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Papillary Glioneuronal Tumor Masquerading as Malignant Brain Tumors: A Case Report

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ABSTRACT
Papillary glioneuronal tumor (PGNT) is a low-grade biphasic tumor that is composed of glial fibrillary acidic protein (GFAP)-positive glial cells and synaptophysin-positive neurons. We report a case of PGNT occurring in the right occipital lobe of a 48-year-old woman who presented with acute headache and left homonymous hemianopsia, the latter of which was difficult to distinguish from malignant brain tumors because of peritumoral brain edema, intratumoral hemorrhage, and intraoperative fluorescence staining. PGNT should be included as one of the differential diagnoses in cases where the tumor shows hemorrhagic change despite decreased perfusion in arterial spin labeling MRI.

Key words decreased perfusion; intratumoral hemorrhage; papillary glioneuronal tumor

Papillary glioneuronal tumor (PGNT) is a low-grade biphasic tumor that is composed of glial fibrillary acidic protein (GFAP)-positive glial cells and synaptophysin-positive neurons. PGNT was first reported in 1998 by Komori et al.,[1] and it is recently identified in the World Health Organization (WHO) 2021 classification as a grade 1 mixed glial–neuronal neoplasm of young adult patients. In this report, we present a case of PGNT with the symptom of acute headache, which was difficult to distinguish from malignant brain tumors.

PATIENT REPORT
A 48-year-old right-handed woman began to suffer from severe headache and consulted a doctor the following day. Computed tomography (CT) scan revealed a cystic lesion with intralesional hemorrhage and calcification in the right occipital lobe (Fig. 1A), and she was referred to our hospital and admitted for surgery. On admission, she was conscious with no motor paralysis and sensory disturbance, but neurological examination showed left homonymous hemianopsia. Brain magnetic resonance imaging (MRI) scan revealed cystic and solid components with peritumoral brain edema (Fig. 1C), and these components were contrast-enhanced using a contrast medium (Figs. 1B and D). In susceptibility-weighted imaging (SWI), a low-intensity lesion, possibly indicative of intratumoral hemorrhage, was extensively noted (Fig. 1E) despite hypoperfusion in arterial spin labeling MRI (Fig. 1F). Based on the tumor contrast enhancement, peritumoral brain edema, and intratumoral hemorrhage, a malignant glioma or a metastatic brain tumor was suspected. The patient underwent tumor removal in the prone position. As malignant glioma was strongly suspected, the cystic tumor and surrounding normal brain tissues were removed until the cerebral falx and cerebellar tentorium were visible on the median and caudal side, respectively (Fig. 2A). The residual yellowish solid component adjacent to the ventricular wall emitted red fluorescence during intraoperative photodynamic testing (Fig. 2B); this finding could easily be misdiagnosed as malignant glioma. The solid tumor was additionally detached from the ventricular wall to achieve gross total removal of the tumor. In addition, as rapid intraoperative diagnosis suggested a malignant glioma (Fig. 3A), the opened ventricle was closed and carmustine (BCNU) wafers were placed to complete the operation. The pathological examination revealed a predominant papillary pattern characterized by multiple layers of GFAP-positive glial cells lining markedly thickened hyalinized vessels (Figs. 3B–D). In addition, synaptophysin-positive neurons were observed between the pseudopapillary structures (Fig. 3E). Immunohistochemical examination revealed a high expression of CD34 (Fig. 3F). The MIB-1 staining index was extremely low. Based on the histological findings above mentioned, a diagnosis of PGNT was achieved. The patient was observed without postoperative chemoradiotherapy, and at the 1-year follow-up, MRI revealed no obvious recurrent lesions (Fig. 1I).

