*The Journal of Laryngology and Otology*
January 1998, Vol. **112,** pp. 61–64

# Clinical Records

# Melanotic neuroectodermal tumour of infancy arising in the maxilla

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**Abstract**
Melanotic neuroectodermal tumour of infancy is an uncommon neoplasm that usually occurs in children aged one year or less. Difficulty in deciding the cellular origin of this tumour has led to numerous names, including congenital melanocarcinoma, melanotic epithelial odontoma, melanotic ameloblastoma, and retinal anlage tumour. Electron microscopy and histochemical studies, however, have now established the neural crest origin. The most frequent site of occurrence is the maxilla followed by the skull, the brain and the mandible. The genital organs are the most frequent extracranial site.

We present two cases of melanotic neuroectodermal tumour of infancy arising in the maxilla.

**Key words: Melanotic neuroectodermal tumour; Infant; Maxilla**

## Introduction

Melanotic neuroectodermal tumour of infancy (MNTI) was first described by Krompecher (1918) who considered it a congenital melanocarcinoma. It is a rare benign lesion that usually is seen in the anterior region of the maxilla (Cutler *et al.*, 1981). Approximately 93 per cent of the lesions reported have occurred in the region of the head and neck; the most common sites being maxilla (68.8 per cent), skull (10.8 per cent), mandible (5.8 per cent) and brain (4.3 per cent) (Judd *et al.*, 1990). MNTI has also been found in the epididymis, thigh, mediastinum, foot, ovary and shoulder by Cutler *et al.*, (1981).

Based on the changing concept of the tumour cell origin, a variety of names have been attributed to the tumour such as melanotic epithelial odontoma, retinal anlage tumour, melanotic prognoma, pigmented adamantinoma, melanotic ameloblastoma, congenital pigmented epulis, melanocytoma and melanotic neuroectodermal tumour of infancy (Anil *et al.*, 1993). Borello and Gorlin (1966) reported a high urinary excretion of vanilmandelic acid (VMA) in a case of MNTI and pointed out the fact that the tumour is of neural crest origin.

Histologically MNTI consists of a biphasic population of epitheloid melanin-containing cells and neuroblastic cells within a prominent stroma (Melissari *et al.*, 1988). The melanin-containing cells can be cuboidal and arranged in alveolar, pseudoalveolar, or glandular-like structures (Mosby *et al.*, 1992).

## Case reports

*Case 1*

A seven-month-old boy was noted by his mother to develop progressive swelling in the left maxillary gingivo-buccal sulcus over a period of several weeks. The child was otherwise well and had no feeding difficulties. He was referred by his family doctor to an oral surgeon. Examination disclosed a firm expansion of the left maxillary alveolar ridge in the premolar region.

Radiographs revealed a radiolucency involving a developing deciduous premolar. Exploration of the region disclosed the developing tooth to be surrounded by a darkly pigmented friable soft tissue which extended into, and obliterated the left maxillary sinus. Darkly pigmented friable material was curretted from the mass within the sulcus and adjacent to the alveolar ridge. Complete excision was not attempted at the time but histological examination was characteristic of a MNTI of infancy. The patient was subsequently referred to us in 1971 for further evaluation and management. He was found to have a firm fullness of the left cheek. The left maxillary alveolus and gingivo-buccal mucosa were expanded by the tumour. The oral mucosa was intact except for the biopsy site. Routine laboratory investigations were normal except for a slight leukocytosis. Urinary VMA was unremarkable. Computed tomograms (CTs) demonstrated an extensive maxillary, infratemporal and orbital floor involvement.

Surgical excision was accomplished by a partial maxillectomy through a gingivo-buccal incision. The tumour was coal-black in colour and multiloculated. Bleeding was minimal. Laterally, the tumour invaded the infratemporal fossa, but was markedly thickened to a depth of approximately 1.0 cm by the mass and deeply pigmented by it.

The orbital floor was curretted away until more normal looking non-pigmented bone was encountered. In so doing the apex of the orbital floor was completely removed resulting in herniation of orbital fat into the

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Accepted for publication: 8 October 1997.

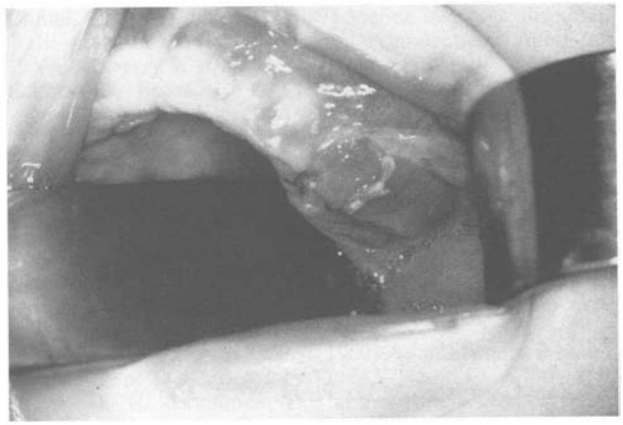

FIG. 1

(*Case 1*). Swelling of the left upper alveolus. Remaining stitch after previous biopsy.

