CLINICOPATHOLOGIC CONFERENCE

An unusual mandibular mass in a child

Karen A. Eley, MBChB, MRCS(Ed), PGCTLCP, FHEA, MSc,[a] Kate Wheeler, MBBS, FRCPCH,[b] Ree Nee Tiam, MBBS, FRCPath,[c] and Stephen R. Watt-Smith, MBBS, BDS, FDSRCS, MD,[d]
University of Oxford and Oxford Radcliffe Hospitals NHS Trust, Oxford, Oxford, United Kingdom
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A 2-year-old boy was referred to the oral and maxillofacial department with a 1-week history of swelling affecting the right mandible (Figure 1). Although this had been noted by his parents and the nurse at his nursery, he had remained asymptomatic and systemically well. There was no history of trauma or dental pain. He had been born at 36 weeks via Cesarean section, and his medical and surgical history was positive only for an uneventful left inguinal hernia repair at 3 months of age. He was meeting all of his developmental milestones, and his childhood immunizations were up to date. On clinical examination there was mild extraoral swelling noted around the right angle and body of the mandible. Intraorally, his dentition was within normal limits, with evidence of good oral hygiene. A 3 × 3 cm firm swelling was noted in the right retromolar region. Systemic examination was unremarkable. Magnetic resonance imaging (MRI) was arranged, and a review appointment made. However, over the course of the following week, there was rapid growth of the mass, which was now associated with pain, particularly when eating, resulting in an emergency hospital admission. Routine hematology and biochemistry results at this time demonstrated a normal full blood count, but elevated C-reactive protein (CRP) of 15 mg/L (normal 0-8 mg/L), and lactate dehydrogenase (LDH) of 408 IU/L (normal 90-235 IU/L). An ultrasound scan of the right mandibular region showed a 3 × 1.8 × 2.5 cm solid mass overlying the right mandible with some deep extension. It did not appear overtly vascular. A radiograph of the mandible was markedly abnormal, with bony destruction, and "sun-ray spiculation" suggesting a degree of osteogenesis. An adjacent soft tissue swelling was noted, and there was evidence of resorption of the overlying teeth. Computerized tomographic (CT) examination of the mandible showed a 6.2 × 4.1 × 8.9 cm mass involving the mandibular condyle, subcondylar region, coronoid process, ramus, and body up to the level of incisor teeth. Marked bony expansion and destruction accompanied by some new bone formation gave rise to characteristic sun-ray spiculation. The mandibular mass was noted to bulge intraorally, extending into the floor of the mouth. There was no significant lymphadenopathy (Figure 2).

DIFFERENTIAL DIAGNOSIS

The differential diagnosis in this case included infective, traumatic, and neoplastic processes. There had been no witnessed trauma, and although pain was an eventual feature, it was absent at first presentation. The dental occlusion was normal, and there were no fractures identified on plain radiography, making trauma a particularly remote possibility. Infection was also deemed to be unlikely in view of his good oral hygiene, with no dental mobility or tenderness to percussion of the teeth. Biochemically, an elevated CRP was nonspecific for a potential inflammatory process, and the white cell count and temperature remained within normal limits.

Attention was therefore turned to possible neoplastic processes, subdivided into 2 broad categories: odontogenic and nonodontogenic tumors. Odontogenic tumors derived from mesenchymal elements of the dental follicle are the most common group of tumors in childhood.[1] However, these rarely present with intra- or extraoral swelling, as was the presenting feature in this case. Normal dental development also made an odontogenic tumor less likely.

Within the nonodontogenic group are giant cell lesions (e.g., giant cell tumors), fibro-osseous lesions (e.g., cherubism, and osteoblastoma), and myxomas. Of these, a fibro-osseous lesion was considered to be a more probable cause.

Cherubism is an autosomal dominant trait with variable penetrance in female subjects, but 100% penetrance in male subjects. First described in 1931,[2] it is

[a]Nuffield Department of Surgical Sciences, University of Oxford.
[b]Department of Paediatrics.
[c]Department of Pathology.
[d]Department of Oral and Maxillofacial Surgery, Oxford University Hospitals NHS Trust.
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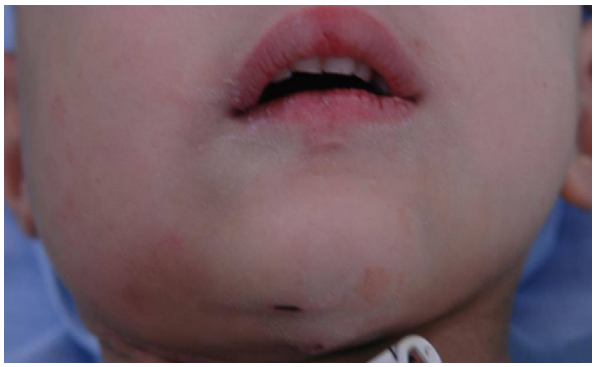

