Melanotic Neuroectodermal Tumor of Infancy with a Negative VMA: A Case Report and Review of the Presentation, Etiology, and Management

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Abstract

Melanotic neuroectodermal tumor of infancy (MNTI) is a rare rapidly growing tumor, which although benign, it is locally aggressive and destructive to the surrounding structures. The maxilla is the most commonly involved site, and MNTI is known to be locally aggressive if left untreated. Neural crest cells differentiate into sympathetic neurons that produce catecholamines. These catecholamines degrade, leaving the residual products homovanillic acid and vanillylmandelic acid (VMA). Because of this, patients with MNTI may have high levels of VMA in their urine and should be tested for this if MNTI is suspected. This is a presentation of a healthy 6-month-old girl with a 1-month history of swelling in the anterior maxilla. A computed tomography (CT) scan revealed a radiolucent lesion of the anterior maxilla, which following biopsy, was histologically diagnosed as MNTI, although the patient had normal levels of VMA. A three-dimensional model was reconstructed from the CT scan and used in planning surgical excision. A differential diagnosis of MNTI should be included in cases of infants presenting with fast growing expansile swelling in the head and neck region.

Keywords ► melanotic ► benign ► tumor ► infant

Melanotic neuroectodermal tumor of infancy (MNTI) is a rare rapidly growing tumor, which although benign, it is locally aggressive and destructive to the surrounding structures. Historically, varying nomenclatures have been used for MNTI, including the following: pigmented ameloblastoma, melanotic progonoma, retinal anlage tumor, melanotic epithelial odontoma, pigmented epulis, melanoameloblastoma, and retinal ameloblastoma. Irrespective of the different terms, MNTI is characterized by its histopathological examination and specific clinical picture. The tumor typically involves the maxilla, however, other sites, such as the skull, mandible, cranial vault, and the extracranial of the mediastinum, long bones of the extremities, and, rarely, the genital organs, have been reported. Most cases occur in the first year of life and present as a solitary, rapidly growing, expansile mass.

Like the neuroblastoma, it is suspected that MNTI has a neural crest cell origin. Neural crest cells differentiate into sympathetic neurons that produce catecholamines. These catecholamines degrade, leaving the residual products homovanillic acid and vanillylmandelic acid (VMA). Because of this, patients with MNTI typically have high levels of VMA in their urine and should be tested for this if MNTI is suspected. It is rare that the histologically confirmed MNTI have a negative urine VMA.

If MNTI is suspected, biopsy should be performed and if histologically proven should then be treated in a timely manner.
with surgical resection to control any further local invasion and structural deformation, regardless of the VMA findings.

**Clinical Report**

A healthy 6-month-old Hispanic female presented to the emergency department with a complaint of bleeding and swelling from the anterior maxilla associated with an erupting and clinically visible tooth #F. The parents had first noticed swelling in the gingiva associated with erupting tooth #F around 1 month prior to presentation. At this time, the parents had taken the child to another facility where they were given a diagnosis of eruption cyst with no further intervention indicated. Approximately 1 month after the initial swelling, the parents noticed the lesion was still enlarging and deforming the maxilla, and with episodes of bleeding. The increased swelling caused feeding difficulties and noticeable facial deformity.

Clinical examination showed a nontender, nonmobile, nonerythematous, nonfluctuant, firm, pigmented lesion of the anterior maxilla (►Fig. 1). A computed tomography (CT) revealed a mass, measuring approximately 2 × 2 cm in size, with expansion of both the labial and palatal cortices (►Fig. 2). The soft tissue was intact, with no ulceration seen from the lesion. Tooth #F was erupted into the oral cavity.

The patient was taken to the operating room, and a biopsy of the tumor was performed under general anesthesia. The specimen removed was approximately 1.7 × 2 cm in size and had a characteristic brownish-black inner surface, raising the suspicion of MNTI (►Fig. 3). Further exploration revealed two additional lesions growing inferior and medial, which were also removed (►Fig. 4). No aggressive removal of the adjacent bony tissues was performed at this time, as the diagnosis was not confirmed.

