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Case Report

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Multimodal Imaging Findings of Cerebral Amyloid Angiopathy Related Inflammation With Unusual Clinical Manifestation: A Case Report

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Cerebral amyloid angiopathy-related inflammation (CAA-RI) is a rare encephalopathy characterized by the coexistence of a perivascular inflammatory reaction in patients with cerebral amyloid angiopathy. CAA-RI diagnosis is challenging as its final diagnosis requires invasive procedures such as autopsy or brain biopsy. Therefore, multimodal imaging approaches with clinical considerations are essential for the probable diagnosis of CAA-RI. In particular, in the case of CAA-RI presented with uncommon clinical symptoms, the need for imaging in diagnosis is further highlighted by difficulties of clinical approaches. Herein, we report a case of CAA-RI with unusual clinical manifestation diagnosed using multimodal imaging including magnetic resonance imaging (MRI) and amyloid positron emission tomography-computed tomography (PET-CT). Multimodal imaging approaches using adequate MRI sequences and PET-CT scans could facilitate the diagnosis of CAA-RI without requiring invasive pathological confirmation.

Keywords: Cerebral amyloid angiopathy; MRI; PET/CT

INTRODUCTION

Cerebral amyloid angiopathy (CAA) is a cerebrovascular disorder characterized by amyloid beta-peptide deposits within the brain's small- to medium-sized arteries [1]. Notably, CAA is a significant cause of lobar intracerebral hemorrhage (ICH) in older adults. It may present with incidental microbleeds or hemosiderosis on magnetic resonance imaging (MRI) [2].

Cerebral amyloid angiopathy-related inflammation (CAA-RI), a subtype of CAA, is characterized by an inflammatory response to vascular deposits of amyloid-β in the brain [3]. CAA-RI and CAA are closely related to each other due to their shared pathological char-

acteristics. However, CAA-RI has noticeable clinical and imaging features distinct from CAA [4,5]. Rather than acute deterioration or mental change due to ICH observed in CAA, CAA-RI presents clinical manifestation of chronic progressive cognitive decline, transient focal neurological episodes, and subacute cognitive disorders or behavioral changes [4,5]. Regarding image findings, patch or confluent white matter hyperintensities on T2-weighted images (T2WI), often asymmetric in subcortical white matter, can be considered an image feature unique to CAA-RI, which is rarely found in CAA [5].

Diagnosing CAA-RI remains challenging as the gold standard requires invasive procedures such as autopsy or brain biopsy. Unfortunately, brain biopsy is an invasive procedure with an increased risk of complications such as hemorrhage, brain edema, and even death. Therefore, imaging assessments and pathological findings play a crucial role in the clinical diagnosis of CAA-RI. For CAA-RI showing uncommon clinical symptoms, the role of imaging in diagnosis is further emphasized due to difficulties in clinical approaches. Herein, we report a case of CAA-RI with unusual visual symptoms diagnosed with multimodal imaging including CT, MRI, and positron emission tomography-computed tomography (PET-CT) scan.

CASE REPORT

Clinical Information

A 77-year-old woman visited Gangnam Severance Hospital with symptoms of sudden vision loss accompanied by dizziness and headache that occurred 6 days before visiting the hospital. Additionally, the patient experienced visual loss repeatedly for a month. However, the patient fully recovered