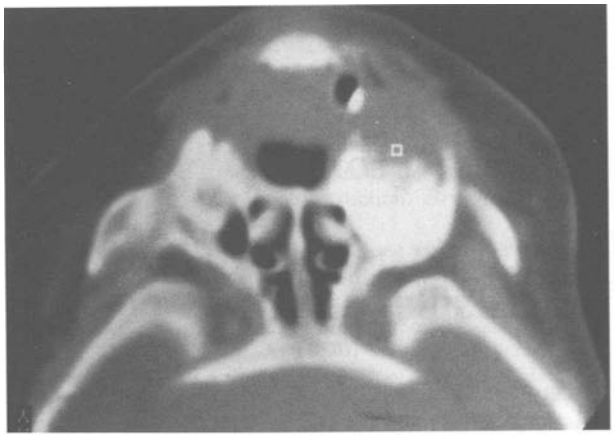

FIG. 3

Axial CT scan through the lower part of the nasal cavity showing the expansive tumour on the left side of the maxilla.

operative field. Small areas of pigmented tumour could be seen in the retro-orbital area, and because of its proximity to the optic nerve, per-operative ophthalmologic consultation was obtained. It was felt that further advances would carry an unacceptably high risk to the nerve. The resection in this area was therefore discontinued. A small buccal flap permitted primary surgical closure of the maxillary defect.

The patient continued to do well in the post-operative follow-up period. He was last seen in 1995 with no clinical or radiographical evidence of recurrence.

*Case 2*

A four-month-old male infant presented with a three-week history of a rapidly growing premaxillary mass (Figures 1–3). This was obviously pigmented, hard, smooth and lacking in mucosal involvement.

A biopsy was performed and the histopathological diagnosis was neuroectodermal tumour. This was supported by a radiographical finding which could be confused with a dentigerous cyst. The patient was otherwise well with no other physical nor laboratory pathological problems. A prompt surgical excision was undertaken. The tumour shelled out easily and was found to involve several dental buds which were sacrified (Figure 4). The dissection was continued until no gross evidence of pigmented tumour could be seen and peripheral curettings were free of tumour. The child has remained free of tumour six years post-operatively.

## Materials and methods

The tissue for light microscopy was fixed in 10 per cent neutral-buffered formalin and embedded in paraffin. Sections were stained with haematoxylin, eosin, saffranin, Masson-Fontana and Schmorl.

Paraffin sections were stained for neuron-specific enolase, cytokeratin (AEI/AE3), synaphtofysin, chromogranin and leu7.

Tissue fragments for electron microscopy study were fixed in a cacodylate-buffered mixture of one per cent glutaraldehyde and four per cent formaldehyde, postfixed in one per cent osmium tetroxide, dehydrate and embedded in an Epon/Araldite mixture.

Ultra-thin sections were contrasted with uranyl acetate and lead citrate and examined under a Philips CM5 transmission electron microscope.

## Results

Microscopically two types of tumour cells were seen. One consisted of groups of small cells with dark, hyperchromatic and scant cytoplasm. The other type exhibited larger pale cells arranged either in solid groups or in a pseudo-alveolar pattern. The tumour cells were surrounded by a dense fibrous stroma (Figure 5).

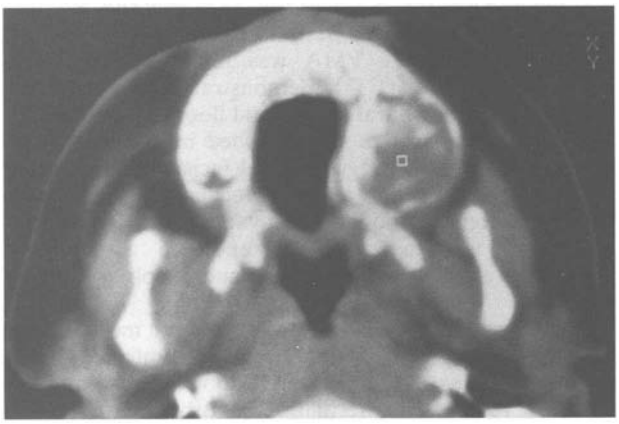

FIG. 2

Axial CT scan through the upper alveolus showing a cystic expansive tumour of the left side.

