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Yoichi Morofuji

Usefulness of intraoperative photodynamic diagnosis using 5-aminolevulinic acid for meningioma with skull invasion: Case report

Yoichi Morofuji, M.D.
Department of Neurosurgery,
Nagasaki University School of Medicine,
Nagasaki, Japan

Takayuki Matsuo, M.D.
Department of Neurosurgery,
Nagasaki University School of Medicine,
Nagasaki, Japan

Yukishige Hayashi, M.D.
Department of Neurosurgery,
Nagasaki University School of Medicine,
Nagasaki, Japan

Izumi Nagata, M.D.
Department of Neurosurgery,
Nagasaki University School of Medicine,
Nagasaki, Japan

Corresponding Author
Yoichi Morofuji, M.D.
Department of Neurosurgery,
Nagasaki University School of Medicine,
1-7-1 Sakamoto,
Nagasaki, 852-8501, Japan.
E-mail: yoichi51@nagasaki-u.ac.jp
Tel: 81-95-849-7375
Fax: 81-95-849-7378

ABSTRACT
OBJECTIVE: We present a case of meningioma where photodynamic diagnosis (PDD) using 5-aminolevulinic acid (5-ALA) was very useful in identifying the skull involvement.
CLINICAL PRESENTATION: An 83-year-old woman presented with a bony hard and immobile bulge in the left forehead. Computed tomography (CT) showed a thickening in the left frontal bone with a flat mass underneath. Magnetic resonance imaging (MRI) revealed that enhancing lesions spread to the dura mater and subcutaneous tissue around the thickened frontal bone, reaching the upper margin of the left orbit.
INTERVENTION: Intraoperative PDD using 5-ALA indicated optimal extent of the excision by showing clear fluorescence of affected tissues. The tumor was totally resected and diagnosed as atypical meningioma. Histopathological examination confirmed consistency of the extent of tumor invasion with affected lesions on PDD.
CONCLUSION: To the best of our knowledge, this is the first case demonstrating the efficacy of PDD using 5-ALA for meningioma with skull invasion. Further studies are warranted as shown in malignant gliomas.

Running title: Photodynamic diagnosis for skull invasion

Key words: 5-aminolevulinic acid, intraoperative photodynamic diagnosis, meningioma, skull invasion

Usefulness of intraoperative photodynamic diagnosis using 5-aminolevulinic acid for meningioma with skull invasion: Case report

Photodynamic diagnosis (PDD) using 5-aminolevulinic acid (5-ALA) has been performed much more frequently in recent years, and it has become an important intraoperative technique. In the field of neurosurgery, due to its convenience and usefulness, PDD is being performed on patients with malignant glioma at many institutions (2, 4, 7, 8, 9). However, to the best of our knowledge, there have been no studies on PDD using 5-ALA in patients with skull lesions. Here, we present a case of meningioma where PDD using 5-ALA was very useful in identifying skull involvement.

Clinical Presentation

An 83-year-old woman complained of headache and a bulge on the left side of the forehead. She had no notable past medical history including head trauma, and prior cranial magnetic resonance imaging (MRI) did not show any abnormalities. She was referred to our department because of the subcutaneous mass with a diameter of about 3 cm had become painful in June, 2006. It was bony hard, immobile and not tender. Cranial computed tomography (CT) showed well demarcated thickening in the left frontal bone, and a flat mass exhibiting isodensity immediately underneath. Destruction of both the inner and outer tables of the skull was confirmed. Contrast-enhanced MRI showed even enhancement spreading to the dura mater and subcutaneous tissue around the thickened bone, reaching the upper margin of the left orbit. Diffuse meningeal enhancement was also seen adjacent to the tumor (Figure 1), suggesting of a rapidly progressing meningioma. In order to intraoperatively determine the extent of tumor excision, PDD using 5-ALA was planned and the written informed consent was obtained. The protocol of the PDD using 5-ALA was approved by the Ethics Committee of the Nagasaki University.

