



Melanotic Neuroectodermal Tumor of Infancy: a Clinicopathological Case Report

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Melanotic neuroectodermal tumor of infancy (MNTI) is a rare neoplasm that affects mainly children under 1 year of age. A 4-month-old boy was referred for evaluation of a lesion with 1 month of evolution. Intra-oral examination detected a firm upon palpation submucosal nodular mass, measuring 1.5 cm in diameter, affecting the anterior maxillary alveolar ridge and covered by a slightly blue mucosa with evident telangiectasia. The patient underwent an incisional biopsy and histological and immunohistochemical analyses revealed nests of AE1/AE3 positive epithelioid cells with abundant melanin pigmentation. Other cell types, resembling neuroblasts, were also present and positive for CD56, synaptophysin and enolase. The diagnosis of MNTI was established and the patient was referred for treatment. Conservative surgical resection was performed along with 3 adjacent teeth under general anesthesia. The patient is in follow-up for 1,5 year without recurrence. Conservative surgical management of MNTI may be an alternative to maxillectomy, contributing to the patient's quality of life.

Key Words: melanotic neuroectodermal tumor of infancy, conservative surgical treatment, neuroectodermal tumors.

Introduction

Melanotic neuroectodermal tumor of infancy (MNTI) is a rare neoplasm that affects mainly children in their first year of life and has a high recurrence rate. More than 90% of MNTIs occurs in the head and neck region, being the maxilla the most commonly affected site followed by the skull, mandible and brain, respectively (1,2).

The disease was first described by Krompecher in 1918 (3) and its origin remained uncertain until Borello and Gorlin propose the neural crest origin in 1966 that could explain the biphasic cellular phenotype present in this tumor (4,5).

Clinically, MNTI presents as a firm mass with rapid and expansive growth that may involve bone and adjacent tissues, often causing tooth displacement. Last reports have shown a slight male prevalence (6). In a systematic review, Rachidi et al. (2015) reported 472 cases around the world. In Brazil, there are published eight cases approximately (8-11). This lesion is usually benign but, there are reports of malignant MNTI (7). The diagnosis is established through histological and immunohistochemical analysis that reveal epithelioid cells, with abundant pigment of melanin and another cell population, that resemble neuroblasts (1). Some patients have elevated levels of vanillylmandelic acid, which may help the diagnosis and support the neuroectodermal origin (12). The differential diagnosis may include rhabdomyosarcoma, neuroblastoma, Ewing's sarcoma and lymphoma (2).

The treatment of choice is surgical resection. However, in very particular situation, such as in inoperable cases, other modalities of treatment including chemotherapy

has been used (13-16).

The aim of this report was to describe the clinical and histopathological features of a case of MNTI where the patient underwent a successful conservative surgical treatment.

Case Report

A 4-month-old boy was referred for evaluation of a swelling in anterior maxilla. His mother first noticed the oral alteration, but she mentioned that no changes in breast-feeding, weight and behavior. His medical history was unremarkable.

Extraorally a swelling on the left anterior maxilla was noticed. Intraoral examination revealed a submucosal well-circumscribed nodular mass, slightly blue with evident overlying telangiectasia, firm on palpation, located on the anterior maxillary alveolar ridge, extending from the midline to the left canine area, measuring about 1,5 cm in diameter (Fig. 1A). The main clinical hypotheses of diagnosis included eruption cyst, the MNTI or a malignant mesenchymal neoplasm.

Cone-beam computed tomography scan performed under sedation showed an expansive mass involving the maxillary bone and alveolar ridge crossing the midline. Inside the lesion was possible to observe at least one tooth completely involved (Fig. 2A).

The patient underwent an incisional biopsy under general anesthesia and, macroscopically, the specimen showed brownish color suggesting melanin pigmentation.

The microscopic analysis revealed two cell populations: one composed by cuboidal cells with epithelioid appearance arranged in nests showing melanin granules and immerse in a dense fibroblastic stroma. (Fig. 3A). Such cells were immunohistochemically positive for AE1/AE3 (Fig. 3B). The other cell population was composed by small cells, roundly shaped-cells, with scanty cytoplasm and dark nucleus resembling neuroblasts. These cells were positive for CD56, synaptophysin, enolase (Fig. 3C, D and E) and negative for chromogranin A. The cellular proliferation index measured by Ki-67 was very low with only some positive cells (Fig. 3F).

