



A Primary Intraosseous Meningioma: A Rare Case of Malignancy with High Proliferative Ability

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Abstract

Primary intraosseous meningioma (PIM) is a rare tumor that arises in the skull. Histopathologically, it is generally described as a slow-growing, benign lesion. However, on rare occasions, PIM presents as a malignancy with high proliferative ability, which requires maximal resection, adjuvant radiotherapy, and subsequent careful follow-up. Because of the rarity of such cases, they present a diagnostic challenge with unusual pathological findings. Herein, we report a case of a primary intraosseous anaplastic meningioma with extensive invasion inside and outside the skull, along with the results of whole-genome analysis. Histopathological diagnosis was a World Health Organization grade 3 anaplastic meningioma. In the literature, only two cases of anaplastic PIM have been reported, so its characteristics and treatment are poorly understood. Our patient was successfully treated with tumor resection, followed by intensity-modulated radiation therapy. Follow-up imaging studies revealed no recurrence or distant metastasis, including to lung, liver, and bone, at 8 months after the surgery.

Keywords

- ▶ meningioma
- ▶ intraosseous
- ▶ anaplastic
- ▶ extensive invasion
- ▶ genetic analysis

Introduction

Primary intraosseous meningioma (PIM) is a rare tumor and a subset of primary extradural meningioma (PEM). The majority of meningiomas are located in the subdural space. In contrast, PEM is located at sites other than the dura, such as the skin, skull, nasopharynx, and lung.¹ PEM accounts for

less than 2% of all meningiomas, and PIM makes up only 14% of PEMs.^{1–3} While only a handful of case reports have mentioned PIM, there are even fewer on anaplastic cases. We report an older patient with anaplastic PIM, who was successfully treated with surgical resection and radiation therapy.

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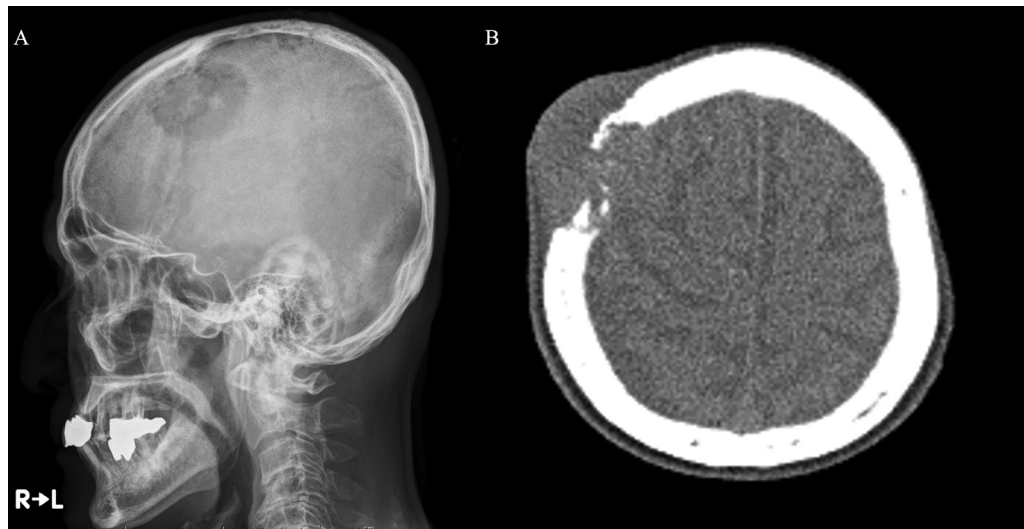


Fig. 1 (A) X-ray photograph showing a 6 × 5 cm osteolytic lesion in the right frontoparietal bone. (B) CT scan showing a large osteolytic lesion with bone destruction. CT, computed tomography.

Case Report

A 78-year-old man, presenting with a growing hard mass in the right frontoparietal bone, was admitted. He had a history of head injury 7 months previously and the mass had appeared 4 months before admission. He did not demonstrate abnormality on a bedside examination. Past medical history, occupational history, and family history were unremarkable. There was no history of weight loss. Routine blood tests were within the normal range.