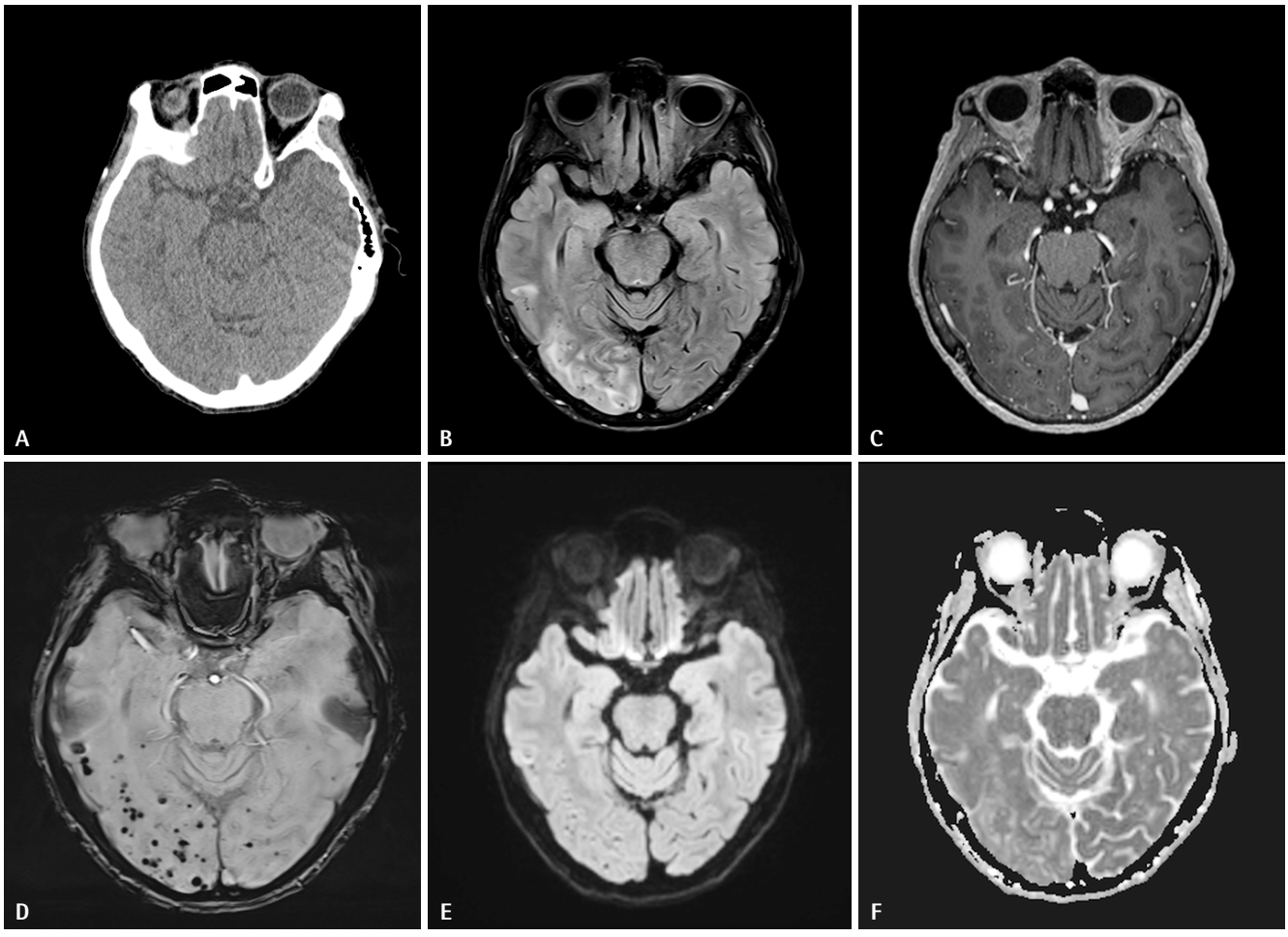

Fig. 1. Initial non-contrast computed tomography (CT) and brain magnetic resonance imaging findings. Axial non-contrast CT (A) shows low-attenuation white matter levels in the right occipital lobe, suggesting edema. On fluid-attenuated inversion recovery (B), cortical and subcortical hyperintensities are noted in the right occipital lobe, suggesting vasogenic edema. No abnormal enhancing lesions were observed in the brain parenchyma on post-contrast T1-weighted images (C). Susceptibility-weighted imaging (D) shows multiple microbleeds scattered in cerebral and cerebellar hemispheres with a prominent distribution in the bilateral occipital lobes. There was no diffusion restriction on diffusion-weighted imaging (E) or apparent diffusion coefficient maps (F).

spontaneously. The most recent event was preceded by a spinning sensation for a few seconds. Visual loss on both sides then lasted for approximately 30 minutes, which also improved spontaneously. The patient had no history of trauma, cancer, fever, night sweats, unexplained weight loss, or other constitutional symptoms. Furthermore, all serum laboratory findings were within normal limits. Initial electroencephalogram (EEG) showed intermittent focal delta-to-theta slow in the right occipital region, suggesting structural lesions.

Imaging Findings

The patient underwent non-contrast brain computed tomography (CT), which revealed a low-attenuated confluent lesion in the right occipital lobe. There was no intra- or extracranial hematoma or hemorrhage on CT. Gadolinium-enhanced brain MRI and magnetic resonance angiography performed the day following symptom onset showed cortical and subcortical T2 and fluid-attenuated inversion recovery (FLAIR) hyperintensities with parenchymal swelling in the right occipital lobe (Fig. 1). No diffusion-restricted or abnormal enhancing lesions were noted in the brain parenchyma. Multiple microbleeds were scattered in cerebral and cerebellar hemispheres with prominent distribution in bilateral occipital lobes. These were also visible on susceptibility-weighted imaging (SWI).

