Case report

Primary osteosarcoma of the skull in teenager

Liliana Vasquez,^{1,2} Víctor Tejada,³ Ivan Maza,¹ Ronald Mendoza⁴¹Pediatric Oncology, Rebagliati Hospital, Lima, Peru²Centro de Investigación de Medicina de Precisión, Universidad de San Martín de Porres Facultad de Medicina Humana, La Molina, Lima, Peru³Department of Head and Neck Surgery, Rebagliati Hospital, Lima, Peru⁴Department of Pathology, Rebagliati Hospital, Lima, Peru

Correspondence to

Dr Liliana Vasquez,
lilianavasq@gmail.com

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SUMMARY

Osteosarcoma of the skull is a rare primary malignant bone tumour in children, representing 1–2% of all cranial tumours. We describe a case of a 17-year-old adolescent with chondroblastic osteosarcoma of the parietal-occipital bone and no distant metastases at presentation treated with neoadjuvant chemotherapy, surgery and, later, concurrent chemoradiotherapy. The patient suffered progressive disease and died 15 months after diagnosis. There are at least 15 paediatric cases of osteosarcoma of the skull described in the literature. Due to its rarity, there are no broad prospective studies on this entity, which has distinctive features when compared to other craniofacial tumours, carrying a worse prognosis. Complete surgical resection is needed for long-term survival, whereas chemotherapy and radiotherapy have still questionable indications.

BACKGROUND

Osteosarcoma is the most common bone malignancy in children. The most frequent locations are large bones of the extremities, whereas approximately 5%–6% occur in craniofacial bones.¹ Most craniofacial osteosarcomas are located in the zygomatic bone. Osteosarcoma of the skull as a primary

tumour is very rare and represents only 1%–2% of skull tumours.² Differential diagnosis must include osteochondroma and chondrosarcoma. Poor survival rates are commonly reported, and published papers are generally limited; so herein we report a case of an adolescent with a primary osteosarcoma of the skull and review of the literature.^{2,3}

CASE PRESENTATION

A 17-year-old man with no prior medical history presented with 5 months of painless cranial lump with progressive growth, headache and nausea. On examination, we found an 18×15 cm mass of heterogeneous consistency in the left parietal-occipital region (figure 1).

INVESTIGATIONS

Skull X-ray demonstrated a dense tumour bone formation with a sunburst-pattern, strongly suggestive of malignancy. (figure 2) Initial MRI showed an expanding lesion of the left parieto-occipital cranial bone with periosteal reaction and invasion of adjacent cerebral parenchyma (figure 3). An open biopsy was obtained. The histopathological diagnosis was chondroblastic osteosarcoma.

Staging studies showed no evidence of distant metastatic disease in chest, abdominal and pelvic CT scans. Whole-body bone scintigraphy revealed focally increased uptake in the cranial vault lesion (figure 4). Initial serum lactate dehydrogenase and alkaline phosphatase level were elevated above the normal range.

TREATMENT

Patient began neoadjuvant chemotherapy with ifosfamide, cisplatin, adriamycin and high-dose methotrexate for 10 weeks (methotrexate, doxorubicin, cisplatin and ifosfamide (MAP-I) regimen). This regimen consisted of a 37-week protocol that included doxorubicin (75 mg/m² for 6 doses), cisplatin (120 mg/m² for 3 doses), high-dose methotrexate (12 g/m² for 11 doses, with leucovorin rescue) and high-dose ifosfamide (9 g/m² for 6 doses). Since the accumulative dose of doxorubicin exceeds 450 mg/m², dexrazoxane was used with each dose of doxorubicin in a ratio 10:1. After neoadjuvant therapy, only minimal (less than 10%) reduction of the tumour size was obtained. Surgery was scheduled at week 13. He underwent left parieto-occipital craniectomy with block resection of the bone tumour. (figure 5) Postresection pathology confirmed a diagnosis of conventional high-grade osteosarcoma with less than 5% of tumour necrosis and compromised margins (figure 6). Radiotherapy

Figure 1 Seventeen-year-old man with left parieto-occipital osteosarcoma.

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Figure 2 Skull X-ray showing tumour bone formation with a sunburst-pattern.

was administered in this patient since a portion of the tumour was seen on a postoperative brain scan, and it was considered as a subtotal resection. Immediate postoperative evolution was favourable, and he underwent adjuvant chemotherapy with concurrent whole-brain radiotherapy at a dose of 39 Gy in 13 fractions followed by a 12 Gy focal boost.

OUTCOME AND FOLLOW-UP

Thirteen weeks after surgery, the patient presented with recurrent epileptic seizures. Follow-up MRI showed multiple extra-axial solid nodular lesions on the left parieto-occipital convexity measuring up to 2.5 cm. Salvage chemotherapy was started but the patient experienced disease progression and died 15 months after diagnosis.

Figure 3 MRI.

Figure 4 Whole-body bone scintigraphy.

