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Maxillofacial Sarcomas: A Single Center Evaluation Study

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Abstract:
Sarcomas of the oral and maxillofacial region are known to arise more often from soft tissue (80%) than from bone/cartilage (20%). They can occur at any anatomical site and at any age[3]. They affect all ages, but, in most reports, adults have an 80-90% predilection while 10-20% affect children[4,5]. Sarcomas demonstrate aggressive biological characters and comprise about 1% of all malignancies.
Aim- *to evaluate the prevalence of patients with head and neck sarcomas managed by the same surgical and medical team at our center over a period of 4 years (2017-2021).*
Methods- *Day registers from the oral diagnosis clinic, surgical day case books and laboratory registers were used to retrieve relevant patient information. Information such as age, gender, tumor size, tumor location, duration of tumor at presentation, and the treatment*
Results - *The data was analysed using the R programming language. The median age of respondents in this study was 38 years, with a female preponderance (55%, n= 22) in a 1:1.2 male: female ratio. Most sarcomas were seen within the fourth decade of life (n=8, 20%), with 57.5% of patients (n = 23) under the age of 40 years. In addition, 14 (35%) of the sarcoma patients were in stages I and II, while 26 (65%) were categorized in stages 111 and 1V of their sarcomas. Nodal involvement was observed most at levels II and III of the head and neck. Staging of lesions was not related to gender, age group, or radiographic presentation.*
There was a positive association (p = 0.0001) between nodal metastasis and post-ablative surgery complications.
Conclusion *- Epidemiological evaluations in different countries are limited. Head and neck sarcomas can occur in any gender or age group. Poor prognosis is associated with tumor size, evidence of metastasis, late presentation for treatment, and advanced staging.*

Keywords: *Sarcomas, mandible, ablative surgery, and chemotherapy*

1. Introduction

Sarcomas of the oral and maxillofacial region are known to arise more often from soft tissue (80%) than from bone/cartilage (20%)[1]. Sarcomas accounted for 5.5 % of malignancies in persons younger than 20 years in North America2. They can occur at any anatomical site and at any age[3]. They affect all ages, but, in most reports, adults have an 80-90% predilection while 10-20% affect children[4,5]. Reports from Africa on the clinical behaviour of oral and maxillofacial sarcomas are sparse and are mostly case reports. Sarcomas demonstrate aggressive biological characters;

most of them are locally invasive with significant potential for metastasis.[6] In all, sarcomas constitute a heterogeneous group of rare neoplasms that comprise about 1% of all malignancies.

They are even rarer in the oral and maxillofacial region and constitute less than 1% of neoplasms occurring in this region.[6–8] Sarcomas of the head and neck region accounted for about 4–10% of all sarcomas.[9] Sarcomas originate from diverse tissue types like muscle, bone, fat, blood vessels, nerves, and more than 50 histopathological subtypes have been identified by the WHO.[10] Most patients with sarcomas have no clear etiology, exposure to ionizing radiation, chemicals, or alkylating substances. However, genetic conditions such as Li-Fraumeni syndrome or type1 neurofibromatosis have been implicated.[10,12] Recent findings also associate specific genetic mutations with the development of some sarcomas.[13]

Sarcomas are associated with high rates of recurrence and mortality. The poor prognosis of most patients with a sarcoma of the head and neck region is due to its aggressive behavior and difficulty in obtaining local control[14,15]. Lymph node involvement is not common (6-1.5%), but distant metastases are observed in approximately 30-50% of patients[15,16]. In various studies, they have an average of 5-year survival rates ranging from 27% to 84%.[6] Despite improvements in chemotherapy and surgical protocols, there are still no clear guidelines for the management of sarcomas: this may be related to a lack of international consensus on classification, grading, and difficulty in their histopathologic diagnosis[11] This paper reports a retrospective evaluation of patients with head and neck sarcomas managed by the same surgical and medical team at our center over a period of 4 years

2. Methods

Day registers from the oral diagnosis clinic, surgical day case books, and laboratory registers at Lagos state University teaching hospital were utilized to retrieve relevant patients' information. These include: Socio-demographic data such as age, gender,

- Location of tumors,
- Duration of tumor at presentation,
- Level of metastasis in the neck,
- Treatment choice,
- The outcome of patients' management, and
- The follow-up periods.

