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Case Report

Melanotic Neuroectodermal Tumor of Infancy: A Case Report and Literature Review

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Abstract

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Melanotic neuroectodermal tumor of infancy (MNTI), first described almost a century back, is of neural crest origin, locally aggressive, a rare biphasic neoplasm of infancy with a slightly higher male preponderance. In the last 100 years since the first description of MNTI, only around 500 cases have been described from 32 countries. We present a 7-month-old female child with 3 × 2 cm hard swelling in the oral cavity and right-side facial region for 3 months. Contrast-enhanced computed tomography scan and contrast-enhanced magnetic resonance imaging scan revealed a hypodense lesion of size 2.5 × 2 × 1.6 cm with relatively well-corticated walls. The lesion appeared to arise from the right maxillary alveolus with erosion of the floor of the maxillary sinus. A 7 × 5 mm tooth was visualized within the lesion. There was minimal enhancement in the postcontrast study. With the following provisional diagnoses—odontogenic keratocyst, dentigerous cyst, and unicystic ameloblastoma—the child underwent excision of the lesion. Intraoperatively, Hopkin's rigid endoscope 4 mm was used to ensure complete tumor removal in the maxillary sinus. Histopathological and immunohistochemistry examination resulted in the diagnosis of MNTI. On 1-year follow-up, the child did not show any signs of recurrence. A high index of suspicion, early diagnosis, and timely treatment are needed to diagnose such a rare tumor, to avoid morbidity, and to plan effective management when an infant presents with facial swelling. It should be complemented with close follow-up to identify recurrence early. Use of endoscope whenever feasible is encouraged by the authors to ensure adequate tumor removal.

Keywords

- biphasic neoplasm of infancy
- Hopkin's rigid endoscope
- infantile neoplasm
- melanotic neuroectodermal tumor of infancy (MNTI)
- vanillylmandelic acid (VMA)

Introduction

Melanotic neuroectodermal tumor of infancy (MNTI), first described almost a century back, is of neural crest origin, locally aggressive, a rare biphasic neoplasm of infancy with a slightly higher male preponderance.[1] MNTI shows a wide geographic variation, however, the highest prevalence of MNTI has been reported from the United States followed by India.[2] Varieties of neoplasms may clinically and radiologically mimic MNTI; however, characteristic histopathological findings aided with immunohistochemistry (IHC)

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studies serve as a cornerstone in the diagnosis of this rare infantile neoplasm.

We report this case considering the rarity of this neoplasm and also to encourage the use of an endoscope whenever feasible for complete excision in recurrence-free survival of the patient. The authors also emphasize the fact that a high clinical suspicion along with characteristic radiological, biochemical, and histopathological findings help in early diagnosis and prompt management of such benign yet locally aggressive neoplasm.

Case Presentation

A 7-month-old female child was brought to the department of otorhinolaryngology by her mother with complaints of swelling in the oral cavity and right-side facial region for 3 months. The swelling was of insidious onset and gradually progressive in nature. It was not associated with any pain, pus discharge and bleeding, or any external skin changes. The child was a known patient of ventricular septal defect (VSD) with mitral regurgitation (MR) on medical management. The patient was born by normal vaginal delivery and was immunized as per age. The child had achieved all developmental milestones as per her age. On examination, the child had stable vitals without any signs of cardiac failure. Local examination revealed fullness on the right-side face and below the right nasal cavity. Oral cavity examination revealed hard swelling of size 3×2 cm in the right upper alveolus and hard palate extending till the midline medially. There was a bulge along the floor in the right nasal cavity. The rest of the examination was unremarkable (►Fig. 1).

The blood investigations of the child were unremarkable. Echocardiography of the child revealed VSD of 5 mm with a left to right shunt and mild MR with normal biventricular function. Contrast-enhanced computed tomography (CECT) scan of the nose and paranasal sinus region and CE magnetic resonance imaging (CEMRI) were advised for the patient. CECT scan revealed a hypodense lesion of size $2.5 \times 2 \times 1.6$ cm with relatively well-corticated walls. The lesion appeared to arise from the right maxillary alveolus with an erosion of the floor of the maxillary sinus. A 7×5 mm tooth was visualized within the lesion. The lesion had obliterated the maxillary sinus and ipsilateral nasal cavity. There was minimal enhancement in the postcontrast study. CEMRI scan revealed well-defined lobulated expansile lesion measuring $2.7 \times 2.1 \times 2$ cm centered in the right anterior alveolar process of the maxilla. The lesion appeared T1/T2 isointense with patchy diffusion restriction on diffusion-weighted imaging. A dental element was noted within the lesion. There was no obvious enhancement on postcontrast study. The following provisional diagnoses were considered—odontogenic keratocyst, dentigerous cyst, and unicystic ameloblastoma. The child was planned for excision of the lesion under general anesthesia (►Fig. 2).

