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Osteosarcoma of the jaws in children

M. E. DONALDSON[1], J. R. GEIST[2] & T. D. DALEY[3]
[1]*Department of Pediatric Dentistry, Nova Southeastern University College of Dental Medicine, Fort Lauderdale, Florida,* [2]*Department of Diagnostic Sciences, University of Detroit Mercy School of Dentistry, Detroit, Michigan, USA and* [3]*Department of Pathology, University of Western Ontario Faculty of Dentistry, London, Ontario, Canada*

Summary. Two cases of osteosarcoma of the jaws in children are reported. One patient was a 13-year-old girl whose first symptoms included nasal and maxillary sinus congestion, followed by epistaxis. She was found to have chondroblastic osteosarcoma extending through the left maxillary alveolar process and sinus. Following surgery and chemotherapy, the patient has been free of disease for 7 years. The second patient, an 8-year-old boy, was diagnosed with juxtacortical (parosteal) osteosarcoma of the mandible, which is a less aggressive variant of the neoplasm. It is believed that this is the youngest patient reported to date with juxtacortical osteosarcoma of the jaws. He was treated by block resection of the right side of the mandible and is free of disease $3^1/_2$ years later.

Introduction

Osteosarcoma is relatively rare in the jaws, and maxillomandibular lesions in children are distinctly uncommon. In most cases the neoplasm pursues an aggressive course, infiltrating through bone and soft tissues at the site of origin and frequently extending into adjacent anatomic structures. A less destructive variant, juxtacortical or parosteal osteosarcoma, generally exhibits a more exophytic growth pattern, with less prominent invasion into trabecular bone. We report two cases of osteosarcoma in the jaws of children, one case representing an infiltrating, destructive lesion, and the other a less aggressive juxtacortical tumour.

Case reports

Case 1

A 13-year-old Caucasian female, who had recently completed orthodontic treatment, complained of enlargement of the left maxillary mucobuccal fold (Fig. 1) as well as symptoms of nasal congestion and maxillary sinusitis. The respiratory problems did not resolve, and the patient subsequently exhibited epistaxis. At that time, computed tomographic examination was performed. A coronal CT (Fig. 2) revealed a poorly defined soft tissue lesion interspersed with irregular radiopaque masses located in the left maxilla and maxillary sinus. The lesion invaded the inferior wall of the sinus, producing a ragged pattern of resorption, and perforated the medial and superior walls. An axial CT (Fig. 3) depicted massive extension of the lesion into the left nasal cavity as well as expansion and destruction of the anterior sinus wall. A radionuclide bone scan exhibited intense accumulations of radioisotope in the left maxilla (Fig. 4), but was negative for systemic lesions. Microscopic examination of the biopsy specimen (Fig. 5) revealed hypercellular osteoid and soft tissue supporting numerous hyperchromatic spindle cells. Prominent masses of chondroid were detected, interspersed with bizarre, pleomorphic cells with hyperchromatic nuclei and atypical mitoses. The diagnosis was chondroblastic osteosarcoma.

Treatment consisted of a hemimaxillectomy followed by nine chemotherapy treatments over a 46-week period. The chemotherapeutic regimen included

Correspondence: J. R. Geist, DDS, MS, 8200 W. Outer Drive, #129, Detroit, Michigan 48219, USA.

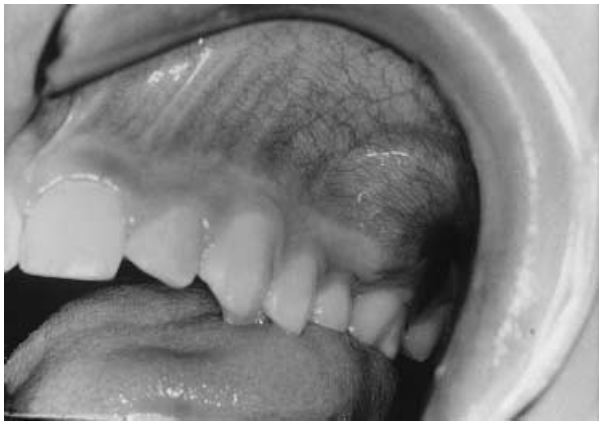

Fig. 1. Gradual, painless enlargement of the left maxillary mucobuccal fold was detected at the end of orthodontic treatment.

