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Fine needle aspiration in the pre-operative diagnosis of melanotic neuroectodermal tumour of infancy

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Abstract
A case of melanotic neuroectodermal tumour of infancy is decribed. The pre-operative diagnosis was made on cytological material obtained by fine needle aspiration. The patient was a three-month-old male infant with a rapidly growing maxillary tumour mass that also involved the pterygomaxillary fossae and the floor of the orbit. In addition to the typical clinical presentation, the cytology is also distinctive showing a dual population of small neuroblastic cells and large melanin-containing epithelial cells. Histological, immunohistochemical and electron microscopic examination of the excised mass confirmed the initial diagnosis. The pre-operative distinction of this tumour from other small round cell tumours of infancy (rhabdomyosarcoma, neuroblastoma, melanoma and lymphoma), is essential in order to plan the most complete resection therefore reducing the possibilities of tumour recurrence. This tumour belongs to a field of pathology with which many otolaryngologists may not be familiar.

Key words: Maxillary neoplasms; Cytodiagnosis; Immunohistochemistry

Introduction

Melanotic neuroectodermal tumour of infancy (MNTI) is a rare, usually benign, histologically distinctive neoplasm that in its classic form occurs in the anterior alveolar ridge of the maxilla (Irving *et al.*, 1993), but is has also been described in other sites. The terms retinal anlage tumour, melanotic progonoma, and melanotic ameloblastoma have also been used to name it, demonstrating the lack of consensus about its histogenesis. In this presentation we describe a case of MNTI emphasizing the usefulness of fine needle aspiration (FNA) cytology in the pre-operative diagnosis. Nowadays patients with MNTI are usually treated by paediatricians in coordination with the oral maxillofacial surgeons (OMS) and only occasionally does an ear, nose and throat (ENT) specialist have the opportunity to be involved in a case like this.

Case report

The patient was a three-month-old male infant that presented with a rapidly growing right maxillary tumour mass and nasal obstruction (Figure 1). No other associated symptoms were present. Pregnancy was uneventful with forceps delivery at the eighth month. The baby had to be watched in the Neonatology Unit for low-birth weight (2.350 kg). Physical examination showed facial asymmetry due to a bluish tumour mass with prominent submucosal vessels and hard consistency to bimanual palpation.

FNA smears revealed a cellular aspirate with two different cell types (Figure 2). The predominant cell population consisted of small, uniform neuroblastic cells with round nuclei and scanty to absent cytoplasm. The second population were oval to cuboidal large melanin-containing cells with eccentrically placed nuclei and moderate amount of cytoplasm. The granules of melanin pigment had a round to rod shape and stained brown with a Papanicolaou, bluish with Giemsa and black with Masson-Fontana. Immunocytochemistry on an ethanol-fixed smear revealed a positive reaction to HMB-45 and cytokeratin in the large pigmented cells and to synapto-

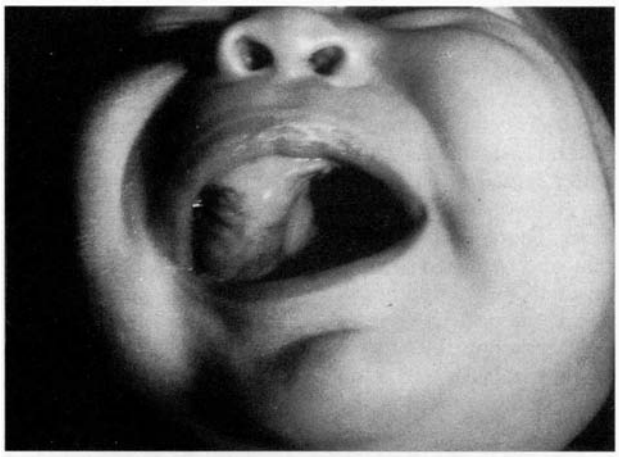

Fig. 1
Clinical pre-operative picture of the infant with the tumour of the anterior maxilla protruding inside the oral cavity.

