Low-Grade Surface Osteosarcoma of the Temporal Bone in Paediatric Patients: A Case Report and Literature Review

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ABSTRACT

PURPOSE OF THE STUDY: Primary osteosarcoma of the temporal bone is an exceedingly rare pathology in the paediatric population. As of now, only 3 cases have been reported in the English literature. We describe the additional case of a 16-year-old girl with an osteosarcoma of the mastoid bone. This study aims to report a rare paediatric case of low-grade surface osteosarcoma of the temporal bone.

MATERIALS AND METHODS USED: A literature review was performed to better understand paediatric osteosarcomas of the head and neck region, to optimize their investigation, to describe their histopathological and radiological characteristics, and to establish the optimal modalities of medical and surgical treatments. The research of previous published data was done using PubMed and Embase library with the keywords mentioned below.

RESULTS: The patient presented with a rapidly progressive left retroauricular lesion over a 3-week period. Radiological studies demonstrated aggressive and invasive features. An open biopsy followed and confirmed the diagnosis of a low-grade surface osteosarcoma. In accordance with the multidisciplinary team, we decided to perform a complete surgical resection with wide surgical margins. We did not administer any adjuvant therapies. A control computed tomography (CT) scan obtained 26 months postoperatively still showed no signs of recurrence.

CONCLUSION: Osteosarcomas are aggressive malignant neoplasms found in the head and neck region in only 6% to 10% of cases. They represent approximately 1% of head and neck cancers, and these are generally high-grade lesions. Temporal bone involvement is rare, particularly for low-grade lesions in paediatric patients. In addition to reporting the fourth paediatric case of primary temporal bone osteosarcoma, this study describes its specific clinical, histopathological, and radiological findings, to improve the management and the prognostic of patients affected with this particular clinical entity.

KEYWORDS: temporal bone, osteosarcoma, low-grade surface osteosarcoma, skull base surgery

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Introduction

Osteosarcomas (OS) are rare malignant bone tumours of mesenchymal stem cells origin. Although these lesions account for less than 1% of overall cancers in adults, OS are the most frequent bone tumours in children and adolescents. They account for 3% to 5% of all malignancies in the paediatric population.[1] Among these, only 6% to 10% will occur in the craniofacial region, most commonly arising from the maxilla, the zygoma, and the mandible.[2] Considering that skull is affected in approximately 1.6% of cases, primary OS of the temporal bone is an exceedingly rare pathology, especially during childhood.[3]

In this report, we describe a paediatric case of low-grade surface OS of the temporal bone.

Case Presentation

A 16-year-old girl was referred to our service for a rapidly progressive left retroauricular lesion incidentally discovered 3 weeks earlier (Figure 1). The patient remained totally asymptomatic and denied any history of trauma or pain. She was otherwise in good health, her only medication being oral contraceptives.

On examination, the lesion was oval shaped, measuring 3 cm × 2.5 cm. It was firm and nontender. The overlying skin was intact. A complete neurotologic examination was performed and did not reveal any anomalies. The left facial nerve function was normal and no cervical lymphadenopathy could be palpated. A computed tomography (CT) scan performed at the medical centre where the patient was first evaluated demonstrated a 2 cm anteroposterior (AP) × 2.5 cm craniocaudal (CC) lesion with highly irregular borders arising from the left mastoid region. A significant periosteal reaction was noted, without any evidence of soft-tissue invasion or intracranial extension.