PET-CT was performed on day 5 of the patient's hospital stay. It showed significant tracer uptake in the gray matter of the parietal, frontal, precuneus/posterior cingulate, and temporal regions. These PET-CT findings suggested pronounced amyloid-β deposition (brain amyloid plaque load score 3) (Fig. 2). Based on the MRI and PET-CT findings, the patient was diagnosed with CAA-RI in the right occipital lobe.

Following diagnosis, the patient underwent steroid pulse therapy for 5 days from the day of hospitalization. Follow-up MRI and EEG were performed on the hospital day 9. Follow-up brain MRI showed decreased extent of hyperintensities involving the right occipital lobe on T2WI and FLAIR. However, scattered microbleeds were still observed in prominent bilateral occipital lobes on SWI (Fig. 3).

DISCUSSION

CAA-RI is an exceedingly rare form of vascular inflammation with an estimated prevalence of 0.13 per 100000 individuals [6]. Histopathologically, the disease is characterized by amyloid-β deposition accompanied by perivascular inflammatory changes [4,5].

The underlying mechanism of CAA-RI remains unclear. Based on the evidence reported thus far, the most plausible hypothesis is that an autoantibody-mediated inflammatory response directed at amyloids can cause perivascular inflammation [7]. Autoantibodies that bind to vascular amyloid-β peptides can inhibit the clearance of amyloid-β from the brain, causing inflammation. Consequently, these pathological effects can increase vulnerability to blood-brain barrier (BBB) damage, microhemorrhage, and vasogenic edema [7].

The most common clinical manifestation of CAA-RI is a subacute cognitive decline (48.0%). Other common presenting symptoms include headaches (32%–38.7%), seizures (32%–36.7%), encephalopathy including confusion and impairment of consciousness (27%–30.7%), motor weakness (16%–20%), and aphasia (14%–16.7%) [8]. However, visual disturbance was only presented in 13%–14.7% of CAA-RI patients [8]. Most of

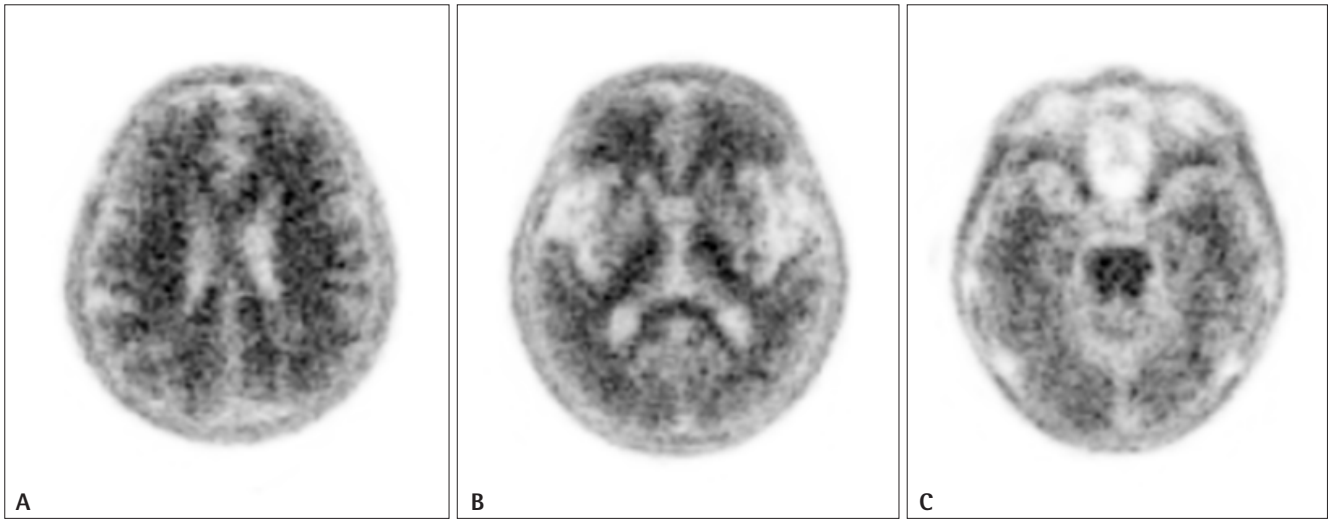

Fig. 2. Positron emission tomography-computed tomography findings. Significant tracer uptake is found in grey matters of the (A, B) parietal, frontal, precuneus/posterior cingulate, and (C) temporal regions, suggesting pronounced β-amyloid deposition (brain amyloid plaque load score: 3).