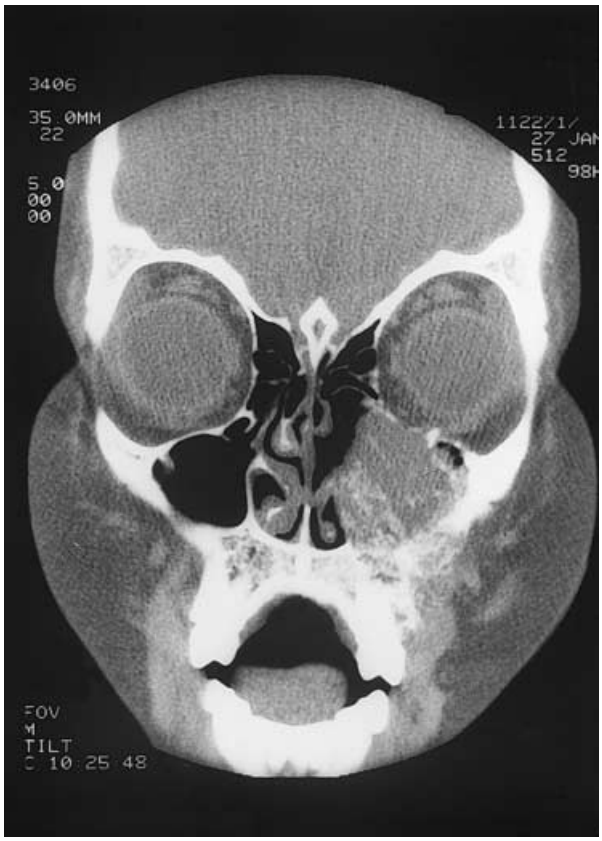

Fig. 2. A coronal computed tomograph (CT) revealed a large soft tissue mass interspersed with hard tissue extending into the left maxillary sinus and causing destruction of the inferior, medial, lateral, and superior sinus walls.

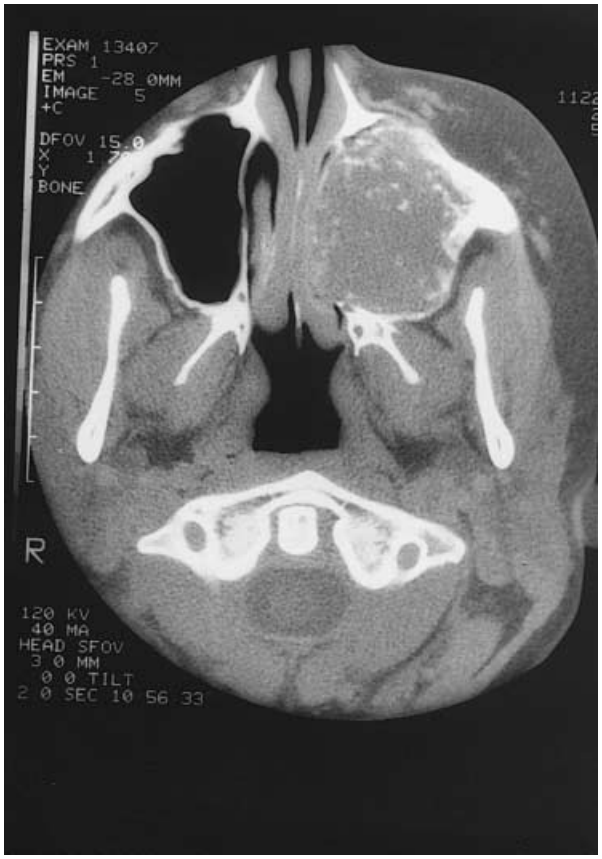

Fig. 3. An axial CT depicted the tumour mass occupying the maxillary sinus and extending into the left nasal cavity. Expansion and resorption of the anterior and posterior-lateral sinus walls were also noted.

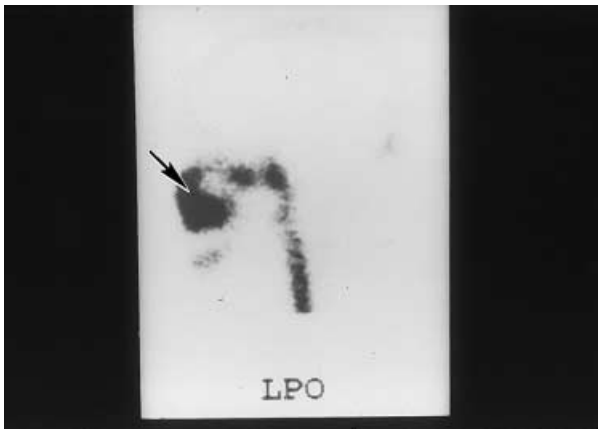

Fig. 4. Radionuclide bone scan demonstrated pronounced uptake of radioisotope in the maxillary lesion (arrow), but no other foci of tumour were detected.

