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CLINICO-HISTOPATHOLOGIC TYPES OF MAXILLOFACIAL MALIGNANCIES WITH EMPHASIS ON SARCOMAS: A 10-YEAR REVIEW
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ABSTRACT

***Background*: Sarcomas are malignant neoplasms that occur anywhere in the human body. Though their occurrence in the head and neck region is rare vis-a-vis other malignancies, their presence is of tremendous concern due to their often grave prognosis.**
***Objective*: To determine the pattern of occurrence, histopathologic types of maxillofacial sarcomas and their proportion to other malignant neoplasms of this region based on archival material accumulated over 10 years (2000-2009).**
***Design*: A combined retrospective and prospective cross-sectional study.**
***Setting*: The University of Nairobi Dental Hospital (UNDH).**
***Subjects*: All cases with a diagnosis of sarcoma registered between 2000-2009 were evaluated.**
***Results*: Of the 528 malignancies recorded over the ten-year period, 427 (80.9%) were of epithelial origin while 101 (19.1%) were sarcomas. Patients with epithelial malignancies were older (54.16 ± 15.94 years) than patients with sarcomas (31.73 ± 16.78) with the differences having been statistically significant. Osteosarcoma was the most commonly occurring sarcoma (29.7%), followed by Kaposi's sarcoma (KS) (28.7%), fibrosarcoma (FBS) (18.8%), and rhabdomyosarcoma (RMS) (9.9%). Sarcomas peaked in the third decade with 70% occurring below the age of 40 years. The maxilla and the mandible were the most afflicted sites in the maxillofacial region accounting for 52%. The patients on average presented to medical personel about nine months after noticing the lesion with the most frequent complaint having been swelling.**
***Conclusion*: The present study confirms the relative rarity of maxillofacial sarcomas. It also provides data on the histopathologic types and demographic characteristics of maxillofacial sarcomas in a select Kenyan population. This information is a contribution to the comprehensive documentation of sarcomas that occur globally and is useful in the provision of baseline data upon which future prospective analytical protocols may arise.**

INTRODUCTION

Whole body sarcomas are relatively rare. In the United States, sarcomas account for approximately 1% of all malignancies with 5 to 15% of these lesions occurring in the head and neck region (1). In Nigeria, a retrospective study by Arotiba *et al*. reported 58 sarcomas (12.37%) out of 469 orofacial malignancies (2). Although head and neck sarcomas occur infrequently in adults, in the paediatric population one in three sarcomas will occur in the head and neck region. Most head and neck sarcomas are of the soft-tissue type with only 20% being of bony or cartilaginous origin (3).

There exist a limited number of reports on individual sarcomas occurring in the maxillofacial region. Most reports are centred on the head and neck region rather than the more limited maxillofacial area. In general, studies on head and neck sarcomas are rare in the English literature. Further, the small number of patients with head and neck sarcomas makes it difficult for prospective studies to be undertaken. Chindia *et al* revealed that, of the 10,897 whole body neoplasms reported between 1982-1991 at the Kenyatta National Hospital in Kenya, 985 were sarcomas among which 16% were found in the head and neck region (4). A clinico-pathologic study by Adebayo *et al* in Nigeria reported that 20% of maxillofacial malignancies were sarcomas with a slight female to male predilection of 1.3:1 (5,6).

Bone sarcomas: Osteosarcoma is the most common primary malignancy of bone, with a reported

incidence of 1:100,000 (7). August *et al* estimated that less than 4% of all recorded osteogenic sarcomas occur in the jaw. The mandible and maxilla are the predominate locations of head and neck osteosarcoma (HNOS), although extragnathic bone as well as soft tissues sites may be affected (10). Adebayo *et al*. Chidzonga *et al* and Chindia *et al* found the mandible to have been the most common site affected (5,11,12). The five-year disease-specific survival rate for patients with HNOS has been poor, with most studies reporting survival rates of 23-37% (7-9,13,14).

Soft tissue sarcomas: Soft-tissue sarcomas (STS) are an uncommon but important problem in head and neck oncology. STS constitute less than 1% of all head and neck malignancies and include many histologic subtypes of varied biological behaviour (1). Fibrosarcomas (FBS) are relatively uncommon tumours and account for 12-19% of soft tissue sarcomas. More than half of all the tumours arise in the lower extremities; approximately 10% occur in the head and neck, most commonly in the sinonasal tract and neck. FBS may arise in patients of any age and a slight male predominance exists. In the African series, no gender bias has been noted with the mandible having been the most common site. Age ranges are similar to those in the western series (5,11).