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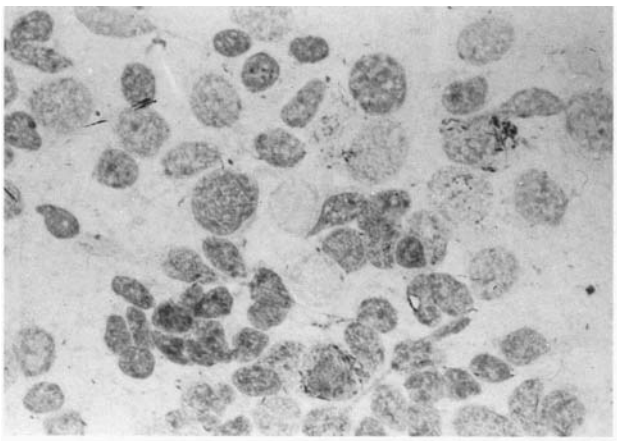

FIG. 2

Cytological smear. Two different cell types: small neuroblastic cells and large cuboidal melanin-containing cells. (Giemsa stain; × 400).

physin in the small round cell group (Figures 3a, 3b and 3c). These clinical, cytological and immunocytochemical findings were consistent with the diagnosis of MNTI.

A full metastatic work-up consisting of an abdominal echography, chest X-ray, urine analysis, haemogram and chemistry profile was within normal limits but for the fact of a slight nonspecific elevation of the alkaline phosphatase and lactate dehydrogenase (LDH). Urinary vanylmandelic acid (VMA) excretion was 1 mg/24 h (normal: 1–14). Computerized tomographic (CT) scan of the head showed a large soft tissue tumour mass involving the frontal and zygomatic processes of the right maxillary bone with osteolytic bony erosion and osteoblastic reactive hyperostosis; the tumour also involved the pterygomaxillary fossae and the floor of the orbit (Figure 4).

Surgical enucleation and curettage was performed under general anaesthesia with nasotracheal intubation to allow better visualization of the surgical field. An incision along the gingivobuccal sulcus was made just over the area of the mass. The mass was excised and 3 to 5 mm of bone was removed as safety margins. Exploration of the orbit revealed neither compromise of the extraocular muscles nor of the optic globe.

Macroscopically, the specimen consisted of a 5 cm submucosal blackish tumour mass that invaded bone and contained two teeth inside. Histologically, the tumour was

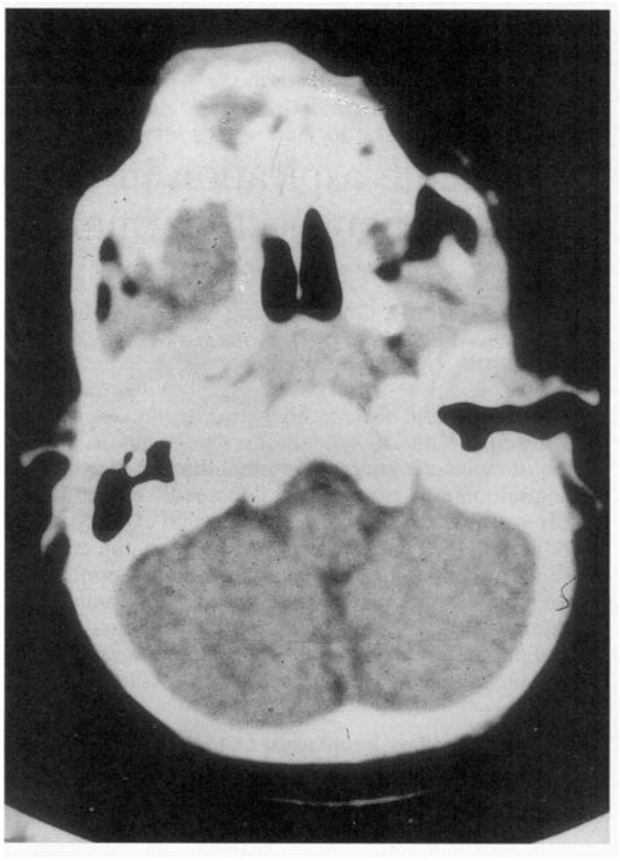

FIG. 4

Axial CT scan demonstrating a soft tissue mass involving the right maxillary bone and pterygomaxillary fossae.

nonencapsulated and composed of a dense fibrous stroma which supported a dual population of small neuroblastic cells and larger melanin-containing epithelial cells (Figure 5). The small neuroblastic cells were tightly arranged into small nests that were often surrounded by pigmented cells in an alveolar or tubular formation. Neither mitoses nor areas of necrosis were seen. Immunohistochemical staining revealed a positive reaction to cytokeratin, HMB-45 and vimentin in the large pigmented cells and to synaptophysin and neuron specific-enolase (NSE) in the small neuroblastic cells (Figures 6a and 6b). Electron microscopy showed an undifferentiated cell

