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FULL PAPER

CT and MRI features of calvarium and skull base osteosarcoma (CSBO)

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Objective: This study aims to assess the CT and MRI features of calvarium and skull base osteosarcoma (CSBO).

Methods: The CT and MRI features and pathological characteristics of 12 cases of pathologically confirmed CSBO were analyzed retrospectively.

Results: 12 patients (age range 9–67 years; 3 male, 9 female) were included in the study. Tumours occurred in skull base (7, 58.3%), temporal (4, 33.3%) and frontal (1, 8.3%). Among all, six patients received radiotherapy for nasopharyngeal carcinoma. According to pathology, 11 out of 12 tumours were high-grade (91.7%). On CT, all the tumours had soft tissue mass penetrated into cortical bone with invasion of surrounding soft tissue. Six tumours were shown to have lytic density and six were mixed density. Matrix mineralization was present in 10 cases (83.3%). On MRI, tumours presented as soft-tissue masses measuring 5.9 ± 2.4 (3.9–8.0) cm. Five tumours

showed low signal intensities on T_1 weighted imaging with seven having heterogeneous signal intensities. One showed low signal intensity on T_2 weighted imaging, two showed high signal intensities and nine heterogeneous signal intensities. All the tumours showed low signal intensities on diffusion-weighted imaging. On contrast enhanced images, seven cases showed heterogeneous enhancement, three showed peripheral enhancement and two showed homogeneous enhancement. Dural tail sign were detected in nine cases.

Conclusion: CSBO is rare, and is commonly associated with previous radiation exposure. A presumptive diagnosis for osteosarcoma should be considered when calvarium and skull base tumours with osteoid matrix and dural tail sign are found.

Advances in knowledge: CT and MR features of CSBO have not been reported. The study helps to identify CSBO and other sarcomas.

BACKGROUND

Osteosarcoma primarily arises in extremities in children and adolescents. Calvarium and skull base osteosarcoma (CSBO) is a disease accounting for not more than 10% of all kinds of osteosarcoma and not more than 1% of all head and neck malignancies. Osteosarcoma of head and neck usually affects patients of 30s or 40s, which is often the result of radiotherapy or chemotherapy.^{1,2} It often occurs in the maxilla and mandible, and is rarely seen in younger or older people. Different from tumours of extremities, the diagnosis of CSBO is challenging due to non-specific symptoms, rarity, and lack of typical radiological characteristics, and it is often misdiagnosed as other diseases. There are few case reports about the imaging manifestations of CSBO,^{3–11}

and no original literature about their imaging features. Therefore, we aim to review the radiological features of calvarium and skull base on MRI and CT of 12 patients and to analyze the clinicopathological features of CSBO patients.

METHODS AND MATERIALS

Between June 2005 and January 2018, 258 patients with histologically proven osteosarcoma were collected at tertiary hospitals. Of all these tumours, the calvarium and skull base were affected in 12 (4.7%) patients. There were three males and nine females aged 9–67 years (mean age, 44.3 years), and they were diagnosed as CSBO based on biopsy ($n = 7$) and open surgical resection ($n = 5$).

CT scans were done on helical 64- or 16-slice CT (Siemens SOMATOM Definition AS 64, Erlangen, Germany; or GE Lightspeed Ultra 16, Milwaukee, WI, USA; 3–5 mm slice thickness; 1.5 pitch; 120 kVp tube voltage; 200–300 mAs, tube current; coronal and sagittal reconstruction thickness, 5 mm with an interval of 5 mm using soft-tissue or/and bone algorithms). An intravenous bolus dose of contrast agents (non-ionic iodinated, 90 ml) was injected at the rate of 3 mm/s.

MRI studies were performed on MRI scanners (GE Signa Excite HD 3.0, USA; or Siemens MAGNETOM Avanto 1.5, Germany) in T_1 weighted [repetition time (TR) 400–650/echo time (TE) 10–25] and T_2 weighted (TR 2,2100–4,010/TE 60–140) sequences. Diffusion-weighted imaging (DWI) sequence was comprised of a single shot spin-echo echo-planar sequence (TR 7000/TE 73) and b-values of 1000 and 0 s/mm². After IV administration of gadopentetate dimeglumine with a dosage of 0.1 mmol/kg (body weight), fat-suppressed T_1 -weighted (TR 460–630/TE 9–25) coronal, axial and sagittal images were performed, with their parameters the same as pre-injection. Section thickness and intersection gap were 5 mm and 1 mm for the axial plane, and 6 mm and 2 mm for the coronal and sagittal planes, respectively.

