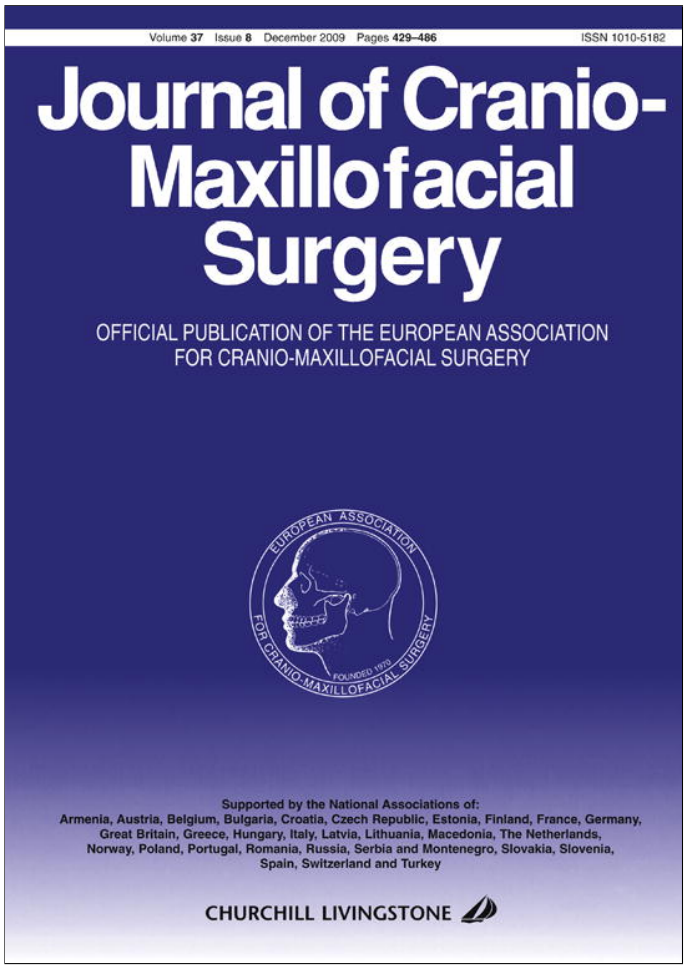

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# Early outcome of three cases of melanotic neuroectodermal tumour of infancy

F. M. A. BUTT, Lecturer, BDS (UoN), FDSRCS (Eng), MDS-OMFS (UoN)[1], S. W. GUTHUA, Professor and Dean, BDS (UoN), MMEDSc (Harvard), DOMS (MGH-Harvard), FCS, FIAOMS[1], M. L. CHINDIA, Associate Professor, Chairman, BDS (UoN), MSc, FFDRCSI[1], F. RANA, Associate Professor, Lecturer, MB, ChB, MMed Path (UoN)[2], T. M. OSUNDWA, Lecturer, BDS (UoN), MDS-OMFS (UoN)[1]

[1]*Department of Oral and Maxillofacial Surgery, University of Nairobi, Kenya;* [2]*Department of Pathology, Aga Khan University Hospital, Nairobi, Kenya*

*SUMMARY.* **Melanotic neuroectodermal tumour of infancy (MNTI)/progonoma is a rare lesion affecting infants. Although it is slow growing and appears benign, it may have malignant potential. Evidently, surgery is the main stay of treatment and close follow-up is recommended for all cases. The literature shows that radiotherapy and chemotherapy may be indicated especially in cases where total surgical extirpation is equivocal. This article contributes three more cases of MNTI surgically managed at our institution. © 2009 European Association for Cranio-Maxillofacial Surgery**

