Malignant Solid Childhood Tumors: Morphological Study in a Tertiary Hospital

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Abstract

Background: Malignancy is the second most common childhood mortality in the developed world. The types of cancer that develop in children are often different types that develop in adult with respect to incidence, type of tumor, underlying familial or genetic aberration and tendency to regress spontaneously or cytodifferentiation. In recent years, identification of specific genes, oncogenes, tumor markers and other biological and pathological factors have played an important role in staging and classifying risk categorization of specific tumors as low, intermediate and high-risk lesions.

Objectives: This study was done to evaluate the incidence and morphological patterns of solid malignant tumors in children.

Method: This hospital based cross-sectional descriptive study was conducted the Department of Pathology, Chattogram Medical College, Chattogram referred from Department of Pediatric Surgery, Chattogram Medical College Hospital, Chattogram. All the cases were subjected to examine histopathological slides with haematoxylin and eosin stain, and IHC done in malignant small round cell tumors and few tumors cases.

Results: An analysis of 43 cases of childhood solid malignant tumors, over a period of a year, was done. The study found that 28 out of 43cases of malignant tumors were seen in boys, whereas 15 casesin girls. The commonest tumor was lymphoma (11 cases) with non-hodgkin's predominance (10 cases), followed by nephroblastoma (10 cases). In addition, the common age group was found 0-4 years (22 cases), with male predominance.

Conclusion: Histopathological diagnosis could be confirmed with IHC in cases B cell non-hodgkin lymphoma, infantile fibrosarcoma, malignant fibrous histocytoma, Ewing's sarcoma / PNET. The frequency of tumors and their distribution was comparable to that report from other studies.

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Introduction

Malignancy is the 2nd most common cause of childhood mortality in the developing world 1st being malnutrition and infection. About 1/650 children develops malignancy before their 15th birthday.[1]

In Bangladesh, there are no perfect cancer registries. Childhood cancers are expected to be high in Bangladesh because of the young population structure – about 30% (47.4 million) of the population is under 15 years old.[2]

Common childhood malignant tumor (almost 80%) arises from haemopoietic elements, lymphnodes, bones and soft tissues. The childhood cancer often the result of DNA changes in the cells that take places very early in life, sometimes even before birth. A few environmental factors, such as radiation exposure, have been linked with some types of childhood cancer. Some children inherit DNA mutation from parents that increases their risk of certain types of cancer. The reason for DNA changes that cause most childhood cancers are not known.[3]

Childhood malignancies differ biologically and histopathologically from those of adults with respect to incidence, type of tumor, underlying familial or genetic aberration and tendency to regress spontaneously or cytodifferentiate[4]. In recent years, identifications of specific gene, oncogenes, tumor markers and other biological and pathological factors have played an important role in staging and risk categorization of specific tumors. Hence there is a need for accurate histopathological reporting in conjugation with ancillary methods.[5] Histological type is important for understanding etiology and progression of disease.

This study aims to provide a comprehensive recent overview on childhood cancers in the Department of Pathology, Chittagong Medical College, Chattogram which would contribute to the understanding of characteristics and provide a basis for the future strategies to deal with childhood cancer.

Method

It is a hospital based cross-sectional descriptive study carried out in the Department of Pathology, Chittagong Medical College, Chattogram over a one year period from 1st January 2017 to 31st December, 2017.

Children of 0-14 years old age diagnosed as malignant tumor, who had undergone operative treatment in the Department of Pediatric Surgery, were included in this study. Patients diagnosed as a case of malignant solid tumor was subjected to detail clinical history and thorough physical examination followed by relevant investigations.

All the specimens sent from Department of Pediatric Surgery were evaluated and stained by haematoxylin and eosin in all cases and immunohistochemistry (IHC) done in malignant small round cell tumors and (few tumors cases). All the necessary and relevant data regarding patients were recorded methodically in pre-designed data sheet.

Statistical analysis

The data were collected from the filled data sheet and statistical analysis was done using the SPSS (Statistic Package for Social Science) Version-20 software package for windows.

