Malignant tumours of childhood in Zaria

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ABSTRACT

Background: The increased prevalence of hitherto uncommon tumours in children in our geographic setting formed the basis for this study. This study aimed to determine the current histopathologic distribution pattern of paediatric malignancies in Zaria. **Materials and Methods**: An eight year (2000-2007) consecutive analysis of malignant tumours in children ages 0 to 15 years in a referral University laboratory. All tissue biopsies were fixed in 10% formalin and processed in wax. Tumours were characterised histologically into tissues of origin and categorised into three age groups; <1 year, 1-5 years and 6-15 years. **Result**: 189 children with malignant tumours were analysed. They showed a male preponderance (M: F; 1.2: 1.0) and their ages ranged from 5 days to 15 years. Tumours of mesenchymal origin were the commonest (115: 60.8%) while epithelial tumours including germ cell tumours accounted for 74 (39.2%) cases. The age group 1-5 years had the highest epithelial tumours while age group 6-15 years had the most tumours with 102 (54%) cases overall. The five commonest tumours over-all were rhabdomyosarcoma, Burkitt lymphoma, retinoblastoma, non-Hodgkin's lymphoma and nephroblastoma. Germ cell tumours affected the ovary predominantly and two of the endodermal sinus tumour cases were seen in the testis of an eighteen month child and sacrococcygeum of a 5 year old girl, respectively. Of the six immature teratoma cases, four were cutaneous in distribution. The vascular tumours included epithelioid haemangioendothelioma, haemangioblastoma and Dabska tumour and they accounted for (5.8%) of all tumours seen. The commonest sites of occurrence of these tumours were the oculo-orbital, jaw, head and neck regions with 82 cases (43.4%) while lymph nodes were involved in 31 (16.4%) cases. **Conclusion**: The distribution and occurrence of malignant tumours in children is age related. Lymphomas were the commonest tumours overall while retinoblastoma and Burkitt lymphoma were the commonest tumours affecting children below 5 years and 6-10 years old, respectively, in our centre. The head region and lymph nodes were the sites of predilection for majority of these tumours.

Key words: Lymphoma, malignant childhood tumour

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INTRODUCTION

Malignant tumours in children are biologically and histologically distinct from adult tumours.[1] They are the leading cause of disease related death in children under 15 years.[1,2] Survival chance improves as the child gets older thus; age plays a significant role in the incidence and types of tumour seen in children as each developmental stage is associated with different disorders and diseases. There is also a remarkable geographic difference in the incidence and pattern of malignant tumour distribution as well the death rate of specific tumours.[3] Many factors such as abnormal development, tumour induction and prevalence of underlying familial or genetic aberrations are implicated in tumorigenesis in children.[1] The increased prevalence of hitherto uncommon tumours in children in our geographic setting formed the basis of this study.

MATERIALS AND METHODS

This is a consecutive analysis of malignant tumours seen in children aged 0 to 15 years from January 2000 to July 2007 in a referral laboratory teaching hospital. All tissue biopsies were fixed in 10% formalin, processed in wax and histology slides were stained with haematoxylin and eosin. Stains such as periodic acid Schiff, reticulin and masson trichome were used for further characterisation of tumours. The tumours were grouped based on tissue of origin into epithelial, germ cell and mesenchymal tumours. The frequency distribution of tumour types was categorized into three age groups; <1 year, 1-5 years and 6- 15 years.

RESULTS

One hundred and eighty nine children with malignant tumours were analysed. They showed a male preponderance (M: F; 1.2:1.0) and their ages ranged from 5 days to 15 years [Table 1].

Tumours were categorised based on tissue of origin: Epithelail - 59, Germ cell - 15 and Mesenchymal- 115 [Tables 2 and 3].

