

# MALIGNANT ORAL-MAXILLARY NEOPLASM IN CHILDREN AND ADOLESCENTS. A RETROSPECTIVE ANALYSIS FROM THE BIOPSY SERVICE AT A SCHOOL OF DENTISTRY IN ARGENTINA

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## ABSTRACT

There are few studies on oral-maxillary lesions in children and adolescents, and reports on malignant neoplasms are scarce. Comparison of available data is difficult due to the different criteria and racial-ethnic origin of the populations in each study. The aim of this work was to perform a retrospective study of malignant oral neoplasms in patients aged up to 20 years diagnosed at a center specialized in histopathological diagnosis of oral diseases between 1990 and 2005. The 24 retrieved cases accounted for 0.9% (n: 2434) of total biopsies in this age group during that peri-

od, and for 8.4% (n: 236) of the tumors. Mean age of the whole population was 9.2 years with even distribution according to sex. The most frequent tumor types were extranodal non-Hodgkin lymphoma (7 cases), osteosarcoma (4 cases) and Ewing sarcoma (3 cases). These data can be considered representative of our population of children and adolescents and serve as a basis for recognition and presumptive diagnosis in clinical practice.

Key words: pediatric pathology, malignant neoplasm, childhood neoplasm.

## NEOPLASIAS MALIGNAS BUCOMAXILARES EN NIÑOS Y ADOLESCENTES. ANÁLISIS RETROSPECTIVO DEL SERVICIO DE BIOPSIAS DE UNA FACULTAD DE ODONTOLOGÍA EN ARGENTINA

### RESUMEN

Los estudios sobre neoplasias bucomaxilares en niños y adolescentes son relativamente poco comunes y escasos los reportes sobre neoplasias malignas. Los datos disponibles son difíciles de comparar debido a diferencias en los criterios de análisis utilizados en cada estudio y origen racial-étnico de la población. El objetivo del presente trabajo fue realizar un estudio retrospectivo de neoplasias malignas bucales en pacientes de hasta 20 años de edad diagnosticados en un centro especializado en diagnóstico anatomopatológico bucal entre 1990 y 2005. Los 24 casos hallados representaron el 0.9% (n: 2434) del total de biop-

sias de este grupo etario en ese periodo y el 8.4% (n: 286) de los tumores. La edad media general fue de 9.2 años, con similar distribución según sexo. Los tipos tumorales más frecuentes fueron los Linfomas No Hodgkin extraganglionares (7 casos), el Osteosarcoma (4 casos) y el Sarcoma de Ewing (3 casos). Estos datos pueden ser considerados representativos de nuestra población infante juvenil y sirven de base para a su reconocimiento y diagnóstico presuntivo en la práctica clínica.

Palabras clave: patología pediátrica, neoplasias malignas, neoplasias infantiles.

### INTRODUCTION

Oral-maxillary neoplasms affecting children and adolescents may be benignant or malignant<sup>1</sup>. In recent years, several studies have dealt with the subject, but they are difficult to compare due to the different assessment criteria used by the authors. The maximum age limits considered are dissimilar<sup>2-9</sup>, the study periods range from 8 to 30 years and most of studies only make some reference to neoplasms within the full range of pathologies found. Those that specifically analyze tumor pathology report data mainly on benignant neoplasms, with little analysis or detail regarding malignant neoplasms<sup>3,10,11</sup>; while others are limited to some particular type of tumor<sup>12-14</sup>. The locations of the neoplasms considered also vary, and while some series include orofacial or oral-max-

illofacial neoplasms<sup>5,15,16</sup>, others are limited only to maxillary neoplasms<sup>10,17</sup>. Moreover, the populations are of different racial-ethnic types<sup>2-5,7-11,15,16,18-20</sup>. Malignant oral-maxillary neoplasm affects all age groups<sup>16,21</sup> and are in eighth place regarding frequency according to current statistics<sup>22</sup>. Nevertheless, they are infrequent in children. According to Keszler et al.<sup>1</sup> in a previous retrospective study on the general distribution of pathologies among children and adolescents, malignant neoplasms represented 1.8% of total lesions diagnosed in this group of patients. Subsequently, Jones et al.<sup>8</sup> reported a frequency of 1% in a study of similar design. When the scope of analysis in literature was limited exclusively to neoplasms, malignant neoplasms were found to have highly variable percentages of frequency