Under general anesthesia the patient was positioned and draped. A right upper sublabial incision was given. The mucoperiosteal flap was elevated. White bony hard swelling was observed. The thin bony covering was broken. Blackish inflamed mucosa present adherent to the maxillary sinus with multiple teeth remnants. The teeth element along with the tumor was removed in piecemeal. Intraoperatively, Hopkin's rigid endoscope 4 mm was used to ensure complete tumor removal in the maxillary sinus. Hemostasis was achieved and the right maxillary sinus was packed with gelfoam soaked with metronidazole antibiotic solution. The mucosal flap was closed with 3-0 Vicryl suture. The

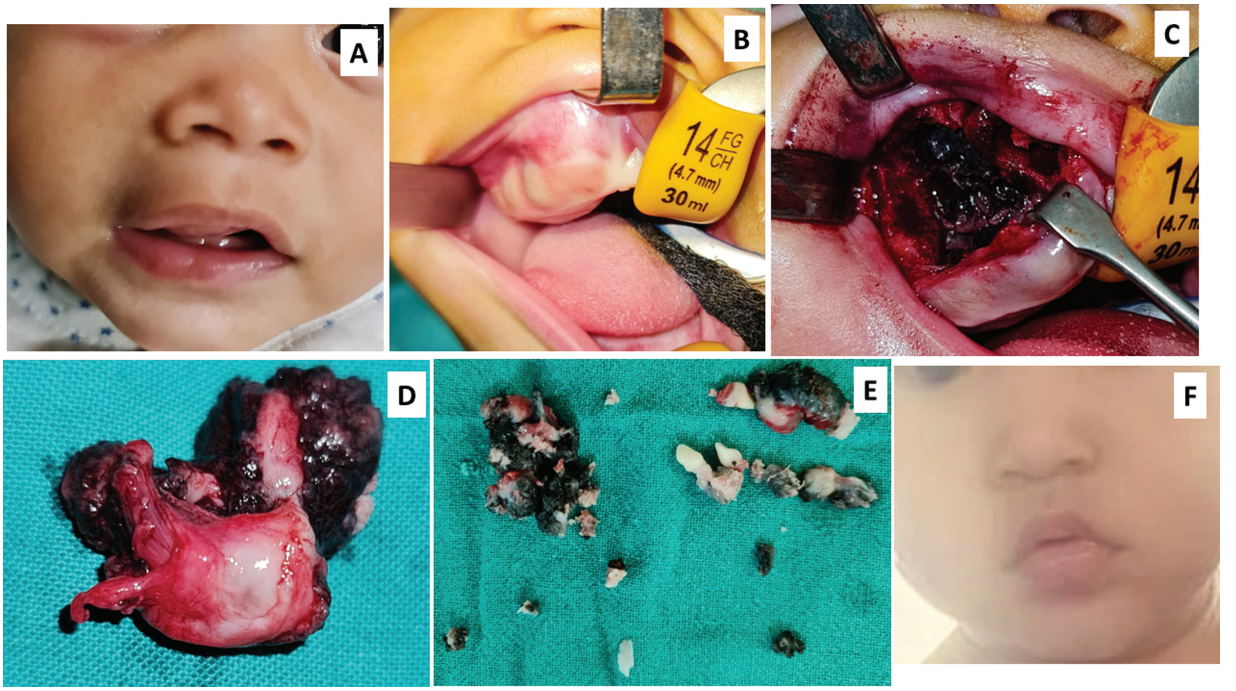

Fig. 1 (**A**) right facial swelling. (**B**) Tumor site involving right alveolus and hard palate. (**C**) Dark brown tumor in situ. (**D** and **E**) Fleshy parts, dark brown parts, and teeth elements from the tumor after removal. (**F**) Child at 12 months' follow-up without any facial swelling.