Intervention

Three hours before the induction of anesthesia, 20mg/kg of 5-ALA was administered orally. She was kept in a dark room for 48hours after drug administration to avoid possible skin phototoxicity. After the scalp incision was made, adhesion between the skull lesion and galea was seen in the area of bone thickening. The skull lesion along with the dura mater was excised as a single mass. Intraoperative PDD showed that tumor itself was highly fluorescent, but the dura mater surrounding the tumor was not (Figure 2). PDD also clearly showed fluorescence from the dipole to the inner table at the stump of the upper orbital margin (Figure 3), while no tumor invasion was observed microscopically. Drilling was performed until the fluorescence disappeared while preserving the outer table. Surgery was completed after confirming the absence of residual fluorescence in the surgical field. Postoperative course was uneventful, and MRI did not show any residual tumors (Figure 4). She was discharged in good health on 9 days after surgery and MRI performed 9 months after surgery showed no evidence of tumor recurrence.

Histology

The tumor on the medial surface of the dura mater grew in a turbinated or fascicular manner, and obviously involved the skull. Tumor cells densely existed from the dipole to the outer table of the skull, and cellular atypia and nuclear fission were seen. The tumor was diagnosed as atypical meningioma (World Health Organization Grade II). No tumor cells were seen in the surrounding the dura mater including the area where contrast enhancement was observed on MRI preoperatively. Tumor cells did exist in the fluorescent orbit-side stump, while no tumor cells were observed in the non-fluorescent bone stump (Figure 5).

Discussion

Fluorescent dyes have long been used to identify brain tumors, first attempted by Moore in 1948 (6). Since then, fluorescent materials and light sources have been developed and improved. At present, PDD using 5-ALA is accepted for its convenience and usefulness, particularly in excising malignant gliomas (2, 7, 8). In addition, randomized control studies on PDD have documented favorable results in glioma excision and progression-free survival (9). To the best of our knowledge, however, no studies on PDD for meningioma with skull invasion have been demonstrated.

In skull tumors or brain tumors with skull involvement, the extent of bone resection is mostly determined based on preoperative imaging and intraoperative findings. However, in clinical settings, it is often difficult to determine the boundary between normal bone and tumor tissues. Therefore, we used PDD in order to identify the extent of skull invasion in the present case. As intraoperative PDD showed lesional fluorescence in the operative field, additional bone resection was needed including the superior wall of the left orbit. By confirming the negative fluorescence within the surgical field, the tumor was completely excised. Histopathological examination confirmed that PDD accurately assessed the extent of skull involvement of the meningioma. While rapid intraoperative pathological diagnosis of bone lesions without demineralization was not technically feasible, the degree of bone invasion was easily assessed on PDD.

Linear thickening and contrast enhancement of the meninges adjacent to meningioma has been called the ‘dural tail signs’, ‘dural thickening’, ‘flare’, or ‘meningeal sign’. However, histological basis of the dural tail with meningioma is not completely understood. In the present case, preoperative contrast-enhanced MRI showed an enhancement of the dura mater adjacent to the meningioma. During the operation, tumor itself was strongly fluorescent, while surrounding dura mater was not. Pathological examination confirmed the existence of tumor cells in the fluorescent area, but none were seen in the non-fluorescent dura mater. These things suggest that PDD using 5-ALA is quite useful in determining the extent of dura mater involvement in meningioma surgery.

5-ALA has been reported to have several adverse effects, such as skin sensitivity (phototoxicity), nausea, vomiting, and transient liver dysfunction. 5-ALA also produces protoporphyrin IX which may increase the risk of phototoxic skin reactions within 48 hours of induction. Therefore, we kept the patient after the administration of 5-ALA in dark surroundings for 48 hours. We have used PDD using 5-ALA according to low-dose regimen in 75 cases so far, but we have never experienced such serious adverse effects.

The reliability of PDD using 5-ALA has not fully verified. Positive reactions to photosensitive materials in non-tumor tissue, in addition, 85% sensitivity even in malignant gliomas have been reported (1, 3, 5, 7). Nevertheless, to the best of our knowledge, this is the first case demonstrating the usefulness of PDD using 5-ALA for meningioma with skull invasion. PDD using 5-ALA is convenient and inexpensive, and because most adverse reactions are avoidable, it may be applied in diagnosing brain tumors other than malignant gliomas.