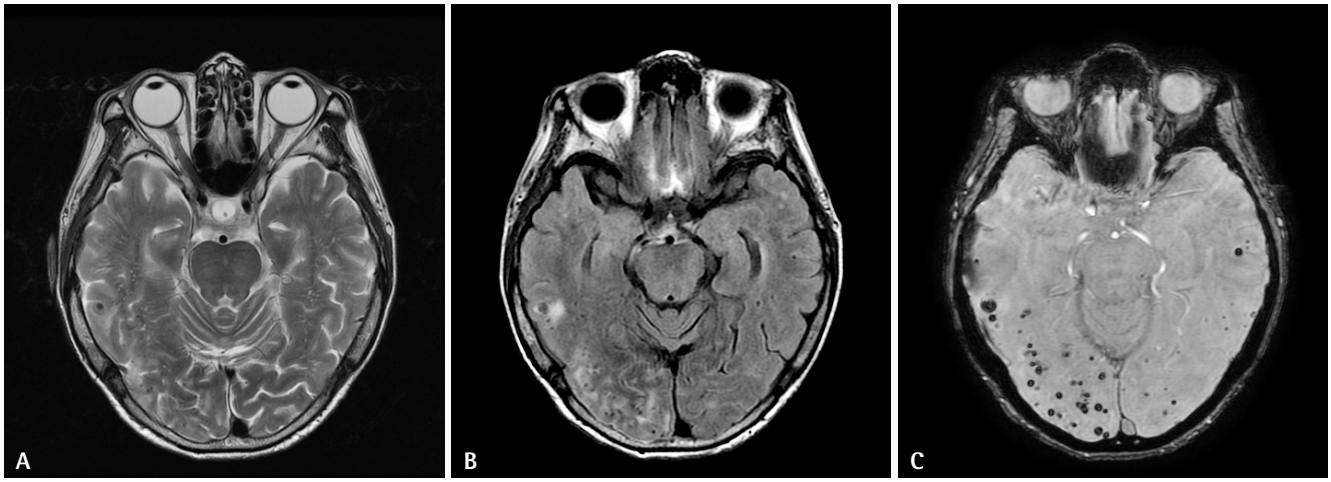

Fig. 3. Follow-up magnetic resonance imaging at 7 days after steroid pulse therapy. On T2-weighted image (A) and fluid-attenuated inversion recovery (B), there was a partial improvement in hyperintensities in the right occipital lobe. However, residual vasogenic edema was still observed. C: No remarkable change was seen in scattered microbleeds in prominent bilateral occipital lobes on susceptibility-weighted imaging.

Table 1. Criteria for the Diagnosis of CAA-RI

Diagnosis	Criteria
Probable CAA-RI	1. Age ≥ 40 years 2. Presence of ≥ 1 of the following clinical features: headache, decrease in consciousness, behavioral change, or focal neurological signs and seizures; the presentation is not directly attributable to an acute ICH 3. MRI shows unifocal or multifocal WMH lesions (corticosubcortical or deep) that are asymmetric, extending to the immediately subcortical white matter. The asymmetry is not due to past ICH 4. Presence of ≥ 1 of the following corticosubcortical hemorrhagic lesions: cerebral macrobleed, cerebral microbleed, or cortical superficial siderosis [10] 5. Absence of neoplastic, infectious, or other causes [5,11]
Possible CAA-RI	1. Age ≥ 40 years 2. Presence of ≥ 1 of the following clinical features: headache, decrease in consciousness, behavioral change, or focal neurological signs and seizures; the presentation is not directly attributable to an acute ICH 3. MRI shows WMH lesions that extend to the immediately subcortical white matter 4. Presence of ≥ 1 of the following corticosubcortical hemorrhagic lesions: cerebral macrobleed, cerebral microbleed, or cortical superficial siderosis [5,11] 5. Absence of neoplastic, infectious, or other causes [10]

CAA-RI, cerebral amyloid angiopathy–related inflammation; ICH, intracerebral hemorrhage; MRI, magnetic resonance imaging; WMH, white matter hyperintensity.

these clinical features were expressed in an encephalopathy/coma pattern (19%–46%) or a multifocal pattern (35%–44%) with multiple simultaneous symptoms. In contrast, a unifocal pattern that appears as only one symptom is relatively rare (10%–20%) [8]. Notably, CAA-RI presenting with only visual symptoms is extremely rare [8].

