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Pattern of presentation and outcome of ophthalmic rhabdomyosarcoma in Ibadan

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Abstract

Background: Rhabdomyosarcoma (RMS) is the most common soft tissue sarcoma, and the commonest primary orbital malignancy in children. Studies on ophthalmic RMS are scanty in Nigeria, and other parts of Africa. This study thus describes the pattern of ophthalmic RMS in Ibadan and treatment outcome.

Method: A retrospective, non-comparative, consecutive, interventional analysis of patients with ophthalmic RMS in an ocular oncology unit of a teaching hospital over 20 years was carried out.

Results: Records of 22 patients, 15 males and 7 females, aged 2 months to 50 years (Median 7 years, Range 5-13 years) were analyzed. All patients presented with visual loss, orbital swelling and proptosis. Histological examination revealed embryonal RMS in 16 (72.7%) patients, alveolar in three (13.6%), pleomorphic in two (9.1%) and "not otherwise stated" in one (4.5%). Treatment outcome was poor as only two (9.1%) patients remained tumour-free 12 and 36 months after diagnosis. Three (13.6%) patients died on admission, while two (9.1%) patients are presently undergoing treatment. Fifteen (68.2%) patients were lost to follow-up, financial constraint and perceived poor response to treatment being the main reasons for incomplete and inconsistent treatment regimen and resultant poor outcome.

Conclusion: Demography and morphology of ophthalmic RMS in Ibadan is comparable to other studies. However, treatment outcome remains poor, mainly due to late presentation, incomplete and inconsistent treatment. Strengthening the national health insurance scheme to cater for the indigent and increased public enlightenment on early presentation of cases may go a long way in improving the outcome in our patients.

Keywords: *Ibadan, Nigeria, ophthalmic, outcome, rhabdomyosarcoma,*

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Résumé

Contexte : Le rhabdomyosarcome (RMS) est le sarcome le plus fréquent des tissus mous, et la plus fréquente tumeur orbitaire primaire chez les enfants. Les études sur les ophtalmiques (RMS) sont rares au Nigeria, et d'autres régions d'Afrique. Cette étude décrit ainsi le motif des ophtalmiques (RMS) à Ibadan et le résultat obtenu des traitements.

Méthode: Une analyse rétrospective, consécutive non-comparative, d'intervention aux patients atteints des ophtalmiques dans une unité d'oncologie oculaire d'un centre hospitalier universitaire de plus de 20 ans a été réalisée

Résultats: Les dossiers de 22 patients, 15 hommes et 7 femmes, âgés de 2 mois à 50 ans (médiane 7 ans, extrêmes 5-13 ans) ont été analysés. Tous les patients présentaient une perte de vision, un gonflement orbital et proptosis. L'examen histologique a révélé le RMS embryonnaire en 16 patients soit (72,7%) alvéolaire sur trois (13,6%), pleomorphic en deux (9,1%) et « aucun cas contraire en un (4,5%). Le résultat du traitement était faible, car seulement deux (9,1%) patients ont été identifiés sans tumeur, 12 et 36 mois après le diagnostic. Trois (13,6%) patients sont décédés pendant l'hospitalisation, tandis que deux (9,1%) patients sont actuellement sous traitement. Quinze (68,2%) patients ont manqué de suivi, pour des raisons financières entrainant une mauvaise réponse au traitement puisque celui-ci est était incohérent et incomplet, expliquant ainsi les mauvais résultats obtenus.

Conclusion: la démographie et de la morphologie des ophtalmiques (RMS) à Ibadan est comparable à d'autres études. Toutefois, le résultat du traitement reste faible, principalement en raison de la présentation tardive, du traitement incohérent et imcomplet.

Le renforcement du système national d'assurance santé à la sensibilisation indigente et accrue du public sur la présentation précoce des cas peut toutefois contribuer à l'amélioration de meilleurs résultats chez nos patients.

