Dental and craniofacial alterations in long-term survivors of childhood head and neck rhabdomyosarcoma

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Objective. Rhabdomyosarcoma (RMS) represents the most common soft tissue sarcoma that affects children. Treatment involves chemoradiotherapy. This study aimed at evaluating the long-term alterations to teeth and cranial bones in children, teenagers, and young adults after oncologic treatment.

Study Design. We conducted a cross-sectional study of patients undergoing treatment for head and neck RMS between 1988 and 2011. We evaluated demographic, clinical, and treatment data and performed panoramic radiography, cephalometry, and photography.

Results. We evaluated 27 long-term survivors, most of whom had been treated between ages 0 to 5 years (51.9%). The total radiation dose applied was 50.4 Gy, and the chemotherapy combination included vincristine, actinomycin D, and cyclophosphamide in 51.9% of the cases. We observed 603 dental alterations, among which 377 (62.7%) occurred in patients ages 0 to 5 years, and root shortening was the most frequent alteration observed (24.2%). With regard to facial bones, 74% of the patients had some level of facial asymmetry, 70.4% had reduced facial depth, 48.4% had mandibles of short size, and 77.8% had reduced facial height.

Conclusions. Children submitted to RMS treatment involving chemotherapy and radiotherapy displayed significant dental and craniofacial alterations, especially when treatment occurred between ages 0 and 5 years. (Oral Surg Oral Med Oral Pathol Oral Radiol 2019;127:272−281)

Rhabdomyosarcoma (RMS) is a malignant neoplasm consisting of embryonic cells that differentiate into skeletal muscle.[1,2] In approximately 35% of the cases, the head and neck region is affected,[3,4] and the histopathologic embryonal subtype of the tumor more likely develops in this region.[1,5] Before the 1970s, treatment often had poor outcome, and only 25% to 30% of children went into remission. However, the use of multiple-agent chemotherapy, followed by radiation, considerably improved the survival rates.[2,6-8] Progress began as more multi-institutional clinical studies were conducted around the world. In the United States, since 1972, studies have been coordinated by the Intergroup Rhabdomyosarcoma Study Group (IRS), and currently, by the Committee for Soft Tissue Sarcoma of the Children's Oncology Group.[9] The IRS group conducted 4 consecutive studies (I−IV) between 1972 and 1997. The 5-year survival rate improved from 55% with the IRS I protocol to 63% with the IRS II protocol and to greater than 70% with the IRS III and IV protocols. The IRS V study is currently under way.[2,7,8,10-13]

In Europe, 2 groups came together to form the European Pediatric Soft Tissue Sarcoma Study Group: (1) the International Society of Paediatric Oncology Malignant Mesenchymal Tumour and (2) the Associazione Italiana Ematologia Oncologia Pediatrica − Soft Tissue Sarcoma Committee − Italian Cooperative Group. The treatment protocols follow the same course. However, differences exist with regard to patient management and philosophic approach.[13]

The treatment of children with RMS follows a multimodal approach that includes systemic (chemotherapy) and local (surgery and/or radiotherapy) interventions.[6-8] The treatment involves complex procedures and must take place in specialized pediatric centers. A multidisciplinary evaluation is crucial to adequate treatment planning, and the team should include a chief surgeon, a dentist, a pediatric oncologist, other specialized surgeons, and a radiotherapist.[14,15]

In cases of RMS involving the head and neck region in children, chemotherapy and radiotherapy cause significant alterations to developing teeth and facial bones, and these changes will persist for the rest of the patients' lives.[16-22] Known prognostic factors determine treatment

Statement of Clinical Relevance

The results of this cross-sectional study provide knowledge about the late toxicities of the treatment for head and neck rhabdomyosarcoma in children and are very important for diagnostic and preventive dental treatments, resulting in a better quality of life for the patients.

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intensity to maximize the chances of a positive outcome and to limit long-term sequelae. The team's dental surgeon has a crucial role in preventing, detecting, and treating late-onset complications; this may not only help improve the patient's quality of life but also provide clues for improvements in future treatment. Here, we describe the main long-term dental and craniofacial alterations in patients who survived head and neck RMS.

