Mandibular Melanotic Neuroectodermal Tumor of Infancy Treated Conservatively With Enucleation

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Abstract: Melanotic neuroectodermal tumor of infancy (MNTI) is an uncommon, rapidly growing neoplasm of neural crest origin that primarily develops in the maxilla of infants during their first year of life. Mandibular lesions are rare and account for about 6% of all cases. Radical surgical excision is usually curative, but patients should be followed up closely because recurrence may occur in approximately 10% to 20% of cases.

In this study, we report a case of mandibular MNTI in a 4-month-old male patient that was conservatively treated with enucleation and curettage and has shown no recurrence 11 years after surgery. Review of the English-language literature revealed that of more than 350 cases of MNTI reported so far, only 23, including the present one, have been encountered in the mandible. Most patients (91.3%) were younger than 1 year, whereas the male-to-female ratio was 1.3:1. Most lesions were treated with wide surgical excision, with only 2 cases being conservatively treated with enucleation. Recurrence was noted in 36.8% of cases at less than 3 months postoperatively.

In conclusion, MNTI lesions in the mandible, albeit rare, show high recurrence rate. However, small-size mandibular MNTI lesions may be successfully treated with conservative enucleation. Close follow-up is highly recommended, in particular during the first 6 postoperative months.

Key Words: Enucleation, infant, mandible, melanotic neuroectodermal tumor of infancy

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Initially described in 1918 by Krompecher,[1] melanotic neuroectodermal tumor of infancy (MNTI) is a rare lesion of neural crest origin that primarily affects infants during their first year of life.[2–5] Most MNTI cases arise in the maxilla, although occurrence in other intraosseous and extraosseous anatomic locations has been described, including the skull, epididymis, testis, and mediastinum.[2–5] Of more than 350 cases reported in the English-language literature between 1918 and 2009, only 22 have been encountered in the mandible, and most of them have been treated with surgical excision.[2–7]

Herein we describe an additional mandibular case of MNTI that was successfully treated with enucleation and curettage and has shown no evidence of recurrence 11 years after surgery. A review of the English-language literature regarding the clinical characteristics, treatment modalities, and therapy outcome of mandibular MNTI cases is also presented.

CLINICAL REPORT

A 4-month-old male infant was referred to the Division of Oral and Maxillofacial Surgery, School of Dentistry, University of Minnesota, for evaluation of a painless mandibular mass, first noticed by his parents 1 week before. His medical history was noncontributory.

Clinical examination showed a 1 × 1-cm well-circumscribed, sessile, nontender, firm mass involving the labial aspect of the right mandibular alveolar ridge (Fig. 1). The overlying mucosa was intact. The clinical features were consistent with an eruption cyst, and aspiration was attempted, but only a small amount of blood was extorted. A computed tomography scan revealed a well-defined, unilocular, osteolytic lesion that had caused expansion and destruction of the buccal cortical bone with displacement of the developing right mandibular deciduous canine (Fig. 2). Based on the clinical and radiographic characteristics of the lesion, a provisional diagnosis of MNTI was rendered. Routine laboratory tests were within normal limits.

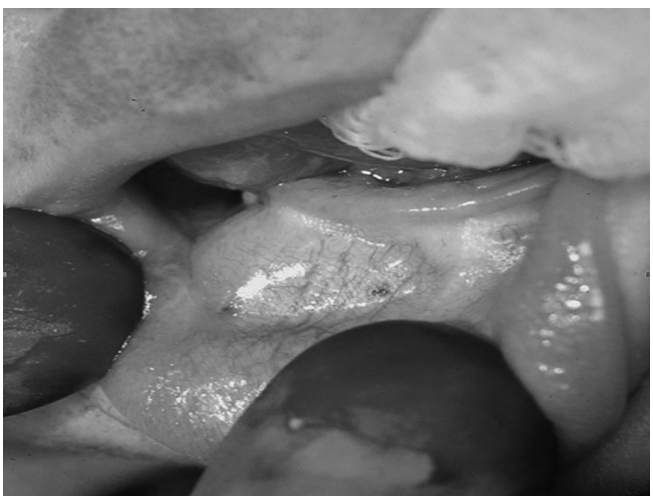

FIGURE 1. A well-circumscribed and sessile mass covered by normal mucosa is seen involving the labial aspect of the right mandibular alveolar ridge.

