Melanotic neuroectodermal tumor of infancy: a histopathological and immunohistochemical study

MENDIS, Balapuwaduge Ranjit Rigobert Nihal, LOMBARDI, Tommaso, TILAKARATNE, Wanninayake MudiyanSELage

Abstract

Melanotic neuroectodermal tumor of infancy is an uncommon neoplasm that normally occurs in the anterior maxilla of children less than 1 year of age. This is a tumor with controversial origin, although neural crest origin is proposed. This case report presents an analysis of histopathological and immunohistochemical findings in this rare tumor.

Reference


DOI: 10.1111/j.2041-1626.2011.0086.x
PMID: 22298524
CASE REPORT

Melanotic neuroectodermal tumor of infancy: a histopathological and immunohistochemical study

Balapuwaduge Ranjit Rigobert Nihal Mendis¹, Tommaso Lombardi¹ & Wanninayake Mudiyanselage Tilakaratne²

¹ Laboratory of Oral and Maxillofacial Pathology, School of Dental Medicine, Faculty of Medicine, University of Geneva, Geneva, Switzerland
² Faculty of Dental Sciences, University of Peradeniya, Peradeniya, Sri Lanka

Introduction

Melanotic neuroectodermal tumor of infancy (MNTI) is an uncommon neoplasm that normally occurs in the anterior maxilla of children less than 1 year of age. A review of the literature shows that 82% of all lesions appear in the first 6 months of life. Most cases in the literature are reports of single-case histories or two-case histories. There are four reports with five cases or more.¹⁻⁴ Since the lesion was first described in 1918,⁵ a total of 355 case reports or case series have been reported in the medical literature.⁶ Extensive reviews of the literature have been made by four groups of authors.⁶⁻⁹

A majority of tumors (92.8%) occur in the head and neck region.⁷ The anterior maxilla is the most common site affected. Lesions have also been reported in the mandible, soft tissues of the cheek, dura, brain, skull, orbit, epididymis, mediastinum, skin, uterus, ovary, thigh, shoulder, scapula, and zygoma. Multicentric distribution of MNTI have also been reported.¹⁰

The mean tumor size reported is 3.5 cm (range: 1.0–10 cm). Exceptionally-large tumors have also been reported.¹¹ As the tumor arises in the area of developing deciduous teeth, the possible presence of odontogenic epithelium in the histological sections must be kept in mind while interpreting these tumors. Although MNTI is accepted as a benign tumor, the lesion invades the bone, and a few cases of malignancy have been reported.¹²,¹³ The rate of recurrence is reported to be 15%. Therefore, careful follow up is needed after conservative surgery. The rarity of the MNTI might result in its misdiagnosis as malignant melanoma, metastatic neuroblastoma, and rhabdomyosarcoma, especially in small biopsies. Therefore, pathologists need to have a clear insight into these tumors. The differential diagnosis involves other small round cell neoplasms, such as Ewing’s sarcoma, peripheral neuroepithelioma, desmoplastic small round cell tumor, peripheral primitive neuroectodermal tumor, and lymphoma.

A further case of MNTI is reported together with the histopathological and immunohistochemical appearances of the tumor.

Keywords
histopathology, immunohistochemistry, melanotic neuroectodermal tumor of infancy, neural crest, pathogenesis.

Abstract
Melanotic neuroectodermal tumor of infancy is an uncommon neoplasm that normally occurs in the anterior maxilla of children less than 1 year of age. This is a tumor with controversial origin, although neural crest origin is proposed. This case report presents an analysis of histopathological and immunohistochemical findings in this rare tumor.


© 2011 Blackwell Publishing Asia Pty Ltd
Case report

A 7-month-old boy presented with a bluish-black growth in relation to the right premaxilla, which had rapidly increased in size during the previous 3 months. Intraorally, the lump extended on the alveolar ridge from the upper right deciduous canine to the upper left deciduous lateral incisor region, and was sessile, soft, non-fluctuant, and not tender.

Past medical history was uneventful, and routine laboratory investigations were within normal limits. Intraoral and extraoral radiography showed a well-defined radiolucent lesion with bone destruction and evidence of developing tooth buds involved in the lesion. Urine level of vanillyl mandelic acid was not done. Excisional biopsy had been performed under general anesthesia with enucleation of the tumor and curettage of the adjacent bone. Three deciduous tooth germs, the upper central incisors, and the upper right lateral incisor attached to the lesion were removed. Periodic review over the past 8 months showed no recurrence of the tumor. The gross pathology specimen was fibrous in consistency and measured 2.0 × 1.5 × 1.3 cm, and the cut surface had a dark blue color.

