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Melanotic neuroectodermal tumour of infancy

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Abstract
The melanotic neuroectodermal tumour of infancy is a rare, pigmented neoplasm that most frequently arises from the anterior maxillary alveolar ridge. It presents in the first few months of life, and usually follows a benign course. A classical case is presented and the clinical, radiological and pathological characteristics are discussed. The importance of early conservative surgical excision is emphasized with, in general, a good prognosis.

This tumour, which many otolaryngologists may not be familiar with, should be included in the differential diagnosis of head and neck neoplasms in infants and young children.

Key words: Maxillary neoplasms, neuroectodermal tumour; Infant

Case report

A four-month-old southeast Asian infant was admitted with a one-month history of a swelling on the left anterior alveolar ridge (Figure 1).

An intraoral examination revealed a smooth, firm, non-tender, non-cystic, mass with normal overlying mucosa, and a normal hard palate.

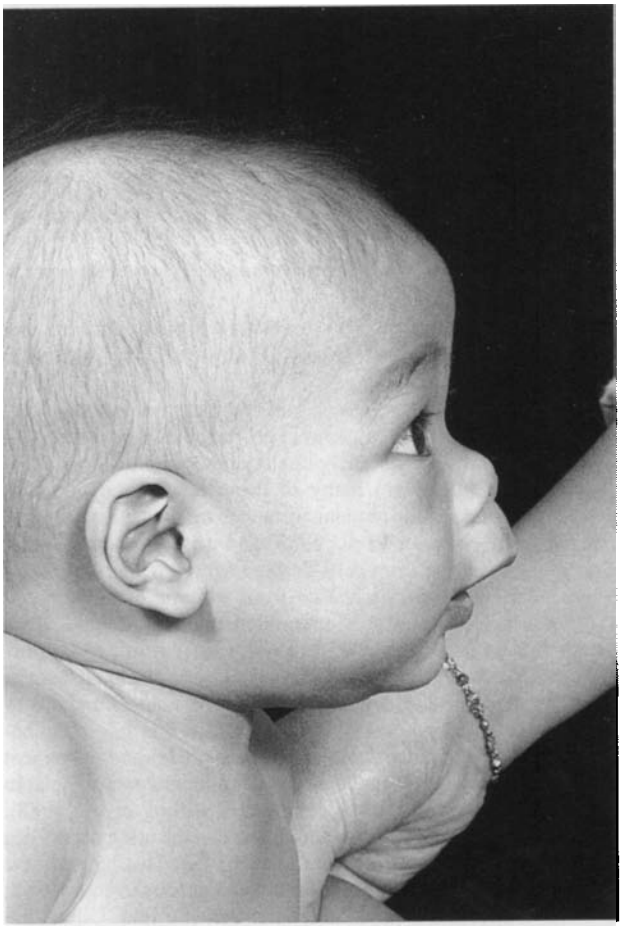

FIG. 1
Pre-operative lateral view demonstrating anterior maxillary swelling.

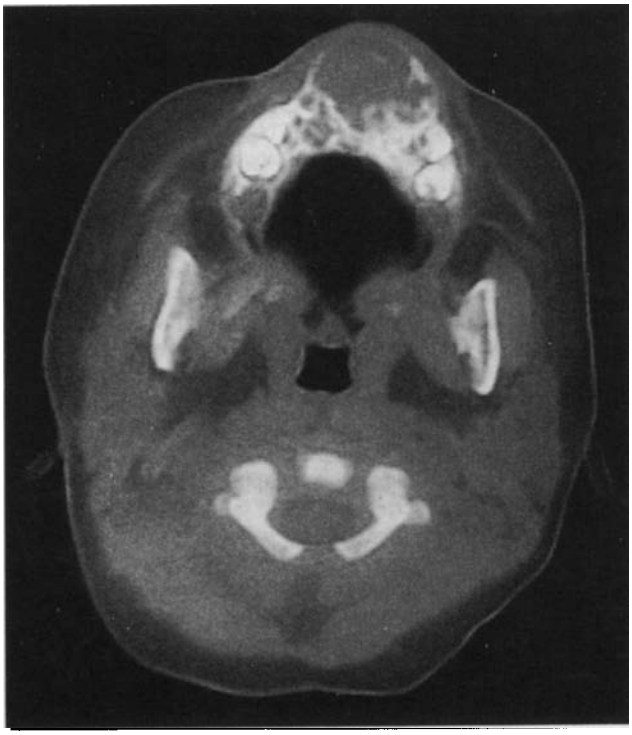

FIG. 2
Axial computerized tomographic (CT) scan demonstrating a left-sided erosive pre-maxillary lesion. The lesion has a central soft tissue density with a shell-like bony rim.