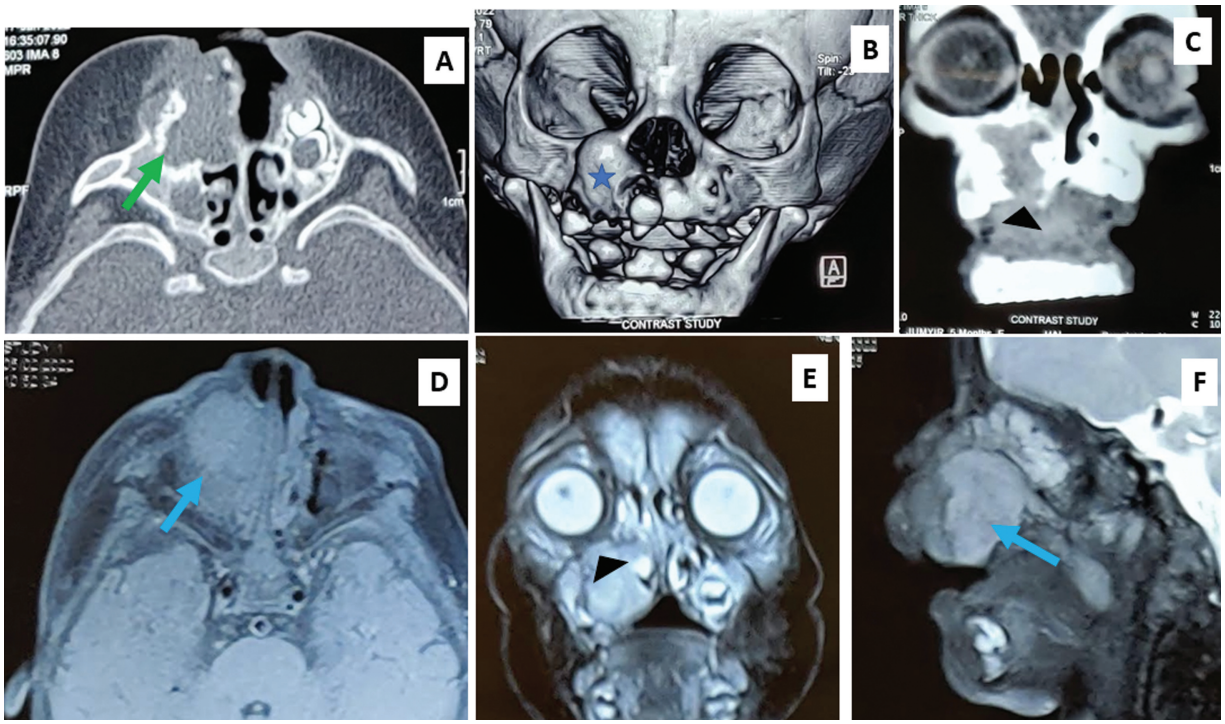

Fig. 2 (**A**) Axial section computed tomography (CT) scan demonstrates tumor obliterating right maxillary sinus (green arrow). (**B**) Three-dimensional (3D) reconstructed computed tomography scan shows the extent of the tumor (blue star). (**C**) Coronal section CT scan causing erosion of right hard palate (black arrowhead). (**D**) T1-weighted axial section magnetic resonance imaging (MRI) scan demonstrating the tumor obliterating the right nasal cavity (blue arrow). (**E**) T2-weighted coronal section MRI scan showing tumor abutting the right orbit (black arrowhead). (**F**) Sagittal section T2-weighted MRI scan shows lobulated tumor (blue arrow).

child was extubated, and an infant feeding tube was inserted. The feeding tube was removed after 48 hours and the post-operative period was uneventful.

On gross examination multiple fragmented tissue bits were noted, the largest bit measuring 2.5 × 1.5 × 1 cm with many smaller remnants measuring around 1.5 × 1 cm each along with dental elements. Histopathological examination revealed tumor cells arranged in predominant cord and trabecular pattern and occasional nests in a dense fibroblastic stroma. The tumor showed a biphasic pattern with small round cells surrounded by larger epithelioid melanin-containing cells. Entrapped cords of odontogenic cells in the stroma were seen. No mitosis or necrosis was noted. On IHC, HMB45 was strongly positive in melanin-containing epithelioid cells. Synaptophysin was positive in smaller cells (►**Fig. 3**). Correlating with the histomorphology and IHC findings a diagnosis of MNTI was made. On 12 months' follow-up following surgery, the child is doing well without any signs of recurrence of the tumor.

