Background: Ewing’s sarcoma is a disease of children and young adults and occurs most often in bone and soft tissues. The intracranial and spinal manifestation of the disease is rare and reported incidence is 1%–6%. **Aims and Objectives:** We conducted this study to determine the surgical outcome of children with skull and spine Ewing’s sarcoma (SSES). **Methods:** This is a prospective analysis of 13 patients of SSES who reported to the Department of Neurosurgery, Nizam's Institute of Medical Sciences, Hyderabad, Telangana, India, between 2014 and 2016. All cases after detailed examination, magnetic resonance imaging, and computed tomography scan were subjected to surgery followed by adjuvant therapy comprising chemotherapy and radiotherapy. Outcome was analyzed at 6 months as well as latest follow-up. Neurological function, local recurrence, primary or secondary nature of the disease, distant relapse, and treatment-related complications were analyzed in this study. **Results:** There were eight female and five male patients with a mean age of 12 years (ranging from 4 to 8 years). Pain was the common presenting feature in all cases. Focal neurological deficits corresponding to the anatomical location was seen in six patients. These 13 cases were distributed anatomically as four cases involving the cloves, two cases with occipital bone and lobe involvement, one case of parietal bone and lobe involvement, and six cases of spinal involvement. Surgery was performed in all cases where gross total excision (Ozge C, Calükolü M, Cinel L, Apaydin FD, Özgür ES. Massive pleural effusion in an 18-year-old girl with Ewing sarcoma. Can Respir J 2004;11:363-5), near-total excision, and subtotal excision was achieved in these 13 cases (Steinbok P, Flodmark O, Norman MG, Chan KW, Fryer CJ. Primary Ewing's sarcoma of the base of the skull. Neurosurgery 1986;19:104-7). Subsequently all cases underwent multiagent chemoradiotherapy. Post surgery pain subsided in 12 (92%) of patients. Ten patients maintained or improved motor function. In seven cranial cases and in six spinal cases, four cases showed improvement whereas three (23%) had deterioration of motor function. **Conclusions:** Surgical outcome of SSES in short-term follow-up is good with current recommended management regimen of maximum excision followed by chemo and radiotherapy. However, metastasis is not uncommon. **Keywords:** Chemoradiotherapy, Ewing’s sarcoma, pseudomeningocele, surgery
The cranial lesions commonly involve the calvarium.\textsuperscript{[2,3]} The skull base remains an infrequent site of primary occurrence.\textsuperscript{[3–5]}

CNS metastases, which account for 2.3\%, occur for bone and soft tissue tumors. The incidence is second to kidneys and adrenal glands metastasis due to ES\textsuperscript{[3]}. These statistics illustrate well the rarity of brain metastases from bone and soft tissue neoplasms in pediatric population. Metastatic lesions carry poor prognosis; the overall mean survival is estimated at 7–16 months, with the majority surviving less than 12 months. Primary ES arising from calvarial bones account for only 1%–4\% of all ES.\textsuperscript{[3]}

**MATERIALS AND METHODS**

- This study was taken up with purpose to determine the surgical outcome in children with skull and spine Ewing’s sarcoma (SSES). It was a prospective study of 13 patients who reported to the Department of Neurosurgery, Nizam’s Institute of Medical Sciences, Hyderabad, Telangana, India, between 2014 and 2016. All cases after detailed examination, skeletal survey, magnetic resonance imaging (MRI), and computed tomography (CT) scan were subjected to surgery followed by adjuvant therapy comprising chemotherapy and radiotherapy. Institutional protocol of chemo and radiotherapy was followed. Outcome was analyzed at 6 months and at latest available follow-up. Neurological function, local recurrence, primary or secondary nature of the disease, distant relapse, and treatment-related complications were analyzed in this study.

**Surgical protocol**

Surgical protocol composed of maximum safe excision of lesion along with the involved bony segment. Duroplasty was performed with neighboring pericranial tissue or fascia lata.