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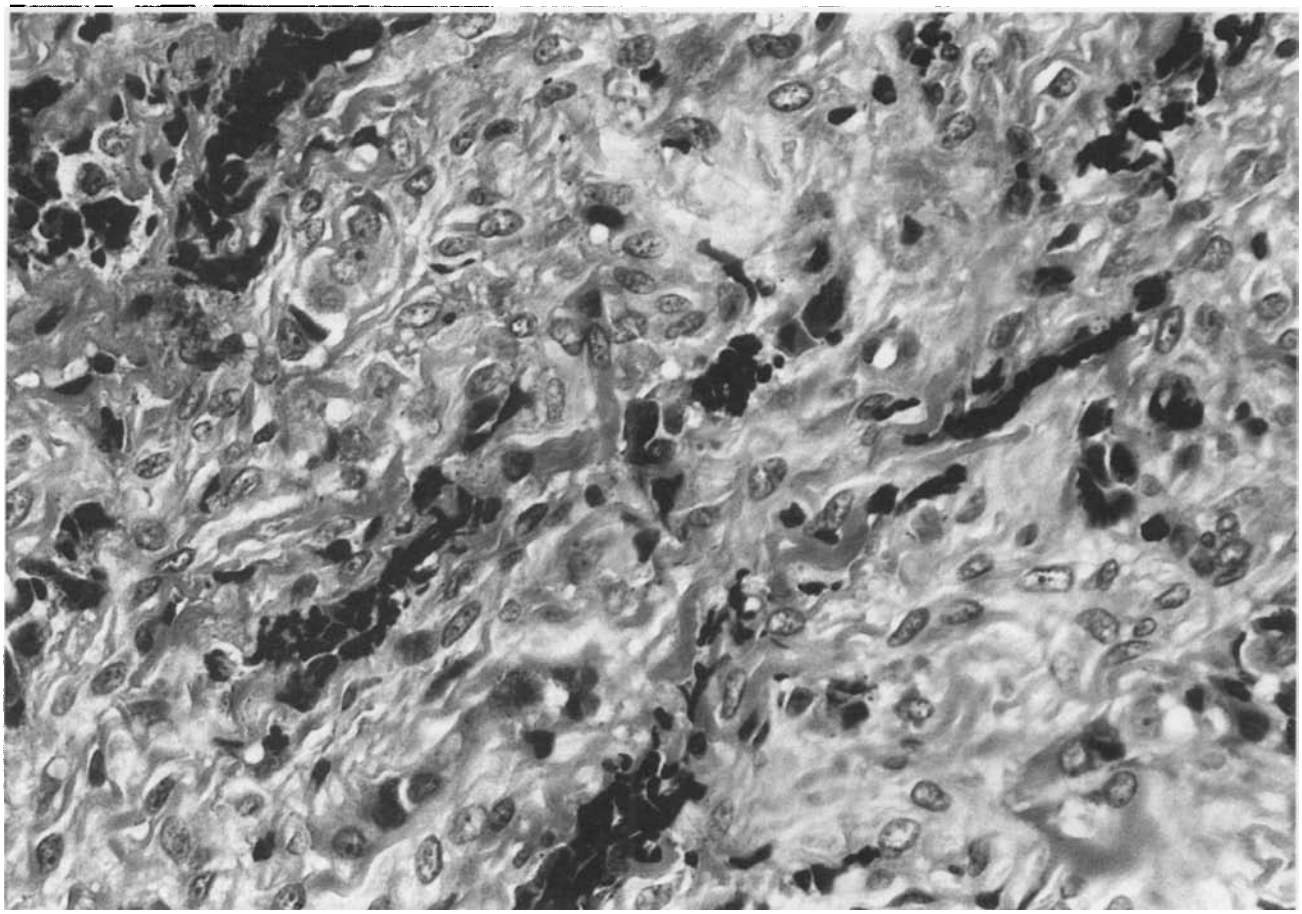

FIG. 3
Cords and clusters of small, dark, neuroblast-like cells lying within a fibroblastic stroma. (H & E; × 100)

A computerized tomographic (CT) scan demonstrated a cystic swelling eroding the premaxilla and situated slightly to the left of the midline. It was of central soft tissue density with a shell-like bony rim (Figure 2). The provisional clinical diagnosis was of fibrous dysplasia.