according to different authors, and there were also differences in prevalent tumor types. According to Das et al.<sup>2</sup> and more recently Shah et al.<sup>20</sup>, malignant neoplasms represented 1.2% and 0.8% respectively of total tumors found in the North American populations studied. In contrast, Sato et al.<sup>11</sup>, Chen et al.<sup>4</sup> and Tanaka et al.<sup>5</sup> reported that frequencies in Asian populations ranged from 2.8% to 7.1%; while according to Arotiba et al.<sup>3</sup>, Kalyanyama et al.<sup>23</sup> and Aregbesola et al.<sup>16</sup>, they ranged from 40% to 51% in African patients. There are very few specific reports on malignant neoplasms in children and most of them refer to a particular type of tumor<sup>12,24-27</sup>. The only series of malignant neoplasms found in updated international literature was recently reported by Ajayi et al.<sup>28</sup> in an African population; and no data on the subject were found for Argentina.

The aim of this work was to conduct a retrospective study of malignant tumor pathology in children and adolescents, from a laboratory specializing in oral pathology that receives samples for histopathological diagnosis from different geographic areas in Argentina.

## MATERIALS AND METHODS

The study material was obtained from the archives of the Surgical Pathology Laboratory of the Oral Pathology Department of the School of Dentistry, University of Buenos Aires. We reviewed the cases with tumor pathology in patients up to 20 years of age from the 1990-2005 period and selected those with a histopathological diagnosis of malignant neoplasm.

The clinical data were obtained from the respective biopsy protocols. All cases were re-evaluated microscopically. New histological sections and immunohistochemical techniques were performed in the cases for which it was necessary for diagnostic definition according to current criteria. The relative frequency of malignant neoplasms was estimated within the total pathologies and the specific tumor pathologies diagnosed for the period. The distribution by sex, age, localization and time of evolution was considered.

## RESULTS

The 24 malignant neoplasms found accounted for 0.98% of the total lesions diagnosed in the 1990-2005 period in children and adolescents (n: 2434), and 8.39% of the total number of neoplasms (n: 286).

The overall mean age was 9.2 years with a range of 2.8 to 20 years and even distribution according to sex. Sixteen cases (66.6%) were intraosseous and eight (33.3%) were located in soft tissues.

Clinical manifestations were rapidly growing, generally asymptomatic 2 to 5 cm tumors. Intraosseous tumors showed expansion of cortical plates, with erythematous mucosa in the area and effacement of the bottom of the sulcus, and radiographs showed an osteolytic lesion with undefined margins, with tooth displacement and rhizolysis. Tumors located in soft tissues had erythematous mucosa, very soft or friable consistency, and were sometimes ulcerated. Presumptive clinical diagnosis was malignancy in 40 % of the cases. Other assumptions included benign neoplasm or pseudo-tumors lesions (20%), and odontogenic lesions (15 %). No diagnosis was made in the remaining cases. The neoplasms found included 14 sarcomas, 7 lymphomas and 3 carcinomas. The sarcoma group included 4 osteosarcomas, 3 Ewing sarcomas, 2 fibrosarcomas, 2 leiomyosarcomas, 2 rhabdomyosarcomas and 1 malignant fibrohistiocytoma. For osteosarcomas, the M:F ratio was 3:1, mean age 11.3 years (7-18) and they were all located in the posterior mandibular area.

For Ewing sarcomas, the M:F ratio was 2:1, mean age 10 years (6-14) and two of the three cases were located in the upper maxilla.

The fibrosarcomas affected females aged 7 to 9 years; both were intraosseous, one located in mandible and the other in upper maxilla.

The 2 leiomyosarcomas affected males in the second decade of life and were located on cheek. The rhabdomyosarcomas affected one male and one female, both aged 5 years, one was intraosseous and the other labial.

All the lymphomas were extranodal non-Hodgkin type. The mean age of these patients was 7.9 years (2.8-16) and the M:F ratio was 1.3:1. Five were located on the maxillaries and two on the soft tissues. All 7 cases were phenotype B. According to the morphological and immunohistochemical study, there were 5 (71%) with high grade of malignancy and 2 with low grade of malignancy. The first group included 2 Large-cell lymphomas, 2 Burkitt lymphomas and 1 Lymphoblastic lymphoma.