Based on the history, as well as the radiologic features, an OS was highly suspected. Consequently, an open biopsy was

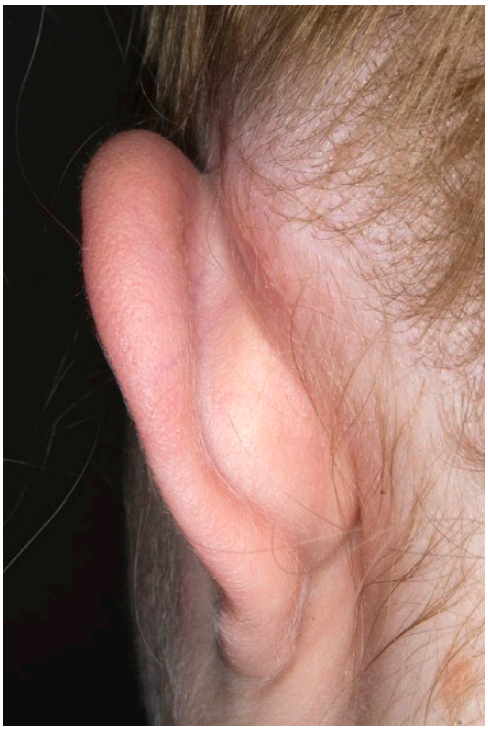

Figure 1. Left retroauricular lesion.

performed for histological confirmation. The first biopsy demonstrated a fibro-osseous lesion without atypia or significant mitotic activity. There was no cartilaginous differentiation; MDM2 immunostaining was negative, and it was not possible to obtain DNA for assessment of GNAS mutation. Immunostaining for CDK4 was not performed in our case. At this point, 3 different diagnoses were considered: fibrous dysplasia, fibrous dysplasia protuberans, and a low-grade surface OS. Considering the highly aggressive radiologic features, decision was made to perform another open biopsy, to exclude a sampling error. The second biopsy demonstrated similar histologic characteristics. Immunohistochemistry for MDM2 was again negative. Polymerase chain reaction (PCR) analysis showed no GNAS mutations in codons 201 and 207. The same differential diagnosis was evoked.

Facing such an important discordance between clinical, radiological, and histopathological characteristics, a multidisciplinary team was consulted. Decision was made to treat the lesion as a primary low-grade surface OS of the temporal bone. A complete surgical resection with wide margins (>1 cm) was suggested. No adjuvant or neoadjuvant therapies were considered justified.

Before surgery, both CT scan and magnetic resonance imaging (MRI) were ordered to optimize surgical planning. The CT scan of the mastoid showed a unique lesion of 2.6 cm anterioposteriorly (AP) × 3 cm cephalocaudaly (CC) × 1.7 transversely (TR) originating from the outer cortex of the left temporal bone. An aggressive periosteal reaction with a sunburst appearance was also described (Figure 2). On the MRI of the mastoid, the lesion had an isointense signal on T1-weighted

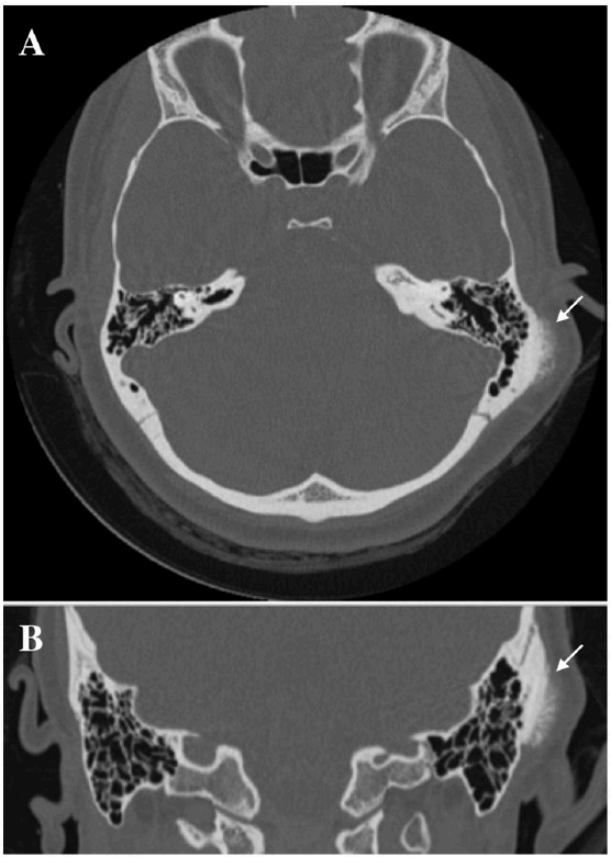

Figure 2. Preoperative noncontrast CT scan showing an ill-defined lesion with sunburst periosteal reaction over the left mastoid bone (arrows). (A) Axial view. (B) Coronal view. CT indicates computed tomography.