Histopathological features

Examination of the sections stained with hematoxylin–eosin confirmed the presence of irregular-shaped tubular or alveolar formations lined by larger epithelioid cells, and also containing small round cells. The larger epithelioid cells are polygonal or polyhedral and contain variable deposits of granules, and in areas arranged in solid cords or strands, thus losing the trabecular structure. The cells do not contain abundant melanin, and show vesicular nuclei, prominent nucleoli, and an esinophilic cytoplasm. The smaller cells are round and basophilic, with a round nucleus and an even chromatin pattern and inconspicuous nucleoli. These cells are neuroblast like with hyperchromatic nuclei, and a scanty rim of cytoplasm (Figures 1a and 1b). In some areas, the tumor tissue was interrupted by single- or multiple-layer strand(s) of odontogenic epithelium (Figure 1c). Special staining for melanin, using Masson–Fontana, demonstrated the presence of melanin in the larger cells lining the trabecular spaces (Figure 1d). The connective tissue is mainly fibrous with moderate vascularization. The tumor is also seen to extend to the surface epithelium without being encapsulated. Evidence of a subepithelial chronic inflammatory cell infiltrate is also evident. Necrosis was absent, and the cells did not show any evidence of mitosis. Invasion of tumor islands in between alveolar bone trabeculae was also evident.

Immunohistochemical staining

Neuron-specific enolase (NSE) showed strong reactivity. The case demonstrated that NSE is present in the larger epithelioid cells and also in the small neuroblastic cells (Figure 2a). Glial fibrillary acidic protein (GFAP) was focally and weakly positive in larger cells, as well as in smaller cells (Figure 2b). HMB-45, the melanoma marker, showed a high immunoreactivity in larger polyhedral epithelioid cells, while smaller cells were negative (Figure 2c). Although the reactivity was not intense, S-100 positivity was observed in the large epithelioid cells, and the smaller cells were non-reactive (Figure 2d).
Discussion

In the literature, almost 19 different names have been used for this tumor,14 reflecting the various conflicting opinions given for the origin of the tumor over the years. However, the World Health Organization classification uses the term MNTI.15 There is also agreement from tissue culture, immunohistochemical, and ultrastructural studies that the tumor is of neural crest ectodermal origin.7,16,17

By light microscopy and electron microscopy, two main cell populations have been identified in this tumor, arranged in mainly tubular or alveolar formations. These formations are lined by large melanin pigment-containing epithelioid cells. In the central area of the trabecular arrangements are irregular nests of small neuroblastic cells possessing scant or fibrillar cytoplasm. These cell populations are arranged in a vascular fibrous stroma. A fibrous capsule is absent. The reported results of immunohistochemical investigations are inconsistent and not homogenous. This warrants further immunohistochemical study.

Many studies showed specific S-100 negativity.11,18–24 In a study of eight tumors, S-100 was negative in six of eight tumors, and positive in two tumors.4 In a series of 19 tumors collected from several centers, S-100 was positive in two cases.2 A series of 12 cases reported S-100 to be positive in two of 12 cases, and negative in the rest.3 Cytokeratin profiles have also been published.22,25

The phenotypic profile of cytokeratin/HMB-45 positivity and S100 negativity seems unusual. The S100 positivity demonstrated in this study is more in keeping with the pathogenesis of this tumor. The NSE positivity for both cell populations is in agreement with that of other studies,2,11,20 and in keeping with the neural crest ectodermal origin of this tumor. In a study of eight tumors, it was shown that seven of eight small cells and six of eight large cells were positive for NSE.4 Focal positivity, which was noted with GFAP, supports the theory of neural differentiation of MNTI. GFAP was positive in three of 12 tumors in one study.3 Recent immunohistochemical studies3,4 have utilized HMB-45 in MNTI. All the studies showed positive staining for epithelioid cells, proving them to be melanocytes actively producing melanin. In one study,3 all 12 tumors studied were HMB-45 positive. This was confirmed by our study, with antibody reactivity corresponding to the localization of the melanin pigment.

In summary, the immune profile of the present case supports the theory of neural crest origin in the pathogenesis of MNTI.

References

4 Barrett AW, Morgan M, Ramsay AD, Farthing PM, Newman L, Speight PM. A clinicopathologic and immunohistochemical analysis of melanotic