Introduction

Rhabdomyosarcoma (RMS) is a malignant neoplasm that is composed of cells with histological features of striated muscle in various stages of embryogenesis [1]. It is the most common soft tissue sarcoma in children accounting for about 5% of childhood cancers and 20% of all malignant soft tissue tumours [2]; and ranks third to neuroblastoma and Wilm's tumour as

an extracranial solid tumour in the United States [3]. There is paucity of data on detailed review of ophthalmic RMS in Nigeria and other parts of Africa, thus, its prevalence is not known and varies widely in different studies. They are usually included in general studies of orbital or childhood tumours in the region. Earlier studies [4,5] in the country reported no case of ophthalmic RMS in the head and neck malignancies reviewed over 10- and 15-year periods respectively. However, in another study [6], 13 cases were seen over a 10-year period.

The purpose of this study is to provide a detailed review of the pattern of presentation of ophthalmic RMS, the treatment outcome, and possible factors influencing the outcome in our patients.

Materials and methods

This is a retrospective, non-comparative analysis in which the records of all patients who had histological examination of orbital tissues in the Pathology Department of University College Hospital (UCH), Ibadan, Nigeria, between 1992 and 2011 were reviewed. UCH is a foremost teaching hospital in Nigeria, with well established Ophthalmology and Pathology departments and Ocular Oncology unit. It receives ocular oncology referrals from all parts of the country in addition to treating general ophthalmic conditions. Patients with tumours undergo tissue biopsy and/or definitive surgical intervention following which tissue specimens are sent to the pathology department for histological diagnoses, and appropriate treatment subsequently instituted after confirmation. Tissue biopsy by surgical incision or excision biopsy or orbital exenteration was done for the patients to obtain adequate tissue specimen for histological examination. Computed tomography scans were carried out to ascertain tumour extension to the paranasal and/or intracranial cavities. Following histological confirmation, patients were commenced on combination of intravenous vincristine, actinomycin-D and cyclophosphamide; and fractionated radiation therapy. The case records of all ophthalmic patients with histological diagnosis of RMS were retrieved from the medical records department and patients with complete records were included in the study and analyzed. Information retrieved from the case records included patients' demographics, presenting complaints, histological type, treatment status and outcome.

Results

Twenty-three patients were seen during this period, of which, 22 with complete records were included in the analysis, comprising 15 males and 7 females. Age ranged from 2 months to 50 years with a median of 7 years (Range 5-13 years). There were only three (13.6%) adult patients (>15 years) in our series (Fig.1). All patients had orbital swelling and proptosis at presentation. Other features included severe visual loss, severe pain and intracranial involvement (Table 1). Three patients presented with presumed secondary orbital tumour spread from a primary lid lesion (1 patient) and paranasal sinuses (2 patients) based on the history of progression of symptoms; while others had primary orbital tumours.

