

Small Round Blue Cell Tumor Retinoblastoma vs. Neuroblastoma

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Abstract:

In histopathology, a small blue cell tumor or small round blue cell tumors refer to tumors comprised of “blue” cell with very scant cytoplasm. As nucleus stains blue and cytoplasm pink, these tumors impart a distinct “blue” appearance”. These cells at low magnification resemble mature lymphocytes which also possess scant cytoplasm. However, they are significantly larger than small lymphocytes and erythrocytes. Leukemia, lymphoma, poorly differentiated carcinomas like oat cell carcinoma and several other primitive tumors may give this picture on histology sections. These tumors can be seen in any age group.^{1&2} Here we report a four month old female child with diagnosed primary lesion of neuroblastoma in the right eye (from an outside laboratory) followed by metastasis to the bone marrow within a period of three months. This was a very rare finding because only 3 cases had been previously reported of Primary Neuroblastoma in the eye and that too with no metastasis. The commonest eye tumor in this age group is of course retinoblastoma which can also present congenitally as well as with metastasis. Immunohistochemistry of both Neuroblastoma and Retinoblastoma give same positivity to the same markers. Hence it is difficult to differentiate the two.

Keywords: Small round cell tumor, Neuroblastoma, Retinoblastoma

Introduction

The highly malignant small round blue cell tumors (SRBCTs) occur in the pediatric, adolescent, and young adult populations in some cases. They generally include Ewing's sarcoma, peripheral neuroectodermal tumor, rhabdomyosarcoma, synovial sarcoma, non-Hodgkin's lymphoma, retinoblastoma, Neuroblastoma, hepatoblastoma, and nephroblastoma or Wilms' tumor. Other differential diagnoses of small round cell tumors include small cell osteogenic sarcoma, undifferentiated hepatoblastoma, granulocytic sarcoma, and intraabdominal desmoplastic small round cell tumor.⁽¹⁾

Accurate diagnosis of these cancers, is essential because the treatment options, responses to therapy, and prognosis vary widely depending on the diagnosis. As their name implies, these cancers are difficult to distinguish by light microscopy, and currently no single test can precisely distinguish these cancers due to their undifferentiated or primitive character. Tumors that show good differentiation are generally easy to diagnose, but when a tumor is

poorly differentiated, identification of the diagnostic, morphological features is difficult and therefore, no definitive diagnosis may be possible. To confirm the diagnosis, pathologists rely on several techniques, including immunohistochemistry, cytogenetics, interphase fluorescence in situ hybridization, and reverse transcription-polymerase chain reaction (RT-PCR). Immunohistochemistry for individual protein markers is used to establish the diagnosis in many instances, but it can only examine a single protein at a time.⁽³⁾ The aim of reporting this case is to highlight the fact that even though it was a diagnosed case of primary Neuroblastoma of the eye, we however feel that it might not be the case because such aggressive tumors of the eye and with metastasis, favor retinoblastoma more. Furthermore, on immunohistochemistry both these tumors give same positivity to same markers and hence differentiating the two becomes a challenge.

Case Report

4 months old female infant, resident of Chitral (Pakistan), presented in children's OPD PIMS, on 4/4/2016 with protrusion of right eye, and swelling of right eye since one month of age. On general physical examination, she had pallor. Rest of the systemic enquiry was unremarkable. There was no family history of similar such disease. The Diagnosis was

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made after getting an incisional biopsy of right eye followed by immunohistochemistry from an outside laboratory (done on 24/3/2016) which revealed FLI, Synaptophysin, Chromgranin and CD56 markers to be positive while Desmin, Myogenin, CD99 and CAM5.2 negative. All these findings were suggestive of Neuroblastoma of eye. Her complete blood picture revealed TLC of 11300, and hemoglobin was 8.3g/dL, with a microcytic hypochromic picture. Her differential leukocyte count included 38% neutrophils, 60% lymphocytes, 2% eosinophils and retics count was 3.7%. Her bone marrow biopsy was performed at PIMS for infiltration. Findings of which were suggestive of Neuroblastoma showing infiltration in the bone marrow as 70% of Mononuclear cells were seen with high N/C ratio and inconspicuous nucleoli lying singly and in classic rosette forms.

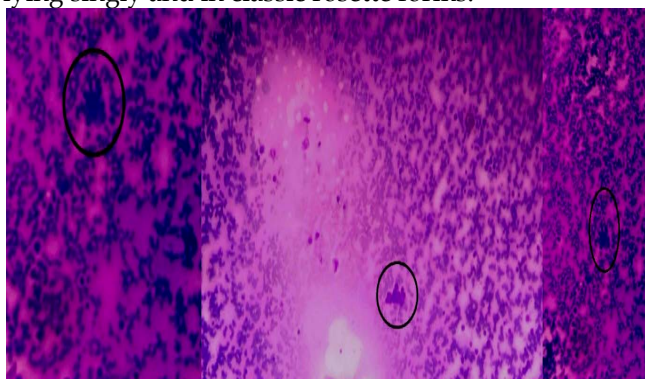


Figure 1. Low power magnification (x100) showing metastatic clumps.

