Case Report

DOI: 10.7860/JCDR/2015/13691.6494

Pathology Section

Cytologic Interpretation of Melanotic Neuroectodermal Tumour of Infancy Involving Cranial Bones: Clue to Diagnosis

ASARANTI KAR[1], PRIYADARSHINI BISWAL[2], SUSMITA BEHERA[3], IPSITA DHAL[4], SURABHI[5]

ABSTRACT

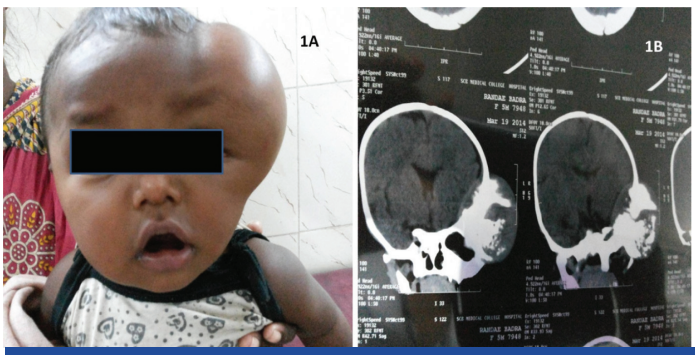
Melanotic neuroectodermal tumour of infancy (MNTI) is a rare, benign but locally aggressive neoplasm of infants commonly affecting the maxilla. It can also involve other areas like skull, mandible, brain and epididymis. The tumour comprise of dual populations of cells like small, basophilic neuroblast like cells and large pigment laden epithelial cells arranged in tubular and pseudoglandular pattern. The proportion of two components varies and therefore the diagnosis can be difficult in absence of the large cells. We describe the cytologic, histologic and immunohistochemical findings in a case of MNTI involving left side orbit with frontal, temporal and parietal bones. The cytologic interpretation could be made due to the suggestive clinical and radiologic findings and detection of large epithelial pigmented cells on thorough searching. The neuroblast like cells was positive for Neuron specific enolase, large cells for HMB-45 and Pan CK. Both the cellular components were negative for desmin. This case report is presented due to its rarity and also to aid the surgical pathologists in diagnosis where the findings are not too straight forward.

Keywords: FNAC, Cranial bones, HMB45, MNTI, PanCK

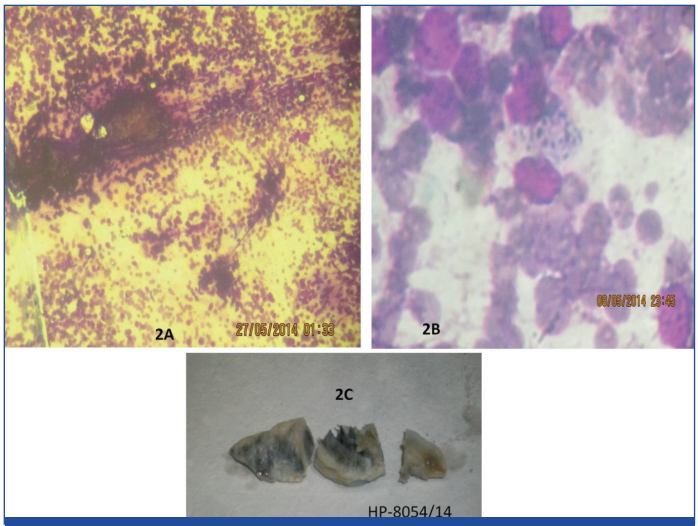
CASE REPORT

A five-month-old female child presented with a large swelling on lateral aspect of left side orbit extending to frontal, temporal and parietal region of skull for 4 months. The mass was rapidly growing in size, around 6 cm in diameter. It was non tender, firm in consistency and fixed to the underlying structures, but the skin over the swelling was free [Table/Fig-1a]. CT Scan showed an extensive tumour outgrowth from left frontal, temporal, parietal bone and lateral wall of orbit with sclerosis of base [Table/Fig-1b]. General examination and imaging studies did not reveal any other mass. From the clinical and radiological findings, provisional diagnosis was small round cell tumour possibly Ewing's sarcoma/peripheral neuroectodermal tumour (PNET).