Pathological, clinical and imaging data were taken. The medical records were reviewed by a radiologist who was trained and had 12 year working experience, and demographic information was harvested, including patients' age, gender, duration of the symptoms, chief complaints, latency of osteosarcoma induced by radiation, history of radiotherapy, primary tumour sites where osteosarcoma may reappear as a secondary lesion, and histologic type. Only patients which did not receive any treatment and had CSBO confirmed by histological examination were included in this report. Baseline tumour characteristics were recorded according to the consensus view on imaging by two radiologists

who were blinded to tumour histological grade and had more than 10 years of experience. CT imaging analysis included (1) mass density; (2) periosteal reaction; (3) matrix mineralization; (4) margins of the mass; and (5) cortical involvement. Mass density could be classified as mixed, lytic, or sclerotic. Cortical involvement and matrix calcification were recorded as present or absent. Periosteal reaction included laminated, spiculated or none. The lesion's margin was recorded as well- or ill-defined.

MR image analysis included (1) lesion location; (2) size of the mass; (3) signal intensities of the lesion on T_2 -, T_1 weighted, DWI, and contrast-enhanced images; (4) presence of dural tail sign (DTS). The longest diameter of the mass defined its size. The lesions' signal intensities on T_2 - and T_1 weighted image and DWI were defined as isointense, low, or high compared to what we saw in the bone marrow of a normal person. They were also classified as heterogeneous or homogeneous. Enhancement patterns on the contrast-enhanced images were defined as peripheral enhancement, heterogeneous or homogeneous. DTS was a tail-like thickening of the enhanced dura mater that extended from the mass on contrast material-enhanced MRI. It was recorded as present or absent.

RESULTS

The clinical characteristics of 12 CSBO patients are listed in Table 1. There were 12 patients in the study cohort, among which 3 (25%) were male and 9 (75%) female with a mean age of 44.3 years (range, 10–67 years). Tumours at the skull base (7 out of 12, 58.3%) were most common, followed by temporal (4, 33.3%), and frontal (1, 8.3%) areas. Seven patients suffered from headache. Four patients experienced a palpable mass. One patient had epistaxis, diminution of vision and vomiting. Symptoms duration ranged from 10 days to 2 years (mean = 132 days). Metastases were found during the initial evaluation in one skull base patient

Table 1. The clinical and histological subtypes in 12 CSBOs

Case no.	Sex	Age (years)	Chief complaints	Duration of symptoms	Prior radiation	Latency (years)	Underlying disease	Histological subtypes
1	M	53	Headache	2 months	Yes	10	No	Osteoblastic
2	F	40	Headache	10 days	Yes	8	No	Osteoblastic
3	M	62	epistaxis	6 months	Yes	9	No	Fibroblastic
4	F	50	Headache	1 month	Yes	12	No	Chondroblastic
5	F	19	Palpable mass	2 months	Yes	2.5	No	Chondroblastic
6	M	57	Palpable mass	5 months	Yes	14	No	Osteoblastic
7	F	56	Headache, palpable mass	1 month	No	-	No	Giant-cell rich
8	F	10	Palpable mass	2 years	No	-	No	Low-grade
9	F	35	Headache	3 months	No	-	No	Osteoblastic
10	F	33	Diminution of vision	1 month	No	-	No	Osteoblastic
11	F	49	Headache, vomiting	five months	No	-	No	Osteoblastic
12	F	67	Headache	1 month	No	-	No	Osteoblastic

CSBOs, calvarium and skull base osteosarcomas.

