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Case Report

Significance of perilesional T1 hyperintense areas in the differential diagnosis of primary adult-type diffuse glioma: A case report ☆,☆☆

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ABSTRACT

Perilesional T1 hyperintensity on magnetic resonance imaging (MRI) of intra-axial brain masses is an unusual feature of the perilesional area, characteristic of cavernous malformations (CMs) and metastatic brain tumors (METs). Here, we report a case of primary diffuse glioma with a perilesional T1 hyperintense area (HIA) on MRI. A 61-year-old woman with transient aphasia visited our hospital. Radiological examination revealed an intra-axial mass with acute/subacute hemorrhaging and calcification in the left frontal lobe. It was presumed to be a CM because of the perilesional T1 HIA. Gross total resection of the tumor was performed, and the pathological diagnosis was anaplastic oligodendroglioma, not otherwise specified by World Health Organization 2016 classification. Histopathological findings in the perilesional T1 HIA indicated hemorrhage involvement in the surrounding white matter. No recurrence appeared after radio-chemotherapy. Perilesional T1 HIAs, characteristic of CMs and METs, are also seen in primary diffuse gliomas. Therefore, caution should be taken when using this sign for the differential diagnosis of intracranial masses.

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Introduction

Preoperative differential diagnosis is essential in deciding the appropriate therapeutic strategy for intra-axial brain masses. Magnetic resonance imaging (MRI) is now used as an optimal modality for diagnosing intra-axial brain masses and advances in MRI sequencing have brought more accuracy to the preoperative process. Brain masses with atypical characteristics are still challenging to diagnose preoperatively, including tumors with recent hemorrhaging.

Perilesional T1 hyperintense areas (HIA) around lesions have been reported as a valuable sign for the differential diagnosis of hemorrhagic masses. This sign has been reported in cavernous malformations (CMs) and metastatic brain tumors (METs) but not primary diffuse gliomas [1–3]. We report a case of primary diffuse glioma that showed a perilesional T1 HIA and was difficult to distinguish from CM.

Case report

A 61-year-old woman who complained of transient aphasia was transferred to our hospital but was asymptomatic on admission and had no significant past medical history. On examination, she was alert and presented no major neurological abnormalities, also denying both headache and nausea. No obvious higher brain dysfunction was detected on admission. Computed tomography (CT) scans revealed a 69 mm diameter intra-axial mass in the left frontal lobe, almost isodense to the brain but containing hematomas and calcifications (Figs. 1A and B). MRI demonstrated a mass showing mixed-signal intensity. The area around the mass showed a high signal intensity on the T2-weighted image (T2WI); however, the same area showed a high signal intensity even on the T1WI (Figs. 2A and B). Gadolinium (Gd)-enhanced MRI showed capsule-like enhancement of the mass while T2*WI detected hemosiderin deposition in the lesion (Figs. 2C and D). The mean T1 signal intensity ratio of the perilesional area to the contralateral white matter was 1.22 (Fig. 2E).

Based on these imaging findings, among several differential diagnoses (including CM and primary glioma), CM seemed the most likely, especially judging from the perilesional T1 HIA and internal calcification. The patient underwent craniotomy and gross total resection of the mass was performed. Intraoperative findings revealed no capsule-like structure around the lesion, but it was gray, slightly hard, and had distinct texturing compared to the surrounding normal white matter. The postoperative course was uneventful. Pathology findings were as follows: anaplastic oligodendroglioma (AOD), not otherwise specified (NOS), World Health Organization (WHO) 2016 classification grade III, same as oligodendroglioma NOS, and central nervous system (CNS) grade 3 as per WHO 2021 (Fig. 3A). Immunohistochemical results also showed mutation of isocitrate dehydrogenase 1 (IDH-1), retained nuclear ATRX, and negative p53 findings. Hemosiderin pigmentation and siderophages were observed in the area that showed perilesional T1 HIA (Fig. 3B).

After surgery, the patient underwent radiotherapy of 60 Gy and 6 cycles of add-on treatment using procarbazine, nimustine, and vincristine. The patient achieved progressive, free survival during a follow-up of approximately 3 years.

