ScientificScholar®
Knowledge is power
Publisher of Scientific Journals

www.surgicalneurologyint.com

Surgical Neurology International

**Editor-in-Chief:** Nancy E. Epstein, MD, Professor of Clinical Neurosurgery, School of Medicine, State U. of NY at Stony Brook.

*SNI: Neuro-oncology*

**Editor**
Mitsutoshi Nakada, MD
Kanazawa University, Ishikawa, Japan

SNI
Open Access

*Case Report*

# Primary and metastatic cerebral Ewing's sarcoma: A case report about a rare entity and literature review

Mariem Mhiri, Amal Abbes, Rihab Ben Dhia, Narjes Gouta, Mahbouba Frih Ayed

Department of Neurology, Fattouma Bourguiba Hospital, Monastir, Tunisia.

E-mail: *Mariem Mhiri - mariemmhiri@yahoo.com; Amal Abbes - amel.abbes07@gmail.com; Rihab Ben Dhia - ribedi@hotmail.fr; Narjes Gouta - narjes_gouta@yahoo.fr; Mahbouba Frih Ayed - mahboubafrih@gmail.com

***Corresponding author:**
Mariem Mhiri,
Department of Neurology,
Fattouma Bourguiba Hospital,
Monastir, Tunisia.

mariemmhiri@yahoo.com

Received: 23 April 2024
Accepted: 28 July 2024
Published: 11 October 2024

**DOI**
10.25259/SNI_316_2024

**Quick Response Code:**

## ABSTRACT

**Background:** Ewing's sarcoma (ES) is a rare malignant tumor primarily affecting young individuals, with cranial localization being particularly uncommon. While intracranial metastatic ES is infrequent, only four cases of intracranial metastatic ES are reported in the literature; it presents unique diagnostic and therapeutic challenges.

**Case Description:** We present a distinctive case of ES to delineate its clinical, radiological, and histopathological characteristics. Our patient, a 33-year-old, manifested symptoms of intracranial hypertension and gait disturbance. Neurological examination revealed a static and kinetic cerebellar syndrome. Imaging studies and stereotactic biopsy confirmed the diagnosis of primary and metastatic cerebral ES. The treatment regimen encompassed chemotherapy and radiation therapy.

**Conclusion:** Our case underscores the importance of considering ES in the differential diagnosis of dural-based lesions exhibiting cystic components and heterogeneous contrast enhancement, particularly in young individuals. Early recognition and intervention hold promise for optimizing patient outcomes.

**Keywords:** Chemotherapy, Ewing's sarcoma, Histopathology, Metastatic

## INTRODUCTION

Ewing's sarcoma (ES) is a malignant small round blue cell tumor primarily affecting bone and soft tissue, constituting approximately 4% of childhood and adolescent malignancies. While it predominantly manifests in bone, extraosseous ES involving the central nervous system (CNS) is rare. Only four cases of primary and metastatic cerebral localization have been documented, representing a mere 1% of all ES localizations [Table 1].[5,13,14] ES commonly presents in the second decade of life, with a notable male predominance.[11] This report presents a unique case of primary and metastatic cerebral ES in a 33-year-old male, aiming to elucidate its clinical, radiological, and histopathological characteristics.

## CASE REPORT

A 33-year-old male presented with a gait disorder and acute headache accompanied by nausea, vomiting, and diplopia. He had no previous medical history. He had experienced persistent hiccups 2 weeks before admission. The endoscopy of the gastrointestinal tract was normal.

He consulted the Department of Neurology due to the persistence of headaches.

Neurological examination revealed signs consistent with a static and kinetic cerebellar syndrome and right abducens cranial nerve paresis. Ophthalmic examination demonstrated bilateral papilledema, while routine blood chemical analysis and complete blood count yielded normal results.

Magnetic resonance imaging (MRI) revealed multiple posterior and anterior cranial masses with heterogeneous enhancement involving the cerebellum and frontal lobe, featuring solid-cystic components. Bilateral transverse venous cerebral thrombosis was noted. Leptomeningeal enhancement was also noted [Figure 1a-c]. According to the MRI features, an infectious cause was suspected. Subsequent examinations, including cerebrospinal fluid (CSF) examination and polymerase chain reaction testing of CSF for tuberculosis, hepatitis, Lyme, Epstein–Barr virus, and HIV serologies, revealed no evidence of abnormalities. No primitive tumor was visualized on computed tomography of the chest, abdomen, or pelvis. Tumor markers were negative.

