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Review

A rare case of cranial Ewing's sarcoma metastasis developing in a patient with a history of occipital glioma surgery: Case presentation in light of the literature

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ABSTRACT

Ewing sarcoma (ES) is an aggressive small round cell malignancy that rarely involves the cranium, either primarily or metastatically. Its sequential occurrence with glioma in the same patient is exceedingly uncommon. We report a 24-year-old man with a history of tibial and abdominal ES who had previously undergone total resection of a left occipital low-grade glioma. This case highlights the rarity of cranial metastatic ES following occipital glioma and emphasizes the importance of long-term surveillance and consideration of possible underlying biological predisposition.

Keywords: Ewing sarcoma, glioma, metastasis.

Ewing sarcoma (ES) is the second most common primary bone tumor seen in children, adolescents, and young adults, and it exhibits a highly aggressive course. This bone tumor can involve not only bone but also soft tissue.[1] Ewing sarcoma cells have a small, round morphology and show high levels of CD99 expression.

Chromosomal translocations involving the FET and ETS gene families play a role in the genetic background of ES. The most common translocation is the t(11;22)(q24;q12) fusion, formed by the fusion of the Ewing sarcoma breakpoint region 1 (EWSR1) gene with the Friend leukemia integration 1 transcription factor. The resulting chimeric protein acts as an oncogenic transcription factor, reprogramming the transcriptome and playing a characteristic role in the pathogenesis of ES.[1,2]

Ewing sarcoma generally involves the trunk and long bones. In the trunk, the pelvis is the most commonly affected site, whereas in the long bones, the femur is most frequently involved. Unlike osteosarcoma, it originates from the diaphyseal region of the bone. Rarely, ES may also show cranial involvement, either as a primary lesion or as a metastasis. In extra-skeletal ES, the most common site of involvement is the chest wall. Despite a multimodal treatment approach in ES (chemotherapy, surgery, and radiotherapy), rapid growth and a tendency for distant metastasis limit the prognosis.[3]

Gliomas are primary brain tumors thought to arise from neural stem or progenitor cells. Histologically, they are classified into subgroups such as astrocytoma, oligodendroglioma, and glioblastoma according to the cells from which

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they originate. In the classification made by the World Health Organization (WHO), gliomas are graded from Grade 1 to Grade 4 according to their degree of malignancy. Each glioma group exhibits a distinct clinical course, treatment response, and genetic signature. Therefore, accurate and early diagnostic classification is of critical importance in the management of patients with glioma. Treatment is based on a combination of surgical resection, radiotherapy, and chemotherapy; however, the prognosis is generally poor, especially in high-grade gliomas.[4]

Although ES and glioma are each well-defined malignancies, their sequential occurrence in the same patient is extremely rare. There are limited data in the literature regarding the consecutive appearance of these two tumors. Reporting this association is important for discussing possible genetic predispositions, treatment-related secondary tumor development, and the need for long-term follow-up. In this study, we present a patient who developed occipital glioma and cranial ES, respectively, and considered publications with possible clinical relevance by reviewing the literature registered in the PubMed search engine between January 2020 and February 2026.

CASE REPORT

A 24-year-old male patient presented with a complaint of headache that had been ongoing for two weeks. On physical examination, his general condition was good; he was conscious, cooperative, and oriented. The Glasgow Coma Scale was 15. On evaluation of the extremities, all four limbs were mobile, and no significant motor deficit was observed. In the patient's medical history, it was learned that he had been diagnosed with diabetes mellitus in 2021 and had undergone a Whipple procedure. Approximately five years earlier, masses had been detected in the tibia and abdomen. As a result of a needle biopsy, he was diagnosed with ES. Subsequently, the patient underwent abdominal mass excision surgery, and the pathological examination confirmed the diagnosis of ES. Radiotherapy was administered for the mass located in the tibia. Written informed consent was obtained from the patient for the publication of this case report and any accompanying images.