Discussion

Rarity of the Tumor

In the pediatric population, head and neck tumors are rare constituting to only 2 to 5% of all pediatric neoplasms.[3] Primary tumors of the jaw are uncommon in pediatric population with the exact incidence estimation being difficult owing to different definitions of pediatric age groups.[4] The World Health Organization classified MNTI under "Other jaw tumor type."[3] The first description of the MNTI was by Krompecher in 1918 and its origin was initially unknown.[2] Recently, the origin of the tumor is believed to be from the neural crest cells.[2,5] In the last 100 years since the first description of MNTI only around 500 cases have been described from 32 countries.[2,6]

It commonly involves the anterior maxilla (62%), skull (15%), mandible (8%), and rarely peripheral bones, testes, and ovaries.[2,6] In our case the location was the anterior maxilla in a female patient. The tumor is usually benign; however, it can grow rapidly with infiltration of bone, soft tissues, etc. Few reports of malignant MNTI have been reported with a metastatic rate of 3%.[6]

Diagnostic Challenges

On CT scan the tumor's bone destruction will be evident with some components demonstrating hyperdense site due to melanin component. In our scenario, the tumor was hypodense with erosion of floor of the maxillary sinus. On MRI scan the tumor will be usually a well-demarcated hypointense mass on T1-weighted and T2-weighted images.[2,7] In our case it was hypointense. The usual differential diagnosis for anterior maxillary mass in patients will be odontogenic keratocyst, dentigerous cyst, and unicystic ameloblastoma.[8]

MNTIs were considered the only melanotic odontogenic tumors for quite a long period of time; however, odontomas, odontogenic fibroma, and ameloblastic fibroma are some of the melanin-containing odontogenic neoplasms as described by Bhanu et al.[9] The presence of melanin pigment and

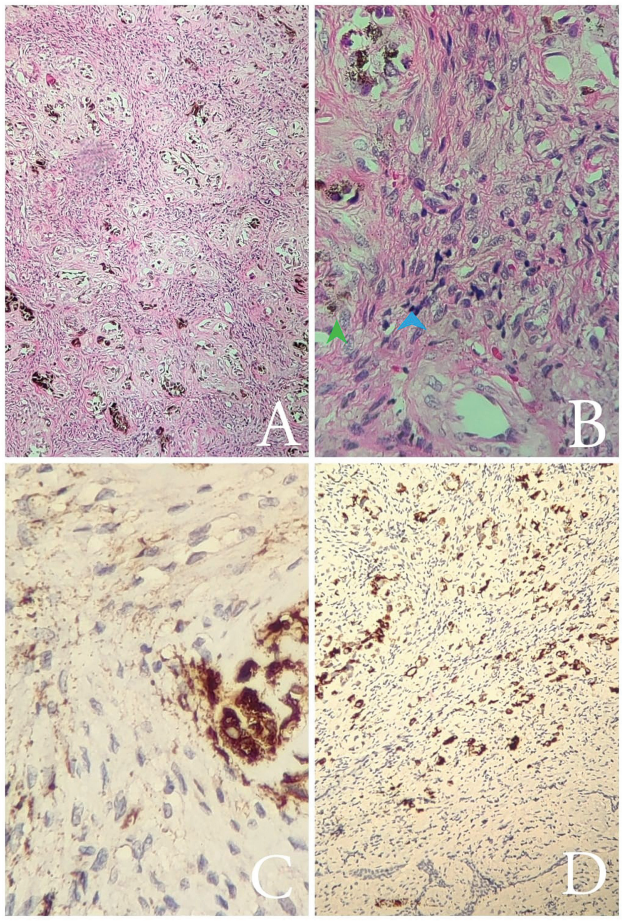

Fig. 3 (**A** and **B**) Histomorphology shows biphasic population of cell with intracytoplasmic melanin. Epithelioid cells are arranged in nests and cords with round nucleus and vesicular chromatin (green arrowhead) admixed with another population of cells arranged in nodular architecture having hyperchromatic small blue nucleus with scant cytoplasm (blue arrowhead) (**A**, hematoxylin, and eosin [H&E], 40×, **B**, H&E, 400×). (**C** and **D**) Immunohistochemistry (IHC) positivity for HMB45 and synaptophysin (IHC, 400×).

characteristic biphasic population of cell is characteristic of MNTI. In our case, various radiological differential diagnoses were ruled out based on histomorphology alone.