An X-ray photograph of the skull showed a 6 × 5 cm osteolytic lesion in the right frontoparietal bone, just across the coronal suture (►**Fig. 1A**). Bone window computed tomography (CT) scan showed a large osteolytic lesion with bone destruction in the same area (►**Fig. 1B**). Magnetic resonance imaging (MRI) using gadolinium–diethylenetriamine pentaacetic acid showed heterogeneous enhancement of the intraosseous mass and homogeneous enhancement of the dura mater (►**Fig. 2D–F**). Brain invasion was not definitively

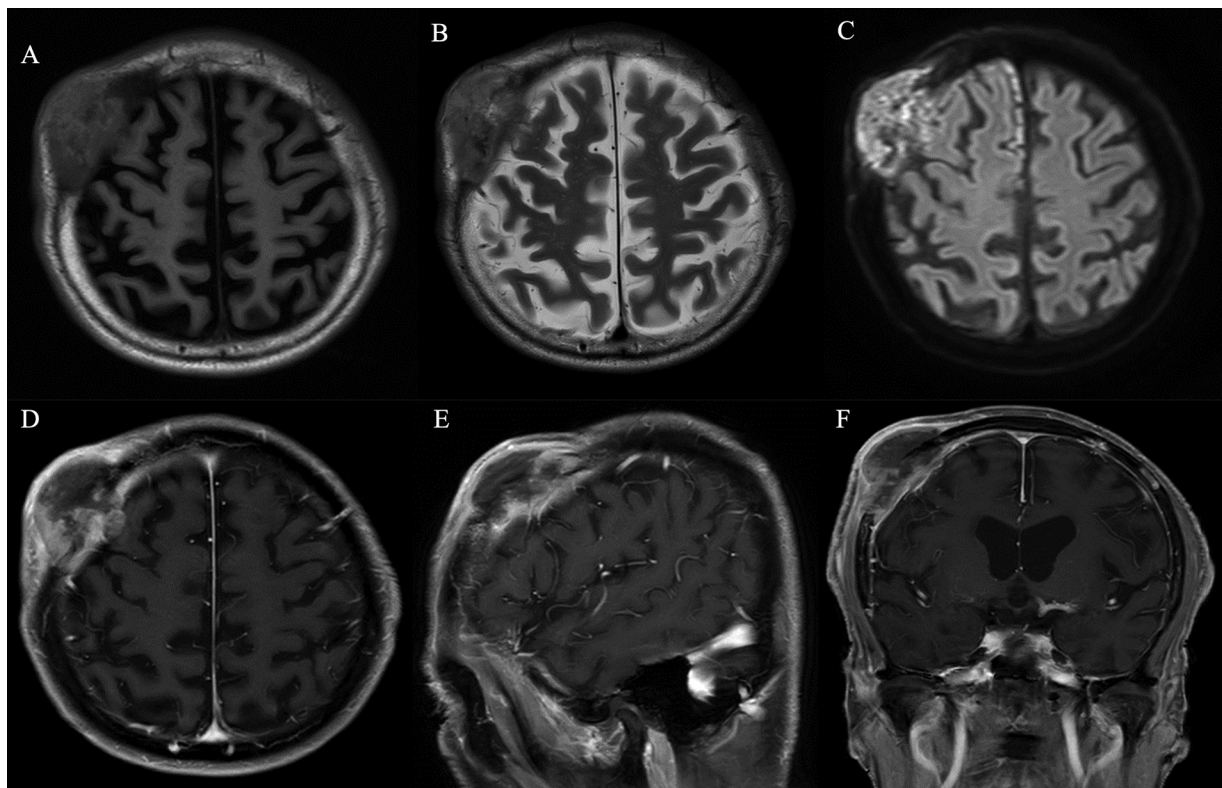


Fig. 2 (A) T1-weighted MRI showing isointensity. (B) T2-weighted MRI showing isointensity. (C) FLAIR images showing heterogeneous high intensity. (D–F) T1-weighted MRI with gadolinium showing heterogeneous enhancement of the intraosseous mass and homogeneous enhancement of the dura mater. FLAIR, fluid attenuated inversion recovery; MRI, magnetic resonance imaging.