Since the outbreak of AIDS, Kaposi's sarcoma (KS) has become the most common type of intra-oral sarcoma. Before the outbreak of HIV infection, KS was a rare form of sarcoma and literature from New South Wales showed an overall incidence of 0.47/million persons. With the advent of HIV infection, the occurrence of KS has rapidly increased and has even reached epidemic proportions in some regions where HIV infection is high. There are some studies which have shown that up to 24% of HIV infected patients have KS (4). Butt *et al* in an evaluation of oral manifestations of HIV infection at a Kenyan provincial hospital documented 13% of oral KS among 61 patients aged 16 years and above (15).
Rhabdomyosarcoma (RMS): A tumour of skeletal muscle origin, is the most common STS in children and adolescents affecting the head and neck (16). RMS has three distinct histopathologic types: alveolar, embryonal and pleomorphic. The embryonal type accounts for 70% of all cases and is particularly common in the oral and peri-oral region (17). In a review of 88 cases in Zimbabwe, Chidzonga *et al* reported that RMS was the second most common sarcoma predominantly in boys and afflicting mainly the maxilla (11). Adebayo *et al* reported RMS to have been the third most common sarcoma behind osteosarcoma and chondrosarcoma. Most were noted to occur in the cheek with 50% of the cases in the first decade (5).
Other sarcomas: Several other sarcomas exist but from the literature they occur rarely in the maxillofacial region. There is need for basic research to better understand these tumours with regard to prompt intervention and clinical management. The aim of this study, therefore was to determine the demographic pattern of occurrence and histopathologic types of maxillofacial sarcomas as well as their proportion to other malignancies at a Nairobi centre, Kenya.

MATERIALS AND METHODS

The study was carried out at the histopathology laboratory of the University of Nairobi Dental Hospital (UNDH).

Data were recorded using a specially designed chart. The data collected included demographic patterns, clinical presentation and the histopathologic variants as previously reported of all maxillofacial malignancies seen over a ten-year period (2000 to 2009). Only the histopathology reports from the UNDH laboratory were used. Recording of individual sarcomas was done utilising the simplified clinical classification of the University of Texas M.D. Anderson cancer centre. The demographic patterns and clinical presentation information were accessioned from the patients' hospital files. Case definition for the study was any sarcoma diagnosed for the first time at the Oral Pathology Laboratory at the UNDH. Recurrent diseases were excluded. Cancer cases were coded according to the International Classification of Diseases. Data were analysed using the statistical package for social sciences version 11.5 with the main outcome measures having been the demographic pattern of occurrence and histopathologic variants of maxillofacial sarcomas.

RESULTS

Demographic distribution of sarcomas as compared to other malignancies of the maxillofacial region showed that over the ten-year period, 525 cases of malignant neoplasm were recorded among which 424 (80.9%) were of epithelial origin while 101 (19.1%) were sarcomas. There were more males 273 (52%) than females 252 (48%). The age range was between 3 to 90 years with a mean of 49.64 years (SD±18.45 years). Patients with epithelial malignancies were older, 54.16 years ±15.94 (95%CI 52.52 - 55.75), than those with sarcomas who had an average age of occurrence at 31.73 years±16.785 (95%CI 28.3735.10). The difference was statistically significant (Mann Z= -10. 266, P<0.01 (0.000). More males had epithelial malignancies than females while there were more females with sarcomas. However, the difference was not statistically significant (X2=2.09, p=0.15). The distribution of maxillofacial malignancies by year is illustrated in Fig. 1.

Age distribution of sarcomas: Among the 101 cases of sarcoma, 46 (45.5%) occurred in males while

55 (54.5%) were found in females with an overall age range of 3 to 90 years. The 20 to 29 year-old age group was the most commonly affected with 28 cases and a significant proportion of sarcomas (70.29%) occurred in patients less than 40 years of age. There was no statistically significant difference in the ages of male (31.19±17.99 years) and female (32.20±15.84 years) patients at first presentation (p=0.770). Table 1 illustrates the distribution of the sarcoma sub-types among the various age groups.