After positron emission tomography (PET)-magnetic resonance imaging (MRI) examinations performed in the medical oncology clinic, where the patient was being followed, revealed an intracranial lesion suspicious for glioma, he was referred to the neurosurgery clinic. In our clinic, 14 months earlier, the patient underwent microsurgical total resection under neuromonitoring and neuronavigation for a left occipital mass that was compatible with low-grade glioma on MRI, as shown in Figure 1. During this surgery, the frozen section result for our patient was reported as low-grade glioma, and the final pathology result also came back as astrocytoma, isocitrate dehydrogenase (IDH)-mutant, central nervous system (CNS) WHO Grade II. No additional treatment was planned following evaluation by the neuro-oncology council. Approximately five months later, he also presented with a palpable subcutaneous swelling in the left parietal region, consisting of a lesion that was soft in some areas. On palpation, the mass measured approximately 5 × 5 cm and had a consistency that was firm in some areas and soft in others. Contrast-enhanced cranial 3T MRI demonstrated heterogeneous intense contrast enhancement causing bone destruction, infiltrating the dura and periosteum, and producing epidural compression, as shown in Figure 2. Surgery was also planned for this new mass.

In the preoperative laboratory evaluation, the complete blood count was within normal limits. The C-reactive protein level was 3.5 mg/L. Random plasma glucose was measured at 141 mg/dL, while the serum lactate level was found to be 5.31 mmol/L. During surgical exploration, the lesion was found to be located entirely extradurally, and the tumor was resected en bloc in total together with the bone, dura, and periosteum. No invasion of the sagittal sinus was observed. Macroscopically, the mass appeared dark reddish-purple in color, highly vascularized, hemorrhagic, and of medium firmness. The resulting defect was reconstructed using allograft dura mater and titanium mesh, as shown in Figures 3a, b.

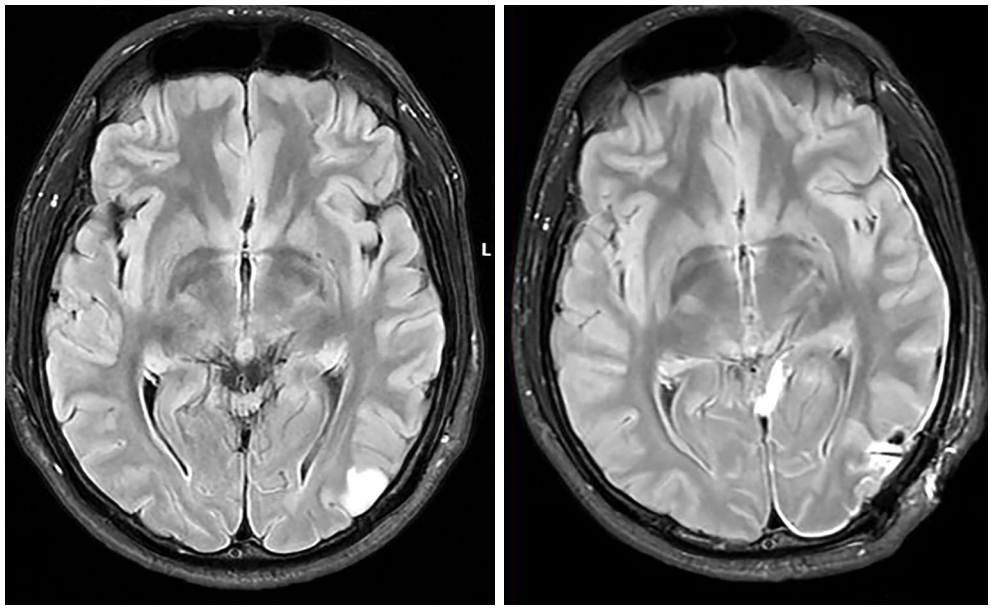


Figure 1. Preoperative and postoperative T2-FLAIR MRI of astrocytoma.
T2-FALIR: T2 fluid-attenuated inversion recovery; MRI, magnetic resonance imaging.