The epithelial tumours comprised of retinoblastoma

Table 1: Frequency distribution of all tumours by gender

Tumour type	Male	Female	Total
Epithelial			
Retinoblastoma	18	9	27
Nephroblastoma	9	9	18
Hepatoblastoma	0	1	1
Squamous cell carcinoma	1	4	5
Basal cell carcinoma	0	1	1
Metastatic carcinoma	3	2	5
Unclassified carcinoma	0	2	2
Germ cell			
Dysgerminoma	0	4	4
Endodermal sinus tumour	2	2	4
Embryonal carcinoma	0	1	1
Immature teratoma	2	4	6
Mesenchymal tumours			
Embryonal rhabdomyosarcoma	11	12	23
Alveolar rhabdomyosarcoma	4	4	8
Burkitt lymphoma	16	11	27
Non-Hodgkin lymphoma	15	3	18
Hodgkin lymphoma	6	3	9
Fibrosarcoma	3	1	4
Osteogenic sarcoma	2	1	3
Chondrosarcoma	1	0	1
Ewing sarcoma	1	1	2
Kaposi sarcoma	2	2	4
Epithelioid haemangioendothelioma	3	2	5
Haemangioblastoma	0	1	1
Dabska tumour	1	0	1
Ganglioneuroblastoma	0	1	1
Malignant peripheral nerve sheath tumour	3	2	5
Neuroblastoma	1	2	3
Total	104	85	189

Table 2: Frequency distribution of common epithelial and germ cell tumours of children

Tumour type	<1 yr	1-5 yrs	6-10 yrs	11-15 yrs	Total
Epithelial					
Retinoblastoma	0	24	3	0	27
Nephroblastoma	1	15	2	0	18
Hepatoblastoma	0	1	0	0	1
Squamous cell carcinoma	0	0	1	4	5
Basal cell carcinoma	0	0	1	0	1
Metastatic carcinoma	0	1	2	2	5
Unclassified carcinoma	0	0	1	1	2
Germ cell					
Dysgerminoma	0	0	3	1	4
Endodermal sinus tumour	0	2	0	2	4
Embryonal carcinoma	0	1	0	0	1
Immature teratoma	3	2	1	0	6
Total	4	46	14	10	74

(27), nephroblastoma (18) and hepatoblastoma (1). Of the retinoblastoma, 7 (26%) cases were histologically well-differentiated tumours while 4 cases were associated with tumour recurrence in the second eye and 17 (63%) children presented with advanced tumour involving the optic nerve. There were two unclassified carcinoma histologically composed of small round blue cells which could not be further characterised due to poor differentiation. Cutaneous tumours included

Table 3: Frequency distribution of mesenchymal tumours by age

Mesenchymal tumours	<1 yr	1-5 yrs	6-10 yrs	11-15 yrs	Total
Skeletal muscle					
Embryonal rhabdomyosarcoma	2	12	6	3	23
Alveolar rhabdomyosarcoma	0	0	4	4	8
Lymphoma					
Burkitt lymphoma	0	7	17	3	27
Non-Hodgkin lymphoma	0	4	5	9	18
Hodgkin lymphoma	0	1	1	7	9
Fibrous tissue					
Juvenile (infantile) fibrosarcoma	1	1	1	1	4
Bone and cartilage					
Osteogenic sarcoma	0	0	0	3	3
Chondrosarcoma	0	0	0	1	1
Ewing sarcoma	0	0	1	1	2
Vascular					
Kaposi sarcoma	0	0	3	1	4
Epithelioid haemangioendothelioma	2	0	1	2	5
Haemangioblastoma	0	0	0	1	1
Dabska tumour	1	0	0	0	1
Neural					
Ganglioneuroblastoma	0	1	0	0	1
Malignant peripheral nerve sheath tumour	1	1	1	2	5
Neuroblastoma	1	1	1	0	3
Total	8	28	41	38	115

squamous cell carcinoma and basal cell carcinoma. Two of the squamous cell carcinoma cases were sequelae of burns injury [Table 2]. Microscopy of the hepatoblastoma showed the epithelial variant and was composed of focal aggregates of fairly uniform polygonal malignant cells having papillary growth pattern predominantly [Figure 1].

Germ cell tumours included dysgerminoma (4), endodermal sinus tumour (4), embryonal carcinoma (1) and immature teratoma (6) [Table 2]. They all affected the ovary except for two cases of endodermal sinus tumour seen in the testis of an eighteen month child and sacrococcygeum of a 5-year old girl, respectively, and four cases of immature teratoma which occurred in the cervical (neck) region with associated respiratory distress in the children. Microscopy of the teratomas showed tumour composed of primitive embryonal cells having ovoid dark to vesicular nuclei arranged in nests, strands and forming tubules in a chondro-fibro-myxoid stroma. Areas of malignant squamous differentiation, rhabdomyosarcoma and undifferentiated neuroepithelial components forming rosettes were also seen [Figure 2].

