Original Article

Orofacial Rhabdomyosarcoma: A 5-year Clinicopathologic Study from Sub-Saharan Africa

Abstract

Background: Rhabdomyosarcoma (RMS) is an aggressive malignant neoplasm of mesenchymal origin. Its common sites of occurrence are the extremities and the genitourinary system, being less frequently seen in the orofacial region. There is paucity of literature, especially from sub-Saharan Africa on orofacial RMS. **Materials and Methods:** Records of all patients managed for orofacial RMS between January 2013 and November 2017 at the Department of Dental and Maxillofacial surgery of Usmanu Danfodiyo University Teaching Hospital were obtained. Data retrieved include sociodemographics, clinical features (including the tumor, node, and metastasis [TNM] stage and Intergroup RMS Study risk classification), histological type, and mode of treatment. Data were recorded and analyzed using IBM SPSS Statistics for Windows version 20 (Armonk, IBM Corp., NY, USA). **Results:** Twenty-one patients were included. There were 17 (81.0%) males and 4 (19.1%) females, giving a male-to-female ratio of 4.3:1. Age ranged from 2 to 76 years (mean [±standard deviation] of 15.8 [±16.8]). Majority of them belonged to the low socioeconomic group. The duration of the symptoms ranged from 2 to 9 months. The midface was the most commonly involved sites. Majority of the cases were nonparameningeal 14 (66.7%). Regional nodal metastasis was clinically present in 9 (42.9%) cases. Embryonal RMS was the most frequently encountered histological type (11 [52.4%]). Treatment was multimodal in 11 (52.4%) cases and 3 (14.1%) had recurrence. **Conclusion:** Orofacial RMS may occur in any age group although it may be more commonly seen in the first decade of life. Unimodal treatment may be successfully deployed in carefully selected cases. Prognosis remains poor in our climes.

Keywords: *Clinicopathologic study, maxillofacial rhabdomyosarcoma, orofacial rhabdomyosarcoma*

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Introduction

Rhabdomyosarcoma (RMS) is an aggressive malignant neoplasm of mesenchymal origin, with a penchant for persistent aggressive growth and a potential for metastasis.[1-3] It is a fairly common pediatric soft-tissue malignancy, representing 6% of all malignancies in children younger than 15 years.[4,5] However, it is less commonly seen among adults, representing <1% of all solid malignancies among them.[6-8] Common sites of its occurrence are the extremities and the genitourinary system, being less frequently seen in the orofacial region.[6,9] Some authors have stated its rarity in the head and neck region.[6,10,11]

Orofacial RMSs have a potential to result in grotesque facial distortions, causing grave esthetic complications.[3,12] Patients often present with varying clinical features, including pain, tooth mobility, spontaneous bleeding, and trismus.[12,13] The clinical features observed is generally dependent on factors such as the site and stage of the tumor.[12,14] All these have a profound detrimental effect on the patients' quality of life.[15,16]

Children generally exhibit better prognosis than adults, with cure being achieved in as much as 70% of cases in the developed countries; especially among those who present early.[17] In contrast, adult cases of RMS have a dismal 20%–40% overall survival rates.[18] Markedly, overall survival rates have improved over the years from as low as 25% in 1970 to as high as 70% in more recent times.[19] This may be attributed to improved understanding of the disease and advent of multimodal treatment methods.[1,3,5,20] Treatment has evolved to become multimodal in nature, involving surgery, chemotherapy, and radiotherapy in different combinations.[20,21] Despite this, mortality rates remain significantly higher in developing countries than in developed

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countries.[14,22] This may be attributable to the high frequency of late presentation among them.[23] There is paucity of literature, especially from sub-Saharan Africa on orofacial RMS. This study aims to present our experience with patients managed on account of orofacial RMS at a tertiary health facility in North western region of the country.

Materials and Methods

Approval for this study was obtained from the Department of Dental and Maxillofacial Surgery, UDUTH. The records of all patients who were managed on account of histologically diagnosed RMS of the orofacial region between January 2013 and November 2017 at the Department of Dental and Maxillofacial surgery of the Usmanu Danfodiyo University Teaching Hospital were retrieved.

