

Children's Mercy Kansas City

SHARE @ Children's Mercy

Manuscripts, Articles, Book Chapters and Other Papers

1-2021

Melanotic Neuroectodermal Tumor Of Infancy

Mohammad H. Almomani

Rebecca M. Rentea

Children's Mercy Hospital

Follow this and additional works at: <https://scholarlyexchange.childrensmercy.org/papers>



Part of the [Surgery Commons](#)

Recommended Citation

Almomani MH, Rentea RM. Melanotic Neuroectodermal Tumor Of Infancy. In: StatPearls. Treasure Island (FL): StatPearls Publishing; Jan 2021.

This Article is brought to you for free and open access by SHARE @ Children's Mercy. It has been accepted for inclusion in Manuscripts, Articles, Book Chapters and Other Papers by an authorized administrator of SHARE @ Children's Mercy. For more information, please contact library@cmh.edu.

NCBI Bookshelf. A service of the National Library of Medicine, National Institutes of Health.

StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan-.

Melanotic Neuroectodermal Tumor Of Infancy

Authors

Mohammad H. Almomani¹; Rebecca M. Rentea².

Affiliations

¹ Jordanian Royal Medical Services

² Children's Mercy

Last Update: December 27, 2020.

Continuing Education Activity

Melanotic neuroectodermal tumor of infancy (MNTI) is a rapidly growing benign tumor arising from the neural crest cells. It typically affects infants and occurs in the head and neck region. MNTI has a total of 500 cases reported since 1918, and it can cause significant morbidity. This activity reviews the evaluation and treatment of melanotic neuroectodermal tumor of infancy and highlights the role of the interprofessional team in the care of patients with this condition.

Objectives:

- Identify the epidemiology of melanotic neuroectodermal tumor of infancy.
- Review the appropriate steps for the evaluation of melanotic neuroectodermal tumor of infancy.
- Outline the management options available for melanotic neuroectodermal tumor of infancy.
- Summarize interprofessional team strategies for improving care coordination and communication to advance the care of melanotic neuroectodermal tumor of Infancy and improve outcomes.

Earn continuing education credits (CME/CE) on this topic.

Introduction

Melanotic neuroectodermal tumor of infancy (MNTI) is a rapidly growing benign tumor that arises from the neural crest. It typically occurs in infants in the head and neck region. It was described for the first time in 1918 by Krompecher, and since the origin was unknown, it was described as congenital melanocarcinoma. Until 1966, this tumor was characterized by variable names (e.g., retinal anlage tumor, pigmented congenital epulis, melanotic progonoma, pigmented teratoma, atypical melanoblastoma, etc.). However, Borello and Gorlin found that the tumor produces vanillylmandelic acid (VMA), which is produced by other types of tumors that arise from the neural crest. [1][2]

MNTI has had 500 cases reported since 1918. The highest prevalence is in the United States, followed by India. There is a slightly higher predominance in males.[3] Since this tumor rarely metastasizes to distant locations, surgical excision is considered the best treatment. However, local recurrence is common. MNTI is considered a locally aggressive tumor because it has a high growth rate. Even though the neoplasm is considered to be of neuroblastic origin because it produces VMA, it is not a common feature. A recent systematic review of jaw lesions found that only 35% of cases had high VMA levels.[1][4]

Etiology

Melanotic neuroectodermal tumor of infancy is a rare neoplasm of neural crest cell etiology. Also, its microscopic features are consistent with this theory, as it appears as biphasic clustered cells.[1] On the genetic and molecular levels, there are few studies on MNTI. Oncogenic BRAFV600E mutation, which was previously known to be associated with melanoma, was reported in 3 cases of femur MNTI lesions.[5]

Another case report of MNTI arising in the fibula was found to have a mutation of CDKN2A on chromosome 9 and RPLP1-C19MC fusion.[6] Also, a molecular analysis of a recurrent case of the mandible detected loss of heterozygosity of chromosome 1p and gain of chromosome 7q, both of these mutations are present in neuroblastoma as well.[7] These demonstrate the need for additional molecular and genetic analysis of this tumor, which will lead to a better understanding of its behavior and hence better treatment protocols that depend on personalized medicine.[8]

