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Melanotic Neuroectodermal Tumor of Infancy

William M Carpenter, DDS, MS, Professor, Chairman, Department of Pathology and Medicine, University of the Pacific Arthur A Dugoni School of Dentistry

Updated: Sep 1, 2009

Introduction

Background

Melanotic neuroectodermal tumor of infancy (MNTI) is a relatively uncommon osteolytic-pigmented neoplasm that primarily affects the jaws of newborn infants. The lesion has had an interesting history since its initial description by Krompecher in 1918 as a congenital melanocarcinoma.[1]

For the next 5 decades, the lesion was reported under a variety of different names as succeeding authors attempted to identify the cell of origin. Some of the terms applied to this lesion included pigmented ameloblastoma, retinal anlage tumor, melanotic progonoma, melanotic epithelial odontoma, pigmented teratoma, atypical melanoblastoma, melanotic adamantinoma, pigmented epulis, retinal choristoma, melanoameloblastoma, and retinoblastic teratoma. These terms reflected theories of suspected origin from the odontogenic apparatus, the pigmented anlage of the retina, or the sensory neuroectodermal tissues.

In 1966, Borello and Gorlin reported a case with high urinary excretion of vanillylmandelic acid (VMA), suggesting a neural crest origin, and they proposed the term melanotic neuroectodermal tumor of infancy.[2] Since then, numerous histochemical, immunohistochemical, electron microscopic, and tissue culture studies have supported the neural crest origin and confirmed the preferred term of melanotic neuroectodermal tumor of infancy.

Pathophysiology

Several patients with melanotic neuroectodermal tumor of infancy (MNTI) have demonstrated a high urinary excretion of VMA. This finding adds credence to a neural crest origin because elevated VMA has been reported in neuroblastoma, ganglioneuroblastoma, pheochromocytoma, and other neural crest tumors. However, the presence of urinary VMA is not diagnostic for MNTI.

Frequency

United States

Approximately 200 cases of melanotic neuroectodermal tumor of infancy (MNTI) have been reported in the literature. An exact number is difficult to discern because of the variety of terms that have been applied to the lesion in the past.[3]

Sex

The sexual predilection for melanotic neuroectodermal tumor of infancy (MNTI) is nearly equal, with a male-to-female ratio of 6:7.

Age

Most patients, by some estimates more than 90%, present with the tumor in the first year of life, usually from age 1-6 months. The mean age of patients with melanotic neuroectodermal tumor of infancy (MNTI) is 4.3 months. Although extremely rare, a few cases of MNTI have been reported in adults, notably, a 23-year-old man, a 24-year-old woman, and a 67-year-old woman.

Clinical

History

- Although melanotic neuroectodermal tumor of infancy (MNTI) is classified as a benign lesion, it is often clinically worrisome because of its rapid onset and alarming local growth rate.
- Often, sucking and feeding are impaired secondary to the swelling.
- The patient is usually asymptomatic.

Physical

- The typical melanotic neuroectodermal tumor of infancy (MNTI) begins as a nonulcerated, lightly pigmented, blue or black lesion on the anterior aspalvato da Windows Internet Explorer 8> Subject: Melanotic Neuroectodermal Tumor of Infancy: [Print] - eMedicine Dermatology Date: Fri, 4 Sep 2009 01:07:54 +0200 MIME-Version: 1.0 Content-Type: multipart/related; type="text/html"; boundary="----=_NextPart_000_044B_01CA2CFC.21FE5FE0" X-MimeOLE: Produced By Microsoft MimeOLE V6.00.2900.5579 This is a multi-part message in MIME format. ------=_NextPart_000_044B_01CA2CFC.21FE5FE0 Content-Type: text/html; charset="Windows-1252" Content-Transfer-Encoding: quoted-printable Content-Location: http://emedicine.medscape.com/article/1079412-print

