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CASE REPORT

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# Recurrent intracranial anaplastic ependymoma with late-onset giant scalp metastasis

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## Key Clinical Message

Ependymomas are primary brain tumors that predominantly affect individuals between 0 and 4 years of age. Although ependymomas have a propensity for recurrence and the potential to spread within the central nervous system through cerebrospinal fluid (resulting in drop metastases), reports of extra-neural metastatic localizations are exceedingly rare in the existing literature. This case report presents a unique and rare instance of recurrent intracranial anaplastic ependymoma with a late-onset giant scalp metastasis.

## Abstract

A 55-year-old male patient with a medical history of partial resection of an atypical supratentorial left temporal ependymoma presented with a recurrent anaplastic ependymoma, which had been managed with surgery and radiotherapy. After a 4-year follow-up, the patient developed a subcutaneous mass in the left parietal region of the scalp. A multidisciplinary team of neurosurgeons and plastic surgeons performed a surgical procedure, which included en bloc removal of the scalp lesion, resection of 1 cm of unaffected skin, and craniotomy to address an osteolytic area in the parietal skull bone. Skin autografts were used for reconstruction. Histological examination confirmed metastasis of anaplastic ependymoma in the scalp. After a delay in starting chemotherapy due to concerns related to the COVID-19 pandemic, the patient eventually initiated chemotherapy, leading to disease stability at a short-term follow-up. Scalp metastases from ependymoma are rarely reported in the literature. Management of such cases necessitates aggressive surgical resection, followed by adjuvant chemotherapy and radiotherapy. A multidisciplinary approach is recommended to ensure effective and targeted therapy, with a focus on preserving aesthetics, particularly in pediatric cases.

**KEYWORDS**

ependymoma, extra-neural, gamma knife, metastasis, recurrent, scalp

## 1 | INTRODUCTION

Ependymomas are primary brain tumors that predominantly occur in children between the ages of 0 and 4 years.[1] While 46% of ependymomas in adults are found in the spine, in pediatric cases, they are overwhelmingly intracranial (90%).[2] These intracranial ependymomas can manifest in various locations, with approximately two-thirds occurring in the posterior fossa and some in the supratentorial space. Anaplastic ependymomas are categorized as World Health Organization (WHO) Grade 3 neoplasms and are characterized by poorly differentiated ependymal cells with intense mitotic activity, microvascular proliferation, and tumor necrosis.[3] Ependymomas often exhibit a propensity for recurrence and the potential to spread to distant regions within the brain and spine via cerebrospinal fluid dissemination (drop metastases). However, reports of extra-neural metastatic localizations are exceptionally rare in the literature.[4] In this report, we present an unusual case of recurrent intracranial anaplastic ependymoma with a late-onset giant scalp metastasis. This case is particularly unique due to the atypical nature of the scalp metastasis and its late onset, which has not been extensively documented in the literature. The rarity of scalp involvement as a site of metastasis from ependymoma is underscored by the limited number of reports, some of which are based on postmortem observations.[5] Notably, our patient's case raises interesting questions about the mechanisms and characteristics of ependymoma metastasis, especially in an extracranial context.

## 2 | CASE DESCRIPTION

A 55-year-old male patient presented with a history of headache and speech disorders. Four years earlier, the patient had undergone a partial resection of an atypical supratentorial left temporal ependymoma, which was followed by a period of disease stability. Upon neurological examination, the patient exhibited phonemic and semantic paraphasia, along with right homonymous hemianopia. Subsequent brain MRI revealed disease progression in the left temporo-parietal region. An extended MRI scan of the entire spine was performed to rule out metastases (Figure 1). Following a brain PET examination utilizing 11C-methionine, which displayed high proliferative characteristics, the patient underwent gross total removal (GTR) of the left temporo-parietal lesion. Histological examination confirmed the presence of an anaplastic ependymoma. A postoperative brain CT scan, conducted within the initial 24 h after surgery, confirmed the complete removal of the lesion (Figure 2). Subsequently, the patient underwent external radiation therapy employing volumetric modulated arc therapy (VMAT), with a total dose of 5940 cGy and fractionated doses of 180 cGy, followed by serial radiological assessments. After a 4-year follow-up, the patient developed