MATERIALS AND METHODS

This cross-sectional study included 88 children, ages of 0 to 15 years, who received treatment for head and neck RMS between 1988 and 2011. The study population was identified through a survey of the Registry of the Cancer Hospital at the Brazilian National Cancer Institute (INCA). In this study, the patients were evaluated in a single moment, during 2015−2016, years after the end of the cancer treatment. We also evaluated demographic, clinical, and treatment data extracted from patient records. Patients underwent panoramic radiography and cephalometric evaluation. Frontal and lateral photographs were taken and used in the assessment of facial symmetry. The study was approved by the Institutional Research Ethics Committee of our institution and followed the guidelines of the Helsinki Declaration. Patients and/or their legal guardians signed the informed consent forms. Teenagers signed an assent form.

Radiographic evaluations

Radiographs were used in the descriptive evaluation of dental alterations and provided a chronologic view of tooth formation and eruption. The following parameters evaluated: partial anodontia, total anodontia, delayed eruption, microdontia, anomalous mineralized structures, reduction of the pulp chamber, absent roots, root shortening, tooth thinning, and precocious root closure.

The evaluation of facial growth relied on linear measurements according to Bimler's cephalometric analysis. Selected measurements included: A'-TM (facial depth), A'-B' (bony overjet), mandibular size (diagonal line of the mandible), and total facial height (facial height).

We also evaluated the frontal, right profile, and left profile photographs of patients. After the photographs were taken, we conducted a clinical analysis of facial symmetry based on previously reported measurements.[23-25] Photographs were taken on the basis of a single standard: patients were asked to sit straight, look forward in alignment with the horizon, and have a relaxed lip posture, and the camera was placed 2 m from the subject. Professional digital cameras were used.

Multimodal treatment

The course of chemotherapy for each patient in this study was administered according to Intergroup Rhabdomyosarcoma Study Group III (1986 to 1996) and IV (1996 to 2011) protocols.[7,8,10-13,17]

For local treatment, patients were submitted to conventional 2-dimensional plan radiotherapy (the treatment fields were defined by bony parameters of the head and neck through radioscopy) and 3-dimensional plan radiotherapy (the treatment fields were defined by head and neck parameters through computed tomography). For the procedure, thermoplastic masks were applied to immobilize the patients in the supine position to allow for daily

Table I. Baseline characteristics of the patients

Characteristics	*N (%)*
Gender	
Female	12 (44.4)
Male	15 (55.6)
Histopathologic diagnosis	
Embryonal	19 (70.4)
Alveolar	7 (25.9)
Mixed	1 (3.7)
Clinical groups	
Group I	- (——)
Group II	21 (77.7)
Group III	6 (22.3)
Group IV	
Age - year (during treatment)	
0−5	14 (51.9)
>5−10	9 (33.3)
>10−15	4 (14.8)
Age - year (Current)	
0−5	—
>5−10	1 (3.7)
>10−15	5 (18.5)
>15−20	8 (29.6)
>20	13 (48.1)
Primary site	
Orbit	7 (25.9)
Parameningeal	
• Orbit with bone erosion	1 (3.7)
• Middle ear/mastoid	1 (3.7)
• Pterygopalatine/parapharyngeal/infratemporal fossa	7 (25.9)
• Nasopharynx and nasal cavity	8 (29.6)
• Paranasal sinus	3 (11.1)
Nonparameningeal	
• Head and neck	00 (—)
Chemotherapy protocol	
VAC	14 (51.9)
VAC + IFO + VP16	5 (18.5)
VA + IFO	3 (11.1)
VA + IFO + DOXO	1 (3.7)
VAC + DOXO	1 (3.7)
Others	3 (11.1)
Radiotherapy	
41.4 Gy	1 (3.7)
45.0 Gy	12 (44.4)
50.4 Gy	14 (51.9)

DOXO, doxorubicin; *IFO,* ifosfamide; *VA,* vincristine, actinomycin; *VAC,* vincristine, actinomycin, cyclophosphamide; *VP16,* etoposide.