Clinical presentation, site distribution and tumour type: Of the 101 sarcomas recorded, 98 had the site of tumour occurrence indicated. The maxilla was the most commonly affected site with 26 sarcomas while 25 were found in the mandible and 17 occurred in the palate. Eleven cases were found in the tongue so that cumulatively, these four sites contributed to 80.5% of the sarcomas. Table 2 shows the distribution of the various sarcoma sub-types according to site. Of all the sarcoma cases analysed, 73 had information regarding the duration between when the patient first noticed the condition to when they first presented to medical personnel. The average duration was 9.9 months (SD=14.91). One case was diagnosed incidentally on routine medical examination while one other patient presented after nine years. For patients who presented with sarcomas, 51 clinical records were located. All but one presented with swelling of the affected site. Other prominent features were pain (37%), bleeding (19%), mobility of teeth (12%), limited mouth opening (10%) and paraesthesia (10%). A case of osteosarcoma was diagnosed incidentally during routine dental examination. Concerning the tissue of origin, 32 sarcomas (31.68%) were of bony or cartilaginous origin while 69 (68.32%) were of soft tissue origin. More females (54.45%) were affected than males (45.54%). However, the differences were not statistically significant. {X^2=1.222; 1df; p>0.05 (p=0.269)}.

Hard tissue sarcomas: Among the osteosarcomas reviewed, the most commonly affected age group was the 10-19 years with most (83.33%) occurring below 40 years of age. The overall mean age at diagnosis was 28.40 years and a statistically significant difference (p=0.019) was observed between the mean age at first presentation in men (21.18±6.91 years) and females (32.58±17.24 years). Among the sub-types of osteosarcoma, 14 (46.7%) were of the osteoblastic sub-type, nine (30%) were fibroblastic while seven (23.3%) were chondroblastic. More females were affected (63.33%) than males (36.67%) with the same trend having been seen among the sub-types. However, the difference was not statistically significant (X^2=0.532; p>0.05 (p=0.892).

Soft tissue sarcomas: Ten lesions of RMS were reviewed which occurred in cases with an overall mean age at diagnosis of 17.77 years with no statistically significant difference observed in the ages of males (17.50±20.46 years) and females (17.88±9.40 years) at first presentation (p=0.291). Five of these were of the pleomorphic sub-type, three embryonal and one was of the alveolar sub-type. An equal number of males and females were affected. More males were affected by the embryonal sub-type while more females were affected by the alveolar and pleomorphic RMS. However, the differences were not statistically significant {X^2=1.48f, p>0.05 (p=1.000)}. Of the eight cases that had the age indicated four were found in the zero to nine year-old age bracket. One case of pleomorphic RMS occurred in the 50-59-year-old age bracket. Majority (87.5%) were seen below 30 years of age.

Over the ten-year period 19 cases of FBS were recorded among which ten (52.63%) occurred in females while nine (47.37%) were in males. The mean age at first diagnosis was 32.16 years with no statistical difference noted in the ages of men (39.56±23.85) and women (25.50±10.80) at first diagnosis (p=0.115). The 20-29 year-old age group was the most commonly affected (n=9) with 73.68% of the cases occurring below the age of 40 years.

KS was the second most frequently occurring maxillofacial sarcoma recorded over the ten-year period (n=29). Majority (72.41%) were found between the ages of 20-50 years. The overall mean age was 36.68 years with no statistical difference (p=0.087) in the age at first presentation of men (33.75±10.80 years) and women (38.29±15.89 years). There was an almost equal distribution between the genders with 15 (51.72%) in males and 14 (48.28%) seen in females.

