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# Skull Base Primary Ewing Sarcoma: A Radiological Experience of a Rare Disease in an Atypical Location

## Authors' Contribution:

Study Design A  
Data Collection B  
Statistical Analysis C  
Data Interpretation D  
Manuscript Preparation E  
Literature Search F  
Funds Collection G

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**Conflict of interest:** None declared

**Patient:** Female, 4-year-old  
**Final Diagnosis:** Skull base Ewing's sarcoma  
**Symptoms:** Gradual visual loss • inability to walk • near blindness • protrusion of eyes • seizure • vomiting • weight loss  
**Medication:** —  
**Clinical Procedure:** Biopsy of the left nasal mass • computed tomography of the brain • magnetic resonance imaging of the brain • nasoendoscope of the left nostril  
**Specialty:** Neurosurgery • Pediatrics and Neonatology • Radiology

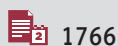
**Objective:** Rare disease  
**Background:** Ewing sarcoma and primitive neuroectodermal tumor are rare tumors grouped under the spectrum of the Ewing sarcoma family of tumors. These highly malignant tumors involve the bones and commonly occur in children. Ewing sarcoma of the skull bone accounts for only 1% of all Ewing sarcomas, with primary skull base Ewing sarcoma occurring in less than 1% of cases. We present a case of skull base Ewing sarcoma with complete symptom recovery and near-total radiological resolution.

**Case Report:** A 4-year-old girl initially presented with a 2-month history of vomiting, poor oral intake, weight loss, and gradual visual deterioration followed by acute symptoms of fever, breathing difficulties, and seizure. Initial computed tomography and magnetic resonance imaging of the brain displayed a large sinonasal mass with extensive regional infiltration and bony destruction and no evidence of distant metastasis. A transnasal biopsy was taken. The histopathology result revealed features of skull base Ewing sarcoma. The child was given a combination of radiotherapy and chemotherapy, to which she responded well, with a minimal residual tumor.

**Conclusions:** Skull base Ewing sarcoma is a rare entity, presenting a challenge to the reporting radiologists. Differential diagnoses of esthesioneuroblastoma, olfactory neuroepithelioma, and, more commonly, sinonasal carcinoma can be misleading since they have similar radiological appearances to skull base Ewing sarcoma, which differs in treatment regimen and prognosis. Therefore, a combination of histopathological appearance, radiographic findings, and clinical correlation is important to determine the correct diagnosis, establish the appropriate treatment regime, and improve the patient's survival.

**Keywords:** Brain Neoplasms • Pediatrics • Sarcoma, Ewing • Skull Base Neoplasms

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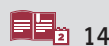
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## Background

Ewing sarcoma and primitive neuroectodermal tumor (PNET) are rare tumors that are grouped under the Ewing sarcoma family of tumors. These 2 tumors are prone to occur in pediatric patients and have highly malignant features [1]. Ewing sarcoma and PNET are also known as small round blue cell tumors because they share close histological similarities and overlapping radiological changes with other tumors such as neuroepithelioma, Askin tumor, and neuroblastoma [2]. These highly malignant tumors tend to occur in a pediatric and young adult age group and predominantly involve the bones. The incidence of skull bone Ewing sarcoma accounts for only 1% of all Ewing sarcomas [3], and primary skull base Ewing sarcoma occurs in less than 1% of cases [4]. We share our experience in this report of this rare case of skull base Ewing sarcoma and the management challenges we encountered in our center.

## Case Report

A previously healthy 4-year-old girl was presented to the Emergency Department with an episode of a generalized tonic-clonic seizure, which self-terminated after 2 min. On further questioning, the patient's parents reported that she had gradual visual loss and vomiting for 2 months that was associated with weight loss, which was followed by a gradual protrusion of the eyes for 1 month. The patient's symptoms started worsening 4 days prior to admission, with increased frequency of projectile vomiting, near blindness with the ability to only perceive light, and the inability to walk. She also had fever followed by seizure on the day of admission. Otherwise, her developmental milestones were appropriate for her age. On physical examination, her Glasgow coma scale score indicated she was completely responsive, with bilateral pupils reactive to the light. However, neurological examinations showed a significant reduction in muscle power and hyperreflexia involving the upper and lower limbs. The cardiovascular, respiratory, and gastrointestinal examinations were unremarkable. Although her random blood sugar level was normal, laboratory tests showed neutrophil leukocytosis and hyponatremia. Meningitis was suspected, and hence she underwent pre-contrast and post-contrast computed tomography (CT) of the head.