Data retrieved included sociodemographics (patients were classified into socioeconomic groups as described by Oyedeji *et al*., clinical features including the TNM stage and Intergroup RMS Study [IRS] risk classification); histological type and treatment were recorded.[24] Tumors were classified based on the site affected as orbital, parameningeal and nonorbital, nonparameningeal.[20,21] Tumors originating from the pterygopalatine fossae, infratemporal fossae, paranasal sinuses, middle ear, base of the skull, and mastoid were grouped as parameningeal.[25] Tumors arising from the orbit or its adnexal structures were termed as orbital tumors.[26] While tumors originating from any other site in the orofacial region outside of the aforementioned ones were classified as nonorbital nonparameningeal.[6,25,27]

The IRS risk classification scheme was utilized to group patients into as culled from Chigurupati *et al*.:[20]

Low risk:
- Embryonal RMS at favorable sites
- Embryonal RMS at unfavorable sites but with complete resection or microscopic residual disease.

Intermediate risk:
- Embryonal RMS at unfavorable sites with gross residual disease
- Metastatic embryonal RMS in children <10 years
- Alveolar RMS at any site.

High risk:
- Patients with metastatic RMS at presentation excepting embryonal RMS in children younger than 10 years.

Data were recorded and analyzed using IBM SPSS Statistics for Windows version 20 (Armonk, NY, USA: IBM Corp.); *P* value was set at 0.05 and results were presented with descriptive statistics.

Results

Twenty-one patients who were histologically diagnosed with RMS were included in this study. There were 17 (81.0%) males and 4 (19.1%) females, giving a male-to-female ratio of 4.3:1. Age ranged from 2 to 76 years (mean ± standard deviation [SD] of 15.8 [±16.8]) [Figure 1]. Majority of them belonged to the low socioeconomic group [Figure 2]. A comparison of the frequency of patients diagnosed with RMS among the socioeconomic groups revealed a statistically significant difference ($P < 0.001$).

All the patients presented with swellings, while 8 (38.1%) presented with an additional clinical feature of spontaneous bleeding. The duration of the symptoms before presentation ranged from 2 to 9 months [Figure 3]. Single site involvement was rarely seen in this series although contiguous involvement of adjacent oral/maxillofacial anatomical regions frequently observed. The midface was more commonly involved than the upper and lower facial thirds [Figure 4]. Majority of the cases were classified as nonparameningeal 14 (66.7%) [Figure 5]. Most of the patients were classified as being in the intermediate- or high-risk classes of the IRS risk classification scheme [Figure 6].

Regional nodal metastasis was clinically present in 9 (42.9%) cases, with the submandibular or upper cervical lymph nodes involved in all cases. Both nodal and distant metastases were present in 3 (14.3%) cases. The sites of distant metastasis were the medial thigh, the scrotum, and the back, respectively. Most of the cases were in TNM pretreatment stages 3 or 4 at presentation [Figure 7]. Embryonal RMS was the most frequently encountered histological type (11 [52.4%]); alveolar histological type was observed in 8 (38.1%) cases, while the pleomorphic histological type was diagnosed in the remaining cases. Multimodal treatment was employed in the management of 11 (52.4%) of the cases. The mean (±SD) of the ages of patients diagnosed with the alveolar, embryonal, and pleomorphic histological types were 19.2 (±19.7), 9.5 (±8.5), and 8.0 (±1.4), respectively. A comparison of the diagnosed histological type according to the age revealed a no statistically significant difference ($P = 0.384$).

Seven (35.7%) cases had primary surgical intervention with adjuvant chemotherapy; of this, debulking and macroscopically complete excision of the tumor was done in 3 and 4 cases, respectively. Four (14.3%) patients

