



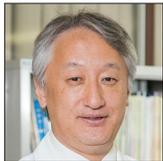
## Case Report

# Acute progression of cerebral amyloid angiopathy-related inflammation diagnosed by biopsy in an elderly patient: A case report

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## ABSTRACT

**Background:** Cerebral amyloid angiopathy-related inflammation (CAA-I) presents with slowly progressive nonspecific neurological symptoms, such as headache, cognitive function disorder, and seizures. Pathologically, the deposition of amyloid- $\beta$  proteins at the cortical vascular wall is a characteristic and definitive finding. Differential diagnoses include infectious encephalitis, neurosarcoidosis, primary central nervous system lymphoma, and glioma. Here, we report a case of CAA-I showing acute progression, suggesting a glioma without enhancement, in which a radiological diagnosis was difficult using standard magnetic resonance imaging.

**Case Description:** An 80-year-old woman was admitted due to transient abnormal behavior. Her initial imaging findings were similar to those of a glioma. She presented with rapid progression of the left hemiplegia and disturbance of consciousness for 6 days after admission and underwent emergent biopsy with a targeted small craniotomy under general anesthesia despite her old age. Intraoperative macroscopic findings followed by a pathological study revealed CAA-I as the definitive diagnosis. Steroid pulse therapy with methylprednisolone followed by oral prednisolone markedly improved both the clinical symptoms and imaging findings.

**Conclusion:** Differential diagnosis between CAA-I and nonenhancing gliomas may be difficult using standard imaging studies in cases presenting with acute progression. A pathological diagnosis under minimally invasive small craniotomy may be an option, even for elderly patients.

**Keywords:** Biopsy, Cerebral amyloid angiopathy-related inflammation, Glioma

## INTRODUCTION

Cerebral amyloid angiopathy (CAA) is pathologically characterized by the deposition of amyloid- $\beta$  proteins in the walls of cortical arteries in elderly patients. Some studies have reported that patients with CAA and inflammation based on vasculitis or perivasculitis present with symptoms such as headache, dementia, and seizure and are recognized as having cerebral amyloid angiopathy-related inflammation (CAA-I).<sup>[2,4]</sup> Magnetic resonance imaging (MRI) typically shows

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a high-intensity area (HIA) on fluid-attenuated inversion recovery (FLAIR) images and low-signal intensity spots described as microbleeds (MBs) on T2 star-weighted images (T2\*WI) of the same lesion.<sup>[8]</sup> The first-line treatment is steroid and immunosuppressive therapy.<sup>[2]</sup> The significance of pathological diagnosis by biopsy is important, but may be waived in cases with illustrative imaging findings with a typical clinical course. Here, we report a rare case of CAA-I presenting with acute pseudotumoral progression in an elderly patient that was successfully treated by biopsy with minimally invasive small craniotomy under general anesthesia.

## CASE REPORT

An 80-year-old woman presented with transient abnormal behavior, initially suggesting mild senile dementia. Computed tomography (CT) revealed a large low-density area in the right temporal, parietal, and occipital lobes [Figure 1a]. The patient was referred to us for further examination. On admission, she had no neurological findings except for a history of the aforementioned symptoms. The lesion was demonstrated as a low-intensity area on T1-weighted images, while an HIA was observed on T2-weighted and FLAIR images [Figure 1b] without enhancement by gadolinium on MRI. Several MBs were observed on T2\*WI in the bilateral temporo-occipital region, which was not predominant in the lesion above [Figure 1c]. Based on the CT and MRI findings, our initial diagnosis was a low-grade glioma with brain swelling, and further, examination was scheduled, including MR spectroscopy, single-photon emission CT, and cerebral angiography. The patient's symptoms progressively worsened for 6 days after admission, leading to comatose left hemiplegia. Repeated MRI also showed aggravation of the brain swelling with no enhancement. Based on acute tumor-like progression, she underwent emergent biopsy with small, targeted occipital craniotomy under general anesthesia with