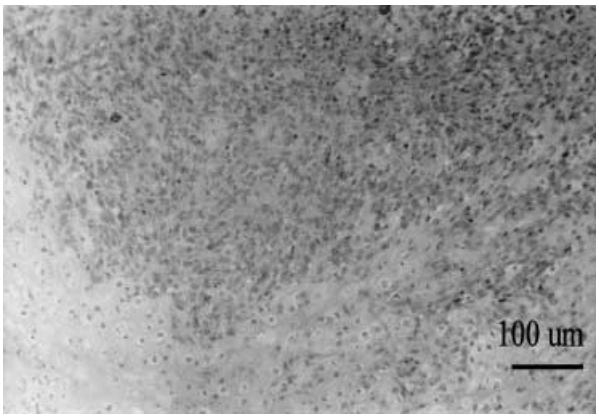

Fig. 5. Photomicrograph of the biopsy specimen revealed osteoid and soft tissue supporting numerous atypical, hyperchromatic spindle cells. A large mass of neoplastic chondroid, interspersed with pleomorphic angular and spindle cells, was also present. (Haematoxylin and eosin, magnification × 66).

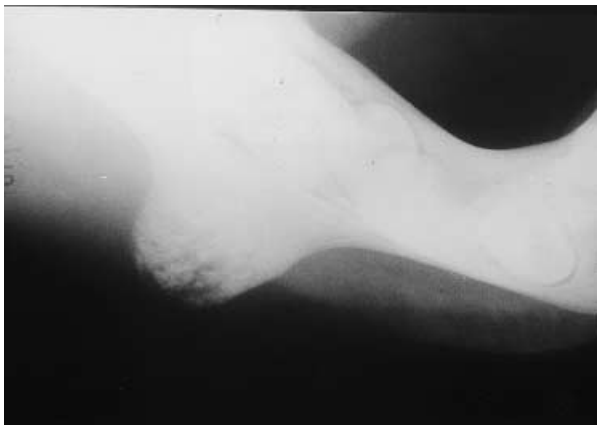

Fig. 6. A cross-sectional mandibular occlusal radiograph revealed an exophytic mass of hard tissue on the buccal aspect of the mandible. The superficial margin was irregular and interspersed with radiolucent tissue. (Courtesy of Dr William L. Fydman, Interface, London, Ontario.).

methotrexate, adriamycin, actinomycin, cisplatin, and cytoxan. Prosthetic reconstruction was accomplished, and the patient has been disease-free for 7 years.

Case 2

An 8-year-old Caucasian male presented for diagnosis of a hard, slowly enlarging lump arising from the outer surface of the right posterior mandible that had been noticed by his mother three months earlier. The abnormality was not tender to palpation, but produced a clinically visible nodular asymmetry of the face. The child was otherwise asymptomatic and in good health. An occlusal radiograph showed a bony radiopaque eruption from the buccal cortical plate, with an irregular radiolucency at its most superficial margin (Fig. 6). Computed tomographs in the coronal (Fig. 7) and axial (Fig. 8) planes revealed the exophytic mass to consist of a non-homogeneous radiopacity with indistinct margins infiltrating the buccal cortex in the area of the second premolar and first molar. The mass approximated the alveolar crest and exhibited superficial extension into the trabecular component of the mandible. The lesion was surgically shaved from the outer surface of the mandible and submitted for microscopic examination.

Histological sections revealed variably calcified trabeculae of bone exhibiting increased cellularity, numerous irregular apposition lines, and focal osteoblastic rimming. The cells within the trabeculae and in the soft tissue stroma exhibited pleomorphism,