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FIGURE LEGENDS

FIGURE 1. Preoperative T1-weighted axial (A) and sagittal (B) MRI with gadolinium showed thickened frontal bone. Enhancement was spreading to the dura mater and subcutaneous soft tissue around the thickened bone. Broad meningeal enhancement was also seen.

FIGURE 2. The tumor fluorescence was evaluated intraoperatively. A, the removed tumor under white light. B, intraoperative PDD confirmed the tumor itself was highly red fluorescent.

FIGURE 3. A, the surgical field after removal of the bone flap. B, PDD showed red fluorescence from the dipole to the inner table at the stump of the upper orbital margin.

FIGURE 4. Postoperative T1-weighted axial (A) and sagittal (B) MRI with gadolinium showed no residual tumor.

FIGURE 5. Photomicrographs of the tumor. Microscopic features showed dense tumor cells, cellular atypia and nuclear fission (A, B). No tumor cells were seen in the non-fluorescent dura mater stump (C) and bone stump (D). Tumor cells were seen in the fluorescent orbit-side stump (E). Hematoxylin-eosin staining ; original magnifications, x25 (A, C, D and E) and x200 (B).

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ARTICLE SUMMARY
We present the first case of meningioma where PDD using 5-ALA was very useful in identifying skull involvement. PDD using 5-ALA may be useful in not only malignant glioma, but also meningioma with skull invasion.

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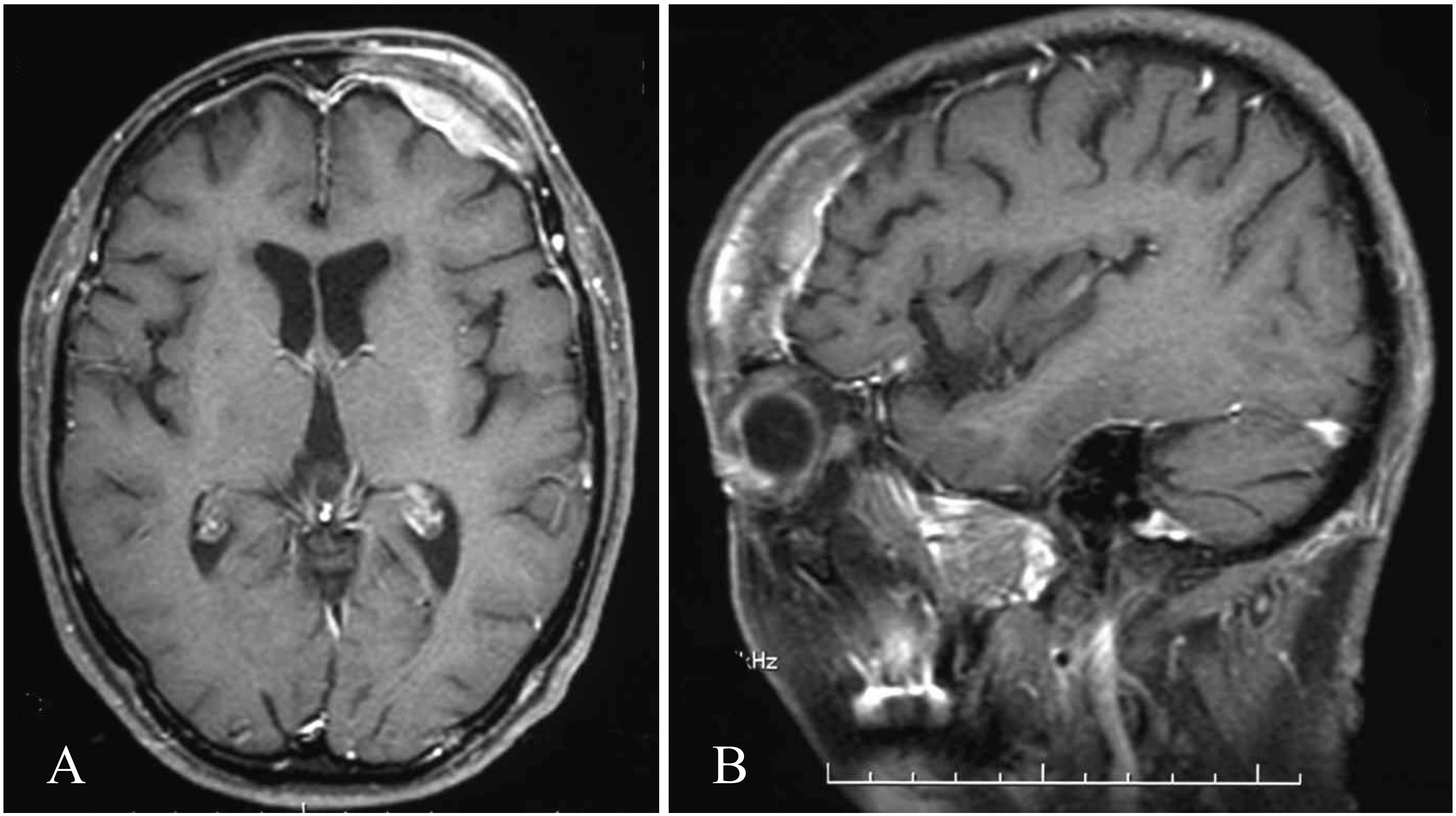