Result

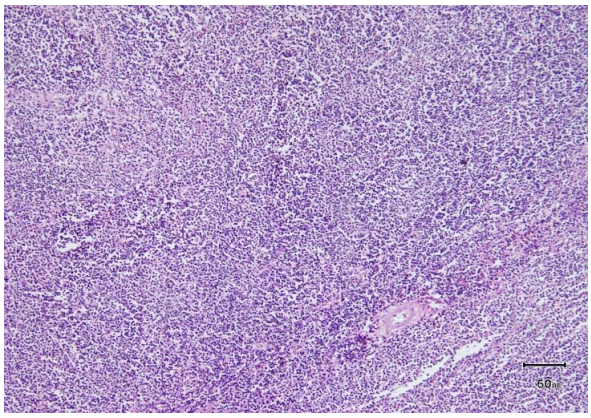
Age incidence ranged from 0-14 years. Patients were divided into 3 age groups. The mean age was 6 years 9 months. 28 (65.1%) cases were seen in boys and 15 (34.9%) cases were seen in girls showing male preponderance. Male and female ratio: 1.87:1.

Table I: Incidence of malignant tumors in different age groups in relation to sex (n=43)

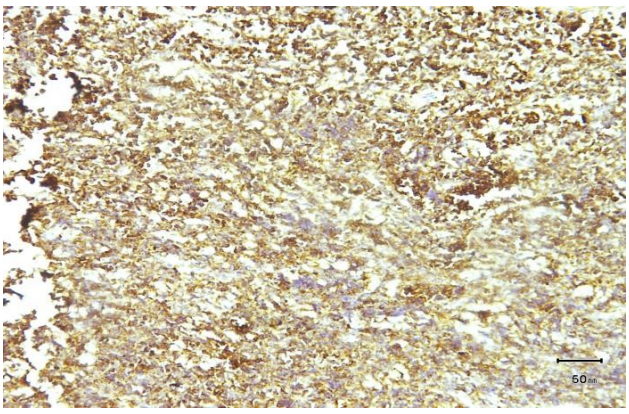
Sex	0-4 Years	5-9 Years	10-14 Years	Total
	n (%)	n (%)	n (%)	n (%)
Male	12(27.9%)	04(9.3%)	12(27.9%)	28(65.1%)
Female	08(18.6%)	04(9.3%)	03(7.0%)	15(34.9%)
Total	20(46.5%)	08(18.6%)	15(34.9%)	43(100%)

Table II: Histological subtypes of tumor in relation to gender (n=43)

Histopathological Diagnosis		Male n. (%)	Female n. (%)	Total n (%)
Lymphoma	Non-Hodgkin's	08 (18.6%)	01 (2.3%)	09 (20.9%)
	Hodgkin's	01(2.3%)	00(0.0%)	01(2.3%)
Nephroblastoma		05 (11.6%)	05 (11.6%)	10(23.4%)
Germ cell Tumor	Immature teratoma	01 (2.3%)	03 (6.9%)	04 (9.3%)
	Dysgerminoma	00 (0.0%)	02 (4.7%)	02 (4.7%)
	Yolk sac tumor	01 (2.3%)	01 (2.3%)	02 (4.7%)
Malignant small round cell tumor		02 (4.7%)	02 (4.7%)	04 (9.3%)
Adenocarcinoma		03 (7.0%)	00 (0.0%)	03 (7.0%)
Ewing's sarcoma/PNET		01 (2.3%)	00 (0.0%)	01 (2.3%)
Chondrosarcoma		00 (0.0%)	01 (2.3%)	01 (2.3%)
Metastatic osteosarcoma		01 (2.3%)	00 (0.0%)	01 (2.3%)
Malignant fibrous histocytoma		01 (2.3%)	00 (0.0%)	01 (2.3%)
Infantile fibrosarcoma		01 (2.3%)	00 (0.0%)	01 (2.3%)
Neuroblastoma		00 (0.0%)	01 (2.3%)	01 (2.3%)
Anaplastic astrocytoma		01 (2.3%)	00 (0.0%)	01 (2.3%)
Invasive squqmous		01 (2.3%)	00 (0.0%)	01 (2.3%)
Total		28 (65.1%)	15 (34.9%)	43 (100.0%)