An incisional biopsy was performed *via* a 'U'-shaped sublabial flap and a buff-coloured specimen was sent for histology. Microscopy of the fixed specimen showed fragments of bone trabecula with a cellular fibrous stroma. Islands of small dark cells were found within the stroma together with larger cells containing pigment (Figures 3 and 4). A Masson Fontana stain confirmed that the pigment was melanin and immunohistochemical staining of the tumour cells was positive with neuron specific enolase. Electron microscopy was not performed. A diagnosis of pigmented neuroectodermal tumour of infancy was made. Urinary levels of vanillyl-mandelic acid were normal.

A subtotal maxillectomy was done *via* a gingivo-buccal sulcus incision and the lesion was completely excised with a macroscopic clearance of 1.5 cm. His recovery following surgery was unremarkable (Figure 5) and there is presently no sign of recurrence 18 months following removal.

Discussion

The first description of a melanotic neuroectodermal tumour of infancy (MNTI), formerly known as a melanotic progonoma, or retinal anlage tumour, was by Krompecher in 1918.

The exact origin of these tumours has been the subject of much controversy. Initially owing to the fact that the tumour cells resembled cells found in the developing retina, it was thought that this was the tissue of origin. This theory proposed that ectopic retinal cells, within the upper jaw, were sequestered as a result of abnormal midface development. The name retinal anlage tumour thus appeared in the literature. This is however unlikely since the retina is completely formed prior to jaw development, and sequestration is therefore unlikely. A second theory proposes an odontogenic origin and these tumours have also acquired the appellations, melanotic ameloblastoma, pigmented ameloblastoma, melanotic progonoma, pigmented congenital epulis and melanotic epithelial odontome. Although this may adequately explain many of these tumours, it does not account for the not infrequent instances arising outside tooth-bearing bone (Johnson *et al.*, 1983) and it is now believed that these tumours arise from cells derived from the neural crest.

The evidence for a derivation from a neural crest stem cell comes from tissue culture, immunohistochemical, and ultrastructural studies (Dehner *et al.*, 1979; Cutler *et al.*, 1981; Stirling *et al.*, 1988). A dual population of cells is characteristic; small lymphocyte-like cells with a prominent nucleus and inconspicuous cytoplasm resembling neuroblasts, and larger epithelioid cells with abundant cytoplasm, pale nuclei and prominent nucleoli, that resemble melanocytes. The latter contain melanin and rarely also vanillyl-mandelic acid (Stirling *et al.*, 1988). Increased levels of vanillyl-mandelic acid in the urine occurs in a small minority of cases (Dehner *et al.*, 1979). This property the MNTI shares with the neuroblastoma and phaeochromocytoma; thus giving further support to a neural crest origin. Ultrastructurally it is possible to demonstrate the presence of premelanosomes and structured melanosomes in these cells (Dehner *et al.*, 1979). Melanin synthesis of this type is seen only in cells of neural crest origin and is distinct from lysosomal neuromelanin seen in the central and sympathetic nervous systems (Stirling *et al.*, 1988).