Fig. 1. Preoperative photograph demonstrating swelling of the right side of the mandible with normal overlying skin.

characterized by bilateral expansion of the jaws within the first few years of life, progressing until puberty and gradually resolving in middle age. The regions most typically affected include the mandibular angle, ramus, retromolar region, and maxillary tuberosity. The dentition is frequently abnormal, with premature loss of the deciduous teeth, and widely spaced, displaced, unerupted, or absent permanent teeth.[3] Radiographically, the lesions, which are typically multilocular, are expansile and radiolucent. In this case, there were a number of features that did not support such a diagnosis. Although the features may be mild in relatives, there were no features identified in any of the family members in this case, and de novo mutations are rare. The radiographic appearances of an isolated lesion, with normal developing dentition, and the rapid growth of the mass were also not in keeping with a diagnosis of cherubism.

Another potential fibro-osseous cause was an osteoblastoma. Osteoblastoma is a rare (<1% of all bone tumors) benign primary bone tumor that is most commonly found in the vertebral column and long bones, with involvement of the maxillofacial skeleton occurring in ~15% of cases.[4,5] Although the majority of cases of osteoblastoma can be managed with simple curettage, there is a small subset of tumors that exhibit locally aggressive behavior and have atypical histopathologic features, often making differentiation from low-grade osteosarcoma difficult.[4] Clinically, osteoblastomas typically present with pain and swelling, with pain being a feature in 90% of cases; however, they may present in the mandible as a painless swelling, as in this case. Radiographic features of osteoblastoma are variable, but are usually of a lucent, well circumscribed, expansive defect that may contain focal calcification and radiopaque areas.[6] Although many of the features of osteoblastoma were in keeping with the presentation in this case, the rapid growth of the mass raised concern of a malignant process.

Appearing to arise from the mandibular bone, rather than the surrounding soft tissue, an osteosarcoma was considered to be the most likely diagnosis. Although an infrequent tumor in the head and neck region, and even more so in children, these tumors often present as a painless mass. Of these head and neck osteosarcomas, 70%-95% occur in the first 2 decades of life, and the body of the mandible is the most frequent site of involvement. Radiologically, osteosarcoma has a lytic and destructive pattern in 35%-45% of cases, a sclerotic pattern in 5%-65%, and a mixed pattern of lysis and sclerosis in 22%-50%.[6] A sunburst pattern, with radiating spicules of bone, is considered to be a characteristic, though infrequently encountered, pattern. This was a key feature identified on imaging in the present case.

Other potential causes to be considered in this case included Ewing sarcoma, fibrous dysplasia, and metabolic bone diseases (though less likely in view of the normal biochemistry results found in this case).

DIAGNOSIS AND MANAGEMENT

In view of the rapid growth of the mass, formal biopsy was performed under general anesthesia. The histopathology of the biopsy specimen was suggestive of a poorly differentiated neuroblastoma. The tumor was positive for NB84a, CD56, and synaptophysin and negative for CD45, CD99, S100, cytokeratin, 34βE12, chromogranin, HMB45, Melan-A, and smooth (desmin) and skeletal muscle markers (MyoD1, Myf4, and desmin). The patient was referred to the pediatric oncology team for further investigation and management. Urinary catecholamines were measured, and he was fully staged with an meta-iodobenzylguanidine (MIBG) scan, a CT scan of his head, and MRI of his chest, abdomen, and pelvis. Bilateral bone marrow aspirates and trephines were undertaken. Further tumor tissue for cytogenetic analysis was obtained from ultrasound-guided core biopsies of the right mandibular mass. The urinary catecholamines were raised, confirming the diagnosis of neuroblastoma. Cytogenetic analysis of the tumor taken from the mandible showed the tumor to be aneuploid, with no *MYCN* amplification and confirmed the presence of segmental chromosomal alterations with a relative loss of 1p in 47 out of 50 cells, a relative gain of 2p in 43 out of 50 cells, and a relative gain of 17q in 47 out of 50 cells examined. This pattern of segmental chromosomal alterations is commonly seen in neuroblastoma. Staging investigations confirmed neuroblastoma infiltration in both the bone marrow aspirates and trephines. The MIBG scan demonstrated a large focus of increased MIBG uptake in the right side of the mandible, and widespread metastatic disease in the spine, pelvis, femora, humeri, and right knee were visible. MRI of the thorax, abdomen, and pelvis con-