Table 2. The CT imaging of all 12 CSBOs

Case no.	Density	Matrix mineralization	Periosteal reaction	Cortical involvement	Margin
1	Mix	Yes	Spiculated	Yes	Ill-defined
2	Lytic	Yes	No	Yes	Ill-defined
3	Mix	Yes	No	Yes	Ill-defined
4	Mix	Yes	No	Yes	Ill-defined
5	Lytic	Yes	Spiculated	Yes	Ill-defined
6	Lytic	Yes	No	Yes	Ill-defined
7	Lytic	No	Laminated	Yes	Ill-defined
8	Mix	Yes	Spiculated	Yes	Well-defined
9	Mix	Yes	Spiculated	Yes	Ill-defined
10	Mix	Yes	Spiculated	Yes	Ill-defined
11	Lytic	Yes	Spiculated	Yes	Ill-defined
12	Lytic	No	No	Yes	Ill-defined

CSBOs, calvarium and skull base osteosarcomas.

who had lung metastases previously but without radiotherapy treatment history. Six patients went through radiotherapy due to nasopharyngeal carcinoma (NPC) (external beam radiotherapy with a dosage of 60–90 Gy in 6–8 weeks). Nasopharyngeal radiation fields usually included two opposite pre-auricular fields. If the patient had a post-styloid area or nasal cavity invasion, a post-auricular or anterior supplementary field was added. The median latency of osteosarcoma induced by radiotherapy (the interval between the end of radiotherapy and the time of diagnosis) was 9.25 years (range 2.5–14 years). Most (11, 91.7%) lesions had microscopically high grades, with only one lesion of low grade. The histology type was osteoblastic in seven cases, chondroblastic in two, and fibroblastic in one, with one rich in Giant cells.

Tumour imaging included CT and MRI, with all the patients taking contrast agents.

Table 2 shows the CT imaging characteristics. Six of the cases had mixed density. Another six had lytic density. Most (10, 83.3%) cases exhibited matrix mineralizations (Figures 1a–6a). Periosteal reaction was seen in seven cases (58.3%), and there were six spiculated periosteal and one lamellar periosteal reaction. All of the cases revealed cortical destruction with a soft mass. Most (11, 91.6%) cases had ill-defined margins, and one had well-defined margins (Figure 1a).

MR imaging results are listed in Table 3. Lesion outbreak at the skull base, temporal, and frontal area was seen in seven, four, and one case, respectively. All 12 cases had soft tissue components. The average size of the mass was around 5.9 cm (range, 3.9–8.0 cm). Five cases (41.7%) had low signal (Figure 2b) while seven (58.3%) had heterogeneous signal (Figures 1b and 3b–6b) on T_1 weighted images. As for T_2 weighted images, heterogeneous signal was seen in nine cases (75%) (Figures 1c and 3c–6c), while two showed high signal with the remaining one showing low signal (Figure 2c). On DWI, all cases showed low

signal (Figures 1d and 4d–6d). Heterogeneous enhancement, peripheral enhancement and homogeneous enhancement were seen on contrast-enhanced images in seven, three and two case, respectively. DTS was detected in nine cases (Figures 1e–6e).

DISCUSSION

Osteosarcoma is one of the most common bone malignancies in the long bones of children and adolescents. However, CSBO is known to be rare with only few studies describing its occurrence in different size population groups.

Primary CSBO is more common in the calvaria than in the skull base, which is the most common site of radiation-induced CSBO.⁶ Our results were similar to previous literature, while skull osteosarcoma more frequently affects the middle skull base.¹² Diagnosis of CSBO is challenging due to the involvement of skull base. It is also challenging to excise the entire tumour lesion due to fear of severing surrounding neurovascular structures, thus resulting in a tendency in recurrence.