Information retrieved were imputed into a data proforma. The continuous variables of age and duration of the lesion were recorded in years and months, respectively.

3. Data Analysis

The data was analysed using the R programming language (R version 4.1.2). Descriptive statistics for socio-demographic variables such as age in range, gender, tumour's location, and lesions' prevalence were determined. Frequencies were obtained and expressed as percentages. Means and standard deviations were used for continuous variables, while proportions and tables were used for categorical variables. Analysis of each diagnosis entailed: the number of samples, male: female ratio, age range, mean age, and standard deviation. Pearson's Chi-Square and Fishers' exact approximation were used to assess the relationship between the socio-demographic and other factors and the lesions. This was also used to assess some lesion characters such as metastatic location, tumour location and stage, outcome, and location while controlling for sex. The mean across the age of the patient, duration of lesions and their relationship to types of sarcomas, and presence or absence of nodal metastasis and recurrence was analysed using Student's T test and ANOVA where necessary. Wilcox rank sum and Kruskal Wallis test were utilised when normality test was breached in the aforementioned variables with attendant post hoc test. Significance was determined at $p \leq 0.05$.

4. Results

This is a retrospective study involving forty treated cases of patients diagnosed with sarcomas at the oral and maxillofacial center over a period of 4 years. The median age of respondents in this study was 38 years, with a female preponderance (55%, n= 22) in a 1:1.2 male: female ratio. The minimum and the maximum age of respondents in the study are 3 years and 96 years, respectively. Most sarcomas were seen within the fourth decade of life (n=8, 20%), with 57.5% of patients (n = 23) under the age of 40 years, while the male gender was equally distributed between the over and under 40 years group, more female patients were observed under the age of 40 years with no statistical significance. The mean duration of lesions prior to presentation is 10.6 months $\pm$ 6.9 months (median = 8.5 months).

Patients' most common conventional radiographic presentation was an ill-defined lytic moth-eaten appearance (n=20, 50%), followed by those with mixed radiopaque – radiolucent appearance (n=14, 35%). Only 15% of all sarcoma patients were presented with a frank osteosclerotic appearance (cotton wool appearance). The median duration of lesions varies significantly between the different radiographic appearances, with osteosclerotic lesions presenting with the highest duration at 12 months and mixed radiopaque-radiolucent lesions presenting with a median of just 6 months ($p = 0.04$). Dunn's post-hoc analysis revealed the significant difference between lytic and mixed radiopaque – radiolucent lesions. Besides these common imaging characteristics, 25% (n = 10) of sarcoma cases showed peculiar radiographic characteristics, mainly sunburst appearance. Our study's median dimensions of sarcoma are 37.5cm, and dimensions vary between different radiographic appearances but with no statistical significance.

14 (35%) of the sarcoma patients were in stages I and II, while 26 (65%) were categorized in stages 111 and 1V of their sarcomas. The median dimensions of lesions in stages III and IV were significantly higher at 48cm relative to the median of 18cm in the cases of stages I and II ($p<0.0001$). Nodal involvement was observed most at levels II and III of the head and neck. Staging of lesions was not related to gender, age group, or radiographic presentation. Nine of the sarcomas

had characterized nodal metastasis (22.5%), while the remaining had nil accessed nodal metastasis. The propensity for nodal metastasis with an increased size of sarcomatous lesions as sarcoma cases had a median dimension of 54cm compared to the median of 32cm for lesions without metastasis at a p-value of 0.01.

The commonest among the sarcomas diagnosed is pleomorphic undifferentiated sarcoma (PUS) n=17, 42.5%), followed by rhabdomyosarcoma (n=12, 30%); osteosarcoma has a prevalence of 27.5%. Several of the sarcomas are located in the mandible (n= 23, 54.4%).

Surgery was the main form of treatment, and in combination with adjuvant chemotherapy, patients were given 23 (54.8%), the highest form of treatment. Five (11.9%) cases also have neck dissection along with tumor ablation surgery and adjuvant chemotherapy. 28 (66.7%) of the cases managed had no recurrence within the first six to twelve months of treatment, and 9 (21.4%) had recurrence five to twelve months post-surgery. Three deaths (7.1%) were recorded in the study, 50% of the subjects were followed up for 1-6 months, and seven patients were either lost to follow-up/ dead (16.7%).