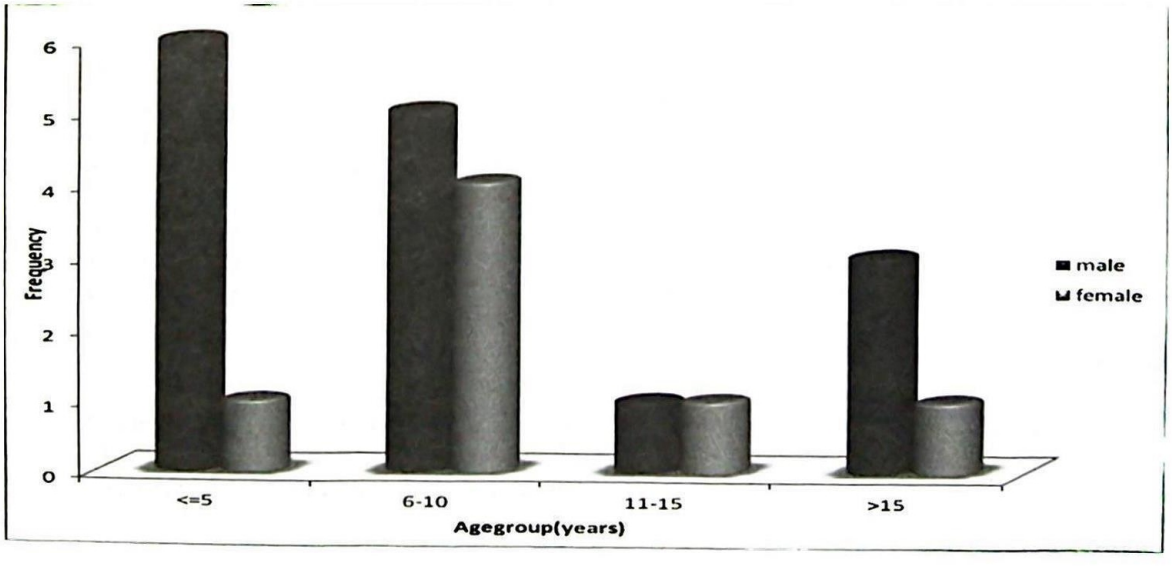

Fig.1: Age and Sex distribution of the patients with ophthalmic rhabdomyosarcoma in Ibadan

Table 1: Clinical features of patients with ophthalmic rhabdomyosarcoma in Ibadan"

Presenting complaint	Frequency	Percent (%)
Orbital/lid mass	22	100
Proptosis	22	100
Severe visual loss	19	86.4
Pain	5	22.7
Intracranial extension	4	18.2
Epistaxis	2	9.1
Leucocoria	2	9.1
Abdominal swelling	1	4.5
Jaw mass	1	4.5
Paraplegia	1	4.5

**More than 1 option possible*

The right orbit was affected in six (27.3%) patients, left in fifteen (68.2%) while one patient (4.5%) had bilateral orbital involvement at presentation. All patients had reduced vision at presentation with visual acuity of ≥6/36 in only three patients (13.6%), and light perception or no perception of light in the remaining (86.4%). Follow-up period in our patients ranged from two months to 40 months with a mean of 10.5±10.1 months.

On histological examination of tissue specimen, 16 (72.7%) patients had embryonal RMS, three (13.6%) had alveolar, pleomorphic was found in two (9.1%) and rhabdomyosarcoma "not otherwise stated" in one (4.5%) patient. Following histological confirmation, all patients were commenced on chemotherapy and 12 (54.5%) patients, in addition, had some radiotherapy treatment. However, only two patients (9.1%) completed their treatment regimen and remained tumour-free at their last clinic visits (12 and 36 months after diagnosis). All other patients were inconsistent with their treatment regimen and did not complete the full course of treatment. Financial constraints and perceived poor response to treatment were the main reasons for poor compliance with treatment.

Two (9.1%) patients remained tumour-free 12 and 36 months after diagnosis while two (9.1%) others are presently undergoing treatment 10 and 40 months after diagnosis. Three (13.6%) patients died while on admission, four (18.2%) discharged themselves against medical advice from admission while on treatment, six (27.3%) developed tumour recurrence after an initial response and subsequently defaulted from further treatment visits, while treatment status was unknown in five (22.7%) patients who were lost to follow-up during their chemotherapy follow-up visits.

Discussion

Rhabdomyosarcoma (RMS) is the most common soft tissue sarcoma in children, approximately 65% are diagnosed in those less than six years of age, with a lower incidence reported among African-Americans and Asians than in Caucasians [7,8]. The head and neck region is the most common site for primary RMS followed by the genitourinary tract and extremities [7-9]. Ophthalmic RMS can be defined as the occurrence of the tumour in any of the tissues in the area of the eye with orbital soft tissues being the most common site, although the eyelids and intraocular tissues can be involved [2,10]. About 25-35% of RMS in the head and neck primarily involves the orbit [11], and in a previous study in Ibadan, Brown and co-worker [9] reported that 28.3% of the patients presented with orbital RMS.

Ophthalmic RMS usually occurs in children, usually in their first decade with a mean age of eight years at diagnosis [9,12]. However, it can present in adults and three of our patients were older than 15 years, similar to findings in other series [13,14]. The slight male preponderance of 2:1 in our study has also been reported in previous studies [9,10]. There are no known factors attributed to this.