images and a hypointense signal on T2-weighted images. It extended superiorly up to the squamous suture, without crossing it. The lesion was strictly confined to the outer cortex of the temporal bone (Figure 3). A complete extension workup was done and did not show any evidence of synchronous osseous disease or distant metastasis.

The patient had a left partial mastoidectomy with gross surgical margins between 1 and 1.5 cm (Figure 4). Following en bloc resection of the tumour, the deficit was corrected with a cervicofacial rotation flap. On definitive pathological analysis, all margins were negative. The lesion was composed of a hypocellular fibrous stroma with spindle cells. There was no atypia and mitotic activity was minimal (1 mitosis/10 hpf). Woven bone with only scant lamellar bone was noted and no prominent osteoblastic population were found along bone trabeculae (Figure 5). These observations combined with the aggressive radiological features supported the final diagnosis of a low-grade surface OS.

The patient had an uncomplicated postoperative course. On her 18-month follow-up visit, she had no signs of local recurrence or distant metastasis. A control CT scan obtained 26 months postoperatively still showed no signs of recurrence.

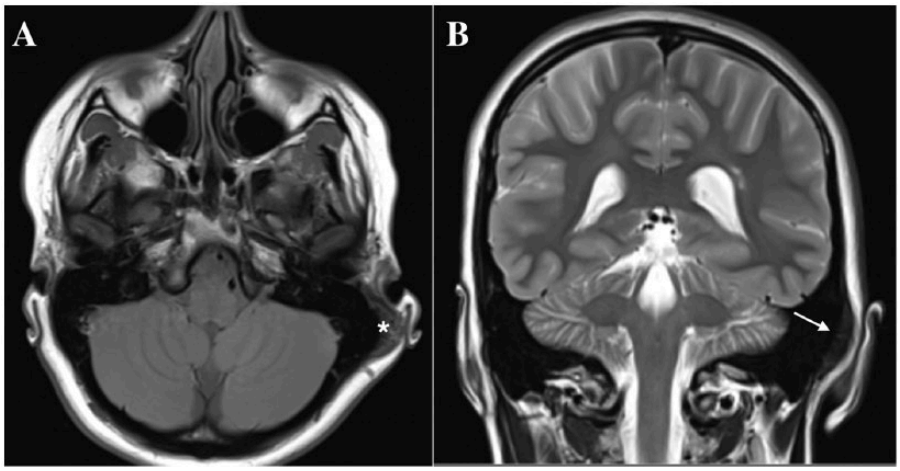

Figure 3. Preoperative MRI. (A) Axial T1W1 with isointense signal lesion (asterisk). (B) Coronal T2W1 with hypointense signal lesion (arrow). MRI indicates magnetic resonance imaging.

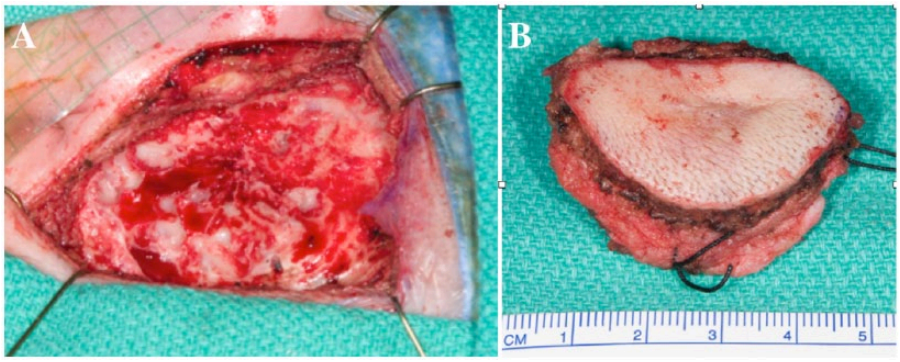

Figure 4. Left partial mastoidectomy with wide surgical margins. (A) Surgical deficit following complete en bloc resection of the tumour. (B) Pathological specimen.