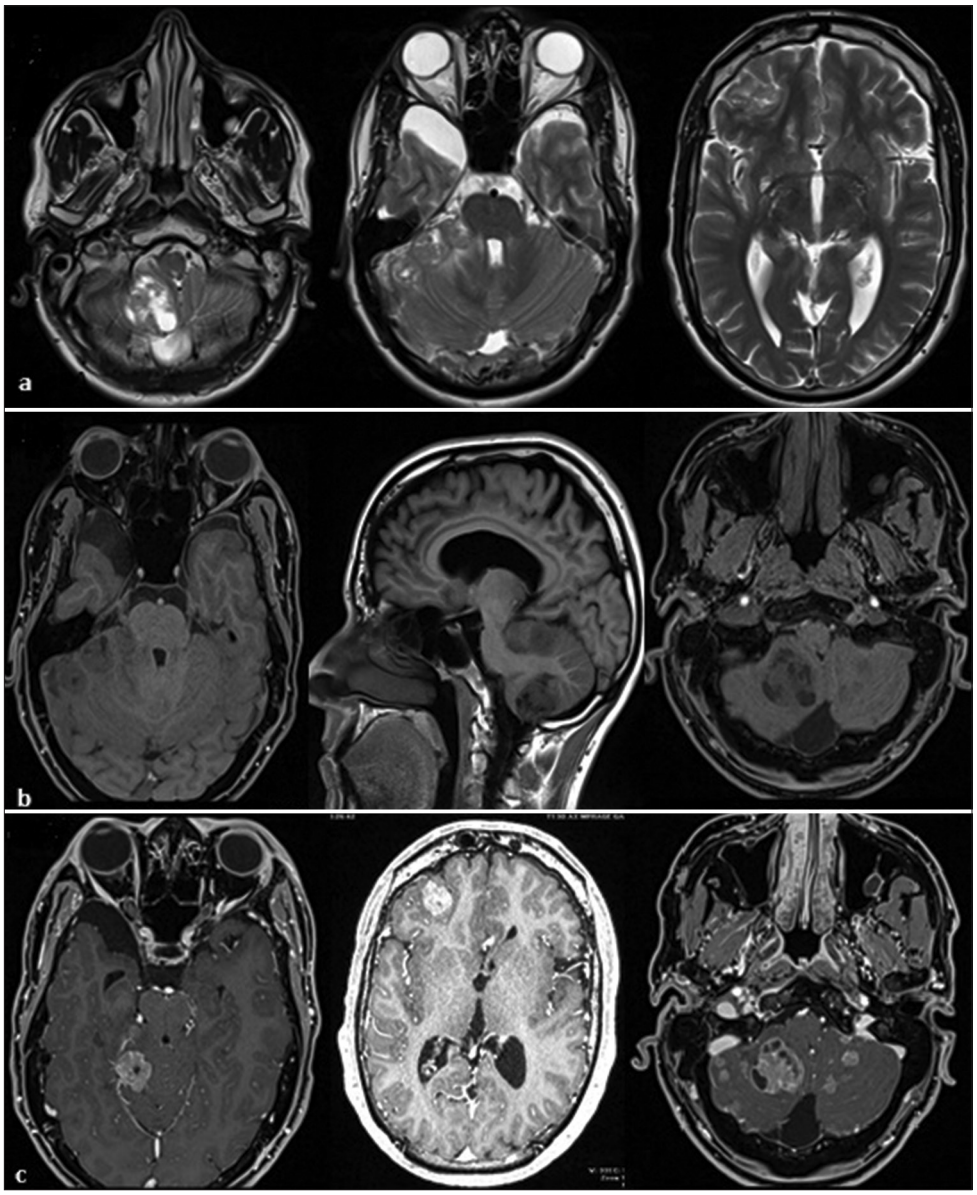


**Figure 1:** (a) T2-weighted images: mixed hyper-intensity/hypo-intensity signals. (b) T1-weighted images: Extra-axial and intra-axial masses with no spontaneous hyperintensity and large area hypointensity. (c) T1 W images after gadolinium injection: solid cystic component mass with significant enhancement.

A stereotactic brain biopsy of the frontal lesion confirmed the diagnosis of ES. Subsequent spinal MRI revealed a metastatic intramedullary lesion on C4 and multiple intradural lesions on the thoracic spinal cord [Figure 2a-d].