There was a positive association (p = 0.0001) between nodal metastasis and post-ablative surgery complications and/or mortality, as all the patients that died between follow-ups had nodal metastasis. In contrast, 33.3% of patients with recurrence between follow-ups had nodal metastasis compared to only 10.7% of patients with no recurrence at follow-up.

5. Discussion

Epidemiological evaluations in different countries are limited. They present different results about the prevalence of various sarcomas 17 Sarcomas accounted for 4% of all the head and neck malignant lesions occurring in the maxillofacial region at our centre. Alishahi et al., in a study from Iran, reported a prevalence of 6%18. Rafindadi and Ayuba reported 4.9%, and Budhy et al. 19 reported a prevalence of 4% of maxillofacial lesions from Indonesia. It is apparent that the sarcomas are rare lesions. The mean age range in the study is similar to what was obtained in several studies18,20. The mandible is more involved than any other anatomical area in the study. A similar report of mandibular involvement is documented by Yamaguchi et al. 9, Alishahi et al. 18, and Fernandez et al. 15

Head and neck sarcomas can occur in any gender or age group like in this study ranging from 3yrs - 96years. In this study, both the young and the adult age groups are implicated in having sarcomas of different types. Several studies have also reported a preponderance of females in head and neck sarcomas.21,22 The gender differences may be due to geographical variation affecting the incidence of different types of sarcomas, age, and gender prevalence18. Genetic and environmental factors can contribute to the development of sarcomas. Several hereditary disorders are also clearly associated with an increased risk of these neoplasms.14

Rhabdomyosarcoma (RMS) is a paediatric sarcoma that rarely occurs in adults.23 Most RMS is diagnosed at young ages; it comprises approximately 4% to 8% of all paediatric cancers14. Therefore, not surprising that five out of the nine cases below eighteen years of age seen in this study are rhabdomyosarcomas. About 35–50% occur in the head and neck, especially in the para-meningeal and non-para-meningeal (tongue, palate, parotid, and other sites) and orbital spaces24. Para-meningeal tumours have the worst prognosis, given their location next to the vital structures, whereas non-para-meningeal and orbital tumours have a better prognosis24. Undifferentiated pleomorphic sarcomas, formerly known as malignant fibrous histiocytoma (MFH), are commonly recognised as an aggressive sarcoma with poor outcomes16. MFHs represent the most common variety of soft tissue sarcoma, but they can also arise in the bone. Only 3% to 10% occurs in the head and neck16. Women tend to present about 10 years earlier than men, but MFHs had been reported to occur more in males. In this study, it occurs more in females 8(57.1%) and mandible 8(57.1%).

Late presentation with extensive tumours was common among the respondent. The average period of the presentation was 10 months in the study. Similar experience of late presentation as a factor was documented by Adebayo et al. 4 and Chidzonga et al. 20 among the African populace. The high cost of medical treatment since several pay out of pocket and the false belief among the populace that local brew concoctions can easily cure the tumours are possible reasons for presenting late. The late presentation can affect the nature of management, encourage tumour spread, increase the size, may result in poor prognosis, and also increase morbidity of surgical intervention21. Several study patients are in stage 1II- IV with neck node involvement. The patient with loco-regional metastasis had neck dissection to remove the various nodes and the tumour ablative surgery as part of our management.

When tumour location is considered, the head and neck sarcomas are associated with the highest rates of local recurrence and the worst disease-specific survival rates14. Studies documented worse survival for patients with high-grade lesions and poorer outcomes with bone involvement.25,26. Three-death was recorded in this study. Two victims had bone-involved sarcomas, and the remaining one had a soft tissue sarcoma. There was evidence of nodal involvement at levels II and III in the neck; all are stage IV high-grade types of sarcomas. Factors such as late presentation, associated metastasis, tumour location, and the stage IV state could have largely contributed to the patients' poor prognosis and outcome. Farhood et al. 25 reported a univariate association of bony involvement with decreased overall survival. At the same time, LeVay et al. 26 demonstrated a multivariate analysis that local extent predicts rates of local recurrence and distant metastases and reduces tumour-free survival. In general, many prognostic factors have been proposed: grade of differentiation, degree of necrosis, location, mitotic count, and tumour size, resulting in several different staging systems in the literature15.

