Primary neuroblastoma of the mandible

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ABSTRACT

Primary neuroblastoma of the mandible is rare with only seven cases reported to date. The diagnosis is made after any possible primary tumour has been adequately investigated for and excluded. We report a one-year nine-month-old girl with a primary neuroblastoma of the mandible and discuss its possible aetiology.

Keywords: mandible, mandibular neuroblastoma, paediatric tumour, primary neuroblastoma

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INTRODUCTION

Metastatic neuroblastoma to the mandible is much more common than a primary neuroblastoma arising from the mandible. A review of the literature reveals only seven reports of primary mandibular neuroblastoma.[1-7] The authors of these reports faced the same problem we encountered, i.e. difficulty in labelling the case as a primary neuroblastoma, given its infrequency. We report a case of a primary neuroblastoma of the mandible seen in our institution and discuss its possible aetiology.

CASE REPORT

The patient is a girl who first presented at one year nine months of age, with swelling and pain in her left jaw in November 2006. As there was no response to a course of antibiotics, a biopsy was done the next month and she was found to have neuroblastoma with N-myc amplification. Resection of the mandibular tumour with insertion of a bone graft (harvested from the right fifth rib) was performed in June 2007 after chemotherapy (three cycles of vincristine, cytoxan, adriamycin and two cycles of cisplatin, etoposide, with the second cycle having half the dose of cisplatin on account of hearing impairment). Computed tomography (CT) performed prior to excision showed the extent of tumour in the mandible (Fig. 1). No other lesion was detected with CT of the thorax, abdomen or pelvis, 18-FDG positron-emission tomography (PET) (Fig. 2) or on a 123I MIBG scan (Fig. 3). The brain CT did not show any abnormality and a bone marrow biopsy of the right iliac crest was negative.

Pathology of the excised tumour showed two areas of viable tumour as well as two positive lymph nodes adjacent to the tumour. As there was dehiscence of the surgical wound, wound revision was performed one month after the initial surgery, supplemented by a bone growth factor injection, resulting in good wound healing thereafter. The girl developed peripheral neuropathy, initially just a footdrop that subsequently progressed to an inability to walk. Magnetic resonance (MR) imaging of the spine showed no cord or nerve root compression and the neuropathy was attributed to chemotherapy.

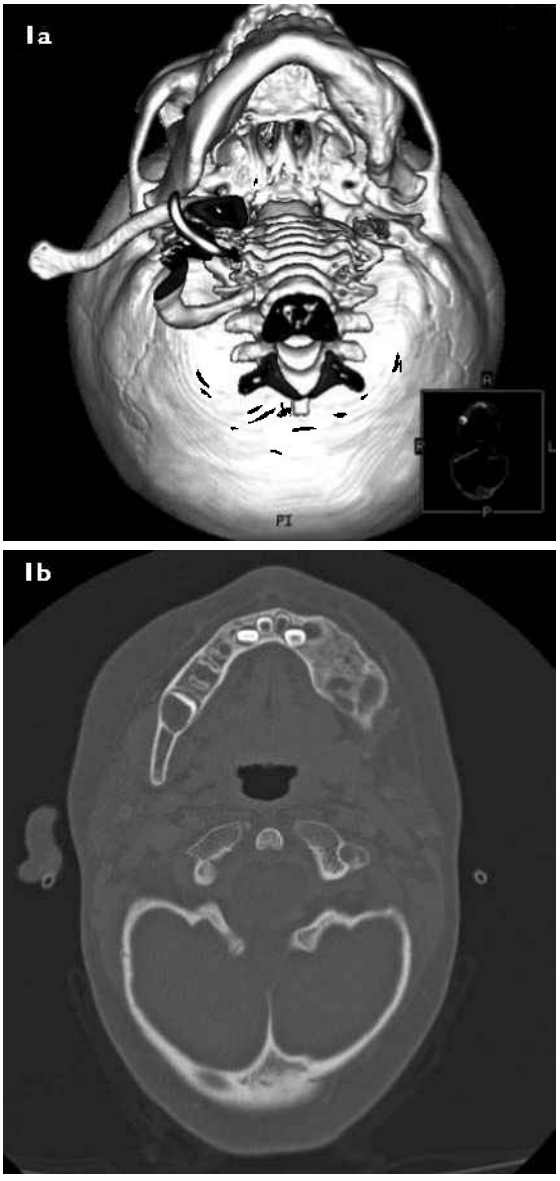

Fig. 1 (a) 3D CT image of the head taken in May 2007 after the biopsy and prior to excision shows an expansile lesion in the body of the mandible extending up into the left ramus. (b) Axial CT image shows that the lesion comprises lucent and sclerotic regions, possibly partly the result of chemotherapy.