DISCUSSION
PGNT is characterized by the pseudopapillary proliferation of GFAP- and S100 protein-positive astrocytes and

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Abbreviations: GFAP, glial fibrillary acidic protein; PGNT, papillary glioneuronal tumor

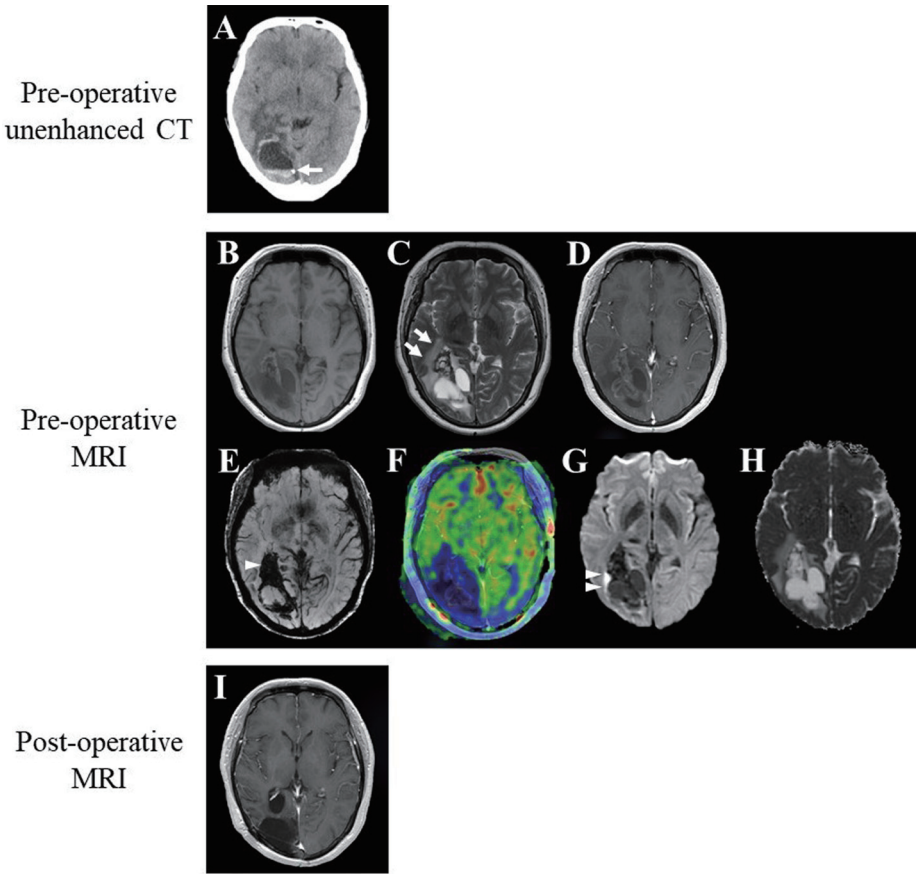

Fig. 1. Preoperative CT and MRI imaging are shown in **A–H**. Unenhanced CT (**A**) shows a cystic space-occupying lesion with hemorrhagic change and calcification (white arrow) in the right occipital lobe. T1- and T2-weighted imaging (**B** and **C**) and contrast-enhanced T1-weighted imaging (**D**) show heterogeneously enhancing lesion with peritumoral brain edema (double white arrow). In susceptibility-weighted imaging (**E**), a low-intensity lesion (white arrowhead), possibly indicative of intratumoral hemorrhage, is extensively noted despite hypoperfusion in arterial spin labeling MRI (**F**). On diffusion-weighted imaging (**G**), the tumor itself shows no diffusion restriction. The perifocal edematous lesion shows partial diffusion restriction (double white arrowhead) with iso-intensity on the apparent diffusion coefficient map (**H**), indicating a T2 shine-through effect. Postoperative contrast-enhanced MRI 1 year after the surgery shows no obvious recurrent lesion (**I**).

