Case report

Cerebral amyloid angiopathy with atypical imaging findings of subarachnoid hemorrhage

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Abstract

Cerebral amyloid angiopathy (CAA) is observed in most cases of nonhypertensive subcortical hemorrhage involving elderly patients. We herein describe the case of a female in whom a convexal subarachnoid hemorrhage was observed at 55 years of age. The cerebral hemorrhage occurred repeatedly; however, no obvious vascular lesions were observed on a cerebral angiography, and no signs of microbleeding or lesions in the deep white matter were identified on magnetic resonance imaging (MRI). Partial excision of the right frontal cortex and hematoma evacuation were performed, and histopathological examination showed deposition of an acidophilic substance with positive staining for Direct Fast Scarlet (DFS) in the cerebral vascular wall. Finally, brain hemorrhage due to CAA was diagnosed. This case suggests that CAA is an important differential diagnosis in patients with localized non-aneurysmal subarachnoid hemorrhage in the convexity sulcus.

Key words: cerebral amyloid angiopathy, subarachnoid hemorrhage, atypical imaging finding

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Introduction

Cerebral amyloid angiopathy (CAA) is a clinical condition in which amyloids are deposited in the cerebral blood vessel wall. CAA usually causes nonhypertensive cerebral hemorrhage in elderly patients^{1–3}. CAA-derived cerebral hemorrhage^{1,2} tends to occur in the subcortical region, both temporally and spatially, in multiple ways. Recently, a complex clinical condition involving subarachnoid hemorrhage and/or multiple episodes of microbleeding in the deep white matter has been reported^{3–6}, and white matter lesions have been identified on head MRI imaging examinations^{7,8}. We

experienced a case of localized subarachnoid hemorrhage that developed at the fornix. Over the next six years, subcortical hemorrhage occurred twice in the right frontal cortex, and CAA was diagnosed based on the results of a histopathological examination. The possibility of CAA should be considered when making the differential diagnosis localized subarachnoid hemorrhage in the convexity sulcus, even in cases without obvious signs of subcortical hemorrhage or microbleeding in the deep white matter.

Case Presentation

The patient was a 55-year-old female without a past medical history. The patient has given informed consent for this case report to be published.

In August 2007, she suffered from numbness in the right arm associated with mild elevation of blood pressure (156/89 mmHg) and was admitted to our hospital. Despite a lack of neurological abnormalities, subarachnoid hemorrhage in the sulcus of the left parietal lobe and a cystic lesion in the deep white matter in the right frontal lobe were observed on head magnetic resonance imaging (MRI) (Figure 1A, 1B). No obvious evidence of a cerebral aneurysm or vascular malformations was observed (data not shown), and the patient exhibited no exacerbation of symptoms following treatment with intravenous medications, without surgical intervention.

Three months later (November 2007), the patient presented with a reduced level of consciousness accompanied by left paresis and aphasia. She was admitted to our hospital for a second time. Intracerebral hemorrhage was observed on head computed tomography (CT) (Figure 1C), although a cerebral angiography reconfirmed the absence of abnormalities in the cerebral vessels. After reinitiating the anti-hemorrhagic medical therapy, the patient's conscious level improved (Glasgow Coma Scale: E3V3M5 on admission, E4V5M6 at discharge). In addition, her performance level

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Figure 1 Imaging findings of the head during the patient's clinical course. A head MRI fluid-attenuated inversion recovery (FLAIR) image was obtained on first admission (A, B). A head CT image was obtained on second admission (C). Head CT (D, E) and head MRI in T2 * images (F) were obtained on third admission. The arrow indicates the subarachnoid hemorrhage in the left parietal lobe (A). The arrowhead indicates the cystic lesion in the right frontal lobe (B).

for activities of daily living gradually recovered as a result of continuous rehabilitation. She was discharged four months later.

Six years after the initial diagnosis (December 2013), the patient suffered from cephalgia and malaise, with no neurological abnormalities. She was admitted to our hospital for a third time. Head CT and MRI examinations revealed intracerebral hemorrhage (Figure 1D, 1E, 1F), whereas a cerebral angiography showed only normal vessels. A pre-dementia score of 27 points (out of 30 total points) was obtained on the mini-mental state examination (MMSE). The hematoma was eliminated via right frontotemporal craniotomy, with partial excision of the right frontal cortex. Although the hematoma contained areas of calcification, no obvious signs of malignancy were detected. Deposition of an acidophilic substance on the vascular wall was observed in the surrounding brain tissue on histopathological exami-

nation. The deposits were positive for Direct Fast Scarlet (DFS) staining (Figure 2). A diagnosis of intracerebral hemorrhage due to CAA was made. The patient's neurological deficiencies promptly disappeared with continuous rehabilitation. She was discharged from the hospital two weeks later, with no further signs of relapse.

Discussion

According to the Boston criteria, CAA is diagnosed as probable in patients over 55 years of age who have been ruled out as having other causes of repeated subcortical hemorrhage. The present case met the Boston criteria for probable CAA⁹.