**Institutional radiation protocol**

Three-dimensional conformal radiation therapy and intensity-modulated radiation therapy were given for 5–7 weeks.

**RESULTS**

There were eight female and five male patients with a mean age of 12 years (ranging from 4 to 18 years). Pain was the common presenting feature in all cases. Focal neurological deficits (FNDs) corresponding to the anatomical location were seen in six patients. These 13 cases were distributed anatomically as four cases involving the clivus, two cases with occipital lobe involvement, one case of parietal lobe involvement, and six cases of spinal involvement. Surgery was performed in all cases; gross total excision,\textsuperscript{[6]} near-total excision,\textsuperscript{[3]} and subtotal excision\textsuperscript{[3]} were achieved in these 13 cases. Subsequently, all cases underwent multiagent chemoradiotherapy. Postsurgery pain subsided in 12 (92\%) patients. Ten patients maintained or improved motor function. In seven cranial cases and in six spinal cases, four cases showed improvement whereas three (23\%) had deterioration of motor function. During follow-up (mean 9 months), of 13 patients, 4 (31\%) had disease-free interval. Five patients (38\%) developed metastatic disease. Of 13 patients, 3 (23\%) developed a local recurrence. One of these patients had paraplegia associated with the local recurrence. Four patients developed treatment-related complications.

**Illustrative case 1**

We present an illustrative case of a 10-year-old child who presented with a history of intermittent headache and vomiting and progressive restriction of movements.
of the right eye for 3 weeks. The child’s neurological deficits included right-sided complete IIIrd, IVth, and VIth nerve palsy and decreased sensations in the right V1 and V2 divisions of the trigeminal nerve. Radiologically there was a lesion noted, involving the sphenoid sinus and the clivus, and sphenoid sinus was destructed [Figures 1A-B and 2A-C].

Decompression of the lesion was performed by microscopic, transnasal-transsphenoidal approach. Frozen section report of a malignant round cell tumor was obtained, and in view of infiltrative nature of the lesion, decompression was restricted to limited debulking. Histological examination showed sheets of small, round cells organized into lobules by variably hyalinized and vascular septae [Figure 3A-D].

**Illustrative case 2**

This 11-year-old child, a previously diagnosed case of ES, presented with recurrence of the tumor and pain at the site of the swelling with no associated FNDs [Figures 4-6].

**DISCUSSION**

The Ewing family of tumors, consisting of ES and its biological counterpart, the peripheral primitive neuroectoderm tumor, constitute an uncommon malignancy of childhood and adolescence with a predilection for soft tissue and bones of the trunk and extremities.[6–9] ES of the cranial bones is a rare entity with only 71 cases reported so far in published literature. It has preponderance for males in the first and second decades of life, with a peak incidence between 5 and 13 years.
Extracranial metastasis from a primary ES in the cranium is exceptional, whereas cranial metastasis from extracranial ES is common.\cite{10}

In ES, classical skull and spine involvement is due to metastasis from the primary focus of bone and soft tissue malignancy. ES is the second most frequent malignant bone tumor in children and is one of the common sarcoma metastasis to brain with a quoted incidence of 56%.\cite{7}

The epidural space or intradural parenchyma gets involved as an extension of the overlying structure.

The peculiarity of our series is that all were of purely either skull or spine involvement but not as metastatic deposits [Figure 7].

However, there is a second mechanism of spread reported in literature, which is said to be of hematogenous spread that leads to direct brain a spinal cord deposit and no overlying bone involvement.\cite{1}

Anatomically in the skull, the parieto-occipital region is the most common area of involvement seen but also involves the frontal and temporal bone. Skull base predilection is negligible. In this series however,
clivus, with six patients having the site for ES, was
the most common region of skull involvement, which
is definitely a noteworthy point to be noted in this
series.