The 3 cases of carcinoma occurred in females in the second decade of life. Two of them were adenocarcinomas, one polymorphic and the other mucoepidermoid; both located in minor salivary glands of

**Table 1: Distribution according to sex and decade of life of the different histological types of malignant neoplasms.**

Histological type	Sex		Age (years)		Total
	M	F	0-10	11-20	
<b>Sarcomas</b>					<b>14</b>
Osteosarcoma	3	1	2	2	4
Ewing Sarcoma	2	1	2	1	3
Fibrosarcoma	0	2	2	0	2
Leiomyosarcoma	2	0	0	2	2
Rhabdomyosarcoma	1	1	2	0	2
Malignant Fibrohistiocytoma	0	1	1	0	1
<b>Non-Hodgkin Lymphomas</b>					<b>7</b>
Low Grade Aggressiveness	2	0	1	1	2
High Grade Aggressiveness	3	2	4	1	5
<b>Carcinomas</b>					<b>3</b>
Squamous Cell Carcinoma	0	1	0	1	1
Polymorphous Adenocarcinoma	0	1	0	1	1
Mucoepidermoid Carcinoma	0	1	0	1	1
<b>Total</b>	<b>13</b>	<b>11</b>	<b>14</b>	<b>10</b>	<b>24</b>

**Table 2: Location of malignant neoplasms according to histological type.**

Histological type	Mand	Max	Cheek	Sulcus Bottom	Lip	Tongue
<b>Sarcomas</b>						
Osteosarcoma	4	1				
Ewing Sarcoma	1	2				
Fibrosarcoma	1	1				
Leiomyosarcoma			2			
Rhabdomyosarcoma	1				1	
Malignant Fibrohistiocytoma			1			
<b>Non-Hodgkin Lymphomas</b>						
Low Grade Aggressiveness	1			1		
High Grade Aggressiveness	2	2		1		
<b>Carcinomas</b>						
Squamous Cell Carcinoma						1
Polymorphous Adenocarcinoma			1			
Mucoepidermoid Carcinoma			1			
<b>Total</b>	<b>10</b>	<b>6</b>	<b>5</b>	<b>2</b>	<b>1</b>	<b>1</b>

cheek mucosa. The other was a squamous-cell carcinoma located on the edge of the tongue in an HIV+ patient (Tables 1 and 2).

Times to progression at the time of consultation recorded in the biopsy protocols were 30 to 60 days for the lymphomas and Ewing sarcoma; and up to 1 year for the osteosarcomas. For the other tumor types it ranged from 25 to 90 days.

## DISCUSSION

The frequency of malignant neoplasms in children and adolescents is highly variable according to data from international literature. While in the African population they represent 40 to 51% according to different authors<sup>3,16,19,23</sup>, in the Oriental population they range from 2.9% to 7.3%<sup>4,5,11</sup>. Data for Caucasian series are also dissimilar. The relative frequency of malignant

**Table 3: Frequency of malignant oral-maxillary neoplasms in children and adolescents according to international series over the past 15 years.**

Author	Year	Population	Age	Total Neoplasms		Malignant Neoplasms	
				N:	n:	%	
Das S et al 2	1993	USA	0-20	299*	3	1.2	
Arotiba GT 3	1996	Nigeria	0-15	174	70	40.2	
Sato M et al 11	1997	Japan	0-15	250	18	7.2	
Chen YK et al 4	1998	Taiwan	0-15	153*	11	7.1	
Tanaka N et al 5	1999	Japan	0-15	105	3	2.9	
Ulmansky M et al 18	1999	Israel	0-15	113*	18	9.5	
Lawoyin JO 19	2000	Nigeria	1-16	209*	82	39.2	
Maaita JK 6	2000	Jordan	0-18	172	16	9.3	
Kalyanyama BM et al 23	2003	Tanzania	0-16	115*	68	43.0	
Al Khateeb et al 7	2003	Jordan	0-19	236	26	11.0	
Tanrikulu R et al 15	2004	Turkey	0-15	46*	6	13	
Aregbesola SB et al 16	2005	Nigeria	0-19	146	74	51.0	
Jones AV et al 8	2006	United Kingdom	0-16	492*	31	6.3	
Ajayi OF et al 28	2007	Nigeria	0-19	353**	47	13.3	
Lima G da S et al 9	2008	Brazil	0-14	100*	8	8	
Shah SK et al 20	2009	USA	0-16	624*	5	0.8	
Present series	2009	Argentina	0-20	286	24	8.04	

\* Only neoplasms are considered

\*\* Includes pseudotumors. S/D on neoplasms exclusively.

