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Frequency of Malignant Solid Tumors in Children

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Abstract

Objective: To find out the frequency of malignant solid tumors in children (<15 years).

Setting: All cases of pediatric malignant solid tumors which were diagnosed in the section of histopathology at the Aga Khan University Hospital, Karachi during the period of two years.

Methods: These tumors were initially evaluated on H&E stained sections and special stains were also performed whenever indicated. The undifferentiated tumors were evaluated immunohistochemically by using a panel of antibodies on sections from routinely processed, formalin fixed, paraffin embedded tissue blocks.

Results: Of two hundred and fifty three (253) consecutive cases of paediatric malignant solid tumors, lymphoma (26.1 %) was the most common tumor followed by central nervous system tumors (16.6%), osteosarcoma (7.5%), rhabdomyosarcoma (6.7%), neuroblastoma (5.1%), Wilm's tumor (5.1%), Ewing's sarcoma (4.7%), retinoblastoma (4.7%), germ cell tumor (4.4%) and primitive neuroectodermal tumor (4%) in order of frequency. In seven cases (2.8%), the nature of lesion remained undetermined even after immunohistochemical staining. Rest of malignant tumors (12.3%) included the rare entities like synovial sarcoma, nasopharyngeal carcinoma, leiomyosarcoma, malignant schwannoma and thyroid carcinoma, etc.

Conclusion: Lymphoma was the most frequent Paediatric tumor. The frequency of childhood central nervous system tumors was quite high as compared to the other series from different regions of Pakistan (UPMA 50:86,2000).

Introduction

Marked variation in the incidence of paediatric malignant tumors has been observed all over the world. Higher incidence of B-cell lymphoma is seen in equatorial Africa and very low incidence of Ewing's sarcoma is noticed in American blacks^{1,2}. Similarly, high prevalence of paediatric tumors is reported from Israel and Nigeria³. Environmental, cultural, racial and genetic factors have been attributed to the variation in the prevalence of the malignant tumors. The study of patterns of malignant tumor in various geographic regions and in different population groups may be helpful to find out the possible etiologic agent. In addition, identification of associations of malignant tumors with a particular condition may provide insight into the pathogenesis of the cancer.

In developing countries, the pediatric malignancies constitute 4.4% to 12.6% of all malignant tumors⁴⁻⁹. In children the most common malignant tumors arise from haemopoietic elements, lymph nodes, bones and soft tissue. About 80% of the tumors belong to these categories⁴. A significant fraction of childhood malignant tumors comprised of small round cell tumors which include rhabdomyosarcoma, lymphoma, Ewing's sarcoma, neuroblastoma, primitive neuroectodermal tumor, medulloblastoma, Wilm's tumor, retinoblastoma, granulocytic sarcoma, desmoplastic small round cell tumor, small cell osteosarcoma, mesenchymal chondrosarcoma, primitive sarcoma of bone and rhabdoid tumors of soft tissue¹⁰⁻¹³. The aim and objective of the present study was to find out the frequency of malignant solid tumors in children under fifteen years.

Material and Methods

This study included 253 consecutive cases of malignant solid tumors which were diagnosed in children under the age of fifteen years in the section of Histopathology at the Aga Khan University Hospital (AKIJH), Karachi during the period of two years (1995-96). Leukemias were excluded from the study. These tumors were initially evaluated on H&E stained sections and special stains such as periodic acid Schiff (PAS), periodic acid Schiff with diastase (PASI), Masson's trichrome and Gomori reticulin were also performed whenever indicated.

The undifferentiated small round cell tumors were evaluated immunohistochemically by using a panel of antibodies on sections from routinely processed, formalin fixed, paraffin embedded tissue blocks. The panel of antibodies varied but mostly included Leukocyte common antigen (LCA), Desmin, Neuron specific enolase (NSE), S-100 and Vimentin by employing peroxidase antiperoxidase (PAP) technique. Other antibodies like PANT (UCHL I), PAN B (L26, CD20), Glial Fibrillary Acidic Protein (GFAP), Neurofilament, Myoglobin, anti smooth muscle actin, Chromogranin A, Synaptophysin, Epithelial Membrane Antigen (EMA), Cytokeratins were also used depending upon the tumor morphology. All antibodies were obtained from Dako Inc., Denmark.