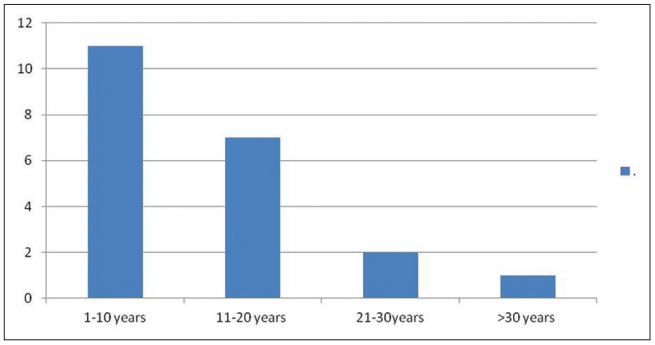

Figure 1: The age distribution of the patients seen

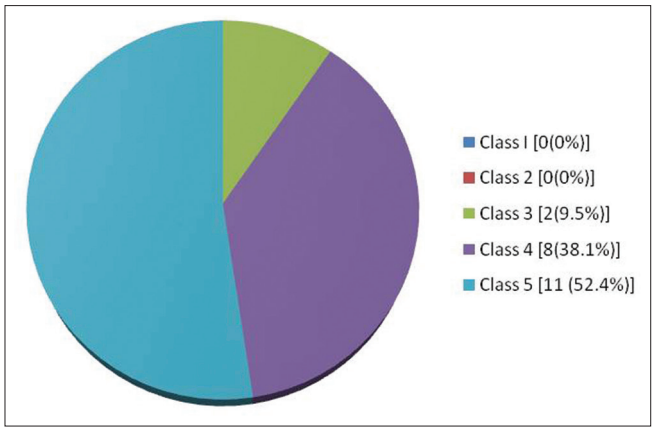

Figure 2: The distribution of patients in accordance with their socioeconomic class

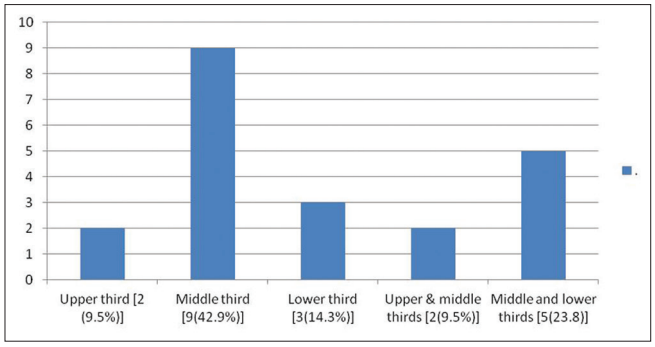

Figure 4: The distribution of the tumors based on site

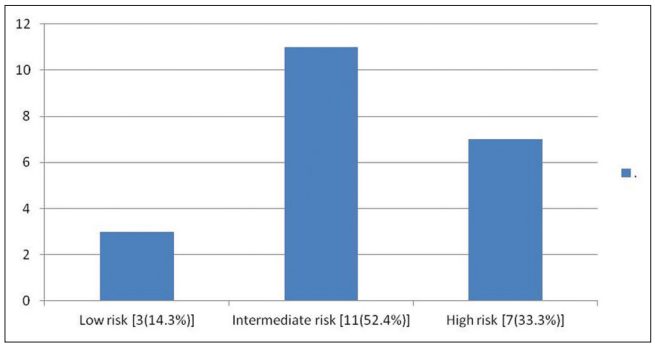

Figure 6: The distribution of patients in accordance with the intergroup rhabdomyosarcoma study risk classification

successfully had neoadjuvant chemotherapy, surgery, and adjuvant chemotherapy. In addition, 6 (28.6%) patients had chemotherapy alone, out of which, 4 (19.1%) patients died during the course of chemotherapy.

Four (19.1%) of the patients, including those with clinical distant metastasis at presentation, died within a few hours/days of admission into the hospital despite urgent resuscitation, thus making institution of definitive treatment impossible. Seven (33.3%) patients were successfully followed up for an average of 7.2 months without any clinical signs of recurrence, while the others were lost to follow-up immediately after hospital