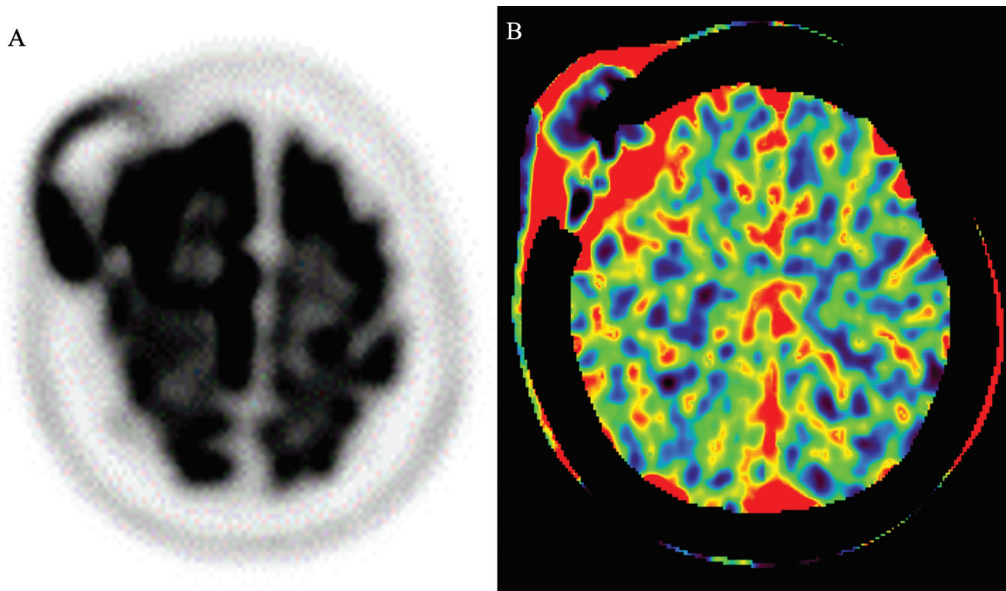


Fig. 3 (A) PET-CT demonstrating a mass lesion with intermediate uptake. (B) Perfusion CT demonstrating an increase in CBV. Note the high vascularity. CBV, cerebral blood volume; CT, computed tomography; PET-CT, positron emission tomography–computed tomography.

revealed. Whole-body contrast-enhanced CT and positron emission tomography (PET) contrast-enhanced CT revealed no solid malignancy except for in the skull. Perfusion CT showed an increase in tumor blood volume, which indicated high vascularity (►Fig. 3B). Given the unusual radiological findings, meningioma, osteosarcoma, metastatic tumor, malignant lymphoma, and epidermoid tumor were listed as possible differential diagnoses.^{2,4}

The patient underwent surgery to obtain a pathological diagnosis and for complete removal of the mass. Tumor invasion was seen subcutaneously, subdurally, and at the surface of the brain (►Fig. 4A, C). The subcutaneous tumor was dissected from the pericranium and removed under the galea. A right frontoparietal craniotomy was performed with multiple burr holes (►Fig. 4B). A round dural incision was made around the tumor invasion. Intraoperative findings showed that the tumor had invaded the brain (►Fig. 4C). Since the cortical vein adhered tightly to the tumor, a small portion of the tumor was not able to be removed. As a result, gross total resection of the extracranial tumor and partial resection of the intracranial tumor were performed. Cranioplasty with a titanium mesh plate

was performed. Postoperative MRI confirmed subtotal removal of the tumor (►Fig. 5).

Histopathological diagnosis was a World Health Organization (WHO) grade 3 anaplastic meningioma. Immunohistochemistry showed positivity for CAM5.2 (►Fig. 6D), AE1/AE3, vimentin, and claudin-1, and negativity for CD34 and signal transducer and activator of transcription 6 (STAT-6). Ki-67 expression was found in approximately 64% of cells (►Fig. 6E) and increased mitotic activity (>20 mitoses/10 high-power fields) was revealed (►Fig. 6C). The tumor cells focally expressed epithelial membrane antigen (EMA), which is one of the diagnostic markers of meningioma. However, only the Golgi apparatus showed EMA staining, not the membrane. CAM 5.2 and AE1/3 are reliable markers of epithelial content, and metastatic lesions also show immunopositivity for them. Since whole-body PET-CT and contrast-enhanced CT ruled out metastases from any solid malignancy, the histopathological diagnosis was meningioma.

We also performed whole-genome analysis with specimens, as part of the HOPE project.⁵ *NF2* was amplified and loss of *CDKN2A/B* was detected (►Fig. 7). *NF2* amplification is frequently seen in meningiomas.