Comprising histological and immunohistochemical findings the diagnosis of MNTI was established and the patient was referred to an oral surgeon, who resected the

tumor along with three teeth. The surgery was performed under general anesthesia. The procedure involved the displacement of the mucoperiosteal flap, followed by osteotomy in which most of the tumor content was removed along with the teeth that were involved by the lesion. Then, the tumor remaining was removed by curettage and osteotomy of the perilesional bone (Fig. 1B, C and D). The patient is in follow up for one year and half without clinical signs of recurrence (Fig. 1E and F) as well as on cone-beam computed tomography that was repeated to control (Fig. 2B). Prosthetic rehabilitation is under consideration

Discussion

In the present case is possible to observe that the clinical

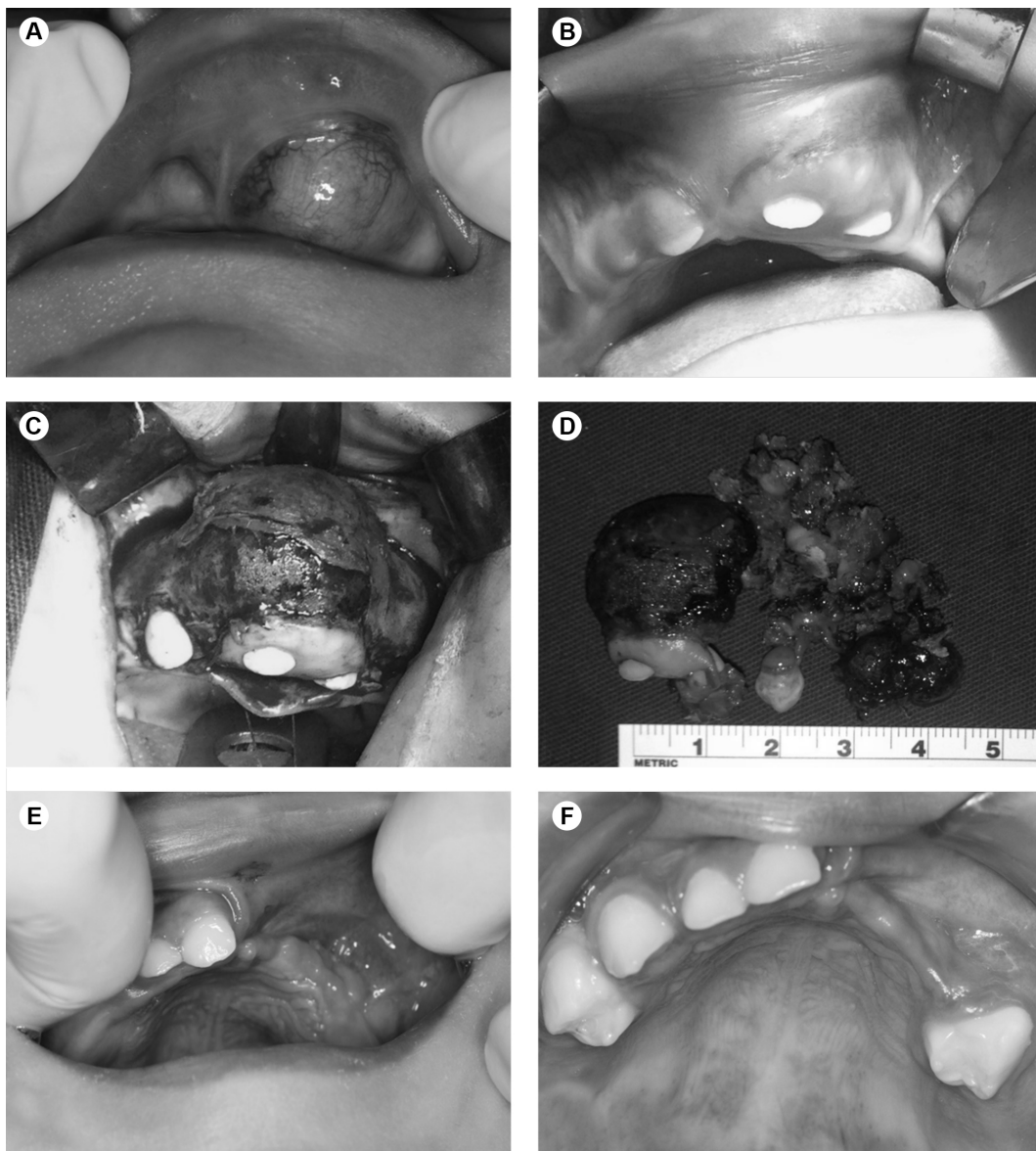


Figure 1. Initial appearance of the lesion showing a well-circumscribed mass, slightly blue with evident telangiectasia on the left maxillary alveolar ridge (A). Clinical appearance of the lesion at the time of surgery (B). Intraoperative view of the tumor (C). Specimen resected after the surgery (D). Clinical appearance 1 year after tumor resection (E) and 1.5 year of follow-up (F).

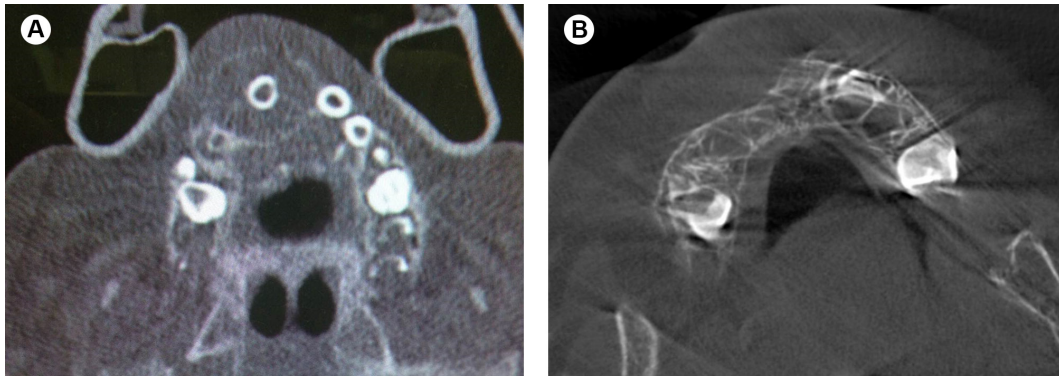


Figure 2. Computed tomography scan showing an expansive mass involving the left maxilla crossing the midline on the day of the diagnosis (A) and 1.5 year after the surgery showing no signs of recurrence (B).