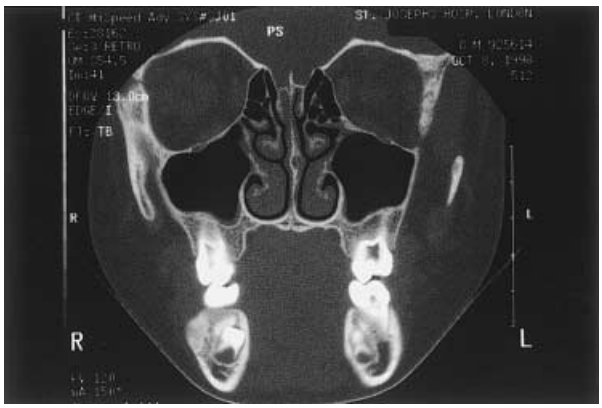

Fig. 7. A computed tomographic bone window image in the coronal plane revealed a mottled, indistinct radiopacity approximating the crest of the right mandibular alveolar process. Poorly defined margins with the buccal cortex and extension into the underlying trabecular bone were also identified.

including spindle and angular cells with hyperchromatic nuclei (Fig. 9). The neoplastic tissue extended to the inferior resection margin and was diagnosed as juxtacortical (parosteal) osteosarcoma, incompletely excised.

Three months later, the boy underwent general anaesthesia for a local block resection of the right posterior mandible and surrounding soft tissues. Microscopic examination revealed tumour in the cortical bone as well as in soft tissue of the overlying mucosa, where a thick band of atypical spindle cells was present. Resection margins were clear. The patient has been free of disease for $3^1/_2$ years since the surgery.

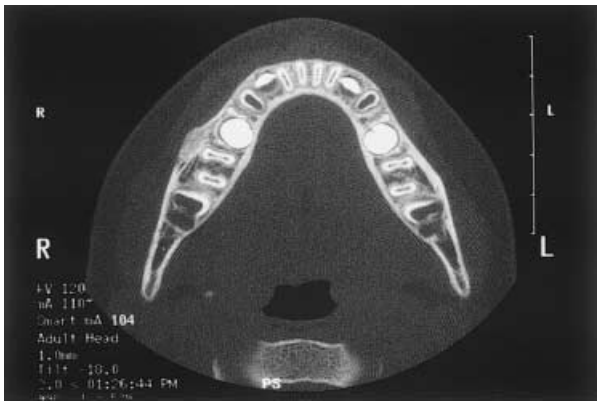

Fig. 8. A computed tomographic bone window image in the axial plane demonstrated some infiltration of the trabecular bone between the second premolar and first molar.

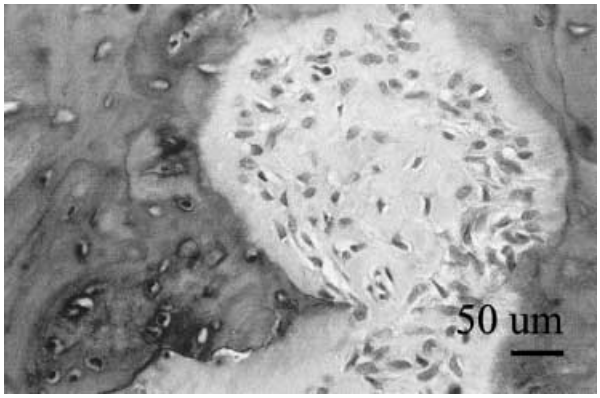

Fig. 9. A photomicrograph of the biopsy revealed hypercellular neoplastic tissue within bone and in the soft tissue stroma. The cells exhibited pleomorphism and nuclear hyperchromatism. (Haematoxylin and eosin, magnification × 370).

Discussion

Osteosarcoma (OS) is the most common primary malignant neoplasm of bone-forming cells, but is still a relatively rare tumour, occurring in approximately 1 per 100 000 persons [1–4]. Many reports of large series indicate that 2% to 13% of osteosarcomas arise in the maxilla and mandible, with most investigations placing the incidence in the 6% to 9% range [1–12]. Garrington *et al*. estimated the incidence of OS in the jaw to be less than one case per million people per year [1].

While OS of the long bones has a peak incidence in the second decade, lesions in the jaws most commonly arise about a decade later, with a peak age in the late 20s to middle 30s [1–18]. Only 6% to 30% of maxillofacial osteosarcomas have been detected in the first or second decade [1,3,7,9,11–15,17,18]. Most investigators have recorded a greater number of maxillofacial OS in males [1,4,7–11,14–16,18], and there appears to be no difference in age between males and females [2,3,5,7,8,10,12,17,18]. The mandible has been reported to be a more likely location than the maxilla in many extensive reports [1–3,7,8,11–18].

Therapeutic radiation has preceded the onset of OS in many documented cases [1,3,4,6,9,13,16,19,20], often for the treatment of retinoblastoma in children and teenagers. It is interesting that patients with hereditary retinoblastoma have a significantly higher frequency of osteosarcoma independent of radiation therapy. This may be related to a deletion on the long arm of chromosome 13, which is known to occur in hereditary retinoblastoma and in many cases of OS [13,19].

