Melanotic neuroectodermal tumor of infancy: A rare case report

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Abstract
Melanotic neuroectodermal tumor of infancy (MNTI) is a rare benign but locally aggressive neoplasm of neural crest origin with a high recurrence rate. It usually affects infants of <1 year of age. Involvement of maxilla of an infant is the most common presentation although cases outside this setting have been reported. We report the case of a 6-month-old male child presenting with intraoral swelling. Radiologically, a tumor was detected in the right maxilla, and wide local excision was done. Histological examination revealed typical biphasic population of cells with deposits of melanin pigment. Immunohistochemistry study was done confirming the diagnosis.

Keywords: Benign tumor of infancy, melanotic epithelial odontome, melanotic neuroectodermal tumor of infancy, melanotic progonoma, pigmented ameloblastoma, retinal anlage tumor, vanillylmandellic acid

INTRODUCTION
Melanotic neuroectodermal tumor of infancy (MNTI) is a rare benign pigmented tumor that most commonly presents in the 1st year of life. It is predominant in boys[1,2] and favors the premaxilla.[2] It is also known as congenital melanocarcinoma, melanotic epithelial odontome, melanotic ameloblastoma, retinal anlage tumor, melanotic progonoma, pigmented adamantinoma, congenital pigmented epulis and melanocytoma. Other known sites of this tumor include the mandible, brain, mediastinum, thigh, epididymis, foot and shoulder. Similar to other tumors of neuroectodermal origin, such as neuroblastoma and pheochromocytoma, MNTI is frequently associated with elevated urinary excretion of vanillylmandelic acid (VMA), a metabolite of epinephrine and norepinephrine. Although an increase in VMA is helpful, this symptom alone is not diagnostic of MNTI.[3,4]

The treatment of choice for this tumor is surgical excision. Because of its relatively high recurrence rate (as high as 45%), cases of MNTI should be monitored closely during the postresection period and beyond. Although locally invasive, the risk of tumor metastasis is approximately 5%. The benefits of adjuvant chemotherapy and radiation therapy to prevent recurrence of the tumor are unproven.[3‑5]

CASE REPORT
A 6-month-old male child presented with feeding difficulty and intraoral swelling noticed at 2 months of age. The swelling was progressively increasing in size. No history of
fever, cold and cough. The child was immunized adequately for the age with no delay in developmental milestones. General examination was unremarkable except for the presence of mild pallor.

On local examination, the swelling was well-defined measuring 3 cm × 2 cm, firm in consistency with smooth overlying
surface. The swelling was nontender and nonpulsatile. The swelling did not bleed on touch. No abnormality was found on systemic examination. A plain radiograph of skull revealed a lytic lesion in the maxilla. On CT scan, an expanded soft-tissue swelling in the right maxillary antrum was noticed. Expansion of the involved bone was seen. Chest radiograph was normal. In view of the above findings, 24 h urine sample was sent for the estimation of VMA, which was found to be normal. Wide local excision of the tumor was done and sends for histopathological examination.

Grossly, the specimen received measures 4 cm × 3 cm × 2 cm and on the serial section, cut surface showed tumor measures 2 cm × 2 cm × 1.5 cm with attached tooth measures 0.6 cm × 0.5 cm × 0.5 cm. The cut surface of tumor showed heterogeneous gray-black appearance. On microscopic examination, the tumor was composed of cells arranged in alveolar pattern separated by fibrovascular stroma [Figure 1]. Two distinctive types of cells were seen – large cells arranged peripherally with abundant cytoplasm, round vesicular nucleus and brown pigment; and small cells with scanty cytoplasm and hyperchromatic round nuclei were seen in the center [Figure 2]. Histological features were consistent with a small round cell tumor favoring melanotic neuroectodermal tumor of infancy. Immunohistochemical studies were done for confirmation. Cytokeratin, [Figure 3] MELAN-A and HMB45 [Figure 4] were positive in large cells and negative for small cells. Neuron-specific enolase (NSE) [Figure 5] and synaptophysin [Figure 6] were positive in small round cells and negative in large cells. S100, CD99, LCA were negative in large and small cells. Thus, a final diagnosis of MNTI was made by correlating HPE and immunohistochemistry (IHC) findings. This case was followed up for the next 6 months without any recurrence.