DISCUSSION

Primary osteogenic sarcomas of the skull are very infrequent and constitute approximately 1.6% of all osteosarcomas.^{2,3} They occur in both genders with the same frequency, unlike osteosarcomas affecting long bones, where there is a clear male predominance.⁴ Osteogenic sarcomas of the skull commonly occurs in the third decade of life, being its appearance later than appendicular osseous tumours, and extremely rare in the paediatric population.^{5,6}

It usually presents as a slow-growing painless or painful cranial mass.⁷ Other common findings are headache and nausea. It is infrequent to find cranial nerve palsies or high blood pressure,

Figure 5 Surgical specimen.

which increase the suspicion of intracranial invasion.^{8–10} The most valuable imaging studies are X-ray, head CT scan and MRI. Histological evidence of bone malignancy is a necessary element for the diagnosis.⁷ There are no specific radiological findings. Usually appearing as osteolytic, osteosclerotic or mixed lesions.¹¹ The specific radiological sunburst sign is observed in 25%–31% of patients and was also present in our patient; which rose suspicion for osteosarcoma.⁶ An angiography is useful to determine blood flow to the tumour and plan a surgical approach. A cranial CT scan allows proper evaluation of the intracranial extension of the tumour and the degree of ossification and calcification, which is useful in the treatment and follow-up.⁶ MRI evaluation does not show calcifications as accurately as CT, but it shows vascular irrigation and tissue surrounding the tumour more clearly.^{12–13} In many cases, it is possible to find elevated levels of lactate dehydrogenase and alkaline phosphatase,¹⁴ as seen in our patient. Pathology of the craniofacial osteosarcomas are described as having a tendency to be less anaplastic and having a lower mitotic index than its appendicular counterparts.⁴ They usually have osteoblastic and chondroblastic patterns.¹⁵

There are at least 150 cases of cranial osteosarcoma reported in the medical literature. Reports on cases of primary paediatric osteosarcoma of the skull are scarce, accounting for

approximately 15 cases.^{2–10, 16–19} Due to the rare nature of its occurrence, there are no prospective studies of this entity. The first review was conducted by Shinoda *et al*²⁰ summarising all reported cases since 1945–1992, a total of 99 cases. In this review, a clear male predominance and an osteoblastic histological pattern were observed. Prognosis was better in those cases where patients presented with no cranial invasion; however, it was not possible to conduct an analysis of the results based on treatment regimens, since the sample of patients was heterogeneous. Furthermore, Chang *et al*⁹ described six patients, children and adults treated with surgical resection and cranial reconstruction. A review of craniofacial osteosarcoma cases describes 22 paediatric cases; however, none of those were cases of primary osteosarcoma of the skull.^{1–5} Patel *et al*²¹ described a young patient with a skull osteosarcoma who received prior treatment with cranial radiotherapy for a posterior fossa ependymoma.

Surgery involving total resection of the primary lesion including a large tumour-free margin of bone tissue and systemic chemotherapy are considered as the treatment of choice.²² The use of radiotherapy remains controversial. Surgical treatment is the most significant contributing factor in achieving a longer survival.^{23–25} However, complete resection of the lesion is seldom achieved. Additionally, there is no consensus on safety margins when performing surgery on the cranium.⁹ At onset, surgery could be considered for small lesions, or if it is possible to obtain negative margins.^{26–27}

Systemic chemotherapy improves prognosis in these patients.^{18–21, 25–26, 28} There is plenty of evidence that neoadjuvant chemotherapy would help reduce tumour size before surgery, improve chances of tumour resection with negative margins, and lengthen the median survival of these patients in inoperable cases, or incomplete resection.^{3–21, 27} Also, adjuvant chemotherapy has improved patients' survival, compared with that of those who did not receive any postoperative treatment.²⁶ Radiotherapy is often prescribed in cases of high-grade tumours with incomplete resection or inoperable.²⁹

Contributing prognostic factors include tumours larger than 5 cm, with poor histological response to neoadjuvant chemotherapy, incomplete resection with positive margins and intracranial invasion.¹⁴ Five-year overall survival among patients with craniofacial osteosarcoma varies between 23% and 63%.^{3–24, 30} Local recurrence occurs in 25%–50% of cases and usually occurs during the first year after initial treatment. Distant metastases are infrequent. Generally, metastases develop within the first 2 years, the lung being the most frequent site. Early lung metastases usually cause death among patients with osteosarcoma in the long bones, while local recurrence is the most common cause of death in patients with craniofacial osteosarcomas.⁶

Figure 6 Biopsy of the tumour showed chondromyxoid matrix and fusiform osteoblastic cells suggestive of chondroblastic osteosarcoma.

Learning points

- ▶ Osteosarcoma of the skull is a rare tumour and literature about its treatment is scarce.
- ▶ Extensive surgery with negative margins of the primary lesion is the most important prognostic factor.
- ▶ Adjuvant and neoadjuvant chemotherapy can lengthen survival.
- ▶ There are very few reported cases of osteosarcoma of the skull in paediatrics, with difficult characterisation of this entity and possible therapeutic schemes.