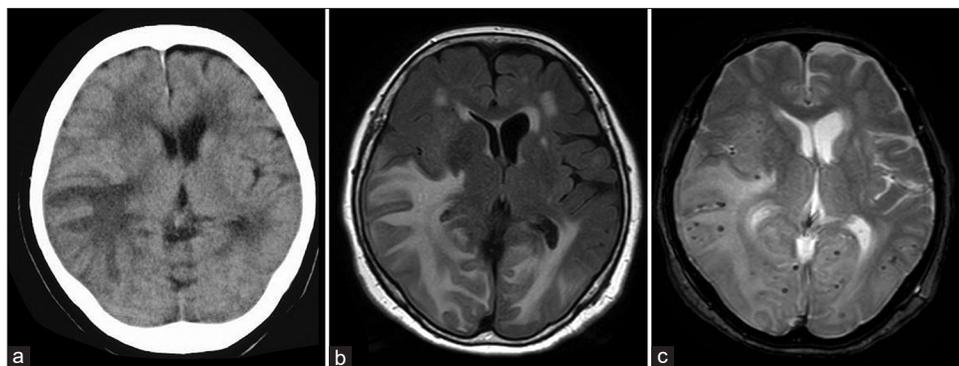
stereotactic navigation. Macroscopic findings of the brain surface suggested brain edema, but they differed from those of a glioma [Figure 2a]. Rapid intraoperative pathological examination did not reveal any neoplastic findings indicative of a glioma [Figure 2b]. At this point, we considered the possibility of CAA-I as a diagnosis considering T2\*WI, even though an extremely progressive clinical course seemed exceptional for CAA-I.

Steroid pulse therapy was started on the day after the surgery with intravenous methylprednisolone 1000 mg/day for 3 days, followed by oral prednisolone 60 mg/day through a nasal feeding tube. Her symptoms gradually improved a few days after the initiation of steroid therapy, and she recovered to an almost arousable state with the left hemiparesis as a manual muscle test (MMT) 3/5 on the 10<sup>th</sup> day. Meanwhile, a permanent pathological diagnosis with specific staining revealed leukoencephalopathy in the white matter without any neoplastic changes. In addition, Congo red staining [Figure 2c] and direct fast scarlet staining [Figure 2d], which are more specific than Congo red staining, suggested the deposition of amyloid- $\beta$  proteins in the cortical arterial wall consisting of CAA-I.

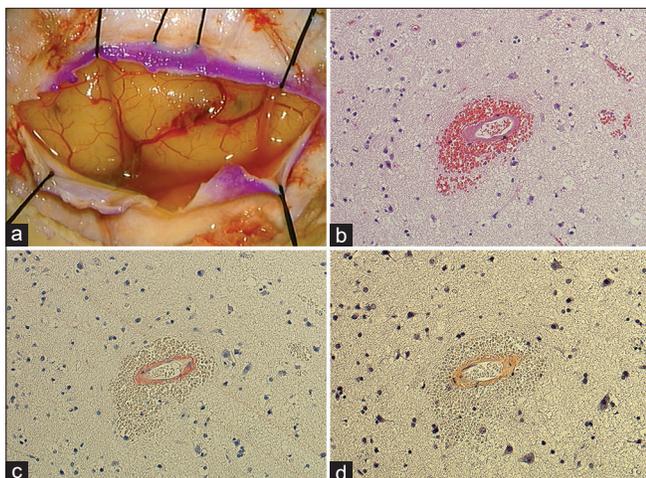
The dose of oral prednisolone was decreased by 10 mg every week for 5 weeks from the 11<sup>th</sup> day and stopped on the 53<sup>rd</sup> day after the initiation of steroid therapy. The HIA on FLAIR decreased gradually in the following 2 months [Figures 3a and b], while her neurological symptoms further improved to clear consciousness with slight left hemiparesis on MMT 4/5. She was discharged on the 57<sup>th</sup> day after the initiation of steroid therapy with independent activities of daily living.

## DISCUSSION

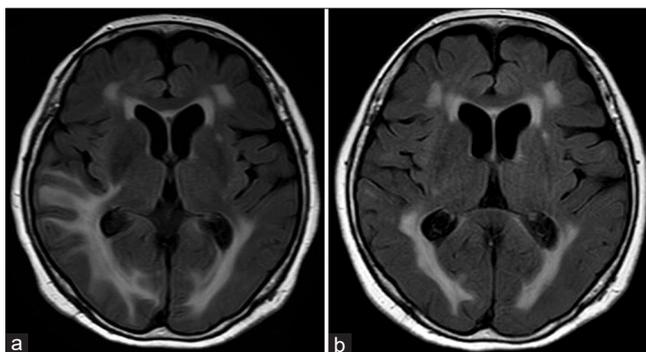
CAA-I is a rare disease that is pathologically characterized by the deposition of amyloid- $\beta$  proteins in the cortical



**Figure 1:** Initial images of CT and MRI. (a) CT showing a low-density area in the right temporal lobe with a midline shift. (b) Fluid-attenuated inversion recovery image of MRI showing a high-intensity area (HIA) in the cortex of the right temporal lobe and occipital lobe combined with an HIA in the white matter indicating vasogenic edema. Periventricular HIAs were also shown in both the anterior and occipital horn of bilateral lateral ventricles. (c) T2 star-weighted MR image showing several low-intensity spots at the margin of the HIA in the right occipital lobe.