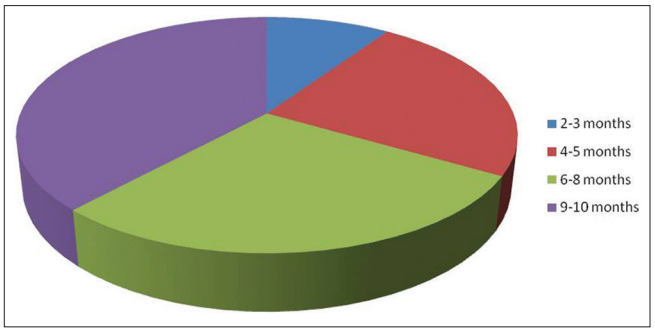

Figure 3: The duration of disease before presentation

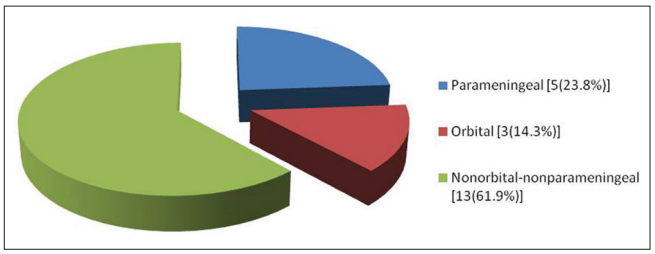

Figure 5: The anatomical site affected by the tumors

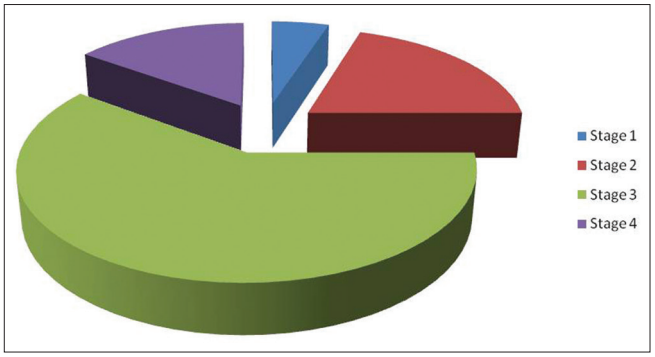

Figure 7: The pretreatment tumor, node, and metastasis disease stage of the patients

discharge. During the follow-up period, 3 (14.1%) were diagnosed of recurrence disease for which they had surgical excision and adjuvant chemotherapy, while the other 4 (19.1%) have remained clinically disease for the duration of the follow-up.

Discussion

A male predominance was observed in this study. This is in agreement with various reports in the literature.[6] Radzikowska *et al*. stated that the incidence of RMS is 1.5 times higher among males compared to females.[6] While this held true in this study, a notable overwhelming male predominance was also observed. However, it contrasts with the report of Chigurupati *et al*. who reported a female predominance in a report of 4 cases of orofacial RMS.[20]

The mean age observed in this study is in consonance with other existing reports on orofacial RMS.[4,28] Several authors

have stated that the modal age group for the occurrence of RMS is the first decade of life.[19,29] This contrasts significantly with the observations in this study. This may be due to the fact that this study focused specifically on orofacial RMS unlike a significant proportion of the contrasting studies which considered RMS of any site. Indeed, some authors have opined stated that RMS is rare in adults and the elderly. Nevertheless, Garduno-Vieyra *et al*. reported a case of orbital RMS in a 96-year-old male.[30]

The observation that most of the patients were of low socioeconomic statuses may indicate a possible higher incidence of this disease among persons of low socioeconomic statuses. The incidence of cancers have been correlated with socioeconomic status.[31-33] Individuals of low socioeconomic status are at a higher risk of experiencing ill health than those belonging to a higher socioeconomic group.[31,32] However, this observation may be influenced by the high prevalence of poverty in our environment.[34,35] High prevalence of poverty may increase the chances that the patients seen would be of low socioeconomic status. Moreover, persons of high socioeconomic status often seek healthcare outside the shores of this country, thus skewing statistics on the incidence of RMS in our climes.[36,37]

Orofacial swellings were frequently observed in this study. This is in concordance with multiple reports in the literature.[4,38,39] Bleeding was a commonly observed feature in this series. This may be related to the detrimental effect of advanced cancer on hemostasis. It may also be associated with the higher chances of sustaining trauma from the opposing teeth among patients with large intraoral masses.