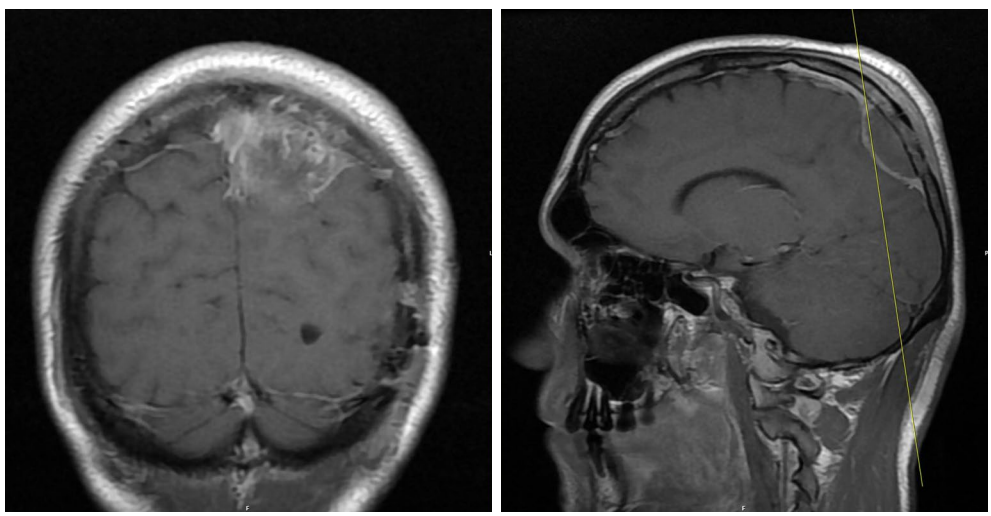


Figure 2. Contrast-enhanced coronal and sagittal MRI obtained five months after astrocytoma surgery and before Ewing metastasis surgery.
MRI, magnetic resonance imaging.

Histopathological evaluation revealed the morphology of a metastatic small round cell tumor infiltrating the bone and soft tissue. On immunohistochemical examination, NKX2.2 was positive, while OLIG2 was negative. In light of these findings, the case was diagnosed as metastatic ES. No loss was detected in DNA repair proteins, specifically mismatch repair (MMR), indicating a proficient MMR despite the presence of multiple primary malignancies.

No chemotherapy was planned for the patient after discussion at the neuro-oncology council, while radiotherapy was administered. A total

