INCIDENCE AND HISTOMORPHOLOGICAL EVALUATION OF PAEDIATRIC NON-HAEMATOLOGICAL MALIGNANT TUMOURS IN A TERTIARY CARE HOSPITAL

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ABSTRACT

BACKGROUND

Paediatric cancers differ markedly from adult malignancies in their distribution by histology, tumour site, and in prognosis. Molecular cytogenetic, immunohistochemistry, and histochemical stains play a major role in determining the exact underlying pathology of various paediatric cancers.

MATERIALS AND METHODS

In this study, we had taken 69 cases of paediatric neoplasms with children presented with paediatric solid tumours and brain neoplasms. Cases with lymph node swelling and haematological malignancies were not included in this study.

OBSERVATION AND RESULTS

This study covered a total of 69 non-haematological paediatric cancers in which 48 were paediatric solid tumours and 21 were CNS neoplasms. Paediatric solid tumours were common in male children than in female children and there was increased incidence in the age group of 3-4 yrs. when the paediatric solid tumours were categorised. Neuroblastoma with incidence of 16.67% (8 cases) predominates over other malignancies followed by ovarian tumours and extra skeletal Ewing sarcoma (5 cases, 10.42%). In 21 CNS tumours observed in this study, 12 cancers were seen in male children (57.14%) and 9 were females (42.86%). Male predominant was noted in CNS neoplasm also and there was increased incidence of cancers during 9-10 yrs. when CNS neoplasms were categorised. Medulloblastoma/PNET predominates with [8 cases (38.09%)], in the age group of 4-11 yrs. followed by astrocytomas, [7cases (33.33%)].

CONCLUSION

In our study, neuroblastoma being the most common abdominal soft-tissue neoplasms. Ewing sarcoma and ovarian neoplasms constitute second most common non-CNS neoplasms. Hepatoblastoma, retinoblastoma, and colorectal adenocarcinomas each constitutes about 8.33% of cases. Embryonal rhabdomyosarcomas was observed in next order frequency and osteosarcoma constitutes about 6.25% of cases. Wilms' tumour was the common form of renal cancer in children. Paediatric CNS neoplasm constitutes about 15.90% with peak age at presentation during 9-10 years and more than 10 yrs. The incidence is also slightly higher in males with M:F of 1.3:1. Medulloblastoma is the commonest childhood neoplasm. Astrocytomas constitute about 33.33% of cases in which 3 cases goes difficulty on diagnosis at light microscopy level. Immunohistochemical marker, GFAP, EMA, and vimentin will help in arriving final diagnosis.

KEYWORDS

Paediatric, CNS Tumours, Incidence.

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INTRODUCTION

Paediatric cancers differ markedly from adult malignancies in their distribution by histology, tumour site, and in prognosis. Unlike incidence pattern in adults where cancer rates tend to rapidly increase with increasing age,[1] relatively wide age variability exists during development with two peaks in early childhood and in adolescence.

It appears that adolescence is a transitional period between the common early childhood malignancies and characteristic carcinomas of adulthood. The mortality rate of cancer in children is approximately 3 to 5 deaths/1 lakh population/year.

In general, there is diversity in the occurrence of paediatric neoplasm all over the world. In this study, the actual incidence and presentation of paediatric neoplasm in semi urban area is evaluated with keen attention to clinical features, role of environmental[2] factors, and consanguinity, and initial cytomorphological evaluation with fine needle aspiration for a proportion of cases. As paediatric neoplasms are often anaplastic cancers, they pose a challenge to surgical pathologists. Paediatric oncology faces unique challenges because treatment with radiation surgery and chemotherapy may adversely affect growth and development and may cause serious long-term medical and psychosocial effect.

Molecular cytogenetics, immunohistochemistry, and histochemical stains play a major role in determining the exact underlying pathology of various paediatric cancers.

This study is undertaken in view of evaluating the actual incidence of paediatric neoplasms in semi-urban area with particular attention to the age, sex, site, and histopathology of

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cancers and also to study the value of immunohistochemistry in final diagnosis of paediatric tumours. In addition, the recent literatures, journals, and research publications regarding paediatric cancers are also immensely reviewed.

MATERIALS AND METHODS

Children and adolescents presented with malignant neoplasms referred during 2003-2005 were included in this study. A thorough clinical evaluation, routine haematological investigations, ultrasonogram, and CT scan (In proportion of cases) were done in each case. A detailed history with particular attention to consanguinity, socioeconomic status, nutrition and radiation, exposure to pesticides, parental occupation, and also similar neoplasms in other family members were also recorded.