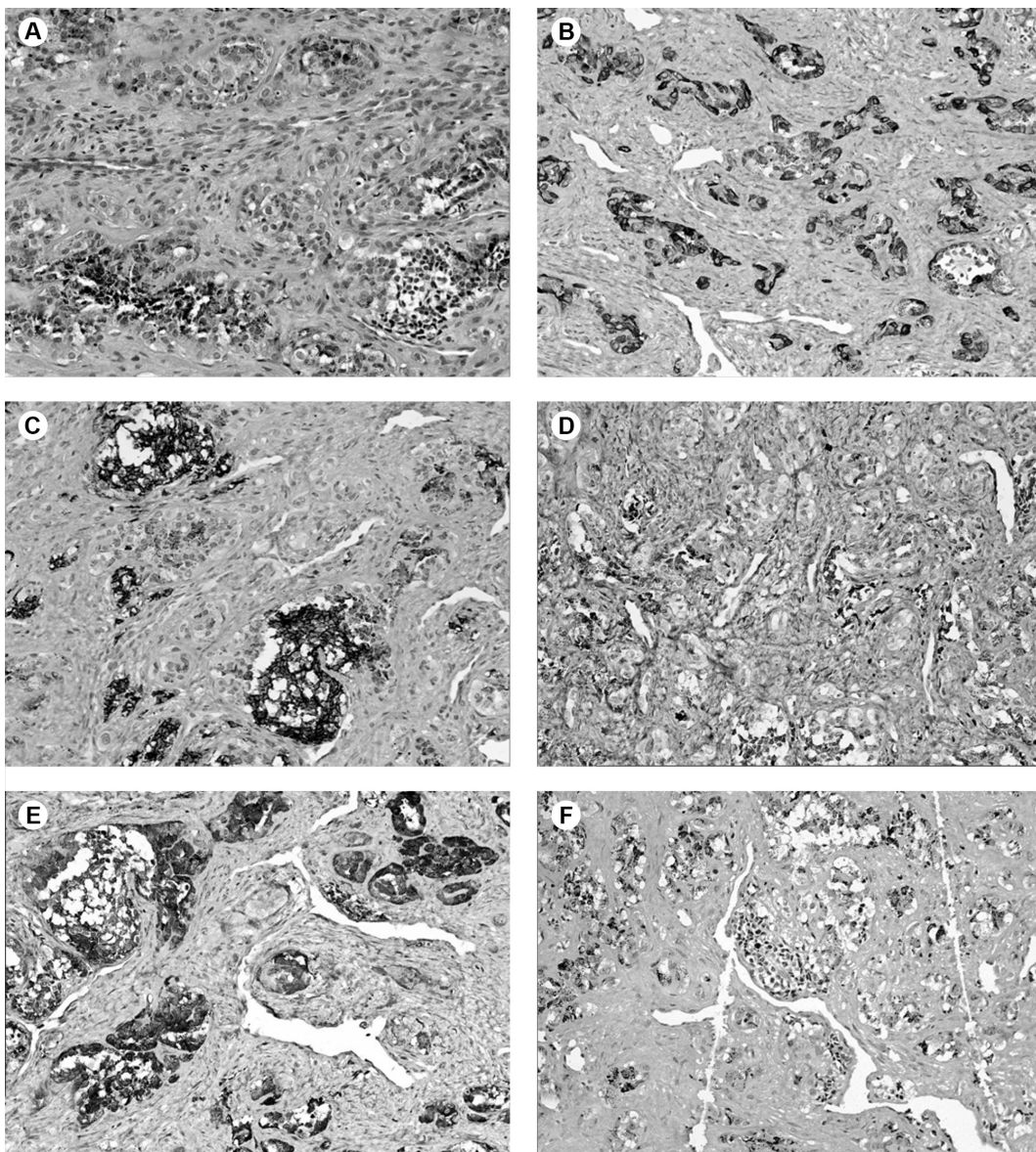


Figure 3. Photomicrographs of histological and immunohistochemical findings showing: (A) profuse melanin cells produced by epithelioid cells immerse in dense fibroblastic stroma (hematoxylin and eosin stain 200 \times). (B) Epithelioid cells were positive for keratin marker (AE1/AE3) (magnification 100 \times). (C) Small neuroblastic like cells showing immunoreactive for CD56 (magnification 100 \times). Both small and large tumor cell positive for neurospecific synaptophysin (D) and enolase (E) markers (magnification 100 \times). (F) Less than 5% of the cells were positive for cellular proliferation index: Ki-67 (magnification 200 \times).

and histological features are similar to other cases reported in English-language literature and, although the MNTI is considered a benign neoplasm, its rapid growth and local aggressive behavior makes the early diagnosis the key for treatment success. The correct and conservative surgical approach provides less damage for important structures and better quality of life to the patients (8).

The diagnosis is possible by the histological observation, once the features are very specific as was the case reported here. Some articles suggest that vanillylmandelic acid serum levels may help on diagnosis once some patients excrete large amounts of this acid. This fact supports the neural crest origin of this tumor. However, it is important to notice that other neuroectodermal tumors also presented high levels of vanillylmandelic acid such as neuroblastomas, ganglioneuroblastomas and pheochromocytomas (12). Therefore, the histological and immunohistochemical analyses are essential to establish the diagnosis (17,18). In the current case the diagnosis was made only by the histological analysis associated to immunohistochemical studies.