Typical CAA hemorrhaging repeatedly occurs in subcortical areas, with the majority of bleeding occurring in the frontal lobe. Taking into consideration the volume of

Figure 2 Histopathological analysis. Brain tissue obtained from the site of cerebral hemorrhage was stained with DFS. (A) Mid-power field ($\times 100$) and (B) high-power field ($\times 400$) views are shown.

the cerebral lobes, such hemorrhage frequently occurs in the occipital, temporal, and parietal lobes^{2, 10}. Moreover, an autopsy report recently showed that amyloid deposition progresses from the occipital lobe¹¹. Although the first hemorrhagic episode in the current case was observed when the patient was middle-aged, the subcortical hemorrhage was limited to the frontal cortex. This presentation is atypical.

The detection of hemosiderin deposition^{2, 5, 12} due to the presence of intracerebral microbleeding and/or white matter lesions^{7, 8} on head MRI is useful for confirming the diagnosis of CAA. Approximately half of CAA cases are accompanied by subcortical hemorrhage or microbleeding¹³, and CAA patients usually have significantly more lesions in the white matter than healthy individuals¹⁴. In contrast, obvious microbleeding in the deep brain white matter or the presence of excessive white matter lesions, known to be typical imaging findings of CAA, were not detected in our patient.

The onset of intracranial hemorrhage at a young age due to CAA is observed in patients with Alzheimer's disease^{1, 2, 11}. Although the present patient's MMSE score was 27 points, which was relatively low for her age (61 years old), this finding did not indicate extreme cognitive impairment. Moreover, because there were no signs of sudden decline in the patient's cognitive function, it is doubtful that the CAA was accompanied by Alzheimer's disease.

Complications of subarachnoid hemorrhage due to CAA^{6, 15, 16} have been reported. Some cases of CAA involve only subarachnoid hemorrhage at the initial onset. Subsequent subcortical hemorrhage within the next two months (20 to 33 days) has also been reported in patients 73 to 77 years of age^{17–19}. Different from what was observed in these cases, our patient suffered from subarachnoid hemorrhage at

a much younger age (55 years old). Furthermore, subsequent intracranial hemorrhage was observed three months and six years later. Regarding these points, our patient had a very rare medical history. Both hematoma-type hemorrhage and subarachnoid hemorrhage have been previously reported at CAA onset in elderly patients. The existence of secondary subarachnoid hemorrhage is ancillary to the imaging diagnosis for CAA due to subcortical hemorrhage^{20–23}. A recent retrospective study of radiological image findings showed that convexal subarachnoid hemorrhage (SAH) may be observed in patients with suspected CAA²⁴. Although that report included 37-year-old patients, pathological confirmation was not obtained. A recent paper also reported the case of a 52-year-old female diagnosed with CAA according to a pathological observation²⁵. The patient showed repeated convexal SAH and intracerebral hemorrhage with hypertension. In contrast, our middle-aged CAA patient presented only with SAH at the time of onset, and cerebral hemorrhage was not observed at the first diagnosis. Several researchers have proposed that convexal SAH is one of the first signs of CAA-related intracranial hemorrhage in patients over 60 years of age^{15, 22, 24, 26}. The current case indicates that limited convexal SAH should also be considered in cases of CAA-related hemorrhage in patients less than 60 years of age.

We herein presented the very rare image findings of a case of CAA in a middle-aged patient. The detection of convexal SAH alone even in middle-aged patients as well as patients over 60 years of age might be one of the first signs of CAA-related intracranial hemorrhage.

Since we determined the pathological diagnosis based on open biopsy specimens, however, surgical treatment should have been critically applied. Our patient suffered

from intracranial hemorrhage three times. Compared with the hemorrhages the first two times, the third hemorrhage was accompanied by a small hematoma and mild clinical symptoms. We never recommended removing the hematoma with surgical treatment. However, the patient and her family strongly wanted to confirm the diagnosis regarding the repeated cases of intracranial hemorrhage. According to the Boston criteria, our patient met the Boston criteria for probable CAA. The practical treatment is not different between probable CAA and probable CAA with supporting pathology. We think that our case does not represent the common treatment course for a probable CAA patient. We recommend restricting surgery to that required to obtain a definitive diagnosis for repeated cases of intracranial hemorrhage with severe outcomes. In addition, surgical treatment with pathological testing should be performed when the patient and patient's family express a strong desire for it.

Conclusion

We emphasize that CAA should be included in the differential diagnosis for subarachnoid hemorrhage with an unknown cause in both elderly and relatively young patients. Furthermore, some CAA cases may involve atypical imaging findings without accompanying microbleeding or white matter lesions. Therefore, caution should be exercised at the time of CAA diagnosis.

Conflict of interest: There are no potential conflicts of interest to disclose. The authors have no personal financial or institutional interests in any of the drugs, materials, or devices mentioned in this article.

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