Radiotherapy remains the primary treatment modality for patients with NPC. With half of our patients presenting with history of prior radiotherapy, it would be logical to postulate that these CSBO were induced by radiation. All the six primary tumours in our study were NPC. This seemed to suggest that cases with radiotherapy history due to a head and neck tumour are more likely to develop osteosarcoma. In particular, osteosarcoma should be taken into consideration if a subject had radiotherapy to treat a craniocerebral tumour and an abnormal soft tissue mass with bony changes in the calvarium and skull base. The median latency after radiation was reported to be of 2.5–14 years. However, it seems that the time of occurrence of osteosarcoma following radiotherapy for NPC is longer than other histological types.^{13,14}

According to the previous literature,^{15–17} the age of CSBO is 26–40 years. In our study, the cases with CSBO had a wider age

Figure 1. (a–e) A 10-year-old female with osteosarcomas in temporal (histological subtypes, low grade). (a) Axial CT on bone algorithm showing mixed lytic and blastic lesion of temporal, suggestive of matrix mineralization (white arrows). (b) Axial T_1 weighted image of its soft tissue component showing heterogeneous signal intensity with patchy low and high signal intensities, suggestive of matrix mineralization (white arrows) and haemorrhage (arrows head). (c) Axial T_2 weighted image of its soft tissue component showing heterogeneous signal intensity with patchy low and high signal intensities, suggestive of matrix mineralization (white arrows). (d) Axial DWI of its soft tissue component showing low signal intensity with patchy high signal intensities, suggestive of haemorrhage. (e) Coronal T_1 weighted contrast-enhanced image showing a markedly enhancing mass in temporal with DTS (white arrow). DTS, dural tail sign; DWI, diffusion-weighted imaging.

range (10–67 years), with their mean age of 44.3 years. Most of the patients (83.3%) diagnosed as CSBO were aged more than 30 years old, which was elder compared to those with osteosarcoma in the extremity. Some authors stated that skull osteosarcoma is more common in males.^{12,17} However, we identified the predominance of CSBO in females in our series, and 75% (9/12) of our patients were female. This is similar to the results of Salvati et al.¹⁸

Figure 2. (a–d) A 50-year-old female with osteosarcoma of middle skull base 12 years after radiotherapy for NPC (histological subtypes, chondroblastic). (a) Axial CT on bone algorithm showing mixed lytic and blastic lesion of middle skull base, suggestive of matrix mineralization (white arrows). (b) Axial T_1 weighted image of its soft tissue component showing low signal intensity. (c) Axial T_2 weighted image of its soft tissue component showing low signal intensity. (d) Sagittal T_1 weighted contrast-enhanced image showing a peripheral enhancing mass in middle skull base with DTS (white arrow). DTS, dural tail sign; NPC, nasopharyngeal carcinoma.

The clinical symptoms of primary skull osteosarcoma vary depending on the tumour site.¹⁸ The main clinical manifestations of CSBO included varying degrees of pain, a swelling or a slow-growing mass, and neurological symptoms such as swelling, headache or dizziness. In cases with nasal cavity involvement, nasal bleeding and a stuffy nose could occur as well as exophthalmos and diplopia with invasion of the orbital cavity. In our study, headache was the most commonly seen symptom, which was in agreement with other studies.^{7,9,11} Meanwhile, the mean symptom duration of our cases was approximately 132 days, which is similar to Guo's finding¹² of 2.9 months in skull osteosarcoma patients (range—20 days–12 months between disease's onset and diagnosis).

Additionally, over 90% of our cases were of high-grade osteosarcoma, and osteoblastic type was more common than fibroblastic or chondroblastic types. This result is consistent with that in previous studies.^{19–21} CT demonstrates osteoid mineralizations best, especially when it is still minimal and able to extend into the soft tissues. The CT features of CSBO were similar to those of osteosarcoma in the extremity.^{22,23} CSBO primarily exhibits osteoblastic and/or osteolysis destruction features, along with an

Figure 3. (a–d) A 40-year-old female with osteosarcoma of right temporal bone (histological subtypes, osteoblastic). (a) Axial CT on bone algorithm showing a lytic lesion of right temporal bone with extraosseous soft-tissue extension, suggestive matrix mineralization (white arrows). (b) Axial T_1 weighted image of its soft tissue component showing heterogeneous signal intensity with patchy high signal intensities, suggestive haemorrhage (white arrows). (c) FLAIR image of soft tissue component showing heterogeneous high signal intensity with patchy low signal intensities, suggestive of matrix mineralization (white arrow). (d) Axial T_1 weighted contrast-enhanced image showing a heterogeneous markedly enhancing mass in right tempus with DTS (white arrow). DTS, dural tail sign; FLAIR, fluid attenuation inversion recovery.