Table II. Frequency of dental alteration

Characteristics	*Simple frequency (%)*	*Average (SD)*	*Median (Min−Max)*
Teeth			
Abnormal teeth	421 (54.7)	15.6 (7.5)	14 (4−32)
Normal teeth	348 (45.3)	12.9 (9.2)	14 (0−27)
Evaluated teeth	769 (100.0)	26.1 (8.6)	28 (0−39)
Dental alteration			
Absent roots	59 (9.8)	2.19 (2.4)	2 (0−80)
Root shortening	146 (24.2)	5.41 (4.6)	5 (0−16)
Root tapering	23 (3.8)	0.85 (1.4)	0 (0−00)
Partial anodontia	42 (6.9)	3.93 (7.4)	1 (0−28)
Total anodontia	64 (10.5)	2.37 (2.5)	2 (0−32)
Microdontia	22 (3.6)	0.81 (1.7)	0 (0−80)
Reduction of the pulp chamber	92 (15.2)	3.41 (4.6)	1 (0−17)
Delayed eruption	26 (4.3)	0.96 (1.3)	0 (0−40)
Anomalous mineralized structures	13 (2.2)	0.48 (0.9)	0 (0−40)
Precocious root closure	104 (17.2)	3.85 (4.3)	2 (0−15)

reproduction of treatment fields. Doses were administered in 1.8 Gy fractions, in 23 to 28 days, 5 days per week, with conventional fractionation and with cobalt 60 or linear accelerator in 2-dimensional and 3-dimensional. Regional lymphatic chains were treated only if compromised, as determined by imaging examinations, or clinically, as indicated on the treatment protocol.

The total dose was based on Intergroup Rhabdomyosarcoma Study Group protocols. Patients with clinical group I tumors did not receive radiotherapy. Patients with clinical group II tumors received radiotherapy at a dose of 41.4 Gy. Patients with clinical group III and IV tumors received radiotherapy at a dose of 50.4 Gy.[7,8,10-13,17]

Table III. Distribution of dental alterations according to primary site and treatment period

	Age group 0 to 5 years			
Primary site	*Dental alterations N (%)*	*Average (SD)*	*Median (Min−Max)*	*P value*
A	165 (43.8)	33.0 (8.7)	29 (26−48)	
B	104 (27.6)	17.3 (6.7)	20 (7−23)	H = 9.94
C	108 (28.6)	36.0 (7.9)	33 (30−45)	(.007)*
TOTAL	377			
	Age group >5 to 10 years			
Primary site	*Dental alterations N (%)*	*Average (SD)*	*Median (Min-Max)*	*P value*
A	83 (45.1)	20.75 (7.81) 7.0 (0.0)	18.0 (15−32)	
B	7 (3.8)	33.0 (4.95) 27.0 (0.0)	7.0 (7−7)	U† = 1.25
C	67 (36.4)		33.0 (21−28)	(.221)
D	27 (14.7)		27.0 (27−27)	
TOTAL	184			
	Age group >10 to 15 years			
Primary site	*Dental alterations N (%)*	*Average (SD)*	*Median (Min−Max)*	*P value*
A	24 (57.1)	12.0 (5,7)	12 (8−16)	
B	06 (14.3)	6.0 (0.0)	6 (6−6)	‡
C	12 (28.6)	12.0 (0.0)	12(12−12)	
TOTAL	42			
TOTAL	603			

*Kruskal-Wallis test.

†Mann-Whitney test.

‡It was not possible to calculate the values of the dental alterations, in relation to the locations, in the age group >10 to 15 years because of the insufficient number in the orbit and pharyngeal sites.Site A: Nasopharynx, nasal cavity and paranasal sinusSite B: Orbit (with or without bone erosion)Site C: Pterygopalatine/parapharyngeal/infratemporal fossaSite D: Middle ear.

Table IV. Frequency of bony alterations

Characteristics	*Simple frequency (%)*	*Average (SD)*	*Median (Min−Max)*
Photographic evaluation			
Harmonic	7 (25.9)	20.1 (7.38)	20.0 (11−29)
Non Harmonic	20 (74.1)	23.1(11.89)	22.0 (6−48)
A' − TM Depth of face			
Short	19 (70.4)	25.4 (11.1)	27.0 (7−48)
Medium	3 (11.1)	14.3 (2.9)	16.0 (1−16)
Big	5 (18.5)	15.6 (7.9)	20.0 (6−23)
A' − B'' Bony overjet			
Class I	9 (33.3)	18.8 (81.0)	21,0 (7−30)
Class II	12 (44.4)	23.3 (13.6)	20,5 (06−48)
Class III	6 (22.2)	25.8 (7.3)	27,5 (15−33)
Mandibular size			
Short	13 (48.1)	28.7 (9.6)	28.0(16−48)
Medium	13 (48.1)	17.2 (8.2)	16.0 (7−32)
Big	1 (3.7)	6.0 (0.0)	6.0 (6−6)
Total face height			
Short	21 (77.8)	25.7 (9.4)	26 (7−48)
Medium	5 (18.5)	11.6 (5.1)	11 (7−20)
Big	1 (3.7)	6.0 (0.0)	6 (6−6)

