Case Report

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Cerebral Amyloid Angiopathy-Related Inflammation: A Case Report and Literature Review

대뇌 아밀로이드 혈관병증 연관 염증: 증례 보고와 문헌 고찰

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Cerebral amyloid angiopathy-related inflammation (CAA-RI) is an encephalopathy caused by inflammation of β-amyloid peptide deposition in cerebrovascular vessels. It is a rare disease that mainly occurs in the elderly and is characterized by rapidly progressive dementia, headache, seizures, and focal neurologic deficits. CAA-RI can demonstrate characteristic brain MRI findings and can be reversed by steroids or other immunosuppressive therapies. Here, we report a case of CAA-RI, which was initially misdiagnosed as a subacute infarction but was diagnosed while reviewing follow-up brain MRI images, and spontaneous remission was achieved.

Index terms Cerebral Amyloid Angiopathy; Magnetic Resonance Imaging; Immunosuppression Therapy; Infarction

INTRODUCTION

Cerebral amyloid angiopathy-related inflammation (CAA-RI) is a rare encephalopathy caused by inflammation of β-amyloid (Aβ) deposited in the cerebrovascular vessels (1, 2). Although inflammatory response to deposits of the Aβ in the brain has been widely studied, there is little relevant information about effect of inflammatory response on vascular Aβ deposits or CAA. Radiologists are familiar with imaging findings of CAA, but they have little knowledge of CAA-RI. In addition, since CAA-RI shows characteristic imaging findings and can be treated after diagnosis, it is important to understand the imaging findings and clinical

course of CAA-RI.

Here, we report a case where CAA-RI was initially misdiagnosed as subacute cerebral infarction, but was finally diagnosed as CAA-RI through subsequent clinical course and follow-up brain MRI.

CASE REPORT

A 77-year-old male visited the emergency room with aphasia that started 5 days ago. He had a medical history of hypertension, hypothyroidism, and arrhythmia, and he was diagnosed with early dementia due to cognitive decline and was being treated with choline alfoscerate. Before admission, he was able to walk, eat meals independently, and communicate briefly. He had poor oral intake 7 days before hospitalization. Vomiting and sagging were observed 5 days before hospitalization. His mental status was drowsy on the date of admission. On brain MRI performed after hospitalization, there was edematous swelling in bilateral parieto-occipital lobe on T2 fluid-attenuated inversion recovery (FLAIR) images (Fig. 1A), and multiple microbleeds in the bilateral parieto-occipital subcortical white matters on gradient-echo (GRE) image (Fig. 1B). Diffusion-weighted image (DWI) (Fig. 1C) show no high signal intensity and apparent diffusion coefficient (ADC) (Fig. 1D) maps showed increased ADC value in the both parieto-occipital area, suggesting vasogenic edema. No enhancement was seen in the both parieto-occipital area on contrast-enhanced T1-weighted images (Supplementary Fig. 1 in the online-only Data Supplement). This MRI finding was considered to be subacute hemorrhagic infarction in the both parieto-occipital area, and he was treated with anticoagulants for a subacute infarction. He was discharged with improved mental status and aphasia symptom. After discharge, he was followed every 3 months in the outpatient clinic and was treated with oral anticoagulant. During follow-up, there were no acute neurologic symptoms other than subjective memory loss.

15 months later, he visited the emergency room for general weakness, and follow-up brain MRI was performed. No acute infarction was seen on DWI (not included), and previously noted vasogenic edema in the both parieto-occipital area disappeared on T2 FLAIR image (Fig. 1E). There was no significant change of multiple microbleeds in the bilateral parieto-occipital subcortical white matters on GRE images (Fig. 1F). There was no newly developed microbleed in the other cerebral hemisphere on GRE images.

