OLGU SUNUMU / *CASE REPORT*

Melanotic Neuroectodermal Tumor of Infancy: A Rare Case Report

İnfantil Melanotik Nöroektodermal Tümör: Nadir Bir Olgu Sunumu

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ABSTRACT

Melanotic neuroectodermal tumor of infancy (MNTI) is a rare, rapidly growing, and pigmented neoplasm of neural crest origin. It predominantly affects the maxilla of infants during the first year of life. A seven-month-old boy presented with a mass approximately 5 cm in diameter in the right oral cavity. On computerized tomography, a lytic expansile lesion was detected in the right maxilla. Microscopically, the tumor consisted of two different neoplastic cell proliferation, located peripherally and centrally, arranged in alveolar clusters within the fibrous connective tissue. Immunohistochemically, peripheral tumor cells showed diffuse staining for Pancytokeratin and HMB-45; the central cells were positive for CD56 and Synaptophysin. MNTI is a rare tumor that can be easily confused with malign small round cell tumors, especially in small biopsies. It has characteristic histomorphological and immunohistochemical findings. Its biological behavior is not fully understood. These tumors can present locally aggressive behavior and a high recurrence rate.

Key words: *melanin; neuroectoderm; infant; tumor*

ÖZET

İnfantil melanotik nöroektodermal tümör (IMNT), nöral krest kökenli, hızlı büyüyen, pigmente nadir bir neoplazmdır. Özellikle bebeklerde, yaşamın ilk yılında, maksillada ortaya çıkar. Yedi aylık erkek çocuk, oral kavitede yaklaşık 5 cm çapında kitle ile başvurdu. Bilgisayarlı tomografide, sağ maksillada ekspansil litik kitle saptandı. Mikroskopik olarak tümör, fibröz bağ dokusu içerisinde, alveolar kümeler şeklinde dizilim gösteren, periferal ve santral yerleşimli, iki farklı neoplastik hücre proliferasyonundan oluşmakta idi. İmmünohistokimyasal olarak periferal tümör hücreleri Pansitokeratin ve HMB-45 ile, merkezi tümör hücreleri CD56 ve Sinaptofizin ile immünopozitif ekspresyon gösterdi. IMNT, özellikle küçük biyopsilerde, malign küçük yuvarlak hücreli tümörler ile tanısal karışıklığa neden olabilen nadir bir tümördür. Karakteristik histomorfolojik ve immünohistokimyasal bulgulara sahiptir. Biyolojik davranışı henüz tam olarak anlaşılamamıştır. Bu tümörler lokal agresif davranış gösterebilir ve yüksek rekürrens oranlarına sahiptir.

Anahtar kelimeler: *melanin; nöroektoderm; infantil; tümör*

Introduction

Melanotic neuroectodermal tumor of infancy (MNTI) is a rare, rapidly growing, and pigmented neoplasm[1]. It was first described by Krompecher[2] in 1918. MNTI originates from the neural crest and comprises comparatively primitive pigment-producing cells. MNTI predominantly arises in the head and neck zone and most frequently involves the maxilla[3]. Various names have been used for this neoplasm because of the unknown cell origin and infrequent occurrence[4]. This report aimed to describe radiological, histopathological, and immunohistochemical features of a rare case of MNTI.

Case Report

A seven-month-old male child was applied to the Otolaryngology clinic with a mass in the right oral cavity for about a month. The mass was initially small but grew rapidly and arrived at the present size during the time. On computerized tomography of the head and neck, a lytic expansile lesion was detected in the right maxilla (Fig. 1a), which had intense homogeneous contrast (Fig. 1b). No other known notable findings existed. During the surgery, a tracheostomy was performed on the patient due to the oral mass. A solid tumor that filled the oral cavity exhibited infiltrative growth into the surrounding maxilla and base of the nose. The tumor was excised for subsequent pathological examination with a preliminary diagnosis of odontogenic myxoma. The defect repair in the maxillary bone was left to the second operation. Macroscopically, this mass was brownish, with well-circumscribed margins, measuring 5×4×2 cm in diameter (Fig. 1c), and had a heterogeneous grayish-black

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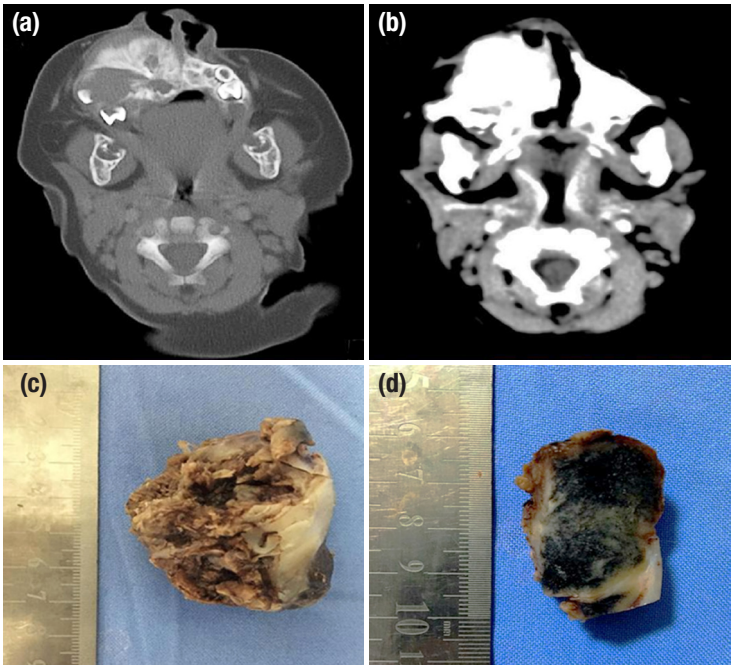