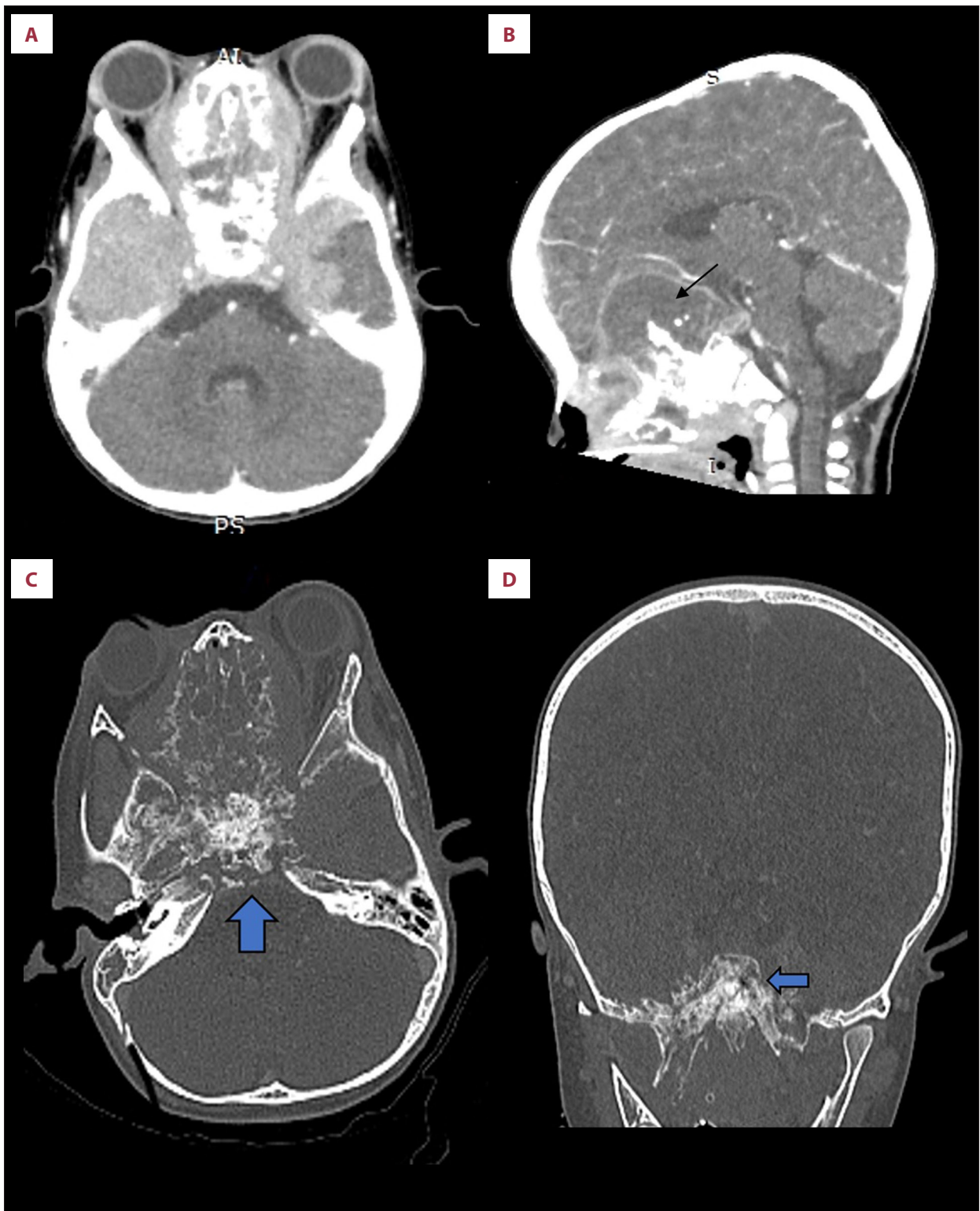
The post-contrast CT scan of the head revealed an infiltrative, ill-defined, predominantly homogenous enhancing mass. This was the presence of a mixed solid and cystic appearance with multiple foci of necrosis and internal calcification arising from the base of the skull, involving the anterior and middle cranial fossa and causing extensive local infiltration (**Figure 1A, 1B**) and local bony erosion (**Figure 1C, 1D**). The mass extended inferiorly, obliterating the sphenoid sinuses, fossa of Rosenmüller, prevertebral space, and masticator space and into the posterior