Tumors in the Ewing’s family of sarcomas are made of
primitive cells, which are cells that have not yet been
decided what type of cell they are. They look blue
to a pathologist because of the staining that is used
when identifying the cancer, so the cells are referred
to as “small round blue cells.” The Ewing’s family of
sarcomas includes the following:

• ES of the bone
• Extrasosseus ES, also referred to as extraskeletal ES
  (tumor growing outside of the bone)
• Primitive neuroectodermal tumor
• Peripheral neuroepithelioma
• Askin’s tumor (ES of the chest wall)
• Atypical ES

The histopathological examination showed
round-to-oval cells arranged in lobules, separated by
a thin vascular channel, having vesicular nuclei, with
indistinct nucleoli. Mitotic figures were seen with
focal areas of necrosis. Few bony trabeculae were seen
embedded in the tumor island. Fat globules seen were
positive for periodic acid Schiff staining.

Clinically localized pain is the hallmark of such tumors
in kids. This is attributed to the involvement of free
nerve endings at the site of tumor. With parenchymal
involvement, however, focal neurological defect becomes
evident corresponding to the anatomical localization. In
this series, 13% of skull cases has FND in addition to
pain all of which correlated to the location of tumor. In
the six spinal cases, 16% has FND. However, progression
of FND was seen in 23% of cases postsurgery and chemo
and radiotherapy.

Radiologically, the X-ray shows a lytic lesion with
mottling and erosion.

Though a classical onion-peel appearance is described,
it is hardly seen. CT scan has a bone destruction
appearance and osteomyelitis-like picture.

MRI shows typically a tumor, and parenchyma is
usually seen separated and pushed from it in case of
the later’s involvement. Bone scan should always be
performed in a suspected case of SSES. Whole-body
positron-emission tomography (PET) scan reveals
a focus in extracranial bone or soft tissue [Figure 8].
T1 sequence is hypointense and T2 is hyperintense.
Contrast PET lesion appears circumscribed and as ↑
takeup. PET, however, is not performed routinely.

Figure 7: Showing Extramedullary tumor involving D12 to L1 and
enhancing on contrast

Figure 8: Bone scan images prior to starting adjuvant therapy
demonstrating increased uptake in the skull base corresponding to
the residual tumor. Note the absence of increased uptake in any
other area
Surgery remains the best treatment modality for such tumor. Classically the dictum of maximally safe resection is followed if it is not amenable to complete excision. A study from the national cancer database by Miller et al.\[11\] showed that surgery at one resulted in the best overall survival for patients with ES of bone. However, due to involvement of eloquent structures, this may not be possible always in SSES where adjuvant therapy needs to be given.

Chemotherapy regimen followed in SSES is the standard combination of vincristine, cyclophosphamide, doxorubicin alternating with ifosfamide, and etoposide. In SSES, because there is a rapid increase leading to serious symptoms of raised intracranial hypertension and FND, preoperative chemotherapy to shrink the size of ES is not advisable as in the case of extracalvarial bony ES.\[8\]

However postsurgical chemo is always advised. We followed our regimen of vincristine, cyclophosphamide, doxorubicin alternating with ifosfamide, and etoposide [Table 1].

This is the recommended regimen with 5-year survival rate of 70%.\[12\]

Radiotherapy with an institutional protocol as mentioned earlier has been given in all our 13 cases. The current literature survey for radiotherapy in ES suggests proton beam therapy. It has an advantage for high precision therapy, especially in sensitive structures such as brain and spinal cord.\[13\]

In this study, all were primary ES affecting CNS. Evaluation also did not reveal any other site of focus in the skeletal system.

Multimodal approaches, including surgery, radiotherapy, and intensive multiagent chemotherapy, have remarkably improved survival in patients with localized ES. By contrast, the prognosis of patients with disseminated ES remains poor.

**Conclusion**

All the cases studied in our study are primary ES affecting CNS. Surgical outcome of ES in short-term follow-up is good with current recommended management regime of maximum excision followed by chemo and radiotherapy. However, metastasis is not uncommon.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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**Conflicts of interest**

There are no conflicts of interest.

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