The current American Joint Committee on Cancer staging system for soft tissue sarcoma is based on histologic grade, tumour size and depth, and the presence of regional nodal or distant metastasis16. Although the staging system is optimally designed for extremity tumours, a significant limitation is its lack of consideration for anatomic and histologic heterogeneity among soft tissue sarcomas. These concerns apply especially to head and neck sites, where primary tumours are relatively smaller at presentation but commonly lie deep in the fascia. Therefore, the system lacks stage

differentiations and thus may provide less accurate prognostic information for head and neck sarcomas than for sarcomas of other sites.

Surgical resection that achieves negative margins remains essential in treating head and neck sarcomas. Several studies from various institutions reveal a significant negative impact on local control and survival rates when nonsurgical management of the primary tumour is used.14 Imputing curative therapy for head and neck sarcoma is essential; however, the major determinant of survival is the control of local and distant recurrence27. Respondents' management in the study mainly involves surgery and chemotherapy either as Neoadjuvant or adjuvant. The study has stated that chemotherapy improves local tumour control; however, its benefit in overall survival remains debatable527. Delivering systemic therapy earlier in the disease course may be more effective against smaller tumour burdens of micro metastatic disease.28 Secondly, induction therapy can give a response that improves the probability of complete resection with negative margins that might not be possible otherwise28. Radiotherapy management of the patients are referred to different institutions in various parts of the country; thus, follow-up records are not readily available.

Patients with head and neck sarcoma have a greater tendency toward local recurrence than distant metastases.28 Surgical resection is the best treatment for sarcomas of the oral and maxillofacial region. Wide resection with clear margins is very important for a favourable survival.9 Selective neck dissection, therefore, is performed only if surgical exposure is required or when either clinically evident nodal metastases or tumour extension to the soft tissues of the neck is present14

6. Conclusion

A multidisciplinary approach form of management using surgery, chemotherapy, and radiotherapy can help achieve local and distant disease control goals. For example, sarcomas of the head and neck may not be common but managing them is challenging and associated with high mortality. In addition, establishing radiotherapy facilities/units at various managing centres will encourage patients to follow up and provide detailed records of patient treatment.

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Characteristic	Osteosarcoma, N = 11[1]	PUS, N = 17[1]	Rhabdomyosarcoma, N = 12[1]
Age (years)	39.4 (21.7)	46.4 (23.6)	32.5 (26.1)
Age_Categories			
over_40	5 / 11 (45%)	6 / 17 (35%)	6 / 12 (50%)
under_40	6 / 11 (55%)	11 / 17 (65%)	6 / 12 (50%)
Gender			
female	6 / 11 (55%)	8 / 17 (47%)	8 / 12 (67%)
male	5 / 11 (45%)	9 / 17 (53%)	4 / 12 (33%)
Duration (months)	11.7 (6.7)	9.7 (5.9)	11.0 (8.5)
Widest_Dimension (cm)	96.4 (140.1)	64.8 (47.5)	29.2 (25.1)
Radiographic Features			
lytic	5 / 11 (45%)	8 / 17 (47%)	7 / 12 (58%)
mixed_lucency	4 / 11 (36%)	8 / 17 (47%)	2 / 12 (17%)
radiopacity	2 / 11 (18%)	1 / 17 (5.9%)	3 / 12 (25%)
Staging			
fair	2 / 11 (18%)	4 / 17 (24%)	8 / 12 (67%)
poor	9 / 11 (82%)	13 / 17 (76%)	4 / 12 (33%)
Nodal_Metastasis			
nil	7 / 11 (64%)	13 / 17 (76%)	11 / 12 (92%)
yes	4 / 11 (36%)	4 / 17 (24%)	1 / 12 (8.3%)
Post-Ablative_Complications			
dead	1 / 11 (9.1%)	2 / 17 (12%)	0 / 12 (0%)
nil recurrence	8 / 11 (73%)	10 / 17 (59%)	10 / 12 (83%)
recurrence	2 / 11 (18%)	5 / 17 (29%)	2 / 12 (17%)