Tumours of mesenchymal origin [Table 3] were the commonest with 115 (60.8%) cases and comprised

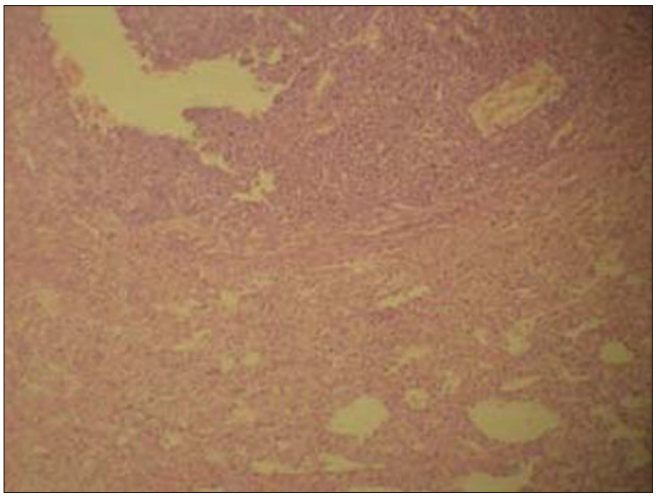


Figure 1: Hepatoblstoma ×40 malignant polygonal cells surrounded by residual hepatocytes

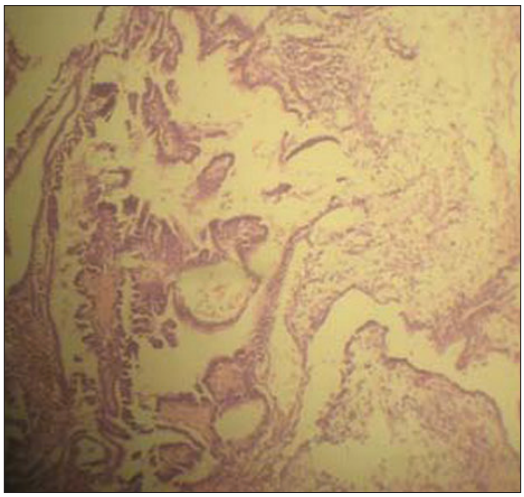


Figure 2: Immature teratoma ×40

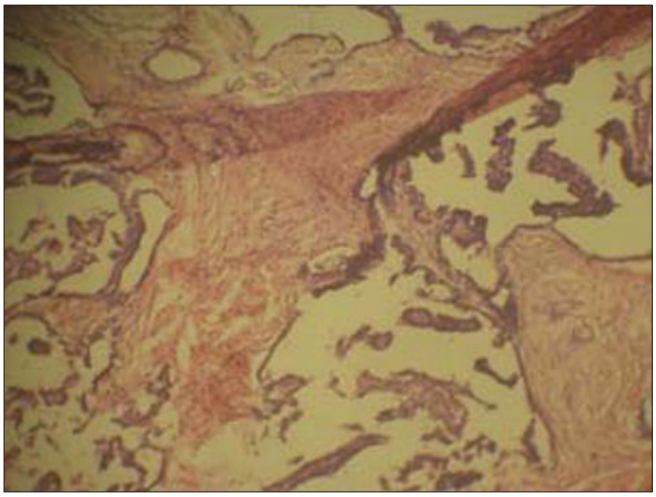


Figure 3: Dabska tumour ×40 Malignant cells in papillary array amidst dilated vascular channels

lymphomas-54 (47.0%), skeletal muscle tumours (rhabdomyosarcoma) - 31 (27.0%), vascular tumours-11 (9.5%), neural tumours - 9 (7.8%), bone tumours - 6 (5.2%) and fibrous tissue tumours - 4 (3.5%). Burkitt lymphoma was the commonest lymphoma with a male prevalence. 16 patients presented with jaw lesions while 11 had lesions in the ovary, kidney and lymph nodes. Of the 15 jaw presentation, 5 children had bilateral jaw masses and 4 cases had associated intra-abdominal masses. The youngest child affected was eighteen months old. Tumours of bone and cartilage also affected older children.

