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Immunohistochemical Evaluation Of Small Round Cell Tumors Of Childhood

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Abstract

Objective: This study was done to evaluate the pediatric undifferentiated small round cell tumors with immunohistochemical staining.
Setting: The present study included consecutive cases of small round cell tumors which were diagnosed in children (<15 years) in the section of Histopathology at the Aga Khan University Hospital, Karachi during the period of two years.
Methods: The group of 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.
Results: The category of undifferentiated small round cell tumors included rhabdomyosarcoma (23.2%), primitive neuroectodermal tumor (17.9%), non-Hodgkin's lymphoma (16.1%), neuroblastoma (14.2%), Ewing's sarcoma (10.7%) in order of frequency. Osteosarcoma (Small cell variant), retinoblastoma and medulloblastoma comprised 1.8% each. In seven cases (12.5%), the immunohistochemical analysis was inconclusive.
Conclusion: Immunohistochemistry is a very valuable diagnostic tool which helps in distinguishing the undifferentiated tumors especially small round cell tumors. The immunohistochemical staining needs to be performed routinely for undifferentiated tumors in diagnostic histopathology (JPMA 49:87, 1999).

Introduction

In developing countries like Pakistan, childhood malignant tumors are not very uncommon. The pediatric malignancies constitute 4.38% to 12.6% of all malignant tumors in developing nations[1-5]. 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 categories[5]. Leukemia constitutes about one third of childhood malignancies and with the other one third being brain tumors and rest are solid tumors[6].

The malignant tumors, included in the category of small round cell tumors pose a great challenge to the histopathologist for precise and conclusive diagnosis as these neoplasms configure a heterogeneous group of malignant tumors. These neoplastic lesions may exhibit a similar morphologic picture and require the application of adjunctive techniques like immunohistochemistry, electron microscopy or cytogenetic studies for further characterization[7]. The category of small round cell tumors of childhood 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 tissue[7-10].

The present study was conducted for the immunohistochemical evaluation of pediatric undifferentiated small round cell tumors and to find out the frequency of these malignant tumors in children under the age of fifteen years.

Material and Methods

This study included 253 consecutive cases of tumors which were diagnosed in children under the age of fifteen years in the section of Histopathology at the Aga Khan University Hospital, Karachi during the period of two years (1995-1996). These tumors were initially evaluated on H&E stained sections and special stains such as periodic acid Schiff (PAS) and periodic acid Schiff with diastase (PA SD) Masson's trichrome and Gomori reticulin were also performed where indicated.

Out of 253 malignant tumors, 124 were those of small round cell tumors. These included fifty six cases in which it was not possible to further characterize the malignant lesion on conventional stains (H&E, PAS, PASD, Reticulin and trichrome). These fifty six cases of 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 included Leukocyte common antigen (LCA), Desmin, Neuron specific enolase (NSE), S-100 and Vimentin by employing peroxidase antiperoxidase (PAP) technique. Other antibodies like PAN T (UCHL1), PAN B (L26,CD2O), Glial Fibrillary acidic protein (GFAP), Neurofilament, Myoglobin, anti smooth muscle actin, Chromogranin A, Synaptophysin, Epithetial membrane antigen (EMA), Cytokeratins were used depending upon the tumor morphology. All antibodies were obtained from Dako Inc . Denmark.

Results

A total of 253 malignant tumors were diagnosed in children under the age of fifteen years which included 124 (49%) cases of small round cell tumors, It was not possible to determine the type of malignant lesions in fifty-six cases of these small round cell tumors on routine conventional stains. These undifferentiated small round cell tumors were further evaluated by using immunohistochemistry. In these 56 cases, 23.2% were rhabdomyosarcoma and 17.9% primitive neuroectodermal tumors (PNET). The results of immunohistochemical analysis of the undifferentiated small round cell tumors are summarised in Table.

Table. Immunohistochemical analyses of SRCT which remained inconclusive on conventional stains (N = 56)

Small round cell Tumors	No. of cases	Percentage
Rhabdomyosarcoma	13	23.2
Primitive neuroectodermal tumor (PNET)	10	17.9
Non-Hodgkin's Lymphoma	9	16.1
Neuroblastoma	8	14.2
Ewing's sarcoma	6	10.7
Osteosarcoma	1	1.8
Retinoblastoma	1	1.8
Medulloblastoma	1	1.8
Inconclusive	7	12.5
Total	56	100

Discussion

The prevalence rate of malignant pediatric tumors is significantly higher in the third world countries as compared to developed nations. In the developing countries, the prevalence rate of childhood tumors has been reported from 4.38% to 12.6% of all tumors[1-5], while in developed countries, pediatric tumors constitute about 2% of all malignant tumors. The significantly increased number of malignant tumors in children in the developing countries as
compared to Western world can be attributed to increased percentage of children in the overall population. Approximately thirty nine percent of the total population of developing countries comprises of children under the age of 15 years while in western countries the pediatric age group constitutes 23% of the total population[12].

Small round cell tumors comprise a significant fraction of pediatric tumors. About one third of pediatric malignant neoplastic lesions comprises of small round cell tumours[6]. McGahay et al reported that 80% of fine needle aspirates from palpable lesions of childhood malignancies revealed small round cell tumors[8]. In the present study small round cell tumors constituted 49% of all pediatric tumors.

Ahmed M et al conducted a study in which the diagnoses of small round blue cell tumors on routine conventional stains were compared with the diagnoses rendered after the immunohistochemical evaluation of these tumors[13]. The concordance rate in their study was 64% and in the remaining 36% cases immunohistochernistry was required for the conclusive diagnosis[13].

McGahay et al used immunohistochemistry and electron microscopy for the conclusive diagnosis in 28% cases of small round cell tumors[8]. In the present series, immunohistochemistry was required in

45.2% cases of small round cell tumors.
In our series, rhabdomyosarcoma comprised a significant proportion of soft tissue tumors while in the previous series, the soft tissue tumors included a significant
number of This is a diagnosis of exclusion and fibrosarcoma like areas are found in many malignant tumors. A higher representation could be attributed to lack of availability of immunohistochernistry.
In our series, the immunohistochemical analysis revealed inconclusive results in seyen cases (12.5%) of small round cell tumors. In about ten percent (10%) of small round cell tumors particularly in the bones, the nature of the lesion remains undetermined even after immunohistochernical analysis[10]. In such cases, the electron microscopy, cytogenetic studies and molecular techniques may be helpful.
With significant advancement in the development of specialised multi-diciplinary treatment protocols for the management of childhood tumors, which have improved the survival rate, an accurate and precise diagnosis of small round cell tumors has become very important. Over the past two decades, immunohistochemistry has emerged as a very valuable diagnostic tool to help in distinguishing the undifferentiated tumors especially small round cell tumors[16,17]. The immunohistochemistry needs to be applied routinely for undifferentiated tumors in the diagnostic Histopathology. This of course needs to be supplemented by the use of cytogenetic studies such as fluorescent in situ hybridisation (FISH) whenever required and available.

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