International Journal of Innovative Studies in Medical Sciences (IJISMS)

ISSN 2457-063X (Online) **www.ijisms.com** *Volume: 2 Issue: 6 | 2018*

Histopathological Patterns of Childhood Rhabdomyosorcoma in Makurdi, North Central Nigeria

JA Ngbea[1*], R.A. Vhriterhire[1], I.O. Akpor[1], M.N. Agwa[1] T.D. Gyenger[1], O.O. Jegede[2], I.B. Achusi[3], K.N. Malu[4], T.J. Ben-Ameh[4].

[1]Department of Anatomical Pathology, and [4]Opthalmology, College of Health Sciences, Benue State University Makurdi.

[2]Department of Morbid Anatomy, College of Health Sciences, Bingham University, Jos. Nigeria.

[3]Department of Anatomical Pathology, Federal Medical Centre Jabi, Abuja.

***Correspondence: Dr. Joseph A Ngbea** Department of Anatomical Pathology, College of Health Sciences, Benue State University, Makurdi, Nigeria.

Abstract: *Rhabdomyosarcoma (RMS) is one of the childhood tumours in children. It is rare in the United States of America accounting for about 3% of all childhood tumours. Most cases are diagnosed in children in their teens, with more than half of them in children younger than 10 years old. This study is to determine the prevalence and pattern of childhood RMS,seen in Benue State University Teaching Hospital Makurdi, Nigeria. It was a 5year retrospective histopathological review of all cases of RMS diagnosed in the Department of Anatomical Pathology, Benue State University Teaching Hospital Makurdi. Archival records and paraffin embedded tissue blocks were retrieved, re-sectioned and stained with haematoxylin and eosin. The tissues were subjected to actin, desmin, and S-100 immunohistochemical stains. Overall,thirty two(32) cases of childhood RMS in children less than 18years of age were histologically diagnose within the review period. Of these 21(66%) were males and 11(34%) were females giving a male to female ratio of 2:1. Embryonal RMS accounted for the highest proportion, followed by alveolar RMS. Head and neck region was the commonest anatomical location for all subtypes. Actin and desmin immunohistochemical stains was strongly positive and S100 negative. This study confirms that embryonal RMS is the commonest subtype accounting for about 56.2% of cases. Head and neck region is the commonest Anatomical site with male preponderance and immunohistochemistry is gold standard for diagnosis.*

Keywords: *Childhood, Rhabdomyosarcoma, North Central Nigeria.*

1. INTRODUCTION

Rhabdomyosarcoma (RMS) is the most common malignant tumour of mesenchymal origin in children and adolescents, accounting for 5% of all paediatrics cancers.[1] It ranked third, after neuroblastoma, and wilms tumour.[2] Estimated 350 new cases of RMS are reported yearly in America between the ages of 0-19years with slight male preponderance in children younger than 6years.[3] Embryonal rhabdomyosarcoma (ERMS) and Alveolar rhabdomyosarcoma (ARMS) are the most common histologic variants.[4] The botyroid and spindle cell variants are also seen. The ERMS mainly occur in the head and neck and genitourinary areas with bimodal age distribution while ARMS occurs in adolescents.[5]

Most cases arise spontaneously, but the disease has been associated with the familial syndromes in 30% of cases like Neurofibromatosis type1 Li-fraumeni syndrome, p53 gene, Rubinstein–Taybi syndrome, Beckwith–weidemann syndrome, Costello syndrome, Noonan syndrome, hereditary retinoblastoma and Gorlin basal cell carcinoma nevus syndrome.[6-10]

RMS is one of the small round blue cell tumour of childhood. The cell of origin for RMS remains a subject of debate, studies has shown that committed muscle stem cells and multipotent mesenchymal stem cells can give rise to RMS.[11,12]

Pathogenesis is not well understood, but as noted, the two histologic variants of RMS in children are ERMS and ARMS. Each of them though with a mesenchymal-derived architecture they have a distinct different cells of origin.[13] PAX7 gene is expressed in ERMS and in the myogenic satellite cells, up regulation of PAX7 expression is seen in ARMS which have PAX3-FKHR or PAX7-FKHR translocation supporting the fact that the two histologic subtypes may originates from different cells.[14]

ARMS tumours have a microscopic appearance that resembles lungs alveoli, chromosomal translocations are detected in 70-80% of ARMS[15]. Translocation t(2:13) (q^{35};q^{14}) occurs in 60% of cases, while translocation t(2:13)(p36;q14) occurs in 20% of ARMS.[15] This results in the expression of chimeric transcription factors PAX3-FKHR (PAX3-FOXO1) or PAX7-FKHR(PAX7-FOXO1) respectively.