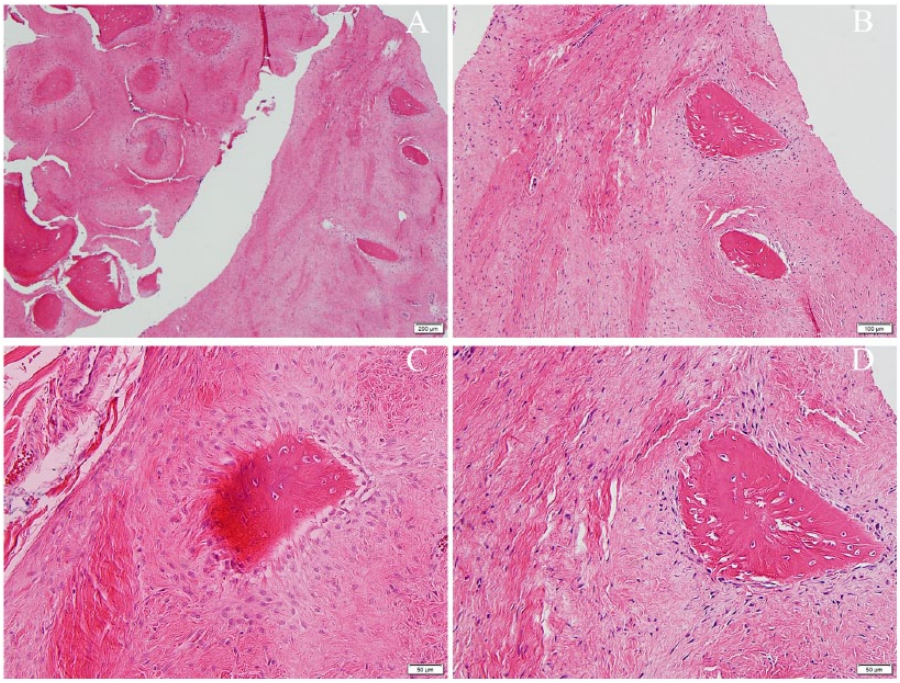

Figure 5. Hematoxylin and eosin (HE) immunostaining. (A) Low power view showing a low-grade fibro-osseous lesion (HE40×). (B) Bland spindle cells in a fibrous background, with islands of woven bone (HE100×). (C) Focus of woven bone which appears to be partially surrounded by osteoblasts (HE200×). (D) Bland spindle cells in a fibrous background, with islands of woven bone (HE200×).

Discussion

Primary OS of the temporal bone is a rare clinical entity. Nowadays, only 3 paediatric cases have been reported in the English literature (Table 1). Although most of the OS are intramedullary in origin, some arise from bone surface and are designated as surface OS. The World Health Organization (WHO) has now classified OS into 8 different categories. Among these, 3 form the surface OS group: parosteal OS, periosteal OS and high-grade surface OS. The parosteal subtype, which was first referred to as 'juxtacortical OS', is the most frequently encountered one. Indeed, it represents between 1% and 6% of all OS.