***Keywords:*** **melanotic neuroectodermal tumour of infancy, progonoma**

## INTRODUCTION

Melanotic neuroectodermal tumour of infancy (MNTI) is a rare benign neoplasm of infancy with a rapid growth pattern which was first described by Krompecher in 1918 as congenital melanocarcinoma. In the literature it has been known by a variety of synonyms including retinal anlage tumour, pigmented congenital epulis, melanotic progonoma, pigmented ameloblastoma, melanotic epithelial odontoma, pigmented teratoma, and melanotic adamantinoma, retinal ameloblastoma (*Clarke* and *Parsons*, 1951; *Lurie*, 1961; *Stowens* and *Lin*, 1974; *Fletcher*, 1995). This reflects great controversy about the cell of origin and pathophysiology of this tumour (*Heba* et al., 2008). In the late 1966s, *Borrello* and *Gorlin* discovered the association between elevated levels of urinary vanillylmandelic acid in the affected infants and suggested that the lesion was of neural crest origin. *Hoshino* et al. in 1994 demonstrated increased urinary levels of catecholamines in MNTI which supported the neural crest origin of the tumour. This tumour is reported to be malignant in 4% of cases and tends to occur in the first year of life and; the anterior maxilla is the most commonly affected (69%), followed by the skull (11%), the mandible (6%), less commonly the brain, mediastinum, thigh, epididymis, foot and shoulder (*Cutler* et al., 1981; *Johnson* et al., 1983). MNTI being a rare lesion poses a challenge to clinicians not only in its diagnosis but also management. According to the literature review there are approximately 250 cases that have been reported (*Retna* et al., 2007). We present three more cases managed that were managed at our institution.

## CASE 1

A 5-month-old child presented to the Oral and Maxillofacial clinic with a maxillary swelling over the anterior maxillary ridge which had been growing progressively for a duration of two months. The mother was concerned as it caused difficulty in breast feeding and asymmetry of the face. Extra-oral examination revealed a lesion elevating the upper lip and causing incompetence. On intraoral examination, there was a round swelling expanding the alveolar ridge, the overlying mucosa had areas of black pigmentation with no ulceration. It was firm, non-tender and the child was unable to approximate the alveolar ridges. The medical history was unremarkable. Under general anaesthesia resection was undertaken with a good margin of healthy tissue. Histopathological examination revealed an MNTI. This patient was followed-up for a period of 24 months.

## CASE 2

A 2½-month-old male presented with a swelling over the right maxilla which had been present for 1½ months. It had grown rapidly causing facial asymmetry and concern to the mother although it was asymptomatic. Examination showed a swelling extending from the right lower eyelid to the lower lip with elevation of the nasal dome and ala and flattening of the nasolabial fold. Intraorally it had areas of black discolouration with an intact overlying mucosa and the edges were well defined with expansion of both the buccal and palatal cortices. On palpation it was firm with no areas of tenderness (Fig. 1). An impression of MNTI