Statistical analysis

For discrete variables, simple frequency distributions and percentages were applied. For continuous variables, arithmetic means, standard deviations, medians, and minimum and maximum values were applied. Comparison of continuous variables was performed with nonparametric Mann-Whitney U and Kruskal-Wallis tests. If the continuous variables had only 2 items to be compared (e.g., dental alterations and gender), the Mann-Whitney U test was applied. If 3 or more items had to be compared (e.g., dental alterations and 3 different age groups), the Kruskal-Wallis test was applied. A significance level of 5% was adopted ($P < .05$).[26] The SPSS software version 24.0 (SPSS Inc., Chicago, IL) was used in the analysis.

RESULTS

Among the 88 patients identified in hospital records, 46 were alive when the analysis was conducted. Seven patients refused to participate, and 12 could not be contacted for lack of current address information in the hospital registry of cancer patients. Thus, 27 individuals participated in the present work, with a median follow-up of 19 years (range 7−34 years). Male individuals constituted the majority of these patients, and most received treatment between ages 0 and 5 years. At the time of the study, 13 patients were ages 20 years or greater (48.1%). The primary site of disease was parameningeal in 20 patients (74%), and a high proportion of these tumors was located in the nasopharyngeal area and nasal cavity (8 of 20; 29.6%). Tumor histopathologic subtype was embryonal in 70.4% of the individuals, and 59.2% of patients presented tumors in clinical group III. Most individuals received vincristine, actinomycin, and cyclophosphamide (VAC) chemotherapy, and the most frequent radiation dose was 50.4 Gy, adopted in 51.9% of the cases (Table I).

The study population had a total of 769 dental elements, among which 421 were abnormal (54.7%; Table II). Patients had 603 dental abnormalities, more frequently represented by root shortening (24.2%), followed by partial and total anodontia (106 cases [17.7%]; see Table II). Upper second molars represented the largest proportion of alterations (10.4%), followed by upper left canines (5.3%; Supplementary Table I).

Patients with tumors in the nasopharyngeal, nasal cavity, and paranasal sinus areas had the highest frequency of alterations (45.1%). Patients who were diagnosed and treated between ages 0 and 5 years had the highest frequency of alterations (n = 377; $P = .016$). In this group of patients, again, the largest proportion of alterations was associated with tumors in the nasopharyngeal, nasal cavity, and paranasal sinus areas (n = 165 [43.8%]; $P = .007$; Table III). When comparing the number of dental alterations among treatment protocols, we observed no significant differences with regard to chemotherapy schemes and radiotherapy doses, as indicated by $P = .454$ and $P = .322$, respectively (Supplementary Table II).

Patients also displayed craniofacial bone alterations. The photographic study revealed asymmetric facial features in 20 individuals (74.1%). Moreover, according to cephalometric analysis, 19 patients (70.4%) had reduced facial depth, and 21 (77.8%) had reduced facial height (Supplementary Table III; Table IV and Figure 1).

In patients with primary tumor of the orbit (n = 8), we evaluated the existence of mandibular dental and bone alterations resulting from chemotherapy because this region would have been outside the irradiation field. Of

