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Histopathologic Characteristics of Childhood Malignant Tumours in a Referral Medical Centre in Nigeria

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Abstract

Background: Diseases of children in most developing countries revolve commonly around infectious disorders and malnutrition. However, other conditions including neoplastic diseases may be unassuming challenges to the attending physician. The objective of this study was to determine the epidemiological and histopathological pattern of malignant tumours among children in a northern Nigerian tertiary health institution.

Materials and Methods: This is a retrospective study of malignant tumours in children aged fifteen years and below diagnosed over a ten year period (1st January 2011- 31st December 2020). Histopathology laboratory records at the Department of Pathology, Federal Medical Centre, Birnin Kebbi, Kebbi state, were reviewed and all diagnoses of malignant tumours were extracted. The findings were compared with similar studies elsewhere.

Results: There were 36 children with confirmed cases of malignant tumours; 22 males and 14 females. The male to female ratio was 1.7:1. The peak age of incidence was 11-15 years. The most common childhood malignant tumours were rhabdomyosarcoma, retinoblastoma, osteosarcoma, non-Hodgkin's lymphoma and squamous cell carcinoma. Head and neck region was the commonest area of affection.

Conclusion: The most common malignant tumours in children in our setting are sarcomas and small round blue cell tumours of childhood affecting predominantly older male children with head and neck regional predilections. Malignant tumours in children though not very common, are an important aspect of paediatric disorders to the attending physician due to their high morbidity and mortality. The diagnosis of such can be challenging to the pathologist, especially in resource constrain environments. High index of suspicion is therefore advocated to detect the tumour in its early stage that is associated with low morbidity and mortality.

Keywords: Childhood, Malignant Neoplasms, Pathology

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Childhood disorders include early congenital disorders, some inborn errors of metabolism, acquired infectious diseases, connective tissue disorders to less commonly occurring benign and malignant neoplastic diseases (1). In developing nations, infectious diseases account for a major cause of childhood morbidity and mortality. Childhood malignant neoplasms account for about 2% of all cancers globally, yet they are the second commonest cause of death in children aged 5-14 years in developed nations (2). Worldwide, about 6% of childhood deaths are due to cancer, however, across the African continent, infectious diseases and malnutrition have long been the primary causes of childhood morbidity and mortality (1). However, with improved healthcare facilities and extensive national immunization programmes, coupled with generally improving socio-economic status, malignant diseases are beginning to account for a significant percentage of childhood morbidity and mortality in Africa (3). Cancer is a significant paediatric problem in several parts of Africa and the rest of the developing world (2). Developing countries contribute an estimated 60% of the total burden of all new cancer cases worldwide (2).

The low prevalence of paediatric malignancies in many sub-Saharan African countries is due to a large number of cases that are never attended to by a physician. Low index of suspicion and poor diagnostic facilities also contribute to low reported prevalence, late diagnosis and poor survival rates of certain types of childhood cancers (4). There is also a remarkable geographic difference in the incidence and pattern of malignant tumour distribution as well the death rate of specific tumours (2). Many factors such as abnormal development, tumour induction and prevalence of underlying familial or genetic aberrations are implicated in tumorigenesis in children (1). This study documents the histopathologic spectrum of neoplastic diseases in children in a relatively new centre with low manpower.

Material and Method

The materials include all submitted surgical biopsy specimens between 1st January 2011 and 31st December 2020 for children aged 15 years and below. Tissue blocks and slides were retrieved from the surgical biopsy records of the Department of Pathology, Federal Medical Centre Birnin Kebbi, Kebbi State Nigeria. The Hospital is the only centre with full histopathologic services covering the entire Kebbi state and some parts of neighbouring Sokoto and Niger States in Nigeria as well as some parts Benin Republic. Relevant histology-stained slides were retrieved and reviewed. Histological slides were retrieved and reviewed by authors; new sections were made where necessary. All specimens were previously fixed in 10% formal saline followed by routine paraffin embedding. Microtome sections were 4µm thick and were stained with Haematoxylin and Eosin. Freshly stained slides were made from stored paraffin embedded tissue blocks in cases of missing slides. Patient's clinical information including age, sex, duration of the clinical symptoms and clinical findings were extracted from the accompanying case cards. The malignant tumours were divided into five categories according to the World Health Organisation (WHO) classification of tumours. These categories were: Small Round Blue Cell Tumour of Childhood, Soft Tissues Tumours, Lymphoreticular tumours, Epithelial Tumours, and Germ cell Tumours.