PAX-FKHR is a protein that stimulates proliferation, induces angiogenesis. Inhibit apoptosis, activates myogenic programme and inhibit simultaneously

terminal differentiation.[16] Twenty percent (20%) of ARMS are translocation negative and fusion-negative ARMS, the molecular characteristics of ARMS is different from fusion- positive ARMS.[17] Other molecular aberration in both ARMS and ERMS include p53, CDKN2A, MYCN,RAS, MET.[18,19]

Though ARMS and ERMS show different histological and genetic characteristics, they also have similar phenotype of defective differentiation, occurring in multiple signaling pathway involving the myogenic transcription factor MyoD.[20]

Studies done within and outside Nigeria have documented the preponderance of ERMS over other types of RMS. In the United State of America (USA) 250-350 cases per year were reported with a higher male preponderance.[21]

The findings of the USA and other African series is comparable with reports from Jos, Kano, Zaria, Ibadan, Ife, Benin and Calabar, Nigeria.[22-24] Benue State University Teaching Hospital, Makurdi is one of the tertiary health centres offering histopathology services in Benue State with an estimated population of 8 million people. This study examines the patterns of rhabdomyosarcoma in Makurdi and compares it with others parts of the country and the world.

2. MATERIAL AND METHODS

This was a retrospective study of 32 histologically confirmed rhabdomyosarcomas seen at the Department of Anatomical Pathology BSUTH Makurdi, between March, 2013 – February, 2017. The specimen consisted of incision, excision and trucut biopsies from various anatomical locations. Fresh tissue slides were cut from paraffin embedded tissue blocks. Each slide was reviewed and the diagnosis was made based on morphological features. Biodata of all cases were retrieved from Laboratory records and collated results were presented in form of tables and micrographs.The tissue were subjected to the following immunohistochemical stains, actin, desmin and S-100.

3. RESULTS

Overall 32 cases of childhood rhabdomyosarcoma were histologically diagnose within the reviw period. Of these, 21(66%) were males while 11(34%) were female with a male to female ratio of 2:1. The commonest anatomical sites were the head and neck regions which accounted for 16(50%) cases followed by the thigh 5(19%), retroperitoneum 4(13%), vagina 4(13%) and testes 2(6%).

ERMS was the highest histological variant with 18(56%) cases consisting of 14 males and 4 females with a male to female ratio of 3.5:1, followed by alveolar 6(19%), pleomorphic 5(16%) and spindle 3(9%).And the highest proportion of cases occur between the ages of 6-15 years. Desmin and myogenin were strongly positive.

Table 1: *Age and Anatomical distribution of childhood rhabdomyosarcoma in BSUTH Makurdi.*

Age group	Head/Neck	Thigh	Retroperitoneum	Vagina	Testis	Total
0-5	2	-	-	-	-	2
6-10	8	2	-	1	-	11
11-15	4	4	3	2	-	13
16-18	2	-	1	1	2	6
Total	**16(50)**	**6(19)**	**4(13)**	**4(13)**	**2(6)**	**32**

Table 2: *Histological subtypes and sex distribution of rhabdomyosarcoma in BSUTH Makurdi.*

Histological subtypes	**Male**	**Female**	**Total**	**%**
Embryonal	14	4	18	56
Alveolar	3	3	6	19
Pleomorphic	3	2	5	16
Spindle	1	2	3	9
Total	**21(66)**	**11(34)**	**32**	**100**

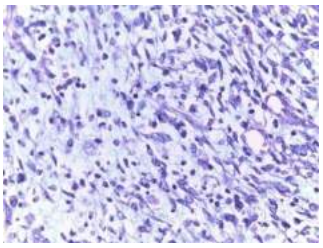

Figure 1: Section show malignant rhabdomyoblasts in a loose fibromyxoid stroma, these cells are round, oval, spindled with prominent eosinophilic cytoplasm. Hyperchromatic, atypical nuclei is also observed (H&E;×20 Objective magnification)

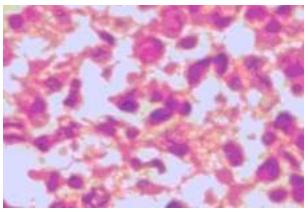

Figure 2: Section shows a pale myxoid stroma with numerous rhabdomyoblast, described with different terms as tadpole cells, straps cells,tennis racquet cells as shown. (H&E;×40 Objective magnification)