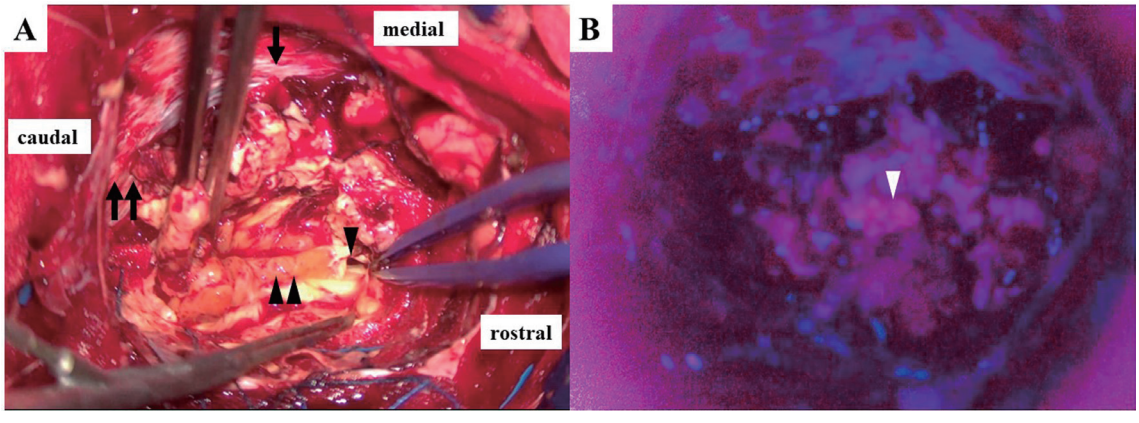

Fig. 2. Intraoperative photographs are shown. The right occipital lobe tumor is resected until the cerebral falx (**A** black arrow) and cerebellar tentorium (**A** double black arrow) are visible on the median and caudal side, respectively. The residual deep-seated tumor with 5-ALA positive fluorescence (**A** double black arrowhead; **B** white arrowhead) is resected, and the posterior horn of the lateral ventricle (**A** black arrowhead) is opened.

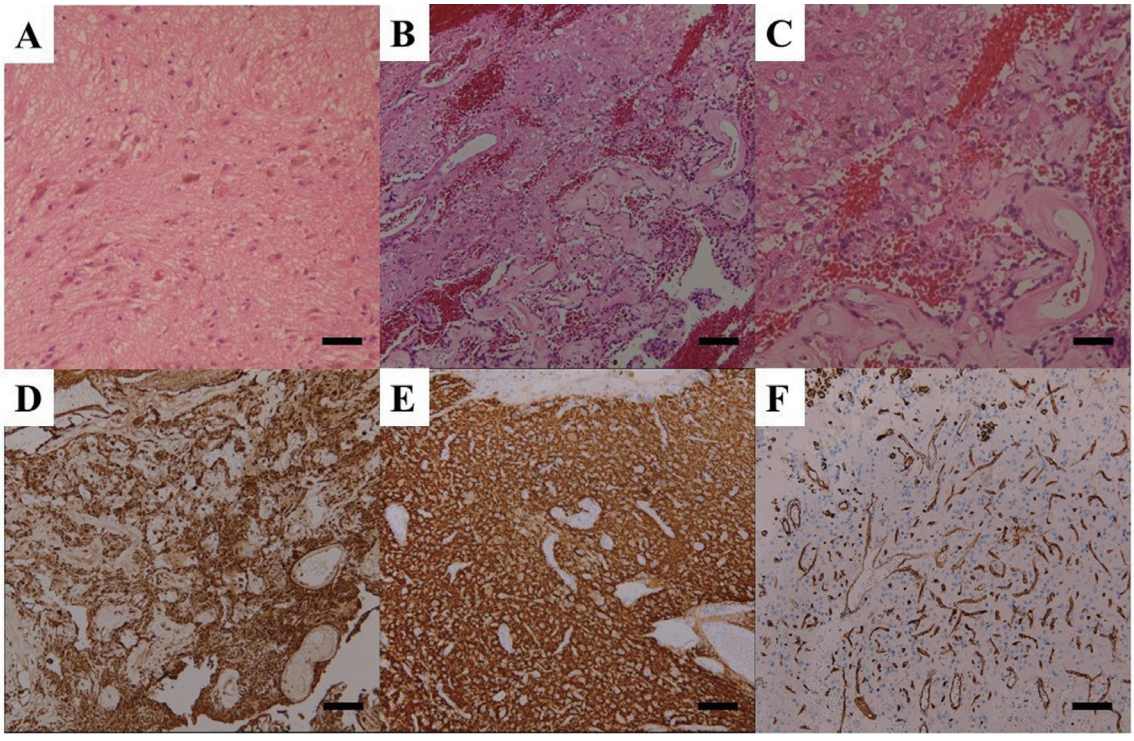

Fig. 3. The intraoperative rapid pathological examination shows proliferation of large or small glia-like cells (**A**). Photomicrographs show GFAP-positive glial cells lining hyalinized vessels and synaptophysin positive nerve cells in the GFAP-negative areas (**B** and **C** hematoxylin and eosin staining; **D** GFAP staining; **E** synaptophysin staining). Immunohistochemical examination reveals a high expression of CD34 (**F**). Bar = 50 μm (**A, C**) and 100 μm (**B**, **D–F**).