Epidemiology

MNTI is a rare tumor. According to the recent systematic reviews, there are only around 500 cases reported worldwide, with the highest reports from the United States, followed by India, Germany, and Brazil. Only 32 countries in the world reported MNTI cases. The prevalence of MNTI is slightly higher in males than females (1.3 to 1). Most reported cases are located in the head and neck region of infants with a mean age of 6.5 months. The maxilla (62%) is the most common site for this neoplasm, followed by the skull (15%) and the mandible (8%). However, in rare cases, it could arise in different locations other than the head and neck, such as ovaries, testis, femur, and others. [3][9]

The metastasis rate for this neoplasm is approximately 3%. This neoplasm is a fast-growing tumor, leading to an aggressive compression of adjacent structures. So, the excision of the tumor is the most common modality of treatment, and local recurrence was 20%.[9]

Pathophysiology

MNTI was thought to be a congenital neoplasm of melanocytes. However, this theory was rejected because neuroblast-like cells were reported histologically, which is not consistent with this description. Another theory states that this neoplasm could arise from retina stem cells. Still, this theory doesn't agree with the location of these lesions since retinal development completes before the jaw, so this theory is not acceptable either.

Odontogenic origin does not explain the lesions in non-head regions. The last and the most acceptable theory proposed that this neoplasm originates from the neural crest, immunohistochemical, and ultramicroscopic findings (see below) support this theory and make it the only logically justifiable one.[1][10][11] A published study on 2 cases suggested that M2 macrophage cells may play a role in the pathogenesis and modeling of this tumor.[12]

Histopathology

Under microscopy, two different types of cells are visualized in MNTI supported by dense fibrous stroma. The characteristics of these cells are the following:

- Large melanin-containing epithelial cells: These epithelial cells, which can be cuboidal or polygonal in shape, are larger than the other type of cells. They are usually found on the periphery of the clustering that is formed by the two types of cells. These cells usually have granules of melanin contained in the large eosinophilic cytoplasm. These cells are positive for NSE, vimentin, cytokeratins, human melanoma black-45 (HMB-45), and dopamine beta-hydroxylase (DBH). Also, these cells can be positive for synaptophysin and epithelial membrane antigen. Rare cases have been reported positive for S100.[8][13][14]
- Small neuroblastic cells: These cells are small basophilic cells, with a small amount of cytoplasm, located in the center of the clustering of cells. These cells are positive for NSE, vimentin, and synaptophysin. Occasionally, this group of cells are positive for glial fibrillary acidic protein (GFAP) and rarely for neurofilament and CD99. Only a few cases have reported positive for S-100, but they are negative for cytokeratins.[8][13][15]

History and Physical

MNTI presents as a fast-growing, painless, bluish swelling in infants less than 12-months old. Due to its rapid enlargement, this lesion causes facial asymmetry but is otherwise asymptomatic. The most commonly reported location for this lesion is the maxilla and skull. The mean size for MNTI is 3.5 cm; however, the size of the largest reported lesion is greater than 20 cm. While males have slightly higher predominance, in older age cohorts >3 years of age, females have a higher prevalence.[9]

MNTI presenting on the skull or intracranially usually have a benign behavior similar to that of lesions that arise in the jaw. However, symptoms may differ based on presenting location, such as seizure, increasing intracranial pressure, and neurologic dysfunction.[9][16] Although MNTI is most frequently located in the head and neck, it can be present in unusual locations, such as ovaries, femur, mediastinum, and shoulder, etc.[17][18][19][20] Although MNTI is locally aggressive and fast-growing, it rarely (3%) metastasizes to distant locations.[21] A systematic review of jaw lesions shows that the most common metastatic site is the orbit.[3]