nasopharynx, causing significant airway narrowing. The mass extended superolateral into the anterior cranial fossa causing displacement of the temporal lobe superiorly with associated adjacent thickened dura enhancement and bilateral cavernous sinus encasement. The mass extended anteriorly involving the bilateral posterior orbit and into the bilateral extraconal space, causing bilateral proptosis.

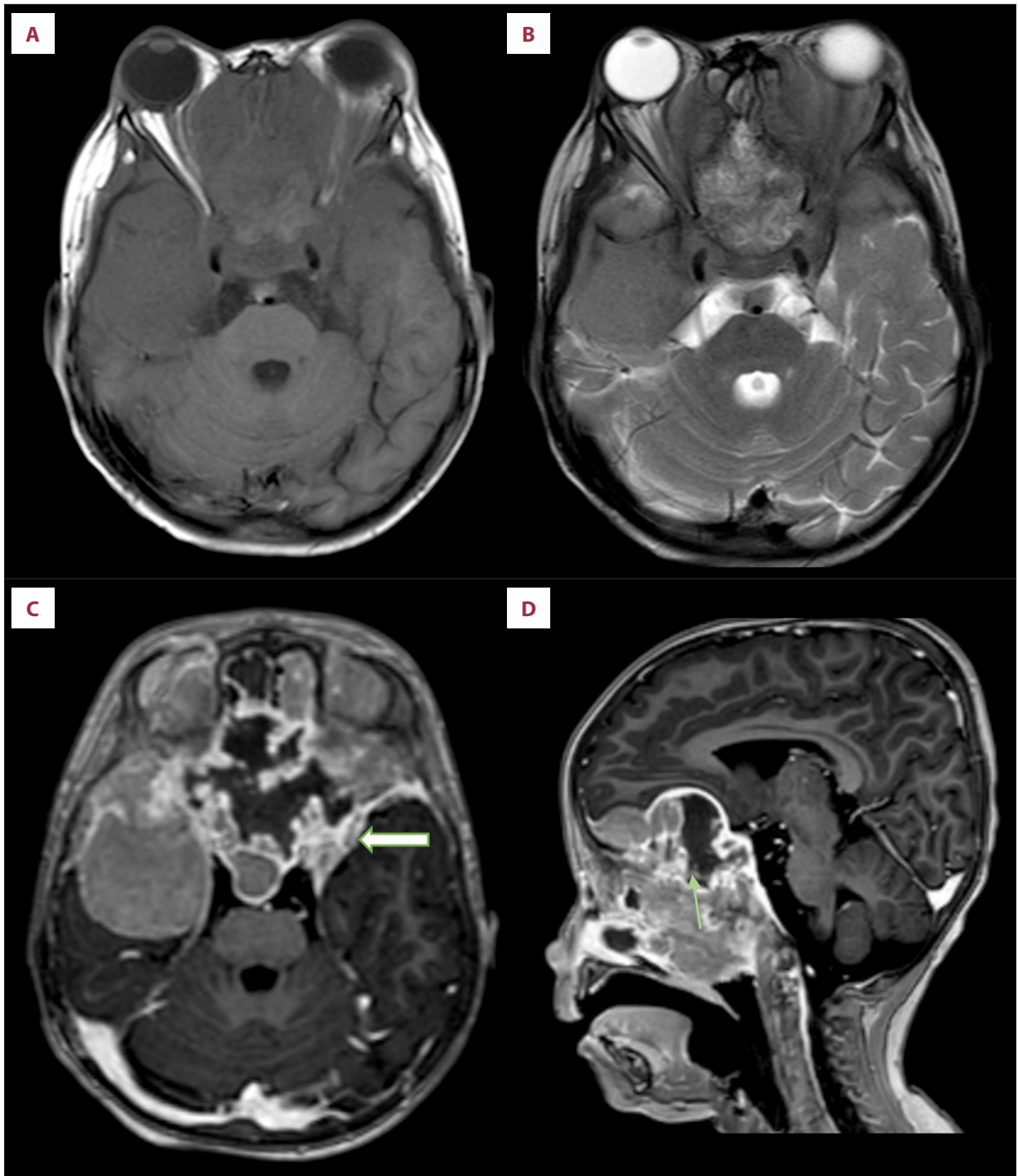
Pre-contrast and post-contrast magnetic resonance imaging (MRI) of the brain was subsequently performed, confirming the findings of the CT and showing an avidly enhancing multilobulated mass displayed as predominantly isointense in the T1-weighted image (**Figure 2A**), a heterogenous high signal in the T2-weighted image (**Figure 2B**), and heterogeneous enhancement in the post-gadolinium study (**Figure 2C, 2D**). This mass demonstrated a significant fluid restriction in diffusion-weighted imaging and apparent diffusion coefficient sequences (**Figure 2E, 2F**). Abnormal signal intensity with contrast enhancement involving the adjacent marrow and the surrounding soft tissue of the nasal nares, nasal septum, and hard and soft palate suggested an infiltration. Therefore, this enhanced the leptomeningeal thickening involving both temporal fossae. There was no focal enhancing lesion seen in the brain parenchyma. Both posterior orbits were involved with the infiltration of the superior, medial, and inferior rectus extra-ocular muscle and optic nerves bilaterally. Otherwise, the brainstem and cerebellum were normal.

