Melanotic Neuroectodermal Tumor of Infancy: Presentation of a Case Affecting the Mandible

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Received: 21 Jan. 2018; Accepted: 31 Jan. 2018

Abstract: Melanotic neuroectodermal tumor of infancy (MNTI) is a rare and distinctive neoplasm of early infancy with rapid expansile growth and a high recurrence rate (1). In the medical literature, the tumor has been referred to a variety of synonyms, such as congenital melanocarcinoma (2), retinal anlage tumor (3), pigmented congenital epulis (4), or melanotic progonoma (5). Krompecherin is the first one who has described this entity in 1918 (2). This tumor can usually be found in young children in the first year of life (6-11). No predilection in gender was described. The majority of tumors (90%) arise in the head and neck and, generally, in the anterior region of the maxilla (80%), but it can also occur at other sites, including the skull (10,8%), mandible (5,8), brain (4,3%), and epididymis (7). Clinically, MNTIs are soft and rapidly growing pigmented swellings. They often destroy the underlying bone and may be associated with displacement of developing teeth (12). It may have a tendency to be locally aggressive (13). Because of these factors, clinical and radiologic findings, as well as histopathologic examination, are required for definitive diagnosis. Despite its rapid and locally destructive growth, MNTI is generally accepted as a benign tumor (14). Recurrence has been observed in 10-15% of patients (15). In addition, few patients with malignant MNTI have been reported in the literature (16-18). The aim of this article was to show the diagnosis and treatment of a 7-month-old patient with melanotic neuroectodermal tumor occurred in the anterior mandible and to demonstrate the effectiveness of the neoadjuvant chemotherapy.

Keywords: Melanotic neuroectodermal; Infancy; Mandible

Introduction

Melanotic neuroectodermal tumor of infancy (MNTI) is a rare and mainly benign neoplasm of early infancy with rapid expansile growth and a high rate of recurrences. Most commonly the lesion affects the maxilla of infants during the first year of life, but it may also occur in the mandible, skull, brain, epididymis, and other rare locations. Common treatment methods include surgical excision and resection of the tumor. The aim of this article was to show the diagnosis and treatment of a 7-month-old patient with melanotic neuroectodermal tumor occurred in the anterior mandible and to demonstrate the effectiveness of the neoadjuvant chemotherapy.

Case Report

A 7-month-old male infant was brought to the Department of Oral and Maxillofacial Surgery with a complaint of swelling in the anterior region of the mandible. His parents noticed “swelling in his lower jaw” at the age of 4 months and reported that the mass was slowly progressed initially and started growing rapidly in the last month. The swelling has caused facial asymmetry and feeding difficulties. There was no history of medication during pregnancy, and no relevant medical history was present. Clinical examination showed a normally developed male infant. No fever or pain was reported by the infant’s parents. Intraoral examination showed a firm, painless, immobile, non-fluctuant, darkly pigmented mass about 8*4 cm in size, bleeding on contact (Figure 1). The lesion had expanded toward the labial surface of the anterior mandibular alveolar ridge. In addition, there were no palpable lymph nodes. The radiologic examination had also been conducted by...
computed tomography (CT). The CT images revealed a homogeneous osteolytic radiolucent tumor with well-demarcated borders arising from the mandibular region as well as bony destruction associated with non-erupted mandibular incisors. There was infiltration of the perilesional soft tissue and multiple cervical nodes. A biopsy specimen from the oral lesion was done, and the histopathologic examination identified a melanocytic neuroectodermal tumor of infancy (keratin +, HMB+, synaptophysin+). Surgical excision was considered difficult and mutilating with an increased risk of incomplete resection. The patient received neoadjuvant chemotherapy with ifosfamide (dose=100 mg/kg for 3 days) and etoposide (dose=5 mg/kg for 3 days). The courses were spaced 21 days apart. From the first course, we noted an excellent clinical response. After six courses of chemotherapy, the tumor measured 3*2 cm with the possibility of suction and well-visualized tongue (Figure 2). The patient had subsequently a surgical excision. The primary tumor volume was 3x2x1.2 cm, and two teeth were found on its surface without an obvious envelope. The side of the suction side was gray and black, with clear boundaries visible. No noticeable tumor invasion was identified in the teeth. Microscopic examination revealed nested, small round cells and larger pigmented cells in the fibrous connective tissue, without evident pathological nuclear fission, necrosis or perineural invasion. Smaller round cells were vimentin/neuron-specific enolase (NSE)/melanoma-associated antigen 45 (HMB45)/synaptophysin (+), and larger cells were cytokeratin (CK)/epithelial membrane antigen (+), with no significant glial fibrillary acidic protein (GFAP)/S-100 staining. Scattered cells exhibited desmin immunoreactivity, and ~2% of the cells were Ki-67(+). The raw surface was covered with a layer of collagen membrane [reinforced with sofratoulle] by suturing it to the surrounding soft tissue margins.