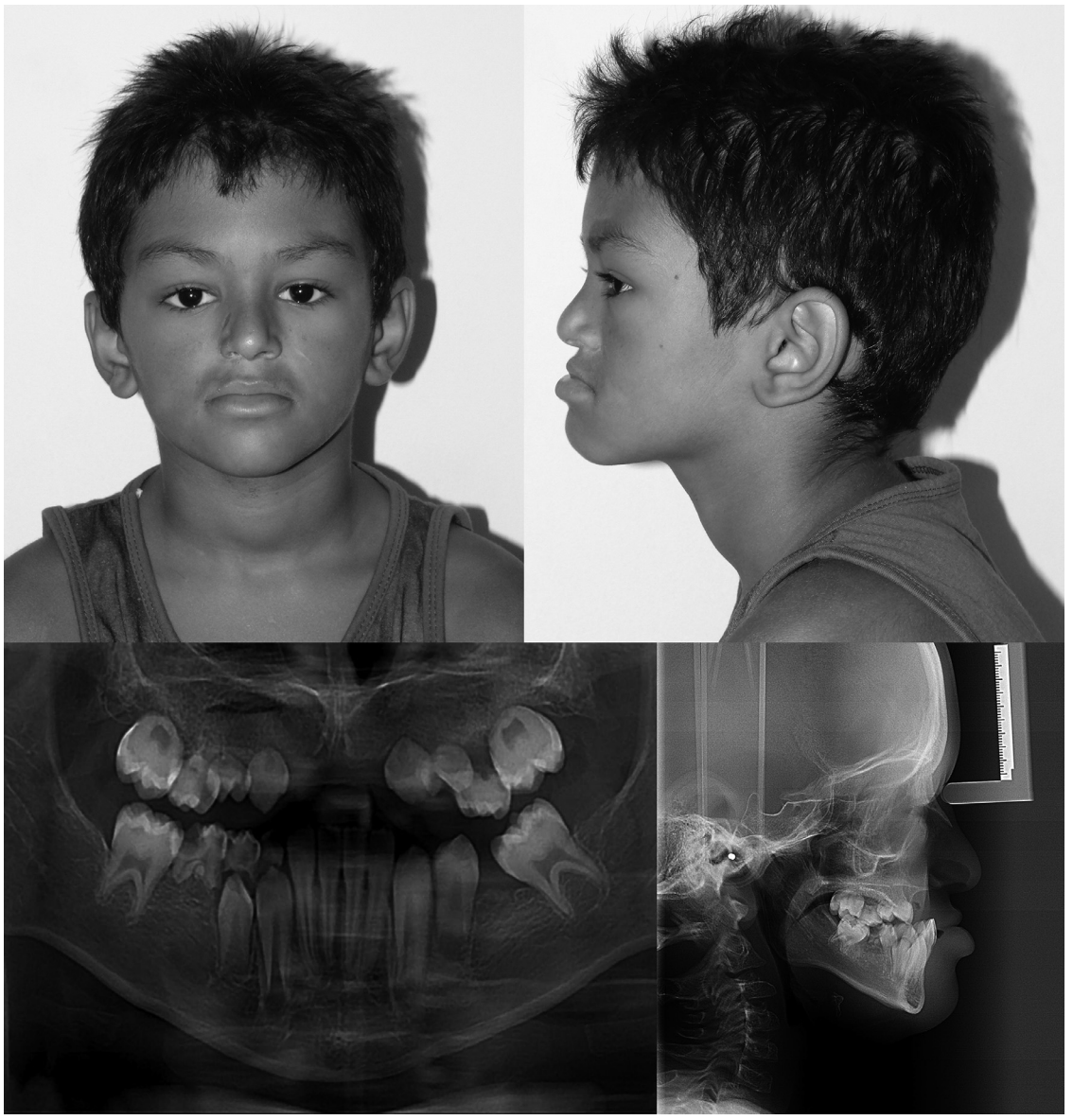

Fig. 1. Nasal cavity tumor, treated at age 2 years. Photographs and radiographic evaluations at age 9 years.

116 teeth evaluated, 50% displayed alterations, more frequently in the form of root shortening (61.5%). Photographic evaluation of these patients showed that 7 individuals (87.5%) had asymmetric facial features, 6 (75.0%) had a short mandible size, and 5 (62.5%) had reduced facial height (Table V). Chemotherapy protocols applied to these patients included VAC (6 individuals, 75%) and VAC + ifosfamide (IFO) + etoposide (VP16) (2 individuals, 25%) (Figure 2).

DISCUSSION

Treatment of head and neck RMS requires a multidisciplinary approach, including chemotherapy, surgery, and radiotherapy.[14,27,28] In most patients, the surgical procedure will only provide biopsy samples for diagnosis, as complete resections are rarely possible.[27]

Prognosis for patients with RMS of the orbit is considered excellent. A recent study involving 306 patients and 4 collaborating groups worldwide indicated that the 10-year overall survival rate was 87%.[29] However, chances of a positive outcome are reduced in parameningeal tumors. A combined analysis was performed in a total of 1105 patients with this presentation of the disease in 10 studies, conducted by European and North American groups between 1984 and 2004. Results indicated that 10-year event-free survival (progression of local or regional disease, relapse, secondary tumors, or death) and overall survival rate corresponded to 62.6% and 66.1%, respectively.[30]