Data presentation

Data were presented in frequency distribution tables and figures including photomicrographs with legends where necessary.

Results

There was a total of 8,961 surgical biopsy specimens received during the ten year (2011-2020) study period. Out of these 750 (8.4%) biopsies were from children aged less than 15 years and 36 out of the 750 surgical biopsy specimens were found to show malignant neoplastic conditions from the various anatomical sites of the body. These formed 4.8% of the surgical biopsies from children aged 15 years and below. There were 22 male and 14 female and a male to female ratio of 1.7:1. Children aged 11-15 years were predominantly affected (47.2%) whereas children 6-10 years were the least affected (Table 1). Head and neck region was the most commonly involved anatomical region (44.4%) (Figure 1).

Figure 1: Regional Distribution of Childhood Tumour (N=36)

Table 1: Age Distribution of Malignant Childhood Tumours

Age group (years)	Frequency (%)
0-5 years	10 (27.8)
6-10 years	9 (25.0)
11-15 years	17 (47.2)
Total	36 (100)

There were 11 cases of small round blue cell tumours of childhood; six cases were rhabdomyosarcoma with two cases from the forearm and a case each from the foot, trunk, mandibular soft tissue and orbital tissue. Five of these were alveolar variants (Figure 2) and a case of embryonal rhabdomyosarcoma seen at the mandibular soft tissue of an eight-year-old female child. The other tumours in this category were five cases of retinoblastoma all arising as orbital soft tissue masses. Overall, these tumours constituted 30.6% of the entire cases. Mesenchymal soft tissue tumours were the predominant malignant neoplasm (Table 2) in this study constituting 33.3% of the tumours. These included five cases of osteosarcoma of the lower leg and arm; three cases arising from the proximal tibia, one at distal femoral end and a case arising at the distal end of the radius in a 15 year-old-male child. Three cases of granulosa cell tumour were seen including two cases arising from the soft tissue of the limbs and a case of granulosa cell tumour (GCT) of bone; all from male children. There were two cases of dermatofibrosarcoma protuberans involving the soft tissues around the inguinal region of a 13-year-old male child and forearm of a four year old female child. The least in this category was a case of malignant fibrohistiocytoma in the soft tissue of the upper back of a 9-year-old female child, and a synovial sarcoma (Figure 3) arising in the left elbow joint of a 15 year old female child.

Figure 2: Photomicrographs of alveolar rhabdomyosarcoma A) low resolution and B) high power view of alveolar pattern of growth of small round blue cell tumour with oval to spindle nuclei. (H&E, A X100, B X400 magnification)

In the category of epithelial malignancies, there were four tumours all arising from protective keratinized squamous epithelial covering of the face; these were moderately to well differentiated squamous cell carcinomas (Figure 4), and two cases of malignant melanoma also

Table 2: Sex Distribution of the Various Tumours (N=36)

SITE	SEX		TOTAL (%)
	MALE	FEMALE	
Rhabdomyosarcoma	4	2	6 (17)
Retinoblastoma	3	2	5 (14)
Osteosarcoma	3	2	5 (14)
Lymphoma	3	1	4 (11)
Squamous cell carcinoma	3	1	4 (11)
Malignant melanoma	1	2	3 (8)
Granulosa cell tumour	3	0	3 (8)
Dermatofibrosarcoma protuberans	1	1	2 (5)
York sac tumour	1	0	1 (3)
Synovial sarcoma	0	1	1 (3)
dysgerminoma	0	1	1 (3)
Malignant fibrohistiocytoma	0	1	1 (3)
Total	22	14	36 (100)

Figure 3: Photomicrographs of synovial sarcoma A) low resolution and B) high power view with typical biphasic growth pattern in which malignant epithelial nest of cells some forming glands were embedded within the malignant spindle cells. (H&E A X 100 magnification, B X 400 magnification)

in skin of the head. In the lymphoreticular category, two cases of Burkitt's lymphoma all affecting the jaw, a case of diffuse large B-cell lymphoma of the cervical lymphoid tissue and a mucosa associated lymphoid tissue (MALT) lymphoma of the colonic mesenteric group of lymphoid tissue in a 15-year-old male child.