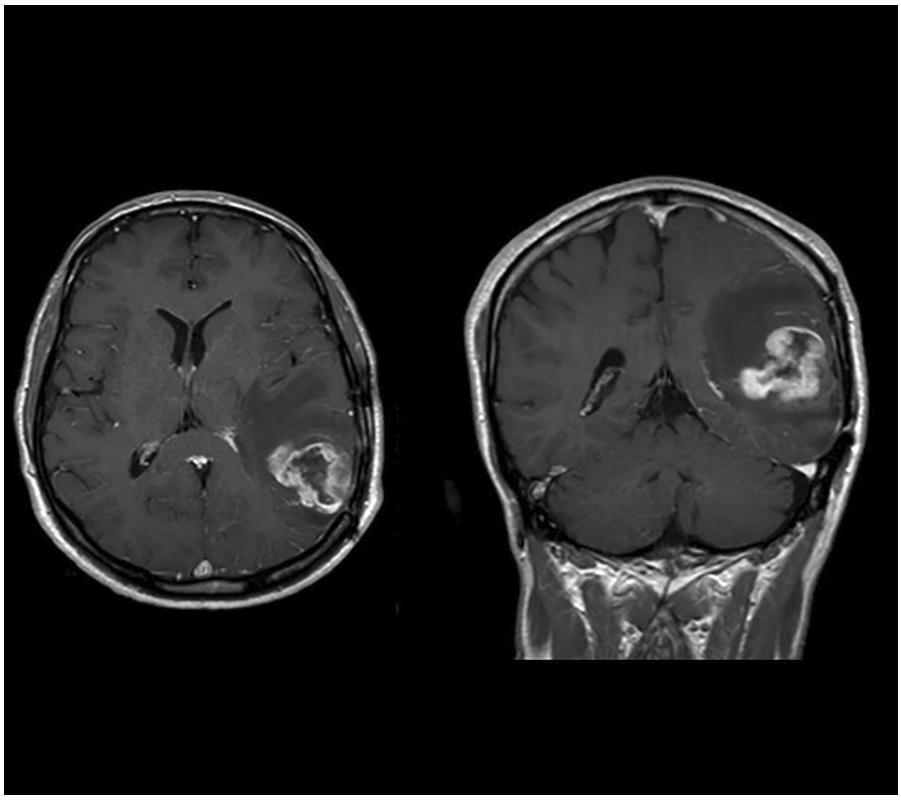

**FIGURE 1** Axial (left) and coronal (right) T1-weighted gadolinium-enhanced MRI sequences illustrating the progression of the residual left temporo-parietal ependymoma.