Table V. Dental and bony alterations in patients who did not receive radiotherapy to the mandible (orbit tumors*)

Characteristics	*N (%)*
Age - year (during treatment)	
0–5	6 (75.0)
5–10	1 (12.5)
10–15	(12.5)
Chemotherapy†	
VAC	6 (75.0)
VAC + IFO + VP16	1 (12.5)
VA + IFO	1 (12.5)
VA + IFO + DOXO	—
VAC + DOXO	—
Others	—
Photographic evaluation	
Harmonic	1 (12.5)
Nonharmonic	7 (87.5)
A' – TM Depth of face	
Short	5 (62.5)
Medium	2 (25.0)
Big	1 (18.5)
A' – B' Bony overjet	
Class I	4 (50.0)
Class II	2 (25.0)
Class III	2 (25.0)
Mandibular size	
Short	6 (75.0)
Medium	1 (12.5)
Big	1 (12.5)
Total face height	
Short	5 (62.5)
Medium	2 (25.0)
Big	1 (11.5)
Dental alterations	
Evaluated teeth	116 (100.0)
Normal teeth	58 (50.0)
Absent roots	2 (1.6)
Root shortening	48 (61.5)
Root tapering	12 (15.4)
Total anodontia	3 (3.8)
Partial anodontia	3 (3.8)
Microdontia	4 (5.1)
Reduction of the pulp chamber	–
Delayed eruption	6 (7.7)
Anomalous mineralized structures	—
Precocious root closure	—

*Orbit (with or without bone erosion).
†Chemotherapy.*DOXO,* doxorubicin; *IFO,* ifosfamide; *VA,* vincristine, actinomycin; *VAC,* vincristine, actinomycin, cyclophosphamide; *VP16,* etoposide.

The increased life expectancy of pediatric patients with cancer will translate into a greater number of long-term sequelae resulting from head and neck RMS treatment. Potential problems include dental and craniofacial bone abnormalities.[31-34]

A retrospective study of survivors of pediatric head and neck RMS analyzed 29 male and female (ratio 1.1:1) patients. Median age at the time of treatment was 4.9 years. Among the patients, 19 (65.5%) had the embryonal form of the tumor. The primary site of disease was the parameningeal area in 20 individuals (69%), including 12 patients (41.4 %) with tumors in the infratemporal fossa and the nasal cavity.[35] These results are similar to ours: our study population had more male patients (55.6%); the predominant histologic type was embryonal (70.4%), as expected of head and neck RMS; and the primary sites were predominantly parameningeal (n = 20 [74%]), specifically in the nasopharyngeal and nasal cavity areas (n = 8 [29.6%]). Tumor location probably explains the number and severity of alterations because in these patients, the middle and inferior areas of the face would be in the frontal and lateral irradiation fields.[16,36] Our patient population was also relatively young at the time of diagnosis (<5 years; 51.9%), a fact that probably contributed to the large number of abnormalities in dental growth and development.[16-22,37,38]

A previous study performed in a Brazilian pediatric oncology unit evaluated morphologic tooth abnormalities in the panoramic radiographs of 137 individuals who were long-term survivors of childhood cancers, including solid tumors and blood diseases.[39] Of the 54 children with solid tumors, 28 (51.8%) developed dental alterations. The authors also indicated that 21 (47%) of the 45 children submitted to chemotherapy and concomitant head and neck radiotherapy had a higher incidence of dental abnormalities. In these patients, taurodontism was the most frequent abnormality (16%). Among younger children (age <6 years) at the time of treatment, 32 of 69 had dental alterations, more frequently including taurodontia (19%), followed by microdontia (13%).[39] Here, we have reported similar findings regarding the higher frequency of alterations among patients treated with chemotherapy and radiotherapy at a younger age (<5 years; 51.8%; $P = .007$). However, the most frequent abnormalities we observed were root shortening (24.2%) as well as total and partial anodontia (17.7%).

In a survey of spontaneous dental malformations in a healthy population, 196 (40.8%) of 480 individuals had at least 1 abnormal tooth.[40] In contrast, we report here 603 abnormalities in 27 patients, an average of 22.33 malformations per patient.