Histological examination demonstrated a highly cellular tumor comprising uniform small round cells with scanty cytoplasm, hyperchromatic nuclei, and frequent mitoses [Figure 3a-c].

Immunolabeling was negative for CD45, glial fibrillary acidic protein (GFAP), chromogranin-A, and cytokeratins. The tumor cells were strongly and diffusely positive for CD99 with predominant membranous staining.

Considering the morphological, immunohistochemical, and molecular results, the final diagnosis was ES/primitive neuroectodermal tumor (PNET).

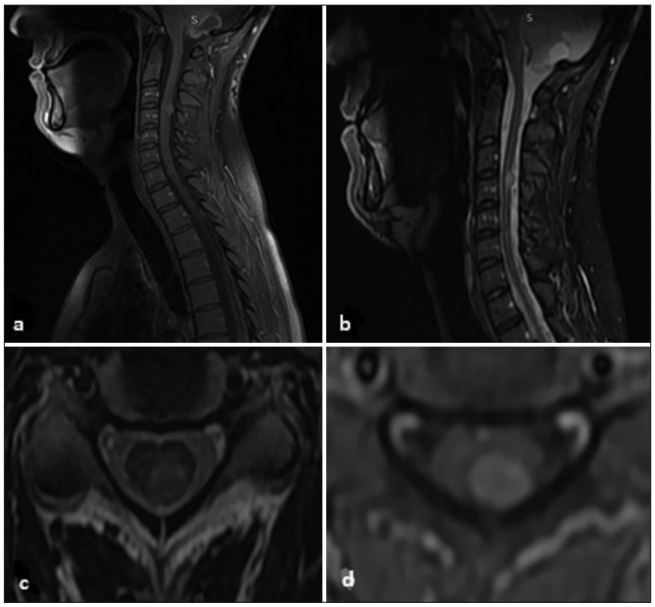


**Figure 2:** (a) sagittal T1-weighted and sagittal T2-weighted (b) revealed a hyperintense T2 mass and multiple subarachnoidal lesions; (c) axial T2-weighted and axial contrast-enhanced T1-weighted (d) images of the cervical spine showed an enhancing tumor.

Due to the metastatic and multifocal nature of the disease, surgical intervention was not feasible. Instead, the patient received chemotherapy and focal irradiation, including six cycles of vincristine-etoposide-carboplatin alternating with vincristine-etoposide-cyclophosphamide, followed by curative radiotherapy with good clinical tolerance (60Gy over 30 fractions). Furthermore, he received three cycles of maintenance chemotherapy with cyclophosphamide and vinorelbine. Unfortunately, the patient died within 16 months of diagnosis.

## DISCUSSION

ES is a rare family of malignancies in the CNS. Primary intracranial ES is extremely rare. It is the prerogative of children and young adults under 20 years old, with a peak incidence between 5 and 13 years old.[11] A male predominance was noted with a sex ratio of 1.6.[11] In order of frequency, it affects the long bones (47%), the pelvis (19%), and the ribs in 12% of cases.[6] James Ewing first described ES; it is a round-cell tumor. It belongs to the family of neuroectodermal tumors which have in common a cytogenetic translocation between chromosome 22 and 11 in the majority of cases.[9,10,12] Most of the central ES results from metastasis from extracranial sites.[12] Primary intracranial ES is a recent entity of CNS PNET. The frontal and parietal localization is the most common.[2] Nevertheless, temporal and occipital localization has also been reported. Clinically, the symptoms are very varied and heterogeneous but not specific.[6] Headache or a syndrome of intracranial hypertension, double vision, epileptic seizure or behavior change, and malaise can be observed.[4] The lack of knowledge of its imaging leads to misdiagnosis.

Our case shows histological features similar to the few cases of CNS-ES previously described in the literature, but it displays different radiological aspects. In our case, masses are multiple and located infratentorial, extra, and intra-axial.