Figure 1
Yearly distribution of maxillofacial malignancies

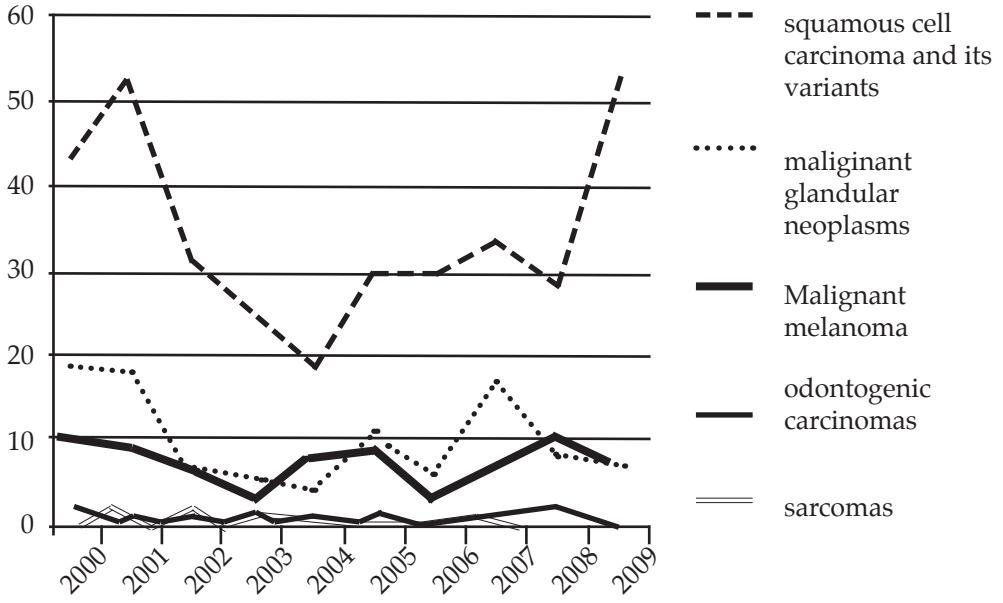

Table 1
Distribution of sarcoma subtypes according to the age groups

Neoplasm	Age of patient in years				
	0-19	20-39	40-59	60+	Total
Osteosarcoma	10	15	2	3	30
Chondrosarcoma	0	1	1	0	2
MFH	0	1	0	0	1
Fibrosarcoma	3	11	3	2	19
Rhabdomyosarcoma	5	3	1	0	9
Angiosarcoma	1	0	0	0	1
Kaposi's sarcoma	2	15	10	2	29
Haemangiopericytoma (H PT)	0	1	0	0	1
Haemangioendothelioma (HED)	0	2	0	1	3
Liposarcoma	0	1	0	1	2
Unclassified	0	0	0	1	1
Total	21	50	17	10	98

Table 2
Distribution of sarcoma types by site

Neoplasm	Site										
	Max	mand	cheek	tongue	FOM	lip	palate	ging/alv	MSG	ill def	Total
Osteosarcoma	15	12	-	-	-	-	-	-	-	1	28
Chondrsarcoma	1	1	-	-	-	-	-	-	-	-	2
RMS	3	2	2	1	-	-	-	-	-	2	10
FBS	5	8	3	-	-	1	-	-	-	1	18
MFH	-	-	1	-	-	1	-	-	-		1
Angiosarcoma	-	-	1	-	-	-	-	-	-	-	1
KS	1	-	1	6	-	-	17	3	-	1	29
HPT	-	-	-	1	-	1	-	-	-	-	2
HED	-	-	-	2	1	-	-	-	-	-	3
MPNST	1	-	-	-	-	-	-	-	-	-	1
Liposarcoma	-	2	-	-	-	-	-	-	-	-	2
Unclassified	-	-	-	-	-	-	-	-	-	1	1
Total	26	28	7	11	1	2	17	3	1	5	

DISCUSSION

Generally, maxillofacial mesenchymal malignancies are rare. In the present study, these neoplasms comprised 19% of all malignant tumours affecting the maxillofacial region. The results show similarity in the occurrence of sarcomas in the maxillofacial region with those seen in Kaduna, Nigeria (5), though these are higher than those seen in European and Asian populations (6,18). This may reflect a racial or ethnic bias with higher incidences of maxillofacial sarcomas seen in Black populations than among the Caucasian stock. In the present study, epithelial malignancies (carcinomas) tended to affect patients in the older age groups while the maxillofacial sarcomas afflicted younger patients. Similar patterns have been described in the western literature (2,4). This implies that genetic factors may have a more significant role to play than environmental influences in the development of maxillofacial sarcomas unlike carcinomas where environmental factors such as tobacco and alcohol usage have been implicated.

Sarcomas can be detected during routine examination for other conditions or due to non-specific signs and symptoms. The presenting features of sarcomas are non-specific and depend on tumour location, size, rate of growth, duration and level of cancer awareness in the individual (1). All but one case seen in this study presented with swelling while a few had pain, mobility of teeth, bleeding from the tumour and trismus. Notably, one case was found incidentally on routine dental examination. The average duration of these lesions was short (mean 9.9 months), as has been reported in other studies, reflecting the rapidity of growth of these lesions. Osteosarcoma was the most frequently diagnosed hard tissue malignant maxillofacial mesenchymal neoplasm in the present study and this is consistent with previous data from this country (4) as well as from other parts of Africa (11,25). From the literature, the most common sarcoma is controversial depending on the age group, site and possibly racial factors. RMS has been documented as the most common soft tissue oral and maxillofacial sarcoma in childhood (19-21) while in adults, osteosarcoma predominates (22-24).