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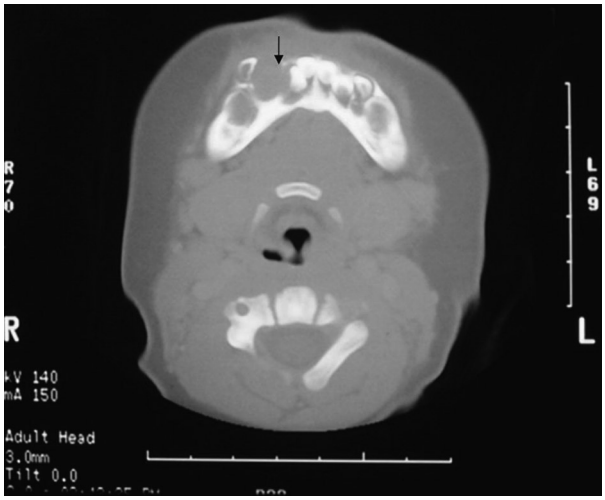

FIGURE 2. Computed tomography scan shows a well-defined unilocular, osteolytic lesion causing expansion and destruction of the buccal cortical bone and displacement of the developing right mandibular deciduous canine.

Surgical excision of the lesion was performed under general anesthesia. A crestal incision was made, and a labial full-thickness flap was reflected, revealing a solid black mass, which was enucleated without difficulty. The bony cavity was carefully curetted and washed. The deciduous canine was extracted, as it was significantly displaced buccally and had no osseous support.

Grossly, black pigmentation was evident in the tumor mass (Fig. 3). Histopathologically, a well-demarcated neoplasm was seen, consisting of a biphasic proliferation of large and small cells that formed nests and cords invested in a fibrous stroma (Fig. 4). The large cells were polygonal and featured ill-defined cytoplasmic membranes, vesicular nuclei with occasionally prominent nucleoli, and variable amounts of intracytoplasmic black pigment, consistent with melanin. The small round cells had scant cytoplasm and basophilic, hyperchromatic nuclei. No features of malignancy, such as nuclear atypia, mitoses, or necrosis, were appreciated. The surgical margins of the specimen were free of tumor cells. The diagnosis of MNTI was rendered.

The postoperative course of the infant was uneventful, and 11 years after surgery, there has been no evidence of recurrence (Fig. 5).

DISCUSSION

Melanotic neuroectodermal tumor of infancy is an uncommon neoplasm that almost always occurs during the first year of life,[2–5] although a few cases have been reported in older patients.[8] The lesion occurs predominantly in the head and neck region (93%) and most commonly in the maxilla (68%–80%).[2–5] A review of the English-language literature between 1918 and 2009 revealed that of more than 350 cases described so far, only 23 cases, including the present one, were located in the mandible (Table 1).[2–17] The mean age of the patients at the time of diagnosis was 10.45 (SD, 26.64) months (range, 1 month to 11 years), whereas the median age was 5 months. Twenty-one (91.3%) of the 23 patients were younger than 1 year, whereas in 18 (78%) of 23 patients, the tumor had developed before the age of 6 months. Thirteen patients were males and 10 were females (male-female ratio, 1.3:1).

Although MNTI is considered a lesion with no sex predilection,[2,5] the results of the present review, albeit restricted to the mandibular cases, showed a slight male predominance. This finding is in agreement with the higher male prevalence of 1.48:1 found by Kruse-Lösler et al[5] in their study of 140 MNTI cases located in various anatomic sites.

Intraorally, MNTI presents as a rapidly growing painless mass with frequent blue or black mucosal discoloration.[5,12]

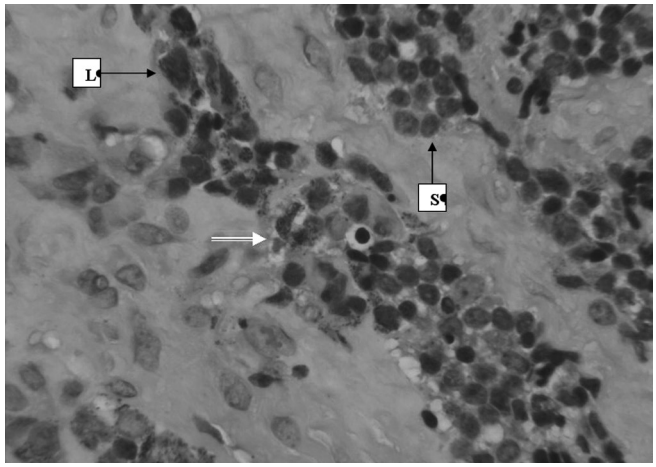

FIGURE 4. Microscopic examination reveals the biphasic cellular population or large polygonal cells (L) and small round cells (S). Melanin pigment is present (white arrow) (hematoxylin-eosin stain, original magnification ×400).

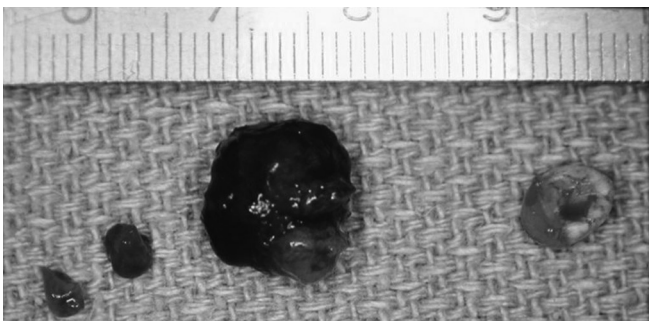

FIGURE 3. Gross examination shows dark pigmentation of the tumor.