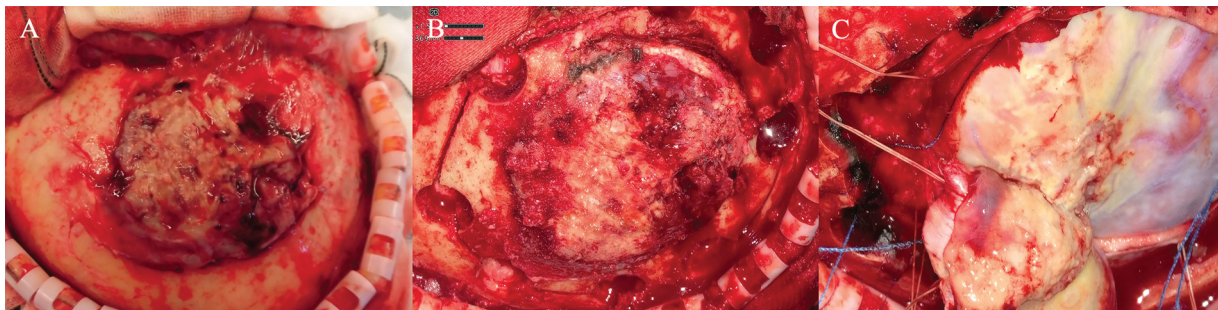


Fig. 4 Intraoperative findings with ORBEYE. (A) The tumor was exposed outside of the skull. (B) A right frontoparietal craniotomy was performed with multiple burr holes. (C) The tumor had invaded subdurally and into the brain and adhered tightly to the cortical vein.

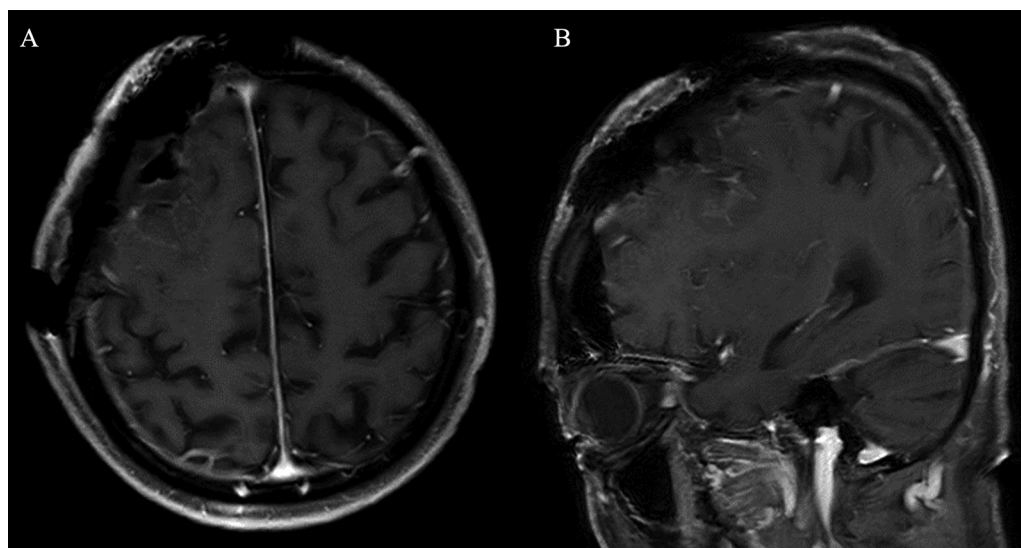


Fig. 5 Postoperative T1-weighted MRI with gadolinium showing subtotal removal of contrast-enhanced lesions. MRI, magnetic resonance imaging