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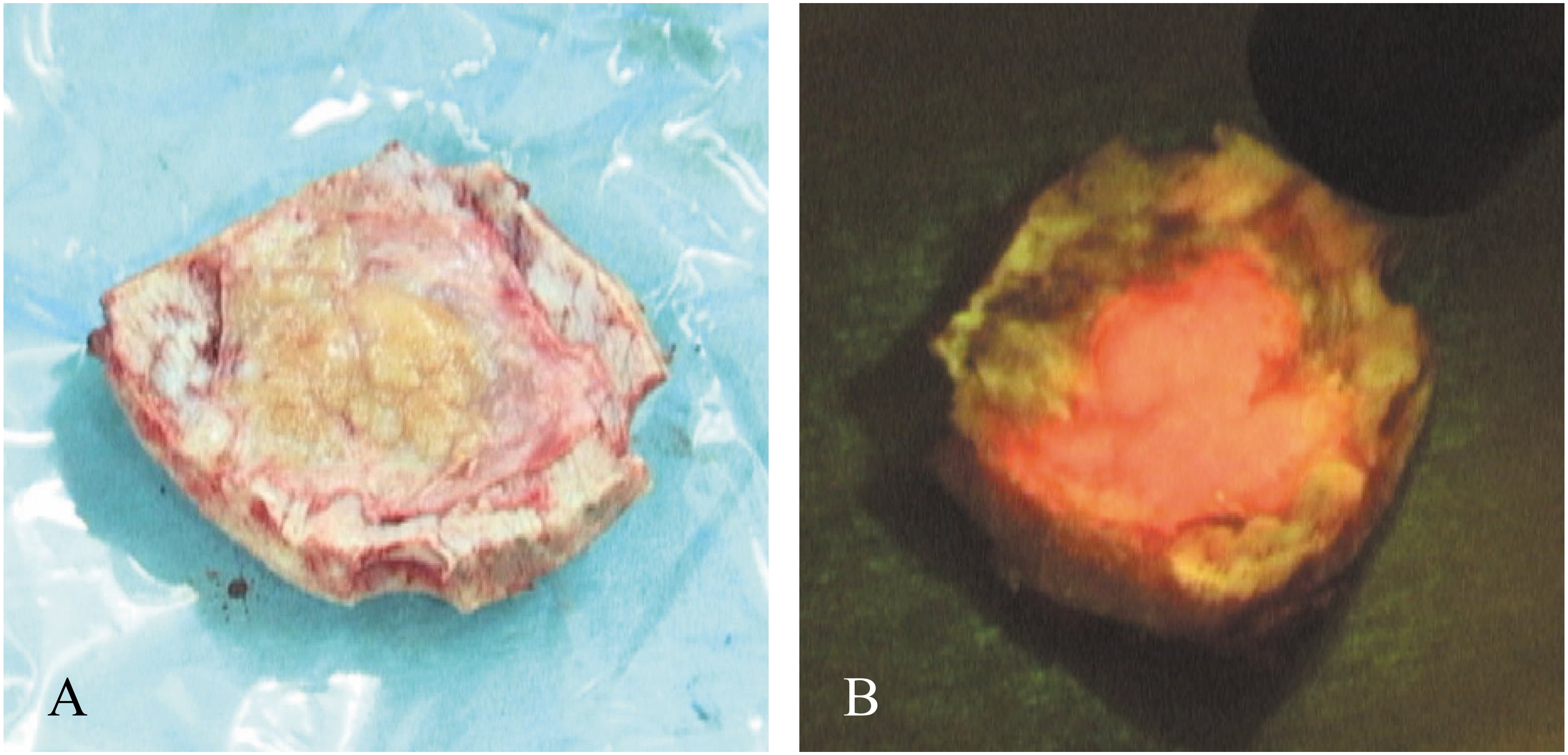