Clinical presentation

Low-grade surface OS, as well as primary head and neck OS, affect older patients compared with their conventional counterpart. Indeed, the peak age of incidence is 30 years, with a slight female predominance (1.3:1). Moreover, patients typically have longer duration of symptoms.[13] Clinical presentation depends on the location of the tumour. When affecting the skull, it may present with various complaints, such as a slowly enlarging lump with or without pain, headaches, cranial nerve palsies or exophthalmos. Consequently, a broad differential diagnoses must be considered, including benign processes such as myositis ossificans, osteoma, osteochondroma, and fibrous dysplasia, as well as malignant entities like periosteal chondrosarcoma and other subtypes of surface OS. Differential diagnosis is also to be made with protuberant fibro-osseous lesion of the temporal bone, also known as Bullough bump.[14] It is particularly important to mention this lesion, as it is surprisingly similar to low-grade surface OS of the temporal bone in its clinical presentation as well as in its pathological appearance.[15] Differentiation between these diagnoses is based mainly on malignant radiologic findings such as periosteal reaction in a sunburst appearance, which was described in our case. Being by definition low-grade lesions, low-grade surface OS carry a good prognosis with a 5e-year overall survival of more than 90%.[16] However, they may dedifferentiate into high-grade surface OS, which convey the same aggressive clinical behaviour as conventional OS.[17]

Radiological findings

On plain X-ray and CT scan, parosteal OS classically presents as an exophytic mass broadly attached to the cortex, with higher bone density in the centre of the lesion compared with the periphery. Cortical bone thickening is often present. Aggressive periosteal reaction is atypical, being more frequent in periosteal OS and high-grade bone lesions.[13] The presence of this aggressive periosteal reaction in a low-grade OS has not been previously described and it differentiates our case from other published reports. Thus, our case does not fit well with the strict definition of parosteal/juxtacortical OS, and the generic terminology of low-grade OS is used. The 'string sign', consisting in a thin cleavage plane separating the normal cortex adjacent to the bone tumour, is seen on both plain X-ray and CT scan in up to 30% and 65% of cases, respectively. Moreover, 41% of low-grade lesions will show signs of medullary invasion. On MRI, osseous components of parosteal OS are generally hypointense on T1-weighted and T2-weighted images. Soft tissues at the periphery of the lesion as well as cortical or bone marrow invasion generally have heterogeneous or hyperintense signal on T2-weighted images and enhance with contrast agents.[16]

Histopathology

Low-grade OS arises from the outer fibrous layer of the periosteum.[18] Histologically, it is typically described as a fibro-osseous lesion composed of mature trabecular bone and fibroblastic spindle cells stroma, with only minimal atypia.[19] Three different patterns are described: (1) the 'streamer pattern', which is the most frequent, is characterized by parallel trabecular bone with intervening spindle cells stroma; (2) the 'fibrous dysplasia-like pattern' features irregular arrangement of trabecular bone, similar to Chinese calligraphy; and (3) the 'desmoplastic fibroma-like pattern' shows a predominance of spindle cells stroma with abundant collagen bundles. Unlike other cases, our case did not fit specifically in these 3 histopathological descriptions. Focal medullary invasion is observed in up to 25% of cases, but it does not have any deleterious effect on prognosis. The detection of GNAS mutation has been of clinical use in the differential diagnosis of bone tumours and is particularly associated with fibrous dysplasia. Although, previous reports suggested that the mutation could also detected in cases of low-grade OS.[20] A recent study by Salinas-Souza et al. analysed pathologic samples of 90 patients with low-grade OS and reported negativity for the GNAS mutation in all cases. These findings and other previous observations support that the detection of GNAS mutation is supportive of the diagnosis of fibrous dysplasia.[21] Furthermore, 2 genes are found to be amplified in parosteal OS: *MDM2* and *CDK4*.[22] Based on previous studies, MDM2 amplification has been reported to occur in 93% of cases of low-grade central OS and in 79% of low-grade parosteal OS.[21] It has also been reported that at least one of these mutations will be positive in 87% to 100% of cases.[23] However, negative staining does not exclude the diagnosis. In our case, MDM2 immunostaining was negative. The concurrent negativity of the GNAS mutation also oriented the diagnosis towards a low-grade OS rather than a fibrous dysplasia in this case.