The paediatric solid tumours and brain neoplasms were examined carefully from the reception itself. Larger specimens were sliced at 1 cm interval without distorting the gross pathology fixed in neutral buffered formalin and processed routinely. 3 to 5 micron sections were cut and stain with routine H. and E. immunohistochemistry with GFAP marker were also performed in doubtful CNS neoplasms.

OBSERVATION AND RESULTS

This study covered a total of 69 non-haematological paediatric cancers in which 48 were paediatric solid tumours and 21 were CNS Neoplasms.

Paediatric Solid Tumours

In this study, 48 paediatric solid tumours were observed in which 25 were male children (52.08%) with age ranging from 1 month to 15 yrs. (Mean age-7.04 yrs.), 23 were female (47.92%) with age ranging from 1 month to 15 yrs. (Mean age-7.08 yrs.).

The following Table No. 1 shows the total number of paediatric solid tumours observed during the period from January 2003 to December 2005. The average incidence is 36.36%.

In Table-2, there was increased incidence of paediatric solid tumours in the age group of 3-4 yrs. followed by more than 10 yrs. and less than 2 yrs.

The Table-2 also shows that the incidence of paediatric solid tumours common in males [25 cases (52.08%)] when compared with females [23 cases (47.92%)].

When the paediatric solid tumours[3,4] are categorised as given in the following Table-3, neuroblastoma with incidence of 16.67% (8 cases) predominates over other malignancies followed by ovarian tumours and extra skeletal Ewing sarcoma (5 cases, 10.42%).

In this study, 4 cases of hepatoblastoma, 4 cases of colorectal adenocarcinoma, and 4 cases of retinoblastoma were also observed. Osteosarcoma, rhabdomyosarcoma, nasopharyngeal and laryngeal neoplasms were observed only in 3 cases respectively.

Likewise, Wilms' tumour.[5,6] once thought to be a common paediatric neoplasm was observed in only one case.

Table-3 also shows one interesting case of melanoma, which is observed at 3 yrs. male child in the intraoral region, testicular tumour is observed at 3 yrs., and adrenocortical neoplasm at the age of 4 yrs.

CNS Neoplasms

In 21 CNS tumours observed in this study, 12 cancers were seen in male children (57.14%) with age ranging from 1-15 yrs. (Mean age 8.33 yrs.) and 9 were females (42.86%) with age ranging from 1-15 yrs. (Mean age 8.77 yrs.).

The average incidence of paediatric CNS neoplasm is 15.90% as given in the following Table No 4 during the period from January 2003 to December 2005.

When the children with CNS Neoplasms were also divided into 6 groups as done in the paediatric solid neoplasms, there was increased incidence of cancers during 9-10 yrs. and more than 10 yrs. (7 cases 33.33%) followed by 2-3 yrs. and less than 2 yrs. (3 cases 14.29%).

Incidence is common in males (12 cases, 57.14 %) as in paediatric solid neoplasms when compared with females (9 cases 42.86%).

The Table No 6 shows paediatric CNS neoplasm distribution.[7,8] Medulloblastoma/PNET predominates with [8 cases (38.09%)] in the age group of 4-11 yrs. followed by astrocytomas [7 cases (33.33%)], and ependymomas [3 cases (14.29%)]. 2 cases of pineoblastoma/pineocytoma and one case of chordoma at the age of 9-15 yrs. and 3 yrs. were also observed.

Immunohistochemistry

Immunohistochemical stains GFAP-for astrocytoma was undertaken and the results were given in the following Table 5.

Sl. No.	Period	Total No. of Non-CNS Malignancy	Paediatric Cases	Percentage
1.	Jan. 2003-Dec. 2003	132	12	9.1%
2.	Jan. 2004-Dec. 2004	198	14	7.1%
3.	Jan. 2005-Dec. 2005	282	22	7.8%

Table 1: Shows Total Number of Paediatric Solid Tumours During 2003-2005

Sl. No.	Age	Male	Female	Total No. of Cases	Percentage
1	<=2	4	4	8	16.67%
2	3-4	11	5	16	33.33%
3	5-6	-	4	4	8.33%
4	7-8	-	2	2	4.17%
5	9-10	4	-	4	8.33%
6	>10	6	8	14	29.17%