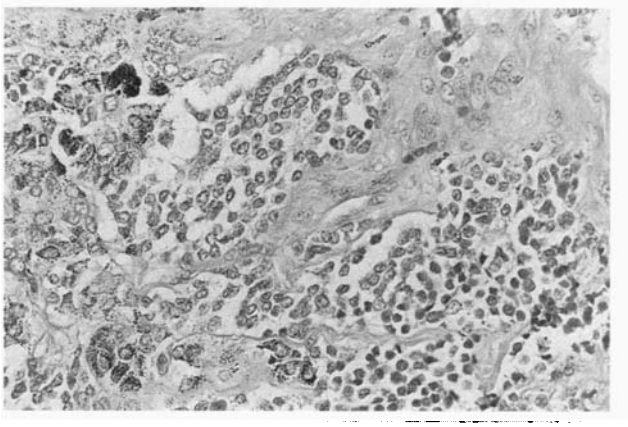

FIG. 3

Cytological smear. Positive immunoreaction for cytokeratin (A), synaptophysin (B) and for HMB-45 (C). (Immunoperoxidase stain; × 500).

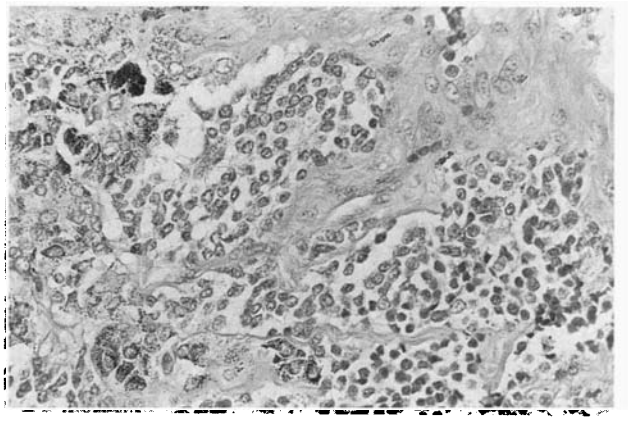

FIG. 5

Histological section of the tumour showing clusters of small neuroblastic cells and large pigmented epithelial cells, surrounded by a dense fibrous stroma. (H & E; × 200).

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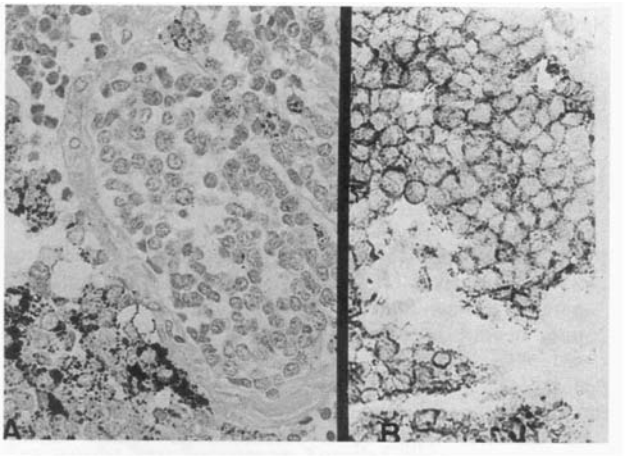

FIG. 6

Histological section. A. Positive immunoreaction for HMB-45 in the cytoplasm of the large pigmented epithelial cells. The small neuroblastic cells are negative. B. Positive immunoreaction for synaptophysin in the cytoplasm of the small neuroblastic cells. The large epithelial cells are negative. (Immunoperoxidase stain; × 200).

population with neuroblastic cells (dendritic processes, microtubules and neurosecretory granules) and pigmented epithelial cells (melanosomes, tonofilaments and desmosomes). DNA content was measured from selected slides and stained with Feulgen in a static cytometer; histograms from both small neuroblastic cells and large pigmented cells showed a uniform cell population with a diploid pattern.