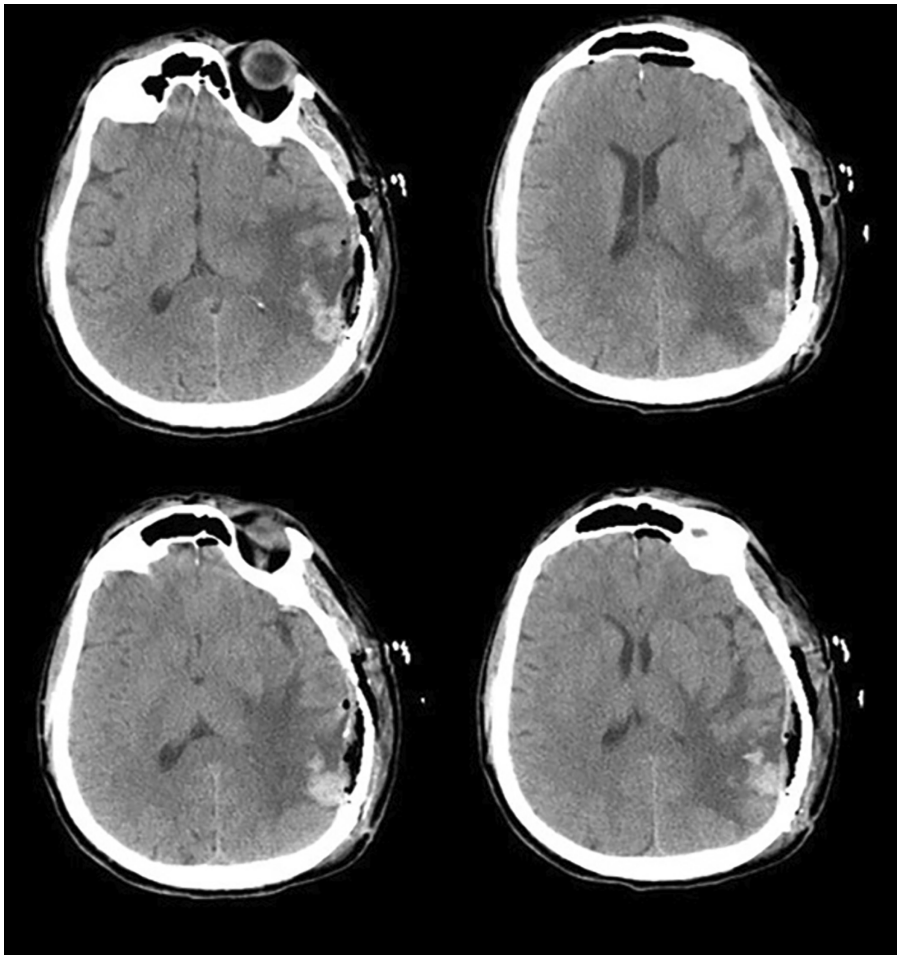

**FIGURE 2** Series of axial brain CT scan images demonstrating the complete removal of the lesion.

a subcutaneous lesion on the scalp in the left parietal region, accompanied by semantic paraphasia as the only neurological symptom. A follow-up brain PET examination using 11C-methionine revealed a probable pericavitary recurrence in the left temporo-parietal region and increased uptake in the left parietal scalp (Figure 3). As a result, the patient underwent hypo-fractionated gamma knife radiosurgery, which entailed treating a volume of 3174 $cm^3$ with a dose of 7 Gy per fraction, a 50% isodose, a total dose of 21 Gy, and a maximal dose of 42 Gy. However, 4 months later, the subcutaneous lesion continued to grow, prompting a new brain MRI, which revealed a 63.36 × 41.26 mm scalp lesion characterized by homogeneous contrast enhancement in T1W 3D-TFE sequences (Figure 4). A multidisciplinary surgical team, consisting of neurosurgeons and plastic surgeons, conducted the subsequent surgical procedure after performing a head CT scan with 3-dimensional reconstructions (Figure 5) (Table 1). The plastic surgeon initiated the surgery by performing an en bloc removal of the scalp lesion and removing an additional 1 cm of unaffected skin. The lesion was found to involve the galea, with infiltration of the periosteum and evidence of an osteolytic area in the parietal skull bone. Extemporary skin biopsies at four cardinal points were sent for histopathological examination, which confirmed the absence of further tumor infiltration. The neurosurgical stage of the procedure involved a craniotomy to excise the osteolytic area, followed by reconstruction with polymethyl methacrylate (PMMA). The bone flap removed during the craniotomy was also subjected to histological examination. The final step of the procedure involved skin closure performed by the plastic surgeon, which included the preparation of two frontoparietal and occipital flaps to cover the bone cement. Additionally, one-third thick skin autografts harvested from the anterior surface of the right thigh were used to cover the skin defect over the right frontal–parietal skull due to the rotation of the flaps (Figure 6A–D). Histological examination of the excised tissue revealed diffuse dermal and subdermal infiltration by poorly differentiated neoplastic cells, characterized by lobular growth patterns and focal areas of necrosis, consistent with scalp metastases from anaplastic ependymoma (Figure 7A–D). Unfortunately, the patient delayed the initiation of chemotherapy due to concerns related to the COVID-19 pandemic. After 4 months, the patient reported the development of new, small, subcutaneous masses at the site of the