Discussion

Oligodendroglioma is a rare type of diffuse glioma requiring IDH-1 or -2 mutations and 1p/19q co-deletion in the genetic diagnosis [4]. These molecular markers are unavailable because this patient was treated before the recent (2021) revised WHO classification of CNS tumors. As such, this tumor would now be classified as “adult-type diffuse glioma” NOS, but other findings strongly suggest the diagnosis of an oligodendroglial tumor. Imaging findings of oligodendroglial tumors are characterized by cortical-subcortical development and calcification, with up to 90% of cases showing coarse calcification on CT [5,6]. MRI will usually find a hyperintense lesion with generally marked heterogeneity on T2WIs. Cystic degeneration, perilesional edema, hemorrhage, and contrast enhancement are not typical features but tend to be observed in high-grade

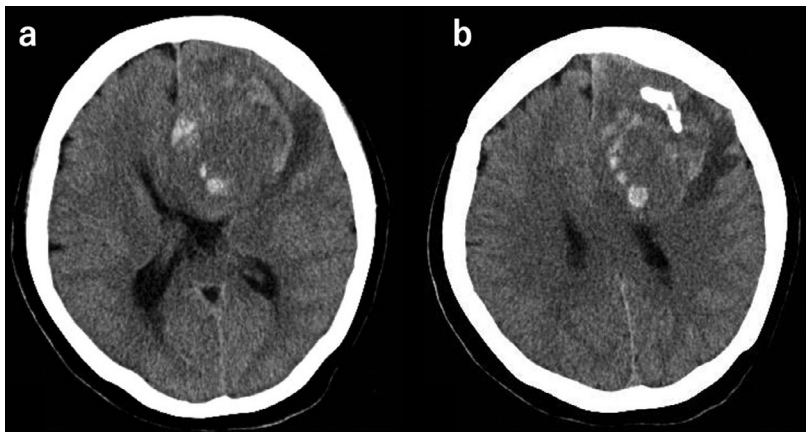

Fig. 1 – Computed tomography (A, B) showing an intra-axial mass with partial hemorrhage and calcification in the left frontal lobe. Partially include a slightly high-density area suspected intratumoral hemorrhage.

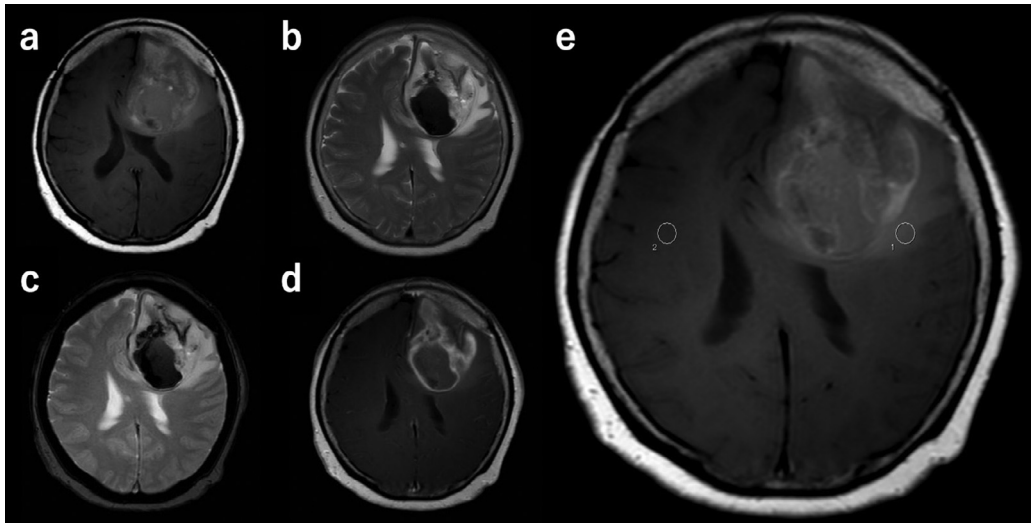

Fig. 2 – T1-weighted images (WIs) (A) showing a perilesional high-intensity area (HIA), which also indicates high intensity on T2WIs (B). T2*WIs (C) suggest hemosiderin deposition and a hemorrhage in the lesion. The lesion rim shows ring-like contrast enhancement by gadolinium (D). MRI Axial T1WIs show regions of interest located in the perilesional T1 HIA (1) and the contralateral white matter (2). The mean T1 signal intensity ratio of the perilesional area to the contralateral white matter is 1.26 (E).