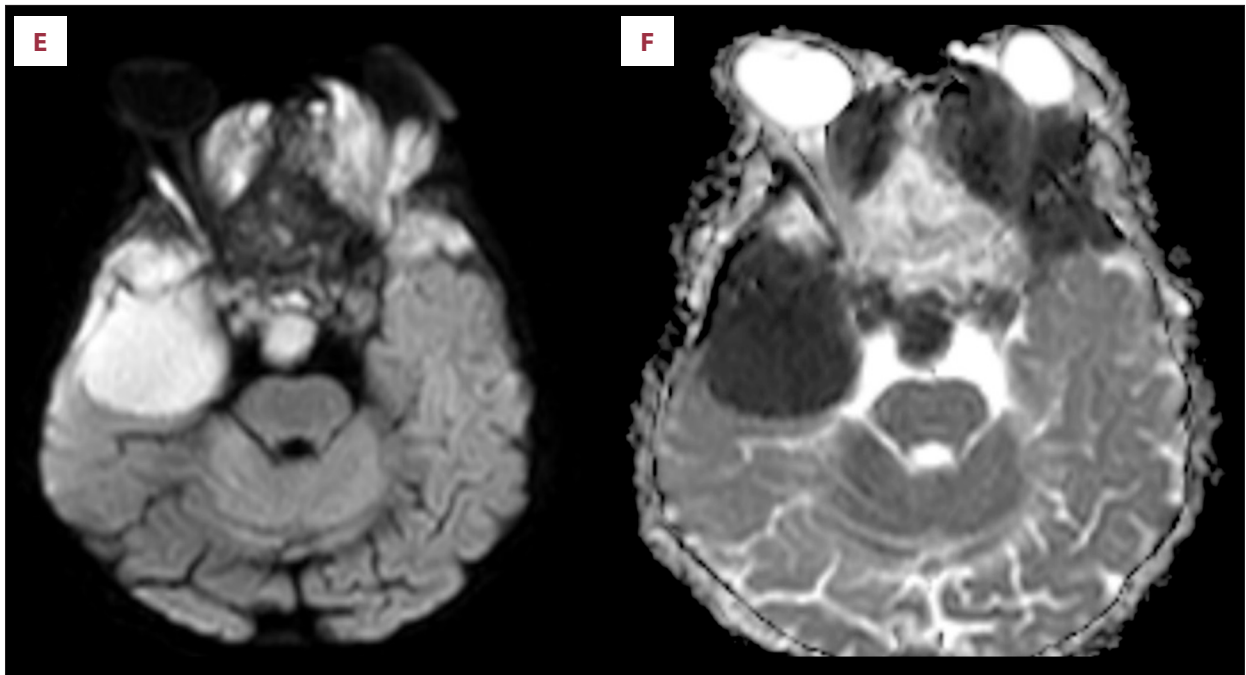
The initial impression was olfactory neuroblastoma or esthesioneuroblastoma with a differential diagnosis of olfactory neuroepithelioma or extraskeletal Ewing sarcoma arising from the paranasal sinus or nasal fossa. Nasoendoscopy examination of the left nostril revealed a fungating mass occupying almost the whole left nasal cavity, obscuring the view from the left inferior meatus. A biopsy sample was taken from the mass on the left nasal cavity, and the histological features suggested a final diagnosis of Ewing sarcoma. Hematoxylin and eosin staining showed sheets of uniformly rounded small cells with hyperchromatic nuclei with a fine granular chromatin pattern within the indistinct cytoplasm. Immunohistochemistry results showed diffusely positive CD99 with a distinctive cytoplasmic membrane pattern. A multidisciplinary discussion was conducted, involving the managing neurosurgeon, pediatric neurologist, and pediatric oncologist. Owing to the location of the tumor and the risk of the surgery, an agreement was achieved for a combination of radiotherapy for local control of the disease and a regimen of 6 cycles of chemotherapy using vincristine, etoposide (VP-16), and carboplatin. The parent's consent was obtained.