Post-operatively, the patient was watched in the intensive care unit (ICU), developing respiratory distress on extubation secondary to oedematous subglottic stenosis. He had to be reintubated and followed by the ICU team for 10 days under systemic corticosteroid therapy (dexamethasone). A CT scan of the head and a total body bone scan were negative three weeks after the surgery without evidence of tumour recurrence one year following its removal.

Discussion

The first description of MNTI was reported by Krompecher (1918); since then approximately just over 200 other cases have also been reported in the English literature. The most frequent site of occurrence is the maxilla (68.8 per cent) (Cutler *et al.*, 1981), usually in the anterior alveolar ridge on one side of the midline, in the region of the incisors. Most of the cases reported are within the head and neck region (92.8 per cent) (Cutler *et al.*, 1981), but it has also been reported in other sites: the skin (Argenyi *et al.*, 1991), epidydimis (Calabrese *et al.*, 1995), extremities (Scheck *et al.*, 1989), uterus (Sobel and Carcangiu, 1994), mediastinum (Misugi *et al.*, 1965) and brain (Hahn *et al.*, 1976). The histogenesis of this tumour is still an issue of debate, however, ultrastructural and immunohistochemical studies have shown certain evidence of neural crest stem cell differentiation (Denher *et al.*, 1979; Navas Palacios, 1980; Pettinato *et al.*, 1991).

MNTI presents before the age of one year and is approximately equally distributed among sexes. The tumour is a non-ulcerative rapidly growing pigmented (blue-black) soft tissue mass that displaces the upper lip. Computed tomography (CT) and magnetic resonance imaging (MRI) are used as extension studies, to determine the amount of bony invasion and the compromise of important structures (optic globe) (Judd *et al.*, 1990; Mirich *et al.*, 1991). Increased levels of vanyl-mandelic acid in the urine occurs in a small minority of cases which are characteristically found in patients with neuroectodermal tumours such as pheochromocytoma and neuroblastoma (Borello and Gorlin, 1966; Denher *et al.*, 1979). In addition to the typical clinical presentation, the cytology and histology are distinctive showing a dual population of small neuroblastic cells and larger melanin-containing epithelial cells. Two previous reports described the cytological picture of MNTI, one located in the maxilla (Rao *et al.*, 1990) and the other in the epididymis (Toda *et al.*, 1996), but none of them describe the immunocytochemistry findings in the aspirate.

The pre-operative distinction of this tumour from other small round cell tumours of infancy and childhood is essential in order to establish the most appropriate definitive therapy; therefore immunohistochemical markers are an excellent help in the differential cytological and histological diagnosis with embryonal rhabdomyosarcoma (desmin and myoglobin positive), metastatic neuroblastoma (synaptophysin and NSE positive), Burkitt's lymphoma (common leukocyte antigen positive) and malignant melanoma (HMB-45 and S-100 positive).

The treatment of choice consists of complete surgical excision with margins and curettage of the underlying bone via a gingivo-buccal sulcus incision or a lateral rhinotomy approach in the case of a large and locally invasive tumour mass (Crocket *et al.*, 1987). An early diagnosis and treatment are important to avoid invasion of important surrounding structures as the optic nerve, and to minimize the extent of bone and soft tissue destruction.

The prognosis of MNTI is favourable if it is compared with other round cell tumours of infancy. Tumour recurrence and persistence occurs in 45 to 60 per cent of the cases and are closely related to incomplete excision (Pettinato *et al.*, 1991). Malignant change occurs in three to four per cent of the tumours and metastatic spread is rare (Cutler *et al.*, 1981; Stirling *et al.*, 1988). Unfortunately the potential for local recurrence or metastasis cannot be predicted from clinical or histological features. Cytometric studies have also been inconclusive in predicting tumour recurrence (Pettinato *et al*, 1991; Kapadia *et al.*, 1993).

In conclusion, MNTI is a rare, usually benign expansile tumour of the anterior maxilla with specific cytological and immunohistochemical findings by FNA. It is important to stress the need of a definitive pre-operative diagnosis by FNA, that will allow us to achieve a complete excision with tumour-free margins in a one-step surgical procedure, thus reducing the probability of developing tumour recurrences. MNTI in most countries are usually diagnosed by paediatricians and depending mainly on the institution it can be treated by the OMS, ENT, plastic or paediatric surgery specialists. Therefore this case sets an example in how the head and neck region does not have well-defined borders among some surgical subspecialties and in particular ENT, OMS and plastic surgery.

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