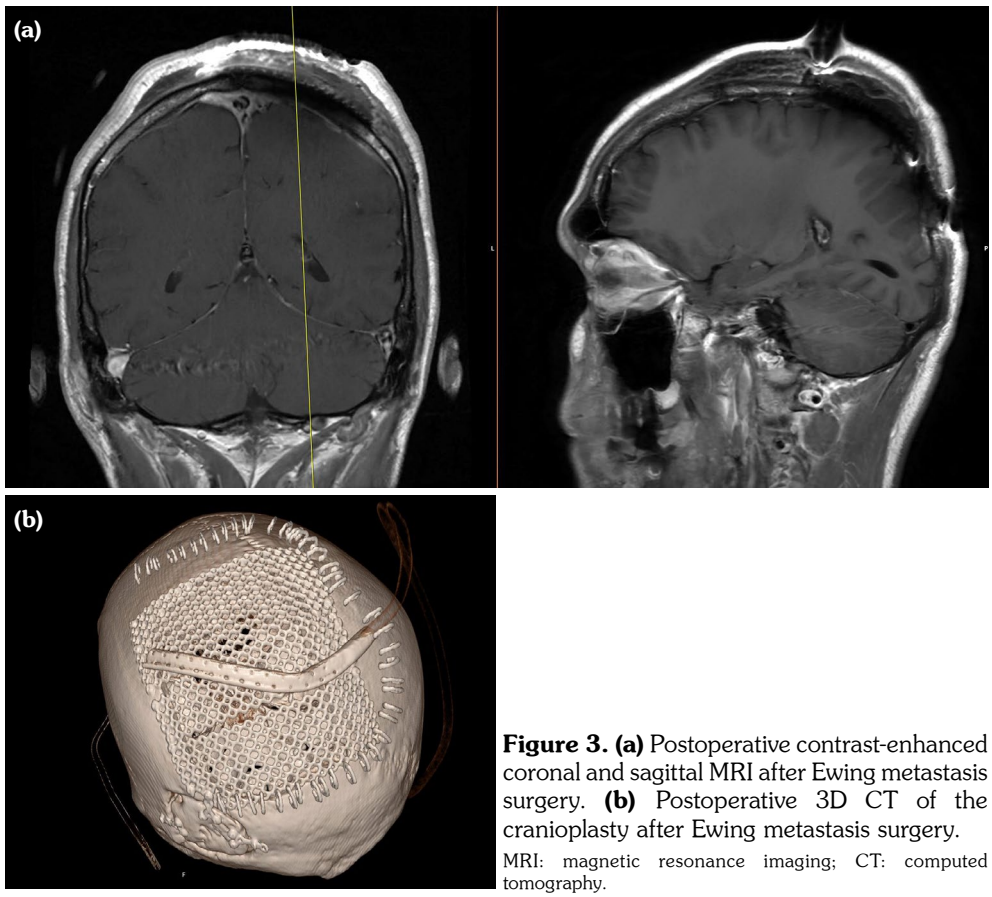


Figure 3. (a) Postoperative contrast-enhanced coronal and sagittal MRI after Ewing metastasis surgery. **(b)** Postoperative 3D CT of the cranioplasty after Ewing metastasis surgery.
MRI: magnetic resonance imaging; CT: computed tomography.

dose of 30 Gy radiotherapy was delivered in fractions. At the 14th month of follow-up since the most recent surgery, the patient had no neurological deficit. Follow-up is ongoing.

DISCUSSION

The presented case reveals an extremely rare clinical scenario in that it demonstrates the development of cranial metastatic ES in an adult patient with a history of previously surgically treated occipital glioma. In addition to the uncommon cranial involvement seen in ES, the coexistence of ES and glioma in the same patient is only rarely reported in the literature. The vast majority of these cases occur in the pediatric age group and present as primary intracranial lesions. This association raises important questions regarding tumor biology, metastatic behavior, and possible underlying predisposition mechanisms. It has been reported in the literature that cranial or intracranial ES cases account for less than approximately 1% of all ESs and represent only 0.03% of all intracranial tumors.[5]

When the localization distribution of cranial ES is examined, the most commonly reported sites are the frontal bone and the nasal cavity (16.7% each). The temporal bone (14.7%), maxilla (13.7%), and mandible (11.8%) are among the relatively more frequent locations. In contrast, parietal region involvement has been reported at a rate of only 4.9%.[6] In the presented case, the lesion located in the parietal bone demonstrates that cranial metastatic ES has exceptional features in terms of both anatomical distribution and clinical presentation. The previously reported cases are summarized in Table 1.

Cranial Ewing sarcoma: Primary versus metastatic disease

When cranially located ES is identified, one of the fundamental questions in clinical management is whether the lesion is of primary

cranial origin or represents a metastatic extension of systemic disease.[7] This distinction is important not only diagnostically but also in terms of prognosis and therapy.

In the presented case, the assessment in favor of metastatic disease is based on the patient's previous diagnosis of tibial ES, the fact that he had entered a remission period after multimodal treatment, and the histopathological demonstration that the cranial lesion was morphologically and immunohistochemically consistent with the previous primary tumor. When these findings were considered together, it was concluded that the current lesion represented a late metastatic extension of systemic disease rather than a primary cranial ES.