Histologically the differential diagnosis includes: neuroblastoma, rhabdomyosarcoma, lymphoma and Ewing's tumour. None of these contain melanin and they are further distinguished

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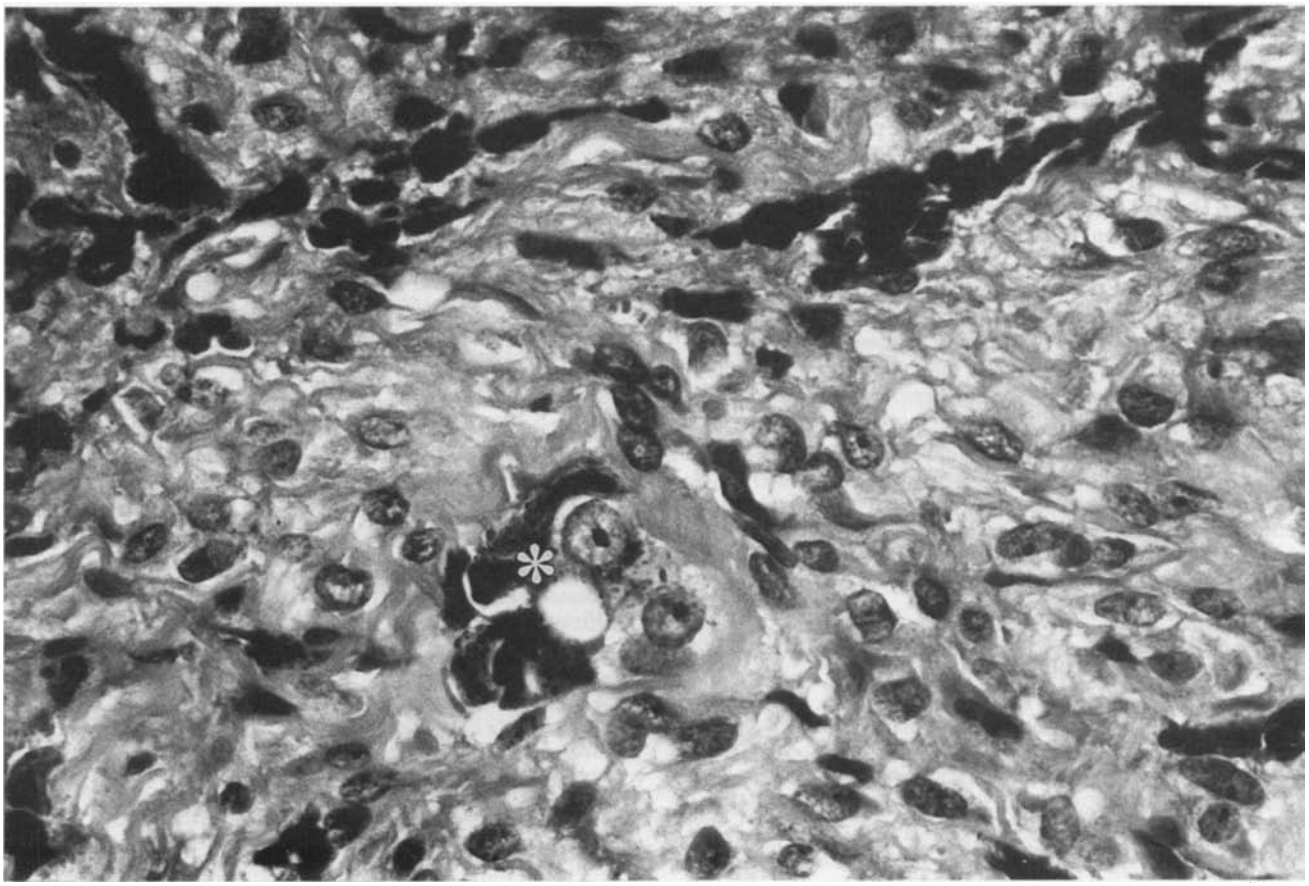

FIG. 4
Associated with the small cells are larger melanocyte-like cells with more abundant cytoplasm containing granular melanin pigment (asterisk). (Masson Fontana; ×160).