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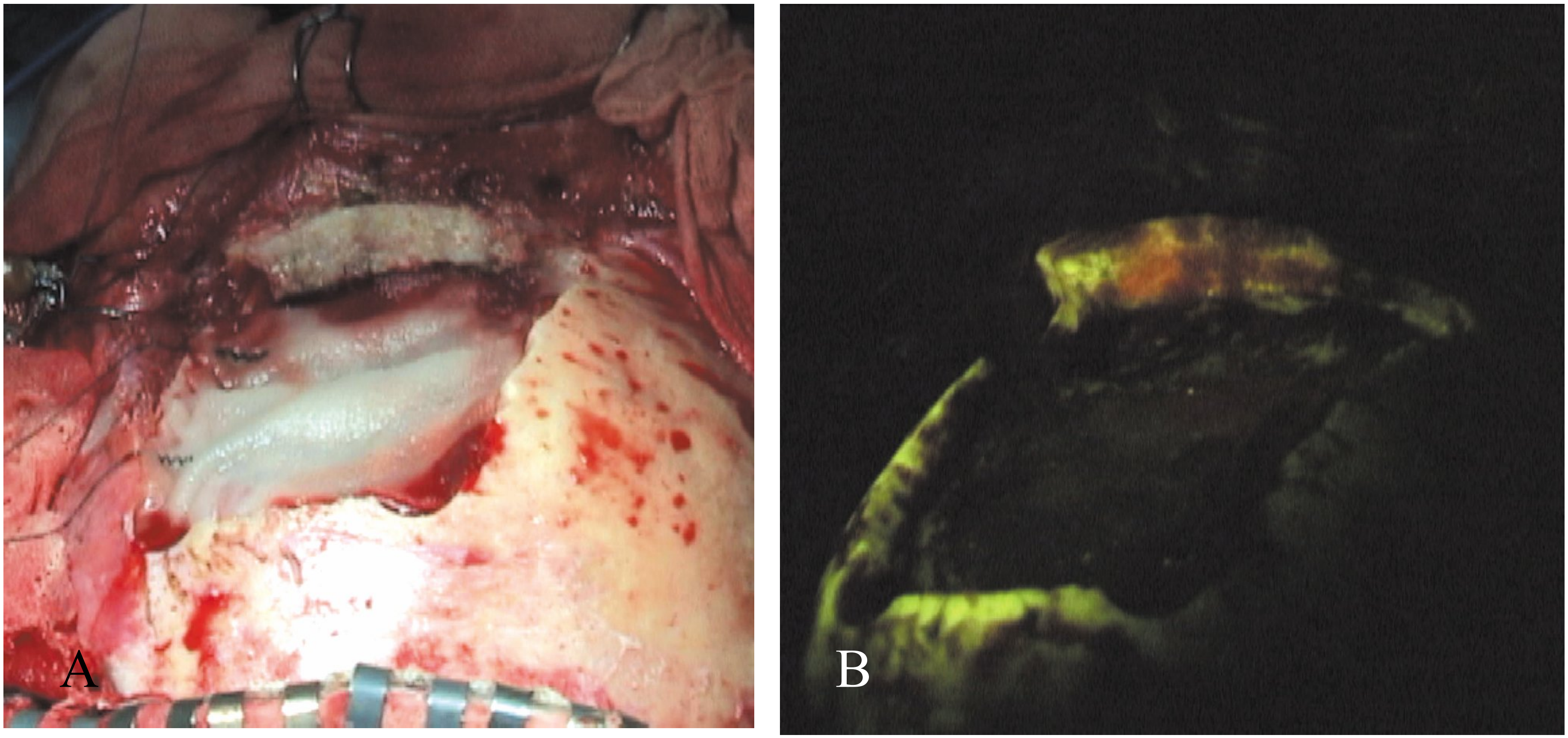