Figer 1: Non-Hodgkin lymphoma (H&E Stain) x 100



Figer 2: CD20+ Non-Hodgkin lymphoma

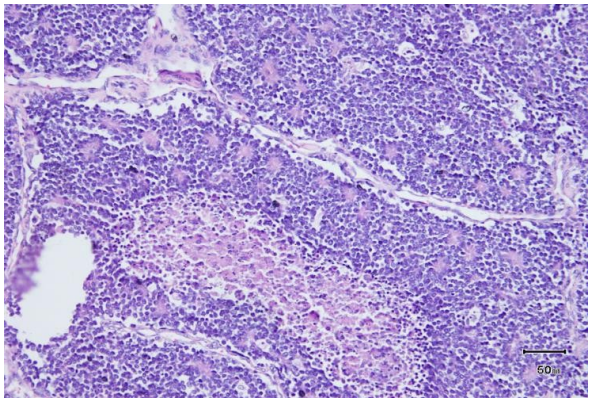


Figure 3. Primitive neuroectodermal tumor (H&E)X400

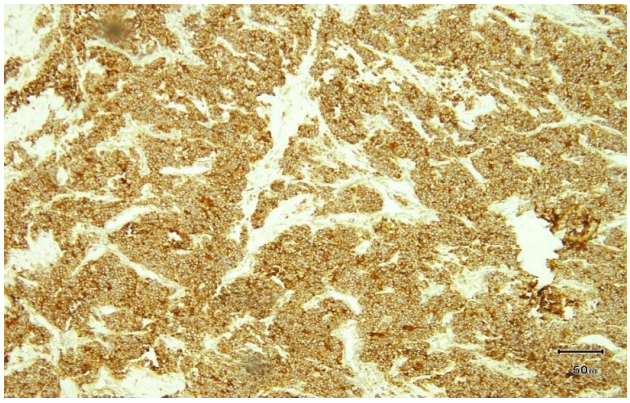


Figure 4: Primitive neuroectodermal Tumor CD99 Stain X 400

Lymphoma is the commonest malignant tumor and it constituted 25.3% of all tumors. 10 cases were Non-Hodgkin's lymphoma and 01 case is Hodgkin lymphoma. Mean age is 8 years. Male is more prevalent than female with male female ratio 9:1, more frequently found in 0-4years age group. Immunohistochemistry CD20 and CD3 are done in selective cases. 6 cases of Non-Hodgkin's lymphoma were B cell origin, CD20 positive and one case was T-cell origin which is CD3 positive. Hodgkin's lymphoma was CD30 negative. 8 cases arose from lymph nodes and 2 cases were soft tissue origin. One of them was diagnosed as a case of malignant small round cell tumor.

Among the renal tumors, only Wilm's tumor (10 cases) was found, with classical triphasic tumors were more prominent feature. The mean age was 4 years 7 months. Male to female ratio was 1:1.

Among the germ cell tumors, 4 cases were noted as immature teratoma: 3 of them arose from sacro-coccygeal region and 1 from ovary; 2 cases were dysgerminoma and 2 cases were yolk sac tumor; 1 case was extra gonadal origin. Female predominance with male female ratio 1:2.5. Mean age was 5 years 7 months.

Table III: Immunohistochemistry in malignant small round cell tumor to confirm the diagnosis

Malignant Small round cell tumor	Immunohistochemical reaction
Non-Hodgkin's lymphoma (Bcell Lymphoma)	CD20(+), CD99(-), Synaptophysin(-)
Desmoplastic small round tumor	Desmin(+), Myogenin (-)
Neuroblastoma	NSE(+) , Myogenin (-)

In this study, four cases were diagnosed as malignant small round cell tumor. For further evaluation, CD20, Myogenin, Desmin, Neuron-specific enulose (NSE), Synaptophysin markers were done. 2 cases were diagnosed as B cell Non-Hodgkin lymphoma, 1 case is desmoplastic malignant small round cell tumor and other was neuroblastoma.

Soft tissue sarcoma comprised 9.3% (4 cases). Mean age was 8 years 4 months, with male female ratio 3:1. 2 cases were histologically diagnosed as infantile fibrosarcoma and malignant fibrous histocytoma. Infantile fibrosarcoma was found, six months old, male

baby, arising from abdomen. Malignant fibrous histocytoma was noted in male, 14 years old. Immunohistochemically both cases showed strong positive for vimentin. A case of desmoplastic small round cell tumor also found. Histologically diagnosed as a case of malignant small round cells arising from intra abdominal cavity and confirmed by desmin. 1 case was PNET/ Ewings sarcoma family. For further evaluation CD99 was recommended.

Colorectal adenocarcinoma accounts for 7% (3 cases) of pediatric malignant tumors in the present study and commonly seen in 10-14years age group. Mean age is 11 years 7 months.

Bone tumor constituted 7% (3 cases): 1 case was metastatic osteosarcoma on the left chest wall; 1 case was Ewing's sarcoma/PNET family; another was chondrosarcoma. Male were predominant with male female ratio 2:1. Immunophenotyping CD99 and S100 were applied for confirming the diagnosis in respectively Ewing's sarcoma and chondrosarcoma.