A study conducted at the Federal University of Rio de Janeiro, investigated tooth loss and anodontia in 1002 healthy children and detected anodontia in 4.6% of the individuals.[41] Work on post-chemotherapy effects revealed an increased risk of dental abnormalities among survivors whose maxillary bones were exposed to radiation in comparison with unexposed patients.[42] The authors reported a dose-dependent risk of abnormalities, including 6 or greater missing teeth. The findings from these studies are in agreement with those of the present study. We identified 42 cases of

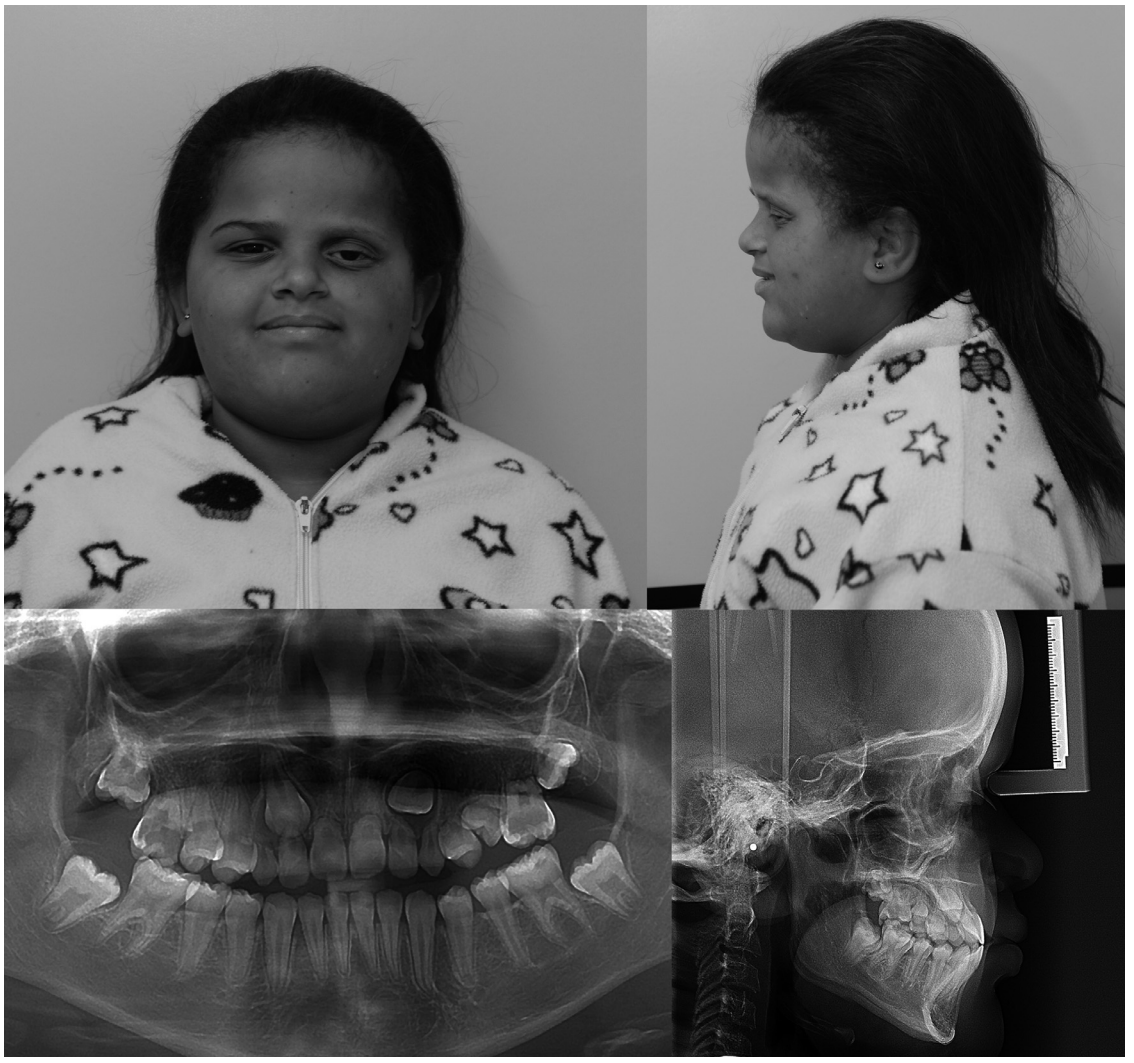

Fig. 2. Left orbit tumor, treated at age 3 years. Photographs and radiographic evaluations at age 10 years.

partial anodontia (6.9%) and 64 cases of total anodontia (10.6%)—a total of 106 cases (17.5%) in 27 patients, representing 3.92 anodontia cases per patient.