Moreover, primary cranial ES is exceedingly rare in the adult age group, and the detection of calvarial and dural involvement in a patient with a history of systemic disease further strengthens the likelihood of metastatic spread.[7] Therefore, this case represents a noteworthy example of ES presenting as an isolated cranial metastasis in adulthood.

Association between Ewing sarcoma and glioma: coincidence or shared predisposition?

Ewing sarcoma and gliomas are two distinct groups of malignancies that differ markedly in terms of histogenesis and molecular driver mechanisms. While ES is a mesenchymal small round cell tumor typically characterized by EWSR1 gene fusions, gliomas are of neuroepithelial origin and are frequently associated with alterations in genes such as IDH1/2, tumor protein p53 (TP53), and alpha thalassemia/mental retardation syndrome X-linked (ATRX).[1,4]

A review of the current literature shows that data regarding the coexistence of ES and glioma in the same patient are extremely limited. One of the reported cases is a mixed tumor displaying the simultaneous presence of intracranial extraosseous ES and glioma.[8] However, that case represents a combined neoplasm histopathologically and therefore differs from two separate primary or metastatic tumor processes developing sequentially. For this

Table 1. Review of the literature

Author (year)	Age / Sex	Type of ES	Glioma presence	Location	Temporal relationship	Treatment	Outcome
Shang et al.[8]	Adult / M	Extraosseous intracranial ES	Yes (glioma, combined tumor)	Intracranial	Synchronous	Surgery + radiotherapy	Limited data
Haveman et al.[7] (2020)	Median 11 year	Primary intracranial ES	No	Frontal, temporal, parietal	-	CTX + surgery ± RT	3-year OS ~70%
Haveman et al.[7] (2020)	~16 year	Extracranial ES with brain metastasis	No	Intracranial metastasis	At diagnosis	CTX + RT	Poor prognosis
Various case reports	Pediatric / adolescent	Primary cranial ES	No	Skull/dura	-	Surgery + RT ± CTX	Variable
Present study	24 / M	Metastatic ES	Yes (astrocytoma, IDH-mutant)	Occipital → parietal	Metachronous	Surgery + radiotherapy	Stable at follow-up

ES, Ewing sarcoma; RT, radiotherapy; OS, overall survival; CTX, chemotherapy; IDH, isocitrate dehydrogenase,

reason, the subsequent development of a distinct glioma in a patient with a history of systemic ES is an almost undescribed phenomenon in the literature.

The development of multiple primary malignancies may be associated with germline tumor suppressor gene mutations. In particular, disruptions in the TP53 pathway have been linked to the development of malignancies with different histogeneses in the same individual.[9] Since TP53 mutations are associated with both sarcomas and CNS tumors, this rare coexistence raises the possibility of an underlying genetic predisposition.[10]

In this context, the presented case constitutes an exceptionally rare example in terms of the sequential occurrence of two malignancies with different histogeneses. The near absence of similar associations in the literature makes the question of whether this represents a coincidental coincidence or a reflection of shared underlying biological mechanisms even more meaningful. Therefore, careful long-term follow-up and, in appropriate cases, genetic evaluation should be considered, especially in such unusual tumor combinations observed in young adult patients.

Role of prior treatment and local factors

Although the main mechanism of metastatic spread is hematogenous dissemination, it is known that the local microenvironment may play a role in the settlement of tumor cells in specific tissues.[11] Previous surgical interventions may alter the local tissue environment by causing vascular remodeling, an inflammatory response, and changes in the blood-brain barrier. These changes may create a favorable "niche" for circulating tumor cells.[12]

In the presented case, the history of systemic ES and the presence of accompanying bone metastases suggest that the cranial involvement was primarily a consequence of hematogenous spread. Nevertheless, the possibility cannot be completely excluded that the previous glioma surgery performed in the left occipital region may have altered the local tissue microenvironment and facilitated metastatic seeding in the anatomically adjacent parietal calvarium. However, the current clinical and pathological data support that the cranial lesion was primarily a metastasis of the systemic disease. In addition, the fact that the patient had not previously received cranial radiotherapy excludes the possibility of a radiation-related secondary tumor.