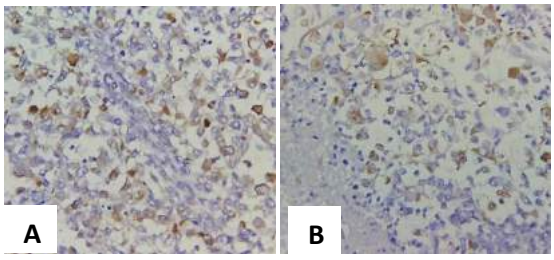

Figure 3: A: Desmin-positive, B: Myogenin-positive,

4. DISCUSSION

In our study, 32 cases of childhood rhabdomyosarcoma were encountered over a 5year period.(Table1) This given average of 6.4 cases per year. In this review embryonal rhabdomyosarcoma was the commonest histologic variant accounting for 56.2% of cases(Table2). This result is however comparable to reports of earlier studies from 54.3% in Jos,69% in Kano, 61.5% in Ibadan, Ife, Benin, and Calabar, Nigeria[22-24] respectively.

Horn and Enterline in the past classified rhabdomyosarcoma as botyroid, embyronal, alveolar and pleomorphic based on morphological appearance of cells.[25] However, with advent of immunohistochemistry, the scheme has changed, what used to be called botyroid is a variant of embryonal rhabdomyosarcoma that principally occurs in hollow organs like vagina, colon, urethral, urinary bladder etc.[26]

The commonest anatomical site in this study was head and neck regions which accounted for 16(50%) of cases. This is consistent with studies done by Mandong and Ngbea in Jos where 21(60%) RMS affected principally the head and neck region.[27] Other centres were head and neck are the predominant site for rhabdomyosarcoma are Kano, Ibadan, Ife, Benin, Calabar[22-24] and Makurdi study by Malu et al who reported an incidence of 40% RMS arising from head and neck.[28] out of which 3(8.6%) were in the orbit. Most ocular RMS occur in the soft tissues of the orbit and in some occasions can arise in other ocular adnexal structures and occur secondarily as post radiation treatment for retinoblastoma and squamous cell carcinoma of the eyelid.[29]

RMS is very rare tumour in adults[30].The tumour is histologically classified into embryonal, alveolar and pleomorphic sub-types.[31] A series of 277 rhabdomyosarcomas study by Ahmad et al[32]. The embryonal variant was the most dominant subtype accounting for 87.4% of cases and occurred between the ages of 0-10years (65.7%) while very few occurred within the ages 21-30years.[33] RMS occur commonly in the head and neck regions. Our study confirms this where (50%) of cases are from head and neck (table 1) followed by the thigh and what was classified as botyroids is ERMS occurring in hollow organs accounted for about 13% of cases.(table 1)

ERMS grossly appears as a soft yellow brown or grey mass with attendant haemorrhages and necrosis, and the principal feature on microscopy is evidence of myogenesis seen as the presence of the rhabdomyoblast at diverse phases of differentiation[34].

Although these tumours arise from striated muscle, many cases in children have been documented in organs such as gall bladder, prostate and urinary bladder where skeletal muscles are absent[35]. Less differentiated tumours exhibit primitive round blue cells while well differentiated display brightly eosinophilic cytoplasm with hyper chromatic nuclei (figure1 and 2) sometimes touting cross striations[36].

In contrast to our study, Ahmad et al in Zaria also observed that retinoblastoma was the most commom childhood malignancy in a review that spanned over 8 years (January 2006 and December 2013) 57.9% were under 5 years of age with a slight male preponderance. This is confirmed by Adewuyi et al. from Radio therapy and Oncology Department of Ahmadu Bello University Teaching Hospital, Zaria who demonstrated retinoblastoma as the most common childhood malignancy referred for radiation between 2005 and 2010[37]. A morphological study of childhood solid tumours seen between January 2000 and 2007 in Lagos University Teaching Hospital by Akinde et al also documented retinoblastoma as the most common malignancy.[38] Other parts of Nigeria such as Enugu, Nnewi, Sokoto, and Abakiliki documented Burkitts lymphoma as the commonest childhood malignancy.[37]

Histologically, the tumour show a loose fibromyxoid stroma with rhabdomyoblast(straps cells) with deep eosinophilia and hyperchromatic nuclei(Figure1 and 2) and and are strongly positive for desmin and myogenin (Figure 3).

5. CONCLUSION

Rhabdomyosarcoma is the most common soft tissue sarcoma in children, ERMS is the commonest variant in our study accounted for 56.2% of cases, Head and Neck region are the commonest anatomical sites with male preponderance as compared with studies in Nigeria and other parts of the World.

6. RECOMMENDATION

We recommended future studies and all cases should be subjected to panels of immunohistochemical makers for confirmation and characterisation of the tumour.

ACKNOWLEDGEMENT

We wish to thank the patients and their families. Special thanks to my colleagues , staff and students of the department of Anatomical pathology for their contributions.

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