Table 2: Shows Age and Sex Distribution of Paediatric Solid Tumours

Sl. No	Solid Tumours	No. of Case	Percentage
1	Malignant Melanoma	1	2.08%
2	Colorectal Malignant Neoplasm	4	8.33%
3	Nasopharyngeal and Laryngeal Neoplasm	3	6.25%
4	Ovarian Tumour	5	10.42%
5	Testicular Tumour	1	2.08%

6	Adrenal Cortical Neoplasm	1	2.08%
7	Retinoblastoma	4	8.33%
8	Neuroblastoma	8	16.67%
9	Hepatoblastoma	4	8.33%
10	Extra Skeletal Ewing Sarcoma	5	10.42%
11	Rhabdomyosarcoma	2	6.25%
12	Low-Grade MPNST	2	4.17%
13	Bone Tumour - Osteosarcoma	3	6.25%
14	Wilms' Tumour	1	2.08%
15	Salivary Gland Tumour	1	2.08%
16	Others	2	4.17%

Table 3: Shows Categorisation of Paediatric Solid Tumours

Sl. No.	Period	Total No. of Neoplasms	Paediatric Cancers	Percentage
1	Jan. 2003-Dec. 2003	18	5	27.78%
2	Jan. 2004-Dec. 2004	21	5	23.80%
3	Jan. 2005-Dec. 2005	32	11	34.37%

Table 4: Total Number of Paediatric CNS Neoplasms During 2003-2005

Sl. No.	Age	Male	Female	Total No. of Cases	Percent
1	<2	1	2	3	14.29%
2	3-4	3	-	3	14.29%
3	5-6	1	-	1	4.76%
4	7-8	-	-	-	-
5	9-10	3	4	7	33.33%
6	>10	4	3	7	33.33%

Table 5: Age and Sex Incidence of Paediatric CNS Neoplasms

Sl. No.	CNS Tumours	No. of Cases	Percentage
1	Medulloblastoma/PNET	8	38.09%
2	Ependymoma	3	14.29%
3	Astrocytoma	7	33.33%
4	Chordoma	1	4.76%
5	Pineoblastoma/Pineocytoma	2	9.52%

Table 6: Categorisation of Paediatric CNS Tumours

Sl. No.	IHC	Marker	Result	Imperssion
1	Central Nervour System Neoplasm			Atypical Teraoid Rhabdoid Tumour
	Astrocytoma- Grade III	GFAP	Positive (+++)	
		VIMENTIN	Positive (+++)	
		EMA	Positive (+++)	
		SMA	Scattered Cells	
	Astrocytoma- Grade II- III	DESMIN	Positive (+++) In Vessels and	Grade II
	Glioblastoma Mulitiforme Grade-IV	GFAP	Very few Tumour cells	Grade II
		GFAP	Negative	
			Positive (++) IN Tumour Cells	
			Positive (++)	

Table 7: Shows Immunohistochemical Stain Results and Interpretations

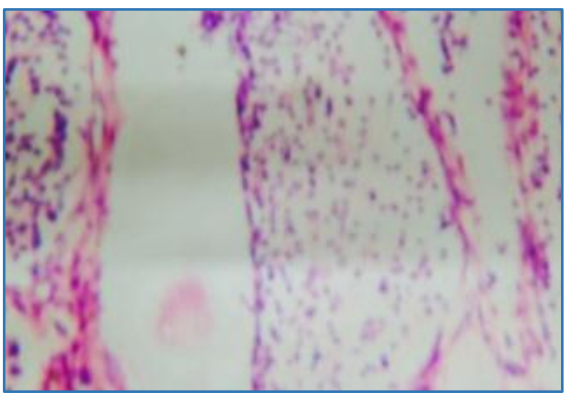

Fig. 1: Neuroblastoma-High Power View Shows the Fine Eosinophilic Network in Between the Tumour Cell Nuclei (Neuropil)

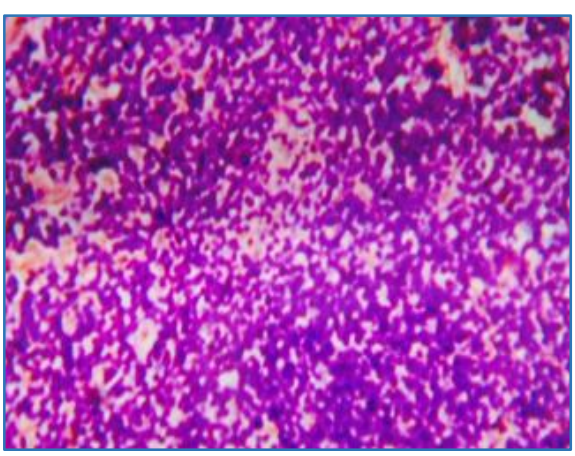

Fig. 2: Extra Skeletal Ewing's Sarcoma/PNET- Tumour Cells Seen Around the Blood Vessels