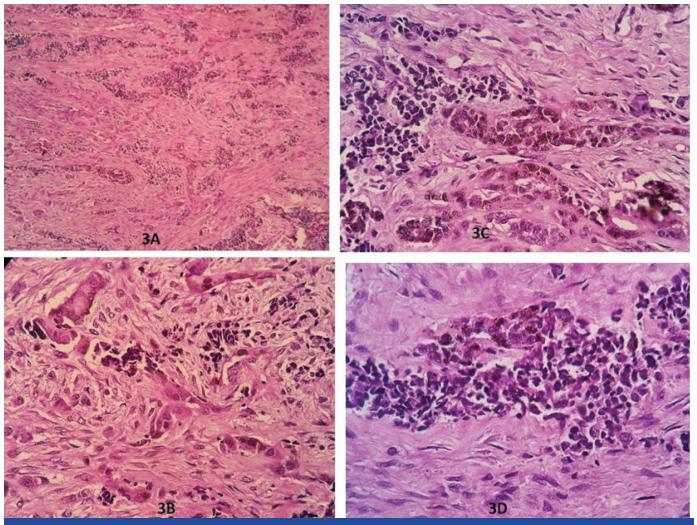
Fine needle aspiration cytology (FNAC) of lesion was done and smears was cellular, revealing mostly small monotonous looking cells with scanty cytoplasm, hyperchromatic nuclei and inconspicuous nucleoli [Table/Fig-2a]. On extensive search, few large cells with moderate amount of eosinophilic cytoplasm, centrally placed vesicular nuclei, focally containing dark brown cytoplasmic pigments were seen [Table/Fig-2b]. From the cytomorphology a provisional diagnosis of small round cell tumour possibly melanotic neuroectodermal tumour of infancy was rendered considering the age, clinical presentation and radiological findings. Other possible differential diagnosis can be Ewing's sarcoma/PNET, neuroblastoma and embryonal rhabdomyosarcoma but due to presence of dual population of tumour cells including large pigmented cells and small neuroblast like cells, the diagnosis of MNTI was preferred. In view of our cytological diagnosis serum vinyl mandellic acid (VMA) was advised. Serum VMA was raised (38mg/g of creatinine). The routine haematological parameters were within normal limit. The girl was planned for debulking of tumour and skin preservation operation was done. The mass was large, attached to skull bones and firm to hard in consistency. Based on these findings the surgeons' operative impression was either osteoid or osteoma/osteogenic sarcoma/Ewings sarcoma or fibrous dysplasia. Only the primary outgrowth from the skull was excised as the inner extension of mass could not be removed. Formalin preserved gross specimen received in Department of Pathology comprised of multiple bits of grayish white



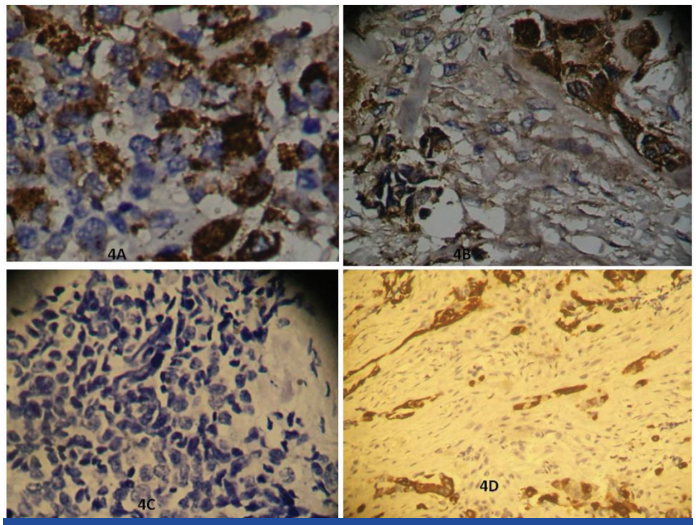
[Table/Fig-1a]: Large expansile growth on Left side of orbit and skull **[Table/Fig-1b]:** CT scan showing large invasive growth with sclerosis of scalp bones