Analysis of age and gender distribution of maxillofacial osteosarcomas in this study noted some trends. The mean ages at first presentation of maxillofacial osteosarcoma were consistent with data from other African studies (5,26) but lower than data from European studies (7,13,14). The lower mean age of occurrence of osteosarcoma is probably influenced by the lower age expectancy in the Kenyan population (52 years in 2006). From the literature, the average age of onset of osteosarcomas of the jaws and craniofacial bones has been reported to present ten to twenty years later than for skeletal lesions; and the histopathological variables are more favourable, distant metastases occur less· frequently and survival rates are higher (27 - 29). Our data also showed that there was no clear gender predilection. The marginal differences in gender predilection seen in the Kenyan studies infer that osteosarcoma may have no real preference for any gender in that population which is in agreement with what has been observed in European or American studies.

There is inconsistency as to the most common site of occurrence of osteosarcoma in the craniofacial region from data gathered in the African selling. Some authors site the mandible as the most afflicted (5,11,26) while others the maxilla (25). Nonetheless, the mandible and maxilla contribute disproportionately to the sites affected within the region (1) as was corroborated in this study. In our series the osteoblastic sub-type of osteosarcoma was the most common similar to a report by Bertoni *et al*. followed by the fibroblastic and chondroblastic sub-types (30). However, other reports have stated that the chondroblastic sub-types are the most common (31). The chondroblastic variant has been proposed to be an adverse prognostic factor while the fibroblastic variant to have had the best prognosis (32) although the largest series to date failed to show any impact of histological sub-type on survival (33). As would be expected, based on evidence elsewhere (39), chondrosarcomas (CHS) were found to have been particularly rare in this series. Only two lesions had been diagnosed over the ten-year period. In general, CHS occurs more often in males, in a ratio of about 2: 1; and there are no pathognomonic signs or symptoms presented (40).

KS has been described as one of the most common malignant tumours in Africa. It is the most common cancer associated with HIV infection, occurring in up to one in four AIDS patients (4). Indeed KS is most prevalent in countries where HIV infection is prevalent. In our report, KS was the second most common maxillofacial malignancy making up 28% with no clear gender predilection, as has been noted in more recent publications (35). It was the most common sarcoma of the head and neck in a report by Chindia *et al*. with a male to female ratio of 3:1 (4). The change in gender affliction trends noted may reflect improved health awareness and treatment seeking behaviour between both genders. The site predilection was in accordance with the findings of other authors with the palate having been the most common site (34,35). With the advent of the highly active anti-retroviral therapy (HAART), the development of KS in AIDS patients has decreased and this may explain the lower prevalence of KS in our study.

Among the soft tissue sarcomas, apart from KS, FBS was diagnosed most frequently accounting for 18.8% of the cases. This is slightly higher than those reported by Chindia *et al*. and Adebayo *et al.* (4,5). In

this series, no clear gender predilection was noted in conformity with literature from other parts of Africa (5). However, this contrasts with a Dutch report by Siootweg and Muller which showed a slight female predominance (36). The mean ages at first diagnosis in this study are consistent with data from both the African (5) and the western literature (36). FBS occur in both the soft and hard tissues of the maxillofacial region. Siootweg and Muller assessed the lesion in the jaws of a Dutch population and found more in the mandible than the maxilla (36). Our findings concurred with most lesions having been found in the mandible (44%) and maxilla (27%) with a few lesions in other sites.

RMS was the fourth most common sarcoma accounting for 9.9% of all tumours reviewed which was similar to other African series (5,11). RMS can occur at any age but the lesion is most common in the first decade of life making it the most common maxillofacial sarcoma in childhood. In our series, 50% of the neoplasms occurred in the first decade thereby corroborating other published series (37,38). RMS may be defined as a malignant tumour of the rhabdomyoblasts and it is estimated to comprise 12 to 56% of all solid malignant tumours in the paediatric age group (37). A review by William *et al* found that among the subtypes, embryonal RMS was the most predominant type in the head and neck accounting for over half the cases with most afflicting younger children (38). The pleomorphic sub-type was the least common and was mostly found in older patients. In our series the pleomorphic sub-type was the most common followed by the embryonal sub-type, with one case seen of the alveolar sub-type. Lack of a centralised sarcoma team may have influenced the results seen in this study with some of the paediatric RMS cases having been seen by medical oncologists. Almost all cases were found below 30 years of age with one case of pleomorphic RMS occurring in the 50-59-year-old age group. From the literature, the occurrence of other sarcomas in the maxillofacial region is rare (1, 5) and this can explain the relatively few cases seen in this study.

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