Evaluation

While MNTI is rare, it should be included in a differential diagnosis in the evaluation of a rapidly growing pigmented mass in the head and neck. Although neural crest-derived neoplasms may produce vanillylmandelic acid (VMA), high levels of urinary levels of VMA are inconsistent but is supportive of the MNTI diagnosis. A cohort study of 18 patients demonstrated that VMA is present in males only.[1][22]

Radiographically, MNTI appears as a hypodense lesion on computed tomography (CT) scans. However, the melanin component of the soft tissue in MNTI will appear as a hyperdense finding. Enlargement of the lesion will lead to the destruction of the bony structures, and this will appear as a "sun-burst" result on the imaging. Therefore, a CT scan is a good choice to determine the extent of the neoplasm for surgical planning.[23] Ultrasonography for peripheral lesions has been performed in a small number of cases. On ultrasound, MNTI lesions appeared heterogeneous, well-demarcated, with decreased vascularization.[24]

On magnetic resonance imaging (MRI), MNTI typically presents as an increase in the T1 signal due to the presence of melanin. However, the common description of MNTI on MRI is a hypointense well-demarcated mass on T1-weighted and T2-weighted. MRI is helpful as it can show the involvement of soft tissues.[23][24]

A definitive diagnosis is obtained by biopsy and immunohistochemical tests to differentiate MNTI from other neoplasms that share similar characteristics.

Treatment / Management

MNTI management is based on reports which demonstrate that complete excision is the best treatment. A 2019 systematic review analyzing the treatment modalities for MNTI, demonstrated that excision appears to be the best choice as it is associated with low recurrence and lower morbidity rates.[4] A few cases were managed with neoadjuvant chemotherapy before surgery, which can decrease the need for wide margins resection, hence decreasing the disfiguring sequences of the surgery.[25][26] Still, excision either with or without additional treatment has quite a high rate of recurrence (22%).[4]

There is a minority of MNTI cases that were successfully treated with chemotherapy alone, without the need for the surgery.[27][28] Chemotherapeutic agents used to treat MNTI are based on the treatment protocols for neuroblastoma and include vincristine, doxorubicin, etoposide, and cyclophosphamide.[29] Bilateral high-frequency hearing loss was reported in a case of MNTI in a ten-year-old female patient who was treated with cisplatin-containing regimen at the age of 8 months.[30] Radiation therapy was reported as an adjuvant therapy with surgery or chemotherapy or both and was reported in only six cases.[9]

Differential Diagnosis

It is not only the clinical characteristics that mislead the diagnosis process, but microscopic findings can be similar to other neoplasms as well. Since MNTI usually presents with only an asymptomatic rapidly growing mass, this will rule out other neoplasms that usually present with other accompanying symptoms.[8]

- Neuroblastoma: Since this neoplasm also originates from the neural crest cells, it can be misdiagnosed initially, especially in small biopsies. However, neuroblastoma forms clusters of cells in a rosette formation, which is not seen in MNTI. On the other hand, the large pigmented epithelial cells that present in MNTI are not found in the neuroblastoma, which will make neuroblastoma negative for cytokeratin and HMB-45. Moreover, neuroendocrine markers of neuroblastoma are absent in MNTI.
- Ewing sarcoma: Compared to MNTI, Ewing sarcomas lack the biphasic appearance of the MNTI. It does not have the melanin-containing cells like MNTI. Also, Ewing sarcoma has its special genetic arrangement (e.g., t(11;22) or (q24;q12)).
- Alveolar rhabdomyosarcoma: This tumor can present in the head and neck region. However, considering its muscular differentiation, this tumor will be positive for desmin and react with myogenin. Necrosis is also present in this tumor, which is rarely present in MNTI.