IHC positivity for HMB45 in epithelioid cells also substantiated the diagnosis of MNTI, whereas uniform negativity for SOX10 ruled out ameloblastomas. Histomorphology and IHC thus serve a vital role in the diagnosis of such rare neoplasms.

Therapeutic Options and Outcomes

The commonly described treatment includes curettage and conservative surgery including resection. There is no difference in recurrence rates between both the modality of treatment according to medical literature.[6] Adjuvant treatment modalities like chemotherapy and radiotherapy have been described for recurrent tumors.[5,10] Chemotherapy agents tried are those used for neuroblastomas. They include cyclophosphamide, etoposide, doxorubicin, and vincristine. There are no established protocols for chemotherapy or radiotherapy for such recurrent tumors.[2,11] However, in recurrent cases, surgery is the preferred therapeutic modality.[5,11] Our patient underwent excision under general anesthesia at 7 months' age, and on a 1-year follow-up the patient had no clinical evidence of recurrence. The patient was posted for CT scan but was lost to follow-up. However, the authors opine that a CT scan on follow-up would have carried more benefits than risks to ensure disease-free status and enabled further action if a small lesion is found before it becomes large, complicating the surgical approach. Age at diagnosis has been described as an important prognostic factor for recurrence of disease with age less than 2 months, 2.5 to 4 months, and after 4.5 months having high risk, intermediate risk, and minimal risk, respectively.[6] This finding correlated with our case. The recurrence rate described so far in the literature is less than 20% and most of the recurrences occur within the first 6 months of therapy.[2,6]

Use of Endoscope

At this point, the authors would like to highlight the use of Hopkin's rigid endoscope 4 mm for cavity inspection to ensure complete tumor removal. Given the small operating field and small patient, the use of an endoscope greatly aids in the surgery. The inaccessible areas like the superior and posterior walls of the maxillary sinus can be best visualized using an endoscope. However, the authors opine that a longer follow-up period with large sample size to evaluate the disease-free status will answer the utility of this modality of management.

Follow-Up

Follow-up of patients is important as the recurrence rate is around 20%.[11] Recurrence increases the morbidity and complicates further surgical resection. Some employ the measurement of urinary vanillylmandelic acid (VMA) levels; however, it can be negative even in recurrent cases.[10] Some employ the use of repeat imaging like CT scan to identify tumor recurrence.[6] The above measures of urinary VMA measurement and repeat imaging may not be possible especially when the patient is from a remote area as in our case. The author recommends that the care givers be counseled about danger signs of recurrence like recurrent swelling, new neurological symptoms, visual disturbance, etc., especially in peripheral center or resource-poor settings.

MNTI as the name implies is predominantly a tumor limited to patients below 1 year of age; however, isolated cases above 1 year are not so uncommon. Kulkarni et al described MNTI in a 2-year-old, Jain et al reports this neoplasm at an unusual age of 10 years, whereas Furtado et al described it in a 13-year-old.[12–15] As more and more cases are getting diagnosed, a clear radiological picture of MNTI in the future is a definite possibility.

Clinical and radiological symptoms are not entirely specific; however, urinary VMA levels are usually elevated except in isolated cases where it appears normal. Complete surgical excision provides the best treatment modality with recurrence-free survival.[2] Nazira et al reported a case of recurrence of MNTI in a 3-month-old child treated by complete enucleation.[16]

Conclusion

A high index of suspicion is needed to diagnose such a rare tumor, to avoid morbidity and to plan effective management when an infant presents with facial swelling. Early diagnosis and timely treatment complemented with close follow-up can reduce the risk of recurrence. Education of care givers to identify any recurrent swelling is of paramount importance as the care givers have the sole responsibility of identifying problems in infants.

Note

The study is reported out after taking proper consent from the patient's caregivers and conforming to the Declaration of Helsinki.

Conflict of Interest

None declared.

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