

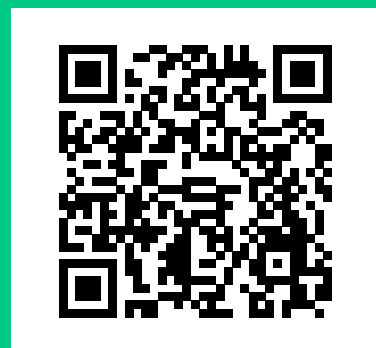
## Rare Case of Intracranial Recurrence of Osteosarcoma: Case Report and Review of Literature

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## ABSTRACT

**Introduction:** Osteosarcoma is the most common malignant bone tumour in children. Though outcome has improved with multimodality treatment, up to one-third of patients develop recurrence. Metastatic disease is seen in 20% of patients with brain metastases being extremely rare in primary or recurrent setting.

**Case presentation:** 13-year-old male presented with pain, swelling over left paravertebral region with imaging showing a destructive lesion of single rib. Diagnosed as high-grade Osteosarcoma and initiated on chemotherapy, primary lesion progressed post 3 cycles. He underwent resection and had completed his treatment. Presented 2 months later with seizures, with CT head suggestive of metastatic recurrence. Patient was offered palliation and had succumbed three months later.

**Conclusion:** Brain metastases are unusual in osteosarcoma patients and they have a poor prognosis. This possibility should be kept when an osteosarcoma patient presents with neurological symptoms.

## INTRODUCTION

Osteosarcoma is the most common malignant bone tumour affecting children, adolescents, and young adults<sup>1</sup>. More than 50% of cases arise in the long bones around the knee. Although survival for patients with high-grade osteosarcoma has improved with multi-agent chemotherapy and aggressive surgical control, up to one-third of patients experience recurrence, which remains challenging to treat. Approximately 15–20% of patients present with metastatic disease at diagnosis, most commonly involving the lungs and other bones. Brain metastases are exceedingly rare, either at initial presentation or during recurrence<sup>2</sup>. Outcomes for children with metastatic disease continue to be poor. Here, we report a rare case of osteosarcoma with both local and intracranial recurrence.

## CASE PRESENTATION

A 13-year-old male presented with complaints of pain and swelling over the left paravertebral region of one month duration. CT Thorax revealed a destructive lesion of the

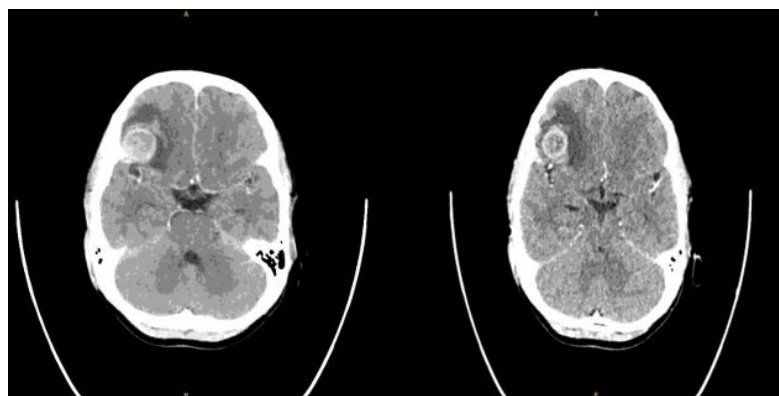
left 7th rib with an associated soft tissue component of 11 × 6 cm. Biopsy from the lesion revealed a high-grade sarcoma with epithelioid and plump spindle cells in an osteoid matrix, suggestive of high-grade osteosarcoma (IHC: ERG-negative, Desmin-negative, SATB2-diffuse weak to moderate positive). CT thorax and bone scans revealed no lung or bone metastases.

He received neoadjuvant chemotherapy with Ifosfamide (3.6 g/m<sup>2</sup>), Adriamycin (60mg/m<sup>2</sup>), and Cisplatin (100mg/m<sup>2</sup>) (IAP), as per our institutional protocol. After three cycles of chemotherapy, response assessment with CT Thorax showed an interval increase in size of the primary lesion with moderate left-sided pleural effusion. He underwent excision of the tumour with resection of the 6th, 7th and 8th ribs and mesh repair of the defect. All four soft tissue margins (both lateral, superior and inferior) were positive for tumour. The histological response was poor, showing 70% viable osteosarcoma cells and only 30% necrosis. A second surgery was not considered because of the risk of morbidity. At the time of treatment, our institutional protocol for osteosarcoma was the IAP protocol, as it was not possible to administer high-dose methotrexate because of resource constraints. including the unavailability of methotrexate level monitoring and intensive supportive care. An alternate regimen was therefore not pursued, and the child received three

additional cycles of IAP chemotherapy followed by surveillance.

Two months later, the child presented with three episodes of seizures of generalised tonic-clonic semiology. CT scan of the head revealed a 2-cm enhancing lesion in the right frontal region with perilesional oedema, most likely representing a metastatic focus (Figure 1). A meningioma was also considered in the differential diagnosis; however, the patient's young age and the absence of any syndrome typically associated with pediatric meningiomas made this less likely. CT thorax revealed multiple soft tissue lesions at the surgical site, the largest 2.3×2cm and an intraspinal deposit at the T6-7 level, suggestive of local recurrence (Figure 2). There were no skeletal metastases on the bone scan.

Given the high clinical and radiological suspicion for metastases, the patient was diagnosed with a recurrence of osteosarcoma. After a discussion with the parents regarding the grave prognosis and limited chance of getting cured with further treatment, the focus of care was shifted to palliation. Consequently, a diagnostic brain biopsy was deemed unnecessary and was not performed. He was given palliative radiotherapy to the left chest wall and brain metastases at a dose of 20Gy in 5 fractions each. Three months later, the child presented with worsening of sensorium and succumbed to his illness.