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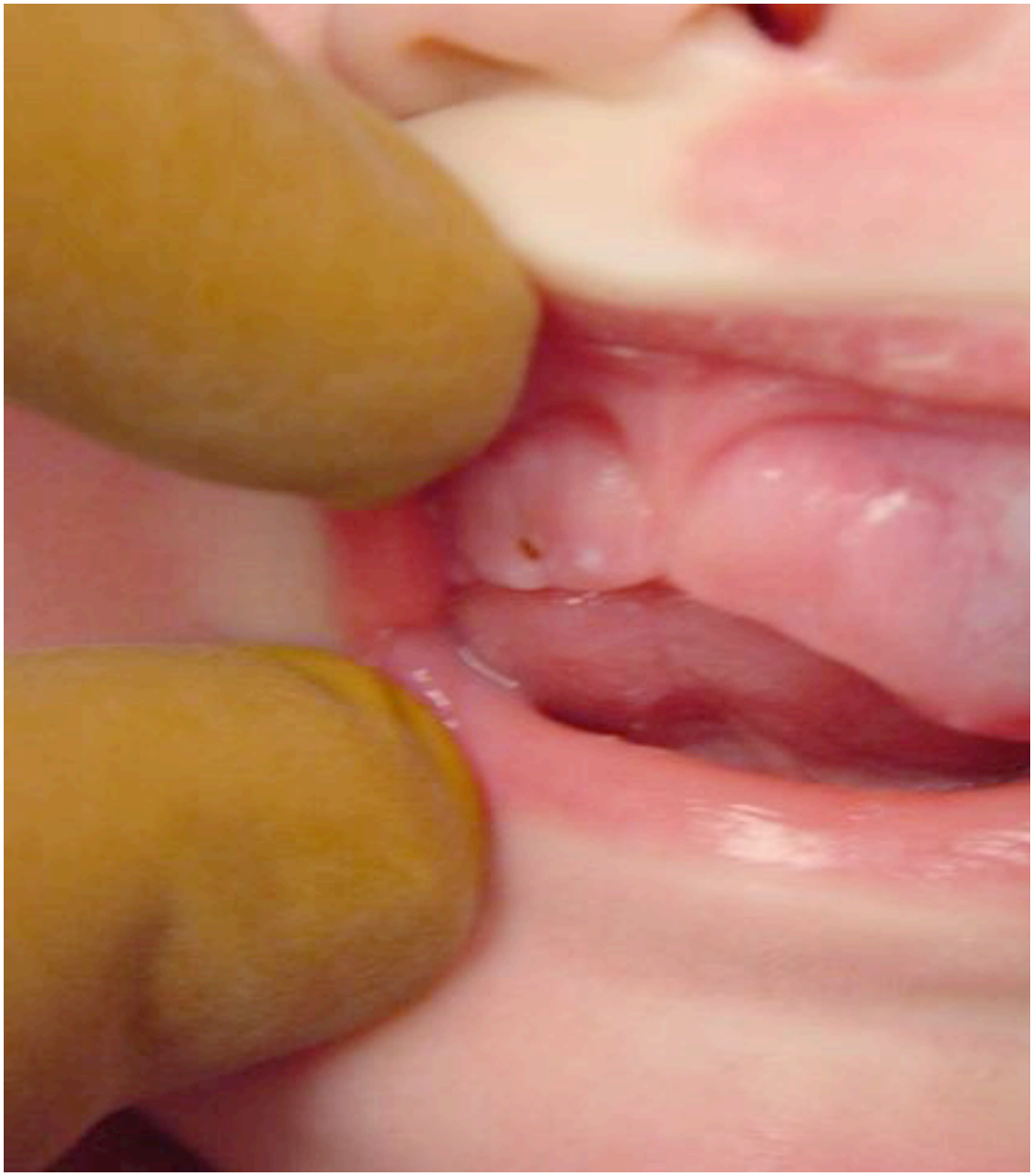
Physical

- The typical melanotic neuroectodermal tumor of infancy (MNTI) begins as a nonulcerated, lightly pigmented, blue or black lesion on the anterior aspect of the maxilla and rapidly expands to form a swelling or a tumescence that is cosmetically obvious to the parents of the infant.



Melanotic neuroectodermal tumor of infancy presents as a rapidly growing bluish mass on the anterior aspect of the maxilla.

- The intraoral lesion appears as a sessile, lobulated mass, often reaching 2-4 cm in diameter by the time of diagnosis.
- Bone destruction and displacement of teeth often occur because of the intraosseous location in the maxilla.
- No thrill or pulse can be elicited from the MNTI. Although the lesion expands rapidly, the overlying mucosa remains intact.
- More than 90% of MNTI occur in the head and neck region, with most on the anterior part of the maxillary ridge. Other common sites include the skull, the mandible, the epididymis, and the brain.[4] Rare lesions have been reported in the shoulder, the skin, the femur, the mediastinum, and the uterus.
- All but 2 of the reported cases have been solitary lesions.

Causes

See Pathophysiology.