Histopathologically, the MNTI is similar to other tumors that contain small round cells. Some tumors with this feature include neuroblastoma, Ewing's sarcoma, rhabdomyosarcoma, peripheral neuroepithelioma, malignant melanoma and lymphoma (1). Clinically, the differential diagnosis of MNTI includes congenital epulis, neuroblastoma, Ewing's sarcoma, rhabdomyosarcoma, eruption cyst, Burkitt lymphoma, Langerhans cell histiocytosis and hemangioma. All these lesions are able to generate oral manifestations as swelling in the anterior maxilla. However, some aspects should be considered to a correct diagnostic hypothesis. Congenital epulis generally is present at birth and in the majority of cases is pedunculated, instead of MNTI, that is sessile and comes up after birth in the most of cases. Neuroblastoma in children affects more commonly the abdomen. Ewing's sarcoma affects mainly teenagers or young adults, being rare before age of five. Rhabdomyosarcoma occurs more frequently on the palate or the tongue. Besides, this malignant tumor can present pain and paresthesia which is rare in MNTI. Lastly, eruption cyst usually presents as a swelling, soft, in anterior gingival mucosa that recovers the crown of unerupted deciduous tooth, generally a superior incisor. The eruption cyst also can present a bluish to brownish color. The coloration of MNTI may be similar but it is more brownish because of the presence of melanin pigment. In the case presented in this article, the eruption cyst was considered as a possible diagnosis, but the child was only 4 months old, which is earlier than the correct eruption period, that occurs around 6 months of life (19).