The most common presenting symptom of OS in the head and neck is swelling [1–13,15,16,21]. Pain has been reported in approximately 50% of patients in some large series [1,2,8,17], although in other reports the occurrence of pain has ranged from 3% to over 80% of patients [3,4,6,7,10,12]. Mucosal ulceration and loosening of teeth can also occur [1–4,8–10]. It is interesting that neither patient in this report complained of pain. In Case #1, the patient's tumour caused symptoms of sinusitis and rhinitis, the result of extension into the maxillary sinus and nasal cavity. Tumours can cause paresthesia of the skin, lip and tongue [1,3,4,7,8,10,15], a symptom that has been related to a decreased chance of disease-free survival [8]. The time between onset of symptoms and the first treatment generally ranges from 3 to 6 months [2–4,6–8,17].

Radiographically, OS usually produces a poorly defined, irregular destructive bone lesion interspersed with radiopaque material [1–4,7–11,14–18]. The indistinct margins correspond to the infiltrative proliferation of malignant osteoblasts and fibrous stroma, while the radiopaque foci represent the tumour bone and/or cartilage produced in many lesions [1,2,12]. The lesion in Case #1 typifies this pattern. Occasionally, the hard tissue produced by the tumour predominates, yielding a largely radiopaque image [1,2,7,8,17]. In numerous cases, no radiopaque component is identified within the radiolucency, in which case the lesion may resemble other malignancies [7–10,16,19]. Computed tomography and magnetic resonance imaging can be helpful in visualizing extramedullary involvement and extension into soft

tissues [7,10,14–16], and is essential for early diagnosis of OS [14].

Osteosarcoma involving the alveolar process may produce symmetrical widening of the periodontal ligament spaces as the neoplasm extends into the ligament [1,3,5,10,15], but this is somewhat rare and not pathognomonic for OS [8,9]. Similarly, the 'sun-burst' or 'sun-ray' pattern of tumour bone produced at right angles to the cortex is seen in no more than a third of all cases of OS [1,3,4,7,8,10–12,15–17]. When this pattern does occur, it indicates that the neoplasm has penetrated the cortex and extended into soft tissue, and is therefore in an advanced stage [11].

Juxtacortical osteosarcoma (JOS), also known as parosteal osteosarcoma, is an uncommon variant of OS that is characterized by a peripheral rather than intramedullary growth pattern [22–29]. JOS is most common in the distal femur, but it occurs in a slightly older age group (most in the third decade) than conventional OS [23,25]. Localized swelling is the most common presenting symptom, and may exist for years before patients seek treatment [22,25]. Pain is reported in approximately 50% of patients [23].

JOS is usually a lobular tumour mass arising on the surface of the affected bone and often encircling it [22–26]. The lesion frequently has a sessile attachment to the cortex with little or no trabecular involvement [22–25]. Invasion of the trabecular bone, if it occurs, is a late consequence [22]. Satellite lesions are also known to arise [23,25]. Radiographic evaluation reveals the base of the lesion to be most radiodense, with less ossification at the periphery, as in Case #2 [22–25]. Although the underlying cortex can exhibit reactive changes such as sclerosis or thickening [22,23], the 'sun-burst' or 'sun-ray' reaction is almost always absent [22–25].

The histological features of JOS resemble well-differentiated osteosarcoma with regular trabeculae of tumour bone and osteoid supported by a fibrous stroma with atypical spindle cells; the soft tissue component predominates at the periphery of the lesion [22,23,25–27]. Chondroid differentiation is observed in many cases of JOS, including Case #2 [23].

Juxtacortical osteosarcoma of the jaws is quite uncommon, with no more than 15 cases reported in the literature [17,18,22–27]. The radiographic and histopathological features of the jaw lesions are similar to JOS of long bones. The average age of patients with maxillomandibular lesions is slightly less than 40 years. Only two of these cases have occurred in the second decade [27]. It appears that our case of JOS in an 8-year-old represents the youngest patient to date with this lesion.