Differential Diagnoses

Other Problems to Be Considered

Consider clinical, radiographic, laboratory, and histologic findings when establishing a proper differential diagnosis for melanotic neuroectodermal tumor of infancy (MNTI). The MNTI often presents as a fast-growing lesion, suggesting a clinical impression of infection or malignant neoplasm. The location in the anterior aspect of the maxilla is consistent with a number of odontogenic cysts and tumors; however, the odontogenic cysts (eg, periapical cyst, dentigerous cyst, odontogenic keratocyst, calcifying odontogenic cyst) occur in an older age group, teenaged through middle-aged adults. The same age differential is noted with respect to the more common odontogenic tumors (eg, ameloblastoma, odontoma, adenomatoid odontogenic tumor, calcifying epithelial odontogenic tumor, ameloblastic fibroma, odontogenic myxoma, odontogenic fibroma).

In addition to a diagnosis of MNTI, the young age of the patient as well as the maxillary location is also compatible with a clinical diagnosis of congenital epulis of the newborn. Many nonodontogenic tumors are possible in the jaws, including central giant cell granuloma, ossifying fibroma, fibrous dysplasia, hemangioma, arteriovenous malformation, craniopharyngioma, Langerhans cell histiocytosis, rhabdomyosarcoma, Ewing sarcoma, and lymphoma. However, only Langerhans cell histiocytosis, rhabdomyosarcoma, Ewing sarcoma, and lymphoma are common in young children.

The radiographic appearance of a maxillary alveolar low-density radiolucency, containing no evidence of calcification, is consistent with any of the odontogenic cysts or tumors. Additionally, many of the aforementioned nonodontogenic lesions may also present with a radiographic appearance similar to that of MNTI.

Once a differential diagnosis is established from the clinical and radiographic findings, histologic evaluation is necessary to determine the final diagnosis. The histologic appearance of MNTI is usually that of a small, dark, cell neoplasm suggestive of neuroblastoma, rhabdomyosarcoma, Ewing tumor, lymphoma, desmoplastic small round cell tumor, and peripheral primitive neuroectodermal tumor. Although the histologic appearance is characteristic, special immunohistochemical stains and electron microscopy may be necessary to make a definitive diagnosis.