Treatment

Nowadays, it is widely accepted that surgical resection, with margins greater than 1 cm, is the treatment modality of

Table 1. Paediatric cases of osteosarcoma of the temporal bone.

AUTHORS (YEAR)	AGE (YEARS)	SEX	TUMOUR TYPE	RAS	LOCATION	SURGICAL RESECTION	NEOADJUVANT/ ADJUVANT THERAPIES	LOCAL RECURRENCE	METASTASIS	SURVIVAL	FOLLOW-UP (MONTHS)
Rand (1961)[4]	**<1**	**M**	**Primary OS[a]**	**No**	**Temporal**	**NS**	**Adjuvant radiotherapy**	**None**	**None**	**Dead**	**348**
Cassentini et al. (1985)[5]	10	F	Secondary OS	Yes	Temporal	Complete	None	None	None	Alive	28
Kellie et al. (1989)[6]	10	F	Secondary OS	Yes	Temporal	Partial	Adjuvant chemotherapy	None	None	Alive	36
Salvati et al. (1993)[7]	**11**	**M**	**Primary OS[a]**	**No**	**Fronto-temporal**	**Partial**	**Adjuvant radiotherapy**	**Yes**	**NS**	**Dead**	**2**
Sharma et al. (1997)[8]	**16**	**M**	**Primary OS[a]**	**No**	**Temporal**	**Partial**	**Neoadjuvant radiochemotherapy**	**Yes**	**None**	**Alive**	**12**
Daw et al. (2000)[9]	NS	NS	Secondary OS	Yes	Temporal	Partial	Adjuvant chemotherapy	Yes	None	Alive	156
	NS	NS	Secondary OS	Yes	Temporal	Partial	Adjuvant chemotherapy	Yes	None	Dead	32
Kim et al. (2004)[10]	18	F	Metastasis	No	Fronto-temporal	NS	NS	NS	NS	NS	NS
Patel et al. (2011)[11]	10	M	Secondary OS	Yes	Mastoid and jugular foramen	Partial	Adjuvant radiochemotherapy	Yes	None	Dead	29
Debnam et al. (2012)[12]	14	M	Secondary OS	Yes	Temporal	Surgery	None	NS	NS	Alive	29
V. Poliquin et al. (case described in this case report, 2019)	**16**	**F**	**Primary OS**	**No**	**Temporal**	**Complete**	**None**	**None**	**None**	**Alive**	**26**

Note: The values in bold are the publications of primary OS.
Abbreviations: NS, not specified; RAS, radiation-associated sarcoma.
[a]Conventional osteosarcoma (high-grade).

choice for low-grade surface OS. When only partial excision can be achieved or when margins are positive, there is a high likelihood of local recurrence with possible dedifferentiation into high-grade lesion. In these cases, reintervention should be performed. Neither chemotherapy nor radiotherapy was shown to be beneficial in the treatment of low-grade surface OS.[17,24] Therefore, complete surgical resection with negative margins was the only treatment in our case.

Conclusions

We describe a rare case of primary low-grade surface OS of the temporal bone. To our knowledge, this is only the fourth paediatric case to be reported in the English literature. We also present a review of all clinically relevant features of parosteal OS. This report demonstrates that correlation between histological, radiological, and clinical characteristics of suspicious bone lesions is essential for reaching an accurate diagnosis and initiating an optimal treatment, to optimize patients' outcome.

Author Contributions

NV-P and MT contributed to conception and design, acquisition of data, analysis, drafting, revision and final approval. GF contributed to conception and design, analysis, drafting, revision and final approval of the manuscript. SL and VB contributed to conception and design, analysis and final approval of the manuscript.

Consent for Publication

Informed consent was obtained directly from the patient.

Ethics Approval and Consent to Participate

The procedures were in accordance with the ethical standards of the CHU de Québec – Université Laval. Ethical approval by research ethics boards was obtained.

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