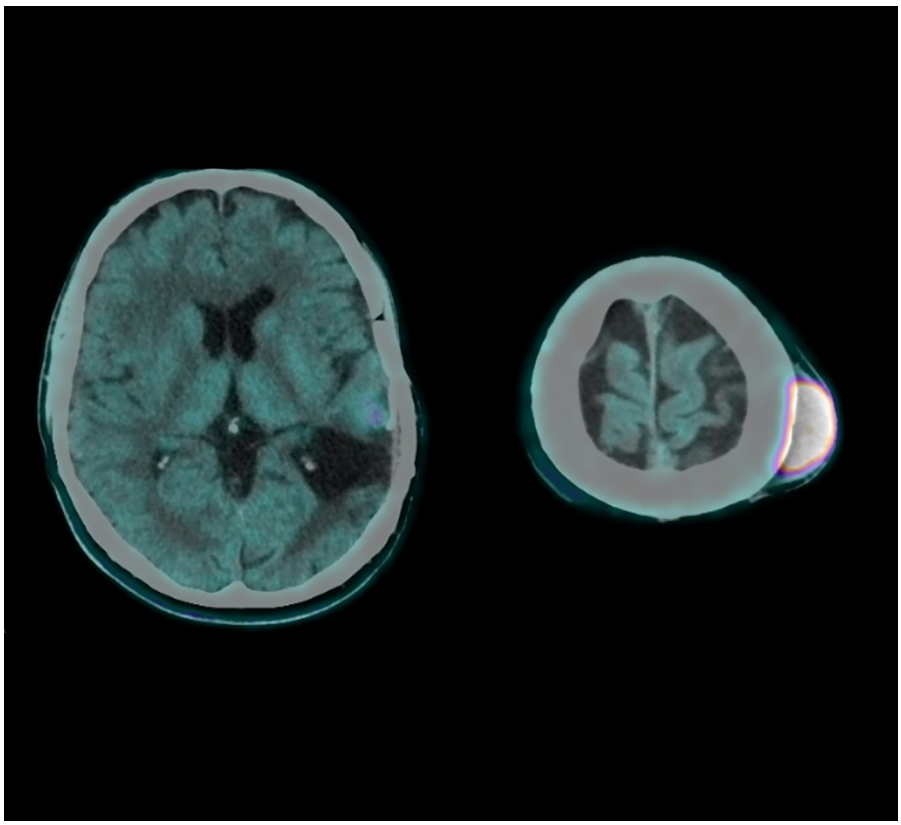

**FIGURE 3** Hybrid brain CT-PET images with 11C-methionine indicating a likely pericavitary left temporo-parietal recurrence (left) and an uptake at the level of the left parietal scalp (right).

previous surgical skin flap, along with cervical lymph node involvement, and intracranial recurrence. Despite these challenges, the skin autografts showed satisfactory healing (Figure 8). Following consultation with a new oncologist, the patient commenced the DEC protocol (comprising cisplatin, etoposide, and cyclophosphamide) with disease stability observed at short-term follow-up.

## 3 | DISCUSSION

Extracranial metastases originating from primary intracranial ependymoma are rare, and the potential mechanisms leading to these metastatic events have been analyzed. Notably, this case report sheds light on the unusual development of late-onset scalp metastases from anaplastic ependymoma, a phenomenon that has not been comprehensively documented in the literature. The rarity of scalp involvement as a site of metastasis from ependymoma is highlighted by the limited number of reports, with some being based on autopsy findings.[5] It is essential to emphasize that this case underscores the distinctive aspects of ependymoma metastasis and prompts further exploration of the mechanisms and characteristics of extracranial metastases.

In rare instances, ependymoma can primarily originate from extraneural/soft tissue sites, such as the inguinal, sacrococcygeal, and mediastinal regions. Distinguishing such cases from extraneural metastases can pose a diagnostic challenge.[6]

The literature includes reports of ependymoma metastases, both within and outside the central nervous system (CNS). Various pathways have been proposed for the development of extracranial metastases from CNS tumors, including hematogenous spread through pathological vessels of the primary tumor, spread via major dural sinuses infiltration, hematogenous, and/or lymphatic dissemination following skull invasion and involvement of extracranial soft tissues (scalp). There is also a debate surrounding the potential role of ventriculoperitoneal shunts in spreading cancer cells.[7,8] Surgical interventions appear to play a significant role as a risk factor for peritumoral metastasis.[7,9] Surgery can disrupt the physiological anatomy of the CNS, allowing malignant cells to gain access to the bloodstream and lymphatic vessels, thus facilitating distant metastasis[10] (Table 2). Extracranial metastases in brain tumors are reported in approximately 0.5%–1% of cases, with ependymomas accounting for 3.7% of such cases in the pediatric population.[11] Common sites for extra-neural metastases of anaplastic ependymomas include the lungs and lymph nodes, suggesting hematogenous and/or lymphogenous spread as the most likely mechanisms for both distant and contiguous metastasis. The mechanism of extraneural spreading of ependymomas is akin to other CNS tumors, such as gliomas and solitary fibrous tumors. In extremely rare cases, ependymomas can primarily originate from