Workup

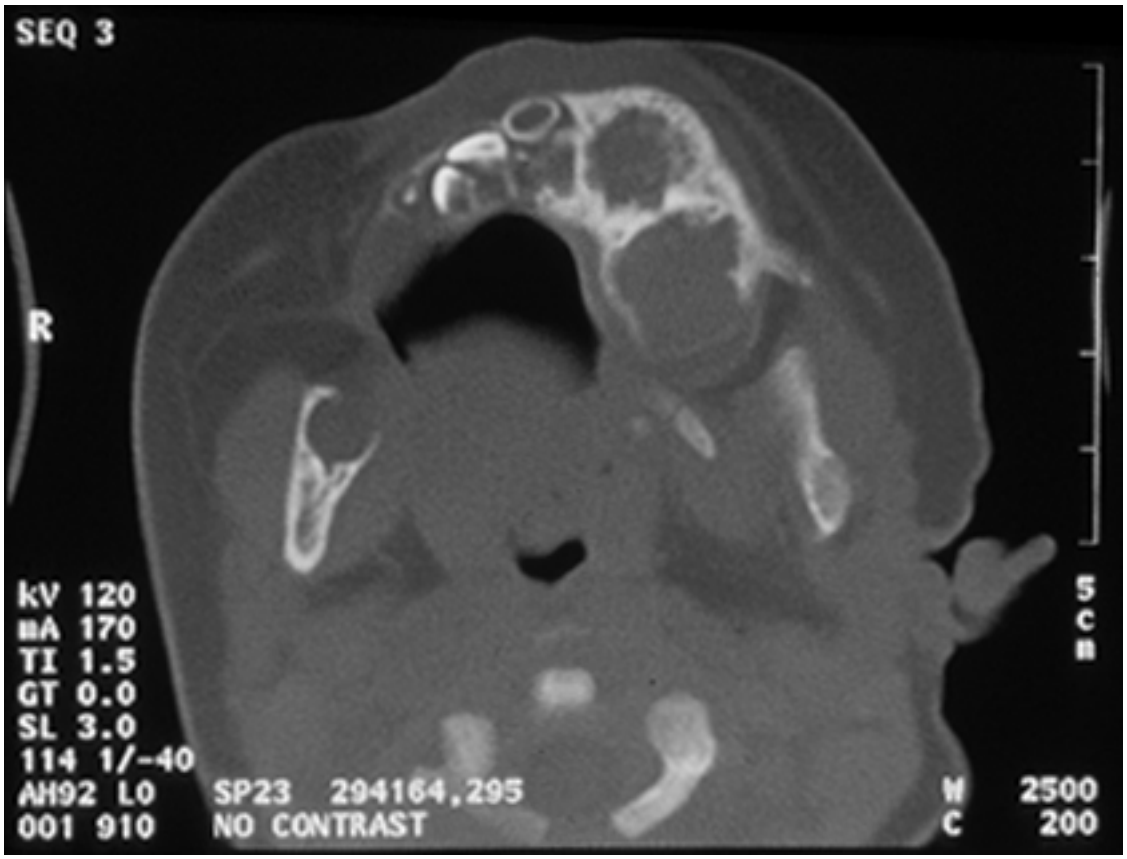
Laboratory Studies

- Typically, the hematologic laboratory values as well as the blood chemistry values are within the reference range. The only noteworthy laboratory value documented in some but not all patients with melanotic neuroectodermal tumor of infancy (MNTI) is an increase in the urinary level of MVA. Elevated MVA has been reported in other tumors of neural crest origin, such as pheochromocytoma, ganglioneuroblastoma, retinoblastoma, and neuroblastoma. As is the case for these lesions, the urinary level of VMA returns to the reference range after surgical removal of a MNTI that has caused elevated VMA. Additionally, no correlation between the presence of elevated VMA and more aggressive or malignant clinical behavior has been shown.

Imaging Studies

- Plain dental radiography, CT scanning, and MRI have been used to evaluate the content and the extent of melanotic neuroectodermal tumor of infancy (MNTI).

- The radiographic appearance of MNTI within bone is a well-circumscribed radiolucency, although diffuse, ill-defined examples have also been reported. The bone is destroyed as the tumor advances, suggesting a malignant process. Although a few cases have been described as multiloculated, most MNTI are unilocular. In its typical premaxillary position, the tumor can displace or destroy the developing deciduous and permanent dentition. The MNTI that occurs predominantly within the marrow spaces of the maxilla and, on plain radiographs, appears as an irregular radiolucency. These characteristics are noted best on maxillary occlusal, sinus views, or periapical images of the involved area.
- CT scanning with intravenous contrast is often used to delineate the margins of osseous involvement.



Axial CT, bone window, noncontrasted scan demonstrates expansile lytic lesion of the left maxilla producing displacement of dental follicles.

- Additionally, MRI with gadolinium contrast can be used to evaluate the bony extent of the lesion. Most MNTI appear as typical soft tissue tumors with nonenhancing heterogeneous tissue density; however, on T1-weighted MRI, for the few MNTI that contain a large amount of melanin, a higher signal intensity often occurs. At no times are flow voids suggestive of a central hemangioma.

Procedures

- Upon completion of the clinical examination of the patient as well as the imaging studies and urinalysis, the definitive diagnosis of melanotic neuroectodermal tumor of infancy (MNTI) is based on the histologic evaluation of a surgical specimen. Grossly, the specimen has a gray, hard, rubbery consistency with foci of blue-black pigmentation. Additionally, entrapped developing tooth buds may be noted in the specimen as MNTI grows in and around the odontogenic apparatus.

Histologic Findings

The histologic appearance of MNTI is unique and characteristic in that a distinct biphasic pattern exists. A moderately vascular fibrous background supports the MNTI. The peripheral borders are faintly noted, at best, by a thin, delicate, fibrous layer; however, most often, this nonencapsulated tumor shows local infiltration into the adjacent bone.