Therapeutic approach and radiosensitivity

The standard approach to the treatment of ES generally relies on a multimodal treatment strategy that includes surgical resection, chemotherapy, and radiotherapy.[13] Particularly in localized disease, when surgical resection is feasible, complete tumor removal is more successful than other methods in achieving cure.[14]

Nevertheless, ES is known to be a radiosensitive tumor compared with many other bone tumors. Therefore, radiotherapy is used as an important treatment option in cases where surgical margins are questionable or in anatomical regions where resection is not feasible.[15]

In metastatic disease, the treatment approach is generally individualized according to the systemic disease burden, the location of metastasis, and the patient's clinical condition. In particular, in metastatic lesions that are symptomatic or carry a risk of local complications, surgical resection and radiotherapy may be applied for palliative purposes or to achieve local control.[16]

In the presented case, *en bloc* surgical resection was performed for the lesion located in the parietal bone and infiltrating the dura and periosteum, and adjuvant radiotherapy was subsequently planned for local control. Since the patient had previously received systemic treatment and the current lesion presented as an isolated cranial metastasis, chemotherapy was not administered; instead, local radiotherapy was preferred in accordance with the decision of the neuro-oncology council. This approach is consistent with the treatment strategies recommended in the literature for achieving local disease control in cranial metastatic ES.

Imaging modalities and follow-up strategy

In ES, imaging plays a central role in accurately determining tumor extent

at diagnosis, evaluating response to chemotherapy, and detecting post-treatment recurrence at an early stage. The main modalities used are MRI, computed tomography (CT), fluorodeoxyglucose-PET/CT or PET/MR, and, when necessary, bone scintigraphy.[17]

The use of PET/MR provides a more accurate assessment of the lesion by simultaneously offering metabolic and high-resolution anatomical data. Owing to these features, it may serve as a guide in biopsy and treatment planning and has the potential to improve diagnostic performance.[18]

Compared with PET/CT, PET/MR stands out by enabling the combined evaluation of metabolic and anatomical data with superior soft tissue contrast. It may contribute to the assessment of soft tissue components, the clearer localization of bone lesions, and the evaluation of early bone marrow involvement. In addition, the significantly lower radiation dose provided by PET/MR represents an important advantage in the follow-up of young patients, who often require multiple imaging studies. These features may contribute to a more comprehensive assessment of disease spread in tumors such as ES.[19]

In the presented case, systemic disease follow-up was performed with PET/MRI, and the cranial glioma lesion was also first detected using this imaging modality. In subsequent follow-up imaging, the metastatic lesion that developed in the parietal calvarium was again evaluated by magnetic resonance imaging. This highlights the importance of advanced imaging methods for the early detection of CNS lesions in patients with a history of systemic sarcoma.

This study has some limitation the rarity of the coexistence of Ewing sarcoma and glial tumors limits the availability of comparable cases in the literature. Although this report presents a single case, it contributes to the limited data regarding the sequential occurrence of these two distinct tumor entities. Further accumulation of similar cases and molecular studies may help clarify whether this association represents a coincidental finding or a potential biological relationship.

In conclusion, this case reflects a clinical scenario involving the development of occipital glioma followed by the emergence of cranial metastatic ES in a patient with a prior history of ES. Although ES rarely metastasizes to the cranium, newly detected cranial or intracranial lesions in individuals with a history of systemic disease should be carefully evaluated for metastatic disease. In addition, this case demonstrates that malignancies with different histogeneses may occur sequentially in the same patient, thereby emphasizing the importance of investigating the possibility of an underlying genetic predisposition. Future studies are expected to better elucidate the biological mechanisms of such rare tumor associations and the optimal follow-up strategies.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

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