**Figure 1:** Contrast-enhancing lesion (2 cm) with perilesional oedema noted in the right frontal region, with sclerosis of adjacent bone- metastasis appears likely



**Figure 2:** CT Thorax images at various time points. **A**-At presentation, **B**-Prior to surgery, **C**-At recurrence

# DISCUSSION

Most osteosarcoma recurrences (80%) present as pulmonary metastases, and other site recurrences are seen in only 2% cases<sup>3</sup>. The large size of the primary tumour and its axial location, as in our case, are established risk factors associated with the risk of recurrence in Osteosarcoma<sup>4</sup>. In addition, the poor histological response to chemotherapy and involved resection margins could have further heightened the risk<sup>5</sup>. While chemotherapy augmentation for poor histological response has not shown proven benefit<sup>6</sup>, the high-risk profile of this case may have justified consideration of an alternative methotrexate-based regimen. The median time to recurrence in relapsed osteosarcoma is approximately 1.6 years<sup>3</sup>. Patients with relapsed osteosarcoma are more likely to survive after the first relapse if they are < 18 years, had localized disease at diagnosis, relapsed 2 or more years after diagnosis and didn't have a combined relapse (bone/lung)<sup>7</sup>. Patients recurring with non-lung distant metastases only or any combination of local relapse, lung metastases and non-lung metastases had comparatively worse overall survival<sup>8</sup>.

Central nervous system (CNS) metastases in osteosarcoma at presentation or at relapse are very rare and have been reported only in a few cases. The mode of CNS metastasis in osteosarcoma is usually hematogenous

and is commonly associated with pulmonary metastases<sup>9</sup>. The postulated mechanism is the migration of tumour emboli from the lung to the brain. Clinical presentation may include seizures, status epilepticus, hemiparesis, raised intracranial tension or stroke-like presentation. Most published reports on CNS involvement in osteosarcoma describe presentations occurring in the primary disease setting, with fewer studies detailing CNS metastases arising during disease progression or relapse. The majority of them have supratentorial CNS involvement. The cerebellar lesion reported by Niaz et al. in a 16-year-old boy is an extremely rare presentation. A distal femur lesion was confirmed as the primary lesion later on workup. The clinical course was rapidly progressive, requiring urgent posterior fossa decompression; however, the child did not survive the postoperative period<sup>10</sup>. Like in our case, most of the reported cases have solitary metastasis. Multiple metastases involving the frontal lobe have been described in a 22-year-old woman who had a stroke-like presentation. The primary lesion in this case was the right iliac bone, an axial site<sup>11</sup>. Both of these cases had pulmonary metastasis too, supporting the hypothesis of tumour emboli migration from the lung. An alternate mode of spread, bypassing the lung, has been reported by Menassa et al. in a 12-year-old boy with osteosarcoma of the fibula and frontoparietal cortical lesions. The patient had a patent foramen ovale, which probably allowed neoplastic cells to reach the brain without being filtered

	Menassa et al. (1997)	Niazi et al. (2009)	Dwivedi et al. (2011)	Marina et al. (1993)
Type of report	Case report	Case report	Case report	A series of 13 patients
Demographics	12 years/Male	16 years/Male	22 years/Female	Ages 4–25 years
Clinical features	Headache, raised ICP	LOC* Cerebellar hemorrhage	Right hemiparesis, LOC*	Headache, seizures, focal deficits
CNS lesion characteristics	Multiple hemorrhagic supratentorial lesions	Hemorrhagic posterior fossa mass	Multiple frontal hematomas	Varied; supratentorial, cerebellar, etc.
Primary tumour site	Left fibula	Right distal femur	Right iliac bone	Mostly long bones
Lung metastases	None	Present	Present	Present in 12/13
Treatment	Biopsy + resection	Posterior fossa decompression	Supportive/emergent	Response to Ifosfamide
Outcome	Not stated	Died	Poor prognosis implied	1 long-term survivor; others died

**Table 1:** Baseline characteristics, treatment, and outcome of patients with brain metastasis; \*LOC-Loss of consciousness

through the lungs<sup>12</sup>. An increased risk of brain metastasis with metastatic disease at presentation or with recurrence at 1 year has been reported in osteosarcoma<sup>13</sup>. Yonemoto et al. recommend regular brain imaging in patients with active pulmonary metastases<sup>14</sup>. Marina et al. had a similar consensus in those with metastatic disease at diagnosis or those who have recurrence within 12 months<sup>15</sup>. The key findings from the literature review are summarised in **Table 1**.

Given the rarity of the disease, there are no guidelines regarding optimal management of brain metastases of osteosarcoma. Effective intracranial control remains difficult as brain metastases from sarcomas are highly radio- and chemo-resistant, and surgical resection is the basic treatment. The achievement of a second complete resection of the disease has been associated with a better long-term survival after recurrence<sup>16</sup>. Our patient had progression of the primary lesion along with intra-cerebral recurrence, which portends a very poor outcome, and unfortunately succumbed to the disease. Given the clinical and radiological evidence in this setting, an alternate diagnosis seems very unlikely. However, the absence of histopathological confirmation is definitely a shortcoming in our case.

## CONCLUSION

Brain metastases are extremely unusual in osteosarcoma patients, and clinicians should be aware of this possibility when an osteosarcoma patient presents with neurological symptoms. Currently, there is no consensus on the optimal management of such patients, and their prognosis is poor.

### Conflict of Interest

The authors declare that there is no conflict of interest.

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