[Table/Fig-2a]: Photomicrograph showing small uniform cells
[Table/Fig-2b]: Large epithelial cells with dark pigments. Diff quik stain X400
[Table/Fig-2c]: Solid grayish white cut surface of MNTI with brown pigmentation



[Table/Fig-3a-d]: Photomicrographs showing dual populations of tumour cells comprising of small neuroblast like cells and large pigment laden cells arranged in tubular pattern. H&E stain X100-400.



[Table/Fig-4]: IHC findings in MNTI.
(a) Positivity of large tumour cells to HMB45. (b) Small cells positive to NSE. (c) Desmin negativity in all cells. (d) Pan CK positivity in large cells.

firm tissue together measuring 4x1x1cm. Cut surface was solid with black pigmentation on surface [Table/Fig-2c]. Gritty sensation was felt on cutting. Multiple sections taken from different areas revealed a biphasic cell population on fibrotic stroma. Large epithelioid cells arranged in tubular, alveolar pattern with moderate cytoplasm containing melanin. Small unpigmented cells resemble neuroblasts, present as sheets and diffusely over a fibrillary matrix background [Table/Fig-3a-d]. Immunohistochemically, the intense cytoplasmic reactivity for HMB 45 and Pan CK in large tumour cells indicated melanocytic differentiation. The small monotonous cells were positive for NSE demonstrating neuroblastic differentiation of tumour cells. Both types of cells were negative for Desmin confirming the diagnosis of MNTI [Table/Fig-4a-d]. So the final diagnosis of MNTI was made. The tumour cells were subjected to Ki67 to know the proliferative potential and it was positive in approximately 10-12% of cells. The patient passed away in the immediate postoperative period due to postoperative complications.

DISCUSSION

Melanotic neuroectodermal tumour of infancy (MNTI) is a rare tumour affecting infants and young children. It is rapidly growing and locally invasive and usually involves head and neck region. The first case of MNTI reported in the literature was designated as “Congenital melanocarcinoma” by Krompecher in 1918 [1]. He described a pigmented tumour of the maxilla associated with a developing tooth and elements of dental lamina in a two-month-old infant. Approximately 250 cases of MNTI have been reported since then in the World literature [2]. Three cases of MNTI were described by Stowens in 1957 which according to him resembled the vomeronasal organ of Jacobson in several ways [3]. Another such case was reported in the maxilla of a three-month-old boy by Borello and Gorlin in 1966 [4]. The growth involves craniofacial region in 90% cases and is rapidly growing and non-ulcerated [5,6]. They often destroy the underlying bone and may be associated with displacement of developing teeth. This tumour almost always develops in young children during the first year of life; only 9% of cases are diagnosed after the age of 12 months [7]. In our case, the lesion developed in a five-month-old infant in orbital region with extensive involvement of cranial bones and the clinical diagnosis was bone tumour extending to soft tissue.

The high level of urinary VMA is useful for diagnosing tumours of neural crest origin. The VMA-to-creatinine ratio is reported when the patient is under 18 years, the urine collection is random or other than 24 hours, or the urine volume is less than 400 mL/24 hours. Since the above patient is only five-month-old, we have measured the VMA: creatinine ratio which was high (Normal-0 to 27 mg/g of CRT). The immunohistochemical staining is variable in MNTI. The large epithelioid tumour cells are positive for cytokeratin, HMB45 and EMA but are usually negative for S100, GFAP, AFP and melan A. In the above case the large cells express HMB45 and Pan CK where as small cells are NSE positive which is compatible with other reports. Complete surgical excision is the treatment of choice in these patients. But patients who are not cured by this can be treated with chemotherapy only, chemotherapy with radiotherapy, chemotherapy before and after the surgical treatment, radiotherapy and surgical treatment or a combination of surgery, chemotherapy and radiotherapy [8]. MNTI generally follows a benign course, but the rate of recurrence is reported to be 15% within one year of initial excision [9]. To assess the biological behaviour immunohistochemical expression of Ki67 and CD99 are observed and when elevated and/or present are considered as indicators of more aggressive tumour growth [10]. Ki67 in this case was approximately10-12% indicating a high proliferative index and worse aggressive behaviour.