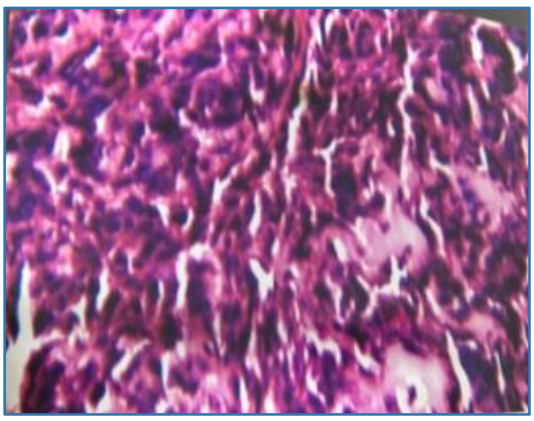

Fig. 3: Osteosarcoma-High Power View Shows Osteoid with Tumour

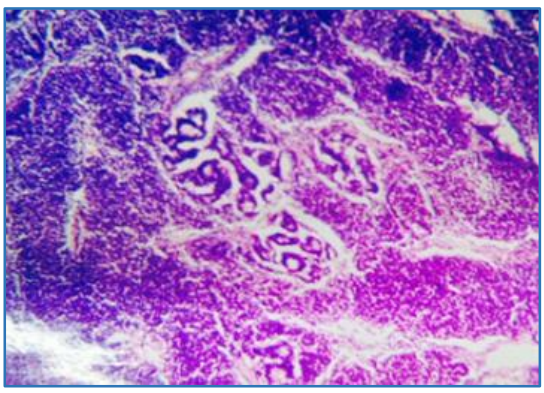

Fig. 4: Wilms' Tumour-Blastemal, Stromal, and Epithelial Tubular Formation

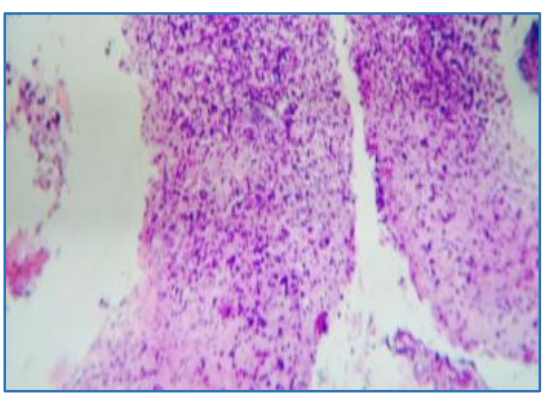

Fig. 5: Atypical Rhabdoid Teratoid Tumour: Scan Power View Shows Increased Cellularity and Microvascular Proliferations

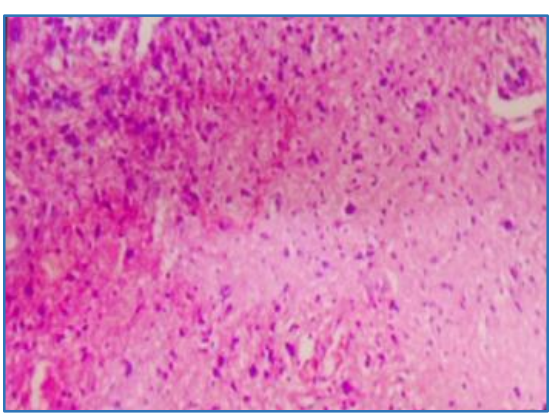

Fig. 6: Atypical Rhabdoid Teratoid Tumour: Low Power View Shows the Bizarre Nature of the Tumour Cells