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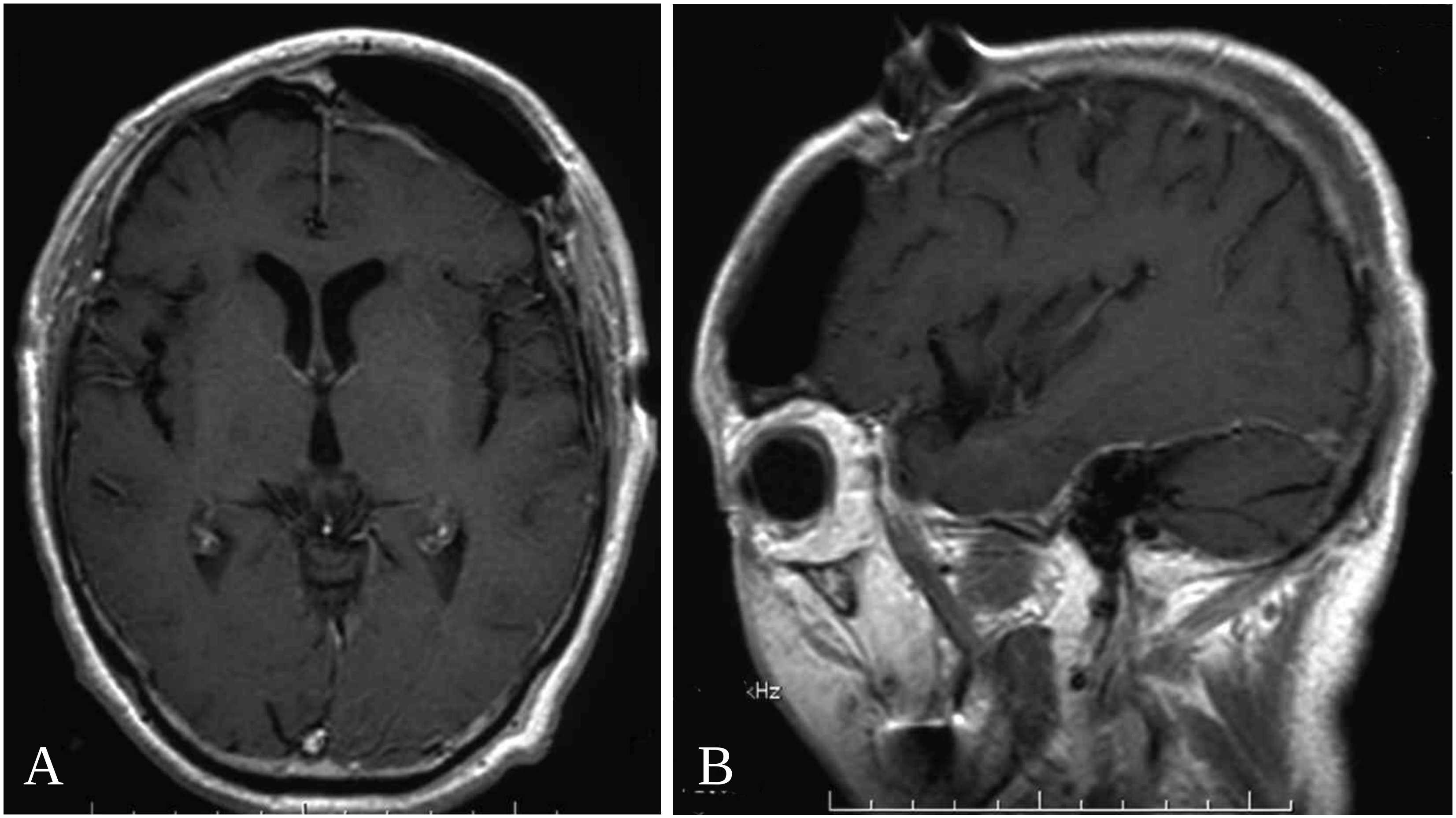