Even though this tumour has been detected around a century back, there are still many unresolved issues which need to be addressed. The exact histogenesis of the tumour is not yet clear for which it is designated by various names. Evidence from tissue culture and immunohistochemical and ultrastructural studies suggest the neural crest as the most commonly accepted tissue of origin for MNTIs. Even though melanin is produced by the tumour it is not evident clinically in the overlying tissue [11]. The cytologic composition includes dual population of cells but the proportion of each component varies in cytology and histology and the diagnosis may be difficult if the large epithelial cells are minimal in number. This happened in present case as the larger cells were difficult to discern in cytology. In such instances, clinical presentation and imaging studies may aid largely in reaching at a diagnosis. In contrast to the paucity of melanin containing cells in cytology, they were abundant in histosections. This indicates the discrepancy in cytologic and histologic morphology of this tumour which may be responsible for missing the diagnosis at first instance and this should be kept in mind while dealing solid tumours of head and neck in infancy.

The radiological studies reveal extensive invasion of this tumour to underlying bones with destruction which also was found in present case, but in contrast the biological behaviour is said to be normal. The nature of MNTI is also controversial. It is well known to be benign in nature but the rapid expansion can be destructive and is harmful for the patient. Approximately 1% of tumours are malignant, only rarely producing metastasis [12]. Yoo et al., recently described a case of malignant MNTI in a 28-month-old female child where metastatic deposits were

found in inguinal sac [13]. This might have occurred due to the ventriculoperitoneal shunt undertaken at eight-month-old as she was born with hydrocephalus. She also had unusual presentation of congenital melanosis with multiple large congenital nevi. Genetic and molecular studies are not yet established in MNTI. Khoddami M et al., performed tests in three cases to establish relationship between small round cell tumours like neuroblastoma and others with MNTI. They detected MYCN gene amplification and deletion of 1p in all 3 cases and presence of the t(11;22)(q24;q12) and the t(11;22)(p13;q12) translocations in 2 of 3 cases . But, there was no genetic basis to link melanotic neuroectodermal tumour of infancy to neuroblastoma, Ewing sarcoma/peripheral primitive neuroectodermal tumour, or desmoplastic small round cell tumour [14].

CONCLUSION

Melanotic neuroectodermal tumour of infancy is a rare osteolytic pigmented tumour of neural crest origin. It commonly involves maxilla in infants during first few months of life. Though benign in nature it usually is rapidly locally invasive and infrequently it may metastasize. It is important for the surgeons and pathologists to keep it as a differential diagnosis while dealing with a small round cell tumour of infants and young children especially involving the head and neck region.

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PARTICULARS OF CONTRIBUTORS:

1. Associate Professor, Department of Pathology, S.C.B. Medical College, Cuttack, India.
2. Assistant Professor, Department of Pathology, S.C.B. Medical College, Cuttack, India.
3. Assistant Professor, Department of Pathology, S.C.B. Medical College, Cuttack, India.
4. Post Graduate, Department of Pathology, S.C.B. Medical College, Cuttack, India.
5. Senior Resident, Department of Pathology, S.C.B. Medical College, Cuttack, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Asaranti Kar,
QRS. No.-JO-1, S.C.B. Medical College, Cuttack-753007, India.
E-mail: asarantikar@yahoo.co.in

FINANCIAL OR OTHER COMPETING INTERESTS: None.

Date of Submission: **Feb 24, 2015**
Date of Peer Review: **May 20, 2015**
Date of Acceptance: **Jul 05, 2015**
Date of Publishing: **Sep 01, 2015**