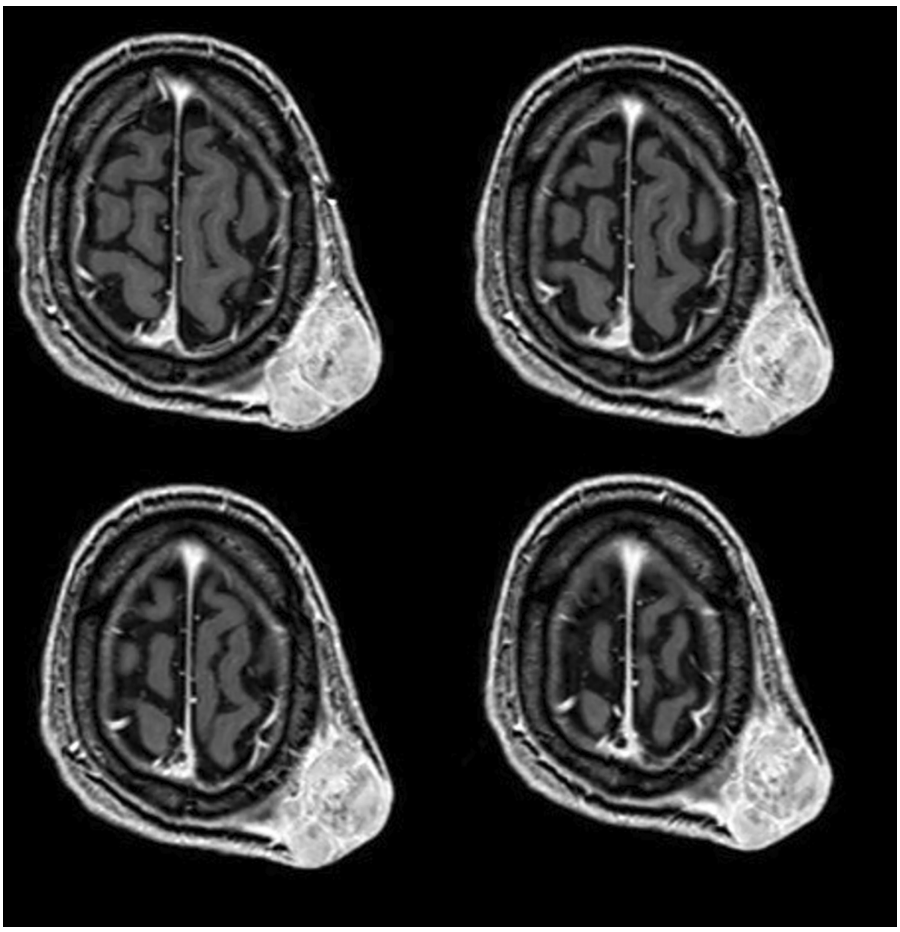

**FIGURE 4** Series of axial T1-weighted Gadolinium-enhanced MRI sequences displaying a 63.36 × 41.26 mm scalp lesion characterized by homogeneous contrast enhancement at the site of the previous surgery skin flap.