**Figure 2:** Intraoperative macroscopic view and pathological examination of biopsy specimen (a) Intraoperative macroscopic view of the occipital lobe showing swelling of the cortex. (b) A histopathological examination (Hematoxylin and eosin staining,  $\times 40$ ) showing the thickened cortical artery wall. (c) An immunohistochemical stain of the same section (Congo red staining,  $\times 40$ ) showing the deposition of amyloid- $\beta$  proteins at the arterial wall. (d) Another immunohistochemical stain (Direct fast scarlet staining,  $\times 40$ ) also showing the deposition of amyloid- $\beta$  proteins.



**Figure 3:** Follow-up images of the fluid-attenuated inversion recovery image of MRI. (a) Image on the 22<sup>nd</sup> day after admission. The high-intensity area (HIA) in the right temporal and occipital lobes was improved compared with the initial image [Figure 1b]. (b) Image on the 55<sup>th</sup> day after admission. The HIA in the right temporal and occipital lobes almost disappeared.

arteries, causing vasculitis or perivasculitis with widespread vasogenic edema. MRI is characterized by a wide HIA on FLAIR concomitant with MBs on T2\*WI in the same lesion without enhancement by gadolinium.<sup>[8]</sup> Ronsin *et al.* describe the significance of T2\*-GRE sequences in the diagnosis of mass lesions in elderly patients resending with subacute cognitive decline and no parenchymal post contrast enhancement, in which we could not perform in this case.<sup>[7]</sup> Symptoms are nonspecific local ones, depending on the site

of the lesion, but they may be accompanied by impaired consciousness in cases of a wide range of lesions. Progression is relatively slow and gradual, lasting from several weeks to several months. Differential diagnoses include infectious encephalitis, neurosarcoidosis, primary central nervous system lymphoma, and malignant glioma.<sup>[7]</sup> Although there are reports that diagnosis can be made only by the above diagnostic imaging techniques,<sup>[6]</sup> it may sometimes be difficult, as in our case. A pathological diagnosis to demonstrate amyloid- $\beta$  deposition at the arterial wall, vasculitis, or perivascular inflammation by biopsy may be required.

CAA-I is known to be relieved by steroid hormones and immunosuppressive agents, such as methotrexate and cyclophosphamide,<sup>[2]</sup> and therapeutic effects of these drugs can be expected in cases with a definitive diagnosis, while a poor prognosis, such as severe morbidity and mortality (20.5% and 37.5%, respectively),<sup>[11]</sup> might be conceivable without adequate treatment. Therefore, the early commencement of medical therapy is desirable to avoid the prolongation of serious symptoms, resulting in a poor prognosis. Even though the accumulation of knowledge on symptomatology, diagnosis, and pathological findings of CAAi, factors relating to the rapid progression and pathological features remain to be determined yet. In our case, the patient initially presented with only transient abnormal behavior. As the possibility of an elderly low-grade glioma<sup>[5]</sup> or a nonenhancing high-grade glioma<sup>[3]</sup> could not be ruled out, several imaging studies, as described above, were scheduled, in addition to the evaluation of the general condition for a biopsy. However, an atypically rapid acceleration of symptoms, “acute pseudotumoral progression”<sup>[7]</sup> leading to hemiplegia and coma, urged us to make an immediate diagnosis.

It might be a choice to start medical therapy by assuming CAA-I without a pathological diagnosis, if we recognized it with emphasizing the findings of MBs on T2\*WI. However, the differential diagnosis of CAA-I from a glioma is not always easy in cases, where the MBs are not limited to the predominant lesion, as in our case. MBs are not rare in elderly patients, even without CAA-I. The risk of a large dose of steroids and immunosuppressive agents due to incorrect diagnosis should not be ignored in elderly patients. Therefore, we deemed it appropriate that pathological confirmation of the diagnosis be undertaken by targeting biopsy with minimally invasive small craniotomy, as wide craniotomy may cause infection due to postoperative steroids and immunosuppressive drugs, particularly in the elderly. Endoscopic or stereotactic surgery, which may be a minimally invasive surgery, is considered an inappropriate option to avoid intraoperative hemorrhage, because vascular specimens should be obtained for the pathological diagnosis of CAA-I to observe findings of vasculitis or perivasculitis.

## CONCLUSION

We report a case of CAA-I, in which an initial diagnosis was difficult between CAA-I and a nonenhancing glioma. A favorable result was obtained with steroid therapy following a pathological diagnosis by biopsy under minimally invasive small craniotomy. This approach may be the choice even for CAA-I in elderly patients, in whom differential diagnosis is difficult using standard imaging studies.

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## Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Nil.

## Conflicts of interest

There are no conflicts of interest.

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