In our case, the patient experienced only recurrent visual loss. There was no cognitive impairment or seizure, a common symptom of CAA-RI. As such, uncommon symptoms appeared in a uniform pattern, making the clinical diagnosis of CAA-RI difficult.

The patient's symptom might be related to vasogenic edema in the right occipital lobe, where the optic radiation and visual cortex are located, which are part of the neurological visual pathway [9]. Therefore, CAA-RI lesions in the occipital lobe may result in visual abnormalities or visual field deficits [9].

Pathologic diagnosis is the gold standard for diagnosing CAA-RI. However, since biopsy is invasive, most clinical cases are diagnosed as CAA-RI according to diagnostic criteria based on clinical and radiological data (Table 1) [5,10,11]. Notably, the diagnostic criteria show high sensitivity (82%) and specificity (97%). They have been proposed to be utilized to avoid the invasive risk of brain biopsy [5]. Consequently, the role of neuroimaging in identifying characteristic radiologic findings of CAA-RI is crucial. In particular, in the case of CAA-RI, which is expressed as an atypical clinical symptom such as in our report, multimodal imaging approaches are helpful for accurate clinical diagnosis.

There are two typical imaging findings of CAA-RI on brain MRI. One is asymmetric patchy or confluent T2/FLAIR hyperintensities of subcortical white matter lesions with or without mass effects [4], as presented in this case. Although many different neurological diseases might exhibit white matter T2/FLAIR hyperintensity, the asymmetrical lobar presentation of white matter T2/FLAIR hyperintensity can be a significant feature of CAA-RI [4]. Usually, lesions do not show diffusion restrictions because vascular inflammation induces loosening of the BBB and causes vasogenic edema [4]. The other significant imaging finding is multiple microhemorrhages at the cortical-subcortical junction. Since the underlying pathology of CAA is essential for diagnosing CAA-RI, detecting microbleeds and cortical superficial siderosis using SWI is greatly helpful for diagnosing CAA-RI [4]. Our case also showed asymmetric confluent white matter hyperintensities on T2WI and asymmetrically multiple microbleeds on SWI as typical CAA-RI imaging findings mentioned above. Furthermore, CAA-RI lesions mostly show little or no gadolinium enhancement.

PET-CT scan can also help in the clinical diagnosis of CAA-RI by identifying underlying amyloid deposition in the brain [10]. Amyloid PET radiotracers such as 11C-labeled Pittsburgh Compound B or Florbetaben can be used to detect and quantify vascular amyloid-β and serve as direct molecular markers for underlying CAA [12]. Notably, patients showed widespread cortical amyloid deposition in a previous CAA-RI study with a PET-CT scan [12]. In contrast, the focal inflammatory region showed relatively reduced amyloid deposits in the acute phase [12], which could be explained by the low retention of amyloid deposition in acute inflammatory lesions [12]. This result is believed to be related to the clearance of amyloid-β by anti-amyloid-β autoantibodies. However, there was no noticeable difference in the uptake of amyloid radiotracers in the right occipital lobe with inflammation in this case.

In conclusion, although CAA-RI is a rare disease that can only be diagnosed through pathological confirmation, multimodal imaging findings could enable a clinical diagnosis of CAA-RI estimated under diagnostic criteria even in cases of CAA-RI with unusual clinical findings.

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

Author Contributions

Conceptualization: Mina Park. Data curation: Jalim Koo, Mina Park. Formal analysis: Jalim Koo, Mina Park. Funding acquisition: Mina Park. Investigation: Jalim Koo. Methodology: Mina Park. Project administration: Mina Park. Resources: Mina Park. Supervision: Han Soo Yoo, Bio Joo, Sung Jun Ahn, Jae-Hoon Lee, Young Hoon Ryu, Sang Hyun Suh. Validation: Mina Park, Jae-Hoon Lee, Young Hoon Ryu. Visualization: Jalim Koo. Writing—original draft: Jalim Koo. Writing—review & editing: Mina Park, Jalim Koo.

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