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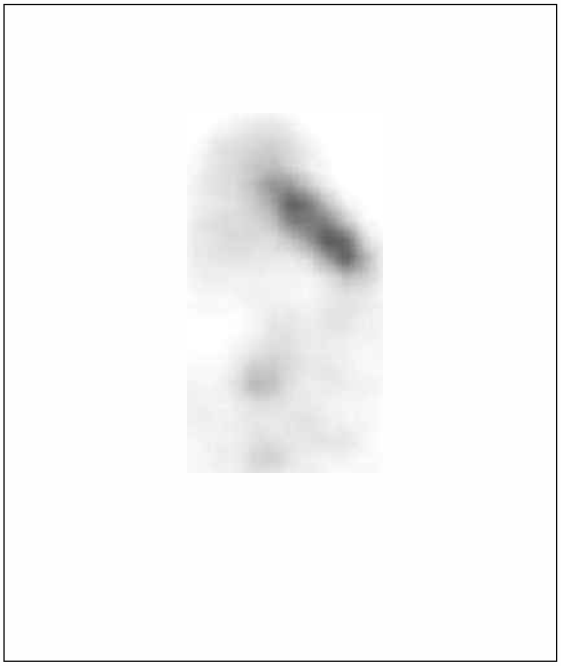

Fig. 2 FDG-PET image shows avid uptake of 18-FDG radiotracer by the mandibular lesion.

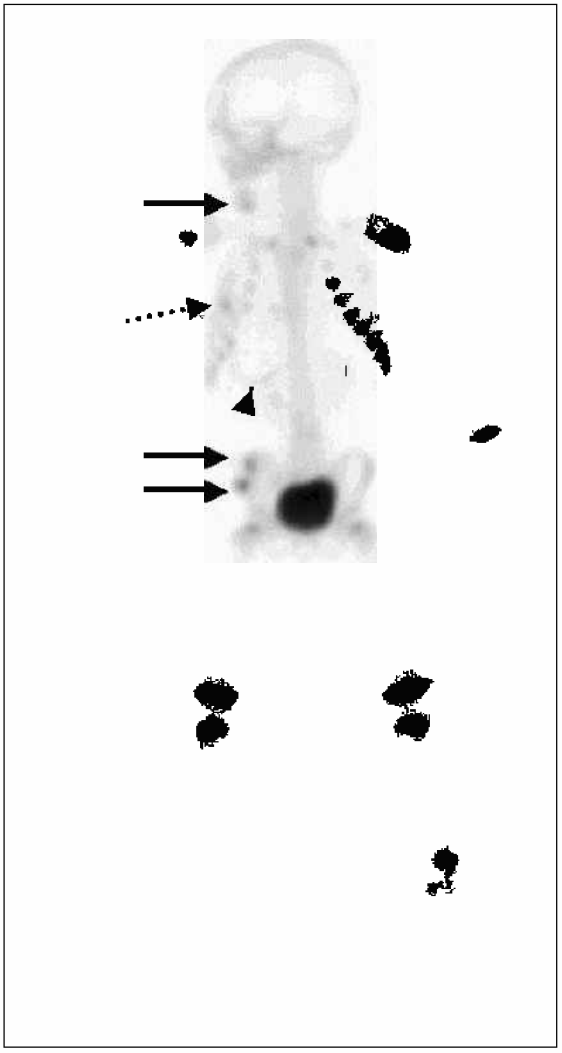

Fig. 3 123I MIBG image shows increased uptake of radiotracer (arrow) by the mandibular lesion. The increased uptake seen in the right iliac crest is a result of the bone marrow biopsy (double arrows). The increased uptake in the anterior right chest is the site where the right fifth rib was harvested for the bone graft (dashed arrow). The tubular structure lying across the right chest is due to a central venous line (arrowhead). No other abnormal focus of increased uptake is seen, particularly in the chest and abdomen, to suggest the presence of a tumour.

The patient underwent autologous bone marrow transplantation because of the positive tumour margins post-resection, regional lymph node involvement and N-myc amplification. Repeat surgery was deemed unsuitable during tumour board discussion in view of the problem with wound healing and cosmesis. A stem cell harvest had been performed after the second cycle of vincristine, cytoxan and adriamycin. With the aid of granulocyte-colony stimulating factor, 13 million CD34+ cells were obtained.

DISCUSSION

Neuroblastomas most commonly arise from within the abdomen (65%), from the adrenal medulla (40%) or anywhere along the sympathetic chain (25%). They can also arise in the thorax (15%), pelvis (5%), neck (3%) and in other sites including the brain.[8] The mandible is an unusual site for primary neuroblastoma,[1-7] although it is frequently seen as a site for neuroblastoma metastases. The importance of labelling this mandibular neuroblastoma as a primary or metastastic lesion lies in the treatment decision for the patient and the prognosis. If the lesion is truly a primary neuroblastoma, this would be a stage 1 disease (using Evans classification) as opposed to a stage 4 disease if it was a metastasis. The various case reports in the literature have shown that it is possible to have a primary neuroblastoma of the mandible, the evidence being that the only focus of neuroblastoma detectable was in the mandible as well as the better than expected survival of these patients. If the mandibular neuroblastoma in these patients were metastases, they would have been stage 4 disease with a 33% survival[9] at best with chemotherapy in contrast to 92% survival for stage 1 disease.[10] The PET scan, which has been proven to be superior to MIBG scans for identifying small neuroblastoma lesions, delineating the extent and localising anatomical sites of disease outside the skull vault, [11] did not pick up other sites of involvement in our patient.