A follow-up of the post-contrast MRI of the brain showed near-total resolution of the tumor, both intracranially and intranasally, with minimal residual marrow changes in the skull bases



**Figure 1.** Post-contrast computed tomography (CT) scan of the brain in the (A) axial and (B) sagittal view showing infiltrative mass with a mixed solid and cystic appearance (black arrow) at the base of the skull, causing extensive local infiltration. Post-contrast CT scan of the brain in the bone setting in (C) axial and (D) coronal view showing mixed bone sclerosis and erosion in the skull base of the anterior and middle cranial fossa (blue block arrows).





**Figure 2.** Magnetic resonance imaging of brain in (A) T1-weighted images and (B) T2-weighted images in axial section showing a predominantly T1 isointense and heterogeneous T2 hyperintense mass. Post-contrast T1 images in the (C) axial and (D) sagittal view showing a solid and cystic nasal mass (green arrow) involving both temporal bones and extending intracranially with dura thickening and enhancement (white arrow block). This mass demonstrates a significant fluid restriction seen in (E) diffusion-weighted images and (F) apparent diffusion coefficient sequences.

of the bones and with persistent bony erosion. Unfortunately, the post-treatment imaging was not available to display in this case report because the images were no longer in our facility or in the parents' possession. The patient's neurological deficit and visual acuity recovered completely. The parents were advised that surgery should be performed to remove the residual tumor. However, the parents refused to continue the girl's treatment in our facility, and she was last seen 6 months after the completion of her radiotherapy and chemotherapy. The parents also defaulted on the child's follow-up.

## Discussion

Tumors of the head and neck can manifest with a vast diversity of clinical presentation, with a differential diagnosis ranging from a simple benign cyst to an aggressive, rapidly growing tumor. An aggressive-looking lesion can have a list of differential diagnoses such as malignant lymphoma, leukemia, rhabdomyosarcoma, neuroblastoma, undifferentiated nasopharyngeal carcinoma, malignant melanoma, PNET, and Ewing sarcoma family of tumors [4].

Skeletal Ewing sarcoma is the second most common bone malignancy in the pediatric population, with a slightly lower predilection than osteosarcoma [3]. However, primary skull base

Ewing sarcoma occurs in less than 1% of all cases of Ewing sarcoma, based on the location [4]. The most common radiological features of Ewing sarcoma are bone destruction with moth-eaten to permeative changes (76% to 82%), aggressive onionskin or spiculated periosteal reaction (58% to 84%), and wide transitional zone (96%). A soft tissue mass was seen in 56% to 80% of Ewing sarcoma cases [3]. Sclerotic changes, as seen in our case, are reported in 32% to 40% of cases [5]. MRI is superior in delineating marrow replacement and cortical destruction, with an associated soft tissue mass seen in 96% of reported cases [5]. MRI can show variable signal intensity in T1, a high signal of a solid component with foci of low signal return from the calcified component in T2, and heterogeneous enhancement in a post-gadolinium study. MRI also demonstrates diffusion restriction and leptomeningeal seeding [6-8].