During the evaluation of a pigmented mass in the head and neck, the differential diagnosis list should also include but not limited to lymphomas, malignant melanoma, and clear cell sarcoma of soft tissue.[8]

Prognosis

Although MNTI mostly presents as a benign neoplasm, malignant behavior is observed in 3% of cases. The 5-year recurrence rate is slightly higher in females than males (25% versus 22%).[9] Clinical and immunohistological presentation of the tumor can predict the prognosis and recurrence rate:

1. Age: Presentation at an age less than 2-months is associated with higher recurrence. Paradoxically, a presentation greater than 12 months is associated with 75 fold mortality.[3]
2. Distant metastasis at presentation is associated with higher recurrence rates and 14-fold higher mortality.[3]
3. Location and size of the lesion: The mandible was found to have the highest recurrence rate (33%), followed by the skull (31%) and the maxilla (19%).[31] The larger size of the lesion (> 5cm) is also associated with a higher rate of recurrence.[16]
4. Model of treatment: Curettage is associated with the highest recurrence rate (61%).[4]
5. Immunohistochemical markers: Although it is rare, the expression of Ki-67 and CD99 on MNTI is associated with more aggressive behavior of the lesion.[32]

Complications

Despite the rarity of MNTI, which makes it difficult to assess the complication of this tumor, this rapidly growing mass may cause facial asymmetry and invade muscles, bony structures and act in a locally destructive manner. Metastasis is rare but has been reported in limited cases. Treatment also can lead to complications as well. For example, surgical excision of the mass may lead to local nerve and tissue injury as well as potential disfiguration. Chemotherapy may cause side effects such as ototoxicity.

Deterrence and Patient Education

Patients' families should be counseled about the high recurrence rate after surgery, and also about the prognostic factors of presentation.

Pearls and Other Issues

The extremely low incidence of MNTI usually makes it a missed differential diagnosis. Lack of familiarity with MNTI leads to misdiagnosis and delay. Delay in diagnosis leads to local tissue invasion.

Enhancing Healthcare Team Outcomes

The diagnosis of MNTI requires a very high index of suspicion. The diagnosis of MNTI must be considered in any rapid-growing mass, especially in the head and neck region. Patients with MNTI are best managed by an interprofessional team approach. Follow up with the patient is important to detect any recurrence at the early stages of the disease and avoid delaying the diagnosis and its complications.

Continuing Education / Review Questions

- [Access free multiple choice questions on this topic.](#)
- [Earn continuing education credits \(CME/CE\) on this topic.](#)
- [Comment on this article.](#)