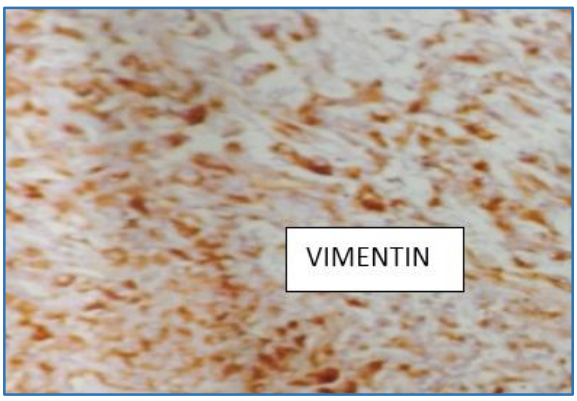

Fig. 7: Atypical Rhabdoid Teratoid Tumour-Vimentin Positive

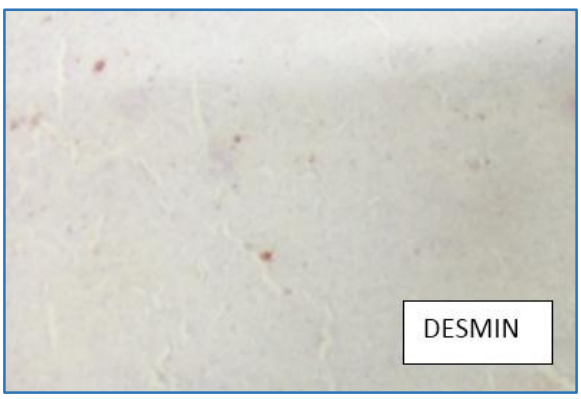

Fig. 8: Atypical Rhabdoid Teratoid Tumour-Desmin Negative in Tumour Cells

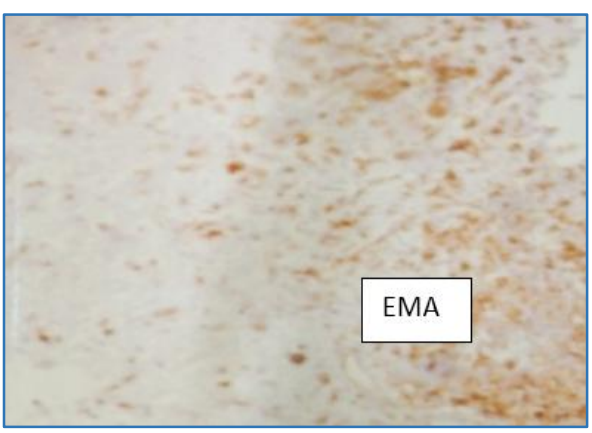

Fig. 9: Atypical Rhabdoid Teratoid Tumour-EMA Positive in Scattered Cells

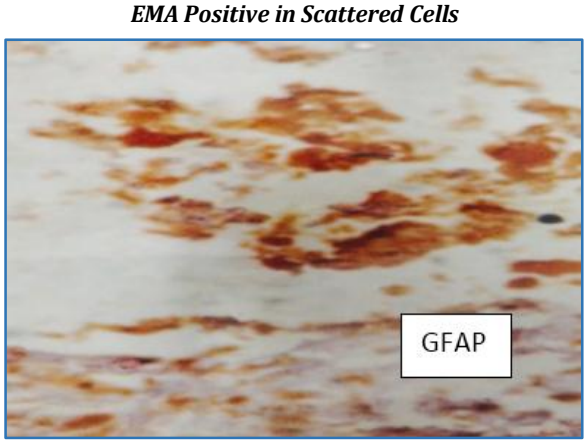

Fig. 10: Atypical Rhabdoid Teratoid Tumour-GFAP Positive in Tumour Cells

DISCUSSION

Although, cancer among children is relatively uncommon. It remains a significant cause of mortality in this population and is second only to accidents as a cause of death in the age group of 5-14 years.

Neuroblastoma (Fig. 1) being the most common abdominal paediatric solid tumours.[8,9] observed in our study as other researches Ewing sarcoma (Fig. 2) and ovarian neoplasms constitute second most common non-CNS tumours.

In this study, hepatoblastoma.[10] retinoblastoma, and colorectal adenocarcinomas each constitutes about 8.33% of cases. Hepatic tumours account for approximately 1% of child malignancies with hepatoblastoma (HB) and hepatocellular carcinoma (HCC) constituting the majority. Because of their rarity generalizations regarding the epidemiology are difficult. Worldwide HB occurs almost twice as often as HCC in children.

Male predominance has been pointed out in the report of Chen et al and our study disclosed a similar result.

Routine newborn screening by paediatrician with physical exam is the only way to find the abdominal mass. But, it is always too late for high stages. In the paediatric literature, several cases have been diagnosed postnatally within 6 weeks after delivery suggesting that HB may arise during foetal life. But, only one case report could be found about antenatal diagnosis of congenital HB in uterus as initial presentation of enlarged foetal abdominal circumference at 36 weeks of gestation. Now, the prenatal sonogram is prevalent and may help in an early diagnosis of liver tumours.