Extraskelatal Ewing sarcoma occurs less often than skeletal Ewing sarcoma. The sarcomas are histologically similar; therefore, it is almost impossible to differentiate between the 2 conditions. A list of proposed criteria to diagnose extraskelatal Ewing sarcoma includes (1) no MRI evidence of bony involvement, (2) no functional uptake of the adjacent bone or periosteum using bone scintigraphy, (3) small round blue cells with no differentiating features on microscopy, and (4) the presence of cytoplasmic glycogen [9,10]. The imaging features for extraskelatal Ewing sarcoma are not specific, probably owing

to the scarcity of reported cases. Radiography, CT, MRI, and nuclear bone scintigraphy are imaging modalities of choice in diagnosing extraskelatal Ewing sarcoma. Soft tissue mass is the most common finding, seen in 87% of the reported cases, with areas of necrosis and hemorrhage. This is demonstrated as areas of low attenuation on CT and high signal intensity on T2-weighted images [11]. Evidence of normal marrow appearance on CT and MRI indicate that there is no bony involvement [11]. Based on CT scans and MRI, the bones of the skull base in the anterior and middle cranial fossa were involved in the present case; therefore, it is unlikely that our patient had extraskelatal Ewing sarcoma. However, an extensive paranasal sinus soft tissue mass with bone involvement may present the possibility of nasal fossa extraskelatal Ewing sarcoma or Ewing sarcoma of the paranasal sinuses with local bony infiltration and intracranial extension.

Clinical presentations of Ewing sarcoma are diverse and depend on tumor aggressiveness. Presentations could be non-specific, and symptoms could be related to high intracranial pressure, focal neurological deficit, or meningism. Our patient presented with symptoms related to high intracranial pressure with manifestations of visual disturbance and neurological deficit, complicated by recent meningism prior to admission. The clinical diagnosis in the patient's initial presentation had already been directed toward a highly aggressive space-occupying lesion.

Histological findings are also important to support the radiological appearance of a tumor. However, both Ewing sarcoma and PNET belong to the group of "small round cell" tumors [2]. Other tumors that belong to this group include non-Hodgkin lymphoma, neuroblastoma, rhabdomyosarcoma, mesenchymal chondrosarcoma, retinoblastoma, desmoplastic small round cell tumor olfactory neuroblastomas or esthesioneuroblastoma, and olfactory neuroepithelioma. Therefore, immunohistochemistry and more advance molecular technologies such as fluorescence in situ hybridization and polymerase chain reaction are essential for differentiation of the tumor subtypes of this family [12].

The treatment options for Ewing sarcoma include surgical resection, chemotherapy, and radiotherapy. According to Shaan M Raza et al (2020), the contraindications of skull base surgery for skull base osteosarcoma, a more common bone tumor involving the skull bases, includes circumferential involvement of major vessels, cavernous sinus invasion, cranial nerve involvement, and inadequate vascularization options [13]. Unfortunately, due to the rarity of skull base Ewing sarcoma, no proper management guidelines have been proposed. However, based on the imaging findings of the child in the present case, which demonstrated cavernous sinus invasion, skull base surgery was contraindicated. Hence, the only possible method of local disease control was radiotherapy. Studies have shown that a combination of surgery and chemotherapy is superior to radiotherapy and chemotherapy in terms of 5-year survival rate and local recurrence rate [14].

## Conclusions

Skull base Ewing sarcoma is a rare entity that can present a challenge to reporting radiologists. Differential diagnoses of esthesioneuroblastoma, olfactory neuroepithelioma, and, more commonly, sinonasal carcinoma can be misleading since they have similar radiological appearances to skull base Ewing sarcoma, which differs in treatment regimen and prognosis. A combination of histopathology appearance, radiographic findings, and clinical correlation is important to determine the correct diagnosis, which will help establish the appropriate treatment regime and improve the patient's survival rate.

## Conflicts of Interest

None.

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