Figure 1. a–d. *Computed tomography (CT) showed an expansive mass measuring 5 × 4 × 3 cm that involved the middle of the anterior maxilla region with bone destruction, extending superiorly and medially* ***(a)****. Contrast-enhanced computed tomography showed a radiolucent osteolytic lesion expanding the surrounding bone* ***(b)****. Macroscopic specimen; a firm, brown-colored, well-demarcated mass* ***(c)****. The cut surface was colored black-gray* ***(d)****.*

appearance on cut sections (Fig. 1d). No foci of hemorrhage, necrosis, calcification, or areas of cystic change were observed. The tumor was microscopic from two distinct types of neoplastic cell proliferation arranged in alveolar nests and irregularly solid sheets within a densely sclerotic fibrous connective tissue stroma (Fig. 2a, 2b). The centrally located cells consisted of small, darkly stained cells with hyperchromatic nuclei and scant cytoplasm. The peripherally located cells were larger epithelioid cells that contained nuclei with vesicular nuclear chromatin and melanin pigment (Fig. 2c, 2d). Necrosis was not seen.

Immunohistochemically, although the peripheral tumor cells showed diffuse staining for HMB– 45 (Fig. 3a), Pancytokeratin (Fig. 3b), and FLI-1, the central cells were positive for NSE, Synaptophysin (Fig. 3c), CD56 (Fig. 3d), and FLI-1. Immunostains for S100, CD99, Melan A, and CD45 were consistently negative in tumor tissue. The final histopathological diagnosis was MNTI. The patient showed no recurrence or metastases in her latest follow-up exam in March 2021.

Discussion

MNTI is a rare, rapid-growing, and pigmented neoplasm arising in infants[4]. It has a mild male preference. MNTI commonly occurs in the first year of life[3]. It has been reported to occur in a small number of patients in older children and adults[5].

MNTI usually arises in the head and neck region. The most common regions are, respectively, the maxilla (68–80%), skull (10.8%), and mandible (5.8%). In our case, it was localized in the maxilla. It can also occur at the mediastinum, epididymis, testis, ovaries, extremities, and brain[7].

MNTI was first described by Krompecher[2] in 1918 as "Congenital melanocarcinoma." In 1966, Borella and Gorlin[8] suggested that these tumors are of neural crest origin because of the high level of vanillylmandelic acid (VMA) in urine, like other neuroectodermal tumors. Also, as these tumors are often seen in infancy, they suggested using the term MNTI[9,10]. Various names have been used in the past for this neoplasm, including "melanotic epithelial odontoma, congenital melanocarcinoma, melanotic progonoma, melanotic ameloblastoma, retinal anlage tumor, pigmented adamantinoma, congenital pigmented epulis, and melanocytoma." Usually, this neoplasm is associated with a rise in urinary VMA excretion, similar to another neuroectodermal neoplasm[6,7].

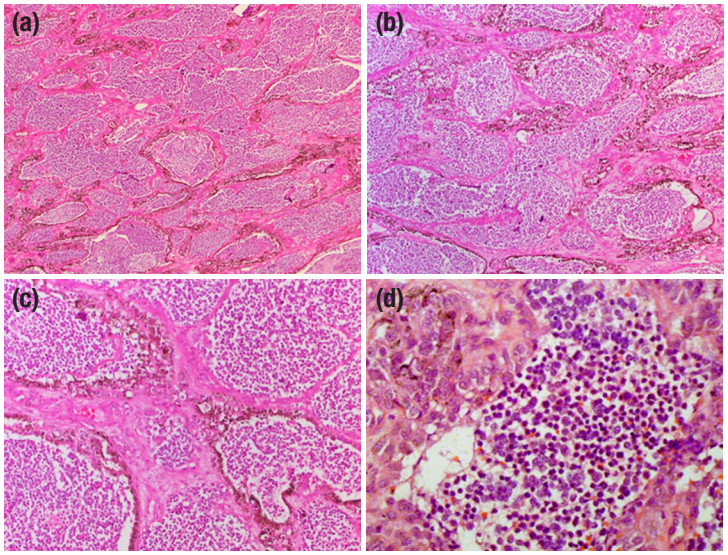

Figure 2. a–d. *Tumor cells are arranged in an alveolar pattern separated by fibrovascular stroma (H&E, 40×)* ***(a)****, (H&E, 100×)* ***(b)****. Biphasic tumor cell population, with large and small cells (H&E 200×)* ***(c)****. Two distinctive types of cells; small cells with scanty cytoplasm and hyperchromatic round nuclei, were seen in the center, and large epithelioid cells with abundant cytoplasm, round vesicular nucleus, and melanin pigment were seen in the periphery (H&E, 400×)* ***(d)****.*