Retinoblastoma is the most common intraocular tumour in childhood[11,12] and the most common tumour of the retina, but it is a rare malignant tumour with a prevalence of about 1/23,000 live births.

Rhabdomyosarcoma.[13,14,15] are malignant neoplasm, which show morphologic, immunohistochemical, and ultrastructural or molecular genetic evidence of primary skeletal muscle differentiation usually in the absence of any other pattern of differentiation.

Soft tissue sarcoma occur with an annual incidence of 8.4 cases/million white children younger than 15 years of age incidence in black children is 50% of that white children.[9]

Malignancies of the kidney (Renal cancers) represented 6.3% of cancer diagnosis among children younger than 15 yrs. of age (Incidence 7.9 per million) and 4.4% of cancer diagnosis for children and adolescents younger than 20 years of age (Incidence of 6.2 per million).

Wilms' tumour was by far the most common form of renal cancer in children. The highest incidence of Wilms' tumour occurred most commonly among children younger than 5 years of age with very low incidence for 10-14 and 15-19 year olds. The highest incidence for Wilms' tumour was in the first 2 years of life followed by steadily decreasing rates with increasing age.

In our study, osteosarcoma constitutes about 6.25% of cases. Osteosarcoma can be defined simply as a malignant tumour in which osteoid or bony matrix is produced by the tumour cells. (Fig. 3). In our malignant mixed germ cell tumours and gonadoblastoma constitute about 10.42% of cases.

In our study, paediatric CNS neoplasm constitutes about 15.90% with peak age at presentation during 9-10 years and more than 10 years. These figures are in contrast with non-CNS tumours in which most of the cases are seen in <5 yrs. of age. The incidence is also slightly higher in males, with M:F of 1.3:1.

In our study, medulloblastoma[16.17] is the commonest childhood neoplasm, which is in correlation with the data provided by the National Cancer Institute as well as the study conducted by the various research workers and authors.[7,10]

TWO MAJOR RISK GROUP CATEGORIES DEFINED BY CLINICAL CRITERIA ARE NOW BEING USED

Average Risk

Children older than 3 years with posterior fossa tumours; tumour is totally or near-totally (<1.5 cc's of residual disease) resected; no dissemination.

Poor Risk

Children 3 years old or younger or those with metastatic disease and/or subtotal resection (>1.5 cc's of residual disease) and/or non-posterior fossa location.

Astrocytomas.[18,19] constitute about 33.33% of cases in which 3 cases goes difficulty on diagnosis at light microscopy level. With immunohistochemical marker, GFAP, 2 cases of grade-II anaplastic astrocytoma yielded positive result where as one case of anaplastic astrocytoma showed positivity for EMA and vimentin in association to GFAP and final impression of atypical teratoid rhabdoid tumour was made (Fig. 7,8,9,10).

Pineoblastoma/pineocytoma constitutes about 9.52% of cases, second most common tumour in the pineal region. Pineal parenchymal tumours arises from pinocytes. Pineoblastoma occurs predominately in childhood. Pineoblastoma is the most malignant variant and is considered a subgroup of PNETS of childhood.

CONCLUSION

In general, because of early detection and progress with therapeutic methods mortality rate due to malignancies as a whole during childhood has been decreasing. Although, mortality of children due to cancer fell in recent years. The incidence of childhood brain tumours is increasing.

In the present study of 69 cases of paediatric cancers evaluated with clinical light microscopy and IHC following conclusions are made and presented.

1. The average incidence of paediatric malignant neoplasm is 2%.
2. The incidence of paediatric neoplasms are increasing trends with new modalities of investigating procedures.
3. No classical epidemiological or socioeconomic cause is identified as an aetiological features in paediatric cancers.
4. Paediatric cancers are common in male children with male to female ratio of 1.5:1.
5. The peak age of paediatric neoplasm is less than 5 yrs. of age.
6. Neuroblastoma is the most common paediatric solid neoplasm.
7. Rare tumours like colorectal adenocarcinoma, melanoma, and nasopharyngeal carcinoma are also occur even in paediatric age groups.
8. Primary CNS neoplasms are relatively rare in children in contrast with western population where brain tumours are common.
9. In case of doubtful histogenesis, immunohistochemistry is very useful for final diagnosis.

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