![Figure 1. Before chemotherapy](image1)

![Figure 2. After chemotherapy and pre-operative aspect](image2)

**Discussion**

Melanotic neuroectodermal tumor of infancy is described in the literature as a benign, non-ulcerated, locally aggressive, rapidly growing pigmented neoplasm that originates from the neural crest (19) and primarily develops in the maxilla of infants during the first year of life. The mandibular localization is very rare. There is a general agreement that the neural crest is the origin of MNTI for the following reasons: the tumor cells are similar to neuroblasts with respect to histologic evaluation; neurosecretory granules can be observed under an electron microscope; and the catecholamine metabolite VMA level increases in the urine (19). Furthermore, the levels of VMA gradually return to normal following tumor resection.

The differential diagnoses of MNTI include neuroblastoma, Ewing sarcoma, rhabdomyosarcoma, peripheral neuroepithelioma, desmoplastic small round cell tumor, malignant melanoma, peripheral primitive neuroectodermal tumor, and lymphoma (20). However, this long list can be reduced to just a few diagnoses based on the clinical and radiologic features. A differential diagnosis can be made according to the typical clinical and imaging appearance of MNTI as well as histopathologic hallmarks, such as the epithelioid and neuroblastoma-like biphasic differentiation of tumor cells and the existence of pigment.

Immunohistochemistry plays a key role in confirming the diagnosis, especially in difficult patients. The fraction of larger epithelioid cells expressed a number of cytokeratins in most patients HMB-45 but rarely S-100 protein (21). The neuroblast-like cells are positive for neuron-specific enolase, CD 56, glial fibrillary acidic protein, and synaptophysin, and the melanogenic cells are positive for HMB-45, epithelial antigen membrane antigen, cytokeratin, and vimentin (22). Expression of Ki-67/CD99 in MNTI, which is quite uncommon, might be correlated with more aggressive growth of the tumor (23).

Conventional radiographs of bony lesions usually show radiolucency with or without irregular margins. It is typical of CT scans to reveal hyperdense masses, but hypodense variants have been reported as well. The CT can accurately define the extent of the lesion and thus provides a good basis for surgical planning. Magnetic resonance imaging shows a hypodense mass with focal areas of hyperdensity (21).

Surgical excision is the typical treatment for MNTI. Individuals with MNTI that are not amenable to surgical management alone may receive other modes of treatment (24). In general, this may be chemotherapy alone (25), chemotherapy with radiotherapy, chemotherapy before
(26), or after surgical treatment (24–28), radiotherapy and surgical treatment (29), or a combination of all, excision, chemotherapy, and radiotherapy (30). The chemotherapeutic regimen included vincristine, vinblastine, dactinomycin, ifosfamide, cyclophosphamide, etoposide, doxorubicin, and liposomal daunorubicin (25,26,31). As described before, chemotherapy may serve as an alternative or adjuvant option in the treatment of widely extended MNTIs. Even so, the primary surgical approach with radical excision will be the preferred procedure and curative in most of the cases.

The biologic behavior of MNTI with rapid and invading growth explains the need for early diagnosis without unnecessary loss of time until treatment. Late diagnosis may be the reason for the difficulty in radical resection because the tumor involves the adjacent critical anatomic structures. Similar aspects should be regarded with the need for close follow-up, especially within the first 6 months postoperatively.

Although MNTI behaves in a benign fashion, recurrences can occur especially within the first 6 months with the need for close follow-up postoperatively. Neoadjuvant chemotherapy helps to reduce the volume of the tumor; then the resection can be complete and less stimulating. This can reduce the prevalence of locoregional recurrence.

References

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