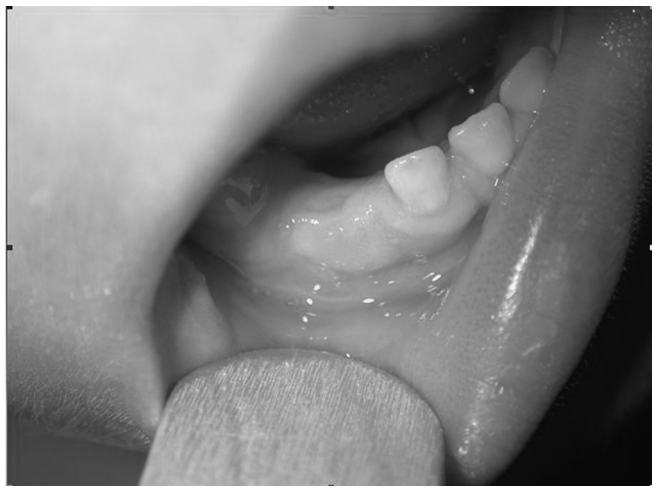

FIGURE 5. The surgical site 7 years after removal of the tumor. At 11 years, there was still no evidence of recurrence.

TABLE 1. Cases of MNTI Located in the Mandible Reported in the English-Language Literature Between 1918 and 2009

Patient	Author	Age, mo	Sex	Treatment	Recurrence/Follow-up
1	Wass, 1948*	5	F	NK	−/2 mo
2	Battle et al, 1952*	1.5	M	RES/HM	+/Soon after surgery
3	Tiecke and Bernier, 1956*	4	M	NK	NK
4	Tiecke and Bernier, 1956*	6	F	NK	NK
5	Kerr and Weiss, 1963*	3	F	NK	−/30 mo
6	Allen et al, 1969*	6	F	NK	−/20 y
7	Baughman, 1978*	2	F	NK	+/1.5 mo after surgery
8	Navas Palacios,[8] 1980	11 y (132 mo)	M	RES/HM	Malignant, died 7 mo after surgery
9	Hupp et al,[3] 1981	5	M	ENU	Lost to follow-up
10	Jerrell and Hill,[9] 1982	2	F	NK	+/NK
11	Melissari et al,[10] 1988	15	M	EXC	−/30 mo
12	Pettinato et al,[11] 1991	3	M	RES	+/3 mo
13	Kapadia et al,[12] 1993	6	F	EXC/CUR	−/3 y
14	Kapadia et al,[12] 1993	5	F	EXC/CUR	−/6 mo
15	Kapadia et al,[12] 1993	6	F	EXC/CUR	−/355 mo
16	Nelson et al,[13] 1995	7	M	ENU	−/18 mo
17	Howell and Cohen,[14] 1996	3	M	RES/HM	+/2 mo
18	Hoshina et al,[15] 2000	1	M	RES/HM at recurrence	+/1.5 mo
19	Eckardt et al,[16] 2001	6	F	RES	−/7 y
20	Barrett et al,[17] 2002	7	M	RES	−/3 y
21	Ahmed et al,[6] 2007	7	M	Preoperative CHE plus RES/HM	−/2 mo
22	Neven et al,[7] 2008	4	M	RES/CHE at 3rd recurrence	+/3 Recurrences at 4 mo, 5 mo, and 1 y after surgery; no recurrence 10 y after chemotherapy
23	Present study	4	M	ENU	−/11 y

*Reviewed by Hupp et al.[3]

MNTI indicates melanotic neuroectodermal tumor of infancy; M, male; F, female; NK, not known; RES, resection; HM, hemimandibulectomy; ENU, enucleation; EXC, excision; CHE, chemotherapy.