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REFERENCES

- Smith RB, Apostolakis LW, Karnell LH, *et al.* National Cancer Data Base report on osteosarcoma of the head and neck. *Cancer* 2003;98:1670–80.
- Chander B, Ralte AM, Dahiya S, *et al.* Primary osteosarcoma of the skull. A report of 3 cases. *J Neurosurg Sci* 2003;47:177–81.
- Chou EK, Chang CS, Chen PK, *et al.* Long-term management of craniofacial osteosarcoma. *J Craniofac Surg* 2009;20:406–9.
- Goepfert H, Raymond AK, Spires JR. Osteosarcoma of the head and neck. *Cancer Bull* 1990;42:347–54.
- Jasnau S, Meyer U, Potratz J, *et al.* Craniofacial osteosarcoma Experience of the cooperative German-Austrian-Swiss osteosarcoma study group. *Oral Oncol* 2008;44:286–94.
- Kanazawa R, Yoshida D, Takahashi H, *et al.* Osteosarcoma arising from the skull--case report. *Neurol Med Chir* 2003;43:88–91.
- Bose B. Primary osteogenic sarcoma of the skull. *Surg Neurol* 2002;58(3-4):234–9.
- Nora FE, Unni KK, Pritchard DJ, *et al.* Osteosarcoma of extragnathic craniofacial bones. *Mayo Clin Proc* 1983;58:268–72.
- Chang CS, Bergeron L, Liao CC, *et al.* Craniofacial reconstruction of primary osteogenic sarcoma of the skull. *J Plast Reconstr Aesthet Surg* 2010;63:1265–8.
- Huvos AG, Sundaresan N, Bretsky SS, *et al.* Osteogenic sarcoma of the skull. A clinicopathologic study of 19 patients. *Cancer* 1985;56:1214–21.
- Mascarenhas L, Peteiro A, Ribeiro CA, *et al.* Skull osteosarcoma: illustrated review. *Acta Neurochir* 2004;146:1235–9.
- Shramek JK, Kassner EG, White SS. MR appearance of osteogenic sarcoma of the calvaria. *AJR Am J Roentgenol* 1992;158:661–2.
- Lee YY, Van Tassel P, Nauert C, *et al.* Craniofacial osteosarcomas: plain film, CT, and MR findings in 46 cases. *AJR Am J Roentgenol* 1988;150:1397–402.
- Kirby EJ, Zhou HH, Morales L. Primary pediatric osteosarcoma of the skull. *J Craniofac Surg* 2011;22:2399–405.
- Gadwal SR, Gannon FH, Fanburg-Smith JC, *et al.* Primary osteosarcoma of the head and neck in pediatric patients: a clinicopathologic study of 22 cases with a review of the literature. *Cancer* 2001;91:598–605.
- van den Berg H, Merks JH. Incidence and grading of cranio-facial osteosarcomas. *Int J Oral Maxillofac Surg* 2014;43:7–12.
- Garland LH, *et al.* Osteogenic Sarcoma of the Skull. *Radiology* 1945;45:45–8.
- Goodman MA, McMaster JH. Primary osteosarcoma of the skull. *Clin Orthop Relat Res* 1976;120:110–4.
- Luna-Ortiz K, Alonso-Calamaco M, Ortiz-Leyva RU. Primary Frontoparietal Osteosarcoma. *J Craniofac Surg* 2017;28:e189–91.
- Shinoda J, Kimura T, Funakoshi T, *et al.* Primary osteosarcoma of the skull--a case report and review of the literature. *J Neurooncol* 1993;17:81–8.
- Patel AJ, Rao VY, Fox BD, *et al.* Radiation-induced osteosarcomas of the calvarium and skull base. *Cancer* 2011;117:2120–6.
- Martin E, Senders JT, Ter Wengel PV, *et al.* Treatment and survival of osteosarcoma and Ewing sarcoma of the skull: a SEER database analysis. *Acta Neurochir* 2019;161:317–25.
- Vener J, Rice DH, Newman AN. Osteosarcoma and chondrosarcoma of the head and neck. *Laryngoscope* 1984;94(2 Pt 1):240–2.
- Ha PK, Eisele DW, Frassica FJ, *et al.* Osteosarcoma of the head and neck: a review of the Johns Hopkins experience. *Laryngoscope* 1999;109:964–9.
- van Es RJ, Keus RB, van der Waal I, *et al.* Osteosarcoma of the jaw bones. Long-term follow up of 48 cases. *Int J Oral Maxillofac Surg* 1997;26:191–7.
- Salvati M, Ciappetta P, Raco A. Osteosarcomas of the skull. Clinical remarks on 19 cases. *Cancer* 1993;71:2210–6.
- Patel SG, Meyers P, Huvos AG, *et al.* Improved outcomes in patients with osteogenic sarcoma of the head and neck. *Cancer* 2002;95:1495–503.
- Smelee LE, Kostense PJ, van der Waal I, *et al.* Effect of chemotherapy on survival of craniofacial osteosarcoma: a systematic review of 201 patients. *J Clin Oncol* 1997;15:363–7.
- Sturgis EM, Potter BO. Sarcomas of the head and neck region. *Curr Opin Oncol* 2003;15:239–52.
- Kassir RR, Rassekh CH, Kinsella JB, *et al.* Osteosarcoma of the head and neck: meta-analysis of nonrandomized studies. *Laryngoscope* 1997;107:56–61.

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