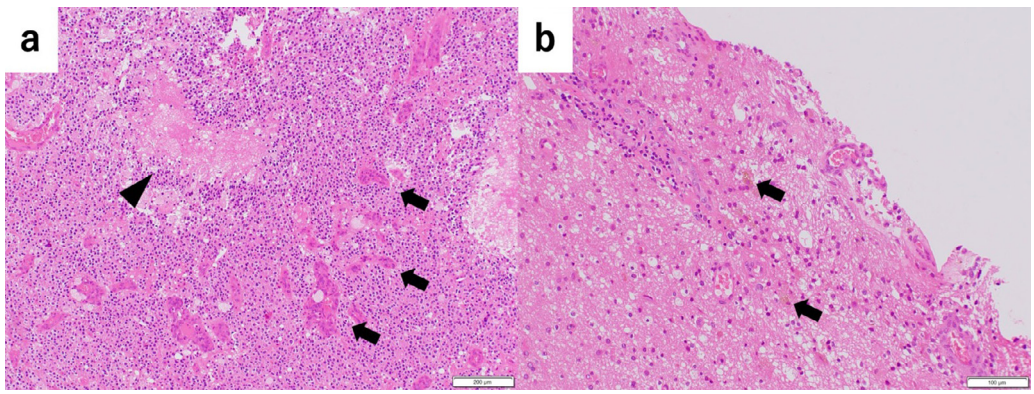

Fig. 3 – Histopathological findings of the tumor (A) show cells with round nuclei and perinuclear haloes. Microvascular proliferation (arrow) and necrosis (arrowhead) are also seen in this field which suggests the high-grade malignancy of this tumor (Hematoxylin and Eosin staining, x100). In the perilesional white matter (B), brown and yellow hemosiderin (arrow) are scattered in the tissue (Hematoxylin and Eosin staining, x200).

lesions reflecting histopathologic findings [6]. These features were seen in our patient and may have reflected grade 3 malignancy.

Conversely, CMs are low-flow vascular malformations, also cited as cavernous angiomas, cavernous hemangiomas, or cavernomas. CMs account for approximately 5%-15% of all central nervous system vascular malformations and MRI is the most reliable diagnostic modality [7,8]. A typical feature of CMs is that T2WI shows a mixed hyper- and hypointensity core within the lesion. Intralesional and perilesional hemosiderin deposition with occasional internal calcification is considered to be the result of repeated subclinical hemorrhages [9,10]. Recently, gradient-echo or susceptibility-enhanced methods have also been reported to help detect CMs while Gd enhancement is also useful [7,11–13].

Perilesional T1 HIA in intra-axial lesions, excluding CMs, is a rare sign. Yun et al. [3] were the first to report it as a supporting finding to distinguish CMs from other hemorrhagic masses with high specificity and selectivity. There have also been reported cases of similar findings in patients with METs or non-neoplastic intracerebral hemorrhages [1,2]. However, there are no current reports of primary adult-type circumscribed/diffuse gliomas presenting with perilesional T1 HIA so far. Typical perilesional brain edema appears at T1 hypointensity and T2 hyperintensity on MRI. Substances that exhibit T1 HIA are methemoglobin, melanin, lipids, proteins,

minerals, and other variants [14], with red blood cells, plasma, and proteins due to extravascular leakage also playing a potential role [1,3]. The T2*WI did not show a signal drop at the perilesional edema in our case, supporting the idea that leaking proteins were the cause of the perilesional T1 HIA.

Angiocentric gliomas are known to exhibit a "T1 hyperintense rim" on MRI scans, a sign similar to the perilesional T1 HIA [15]. However, the cause of this sign is yet to be defined [15–17]. It is described as "intrinsic hyperintensity," showing the rim is in the tumor itself. On the other hand, in our case, perilesional T1 HIA was found in the perilesional brain edema area, probably due to the mass effect of the lesion. These 2 signs differ in their location.

In ultrastructural studies, CMs were shown to have thin walls, lacking subendothelial support, which could result in increased vascular permeability [18,19]. Also, the high-grade features of oligodendroglial tumors, such as microvascular proliferation, suggest the increased microvascular permeability of immature microvessels [20]. Blood-brain barrier disruption due to these pathophysiological features of the lesion may contribute to microhemorrhaging and leakage of plasma and protein into the perilesional white matter.

To our best knowledge, this case is the first report on perilesional T1 HIA in a primary glioma. From the patient's symptoms and imaging features, the patient was assumed to have acute or subacute hemorrhage from the primary lesion and repeated subclinical hemorrhages in the lesion. In this patient, acute or subacute hemorrhaging from the tumor appeared to have resulted in leakage of plasma and protein. In addition, histopathological findings, such as hemosiderin pigmentation and siderophages in the perilesional white matter, support the association with past hemorrhages. Since, in almost all patients with perilesional T1 HIA, acute or subacute hemorrhagic events have been reported, the presence of an intra- or perilesional hemorrhage must be associated with this sign. Subclinical repeated hemorrhages are not common in oligodendroglial tumors but are commonly observed in CMs. The presence of repeated hemorrhages and increased vascular permeability could be causative for the perilesional T1 HIA in our case. Although perilesional T1 HIA is almost characteristic of CMs, such MRI findings do not always rule out primary glioma.

Conclusions

Perilesional T1 HIA was present in primary glioma with acute and subacute hemorrhaging. This seems to be associated with the T1 HIA of the perilesional white matter. Although perilesional T1 HIA was thought to be a characteristic of CMs, the same MRI findings may be present in primary adult-type diffuse gliomas and, as such, care must be taken in the differential diagnosis.

Patient consent

Appropriate written informed consent was obtained from the patient for the publication of this case report and images.

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