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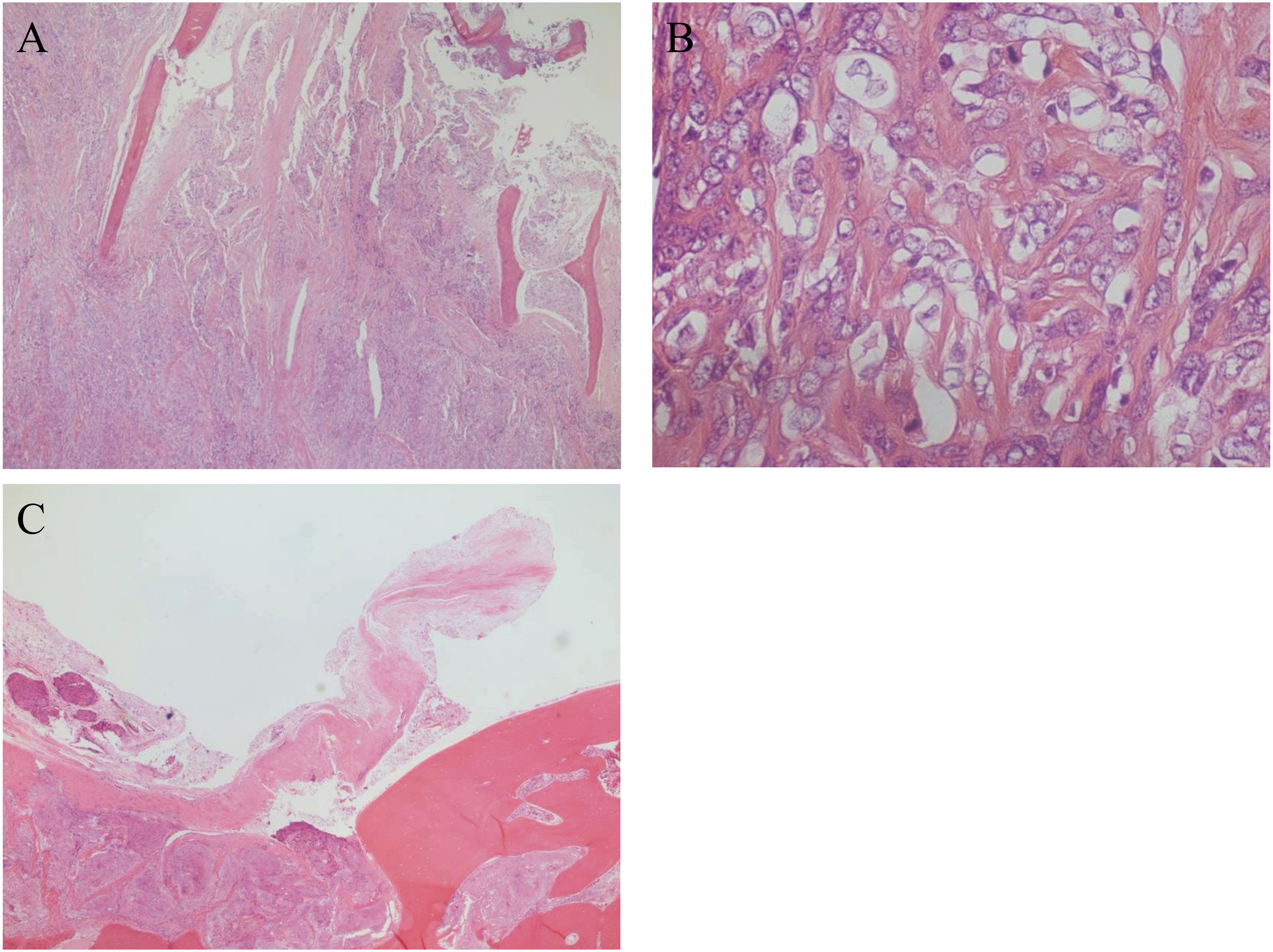