References

1. Borello ED, Gorlin RJ. Melanotic neuroectodermal tumor of infancy--a neoplasm of neural crest origin. Report of a case associated with high urinary excretion of vanilmandelic acid. *Cancer*. 1966 Feb;19(2):196-206. [PubMed: 4285905]
2. Mengide JP, Jaimovich SG, Lubieniecki FJ, Rugilo C, Lamas G, Mantese B. Melanotic neuroectodermal tumor of infancy arising from the skull: report of an unusual case, review of the literature, and a diagnostic approach. *Childs Nerv Syst*. 2020 Mar;36(3):469-475. [PubMed: 31897638]
3. Pontes FSC, de Souza LL, Uchôa DCC, Joaquim AMC, do Nascimento LS, da Mata Rezende DDS, Pontes HAR. Melanotic neuroectodermal tumor of infancy of the jaw bones: Update on the factors influencing survival and recurrence. *Head Neck*. 2018 Dec;40(12):2749-2756. [PubMed: 30390348]
4. Chrcanovic BR, Gomez RS. Melanotic neuroectodermal tumour of infancy of the jaws: an analysis of diagnostic features and treatment. *Int J Oral Maxillofac Surg*. 2019 Jan;48(1):1-8. [PubMed: 30170777]
5. Gomes CC, Diniz MG, de Menezes GH, Castro WH, Gomez RS. BRAFV600E Mutation in Melanotic Neuroectodermal Tumor of Infancy: Toward Personalized Medicine? *Pediatrics*. 2015 Jul;136(1):e267-9. [PubMed: 26122804]
6. Barnes DJ, Hookway E, Athanasou N, Kashima T, Oppermann U, Hughes S, Swan D, Lueerssen D, Anson J, Hassan AB. A germline mutation of CDKN2A and a novel RPLP1-C19MC fusion detected in a rare melanotic neuroectodermal tumor of infancy: a case report. *BMC Cancer*. 2016 Aug 12;16:629. [PMC free article: PMC4983003] [PubMed: 27519597]
7. Neven J, Hulsbergen-van der Kaa C, Groot-Loonen J, de Wilde PC, Merckx MA. Recurrent melanotic neuroectodermal tumor of infancy: a proposal for treatment protocol with surgery and adjuvant chemotherapy. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2008 Oct;106(4):493-6. [PubMed: 18602297]
8. Soles BS, Wilson A, Lucas DR, Heider A. Melanotic Neuroectodermal Tumor of Infancy. *Arch Pathol Lab Med*. 2018 Nov;142(11):1358-1363. [PubMed: 30407852]
9. Rachidi S, Sood AJ, Patel KG, Nguyen SA, Hamilton H, Neville BW, Day TA. Melanotic Neuroectodermal Tumor of Infancy: A Systematic Review. *J Oral Maxillofac Surg*. 2015 Oct;73(10):1946-56. [PubMed: 25936939]
10. Cutler LS, Chaudhry AP, Topazian R. Melanotic neuroectodermal tumor of infancy: an ultrastructural study, literature review, and reevaluation. *Cancer*. 1981 Jul 15;48(2):257-70. [PubMed: 6263455]
11. Bouckaert MM, Raubenheimer EJ. Gigantiform melanotic neuroectodermal tumor of infancy. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 1998 Nov;86(5):569-72. [PubMed: 9830649]
12. Strieder L, Carlos R, León JE, Ribeiro-Silva A, Costa V, Kaminagakura E. Protumorigenic M2-like phenotype cell infiltration in the melanotic neuroectodermal tumor of infancy. *Oral Surg Oral Med Oral Pathol Oral Radiol*. 2016 Feb;121(2):173-9. [PubMed: 26686956]