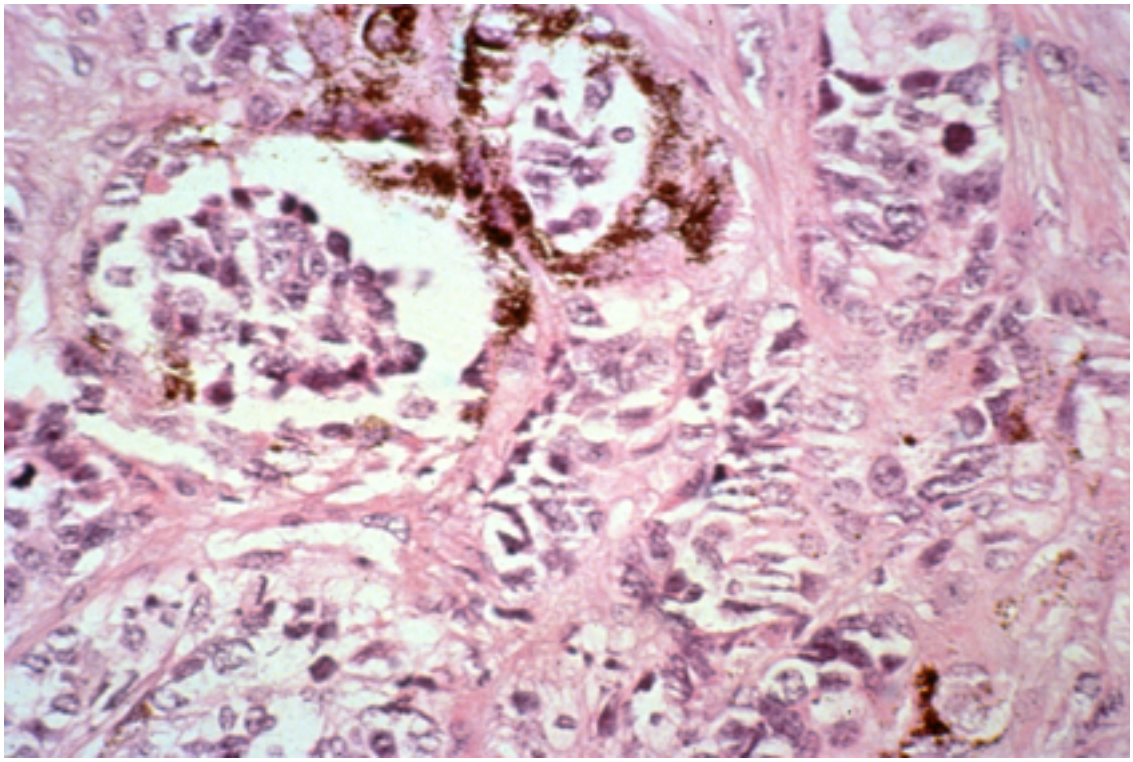
One portion of the lesion contains large polygonal cells arranged in sheets or alveolarlike structures. These large cells appear, under hematoxylin and eosin staining, to have pale abundant cytoplasm and pale nuclei with finely dispersed chromatin. These cells often contain the melanin pigment that gives the MNTI its blue-black clinical appearance.

Fontana stain can be used to enhance the demonstration of the melanin pigment. The cuboidal polygonal cells are at the periphery of the alveolar spaces, while the central portion contains the second smaller characteristic cell type. These cells are lymphocytelike or neuroblastlike with small, dark nuclei and little, if any, cytoplasm. These cells occasionally also form isolated clusters of their own within the fibrous stroma. Throughout the lesion, mitoses are rare but, when present, are normal in appearance. Cellular pleomorphism is scant. The few reported malignant cases of MNTI have little variation from the description above other than an increase in mitoses (3 or more per high-power field), hypercellularity, and focal necrosis.[5] The malignant diagnosis is more one of increased growth rate, infiltration, and metastases. Metastatic lesions have been described in the lymph nodes, the liver, the adrenal gland, the spinal cord, and a variety of other sites.

Immunohistochemistry is of assistance in cases that are more difficult to diagnose. The cuboidal cells express cytokeratin as well as melanoma-associated antigen (HMB-45), but they are usually negative for S-100. Some cells are also positive for vimentin, epithelial membrane antigen, glial fibrillary acidic protein, neuron specific enolase (NSE), and synaptophysin.

Electron microscopic examination demonstrates ultrastructural evidence of neural, epithelial, and melanocytic features. Fine, delicate cytoplasmic fibers are suggestive of neurofibrils, reminiscent of glial tissue. Typically, some of the cells demonstrate neurosecretory granules. Evidence exists of basal laminae and interdigitating desmosomal attachments to adjacent cells, which is suggestive of epithelial features in some cells. Finally, melanosomes are noted in many of the cuboidal cells.

The polygonal cells noted for their melanin production have been cultured in vitro. These cells developed long dendritic processes suggestive of their neural crest origin. Additionally, melanotransferrin expression has been noted with DNA analysis of these cells. The other small, dark, neuroblastlike cells have also been studied; however, to date, no molecular genetic basis to link MNTI to neuroblastoma is apparent.