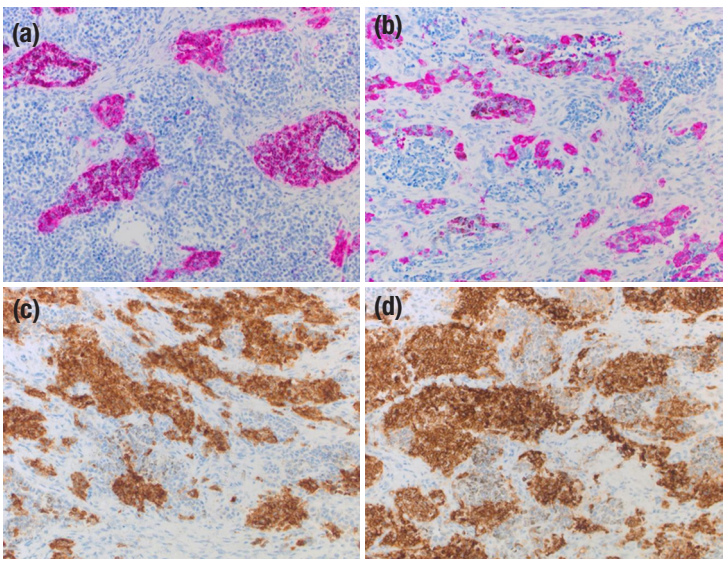

Figure 3. a–d. *Large epithelioid cells were positive for HBM-45* ***(a)*** *and PanCK* ***(b)****, and small cells were positive for Synaptophysin* ***(c)*** *and CD 56 (IHC, ×200)* ***(d)****.*

In the preoperative period, catecholamines such as VMA, noradrenaline, adrenaline, and neuron-specific enolase secreted by tumor cells support that the tumor is of neural crest origins such as pheochromocytoma and neuroblastoma. Following the surgery, these catecholamines are returned to normal levels[4,11].

Radiologically, the tumor introduces as a well-circumscribed radiolucent lytic lesion within the bone that may have features concerning local destruction. Computed tomography scans generally display a hyperdense tumor due to the presence of melanin and emphasize bone remodeling and expansion. Magnetic resonance imaging generally shows a demarcated, enhancing, and hypointense tumor on T1- and T2-weighted imaging[6,12].

Histomorphological findings show similar features in almost all MNTI cases published in the literature. Tumour includes two types of cells: one of them has

a small, less-differentiated, primitive appearance and scant cytoplasm, and the other one is a large epithelioid cell, which has a differentiated appearance, pale abundant cytoplasm, and includes melanin pigment. These characteristic cells are arranged in alveolar nests and solid sheets within a densely fibrous stroma. Mitoses or pleomorphism were not seen. The small cells were strongly positive for synaptophysin, an immunohistochemical marker supporting the neuroendocrine features of this tumor. Staining of the larger cells with pan-cytokeratin and HMB-45 supported epithelial differentiation and features seen with melanocytic differentiation[13]. Also, in our case, expression was observed in both cell populations for FLI-1.

The differential diagnosis of MNTI contains other small round blue cell neoplasms of infants, particularly neuroblastoma, Ewing sarcoma, alveolar rhabdomyosarcoma, desmoplastic small round cell tumor, and lymphoma. Also, melanogenic tumors of soft tissue should be considered in different diagnoses. It can be difficult to distinguish MNTI from other neuroendocrine tumors such as neuroblastoma, especially in small biopsy specimens. Typical features of MNTI, such as the biphasic population of epithelioid and primitive neurogenic cells, its characteristic immunohistochemical findings, and the clinical symptoms, can help distinguish it from other neoplasms[5,6].

Although MNTI cases are generally considered benign, their biological behavior is not fully understood. These tumors grow rapidly and present locally aggressive behavior and a high recurrence rate. It has been reported that cases show more aggressive behavior in tumors, where the small cell component is dominant, and the large cell component is not evident. However, there are no established criteria for distinguishing benign from malignant lesions[3]. The treatment option is generally surgical excision, as it was in the present case. In the literature, some studies point out that there is no difference between curettage and resection in recurrence rate[4]. In cases where accurate surgical eradication is not possible, radiotherapy and chemotherapy are potential alternative treatments. However, this is controversial[6,13].

Conclusion

MNTI is a rare tumor that can be easily confused with malign small round cell tumors, especially in small biopsies. Characteristic histomorphological and immunohistochemical findings are useful in the differential diagnosis. Knowing MNTI can prevent unnecessary preoperative and radical surgical treatments. These patients need to be followed up closely due to locally aggressive behavior and high recurrence rates.

Conflict of Interest

There are no conflicts of interest.

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