Figure 4: Photomicrographs of well differentiated squamous cell carcinoma. A) low resolution and B) high power view of polygonal cells with keratin formation (H&E, A X 100 magnification B X 400 magnification)

Discussion

Childhood malignant neoplastic diseases pose a lot of challenges to the attending physician in resource constrained environments like ours. This stems from the rarity of these diseases to inadequate manpower and lack of modern diagnostic facilities. In addition, the patronage of traditional medical providers further delays presentation of the patients to the hospital. The distribution pattern of these tumours in our study was age related and showed a male preponderance. The age group 11-15 years had the highest malignant tumours and rhabdomyosarcoma was the commonest with male predilection. Rhabdomyosarcoma, a skeletal muscle tumour is one of the most common soft tissue sarcomas in the African child in most reports (5-8). Our findings showed a similar pattern, however, the peak age was contradictory to most reports, where the peak age of incidence was less than five years (4,6-8). In this study fifty percent of the children were between the ages of 6-9 years. In Ilorin, North-central Nigeria, most of their patients were in the age group of 10-14 years and in Ibadan, South-western Nigeria, the finding was that of the age group between 2 and 4 year (4,7).

Retinoblastoma was one the most common childhood tumours in this study. Retinoblastoma is derived from differentiated primitive neuroectodermal cells and has a worldwide distribution while its incidence reduces with age, with no associated racial preference or gender bias (1,3). Retinoblastoma has a high incidence in Africa, similar to our findings; it was the second most frequent solid tumour in Ibadan and Lagos (9,10). In Ilorin and Zaria, majority of their patients presented with extra-ocular advanced disease (4,11). Extra ocular advanced disease is commonly seen in most developing countries where patients would have exhausted all unorthodox means of treatment before hospital presentation. In Europe and America, it is less common, accounting for 4.5% of tumours in Europe (3).

Sarcomas are common malignant lesions in children. Generally, sarcomas outnumber carcinomas in children. The most common sarcoma in our study was osteogenic sarcoma. Osteosarcoma, the most common type of primary malignant bone tumour, is defined by the presence of malignant mesenchymal cells producing osteoid or immature bone. It accounts for 30–80% of the primary skeletal sarcomas and is the most common bone malignancy. Primary osteosarcomas typically arise in the extremities, with a predilection for the metaphyses of long bones (12). All the cases seen in this study occurred in the long bones. Among lympho-reticular malignancies, Burkitt's lymphoma predominated in the index study entirely affecting the jaw similar to what is seen in endemic environments like ours. However, presentation in other sites like ovary, kidney and lymph nodes has been reported in the endemic areas (11,14).

Carcinomas are generally rare in children, though few cases have been reported with particular associations to certain environmental and genetic factors (15). Such associations were seen in squamous cell carcinoma of the skin and anogenital mucous membrane, mostly associated with human papilloma virus infection, basal

cell carcinoma associated with some congenital syndromes such as basal cell nevus syndrome, xeroderma pigmentosum, or nevus sebaceous and in areas of intense ultraviolet (UV) radiation exposure (16,17). We documented a few cases of squamous cell carcinoma and malignant melanoma, however, such associations could not be demonstrated in this report because of lack of other diagnostic facilities including human papilloma virus (HPV) study and typing.

The most common childhood malignant tumours irrespective of histiogenic origin were rhabdomyosarcoma, retinoblastoma, osteosarcoma, non-Hodgkin's lymphoma and squamous cell carcinoma. Head and neck was the commonest site of affectation, with predilection for the male child in older age group. These tumours showed specific age related occurrence and distribution patterns. The soft tissue sarcoma affected older children while the epithelial tumours predominated in the younger age group.

Conclusion

Malignant tumours in children though not very common, are an important aspect of paediatric disorders to the attending physician due to their high morbidity and mortality coupled with late presentation due to factors outlined in this study. The diagnosis of such tumours can be challenging to the pathologist, especially in resource constrained environments with inadequate manpower, lack of diagnostic facility for other ancillary and molecular investigations and economic realities of the present time. High index of suspicion is therefore advocated to detect the tumour in its early stage that is associated with low morbidity and mortality.

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