irregular tumour margin on CT. The mixed and sclerotic radiological pattern in the calvarium and skull base is highly indicative of osteosarcoma, and it should be differentiated from chondrosarcoma, lymphoma, and metastases. Osteoid mineralization was seen in 83.3% of our patients, which was typical and the same as that of tubular bone osteosarcoma. Aggressive reactions are comprised of spiculated (sunburst or hair-on-end), disorganized, laminated, or Codman triangle reaction patterns.²⁴ In our study, CSBO with spiculated periosteal reaction was common ($n = 5$) but that with lamellar periosteal reaction was rare ($n = 1$). Bone destruction without periosteal reaction was also found in some CSBO cases. The findings above are consistent with Wang et al.' study²² in which periosteal reaction was found in 62% patients and more frequent than laminated.

MRI is now regarded as the best imaging method to evaluate a primary lesion and the relationship with surrounding structures. For depiction about bone marrow and soft-tissues infiltration,

Figure 4. (a–e) A 49-year-old male with osteosarcoma of skull base (histological subtypes, osteoblastic). (a) Axial CT on bone algorithm showing mixed lytic and blastic lesion of middle skull base, suggestive of matrix mineralization (white arrows). (b) Axial T_1 weighted image of its soft tissue component showing heterogeneous signal intensity with patchy low signal intensities, suggestive of matrix mineralization (white arrows). (c) Axial T_2 weighted image of its soft tissue component showing heterogeneous signal intensity with patchy low signal intensity, suggestive of matrix mineralization (white arrows). (d) Axial DWI of its soft tissue component showing low signal intensity. (e) Axial T_1 weighted contrast-enhanced image showing a heterogeneous enhancing mass in skull base with DTS (white arrow). DTS, dural tail sign; DWI, diffusion-weighted imaging.

MRI is better compared to CT, which shows cortical destruction and expansile masses. In our study, the masses showed heterogeneous ($n = 7$) or low ($n = 5$) signal in T_1 weighted images. They also showed low ($n = 1$), high ($n = 2$) or heterogeneous

Figure 5. (a–e) A 35-year-old female with osteosarcoma of frontal bone (histological subtypes, osteoblastic). (a) Axial CT on bone algorithm showing mixed lytic and blastic lesion of frontal bone, suggestive of matrix mineralization (white arrows). (b) Axial T_1 weighted image of its soft tissue component showing heterogeneous signal intensity with patchy low signal intensities, suggestive of matrix mineralization (white arrows). (c) Axial T_2 weighted image of its soft tissue component showing heterogeneous signal intensity with patchy low signal intensity, suggestive of matrix mineralization (white arrows), and with peritumoral oedema. (d) Axial DWI of its soft tissue component showing low signal intensity. (e) Sagittal T_1 weighted contrast-enhanced image showing a peripheral enhancing mass in frontal bone with DTS. DTS, dural tail sign; DWI, diffusion-weighted imaging.

($n = 9$) signal in T_2 weighted images. The masses could contain haemorrhage, necrosis or even osteoid matrix, which are often seen in osteosarcoma.²⁵ Gd-DTPA-enhanced and non-enhanced MR imaging is significant due to its ability of enhancing tissue characterization. Sometimes these peripheral or heterogeneous enhancements are related to different components such as haemorrhage, osteoid matrix or necrosis within the tumour mass.²⁶ In this study, although the MRI appearance of osteoblastic osteosarcoma is non-specific and rarely distinguishable from other

Figure 6. (a–e) A 33-year-old female with osteosarcoma of skull base (histological subtypes, osteoblastic). (a) Axial CT on bone algorithm showing mixed lytic and blastic lesion of skull base, suggestive of matrix mineralization (white arrows). (b) Axial T_1 weighted image of its soft tissue component showing heterogeneous signal intensity with patchy low signal intensities, suggestive of matrix mineralization (white arrows). (c) Axial T_2 weighted image of its soft tissue component showing heterogeneous signal intensity with patchy low signal intensity, suggestive of matrix mineralization (white arrows), and with peritumoral oedema. (d) Axial DWI of its soft tissue component showing low signal intensity. (e) Sagittal T_1 weighted contrast-enhanced image showing a heterogeneous enhancing mass in skull base with DTS. DTS, dural tail sign; DWI, diffusion-weighted imaging.