13. Dehner LP, Sibley RK, Sauk JJ, Vickers RA, Nesbit ME, Leonard AS, Waite DE, Neeley JE, Ophoven J. Malignant melanotic neuroectodermal tumor of infancy: a clinical, pathologic, ultrastructural and tissue culture study. *Cancer*. 1979 Apr;43(4):1389-410. [PubMed: 221089]
14. Mendis BR, Lombardi T, Tilakaratne WM. Melanotic neuroectodermal tumor of infancy: a histopathological and immunohistochemical study. *J Investig Clin Dent*. 2012 Feb;3(1):68-71. [PubMed: 22298524]
15. Kapadia SB, Frisman DM, Hitchcock CL, Ellis GL, Popek EJ. Melanotic neuroectodermal tumor of infancy. Clinicopathological, immunohistochemical, and flow cytometric study. *Am J Surg Pathol*. 1993 Jun;17(6):566-73. [PubMed: 8392815]
16. Ren Q, Chen H, Wang Y, Xu J. Melanotic Neuroectodermal Tumor of Infancy Arising in the Skull and Brain: A Systematic Review. *World Neurosurg*. 2019 Oct;130:170-178. [PubMed: 31295620]
17. Liu Z, Li M, Tang X, Xiao Y, Xiao Z, Li Y. Melanotic neuroectodermal tumor of infancy in ovary: A rare case report. *Medicine (Baltimore)*. 2019 Dec;98(49):e18181. [PMC free article: PMC6919528] [PubMed: 31804335]
18. Elli M, Aydin O, Pinarli FG, Dagdemir A, Dabak N, Selcuk MB, Acar S. Melanotic neuroectodermal tumor of infancy of the femur. *Pediatr Hematol Oncol*. 2006 Oct-Nov;23(7):579-86. [PubMed: 16928653]
19. Marchevsky AM. Mediastinal tumors of peripheral nervous system origin. *Semin Diagn Pathol*. 1999 Feb;16(1):65-78. [PubMed: 10355655]
20. BLANC WA, ROSENBLATT P, WOLFF JA. Melanotic progonoma (retinal anlage tumor) of the shoulder in an infant; a case report. *Cancer*. 1958 Sep-Oct;11(5):959-63. [PubMed: 13585349]
21. Batsakis JG. Pathology consultation. Melanotic neuroectodermal tumor of infancy. *Ann Otol Rhinol Laryngol*. 1987 Jan-Feb;96(1 Pt 1):128-9. [PubMed: 3028235]
22. Chaudhary A, Wakhlu A, Mittal N, Misra S, Mehrotra D, Wakhlu AK. Melanotic neuroectodermal tumor of infancy: 2 decades of clinical experience with 18 patients. *J Oral Maxillofac Surg*. 2009 Jan;67(1):47-51. [PubMed: 19070747]
23. Fowler DJ, Chisholm J, Roebuck D, Newman L, Malone M, Sebire NJ. Melanotic neuroectodermal tumor of infancy: clinical, radiological, and pathological features. *Fetal Pediatr Pathol*. 2006 Mar-Apr;25(2):59-72. [PubMed: 16908456]
24. Haque S, McCarville MB, Sebire N, McHugh K. Melanotic neuroectodermal tumour of infancy: CT and MR findings. *Pediatr Radiol*. 2012 Jun;42(6):699-705. [PMC free article: PMC3526662] [PubMed: 22430481]
25. Maroun C, Khalifeh I, Alam E, Akl PA, Saab R, Moukarbel RV. Mandibular melanotic neuroectodermal tumor of infancy: a role for neoadjuvant chemotherapy. *Eur Arch Otorhinolaryngol*. 2016 Dec;273(12):4629-4635. [PubMed: 27107579]
26. Davis JM, DeBenedictis M, Frank DK, Lessin ME. Melanotic neuroectodermal tumor of infancy: a wolf in sheep's clothing. *Ann Otol Rhinol Laryngol*. 2015 Feb;124(2):97-101. [PubMed: 25030945]
27. Kumari TP, Venugopal M, Mathews A, Kusumakumary P. Effectiveness of chemotherapy in melanotic neuroectodermal tumor of infancy. *Pediatr Hematol Oncol*. 2005 Apr-May;22(3):199-206. [PubMed: 16020102]
28. Woessmann W, Neugebauer M, Gossen R, Blütters-Sawatzki R, Reiter A. Successful chemotherapy for melanotic neuroectodermal tumor of infancy in a baby. *Med Pediatr Oncol*. 2003 Mar;40(3):198-9. [PubMed: 12518354]
29. Emmerling MR, York TA, Caccamese JF. Melanotic Neuroectodermal Tumor of Infancy: Case Report and Review of Management. *J Oral Maxillofac Surg*. 2019 Feb;77(2):315-320. [PubMed: 30392845]
30. Hojan-Jeziarska D, Chomiak A, Czopor A, Matthews-Kozanecka M, Majewska A, Urbaniak-Olejnik M, Matthews-Brzozowska T. Ototoxicity after platinum-based chemotherapy in the treatment of melanotic neuroectodermal tumour of infancy. *Oncol Lett*. 2020 May;19(5):3411-3416. [PMC free article: PMC7115066] [PubMed: 32269613]
31. Kruse-Lösler B, Gaertner C, Bürger H, Seper L, Joos U, Kleinheinz J. Melanotic neuroectodermal tumor of infancy: systematic review of the literature and presentation of a case. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2006 Aug;102(2):204-16. [PubMed: 16876064]
32. Barrett AW, Morgan M, Ramsay AD, Farthing PM, Newman L, Speight PM. A clinicopathologic and immunohistochemical analysis of melanotic neuroectodermal tumor of infancy. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2002 Jun;93(6):688-98. [PubMed: 12142876]

Copyright © 2021, StatPearls Publishing LLC.

This book is distributed under the terms of the Creative Commons Attribution 4.0 International License (<http://creativecommons.org/licenses/by/4.0/>), which permits use, duplication, adaptation, distribution, and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, a link is provided to the Creative Commons license, and any changes made are indicated.

Bookshelf ID: NBK560596 PMID: [32809431](#)