Treatment of conventional osteosarcoma almost always involves surgery with wide resection to attain clear margins [1–13,15,21,30,31]. Local recurrence has been a significant problem among those treated with surgery alone in some series of head and neck OS [4,6,7,9,11,13,30,31], and when clean surgical margins are not obtained the outcome is almost always poor and often fatal [6–8,30,31]. A recent review of the treatment of 18 osteosarcomas in children (11 in the jaws or palate) at one institution revealed that surgical removal of less than 95% of the tumour resulted in significantly higher frequency of local recurrence and significantly poorer survival rates compared to treatment with greater than 95% excision and/or negative surgical margins [30]. Another report of 44 cases of OS, including 20 in the maxilla and 18 in the mandible, concluded that clear surgical margins were the only significant factor in overall survival and disease-specific survival [31]. In addition, patients younger than 18, particularly those with retinoblastoma-related OS, had a significantly increased risk of local recurrence [31]. One problem that complicates surgical management of head and neck OS, most notably in the maxilla, is the difficulty in obtaining adequate surgical margins due to the complex anatomy of the region [30,31]. In one report, lesions of the maxilla and skull were significantly more likely than mandibular OS to have positive margins [31].

Although radiation therapy alone is ineffective [1,2,7,10], adjuvant radiation treatment has been used, either pre- or post-operatively to control residual tumour or recurrent disease [2–4,6,10,11,13,16]. Some authors believe that radiation should be used only as an adjunct to surgery and chemotherapy in cases that are not completely resectable or at sites of recurrence [2,5,11]. Adjuvant radiation therapy has been recommended for patients if the surgical margins of the lesion are questionable or positive [31].

Chemotherapy, when applied in association with surgery, has been reported to significantly increase the survival rate and reduce the frequency of recurrence and number of metastases in some osteosarcomas, consistent with the findings in Case #1 [2,4,8–10,13,19,32]. The beneficial effects of chemotherapy in head and neck OS are not as well established as in OS of the long bones, where

postoperative chemotherapeutic agents often permit limb-sparing surgery [19]. In a review of head and neck OS patients at one treatment centre, neoadjuvant chemotherapy did not significantly decrease distant metastases or improve local control or disease-specific survival [31]. These findings may be related to the fact that most of the patients treated with chemotherapy had larger and higher-grade tumours, and many had been irradiated for retinoblastoma [31]. However, recent research suggests that postoperative chemotherapy may not increase survival rates and may in fact predispose to development of a second malignancy [33]. It should be kept in mind that conclusions regarding the efficacy of chemotherapy are hard to reach due to the diversity of agents and regimens employed over the years [30].

The prognosis of patients with OS has been reported to be statistically better with these factors: absence of paresthesia as a symptom, smaller tumour size, adequacy of surgical removal (margins clear of tumour), a more differentiated histological grade of the lesion, and younger age of the patient [4,6,8–10,12], with the possible exception of children also diagnosed with retinoblastoma [31]. Increasing age may be related to recurrence after treatment [8]. However, there is no statistical correlation between radiographic appearance and survival [8] or between histological type and survival [1]. Many institutions report 5-year survival rates that range from 10% to 47% [3–9,11,30]. Patients with mandibular lesions have been reported to have a longer median survival time than those with OS of the maxilla, and tumours in the maxillary sinus are believed to have the worst prognosis [1]. The risk of distant metastases with OS of the head and neck varies widely in different reports [1,2,7,11,13,19], but death usually results from extension into the skull [2,10,21].

JOS is also treated with resection but the prognosis is better, reflective of the lack of invasion and the usually low-grade nature of the tissue. Postoperative recurrence is rare, and generally follows limited surgery [23,27].

Résumé. Deux cas d'ostéosarcome des mâchoires chez l'enfant sont rapportés. Chez une jeune fille de 13 ans, les premiers symptômes ont compris une congestion des sinus maxillaire et nasal puis un épistaxis. Il a été diagnostiqué un ostéosarcome chondroblastique s'étendant à travers le sinus et les procès alvéolaires maxillaires gauches. Après chirurgie et chimiothérapie, le patient a été sans problème pendant 7 ans. Chez le second patient, un garçon âgé de 8 ans, un ostéosarcome juxtacortical de la mandibule a été diagnostiqué, variante moins agressive de tumeur. Il s'agirait du plus jeune cas rapporté à ce jour d' ostéosarcome juxtacortical des mâchoires. Il a été traité par résection de bloc du côté droit de la mandibule et n'a plus connu de problème depuis 3 ans $^1/_2$.