A review of the literature shows that the PNET is defined as an enhancing solid mass with hemorrhagic and cystic

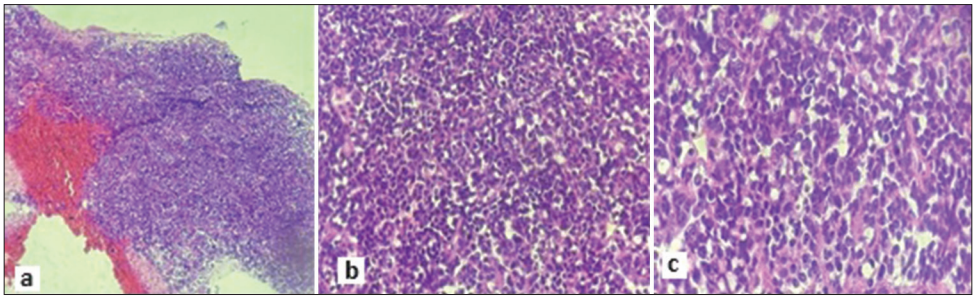


**Figure 3:** Histopathological, histochemical features of meningeal Ewing's sarcoma. (a) Small round tumor cells arranged in solid with hyperplasia of interstitial collagen fibers around cells. (b and c) small undifferentiated tumor cells with round, uniform and hyperchromatic nuclei.

**Table 1:** Reported cases in the literature for primary and metastatic intracranial Ewing's sarcoma.

| | Author/ year | Age/ gender | Location on imaging | Presentation | Positive IHC | Positive molecular results | Treatment | Follow up/ outcome | Reference |
|---|---|---|---|---|---|---|---|---|---|
| 1 | Haguenard AL. *et al.*, (2021) | 34/M | Multifocal intracranial lesions, Lumbar lesion L5 | Vomiting, headaches and Lumbago | CD99 | *t*(11;22) by RT-PCR | Hemilaminectomy Radiation cisplatin, Cytoxan, and vincristine | 6 months | (5) |
| 2 | Weil et al., (2001) | 21/M | T10–11 , L1–2, 2 parietal lesions | Thoracic back pain, lower extremity weakness | NSE, cytokeratins, vimentin, MIB-1 | *t*(11;22) by RT-PCR | Surgery: STR cranial & spinal lesion; chemo: VCR, DXR, CPM, ETP, IFO; Radiation: craniospinal radiation | Alive at 30 months | (14) |
| 3 | VandenHeuvel et al., (2015) | 61/M | Fronto-temporal lobe | Slurred speech, facial droop, hemiparesis | CD99 | *t*(11;22) by RT-PCR | Surgery: STR; no adjuvant chemo or radiation | Lost at follow up | (13) |
| 4 | Weil et al, (2001) | 67/F | Cerebellar pontine angle | Headache, slurred speech, hearing loss | CD99 | ? | Treatment: Treated with surgical resection and palliative radiation | Patient had no progression of symptoms for 13 months, followed by rapid decline and death | (14) |

components.[1] Similar to the reported cases in the literature, the lesion in our case was isointense T1 with intense contrast enhancement. Rarely the tumor was described with spontaneous contrast on weighted MRI T1.[1,8]

ES can be misdiagnosed as meningioma because it frequently arises from meninges. It manifests two different patterns of meningeal involvement characterized by diffuse involvement of leptomeninges or localized dural-based mass.[11]

ES mostly occurs as a single lesion. It is mostly intraparenchymal, located supratentorial or, less frequently, in the spinal cord.[1] In our case, masses are multiple and located infratentorial intra- and extra-axial.

Immunohistochemistry for CD99 is characteristic of ES/PNET, but it is not specific because immunopositivity can also be expressed in other primary small cell tumors of the CNS. The pattern of staining is usually cytoplasmic in these tumors.[7]

However, central PNET is frequently negative for CD99 staining.[3] Genetic testing for the rearrangement of the EWSR1 gene is important for the diagnosis. The chromosomal translocation t(11, 22)(q24; q12) is pathognomonic.[11,12]

It consists of the fusion of the human FLI gene on chromosome 11q24 with a gene EWS on chromosome 22q12, causing oncogenic conversion of the ES gene. It is found in over 90% of peripheral PNET-ES. The distinction of intracranial ES/PNET from central PNET is important for treatment and prognosis.

The therapeutic recommendation for ES indicates surgery when it is possible or combining systemic chemotherapy with focal irradiation.[2,4] Treatment options in patients with cerebral ES include chemotherapy, surgery, and/or radiation therapy (RT).

Drug combinations of chemotherapy include vincristine-ifosfamide-doxorubicin-etoposide therapy.[2] RT is indicated in patients with metastatic tumors. Chemotherapy in the treatment of ES has shown rates of long-term survival.[2] Overall survival (OS) is about 70% in patients with no localized disease; however, OS is lower than 30% in patients with metastatic disease.[4]

The prognostic factors influencing intracranial extraosseous ES have not been identified yet. In general, a worse prognosis is associated with the presence of metastatic lesions at the time of diagnosis, infratentorial localization, involvement of bone, atypical histology, age at presentation >14 years old, and a tumor volume >200 mL.[2]

## CONCLUSION

Primary and metastatic intracranial ES at diagnosis is exceedingly rare. Our case revealed the most atypical radiological features of all reported cases.