The vascular tumours accounted for 5.8% of all tumours and included epithelioid haemangioendothelioma, Kaposi sarcoma, haemangioblastoma and Dabska tumour (malignant endothelial papillary angioendothelioma) which was composed of dilated vascular channels arranged in papillary array histologiclly [Figure 3]. The latter two lesions were seen in the soft tissues of the head and the neck in a 12 year old girl and a 7 weeks old male infant, respectively. All the four children with Kaposi sarcoma were HIV sero-positive.

The commonest sites of occurrence of tumours were the orbito-ocular, jaw, head and neck regions with 82 cases (43.4%) while lymph nodes were involved in 31(16.4%) cases. Other tumour sites included the kidney, ovary, testis, retroperitoneum, liver, bone and skin. Majority of the children presented with advanced disease.

DISCUSSION

Malignant childhood neoplasms commonly arise in haematopoietic and nervous tissues and account for two percent of all malignancies.[1,3] They accounted for 5.6% of all malignancies within the study period, comparable to reports of 4.3% and 12.5% from Pakistan and Ibadan, Nigeria, respectively.[4,5]

The distribution pattern of these tumours is age related and showed a slight male preponderance. The age group 1-5 years had the highest epithelial tumours and retinoblastoma was the commonest with a male predilection. Retinoblastoma derives from differentiated primitive neuroectodermal cells and has a worldwide distribution while its incidence reduces with age, with no associated racial preference or gender bias.[6-10] Over 60% of our patients presented with extra-ocular advanced disease as is commonly seen in most developing countries where patients would have exhausted all unorthodox means of treatment before hospital presentation while four children had tumour involvement of the second eye which accounted for 14.8% of cases. Bilateral retinoblastoma occurs in 30%

of patients while over 90% of the hereditary form present with bilateral disease.[11] 15% bilateral disease was also reported from Ilorin, North Central Nigeria.[12]

Fifty-four percent of all our tumours occurred in the age group 6-15 years while the 6-10 years age group had the most mesenchymal tumours. Neonates and infants had the least tumours. This is not surprising because this age group is more prone to adaptation problems and developmental anomalies.

Lymphoma was the commonest tumour overall and Burkitt lymphoma predominated with majority of cases affecting the 6-10 year age group. The jaw predictably was the commonest site of presentation in our endemic zone, though some children presented with tumours in the ovary, kidney and lymph nodes. Sporadic cases commonly present with intra-abdominal masses[13] however, we could not determine the sporadic ones in these series due to absence of facility for cytogenetic studies. Non Hodgkin lymphoma (NHL) was predominant in boys and accounted for 9.5% of overall tumours in our series. It is a highly aggressive tumour in young children and constitutes 6% of childhood tumours. NHL has also been linked with immunodeficiency states induced by drugs, viral infection and genetic diseases.[3]

Rhabdomyosarcoma, a malignant skeletal muscle tumour was the second commonest overall with the embryonal variant accounting for over 70% of cases. They were located in the head and neck region predominantly. Rhabdomyosarcoma was also the commonest soft tissue sarcoma in children under 15 years in Ibadan and the embryonal variant accounted for 61.5% of their cases while the alveolar subtype was prevalent in the lower limbs of children below 10 years in a clinical review in Jos.[14,15]

Germ cell tumours have varied histologic subtypes though of common histogenetic origin and are seen in sites where primitive or embryonal cells are found.[1,16,17] Immature teratoma was the commonest seen and occurred in the neck region in infants and very young children. The neck region is not an uncommon site though the sacrococcygeum, ovary, testis are more frequent sites of occurrence.[1,16-19] Foci of adenocarcinoma, squamous cell carcinoma and sarcomatoid differentiation as seen in some of the cases are not uncommon finding in malignant teratoma.[20-22]

The vascular tumours in children are mostly benign and comprise haemangiomas.[23,24] Our malignant cases accounted for 5.8% of overall tumours seen and included rare tumours such as haemangioblastoma and Dabska tumour. Neural, bone and fibrous tissue tumours were the least in this series.

The five commonest tumours irrespective of histiogenic origin were Burkitt lymphoma, retinoblastoma, rhabdomyosarcoma, NHL and nephroblastoma while their distribution and occurrence were age related. Epithelial tumours were more frequent in children under five years while mesenchymal tumours favoured older children. The head and neck regions and lymph nodes were the sites of predilection for majority of the tumours. The lack of facility for immunohistochemical and cytogenetic studies, which would have enabled us to determine tumour biology of these lesions, was a limitation in this study.

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