Zusammenfassung. Zwei Fälle von Osteosarkom im Kieferbereich bei Kindern werden vorgestellt. Ein Patient war ein 13 jähriges Mädchen, dessen erst Symptome Nasenverstopfung und eine eingeengte Kieferhöhle waren. Bei ihr wurde ein chondroblastisches Osteosarkom mit Befall der linken maxillären Kieferhöhle sowie des Alveolarfortsatzes festegstellt. Nach chirurgischer Behandlung und Chemotherapie blieb sie bislang 7 Jahre rezidivfrei. Der zweite Patient, ein 8 jähriger Junge, wies ein juxtacorticales Osteosarkom der Mandibula auf, eine weniger aggressive Variante der Neoplasie. Dies ist vermutlich der jüngste bisher beschriebene Patient mit dieser Form des Osteosarkoms. Er wurde mittels Blockresektion der rechten Mandibula behandelt und ist seit $3^1/_2$ Jahren rezidivfrei.

Resumen. Se informa de dos casos de osteosarcoma en niños. El primer paciente fue una niña de 13 años, cuyos primeros síntomas incluyeron congestión nasal y sinusal, seguida de epistaxis. Se encontró que era un osteosarcoma condroblástico que se extendía a través del proceso alveolar y el seno maxilar izquierdo. Después de la cirugía y quimioterapia, la paciente se ha mantenido sana durante siete años. Al segundo paciente, un niño de 8 años de edad, se le diagnosticó un osteosarcoma yuxtacortical (parosteal) mandibular, el cual es una variante menos agresiva de la neoplasia. Se cree que este es el paciente con osteosarcoma yuxtacortical mandibular más joven de que se ha informado. El tratamiento constó de una resección en bloque del lado derecho de la mandíbula. El paciente se mantiene sano después de tres años y medio.

References

1 Garrington GE, Scofield HH, Cornyn J, Hooker SP. Osteosarcomas of the jaws. Analysis of 56 cases. *Cancer* 1967; **20** (3): 377–391.

2 Forteza G, Colmenero B, Lopez-Barea F. Osteogenic sarcoma of the maxilla and mandible. *Oral Surgery, Oral Medicine, Oral Pathology* 1986; **62** (2): 179–184.