Physicians should consider the possibility of this rare tumor, especially in young people with dural-based lesions with cystic components and heterogeneous contrast enhancement. Histological and genetic features of the tumor are important for guiding treatment decisions and predicting prognosis.

### Ethical approval

The Institutional Review Board approval is not required.

### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

### Financial support and sponsorship

Nil.

### Conflicts of interest

There are no conflicts of interest.

### Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

## REFERENCES

1. Batur A. Conventional and advanced MR imaging findings of primary Ewing sarcoma of the tentorium: A case report with literature review. Br J Neurosurg 2021;37:1322-25.
2. Cherif El Asri A, Benzagmout M, Chakour K, Chaoui MF, Laaguili J, Chahdi H, *et al*. Primary intracranial pPNET/Ewing sarcoma: Diagnosis, management, and prognostic factors dilemma-a systematic review of the literature. World Neurosurg 2018;115:346-56.
3. Dedeurwaerdere F, Giannini C, Sciot R, Rubin BP, Perilongo G, Borghi L, *et al*. Primary peripheral PNET/Ewing's sarcoma of the dura: A clinicopathologic entity distinct from central PNET. Mod Pathol 2002;15:673-8.
4. Haveman LM, Ranft A, Van den Berg H, Klco-Brosius S, Ladenstein R, Paulussen M, *et al*. Primary and metastatic intracranial Ewing sarcoma at diagnosis: Retrospective international study and systematic review. Cancers (Basel) 2020;12:1675.
5. Huguenard AL, Li YD, Sharifai N, Perkins SM, Dahiya S, Chicoine MR. Multifocal primary central nervous system Ewing sarcoma presenting with intracranial hemorrhage and leptomeningeal dissemination: Illustrative case. J Neurosurg Case Lessons 2021;1:CASE2042.
6. Ibrahim GM, Fallah A, Shahideh M, Tabori U, Rutka JT. Primary Ewing's sarcoma affecting the central nervous system: A review and proposed prognostic considerations. J Clin Neurosci 2012;19:203-9.
7. Kazmi SA, Perry A, Pressey JG, Wellons JC, Hammers Y, Palmer CA. Primary Ewing sarcoma of the brain: A case report and literature review. Diagn Mol Pathol 2007;16:108-11.
8. Ke C, Duan Q, Yang H, Zhu F, Yan M, Xu SP, *et al*. Meningeal Ewing sarcoma/peripheral PNET: Clinicopathological, immunohistochemical, and FISH study of four cases. Neuropathology 2017;37:35-44.
9. Roosen N, Lins E. Primary Ewing's sarcoma of the calvarial skull. Neurochirurgia (Stuttg) 1991;34:184-7.
10. Salunke PS, Gupta K, Malik V, Kumar N, Le H, Cai C, *et al*. Primary Ewing's sarcoma of cranial bones: Analysis of ten patients. Acta Neurochir (Wien) 2011;153:1477-85.
11. Sohail AH, Sachal M, Maan MA, Soban M, Khan MS, Bari ME. Primary intracranial extraosseous Ewing's sarcoma. Childs Nerv Syst 2019;35:541-5.
12. Tanboon J, Sitthinamsuwan B, Paruang T, Marrano P, Thorner PS. Primary intracranial Ewing sarcoma with an unusually aggressive course: A case report and review of the literature. Neuropathology 2012;32:293-300.
13. VandenHeuvel KA, Al-Rohil RN, Stevenson ME, Qian J, Gross NL, McNall-Knapp R, *et al*. Primary intracranial Ewing's sarcoma with unusual features. Int J Clin Exp Pathol 2015;8:260-74.
14. Weil RJ, Zhuang Z, Pack S, Kumar S, Helman L, Fuller BG, *et al*. Intramedullary Ewing sarcoma of the spinal cord: Consequences of molecular diagnostics. Case report. J Neurosurg 2001;95 2 Suppl:270-5.

**How to cite this article:** Mhiri M, Abbes A, Ben Dhia R, Gouta N, Frih Ayed M. Primary and metastatic cerebral Ewing's sarcoma: A case report about a rare entity and literature review. Surg Neurol Int. 2024;15:367. doi: 10.25259/SNI_316_2024