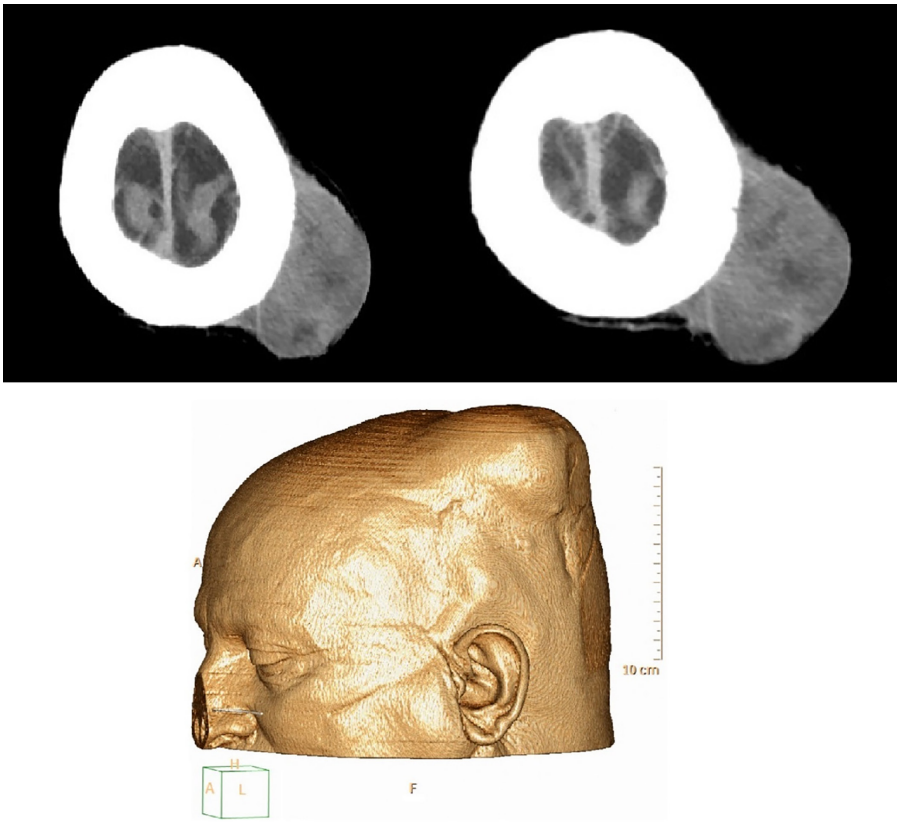


**FIGURE 5** Series of axial brain CT scan images (top) along with 3-dimensional reconstruction (bottom) presenting a large left temporo-parietal scalp lesion.

**TABLE 1** Summary of imaging findings.

| Imaging modality | Findings |
|---|---|
| Brain MRI (Figure 1) | - Progression of left temporo-parietal residual ependymoma<br>- Extensive T1-weighted Gadolinium-enhanced sequences<br>- Evidence of disease progression |
| PET with 11C-methionine (Figure 3) | - Pericavitary left temporo-parietal recurrence<br>- Uptake at the level of the left parietal scalp |
| Brain CT scan (Figure 5) | - Giant scalp lesion with homogeneous contrast enhancement<br>- Osteolytic area on the parietal skull bone |

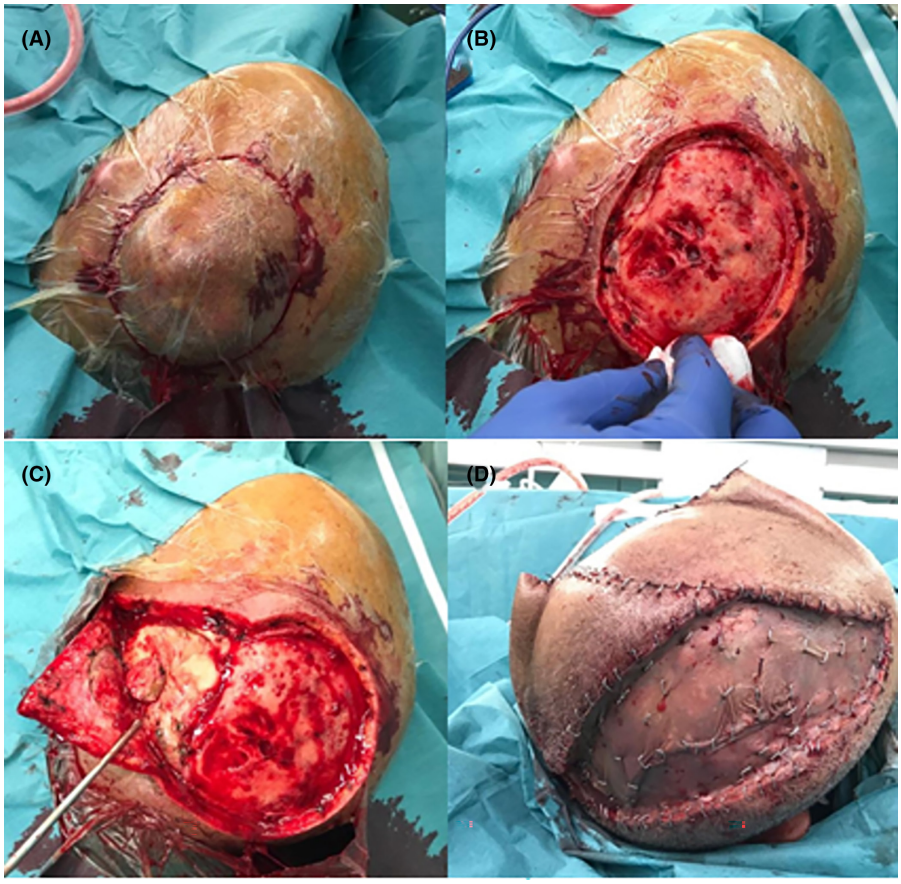


**FIGURE 6** Intraoperative images depicting a step-by-step surgical procedure, including the en bloc removal of the scalp lesion with an extension of 1 cm of unaffected skin (A, B), craniotomy involving the removal of the osteolytic area and reconstruction with PMMA (C), and skin closure involving frontoparietal and occipital rotation flaps and a one-third thick skin autograft obtained from the anterior surface of the right thigh to cover the skin defect over the right frontal–parietal skull (D).