**DISCUSSION**

Krompecher first described the tumor as “congenital melanocarcinoma” in 1918. Since then it has been known by a variety of names. Borello and Gorlin suggested the term “Melanotic Neuroectodermal Tumor of Infancy” which has now been universally accepted. It frequently involves the maxilla of infants <1 year of age with a moderate predominance in males. Occasional reports in adults have been widely believed to be misdiagnoses. Extramaxillary locations reported include the mandible, skull, long bones, epididymis, mediastinum, soft tissues of extremities and cheek and even brain.

MNETI was previously thought to be of odontogenic origin, but immunohistochemical and ultrastructural studies, occasional demonstration of neuronal differentiation and VMA production have confirmed the neural nature of this neoplasm. Increased preoperative serum levels of noradrenaline, adrenaline, VMA, and neuron-specific enolase which returned to normal following surgery and chemotherapy have been reported. The variable expression of immunohistochemical markers in different studies suggests that MNETI is a primitive neuroectodermal tumor with polyphenotypic expression of neural and epithelial markers, melanin production, occasional rhabdomyoblastic, glial, ganglionic and osseous differentiation and no photoreceptor differentiation.

There is no typical biological behavior of MNTI. Although it is locally fast-growing and is considered benign, recent studies have indicated that the local recurrence rate following conservative resection is 10%–60%, with 6.5% of cases also showing distant metastasis. Recurrence may occur due to the invasion of the tumor edge into the bone, difficulty in complete resection due to a tumor with no envelope or multicenter growth.

The differential diagnosis of MNTI are listed in Table 1. However, this long list can be reduced to just a few based on the clinical and radiological features.

Conventional radiographs of bony lesions usually reveal radiolucency with or without irregular margins. Typically, computed tomography (CT) scans reveal hyperdense masses, but hypodense variants have also been reported. CT can accurately define lesion extent and thus, provides a good basis for surgical planning. Melanotic neuroectodermal tumors of infancy tend to be isointense on T1-weighted images and slightly hyperintense on T2-weighted images. Furthermore, there may be an inhomogeneous increase in signal on T1-weighted images, which also may reflect intratumoral melanin, whereas T2-weighted images visualize the tumor as isointense or hypointense to gray matter. Contrast enhancement is usually quite marked.

| Table 1: The differential diagnosis of Melanotic neuroectodermal tumor of infancy |
|-----------------------------------------------|
| **The differential diagnosis of Melanotic neuroectodermal tumor of infancy includes** |
| **Category** | **Condition** |
| Developmental cysts | Nasopalatine cyst, globulomaxillary cyst |
| Odontogenic lesions | Odontoma, ameloblastoma, ameloblastic fibroma, odontogenic myxoma, adenoameloblastoma, odontogenic keratocyst |
| Nonodontogenic nonneoplastic lesions | Central giant cell granuloma, fibrous dysplasia, and arteriovenous malformation |
| Nonodontogenic neoplastic lesions | Rhabdomyosarcoma, Burkitt’s lymphoma, Langerhans cell histiocytosis, Ewing sarcoma |
Characteristically, histology of the lesion shows dual population of cells. One is large, polygonal cells resembling melanocytes with brown pigment and the other small, neuroblastic-like round cells with condensed chromatin. This similar feature is noted in the present case. IHC markers are useful in differentiating MNTI from various other small cell tumors of infancy such as embryonal rhabdomyosarcoma in which desmin and myogenin are positive; Burkitt’s lymphoma where leukocyte common antigen is positive and malignant melanoma which gives positivity to HMB45 and S100. In the present case, IHC positivity for HMB45 and NSE indicates melanocytic and neuroblastic differentiation of the tumor cells, respectively, thus confirming the diagnosis of MNTI. [5,6,13]

Complete surgical excision, with negative margins, can be performed without prior biopsy. This approach avoids unnecessary anesthetic risks and reduces lesion manipulation, which is important because it has been reported that tumors appear to grow faster at previous biopsy sites. A conservative approach, consisting of local excision and curettage, has been adopted for the management of MNTI. However, the extent of surgical excision is debatable because these tumors may have the potential to behave in a malignant fashion. [10]

CONCLUSION

Melanotic neuroectodermal tumor of infancy should be included in the differential diagnosis of skull lesions in infants. In summary, the importance of early detection and intervention in cases of MNTI cannot be overstated because of the rapidly destructive and invasive nature of this lesion. As pointed out in this case report, a number of known pathologic entities can present in the oral cavity of infants, but MNTI can be confirmed by its characteristic radiographic and histologic appearance.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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