Results

A total of 5716 malignant tumors were diagnosed in the department of histopathology of the Aga Khan University Hospital, Karachi during the period of two years from January 1995 to December 1996. During this period, 38985 biopsies were received in the department of histopathology. Two hundred and fifty three (253) malignant tumors were encountered in children below the age of fifteen years during the study period.

The frequency of different paediatric tumors was analysed after the characterisation of undifferentiated tumors with the help of immunohistochemical techniques. The results are summarised in Table 1.

Table. Frequency of malignant solid tumors in children (<15 years).

Malignant tumors	Male	Female	Total	%
Lymphoma	56	10	66	26.1
Non-Hodgkin's lymphoma	31	6	37	14.6
Hodgkin's disease	25	4	29	11.5
CNS tumors	20	22	42	16.6
Osteosarcoma	7	12	19	7.5
Rhabdomyosarcoma	7	10	17	6.7
Wilm's tumor	9	4	13	5.1
Neuroblastoma	4	9	13	5.1
Ewing's sarcoma	10	2	12	4.7
Retinoblastoma	8	4	12	4.7
Germ cell tumor	1	10	11	4.4
Primitive neuroectodermal tumor (PNET)	8	2	10	4
Undifferentiated SRCT	6	1	7	2.8
Miscellaneous	15	16	31	12.3
Total	151	102	253	100

Lymphoma was the commonest malignant tumor seen in children and it constituted 26.1% of all paediatric tumors. Non-Hodgkin's lymphomas (14.6%) were more prevalent than Hodgkin's disease (11.5%). Non-Hodgkin's lymphoma was more frequent in males as compared to females with a male to female ratio of 5.6:1. Hodgkin's disease was also more common in males with a male to female ratio 6.3:1. The most frequent histological type of Hodgkin's disease was mixed cellularity (59.3%) followed by nodular sclerosing (22.2%), lymphocytic predominant (14.8%) and lymphocytic depleted type (3.7%) in order of frequency.

Non-Hodgkin's lymphoma was more frequent in the age group of¹⁰⁻¹⁴ years while Hodgkin's disease was more common in the age group of 5-9 years.

Malignant tumors of central nervous system (CNS) were the second most common neoplastic lesions and these made up 16.6% of all paediatric malignant disorders. The CNS tumors were more common in the age group of 10-14 years.

Osteosarcoma constituted 7.5% of all childhood neoplasms with male to female ratio of 1:1.7. This tumor was more prevalent in the age group of 10-14 years.

Rhabdomyosarcoma constituted 6.7% of all paediatric malignant neoplasms. The most frequent sites for these tumors were head and neck region (53%), followed by upper and lower extremities (29.4%) and genitourinary region (17.6%) respectively.

Wilms' tumors comprised 5.1% of all tumors and these tumors were more common in male with male to female ratio 2.2:1. Wilms' tumor was relatively more frequent in the right kidney as compared to left side with a ratio of right to left kidney 1.2:1.

Neuroblastoma comprised 5.1% of all paediatric tumors and it was more prevalent in females with male to female ratio of 1:2.2. Neuroblastoma was more prevalent in the age group of 0-4 years.

Ewing's sarcoma constituted 4.7% and primitive neuroectodermal tumor (PNET) comprised 4% of all malignant tumors. Ewing's sarcoma and primitive neuroectodermal tumors (PNET) were more common in males with male to female ratio of 5:1 in Ewing's sarcoma and 4:1 in primitive neuroectodermal tumor (PNET).