The biphasic population of cells demonstrates alveolar structures lined by cuboidal epithelioid cells demonstrating granules of dark-brown melanin pigment. The second cell type is neuroblastic in appearance and consists of small, round, hyperchromatic cells.

Treatment

Surgical Care

The treatment of choice for melanotic neuroectodermal tumor of infancy (MNTI) is surgical excision, and it is usually curative. This treatment can usually be accomplished with a partial maxillectomy by using a Weber-Fergusson incision and a facial degloving approach. Teeth, developing teeth, and the adjacent bone must be sacrificed when they lie near the borders of MNTI, since many clinicians advocate that a 5-mm margin of healthy tissue be included with the surgical specimen.[6]

The possibility of local recurrence is a problem that has been documented to range from 10-60% of patients depending on the study quoted. Overall, the average recurrence rate is 15-20%. The recurrent lesions, possibly secondary to inadequate excision or multicentricity, usually become apparent within the first year after surgery. In instances of inoperable recurrence or where clear margins are impossible to obtain, radiation therapy and/or chemotherapy have been used, but too few examples exist for preferences to be established.[7]

Although MNTI is an aggressive benign tumor, malignant variants have been reported, ranging from 1.5% of total MNTI to 2.1% of the maxillary subset.[8] Metastatic spread of MNTI occurs infrequently, in less than 5% of malignant cases. Management of these rare cases is different. Few, if any, parameters exist, either clinically or histologically, to predict the development of metastatic lesions. In a few cases reported as malignant, the histologic features have taken on a neuroblastomalike appearance.

Follow-up

Further Outpatient Care

- Address the documented 15-20% recurrence rate of melanotic neuroectodermal tumor of infancy (MNTI) in the postoperative care by monitoring the patient with physical and radiographic examination at monthly intervals for the first postoperative year.
- Permanent reconstruction of the maxillary alveolus and missing dentition may have to be delayed until after growth is completed, often in the teenage years. In the interim, transitional removable partial dentures may be necessary. The skills of an orthodontist, prosthodontist, oral surgeon, and/or dentist may be required, based on the extent of the missing structures, to correct any functional and cosmetic deformity.

Prognosis

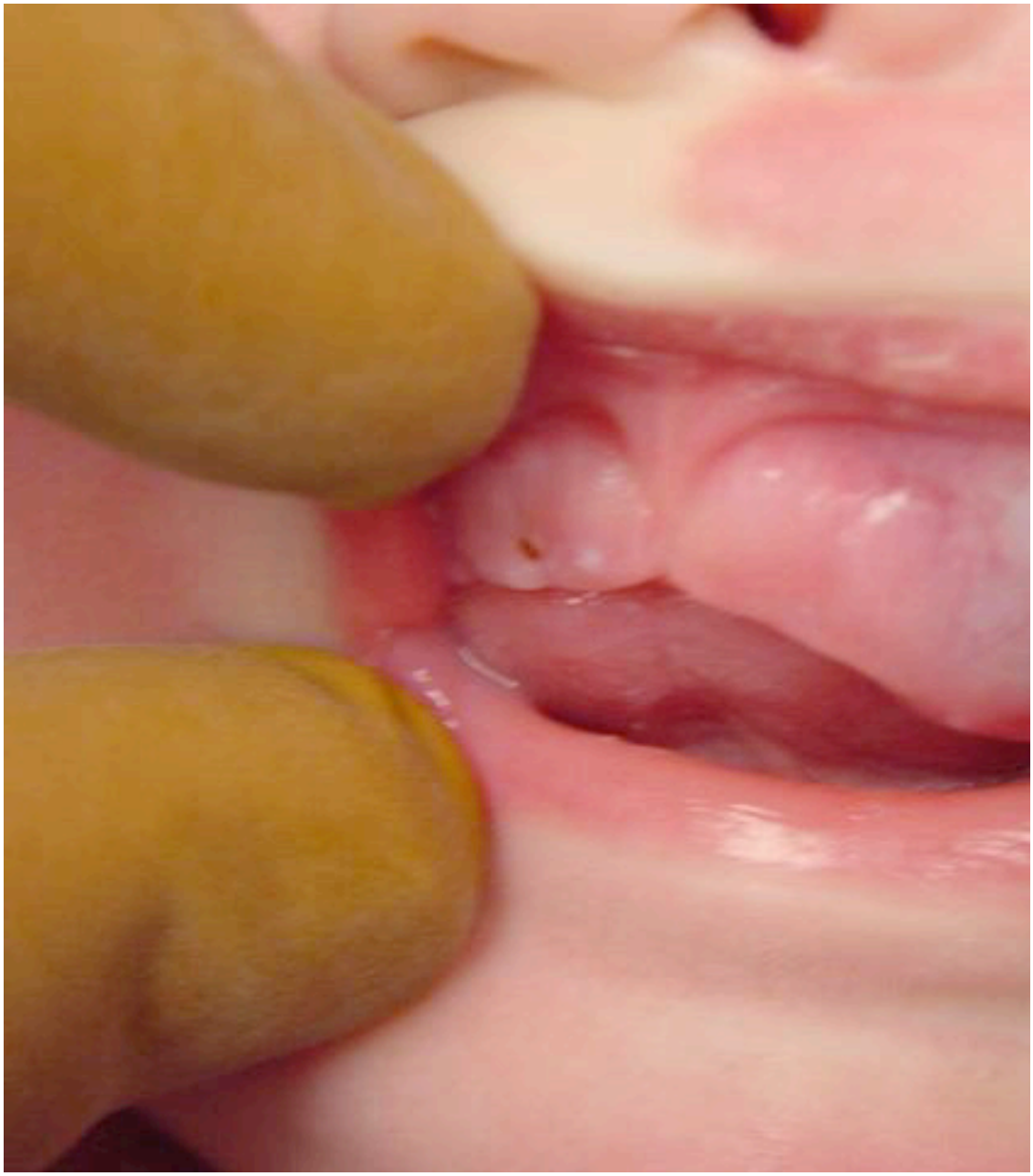
- Most melanotic neuroectodermal tumors of infancy (MNTI) are benign and effectively managed by aggressive surgical excision. Reconstruction may be challenging. Approximately 1% of tumors are malignant, with only rare tumors producing metastases.