Rhabdomyosarcoma is generally classified histologically as embryonal (57%), alveolar (19%), botryoid (6%), plemorphic (1%), and others too undifferentiated (10%) or heterogeneous (7%) for specific classification [15]. Over 70% of the patients in our series had histological diagnosis of embryonal rhabdomyosarcoma while less than 25% had alveolar. This is in keeping with the results of Intergroup Rhabdomyosarcoma Study Group [12] and reports from other studies [2,9,10]. However, we found two cases of pleomorphic rhabdomyosarcoma in our series despite the uncommon presentation of this variant in the orbit [2].

The commonest presentation in our patients was proptosis with or without a palpable mass, similar to previous reports [10,16]. Space-occupying lesions in the orbit usually manifests early with proptosis being a closed bony cavity. Poor vision was another common presentation in our patients and about 90% presented when the vision in the affected eye was either light perception or no perception of light, and, with an average duration of symptoms of 28 weeks, indicate late presentation of patients to our facility. Delayed presentation of patients is a major poor prognostic factor to the management of ocular conditions in our region [17] and this pattern of presentation is similar to findings in previous studies [4,6] in the region. This, however, is at variance with

reports [10,16] from developed countries where patients present early before the tumours become advanced. Two of our patients, aged 18 and 49 years, presented with epistaxis as the earliest symptom and were found to have paranasal sinus involvement of the tumour. The paranasal sinus accounts for the tumor site in about 10-15% of RMS involving the head and neck region and these tumours readily spread to the adjacent structures including the orbits [18,19]. The primary site of these tumours in our patients was difficult to ascertain precisely, due to late presentation but it seems likely they started from the paranasal sinuses due to history of epistaxis preceding the ophthalmic symptoms.

One of our patients presented with bilateral orbital involvement. This four-year-old girl with histological diagnosis of alveolar RMS presented with metastatic disease to the other orbit, lymph nodes, abdomen and spinal cord, giving rise to paraplegia; and died while on admission. This is an uncommon presentation of the disease [20,21] but supports the fact that alveolar histological type has the worst prognosis and a greater frequency of systemic disease [22].

There was intracranial tumour spread in four patients when they presented to our facility, again indicating late presentation in our patients. Two patients also developed intracranial spread during the course of their treatment, and were found to be inconsistent with the treatment regimen. Intracranial tumour spread is an uncommon presentation of ophthalmic RMS in developed countries where patients present early, and is usually associated with the parameningeal disease [23]. It carries a poorer prognosis for the patients [24] and of the four patients, one died while on admission, two defaulted from further treatment due to perceived poor response to treatment and the last patient is still undergoing chemotherapy. One of the two patients who developed intracranial tumour extension while on treatment underwent neurosurgical tumour excision and is presently on further treatment while the second has been lost to follow-up. The third patient who died while on admission was the youngest patient in our series with a primary upper eyelid mass, secondarily involving the orbit, and histologically diagnosed as embryonal RMS. The clinical condition deteriorated and he died after 3 courses of chemotherapy.

Overall, the outcome of ophthalmic RMS is still poor in our patients with only two patients being tumour free at their last follow-up visits. These were the only patients who completed their treatment regimen. Three patients died on admission. Eleven patients were inconsistent with their treatment visits, and eventually defaulted from further follow-up treatment visits. Treatment was greatly hampered by financial constraints. This is at variance with reports from developed countries where the prognosis for ophthalmic RMS had improved from an initial dismal outcome [25] to a more favourable outcome [12,26,27] with over 90% survival at 3 years. Late presentation to the appropriate health facility with incomplete and inconsistent treatments in our patients might have been responsible for this. The retrospective nature of this study is however a limitation to a detailed description of the clinical presentation and classification of tumours in the patients.

In conclusion, the demography and morphology of ophthalmic RMS in Ibadan is comparable to other centres. However, the outcome in our patients which could have been comparable with what obtains in developed countries remains poor, mainly due to late presentation and incomplete and inconsistent treatment. Strengthening the national health insurance scheme to cater for the indigent and increased public enlightenment may significantly improve the treatment outcome in our patients.

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