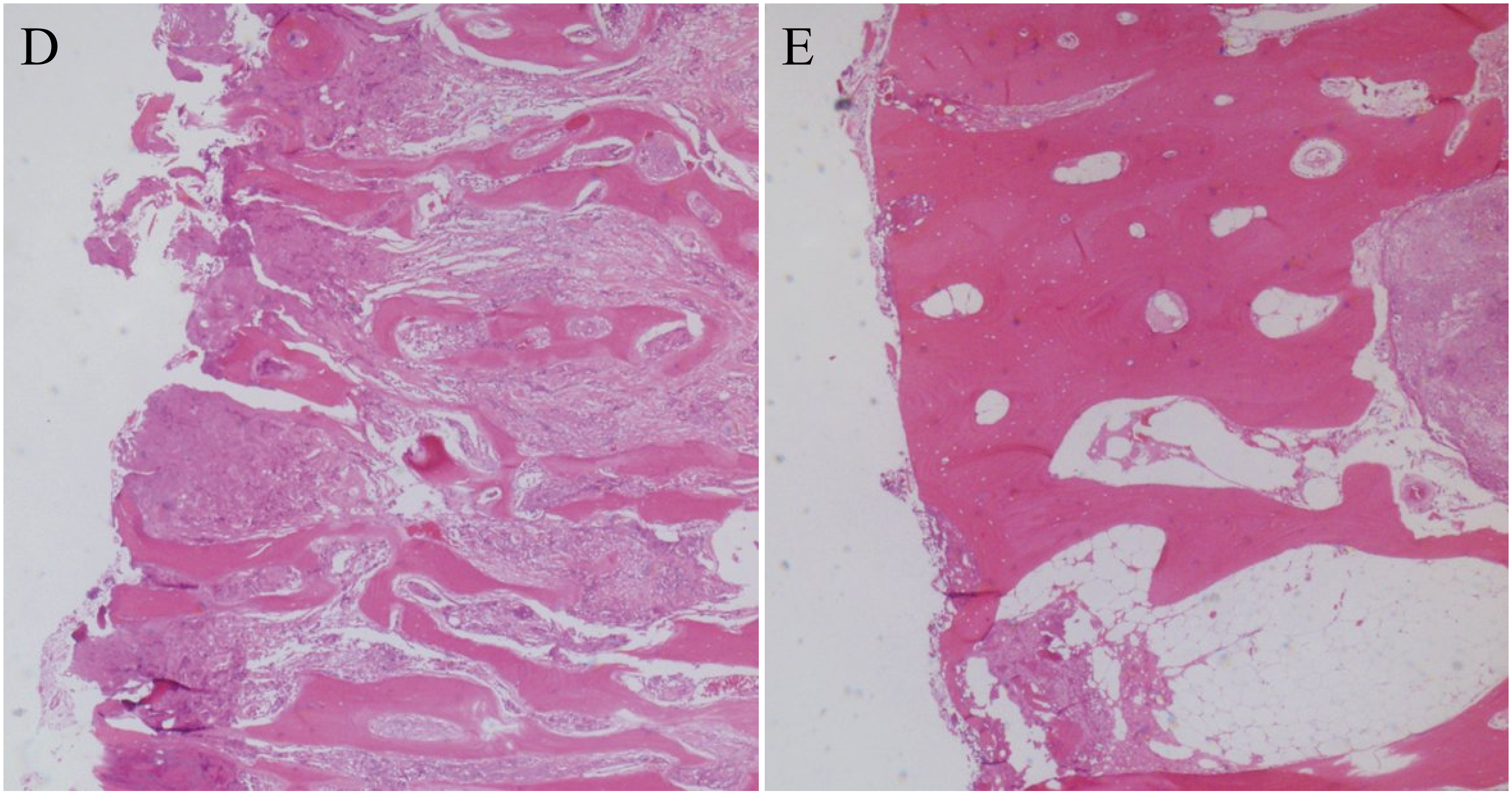
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