Table 1: Descriptions of the Variables across Types of Sarcomas

[1]Mean (SD); N / N (%)

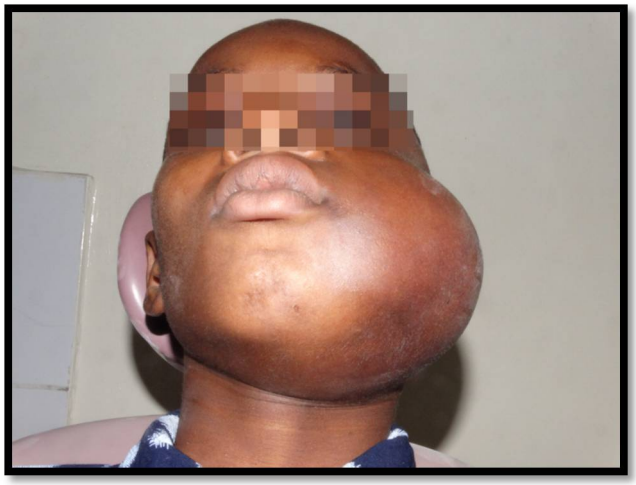

Figure 1: Showing Mandibular Rhabdomyosarcoma

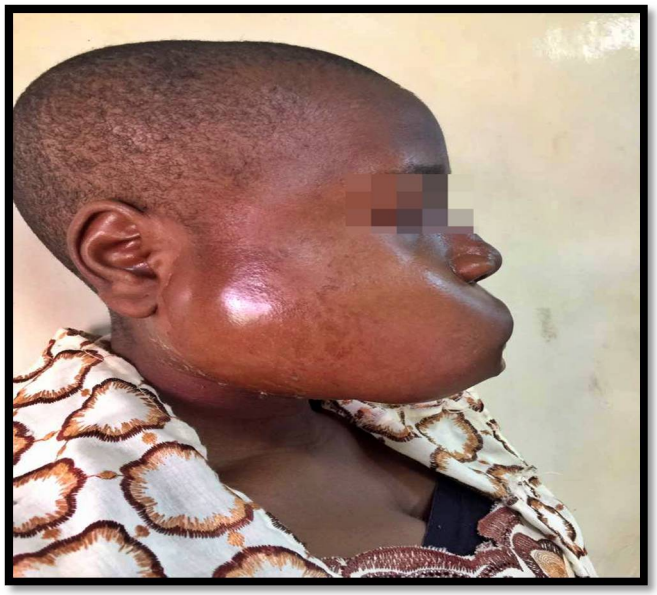

Figure 2: Clinical

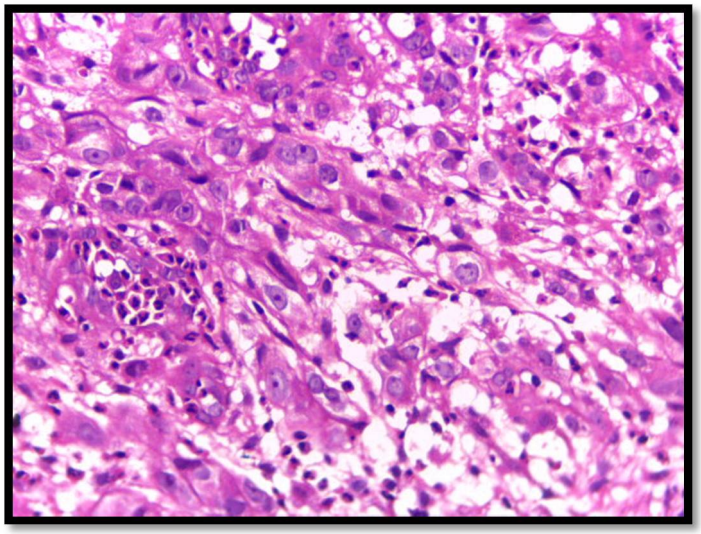

Figure 3: Photo Micrograph of Rhabdomyosarcoma