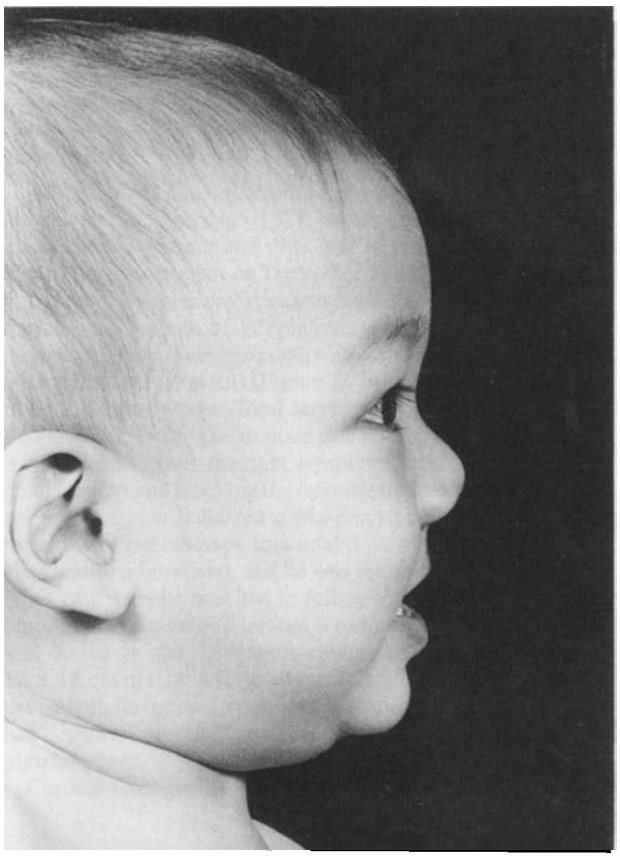

FIG. 5
Lateral view demonstrating post-operative appearance.

by immunohistochemistry and electron microscopy. Malignant melanoma is virtually unheard of in infancy and confusion is thus unlikely.

The MNTI falls into a group of peripheral primitive neuroectodermal tumours that arise outside the central or sympathetic nervous system. This group also includes many of the so-called Ewing's sarcomas and Askin's tumour: the malignant thoraco-pulmonary round cell tumour of childhood (Stirling *et al.*, 1988). The MNTI is unique in that unlike other tumours in this group its behaviour is almost invariably benign.

In a review of all cases reported up to 1981 92.8 per cent of lesions were in the head and neck, with the maxilla being the most frequent site (68.8 per cent). Other sites include the skull (10.8 per cent), mandible (5.8 per cent), and brain (4.3 per cent) (Cutler *et al.*, 1981). The MNTI has also been found in the mediastinum, shoulder, thigh, epididymis, ovary, uterus, and foot (Cutler *et al.*, 1981). It is distributed equally between the sexes, and most commonly presents as a nonulcerative, fast growing, soft tissue mass displacing the upper lip. Overlying pigmentation is common and a blue–black discolouration is observed in most cases. The majority present in the first three months of life, and 95 per cent before the age of one year.

Plain radiographs, and computerized tomographic scanning usually demonstrate a benign picture, a radiolucency with sharp margins and displacement of surrounding bone and tooth buds. Rarely however, rapid growth can result in bone invasion giving a lesion with poorly demarcated borders, and in such cases developing teeth may be seen to be floating within the lesion.

The treatment is surgical, and debate has centred on the extent of surgical excision. Most now favour a conservative approach (Hupp *et al.*, 1981; Judd *et al.*, 1990), *via* a gingivo-buccal sulcus incision or lateral rhinotomy approach (Crockett *et al.*, 1987). If technically possible, complete resection is recommended, but

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when radical surgery would be mutilating then local excision with curettage of the underlying bone is sufficient. This approach is based on the observation that tumour remnants tend to disappear, and it has been proposed that central stimulatory cells exist, and when removed, death of the peripheral invading cells will occur (Soderberg and Padgett, 1941).

Invasion of vital structures, including the optic nerve has been described (Judd *et al.*, 1990), early intervention is thus essential to minimize the extent of tissue destruction caused by tumour growth.

The prognosis of this rare tumour is more favourable than other similar infantile tumours. Local recurrence occurs in 10 to 15 per cent (Cutler *et al.*, 1981) but most cases are eventually cured, with repeated conservative surgery, when recurrences emerge. Malignant change occurs in three to four per cent (Cutler *et al.*, 1981; Stirling *et al.*, 1988) and metastatic spread is rare. Interestingly in those cases showing unequivocal malignant change with lymph node metastasis, the malignant element appears to arise in the neuroblastic portion and has features of neuroblastoma (Navos Palacios, 1980). There are however unfortunately no reliable features, either clinical or histological, that will predict those that will ultimately undergo malignant transformation.

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