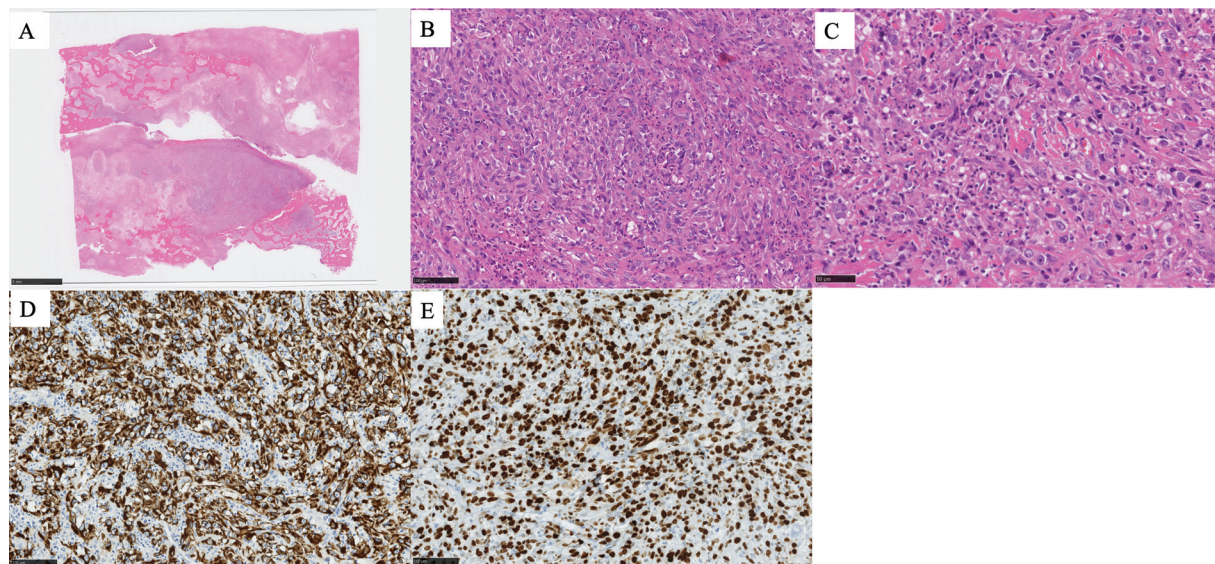


Fig. 6 (A) Hematoxylin and eosin (H&E) stain showing infiltration of atypical cells into and outside of the skull ($\times 0.4$). (B) H&E stain showing proliferation of atypical cells ($\times 20$). (C) H&E stain showing increased mitotic activity (>20 mitoses/10 high-power fields) ($\times 40$). (D) CAM 5.2 stain showing strong positivity ($\times 40$). (E) Ki-67 expression is found in $\sim 64\%$ of cells ($\times 40$). Note the high proliferative ability.

The postoperative course was uneventful and the patient was discharged home 2 weeks after the surgery. One month after the surgery, the patient underwent intensity-modulated radiotherapy (IMRT) with a total dose of 60 Gy in 30 fractions for the residual tumor. Follow-up MRI 9 months after the radiation therapy showed no recurrence of the tumor.

Discussion

According to the 2021 WHO classification, anaplastic meningiomas are diagnosed with increased mitotic activity (>20 mitoses/10 high-power fields), loss of *CDKN2A/B*, or *TERT* promoter mutation.⁶ WHO grade 3 PIM is extremely rare. Omofoye et al reviewed 111 cases of PIM and found that only two of them were WHO grade ^{3,7,8} (–Table 1). In our

case, the tumor component was localized mainly in the skull. The histopathological diagnosis was anaplastic intraosseous meningioma, but undifferentiated sarcoma of intraosseous origin was also considered. However, since *NF2* was amplified, undifferentiated sarcoma was unlikely. Finally, based on the extensive immunohistochemistry panel and review by pathologists, the diagnosis of anaplastic intraosseous meningioma was reached.

Grade 3 meningiomas generally exhibit high rates of recurrence and mortality. In one report, grade 3 meningiomas and one-third of grade 2 meningiomas recur within 20 months.³ The recurrence rate was found to be significantly associated with the WHO tumor grade. In another report, aggressive atypical or anaplastic meningiomas were reported to have high mortality of 29%.⁹ As for molecular