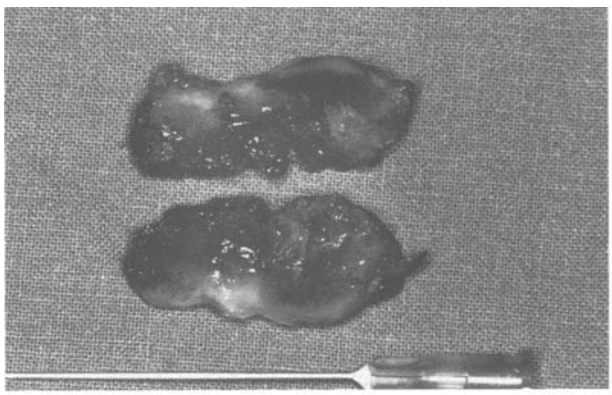

FIG. 4

Excised bluish-dark tumour measuring 2 × 2 cm and cut in two pieces.

https://doi.org/10.1017/S0022215100139908 Published online by Cambridge University Press

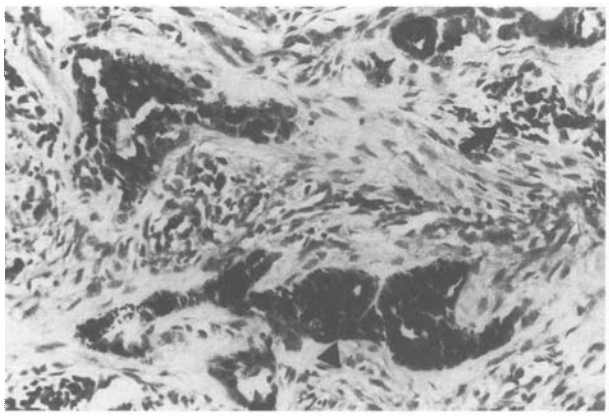

FIG. 5

(*Case 1*). Photomicrograph showing that the large tumour cells contain melanin granules, while the small dark cells do not (Masson-Fontana; × 225).

Masson-Fontana stain revealed abundant melanin granules in the larger cells, while the smaller cells were non-pigmented (Figure 6).

Antiserum to neuron-specific enolase and to cytokeratin (AEI/AE3) exhibited positive tumour cells. Synaptofysin showed a weak positivity while leu7 and chromogranin were negative. Electronmicroscopically, some of the tumour cells contained abundant pre-melanosomes and melanosomes in their cytoplasms and some had membrane-bound small electron dense granules. The latter were of a neuroendocrine nature.

## Discussion

The melanotic neuroectodermal tumour of infancy is very much debated and controversy exists concerning its histogenesis.

The most widely accepted theory is that the neoplasm orginates from the neural crest cells. This theory has received support from embryological, ultrastructural and biochemical evidence (Gotcher *et al.*, 1980). It has also been supported by the fact that the lesion secretes large amounts of VMA, which is characteristic of other tumours of neural crest origin such as pheochromocytoma, neuroblastoma and ganglioneuro-blastoma (Brekke and Gorlin, 1975).

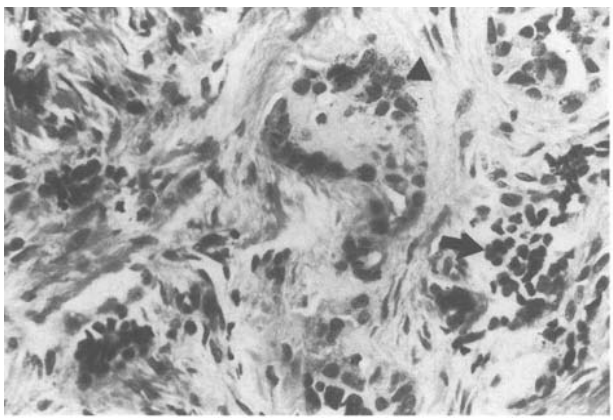

FIG. 6

(*Case 1*). Photomicrograph showing two types of tumour cells: groups of small cells with hyperchromatic nuclei and scant cytoplasm, and larger pale cells containing granular melanin pigment and pattern. The cells are surrounded by dense fibrous stroma. (H & E; × 360).

TABLE I

DIFFERENTIAL DIAGNOSES OF MNTI

| | |
|---|---|
| • Odontogenic cysts | |
| Palatal and dental laminal cysts of the newborn | |
| Eruption cysts and haematoma | |
| • Odontogenic tumours: | |
| Congenital gingival granular cell tumour | Histocytosis X |
| Pyogenic granuloma | Fibrosarcoma |
| Haemangioma | Chondrosarcoma |
| Lymphangioma | Rhabdomyosarcoma |
| Neuroblastoma | |

From the clinical point of view, MNTI has to be differentiated from other maxillary swellings in infancy as shown in Table I. However, the correct diagnosis cannot be achieved unless histopathological examination is performed (Forrester *et al.*, 1981).

MNTI is widely accepted as a benign neoplasm and the management has usually been conservative with local excision and curettage. However, a recurrence rate of 15 per cent has been reported (Block *et al.*, 1980) and attributed to incomplete removal of the primary lesion, dissemination of neoplastic cells during surgery and multicentricity (Nagase *et al.*, 1983).

Malignant behaviour has been reported in five out of 158 cases of MNTI reviewed by Culter *et al.* (1981), although in some of these cases the histological appearance is more similar to neuroblastoma than that of MNTI (Shokry *et al.*, 1986).

## Acknowledgement

We are indebted to doctor Jahn M. Nesland, Department of Ultrastructural Pathology, The Norwegian Radiumhospital, Oslo, Norway, for carrying out the immunohistochemical and electron microscopic studies.

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