Table IV: Distribution of tumor in relation to age groups (n=43)

Diagnosis	Age			
	0-4 Years n(%)	5-9 Years n (%)	10-14 Years n (%)	Total n (%)
Nephroblastoma	08(18.6%)	01(2.3%)	01(2.3%)	10(23.3%)
Non-Hodgkin's lymphoma	02(4.7%)	03(7.0%)	01(2.3%)	06(14.0%)
Bcell Lymphoma	03(7.0%)	00(0.0%)	01(2.3%)	04(9.3%)
Hodgkin's lymphoma	00(0.0%)	00(0.0%)	01(2.3%)	01(2.3%)
Immature Teratoma	03(7.0%)	00(0.0%)	01(2.3%)	04(9.3%)
Adenocarcinoma	00(0.0%)	00(0.0%)	03(7.0%)	03(7.0%)
Dysgerminoma	00(0.0%)	01(2.3%)	01(2.3%)	02(4.7%)
Yolk sac tumor	01(2.3%)	01(2.3%)	00(0.0%)	02(4.7%)
Ewing's Sarcoma	01(2.3%)	00(0.0%)	00(0.0%)	01(2.3%)
PNET	00(0.0%)	00(0.0%)	01(2.3%)	01(2.3%)
Chondrosarcoma	00(0.0%)	00(0.0%)	01(2.3%)	01(2.3%)
Metastatic osteosarcoma	00(0.0%)	00(0.0%)	01(2.3%)	01(2.3%)
Infantile fibrosarcoma	01(2.3%)	00(0.0%)	00(0.0%)	01(2.3%)
Malignant fibrous Histocytoma	00 (0.0%)	00(0.0%)	01 (2.3%)	01 (2.3%)
Desmoplastic small round cell tumor	00 (0.0%)	01 (2.3%)	00 (0.0%)	01 (2.3%)
Neuroblastoma	01 (2.3%)	00 (0.0%)	00 (0.0%)	01 (2.3%)
Anaplastic astrocytoma	00 (0.0%)	00 (0.0%)	01 (2.3%)	01 (2.3%)
Invasive squamous cell carcinoma	00 (0.0%)	00 (0.0%)	01 (2.3%)	01 (2.3%)
Total	20 (46.5%)	08 (18.6%)	15 (34.9%)	43 (100.0%)

Discussion

Most of the childhood malignant tumors occur below the age of eight years, although wide age variability exists in children.[6] In present study, 14 years was considered as the pediatric age with infancy as a separate age group. The peak occurrence of tumors was found in 0-4 year's age.

Table V: Comparison of age group distribution of tumors in various studies

SI.No.	Series	Birth-4 years	5-9 years	10-15 years
1	Jain *et al.*(1975)[9]	42.3%	22.2%	35.5%
2	Chandrashekar*et al. (2015)*[4]	27.3%	31.8%	40.9%
3	Dewani*et al.*(1972)[7]	47.2%	40.9%	11.9%
4	Jussawala & Yeole. (1984)[8]	42%	29%	29%
5	Present study	46.5%	18.6%	34.9%

The overall incidence of malignant tumors of childhood was more in male (M: F=1.53:1) patients. This observation has been made uniformly in literature by author. Male predominance is noted in all age groups and female predominance in germ cell tumor by Lee et al[10] and Miler et al,[11] In present study, male predominant in all age group of tumor except germ cell tumors. Male and female ratio: 1.86:1.

The commonest tumor comprised of lymphoma (11cases, 25.3%). Similar results were reported by Sharma et al,[13] and Baneerjee et al.[14] NHL was more frequent than Hodgkin. Non-Hodgkin lymphoma represented 23.3% whereas Hodgkin 2.3%. Non-Hodgkin lymphoma commonly expressed in 0-4 years age group in this study. Patients presented with swelling, pain, fever, and loss of weight with the duration ranging from one month to year. IHC CD20 was applied in 6 cases and revealed B cell origin Non-Hodgkin lymphoma.

Wilm's tumor is common renal tumour that is 100% as compared to the 78.4% by Louisa et al. This difference may be due to small sample size in present study. Male and female ratio is 1:1. Whereas in the study of Paul et al,[6] 11 infantile Wilm's tumor found the male to female ratio was 2.3:1. Husain et al.[2]found that Wilm's tumor was slightly more common in girls in whom it tends to present at an older age.