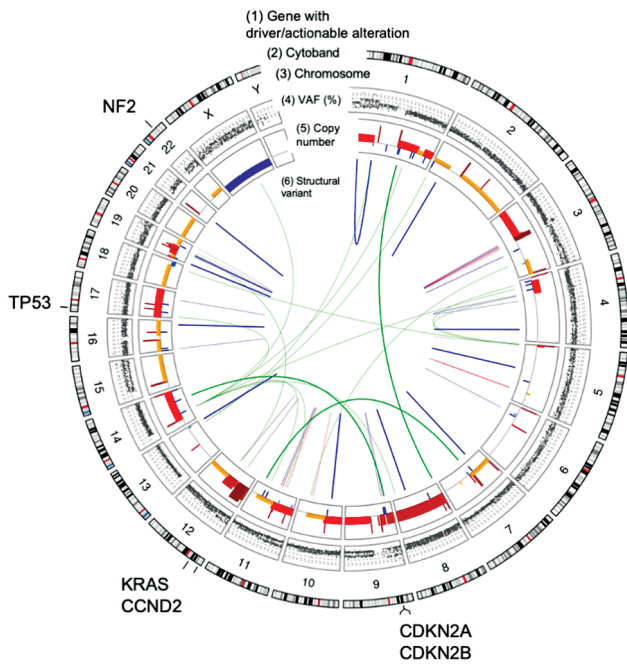


Fig. 7 In the whole-genome analysis with specimens, *NF2* was amplified and loss of *CDKN2A/B* was detected.

analysis, several studies have shown that *CDKN2A/B* alteration is correlated with recurrence.¹⁰ In grade 3 meningiomas, deletion of *CDKN2A/B* appears to have prognostic value.¹¹

Histopathological diagnosis without molecular classification has been established for meningiomas. Meanwhile, molecular diagnostics have also been incorporated that. Meningioma is classified as a benign tumor and can be completely treated by surgical removal, if gross total resection is achieved. However, in cases of repeated recurrence and those where the tumor is difficult to remove, such as skull base meningioma, the value of genomic diagnosis, and the possibility of subsequent molecular-targeted therapy are considered.

In general, meningiomas arise from arachnoid cap cells, most of which occur in the subdural space. Meningiomas that occur in the epidural space are rare due to the result of the ectopic arachnoid cap cells.^{1,3} Lang et al. collectively defined them as PEM.¹² In our case, the tumor that initially developed inside the skull extensively invaded outside the skull. Intraoperatively, a high proportion of the tumor component was clearly present in the skull, and we made a diagnosis of PIM. Several theories have been proposed on the exact origin of PIM.¹³⁻¹⁵ First, it was suggested that these cases originate from arachnoid cap cells that get trapped in the cranial sutures during embryogenesis or molding of the cranium at birth. Another theory proposed that they originate from arachnoid cap cells through blood vessels or nerves that cross the skull.¹³⁻¹⁵ Trauma with skull fracture has also been proposed as a causative factor. In this case, part of the dura mater would be taken into the fracture at the time of trauma, subsequently forming a tumor over time.^{16,17} The cause of our case is unclear, although there are several theories.

Table 1 The reported cases of primary intraosseous meningioma, World Health Organization grade 3

Case	Age	Sex	Symptom	Tumor location	Cranial suture involved	EOR	Pathology	Time to recurrence	Publication year
1	42	Male	Facial nerve paresis	Rt temporal	Yes	STR	Anaplastic	1.3 y	1993 ⁷
2	70	Female	Scalp mass	Lt parietal	No	GTR	Anaplastic	2.5 y	2006 ⁸
Present case	78	Male	Scalp mass	Rt frontoparietal	Yes	STR	Anaplastic	N/A	N/A

Abbreviations: EOR, extent of resection; GTR, gross total resection; Lt, left; N/A, not available; Rt, right; STR, subtotal resection.

We successfully treated the presented case with tumor resection, followed by IMRT. Preoperatively, the tumor grew larger in a short period of time and imaging findings suggested an atypical or anaplastic meningioma. Therefore, early diagnosis, total removal, and subsequent radiotherapy were required. Cranioplasty with a titanium plate was also required. Generally, anaplastic meningioma portends a high likelihood of recurrence and the possibility of extracranial metastasis, most commonly involving the lung, liver, and bones.¹⁸ Not only MRI of the surgical site but also radiological follow-up for metastases to other organs is needed to ensure meticulous care. In addition, calvarial meningioma often develops as a painless tumor, which exerts less pressure on the brain.¹⁶ Neurological signs are often rare and the diagnosis may be delayed. When encountering these cases in a clinical context, care is required.

Conclusion

We experienced a rare case of primary intraosseous anaplastic meningioma with extensive invasion inside and outside the skull. As for the origin of such cases, several theories have been proposed. Early diagnosis, total removal, and subsequent radiotherapy may contribute to an improved outcome. In addition, meticulous care is needed in such cases because of the high recurrence rate and the possibility of extracranial metastasis.

Conflict of Interest

None declared.

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