurrence
			Tumor	Site	Disease-free survival (y)	
1	Rhabdomyosarcoma	Maxillary sinus	Papillary	Thyroid	15	
2	Rhabdomyosarcoma	Maxillary sinus				
3	Rhabdomyosarcoma	Parameningeal				X
4	Rhabdomyosarcoma	Maxillary sinus				
5	Lymphoepithelioma	Rhinopharynx	Squamous cell carcinoma	Mandible	10	
6	Lymphoepithelioma	Rhinopharynx				X
7	Retinoblastoma	Ocular	Osteosarcoma	Femur	7	X
8	Retinoblastoma	Ocular				
9	Undifferentiated carcinoma	Nasal cavity				
10	Ewing sarcoma	Mandible				
11	Langerhans cell histiocytosis	Mandible				
12	Pleomorphic sarcoma	Maxillary sinus				X

to Stolze et al., the type of cancer treatment and age at diagnosis influence dental disorders. Patients under 5 years of age are more susceptible to dental changes, as most permanent tooth development begins before this age[16]. Dental development begins in the fourth month of intrauterine life and continues until adolescence, when crowns are formed and roots are closed, respectively[17]. Odontoblasts are more susceptible to the effects of antineoplastic therapy only before the formation of the dentinal matrix[18]. The minimum toxic dose for dental developmental abnormalities is unknown, suggesting that the dose to the teeth should be kept as low as possible, particularly in younger patients, with special effort to keep doses <20 Gy in patients <4 years old[7]. In our study, the mean age at diagnosis was 5 years, which explains that 93% of our sample presented one type of teeth alteration.

At birth, the development of the first molars begins, the incisors and canines develop in the first year of life, and the premolars and second molars in the second and third years of life, respectively[12]. The information about the development of teeth is important, not only for reasons of diagnosis and treatment but also for more detailed purposes of research. Knowledge about general acceleration or retardation of calcification of the teeth of an individual is important mainly to the orthodontist to determine the treatment[8]. Regarding dental development alterations, root alterations are more prevalent, followed by agenesis and microdontia[16,19]. In our study, our findings align with those reported in the literature. Root malformation was found in all patients. Notably, premolars and molars were the most affected, as they are the last germs to initiate their formation, which correlates with the patient's age at the time of treatment.

Jensen et al. investigated the incidence of second primary cancer among pediatric head and neck cancer patients. Among 234 pediatric patients, six presented a second primary cancer, corresponding to an overall standardized incidence rate of 4.8. No patients were diagnosed with more than one second primary cancer[20]. In our study, we observed 33% of relapse and patients with more than one second primary cancer. Another side effect of radiation is osteoradionecrosis, the irradiated bone undergoes changes based on an imbalance between the synthesis and degradation of irradiated bone tissue, where radiation induces a fibroatrophic process in endothelial cells and connective tissue cells. Therefore, some surgical bone procedures, such as exodontias, may present delay and difficulty in bone repair, inducing necrosis[21]. Furthermore, the facial asymmetries caused by radiotherapy at an early age have important psychosocial implications, and the asymmetries worsen with growth during puberty[22]. In our study, facial asymmetries were observed, and no case of necrosis has been related so far.

The various maxillofacial alterations identified in this study often increase the risk of oral and dental health problems in childhood cancer survivors. These individuals require regular dental care to monitor potential side effects and begin early treatment[23]. However, there is limited literature on the oral rehabilitation of these patients, necessitating individualized treatment plans. Recent evidence on the rehabilitation of childhood cancer survivors includes a systematic review, which evaluated long-term dental management in nine patients through six case reports, all showing significant dental late effects[24].

Orthodontic treatment is often controversial and usually contraindicated in these patients due to atypical root morphology, which increases the risk of pathological mobility and further root resorption[25]. In one case report, a patient underwent orthodontic treatment to correct malocclusion; however, this patient did not have root defects, but rather hypodontia and an underdeveloped residual ridge[26]. Most case reports favored restorative treatment combined with prosthodontic rehabilitation to enhance function, preserve bone structures, and improve aesthetics[24]. However, radicular malformations result in reduced periodontal support, making the dentition susceptible to mobility from occlusal forces and the progression of periodontal disease, leading to unpredictable tooth loss and contraindicating dento-mucosally supported prostheses.

Unpredictable tooth loss is a significant concern for clinicians, as we must strive to prevent it but recognize that it can still occur. This issue was exemplified in a case report showing that 32 years after treatment, a patient with severe root defects had lost multiple teeth and suffered severe facial deformity[26]. There is limited long-term evidence on the prognosis of teeth with atypical root morphology or significantly shortened roots, highlighting the need for close monitoring. The absence of many teeth or edentulism presents a potential future challenge that may need to be addressed with prosthetic rehabilitation[24].

Another piece of information to consider, radiotherapy during childhood can lead to atrophic maxillary alveolar ridges with unfavorable anatomy (bone hypoplasia), necessitating the placement of endosseous implants to provide retention for dental prostheses[27]. However, the placement of dental implants in these

patients can pose challenges, including compromised healing, reduced osseointegration, and the risk of serious infections such as osteoradionecrosis[21]. Despite the absence of studies reporting the success of implants placed for survivors of head and neck cancer in childhood, it is noteworthy that implant survival in patients who have undergone radiation therapy for head and neck cancer in adulthood exhibits a significantly lower success rate[28].

Hyposalivation, a common late effect of head and neck radiotherapy in adults, also impacts children undergoing antineoplastic treatment[29]. Saliva plays a crucial role in maintaining oral health and function. Complications from salivary dysfunction, such as increased susceptibility to dental caries and difficulties in swallowing, chewing, and speech, significantly reduce quality of life. Studies on salivary gland function in childhood cancer survivors have revealed lower stimulated and unstimulated flow rates compared to healthy controls, highlighting the heightened risk of dental caries[30]. This underscores the importance of supervised fluoride application and regular dental monitoring for preventive care. Referral to specialists in restorative dentistry or consultants is essential for appropriate treatment and restoration if caries develop.

CONCLUSION

In our study, the presence of bone and dental alterations was observed, with bone hypoplasia and alterations of root development being the most prevalent. Understanding the side effects of cancer treatment during childhood is essential for providing optimal care to these individuals. Due to the limited evidence on oral rehabilitation and dental care for childhood cancer survivors, personalized treatment planning is crucial for each case based on considerations presented in this study. For children who have undergone head and neck radiotherapy, uncertainties persist regarding the long-term viability of implant-supported prostheses, with potential risks of osteoradionecrosis.

AUTHORS' CONTRIBUTIONS

KHSN: Conceptualization, Data curation, Investigation, Writing – review & editing. RES: Investigation, Conceptualization, Writing – original draft, Writing – review & editing. FAA: Methodology, Project administration, Resources, Visualization, Writing – review & editing. CMLC: Methodology, Project administration, Resources, Visualization, Writing – review & editing. JPA: Conceptualization, Project administration, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing.

CONFLICT OF INTEREST STATEMENT

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Ethics approval: This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of the Hospital (no. 5.099.339).

Consent to participate: Informed consent was obtained from all individual participants included in the study.

Consent to publish: The authors affirm that human research participants provided informed consent for publication of the images.

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