the proliferation of synaptophysin- and NeuN-positive neurons around hyalinized vessels.[2] According to the 2021 WHO classification of central nervous system tumors, PGNT is classified as a grade 1 tumor, and total resection is generally considered to be conducive to a favorable prognosis. The mean age of patients at the onset is relatively lower (26.9 ± 16.3 years), and the male-to-female ratio is 1.42:1.[3] The most common site of occurrence of PGNT is the frontal lobe (32.1%), followed by the temporal (21.6%) and parietal (11.9%) lobes.[3] Overall, PGNT occurs near the cerebral ventricles in 78.4% of cases,[4] suggesting a possible origin from the germinal zone of the subependymal plate.[1] Typical imaging findings include cystic and solid lesions that lack peritumoral edematous changes, with calcification in 25% of the cases.[3] The effects of contrast enhancement in the cystic and solid areas vary from case to case.[5]

In the present case, the patient presented with signs of peritumoral cerebral edema and intratumoral hemorrhage, which led to the misdiagnosis of malignant brain tumors, including malignant glioma, malignant lymphoma, and metastatic brain tumor. There have been sporadic reports of PGNT cases with similar findings as follows. Myung et al. reported that 13.7% of cases presented moderate or advanced peritumoral edema.[4] In even rarer cases, intratumoral and intraventricular hemorrhage triggered the onset.[6–8] Given the high immunohistochemical expression of CD34 as shown in the present case, peritumoral edema and intratumoral hemorrhage in PGNT cases may result from intratumoral growth of hyalinized microvessels rather than increased feeding vessels surrounding the tumor. Although malignant brain tumors could not be completely ruled out given the possibility of decreased perfusion imaging due to intratumoral hemorrhage, PGNT should be included as one of the differential diagnoses in case that the tumor shows hemorrhagic change despite decreased perfusion in arterial spin labeling MRI. Yadav et al.[9] previously reported a rare case of recurrent PGNT showing focal area of diffusion restriction and raised perfusion. MRI findings above mentioned vary depending on the tumor aggressiveness, and further accumulation of PGNT cases are warranted.

Other than the MRI findings mentioned above, the present case could also have been misdiagnosed as a malignant brain tumor based on the following intraoperative findings: (1) the solid component emitted red fluorescence during the intraoperative photodynamic

diagnosis, and (2) the results of the rapid intraoperative diagnosis using only one sample from one site indicated a malignant glioma. To the best of our knowledge, only one case of intraoperative fluorescence in PGNT has been reported in the relevant literature (Labrador et al.)[10]; therefore, the former finding was extremely rare. Additionally, Labrador et al. reported intraoperative fluorescence in other cases of benign brain tumors.[11] Based on these reports, it should be noted that photodynamic testing is not specific to malignant brain tumors. Regarding the latter finding, if PGNT had been predicted from the preoperative imaging findings mentioned above, an accurate rapid intraoperative diagnosis could have been achieved by using multiple pathological specimens, focusing on the presence of biphasic cell patterns composed of glial and nerve cells.

We reported a case of PGNT with the symptom of acute headache, which was difficult to distinguish pre- and intra-operatively from malignant brain tumors because of peritumoral brain edema, intratumoral hemorrhage, and intraoperative fluorescence staining. In conclusion, hemorrhagic change despite decreased perfusion in arterial spin labeling MRI could be useful for the differential diagnosis of PGNT from other malignant brain tumors.

Informed consent: We explained and received verbal informed consent from the patient.

The authors declare no conflict of interest.

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