Malignant germ cell tumors in the ovaries of very young children are rare in condition[1]. Weinblatt and Ortega, 1982 noted dysgerminoma as the commonest tumor.[16] In this study, 7 cases were malignant germ cell tumors. Among them 3 cases were gonadal origins. Rest of them arose from extragonadal site, and two cases of dysgerminoma in ovary were documented. It is more common in gonadal tumor in patient with gonadal dysgenesis.[17] Tumors with syncytiotrophoblastic giant cells have the same prognosis as tumors in which they are absent.[18]

Table VI: Histological types of tumor in different series

Histological subtypes	Banerjeeet al. (1984)[14]	Sonal etal. (2004)[13]	Chandrashekhar et al. (2015) [4]	Present Study
Lymphomas	25.92%	21.41%	31.81%	25.3%
Renal Tumors	8.5%	19.48%	9.09%	23.3%
GermCell Tumors	3.8%	8.44%	13.63%	18.7%
Bone Tumors	10.52%	9.74%	12.12%	7%
Soft tissue tumors	14.3%	7.79%	19.69%	9.3%
Brain Tumors	15.32%	9.74%	7.57%	2.3%
Retinoblastoma	8.7%	6.49%	3.03%	0.0%
Neuroblastoma	4.5%	3.89%	3.03%	4.7%
Others	8.5%	20.12%	-	9.3%
Total	100%	100%	100%	100%

In this study, two cases of yolk sac tumor was locates at testis and intra abdomen. Both of them had shown elevated level of AFP. One case of yolk sac tumor, in testicular origin, at the age of 8 years and other one of female patient with 45 days arising from intra abdomen.

Soft tissue sarcoma comprises 9.3% of pediatric malignancy. Two cases are histologically diagnosed as infantile fibrosarcoma and malignant fibrous histocytoma. Infantile fibrosarcoma is found, six months old, male baby, arising from abdomen. Malignant fibrous histocytoma is seen in male, 14 years old. Immunohistochemically both cases show strong positive for vimentin. A case of desmoplastic small round cell tumor is also found. Histologically it is diagnosed as a case of malignant small round cells arising from intra abdominal cavity and confirmed by desmin.

Bone tumor constitutes 7% of pediatric malignant tumors in this study: one case is metastatic osteosarcoma arising from the left chest wall; one case is Ewing's sarcoma/PNET family; another is chondrosarcoma. Male are predomident, and male female ratio is 2:1. Immunophenotyping CD99 and S100 are applied for confirming the diagnosis in respectively Ewing's sarcoma and chondrosarcoma.

In this study, colorectal adenocarcinoma account for 7% (3cases) of pediatric malignant tumor and commonly seen in 10-14 years age group which is similar to the study of Tonbary et al. 2012.[19] Among the three cases, tumor arises from appendix, descending colon and rectum, respectively.

In this study, four cases of malignant small round cell tumor are documented .Male to female ratio is 1:1. Out of four cases of small round cell tumor, three cases arose from intra abdominal mass and one case from axillary swelling. For further evaluation of immunohistochemistry of CD20, CD3, Myogenin, Desmin, Vimentin, Neuron-specific enulose (NSE), Chromogranin, Synaptophysin markers are done. Two cases were diagnosed as B cell Non- Hodgkin lymphoma as well as one case was diagnosed as desmoplastic malignant small round cell tumor and other was as neuroblastoma.

In this study, one case is noted as anaplastic astrocytoma; Pilocytic astrocytoma, the most

common type of astrocytoma in children, is a low grade tumor that typically arises in the cerebellum. One case of invasive squamous cell carcinoma is documented in the study, arose from retro-molar mass, male, 10 years old patient. No predisposing factor was elicited.

Because of unwanted technical fault like delayed cold ischemic time and fixative time, negative result of IHC was found.

Conclusion

In this study, histopathological diagnosis could be confirmed with IHC in following cases: B cell non-hodgkin lymphoma, infantile fibrosarcoma, malignant fibrous histocytoma, Ewing's sarcoma / PNET. The frequency of tumors and their distribution is comparable to that report from other studies. The early onset and the embryonal nature of the major pediatric tumors suggest a prenatal origin and role of genetic factors. Infection, exposure to drugs and chemicals during pregnancy are other contributory factors. Accurate incidence of data is important in the planning and evaluation of clinical trial. Documentation of cases, advanced diagnostic methods like IHC, cytogenetic studies and treatment modalities with close follow up is needed to achieve better statistical evaluation of the problem.

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