In a study of head and neck RMS, 22 survivors were divided into groups on the basis of age at the time of treatment. Patients were treated with radiation doses ranging from 34 to 67 Gy and chemotherapy. The authors found severe dental abnormalities, including premature arrest of root formation (n = 12), hypodontia (n = 11), and microdontia (n = 5).[34] Again, these results are in agreement with our findings, showing that among 27 patients treated with a radiation dose of 41.4 to 50.4 Gy, as well as chemotherapy, 421 abnormalities were detected in 769 evaluated teeth (54.7%). Severe abnormalities included root shortening (24.2%), partial and total anodontia (n = 106 teeth [17.5%]), premature closure of the permanent root (n = 104 teeth [17.2%]), and delayed eruption (n = 92 teeth [15.2%]). Increased frequency of these alterations may be explained by the high doses of radiation that targeted the left, right, and frontal facial fields of our patients, and probably killed ameloblasts and odontoblasts, regardless of their stage in the cellular cycle.[16,18,19,43,44]

A Danish study compared 150 children who survived cancer and received chemotherapy before age 8 years with a control group of 193 healthy children.[45] Among children of the first group, microdontia affected 88 premolars and permanent molars (19.3%), whereas no cases occurred among the control group children. Moreover, 27 cases of premolar and molar hypodontia affected 14 cancer survivors (9.3%) in comparison with 18 cases in 8 children of the control group (4.1%). The authors observed that earlier exposure to chemotherapy correlated with higher frequency of hypodontia.[45] Yet another study of pediatric

cancer survivors evaluated, 5 years after treatment, 106 patients whose average age was 5 years at the time of treatment.[46] The authors reported a dose-dependent association of cyclophosphamide by using the Holder Defect Index and described the occurrence of hypodontia, microdontia, and alterations to crown/root proportions as assessed by panoramic radiographies.

Other chemotherapy drugs, such as vincristine[47-50] and alkylating agents[40,46] were associated with dental abnormalities in survivors of pediatric cancer. These abnormalities may result from the inhibitory effects of vincristine on the secretion of dentin collagen matrix by odontoblasts.[49,50] In the present study, 8 (29.6%) of 27 patients had primary tumor of the orbit. Radiation treatment in these patients focused on the eye area—zygomatic bone and frontal/oblique exposure of the eye. Nevertheless, these individuals displayed alterations to the mandible, which was outside of the irradiation field, and this could be explained by the use of VAC treatment (6 of 8 [75%]). In these cases, alterations included 58 (50%) of 116 abnormal teeth, 78 dental alterations (0.67 alteration/-dental element), and root shortening (n = 48 [61.5%]), suggesting that chemotherapy also causes long-term alterations to bone and dental structures.[16,35,36,51-56]

A cephalometric assessment included patients who had survived acute lymphoid leukemia before age 10 years. Among these individuals, those who received chemotherapy and radiotherapy (24 Gy) before age 5 years had a high incidence of craniofacial abnormalities (18 of 20 [90%]). The mandible was severely affected in this group, according to cephalometric parameters.[57]

Overall, up to 80% of the children who receive radiotherapy to the craniofacial region and survive the disease will develop maxillofacial abnormalities.[58,59] The intensity and frequency of these abnormalities are inversely proportional to age at time of treatment and directly proportional to the doses of chemotherapy and radiotherapy.[57] These reports corroborate our findings. The highest frequencies of abnormalities were 77.8% (low facial height), 70.4% (low facial depth), and 74.1% (nonsymmetric features) and were possibly potentiated in the lower age groups (<5 years) and higher-dose treatments.

CONCLUSIONS

Chemotherapy and radiotherapy for the treatment of head and neck RMS can result in alterations to dental and bone development, especially when treatment occurs at a young age (<5 years). Our results suggest that chemotherapy alone can also affect bone and dental growth and development. The high frequency of alterations warrants a multidisciplinary approach, and semiannual follow-ups for the early detection of problems and for improving the quality of life in these patients.

SUPPLEMENTARY MATERIALS

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.oooo.2018.12.012.

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