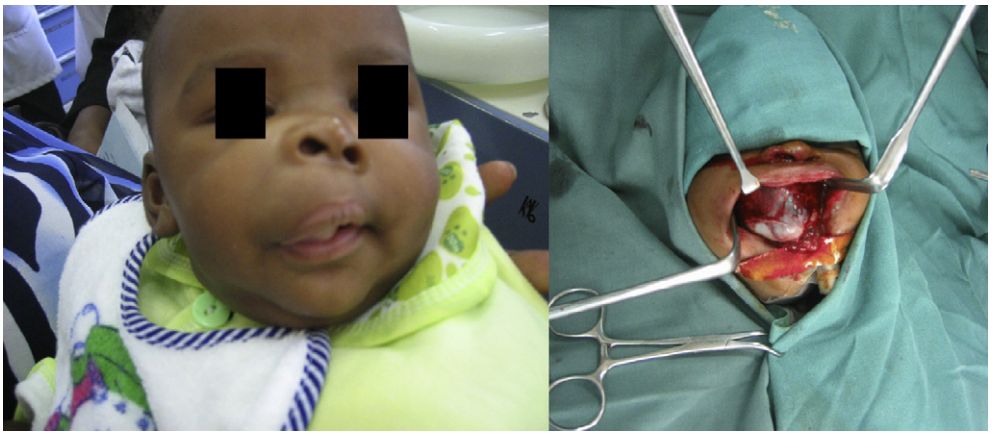

**Fig. 1** – Clinical presentation of MNTI in a 2½ month old baby.

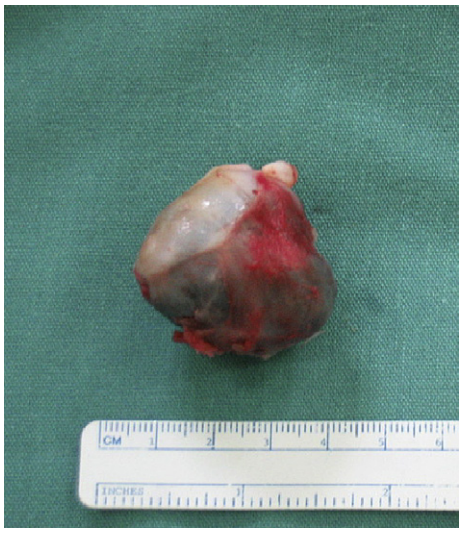

**Fig. 2** – Appearance of the excised specimen.

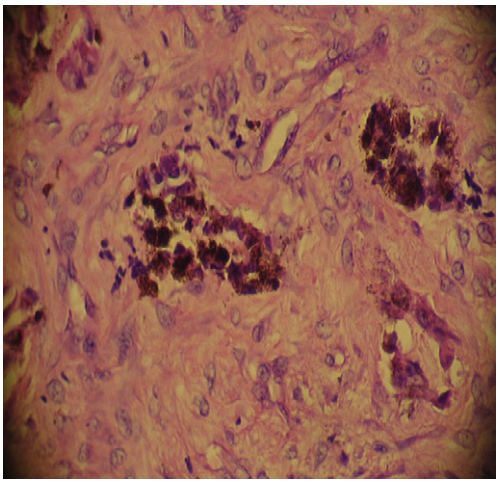

**Fig. 3** – Photomicrograph depicting the histopathological features of MNTI (Magnification x40, Haematoxylin & Eosin stain).

was made. Under orotracheal intubation the lesion was excised with three of the developing tooth buds in situ. A deformity was left which was closed partially by advancement of labial and palatal flaps. The gross specimen measured 3 cm × 3.5 cm × 4 cm (Fig. 2). Histopathological examination revealed a progonoma (Fig. 3). At two months post-operative follow-up the patient was doing well and remains under regular review.

## CASE 3

A 2-year-old girl presented with an intrabony lesion on the left side of the face which had started as a small swelling and had progressively increased in size over 12 months. The onset was insidious without symptoms but the lesion caused deformity of the face and hence the reason for consultation. The medical history was unremarkable. Extra-oral examination showed a swelling over the left maxilla extending from the lower eyelid to the angle of the mouth on the same side causing a deviation to the left side of the face. It measured 5 cm in the widest dimension with normal overlying skin. Intraorally the lesion caused obturation of the left buccal sulcus and appeared as if it arose from the maxillary sinus causing bone expansion (Fig. 4). The rest of the hard and soft tissues were normal including the presence of a complete set of the deciduous dentition. An antero-posterior view of the skull showed an ill-defined radio-opacity over the left maxilla and antrum. A computed tomography (CT) scan outlined a clearly delineated lesion causing opacification of the left maxillary sinus with destruction of its lateral wall (Fig. 5). Under orotracheal intubation the lesion was exposed via a Weber–Ferguson incision (Fig. 6). The lesion was excised with a good margin of about 5 mm of normal tissue. Two fragments were removed one measuring 4.5 cm × 3.0 cm × 2.5 cm and the other 3.0 cm × 2.5 cm × 2.0 cm (Fig. 7). The resulting defect was primarily closed. Microscopic examination revealed features of MNTI. This patient has been reviewed for three years since and remains well.

## DISCUSSION

It has been documented that the best form of treatment for MNTI is surgical removal with preservation of vital structures (*Blank* and *Runckel*, 1980). Successful primary