extraneural or soft tissue sites, further complicating the differential diagnosis from extracranial metastasis.[6] It is worth noting that the response to chemotherapy can differ significantly between extracranial and intracranial disease. The consensus is that CNS tumors typically respond poorly to chemotherapy due to limited blood–brain barrier penetration. However, when considering the extracranial location of scalp metastasis, a much more favorable response should be anticipated. Therefore, the use of chemotherapy should be strongly considered in the management of these patients. The patient's delay in initiating chemotherapy, prompted by concerns related to the COVID-19 pandemic, highlights the impact of external factors on treatment decisions and underscores the importance of addressing such issues effectively to ensure timely and appropriate care. In conclusion, extraneural metastases secondary to anaplastic ependymoma are rare, and the possible mechanisms of onset have been analyzed. Late-onset scalp metastases from anaplastic ependymoma have not been well-documented in the literature and require extensive and radical surgical resection with adjuvant chemotherapy and radiotherapy.[12–16] In these complex cases, we suggest a multidisciplinary evaluation to carry out aggressive and targeted therapy, while also emphasizing the importance of preserving good aesthetics, especially in pediatric cases. The present case provides unique insights into the mechanisms and characteristics of extracranial metastases in ependymomas, underscoring the need for further research in this area.

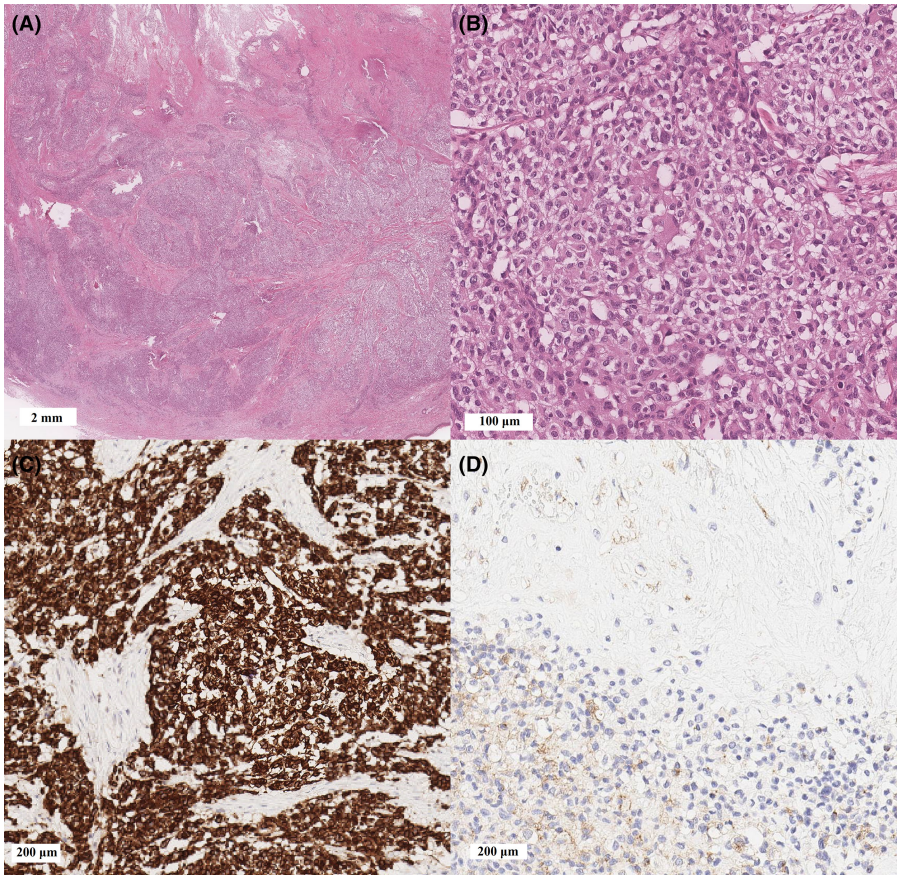


**FIGURE 7** Histological examination images showing widespread dermo-ipodermal infiltration by poorly differentiated neoplasm (H&E) (A), neoplastic elements with lobular pattern of growth, small round nuclei, eosinophilic and focal clear cytoplasm (H&E) with focal areas of necrosis (B). Additionally, images depict diffuse and strong immunostaining for GFAP (glial fibrillary acidic protein) (top) and focal immunostaining for EMA (epithelial membrane antigen) (C, D).