About the treatment, surgical resection is the modality

of choice in the majority of cases, as it was in the present case. Some studies support that there is no difference between curettage and resection in recurrence rate (2). However, other studies recommend that a margin of 5 mm of healthy tissues would be enough, including the removal of soft tissues and teeth that occasionally are involved by the lesion (18). Total or partial maxillectomy may be used depending on the extent of the tumor. Chemotherapy has been used in association with surgery, particularly when the tumor can not be totally resected, if there is history of recurrences, if the tumor has a malignant aspect on histology or if there are metastasis. Several chemotherapeutic protocols have been suggested, but there are no gold standards (13,14,16). It is observed that chemotherapy has a partial effect, with good results in neuroblastic areas of the tumor and poor results in epithelial areas (15).

Malignant MNTI is rare and approximately 25 cases have been reported in the literature (18). Metastasis from MNTI of maxilla or mandible occurs in the regional lymph nodes and consequently the prognosis is poor and the patients die because of the tumor progression (18).

As far as prognosis is concerned, Rachidi et al. (2015) found that patients younger than 2 months of age in the diagnosis moment would have more chance to develop recurrences, suggesting that age at diagnosis can be an important prognostic indicator. In turn, patients diagnosed after four months and half of age would have a less risk of recurrence. The rate of local recurrence is around 20% and the sites more affected are the maxilla following by the skull and brain, being that the most part of recurrences happens within four months after the surgery (1). In the current patient no recurrences were observed so far.

As mentioned before, MNTI basically affects children up to one year and the treatment consists in surgical approaches. Therefore, rehabilitation is an important aspect to consider for improving the oral functions. The rehabilitation process will depend on various aspects such as the extension of the surgery, involved structures and number of removed teeth. Possible alternatives consist in obturator prostheses to correct feeding when there is oroantral communication and space maintainer to ensure the correct replacement of the loose teeth in the future by dental implants or conventional prostheses (20). More extensive rehabilitation also can be an approach when a radical management is necessary, such as reconstruction with bone graft (17). In the current patient, rehabilitation has been planned.

In summary, considering the potential of local destruction, the rate of recurrences and the possible mutilation from surgery, this case represents a good example that the early diagnosis allowed an adequate conservative

surgical treatment of MNTI, that culminated in minimum sequels to the patient. These aspects must be emphasized to improve the clinical management of this lesion. In addition, close follow-up and correct rehabilitation will be able to ensure the proper development of the child.

Resumo

Tumor neuroectodérmico melanótico da infância (TNMI) é um neoplasma raro que afeta principalmente crianças com idade abaixo de 1 ano. Um menino de 4 meses foi referenciado para avaliação de uma lesão com 1 mês de evolução. O exame intra-oral detectou uma massa nodular submucosa firme à palpação, medindo 1,5 cm de diâmetro, afetando rebordo alveolar anterior da maxila e recoberta por mucosa de coloração levemente azulada com telangiectasia evidente. O paciente foi submetido à biópsia incisional e as análises histológica e imunohistoquímica revelaram ninhos compostos por células com abundante pigmento de melanina, positivas para AE1/AE3. Outro tipo celular, semelhante à neuroblastos, também estava presente e foram positivas para CD56, sinaptofisina e enolase. O diagnóstico de TNMI foi estabelecido e o paciente encaminhado para tratamento. Ressecção cirúrgica conservadora sob anestesia geral ao longo de 3 dentes adjacentes foi realizada. O paciente está em acompanhamento há 1 ano e meio sem sinais de recorrência. O tratamento cirúrgico conservador do TNMI pode ser uma alternativa à maxilectomia, contribuindo para a qualidade de vida do paciente.

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