Most of the patients in this series were adjudged to have presented late. This is because of the aggressive nature of RMS and its relatively rapid growth rate.[38,40] Late presentation by patients is a common occurrence in our environment, and the reasons for this are diverse, ranging from financial to sociocultural.[41,42]

Reported modal site for oral involvement is inconsistent; however, there are strong indications that most occur in the palate or tongue.[30] Multiple site involvement was frequently recorded in this study majorly due to contiguous spread of the tumor. We opine that this is largely secondary to late presentation and the propensity of the tumor for relatively rapid growth. However, history was quite indicative of the primary site of occurrence. A slight majority of the cases were nonparameningeal. This is in consonance with the assertion that 59% of all head and neck RMS are located in non-parameningeal sites.[25] Parameningeal RMS exhibits a poorer prognosis, which may be related to its tendency to invade the base of the skull and to achieve intracranial involvement.[6,10,43]

Most of the patients were in the intermediate- or high-risk classes of the IRS classification at presentation. This was mainly because most of them presented late as evidenced by the large, extensive lesions observed among them. Submandibular nodal involvement was seen quite frequently, and obvious metastatic lesions were seen in some of the patients. These contributed to the relatively worse classifications that the patients belonged to. The TNM classification system also gave a similar trend, with most of the patients in classes with the worst prognosis.

Nodal metastasis was a common feature of the disease in this series. This is in contrast to some reports in the literature that suggest that head and neck RMS rarely spread to regional lymph nodes.[44] Notably, late presentation seen among these patients may have altered the behavior of these tumors by increasing the chances of regional lymph node involvement. The sites of metastasis detected in this study contrast with the report by Dagher and Helman, who stated that the most common site of metastasis is the lung.[44]

Plain radiographs were used in assessing metastasis in this study. This was due to the inability of the patients to afford other more appropriate investigations. Magnetic resonance imaging is considered the gold standard for evaluating RMS of soft tissues because of its superior ability to characterize soft tissues.[2,14,45,46] However, other imaging modalities such as plain radiographs, computed tomography scans, and ultrasonography have been used successfully.[45,46] Bone scintigraphy has been utilized to assess bone metastasis.[45,46]

Embryonal RMS was the more commonly diagnosed histological type in this study. This is in consonance with several reports in the literature.[6,29] Embryonal RMS exhibits a better prognosis than the other histological types. The pleomorphic histological type has also been described; it is rare and typically seen among patients older than 45 years.[29] Histological subtypes such as the botyroid and spindle cell variants have also been documented.[47] Histological differentials of RMS include neuroblastoma and Ewing's sarcoma.[29,48,49] Differentiating RMS from its differentials is quite challenging; hence, newer techniques of diagnosis such as immunohistochemistry and cytogenetic analysis have been deployed.[50,51]

More recently, multimodal treatment involving surgery, chemotherapy, and radiotherapy in various combinations is often advocated.[6,7,14] However, treatment is often patient-specific, depending on the risk classification and stage of the disease, among other factors.[20,21] The site of the lesion also influences choice of the mode of treatment.[26] Orbital tumors are amenable to radiation alone or a combination of chemotherapy and radiotherapy, offering survival rates as high as 95%.[26] In our experience, the ability of the patient to withstand the stress of proposed treatment modality also played a role.

Achievement of surgical sterility where possible improves the prognosis significantly.[6,7] Radical surgery is often limited by the presence of vital structures, especially in patients with parameningeal form of RMS. Furthermore, radical surgical resection may result in severe esthetic and functional limitations. The array of treatment modalities employed in this study was severely limited by financial incapacitation on the part of the patients, and patients' inability to withstand some treatment modalities as a significant proportion of them was unstable at presentation.

Follow-up of the patients was quite challenging; thus, specific details on the long-term survival of the patients were difficult to obtain. Patients in our environment often miss appointments or do not report back to the hospitals for review.[52,53] This may be due to financial encumbrances since most patients in our climes make out-of-pocket payment for their healthcare.[54] Furthermore, patients often engage in unorthodox treatment before or after hospital treatments, with a significant proportion of them dying at home.[55,56] Such deaths often go unreported and unrecorded in our environment.[57]

Some authors have associated the occurrence of RMS in the head and neck region with better prognosis.[9,11,27] The proposed reason for this was the high visibility of the head and neck resulting in possible earlier detection than when it occurs in other relatively obscure sites.[3]

Conclusion

Orofacial RMS may occur in any age group although it may be more commonly seen in the first decade of life. Unimodal treatment may be successfully deployed in carefully selected cases. Late presentation is a commonly seen situation in our environment; hence, there is a need for institution of public health promotion. In addition, public health reforms to reduce the prevalence of out-of-pocket payment should be commenced.

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Conflicts of interest

There are no conflicts of interest.

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