A few theories have been proposed to explain the possibility of a primary neuroblastoma of the mandible,

one being a primary neuroblastoma giving a metastasis to the mandible before spontaneously regressing. This appears to be supported by cases of spontaneously disappearing neuroblastomas.[12] However, this theory of the primary tumour spontaneously regressing while leaving the mandibular metastasis to proliferate does not seem logical, as the primary tumour would be expected to have identical genetic material as its metastasis and should behave similarly. Faulty migration of neural crest cells into the mandible in the embryo is the other hypothesis that has been proposed for the possibility of neuroblastoma in the bony mandible, given that skeletal tissue is derived from mesoderm and not ectoderm. A more recent publication states, however, that the facial bones are unique and they arise from mesenchyme derived from ectodermal neural crest, unlike the rest of the skeletal tissues in the trunk and appendages which are mesodermal in origin.[13] Thus, this suggests that it is not a failure of migration but rather a failure of regression of these cells that would result in the development of neuroblastoma. The high incidence of normal healthy children found to have a natural antibody against neuroblastoma which indicate that they once harbored neuroblastomas supports this.[14] More compelling evidence comes from a Japanese study which detected IgM antibodies against neuroblastoma in healthy volunteers and 82 patients with non-malignant surgical disease.[15]

Thus, primary neuroblastoma of the mandible is rare but has been described, possibly due to a lack of regression of neural crest derivatives in the mandible from an inadequate immune response. Nevertheless, given the rarity of such a condition, the diagnosis of a primary neuroblastoma of the mandible should be made only after exclusion of any possible primary tumour.

REFERENCES

1. Burkes EJ Jr, Kelly DE. Primary mandibular neuroblastoma. J Oral Surg 1980; 38:128-31.
2. Muldoon CJ. Neuroblastoma of the mandible. S Afr J Surg 1973; 11:153-4.
3. Barsekow F. [Neuroblastoma of the mandible - case report]. Dtsch Zahnarztl Z 1981: 36;173-4. German.
4. Antoine P, Raphael B, Bachelot H, et al. [Primary neuroblastoma of the mandible. Apropos of a case]. Rev Stomatol Chir Maxillofac 1984; 85:314-9. French.
5. Vautier E. [Neuroblastome avec atteinte osseuse isolee, de bon prognostic. Metastase ou tumeur primitive? (a propos de deux observations chez de grad enfants)]. These Med 1982. French.
6. Ihrai H, Jidal B, El Gbouri H. [Neuroblastoma: primary mandibular localization]. Maroc Med 1986; 8:285-91. French.
7. Kushner BH, Kramer K, Cheung NK. Chronic neuroblastoma. Cancer 2002: 95:1366-75.
8. Schofield D, Cotran RS. Diseases of infancy and childhood. In: Contran RS, ed. Robbins Pathologic Basis of Disease. 5th ed. Philadelphia: WB Saunders, 1994: 459-61.
9. Kaneko M, Tsuchida Y, Mugishima H, et al. Intensified chemotherapy increases the survival rates in patients with stage 4 neuroblastoma with MYCN amplification. J Pediatr Hematol Oncol 2002; 24:613-21.
10. Haase GM, Atkinsonb JB, Stramb DO, Lukens JN, Matthay KK. Surgical management and outcome of locoregional neuroblastoma: Comparison of the Childrens Cancer Group and the International Staging Systems. J Pediatr Surg 1995; 30:289-95.
11. Kushner BH, Yeung HW, Larson SM, Kramer K, Cheung NK. Extending positron emission tomography scan utility to high-risk neuroblastoma: fluorine-18 fluorodeoxyglucose positron emission tomography as sole imaging modality in follow-up of patients. J Clin Oncol 2001; 19:3397-405.
12. Reynolds CP. Ras and Seppuku in neuroblastoma. J Natl Cancer Inst 2002; 94:319-21.
13. Carlson BM. Human Embryology and Developmental Biology. St Louis: Mosby, 1994.
14. Ollert MW, David K, Schmitt C, et al. Normal human serum contains a natural IgM antibody cytotoxic for human neuroblastoma cells. Proc Natl Acad Sci USA 1996; 93:4498-503.
15. Fukuda M, Nozaki C, Ishiguro Y, Horibe K. Distribution of natural antibody against human neuroblastoma among children with or without neuroblastoma. Med Pediatr Oncol 2001; 36:147-8.