The patient was discharged on postoperative day 1. The 1-week postoperative checkup was uneventful, and the patient was seen to be tolerating feeds with no issues. The histology of the lesion revealed characteristic large epithelioid cells with associated melanin pigment admixed with small hyperchromatic basaloid neuroblast-like cells, confirming the diagnosis of MNTI (►Fig. 5). On clinical examination at the 2-week follow-up, the postsurgical swelling was seen to have resolved, but another suspicious expansile lesion was seen inferior to the previous site. The CT scan was used to print a three-dimensional (3D) model to aid in planning the resection margins (►Fig. 6). The patient was taken back to the operating room for definitive surgery. At the time of this surgery, a straight catheterization was performed to assess for urinary levels of VMA, which was 11.9 mg/g, which is within the normal range of 0 to 25 mg/g. During the surgery, additional foci of lesion were noted beyond the areas demonstrated by the model. It was therefore necessary to remove a greater quantity of bone than was originally planned (►Figs. 7 and 8).
The postoperative period was uneventful, and the patient was discharged to home 2 days following surgery. Good oral feeding was observed prior to discharge. There was no evidence of recurrence during the 6-month follow-up period.

**Discussion**

Melanotic neuroectodermal tumor of infancy was first described by Kompecher in 1918 as a tumor of infancy, and most cases are identified in the first year of life. There are currently less than 400 cases of MNTI reported in the literature; with approximately 65% of them occurring solely in the maxilla. Around 90% of cases occur in the head and neck region, while rare instances have been reported in other areas, such as the mediastinum, long bones of the extremities, and genital region.

There are different opinions regarding the origin of this rare tumor. However, the consensus favors a neuroectodermal origin as the root cause. Biochemical analysis corresponding to high levels of urinary VMA found in some patients with MNTI supports the theory of a neuroectodermal origin, although does not confirm it. As demonstrated in this case, however, MNTI diagnosis should not be dependent on VMA levels as not every patient with MNTI will have increased levels of VMA. Clinical examinations of these patients will frequently reveal a pigmented neoplastic growth. If the lesion affects the tooth-bearing alveolus of the maxilla or mandible, if large enough, will displace the teeth or tooth buds in these areas. Diagnostic studies, such as CT scanning or plain radiography, are useful in delineating the size and extent of local destruction from the tumor, but no confirmatory diagnosis can be achieved from radiographs alone. Clinical assessment with diagnostic biopsy continues to be the basis for MNTI confirmation.

In the case presented here, a 3D model aided in treatment planning the amount of bone removal required during the definitive treatment. The accuracy of such treatment planning may come into question as conventional CT scan may not be able to pick up the small satellite lesions as was seen in our patient, but the fact that it can help the surgical team in preparation for the procedure and aid in surgical discussion with family members added a valuable component to the treatment process.
Surgical treatment is the typical treatment modality for MNTI, with some clinicians advocating an en bloc excision of the affected site to safeguard against recurrence.\(^8\) Conversely, because of its benign nature, some authors have advocated conservative treatment with simple local excision and curettage.\(^9\) There is a high recurrence rate of 12 to 31\% with most recurrences emerging within 4 weeks of surgical treatment.\(^7\) This may be due to incomplete resection of the lesion or the difficulty in ensuring a clean surgical margin.

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Conclusion

In our case, the initial surgical treatment was simple local excision with nonaggressive curettage for confirmatory biopsy. By the time the second and definitive surgical treatment was performed, 3 weeks later, there was already additional expansion of either recurrent or previously nonexcised lesions into the previous surgical site. The use of a 3D-printed model created from the CT scan offered an alternative way to discuss treatment plan with the patient's family, aided in the surgical planning, and in visualizing the amount of aggressive bone resection needed to be done to achieve clear surgical margins. Predicting the exact recurrence of this highly aggressive tumor is impossible, and close follow-up should be implemented, especially in the cases treated with simple enucleation and curettage.

Conflicts of Interest
None declared.

References