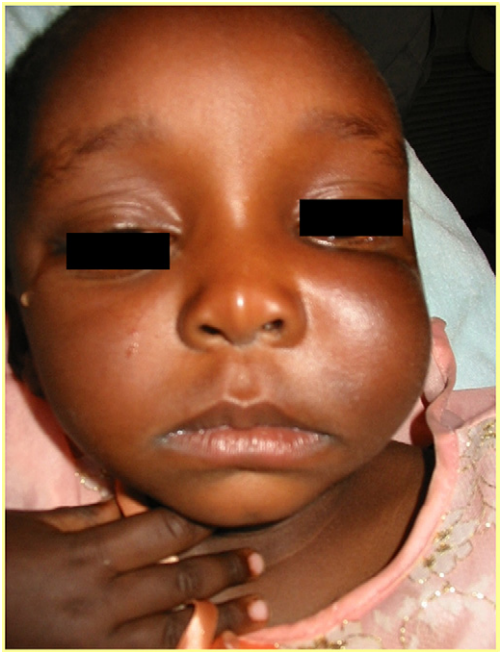

**Fig. 4** – Clinical presentation of a 2-year old with MNTI in the left maxillary.

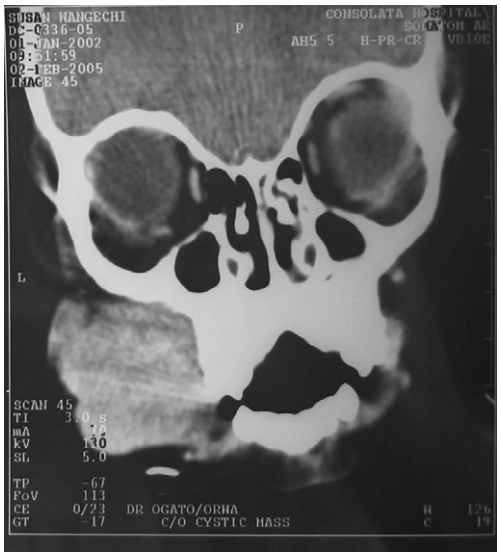


**Fig. 5** – Coronal CT scan of the maxilla showing clearly delineated lesion emanating from the maxillary antrum.

excision has been reported to occur in 85–90% of all cases (*Clarke* and *Parsons*, 1951). Although classified as a benign lesion, the average recurrence rate is 15–20% and, may be as high as 50% among cases without wide resection. Recurrences have been reported in the first several weeks post-operatively and it is skewed towards younger patients. This has been reported in children who were at twelve weeks of age or younger possibly due to an aggressive form of MNTI (*Lurie*, 1961). In 2000, *Kaya* et al. examined two cases of MNTI and found that adjuvant therapy such as chemotherapy and radiation should be reserved for cases where resection with clear margins is impossible (*Heba* et al., 2008). *Sailukar* in 2007 administered a regime of neoadjuvant chemotherapy consisting of

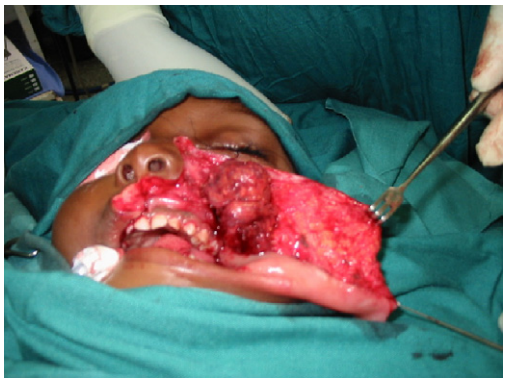

**Fig. 6** – Intra-operative photograph of the lesion exposed via a modified Weber-Ferguson incision.

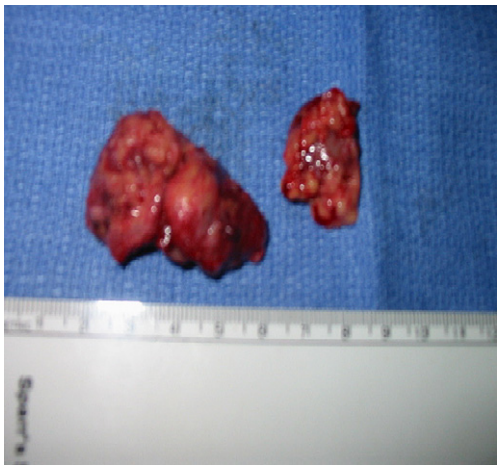

**Fig. 7** – Photograph of the gross specimen excised in two fragments.

vincristine, cyclophosphamide and dactinomycin for a three-month-old child with MNTI and achieved 10% regression in the mass in two weeks showing a poor response to the treatment (*Krompecher*, 1978). Radiotherapy and combination chemotherapy including vinblastine, ifosphamide, etoposide, cyclophosphamide, doxorubicin and dactinomycin has been advocated for inoperable recurrences or margin positive resections (*Sailukar* et al., 2007). Therefore, the utility of chemotherapy and radiation in the treatment of MNTI remains unclear and controversial (*Lurie*, 1961).