Miscellaneous

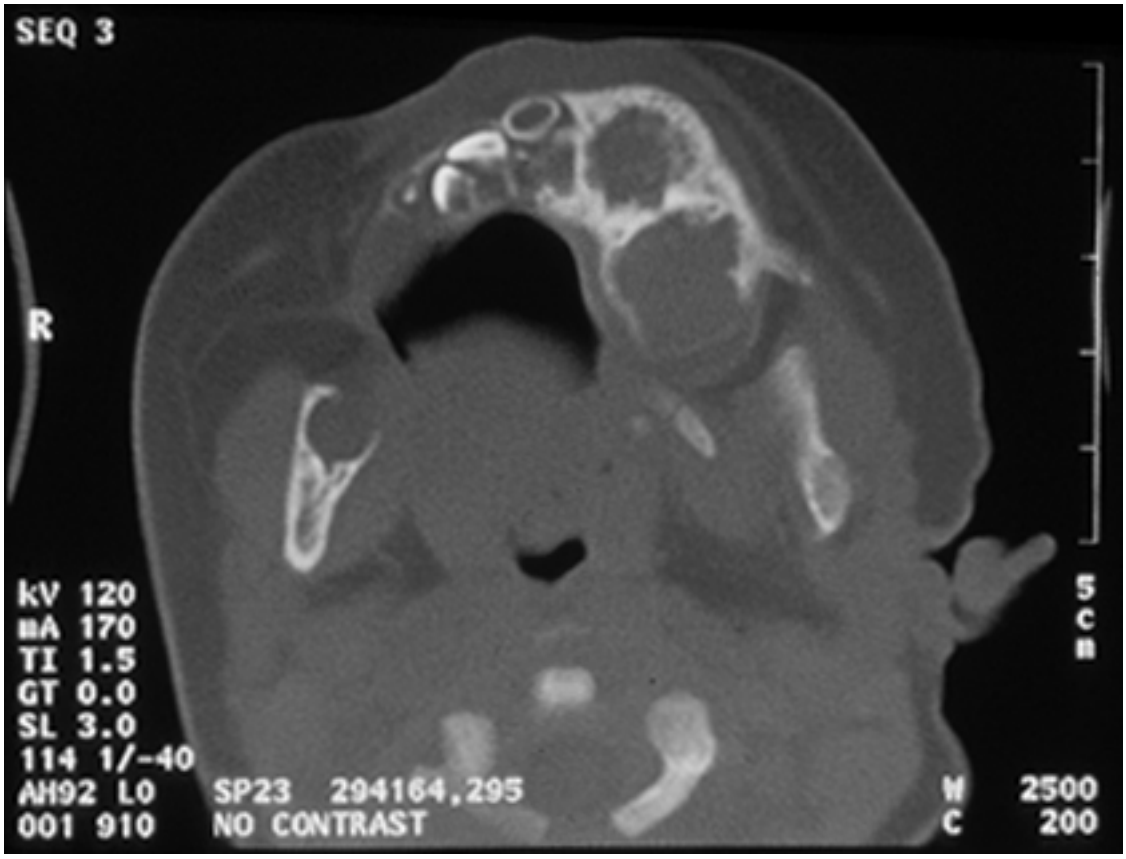
Medicolegal Pitfalls

- The rapid clinical growth rate could lead to the possibility of diagnosing melanotic neuroectodermal tumor of infancy (MNTI) as a malignant lesion with subsequent overtreatment. Care must be taken to obtain a complete workup of the patient and to evaluate the histopathology to prevent this misdiagnosis.

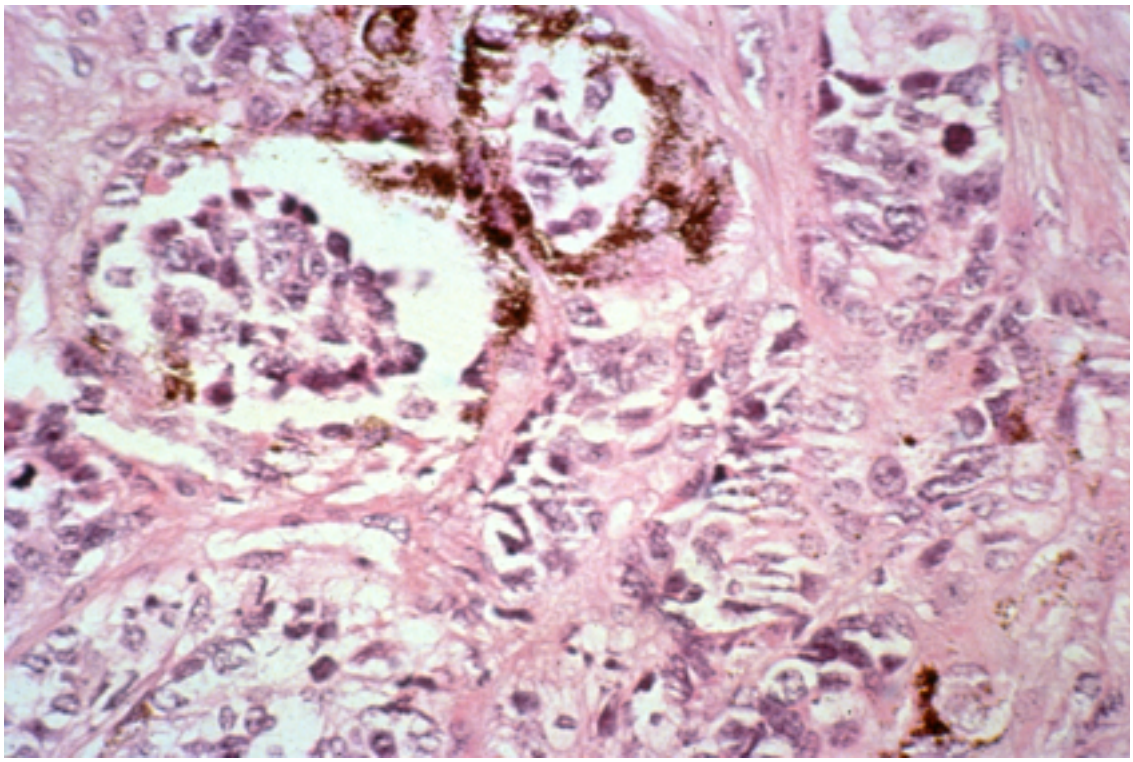
Multimedia



Media file 1: Melanotic neuroectodermal tumor of infancy presents as a rapidly growing bluish mass on the anterior aspect of the maxilla.



Media file 2: Axial CT, bone window, noncontrasted scan demonstrates expansile lytic lesion of the left maxilla producing displacement of dental follicles.



Media file 3: The biphasic population of cells demonstrates alveolar structures lined by cuboidal epithelioid cells demonstrating granules of dark-brown melanin pigment. The second cell type is neuroblastic in appearance and consists of small, round, hyperchromatic cells.

References

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