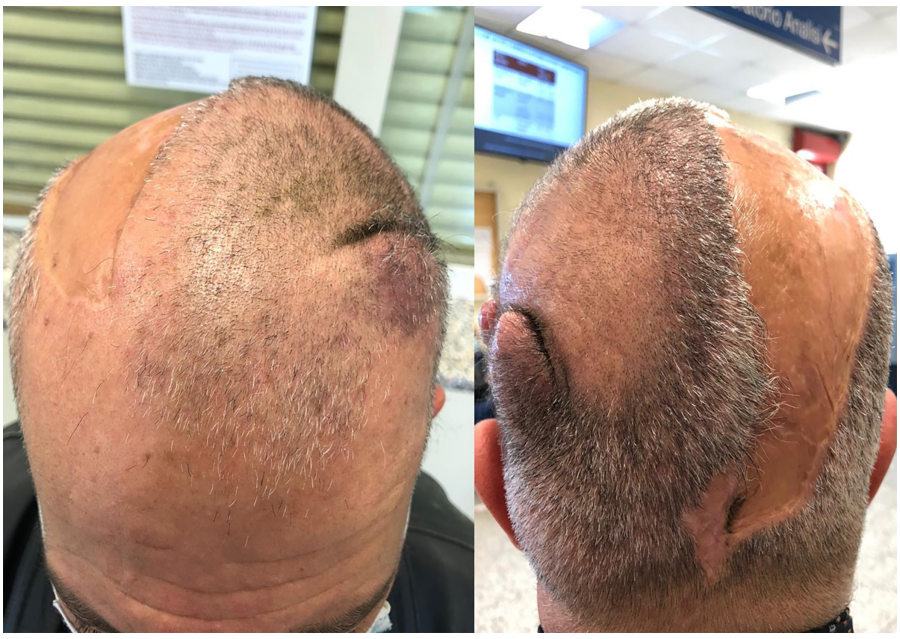

**FIGURE 8** Views of the frontal (left) and posterior (right) scalp demonstrating satisfactory healing of the skin autograft.

## 4 | CONCLUSION

Extraneural metastases secondary to anaplastic ependymoma are rare and the possible mechanisms of onset have been analyzed. Late-onset scalp metastases from anaplastic ependymoma have not been well documented in the literature and require extensive and radical surgical resection with adjuvant chemotherapy and radiotherapy. In these complex cases, we suggest a multidisciplinary evaluation to carry out aggressive and targeted therapy, while also emphasizing the

**TABLE 2** Mechanisms of ependymoma metastasis.

| Mechanism | Description |
|---|---|
| Hematogenous spread | Spread of malignant cells through the bloodstream, potentially via pathological vessels of the primary tumor |
| Lymphatic spread | Dissemination of cancer cells via lymphatic vessels, possibly involving lymph nodes in the metastatic process |
| Skull invasion and extracranial soft tissue involvement | Metastasis facilitated by tumor invasion of the skull and adjacent extracranial soft tissues, including the scalp |
| Surgical manipulation | Surgical procedures can disrupt the physiological CNS anatomy, allowing malignant cells to access blood and lymphatic vessels, potentially leading to metastasis |
| Ventriculoperitoneal shunts | Controversial mechanism that involves the potential spread of cancer cells via ventriculoperitoneal shunts, although its role remains debated |

importance of preserving good aesthetics, especially in pediatric cases. This case report offers valuable insights into the mechanisms and characteristics of extracranial metastases in ependymomas, particularly with the unique presentation of late-onset giant scalp metastasis. These findings underscore the need for further research to better understand the mechanisms of metastasis and to develop more effective treatment strategies.

## AUTHOR CONTRIBUTIONS

**Gianluca Scalia:** Conceptualization; data curation; formal analysis; investigation; supervision; validation; writing – original draft; writing – review and editing. **Gianluca Ferini:** Data curation; funding acquisition; supervision; validation; visualization. **Bipin Chaurasia:** Resources; supervision; validation; visualization. **Francesca Graziano:** Validation; visualization. **Stefano Priola:** Conceptualization; supervision; validation; visualization. **Paolo Amico:** Data curation; formal analysis; validation; visualization. **Giuseppe Emmanuele Umana:** Conceptualization; supervision; validation; visualization; writing – original draft; writing – review and editing.

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## CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

## DATA AVAILABILITY STATEMENT

Data sharing not applicable—no new data generated or the article describes entirely theoretical research.

## CONSENT

A written informed consent has been obtained from the patient to publish this paper.

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