The diagnosis is based on the knowledge of the disease and experience. Since the discipline of paediatric Oral & Maxillofacial surgery has advanced, second opinion regarding the diagnosis should be sought. In addition, incisional biopsy followed by histopathological examination by a competent pathologist with head and neck pathology experience is advised. Although some reports have indicated that the MNTI cells are cytokeratin and HMB 45 (human melanoma block) positive and S-100 negative (*Barrett* et al., 2002), because of our limitations the specimens were not subjected to these tumour markers and, therefore, histodiagnosis was based purely on the nature of cells as depicted in Fig. 3.

All three of our patients had excision with a healthy margin of tissue with respect for the vital structures. The longest follow-up in these series has been three years and none of the

patients have shown signs of recurrence. The recurrence rates mandate a close and long-term follow-up as the child continues to grow. Our recommended surgical approach is intra-oral method to avoid facial scars and minimize disfiguring the patient. However, in case 3, because of the extent and location of the tumour, it was not possible to remove the entire tumour with a good margin via the intraoral route.

## CONCLUSION

According to the literature review and our experience the role of chemotherapy and radiotherapy appears controversial and ought to be reserved for malignant lesions. Infants should be spared from the adverse side effects of chemo- and/or radiotherapy if surgery is a curative option.

## References

Barrett AW, Morgan M, Ramsay AD, Farthing PM, Newman L, Speight PM: A clinicopathologic and immunohistochemical analysis of melanotic neuroectodermal tumor of infancy. Oral Surg Oral Pathol Radiol Endod 93: 688–698, 2002

Blank E, Runckel DN: Melanotic progonoma. Case report 119. Skeletal Radiol 5: 179–182, 1980

Borrello ED, Gorlin RJ: Melanotic neuroectodermal tumor of infancy – a neoplasm of neural crest origin. Cancer 19: 196–206, 1966

Clarke BE, Parsons H: An embryological tumor of retinal anlage involving the skull. Cancer 4: 78–85, 1951

Cutler LS, Chaudhry AP, Topozian R: Melanotic neuroectodermal tumor of infancy. An ultrastructural study, literature review and re-evaluation. Cancer 48: 257–270, 1981

Fletcher C: Melanotic neuroectodermal tumour of infancy. Clinical pathology, immunocytochemical and flow cytometry study. Am J Surg Pathol 17: 566–573, 1995

Heba S, Shagufta S, Khaled B, Abdulhafez AS: Melanotic neuroectodermal tumour of infancy; review and case report. J Pediatr Surg 43: E25–E29, 2008

Hoshino S, Takahashi H, Shimura T, Nakazawa S, Naito Z, Asaro G: Melanotic neuroectodermal tumor of infancy in the skull associated with high serum levels of catecholamines; case report. J Neurosurg 80: 919–924, 1994

Johnson RE, Scheithauer BW, Dahlin DC: Melanotic tumour of infancy: a review of seven cases. Cancer 52: 661–663, 1983

Kaya S, Unal OF, Sorac S, Gedicoglu: Melanotic neuroectodermal tumor of infancy. Report of two cases and review of literature. Int J Pediatr Otorhinolaryngol 52: 169–172, 2000

Krompecher E: Zur histogenese und sonstiger Kiefergeschwulste. Beitr Pathol Anat 64: 165–197, 1978

Lurie HI: Congenital melanocarcinoma, melanotic adamantinoma, retinal anlage tumor, progonoma and pigmented epulis of infancy. Cancer 14: 1090–1108, 1961

Retna KN, Sreedharan S, Balachandran D: Melanotic neuroectodermal tumor of infancy: a case report. J Indian Soc Pedod Prev Dent 25(3): 148–151, 2007

Sailukar M, Bhagwat R, Seth T: Melanocytic tumour of infancy. J Indian Assoc Pediatr Surg 12(3): 136–137, 2007

Stowens D, Lin TH: Melanotic progonoma of the brain. Hum Pathol 5: 105–113, 1974

**Dr F.M.A. BUTT**
P.O. Box 25361, Code 00603
Nairobi, Kenya

Mobile: 0722 703347
Fax: +254 20 271 0712
E-mail: fawzia_butt@yahoo.co.uk

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