Retinoblastoma was 4.7% of all malignant neoplastic lesions. It was more prevalent in males as compared to females with male to female ratio of 2:1. The retinoblastoma was more common in the age group of 0-4 years. The occurrence of retinoblastoma was more frequent in left eye as compared to right side with right to left eye ratio of 1:1.7.

The germ cell tumors comprised 4.4% of all malignant tumors in children. These tumors were more common in females with male to female ratio of 1:10. In the seven cases (2.8%), the nature of lesion remained undetermined even after immunohistochemical staining. The miscellaneous category (12.3%) comprised of rare entities like synovial sarcoma, nasopharyngeal carcinoma, thyroid carcinoma, leiomyosarcoma and malignant schwannoma, etc.

Discussion

In developed countries the prevalence of childhood cancer (2%) is low¹⁴, while in third world countries it ranges from 4.38% to 12.6%⁴⁻⁹. The data from the developing countries may not depict the real picture and actual number may be higher than this figure. The majority of the population of third world countries lives in rural areas where the medical facilities may not be appropriate. Poor substandard or non-availability of diagnostic facilities, small number of oncology centres and lack of comprehensive national tumor registry may contribute to the under reporting of the cases of malignant tumors.

In spite of these factors the higher prevalence of childhood malignant tumors in the developing countries as compared to Western world can be attributed to increased percentage of children and young people while considering the overall population. Approximately 74% of the total population of the world live in the developing countries. Thirty nine percent (39%) of the population of developing countries is of children under the age of 15 years while in Western countries the paediatric age group, constitutes 23% of the total population¹⁵. In Pakistan, approximately 44.5% of the total population is below the age of fifteen years¹⁶. In the present study, paediatric tumors comprised 4.4% of all malignant tumors diagnosed in the section of histopathology.

After the characterisation of undifferentiated tumors with the help of immunohistochemistry, the frequency of paediatric malignant solid tumors was analysed. Malignant lymphoma was the most common tumor seen in children and it constituted 26.1% of all paediatric tumors. A relatively higher frequency of non-Hodgkin's lymphoma (36%) has been reported in a series from Armed Forces Institute of Pathology (AFIP) Rawalpindi¹⁷. Non-Hodgkin's lymphoma and Hodgkin's disease were

more frequent in males as compared to females. The other series also reported a similar observation⁸⁻²⁰.

Tumors of central nervous system (CNS) were the second most common malignant neoplastic lesions in children and these constituted 16.6% of all paediatric tumors. In our series, the frequency of tumors of central nervous system (CNS) is quite high as compared to other series of childhood tumors such as 3.8% by Zaidi et al.¹⁸ and 4.1% by Zaman et al.²¹ 7.1% reported by Haneef et al.²⁰, 9% by Khan et al.¹⁹. High prevalence rate of retinoblastoma was reported in the earlier studies conducted in different centres in Pakistan. Retinoblastoma was the most common malignant tumor in children described by Haneef et al.²⁰ and it comprised 27.8% of all paediatric tumors. A higher figure of 16% was reported by Khan et al.¹⁹ 15.9% by Zaidi et al.¹⁸ and

11.3% by Zaidi et al.²¹, But retinoblastoma was not among the five most common malignant tumors of childhood in a series from AFIP, Rawalpindi¹⁷.

In our series, the retinoblastoma constituted 4.7% of all paediatric tumors. One possible factor for the low frequency of retinoblastoma may be less referral of eye cases to Aga Khan University Hospital (AKUH).

In the previous series, the soft tissue tumors included a significant number of fibrosarcoma^{18,19}. But in the present study, rhabdomyosarcoma comprised a significant fraction of soft tissue tumors, which could be attributed to the use of immunohistochemistry in the diagnostic histopathology.

This study concluded that Lymphoma was the most frequent pediatric tumor. To get an exact prevalence of childhood cancers, adequate oncology centres with diagnostic facilities and a national tumor registry is necessary.

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