**Table 4: Histological types of malignant neoplasms found in children and adolescents compared to data from literature.**

Author	Type of Neoplasm						Total
	Sarcomas		Lymphomas		Carcinomas		
	n	%	n	%	n	%	n
Arotiba et al 3	17	26	40	61	8	12	65*
Sato et al 11	5	29	9	53	3	18	17*
Aregbesola et al 16	5	7	67	90	2	3	74
Ulmansky et al 18	4	25	9	56	3	19	16*
Lawoyin et al 19	20	24	62	75	0	0	82
Kalyanyama et al 23	5	7	60	88	3	4	68
Ajayi et al 28	17	36	25	53	5	11	47
Al-Khateeb et al 7	7	38	7	38	4	22	18*
Present series	14	58	7	29	3	12	24

\* Excluding cases of metastasis, nasopharyngeal neoplasms and/or epidermal melanomas

neoplasms in this series is similar to that reported by Jones et al.<sup>8</sup> and Ulmansky et al.<sup>18</sup>, but considerably higher than those reported by Das et al. in 1993<sup>2</sup> and recently by Shah et al.<sup>20</sup>. Although these differences may be due to geographic conditions and/or racial groups studied, even the variations observed between studies with the same geographic origin suggest that they may also be partly due to the different criteria used by the different authors to study them (Table 3). In this study, malignant neoplasms were evenly distributed according to sex and age; nevertheless,

variations were found when specific tumor types were considered. Both sarcomas and lymphomas predominated in males, but while the former were distributed evenly over the first and second decades of life, the latter prevailed in the first decade. Sarcomas in general were the most frequent neoplasms (58%), followed by lymphomas (29%). These data differ from those reported by most authors, who find that lymphomas are the most common tumor type in this age group<sup>3,11,16,18,19,23,28</sup> or report equal numbers of cases for both entities<sup>7</sup> (Table 4).

**Table 5: Types of sarcoma found in this series and in data from literature.**

Author	Type of Sarcomas							Total n
	Osteo sarcoma n	Ewing Sarcoma n	Fibro sarcoma n	Leiomyo sarcoma n	Rhabdomyo sarcoma n	Malignant Fibrohist n	Other *	
Arotiba et al 3	0	1	1	0	6	4	5	17
Al-Khateeb et al 7	1	0	0	0	6	0	0	7
Aregbesola et al 16	1	0	0	1	3	0	0	5
Sato et al 11	0	0	4	0	1	0	0	5
Ulmansky et al 18	0	0	3	0	1	0	0	4
Ajayi et al 28	4	3	3	0	4	2	1	17
Present series	4	3	2	2	2	1	0	14

\* Includes cases of Kaposi's sarcoma, neurofibrosarcoma, undifferentiated sarcomas, myxosarcoma.

In this series, sarcomas included lesions with different kinds of histogenesis, but osteosarcomas prevailed, which was another difference with the data from literature. According to Arotiba et al.<sup>3</sup>, Al Khateeb et al.<sup>7</sup> and Aregbesola et al.<sup>16</sup>, rhabdomyosarcoma was the most frequent sarcoma; Sato et al.<sup>11</sup> and Ulmansky et al.<sup>18</sup> report a higher frequency of fibrosarcomas, while Ajayi et al.<sup>28</sup> report the same number of osteosarcomas and rhabdomyosarcomas (Table 5).

Carcinomas were the least frequent, in agreement with reported data<sup>7,16,18</sup>. This kind of tumor is infrequent in patients under 20 years of age and extremely rare in the first decade of life<sup>21</sup>. The three cases found were from females aged 15 to 20 years, and corresponded to 2 adenocarcinomas in minor salivary glands and 1 squamous cell carcinoma on lingual mucosa. The histological type of the salivary neoplasms reported in different series is variable and, due to the low number of cases reported, not comparable. This series includes one mucoepidermoid carcinoma and one polymorphic adenocarci-

noma. These two types of tumor have been reported as the most frequent in a study performed exclusively on neoplasms of the major and minor salivary glands in a Chinese population<sup>29</sup>. The etiological factors of squamous cell carcinomas in adolescents have been widely discussed. The possibility of tobacco and alcohol having a carcinogenic effect of on young patients is low because exposure time would be relatively too low to establish a cause-effect. Nevertheless, other factors such as genetic predisposition, viral infections and states of immunodeficiency, among others, may condition their development<sup>30</sup>. The case included in this series corresponded to an HIV+ patient. Malignant neoplasms in children and adolescents are infrequent, but are usually high-degree, with rapid progression and potentially life-threatening, therefore an early diagnosis is vital. The data presented in this series may be considered representative of our environment and serve as a basis for recognition and presumptive diagnosis in clinical practice prior to biopsy.

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#### CORRESPONDENCE

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