kinds of sarcoma with heterogeneous post-contrast enhancement and T_2 hyperintense signal, the peripheral rim enhancement seen in Gd-enhanced MRI suggested a chondroblastic osteosarcoma. This was in accordance with the past literature.²⁷ The DTS is seen in contrast material-enhanced MRI as a tail-like enhanced dura mater thickening extending from a mass. Connective tissue expansion and hypervascularity may be the

Table 3. The MR imaging of all 12 CSBOs

Case no.	Location	Size (cm)	T ₁ WI	T ₂ WI	DWI	CE	DTS
1	Temporal	3.9	Low	High	Low	Hom	Yes
2	Temporal	8.0	HT	HT	Low	HT	Yes
3	Skull base	6.3	HT	HT	Low	HT	Yes
4	Skull base	7.4	Low	Low	Low	Peripheral	Yes
5	Skull base	7.1	HT	HT	Low	Peripheral	Yes
6	Skull base	4.8	Low	High	Low	HT	No
7	Temporal	3.9	Low	HT	Low	Hom	No
8	Temporal	4.3	HT	HT	Low	HT	Yes
9	Frontal	4.6	HT	HT	Low	Peripheral	Yes
10	Skull base	8.0	HT	HT	Low	HT	Yes
11	Skull base	6.7	HT	HT	Low	HT	Yes
12	Skull base	6.2	Low	HT	Low	HT	No

CE, Contrast-enhancement; CSBOs, calvarium and skull base osteosarcomas; DTS, dural tail sign; DWI, diffusion-weighted imaging; HT, heterogeneous.

possible reasons to this sign. Among all these causes, tumour invasion is very important to the surgical recurrence and prognosis of the cancer and awareness of invasion is important for the therapeutic plan. The DTS, although not pathognomonic, seems to look like meningioma. Direct tumour invasion or reactive meningeal changes may result in DTS or extra/intra-axial cranial lesions with adjacent meningeal enhancement but look like meningioma, chloroma, neuroma, metastases, lymphoma, pituitary diseases, gliomas, cerebral Erdheim-Chester disease or granulomatous disorders.^{28,29} More and more tumours other than meningioma show this sign, although it is rare in skull bone tumours.^{30–32} In our study, 75% of all CSBOs showed DTS on contrast-enhanced MRI. The same proportion has been quoted in previous reports,^{7,10,13,33} although not specifically discussed in the past.

The early diagnosis and treatment of CSBO are clinically significant, and its diagnosis should be considered when patients show the imaging characteristics or symptoms described previously.

This study also have some limitations. First, we had only limited cases, which was due to the rarity of osteosarcoma in the calvarium and skull base. Second, alternative CT or MRI scanners and protocols were used. The technical bias was unavoidable because the data were not collected from the same hospital. Third, our study focused on the MRI and CT aspects of CSBO

and many clinical outcomes or treatment strategies were not deeply discussed. Follow-up was lost in many patients. Finally, the shortcoming of retrospective studies was available. However, it is difficult to conduct a prospective study due to the rarity of osteosarcoma in calvarium and skull base.

CONCLUSIONS

CSBO is uncommon, which is closely related to radiation exposure. Characteristics of osteoblastic CSBO on MRI are non-specific and are often confused with other sarcoma which had T₂ hyperintense signal and heterogeneous enhancement. However, peripheral rim enhancement on Gd-enhanced MRI suggests chondroblastic CSBO. Features mostly do not differ from those of typical osteosarcoma in extremity bones, apart from patients who are older and have spiculated periosteal reaction. An initial diagnosis of CSBO should be taken into consideration for patients aged over 40 years when tumours have matrix mineralization and DTS. Due to these uncommon sites and challenges in discerning osteosarcoma from other commonly seen tumours, remembering these radiological and clinical features will facilitate CSBO diagnosis greatly.

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