3 Tanzawa H, Uchiyama S, Sato K. Statistical observation of osteosarcoma of the maxillofacial region in Japan. *Oral Surgery, Oral Medicine, Oral Pathology* 1991; **72** (4): 444–448.
4 Clark JL, Unni KK, Dahlin DC, Devine KD. Osteosarcoma of the jaw. *Cancer* 1983; **51** (12): 2311–2316.
5 Slootweg PJ, Muller H. Osteosarcoma of the jaw bones. Analysis of 18 cases. *Journal of Maxillofacial Surgery* 1985; **13** (4): 158–166.
6 Delgado R, Maafs E, Alfeiran A *et al*. Osteosarcoma of the jaw. *Head and Neck* 1994; **16** (3): 246–252.
7 Bertoni F, Dallera P, Bacchini P, Marchetti C, Campobassi A. The Istituto Rizzoli-Beretta experience with osteosarcoma of the jaw. *Cancer* 1991; **68** (7): 1555–1563.
8 August M, Magennis P, Dewitt D. Osteogenic sarcoma of the jaws: factors influencing prognosis. *International Journal of Oral and Maxillofacial Surgery* 1997; **26** (3): 198–204.
9 Lewis M, Perl A, Som PM, Urken ML, Brandwein MS. Osteogenic sarcoma of the jaw. A clinicopathological review of 12 patients. *Archives of Otolaryngology and Head and Neck Surgery* 1997; **123** (2): 169–174.
10 Doval DC, Kumar RV, Kannan V *et al*. Osteosarcoma of the jaw bones. *British Journal of Oral and Maxillofacial Surgery* 1997; **35** (5): 357–362.
11 Vege DS, Borges AM, Aggrawal K, Balasubramaniam G, Parikh DM, Bhaser B. Osteosarcoma of the craniofacial bones. *Journal of Cranio-Maxillo-Facial Surgery* 1991; **19** (2): 90–93.
12 Chindia ML, Guthua SW, Awange DO, Wakoli KA. Osteosarcoma of the maxillofacial bones in Kenyans. *Journal of Cranio-Maxillo-Facial Surgery* 1998; **26** (2): 98–101.
13 Mark RJ, Sercarz JA, Tran L, Dodd LG, Selch M, Calcaterra TC. Osteogenic sarcoma of the head and neck. The UCLA experience. *Archives of Otolaryngology and Head and Neck Surgery* 1991; **117** (7): 761–766.
14 Bianchi SD, Boccardi A. Radiological aspects of osteosarcoma of the jaws. *Dentomaxillofacial Radiology* 1999; **28** (1): 42–47.
15 Givol N, Buchner A, Taicher S, Kaffe I. Radiological features of osteogenic sarcoma of the jaws. A comparative study of different radiographic modalities. *Dentomaxillofacial Radiology* 1998; **27** (6): 313–320.
16 Lee YY, Van Tassel P, Nauert C, Raymond AK, Edeiken J. Craniofacial osteosarcomas. plain film, CT, and MR findings in 46 cases. *American Journal of Roentgenology* 1988; **150** (6): 1397–1402.
17 Adekeye EO, Chau KK, Edwards MB, Williams HK. Osteosarcoma of the jaws – a series from Kaduna, Nigeria. *International Journal of Oral and Maxillofacial Surgery* 1987; **16** (2): 205–213.
18 Regezi JA, Zarbo RJ, McClatchey KD, Courtney RM, Crissman JD. Osteosarcomas and chondrosarcomas of the jaws: immunohistochemical correlations. *Oral Surgery, Oral Medicine, Oral Pathology* 1987; **64** (3): 302–307.
19 Goorin AM, Abelson HT, Frei E III Osteosarcoma: fifteen years later. *New England Journal of Medicine* 1985; **313** (26): 1637–1643.
20 Homa DM, Sowers MFR, Schwartz AG. Incidence and survival rates of children and young adults with osteogenic sarcoma. *Cancer* 1991; **67** (8): 2219–2223.
21 Okinaka Y, Takahashi M. Osteosarcoma of the maxilla: report of a case and review of the literature concerning metastasis. *Journal of Oral and Maxillofacial Surgery* 1997; **55** (10): 1177–1181.
22 Solomon MP, Biernacki J, Slippen M, Rosen Y. Parosteal osteogenic sarcoma of the mandible. *Archives of Otolaryngology* 1975; **101** (12): 754–760.
23 Bras JM, Donner R, van der Kwast WAM, Snow GB, van der Waal I. Juxtacortical osteogenic sarcoma of the jaws. *Oral Surgery, Oral Medicine, Oral Pathology* 1980; **50** (6): 535–544.
24 Bianchi SD, Boccardi A, Pomatto E, Valenti G. Parosteal osteosarcoma of the maxilla. *Dentomaxillofacial Radiology* 1997; **26** (5): 312–314.
25 Millar BG, Browne RM, Flood TR. Juxtacortical osteosarcoma of the jaws. *British Journal of Oral and Maxillofacial Surgery* 1990; **28** (2): 73–79.
26 Minic AJ. Periosteal osteosarcoma of the mandible. *International Journal of Oral and Maxillofacial Surgery* 1995; **24** (3): 226–228.
27 Patterson A, Greer RO Jr, Howard D. Periosteal osteosarcoma of the maxilla: a case report and review of the literature. *Journal of Oral and Maxillofacial Surgery* 1990; **48** (5): 522–526.
28 Unni KK, Dahlin DC, Beabout JW, Ivins JC. Parosteal osteogenic sarcoma. *Cancer* 1976; **37** (5): 2466–2475.
29 Unni KK, Dahlin DC, Beabout JW. Periosteal osteogenic sarcoma. *Cancer* 1976; **37** (5): 2476–2485.
30 Daw NC, Mahmoud HH, Meyer WH, Jenkins JJ, Kaste SC, Poquette CA *et al*. Bone sarcomas of the head and neck in children. The St. Jude Children's Research Hospital experience. *Cancer* 2000; **88** (9): 2172–2180.
31 Patel SG, Meyers P, Huvos AG, Singh B, Shaha AR, Boyle JO *et al*. Improved outcomes in patients with osteogenic sarcoma of the head and neck. *Cancer* 2002; **95** (7): 1495–1503.
32 Meskens M, Burssens A, Hoogmartens M, Fabry G. Osteogenic sarcoma in children: a retrospective study of 58 cases. *Acta Orthopaedica Belgica* 1993; **59** (1): 64–68.
33 Berend KR, Pietrobon R, Moore JO, Dibernardo L, Harrelson JM, Scully SP. Adjuvant chemotherapy for osteosarcoma may not increase survival after neoadjuvant chemotherapy and surgical resection. *Journal of Surgical Oncology* 2001; **78** (3): 162–170.