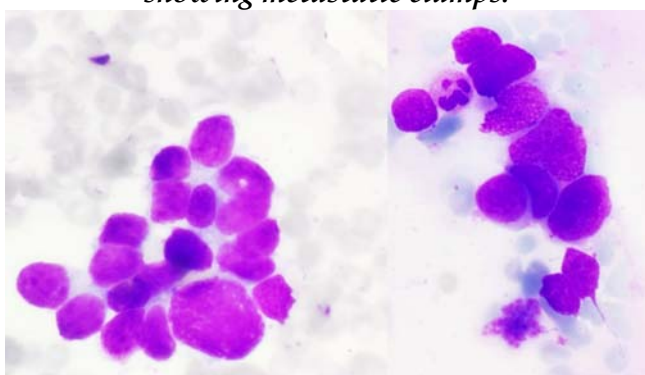


Figure 2. High power magnification (x1000) showing classical rosette pattern of cells

Discussion

Many of the pediatric solid tumors categorized as small blue round-cell tumors can be differentiated on immunohistochemistry but retinoblastoma and Neuroblastoma give same positivity to the same markers. So it difficult to differentiate them and they

should be considered in the differential diagnosis of neonatal orbital tumors.

Neuroblastoma is by far the most common cancer in infants (less than 1 year old). It accounts for about 7% of all cancers in children (4) but rarely, does Neuroblastoma represent primary Lesions in the orbit, where they may arise from the ciliary ganglion. So far, only three cases have been reported of Primary Neuroblastoma. The most recent one was reported in 2014 in Japan's pediatric international journal (5), Inzawa N et al described primary Neuroblastoma in a 1-month old boy without metastasis. The rest of two cases were reported in Japan and India in 2006 and 2012 respectively(6)(7). No evidence of metastasis to bone marrow was reported in these three cases. On the other hand Retinoblastoma is the most common primary ocular malignancy of childhood. It makes up 3% of all cancers diagnosed in children before the age of 15.(8) Generally, 3 out of 4 children have the disease in one eye, while 1 in 4 children have the disease in both eyes. Choroidal invasion of retinoblastoma is a risk for metastases, especially if it is associated with any degree of optic nerve invasion. (9)

The following table shows the differences between the two tumors which might help us in the proper diagnosis.

Feature	Neuroblastoma	Retinoblastoma
Age of presentation	Younger than 2 years. Median age of diagnosis is 17 months.	Usually before 5 years of age
Symptoms	Depends on primary tumor locations.	Most common is leukocoria. Others include Bulging of eyes, vision problems and eye pain
Morphology	Small, round and blue, and rosette patterns (Homer Wright rosettes)	Flexner-Wintersteiner rosettes
Immunohistochemistry	Positive for NSE, S-100, chromogranin and synaptophysin	Positive for NSE, S-100, chromogranin and synaptophysin

Neuroblastoma generally occurs in very young children; the median age at diagnosis is 17 months. The tumors arise in tissues of the sympathetic nervous system, typically in the adrenal medulla or paraspinal ganglia, and thus can present as mass lesions in the neck, chest, abdomen, or pelvis. Primary tumors in the

neck or upper chest can cause Horner’s syndrome (ptosis, miosis, and anhidrosis), and tracheal deviation with resulting stridor. Tumors along the spinal column can expand through the intraforaminal spaces and cause cord compression, with resulting paralysis.⁽¹⁰⁾

Retinoblastoma (Rb) is an embryonal tumor of the retina and is the most common malignancy of the eye in children. Onset generally occurs between the third month of pregnancy and 5 years of age. Initial signs are confined to the eye. The most common and obvious sign is an abnormal appearance of the pupil, leukocoria. Other less common signs and symptoms are deterioration of vision, a red and irritated eye, and bulging of the eyes. As the tumor progresses, patients are at a higher risk of developing metastatic disease. Metastases occur most commonly in the CNS, bones, bone marrow and liver.⁽⁸⁾

Both Retinoblastoma and Neuroblastoma demonstrate a small round-cell tumor of neuroepithelial origin. Flexner-Wintersteiner rosettes (relatively specific for Rb), and Homer Wright pseudorosettes may be seen on microscopy. Neuroblastomas are characteristically positive for neuron-specific enolase (NSE) which is an isoenzyme of the glycolytic enzyme, enolase, which has been shown to be highly specific for neurons and neuroendocrine cells. Other markers evaluated in neuroblastoma include S-100, chromogranin, and synaptophysin, which are not usually helpful in distinguishing undifferentiated and poorly differentiated tumors.⁽¹⁾ These same Markers also positive for retinoblastoma. ⁽¹¹⁾

So we have made a conclusion that these tumors are difficult to differentiate since they have the same morphology and immunohistochemistry results. The exact diagnosis is always a challenge and common things should always be considered first. Hence retinoblastoma is more likely to have been the diagnosis in our case as the patient was younger than 5 years, had eye symptoms, classical rosette pattern on

histology signifying presence of metastasis that was aggressive in nature. All these features favor retinoblastoma more than neuroblastoma at this age.

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- A. Conception, Synthesis and Planning of the research
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- C. Interpretation, analysis and discussion