Radiographically, bone erosion may be seen initially, but as the tumor grows, bone destruction is evident. In some cases, erupted or developing deciduous teeth may be involved in the lesion, and tooth displacement, as in our case, may be seen.[7,14–16,18,19] Occasionally, slight radiopacities featuring a "sun ray" pattern may be present,[3,7] probably due to mild calcification along vessels.[7]

Because of the rapid enlargement and associated bone destruction, the differential diagnosis includes infections and tumors encountered during infancy, such as Langerhans cell histiocytosis, Ewing sarcoma, rhabdomyosarcoma, osteosarcoma, and malignant lymphoma.[3,5,20] In some patients, elevated levels of urinary vanillylmandelic acid, a finding supportive of the neural crest origin of the tumor, may be of diagnostic help.[2,19] Vanillylmandelic acid levels should return to normal after removal of the tumor.[14,21]

Microscopic examination, revealing the biphasic cell population of large epithelioid cells with intracellular melanin granules and smaller, round, neuroblast-like cells in a variably vascularized fibrous stroma, is usually diagnostic.[5,20] In ambiguous cases, when other pediatric small round cell neoplasms, such as neuroblastoma, rhabdomyosarcoma, malignant melanoma, lymphoma, or Ewing tumor, are considered in the differential diagnosis, immunohistochemical and molecular studies are helpful. Epithelioid cells react for keratins, HMB-45, vimentin, epithelial membrane antigen, and rarely for S100 protein, whereas the small cells principally express CD56 and synaptophysin. Both cell populations are positive for neuron-specific enolase.[5,7,11–15,20] The increased expression of Ki-67 may be correlated with a more aggressive behavior, as has been suggested in cases with malignant transformation.[17] In such cases, increased cellularity, nuclear atypia, necrosis, and hemorrhage are usually seen.[8,11,12]

Treatment of choice for MNTI lesions is wide resection with 5-mm free margins and removal of the involved teeth.[2–24] However, as it was the case in our patient, enucleation may be curative for lesions easily detached from the bone. In extensive, recurrent multifocal lesions, a more aggressive surgical approach with adjuvant chemotherapy before or after surgery may be indicated.[7] Chemotherapy alone[23] and radiotherapy, either alone or in combination with chemotherapy, and resection have also been proposed.[5] Information on treatment modality was available in 16 of the 23 mandibular cases and on follow-up in 20 of the 23 cases. Fourteen cases were treated with surgical resection or excision and curettage, whereas 2 were treated with enucleation. Hemimandibulectomy, either initially or after recurrence, was performed in 5 cases. One patient was unsuccessfully medicated with chemotherapy consisting of isofosfamide, vincristine, actinomycin D, carboplatin, etoposide, and doxorubicin before surgery, due to an initial diagnosis of primitive neuroectodermal tumor.[6] Interestingly, histologic examination of the biopsy specimen after excision showed no signs of small round cells of MNTI that were evident in the initial biopsy. In another patient, a neuroblastoma chemotherapy protocol consisting of vincristine, isofosfamide, carboplatin, and etoposide was used after the third recurrence, and he has been free of disease 10 years

after.[7] In both cases, a reduction of the neuroblast-like cell type of the lesions was noted, perhaps due to the genetic similarity between MNTI and neuroblastoma.[7] Neuroblast-like cells are considered the more aggressive component of MNTI, and as have been shown in previous studies, this population increases in malignant transformation.[8,11,12,20]

In our case, the small size of the lesion and the easy detachment from the surrounding bone were indicative of a benign course. Therefore, when it comes to mandibular lesions, conservative surgical treatment as the first choice is suggested. Radical resection or even hemimandibulectomy may be spared for extensive or recurrent lesions because of the functional and cosmetic disturbance that may cause the patients. Radical surgery of extensive mandibular lesions is more easily performed compared with maxillary lesions.

Local recurrence is seen in approximately 10% to 20% of MNTI cases in general,[2,5] although higher rates rising up to 60% have also been reported.[11,12] Recurrences are thought to result from incomplete excision or diffuse bone marrow invasion by tumor cells because of the lack of a fibrous capsule, tumor dissemination during surgery, or multicentricity of the lesion.[15,22] Of the 19 benign cases of mandibular MNTI with available relevant data, 7 cases recurred in a period of 1.5 to 4 months (mean time, 2.4 months; available data in 5 of 7 cases). Mean age of these patients was 2.35 months (range, 1–4 months; 6 of 7 were <3 months old) as opposed to a mean age of 6.41 months (range, 3–15 months; 11 of 12 were >3 months old) of those who had shown no signs of recurrence in a follow-up period of 2 to 355 months (mean time of follow-up, 80.9 months).

Malignant transformation accounts for 2% to 7% of all reported cases regardless of the site.[3,5] Regional or distant metastasis has been described in less than 5% of malignant cases.[5] Only 1 (4.3%) of the 23 mandibular MNTI cases was malignant,[8] suggesting a lower prevalence than that reported for the skull and the brain.[2–5] So far, no reliable markers for predicting the outcome of MNTI have been defined. Vanillylmandelic acid levels do not seem to correlate with its biologic behavior, but aneuploidy has been associated with an increased risk for recurrence.[11,20]

In conclusion, we reported a rare example of mandibular MNTI that was successfully treated with enucleation. Such treatment should be favored for small mandibular MNTI lesions. Because recurrence develops usually within 3 months and in patients younger than 3 months, close follow-up is highly recommended.

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