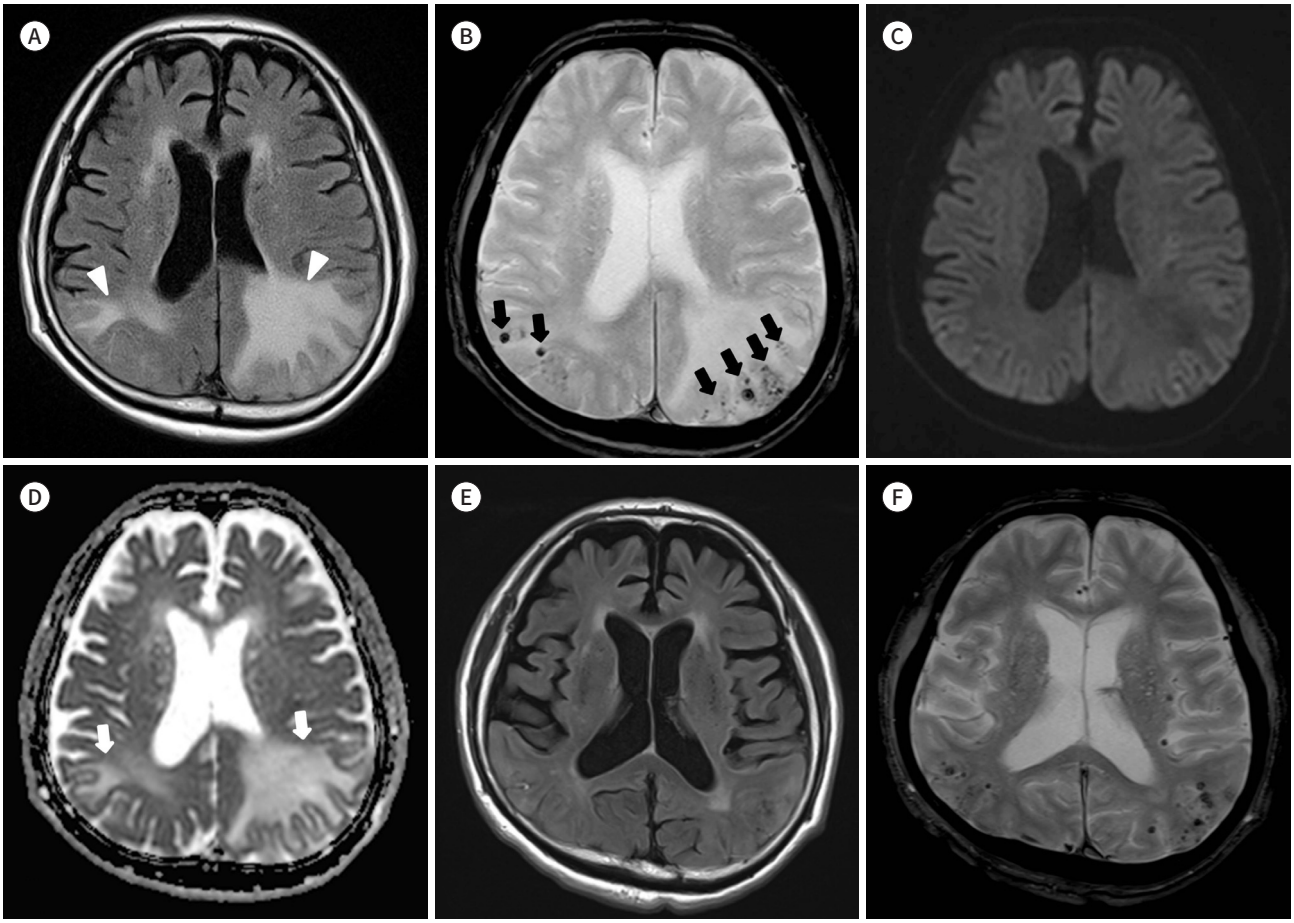
As a result of reviewing the patient's clinical course and brain MR images, CAA-RI could be finally diagnosed.

This study was approved by the Institutional Review Board of Ewha Womans University Mokdong Hospital assigned IRB No. 2022-07-026 and the requirement for informed consent was waived.

DISCUSSION

Our patient presented with acute neurological symptoms, drowsiness and aphasia. MRI findings included vasogenic edema with microbleeds in bilateral parieto-occipital area which could also be observed in subacute infarction. Our initial diagnosis was subacute infarction.

Fig. 1. Initial and follow-up MR images of the patient with cerebral amyloid angiopathy-related inflammation.
A. The T2 FLAIR image shows, asymmetric, edematous swelling (arrowheads) in the bilateral parieto-occipital areas.
B. The GRE image shows multiple microbleeds (arrows) in the bilateral parieto-occipital and subcortical white matter.
C. The diffusion-weighted image shows no high signal intensity in either of the parieto-occipital areas.
D. The ADC map shows an increased ADC value (arrows), suggesting vasogenic edema in both parieto-occipital areas.
E. The follow-up brain MRI was obtained 15 months after the first brain MRI. The follow-up T2 FLAIR image shows that the edema in both parieto-occipital areas has almost disappeared.
F. Multiple microbleeds in both parieto-occipital and subcortical white matter are not significantly changed on the T2 GRE image.
ADC = apparent diffusion coefficient, FLAIR = fluid-attenuated inversion recovery, GRE = gradient-echo



However, considering the clinical course and spontaneous regression of the lesion in the follow-up brain MRI, the final diagnosis of CAA-RI was reached.

CAA is a vascular disease in which Aβ is deposited on the tunica adventitia and tunica media of blood vessels in the brain (2). Deposited Aβ gives damage to vascular media and adventitia, resulting in loss of integrity of vessel wall (3). This can lead to vascular rupture with secondary microbleeds and hematoma or vessel lumen obliteration. In some patients, activation of a proinflammatory cascade leads to perivascular inflammation with or without vasculitis, which is described as CAA-RI (3).

Diagnosis of CAA-RI is often delayed and sometimes missed. Definite diagnosis requires histological confirmation, but stereotactic biopsy may cause complications such as hemorrhage. According to the diagnostic criteria of CAA-RI, probable CAA-RI can be diagnosed

when there are these all of the following: 1) acute or subacute onset of symptoms; 2) 40 years of age or older; 3) at least 1 typical clinical feature(headache, mental status or behavioral change, focal neurologic signs, and seizure); 4) MRI shows patchy or confluent T2 or fluid attenuation inversion recovery (FLAIR) hyperintensity which is usually asymmetric; 5) evidence of pre-existing CAA(multiple cortical and subcortical hemorrhages or microhemorrhages and/or recent or past lobar hemorrhage) on susceptibility weighted image (SWI) sequences; 6) absence of neoplastic, infectious, or other causes (4, 5). The proposed diagnostic criteria allow diagnosis of probable CAA-RI without brain biopsy (4, 5).

MRI findings of CAA-RI are asymmetric patchy or confluent T2/FLAIR hyperintensity in white matter, suggesting vasogenic edema (3). Microbleeds at the cortical-subcortical junction on SWI are strong imaging markers to support diagnosis (3). These two findings are sufficient imaging findings to diagnose probable CAA-RI without brain biopsy.

The most common symptom of CAA is intracerebral hemorrhage (ICH), but the most common symptom of CAA-RI is cognitive decline in acute or subacute manner (6). Other symptoms include seizures, headache, encephalopathy (confusion, impairment of consciousness), motor weakness, and aphasia (6).

The course of the CAA-RI is variable. According to previous report, course of CAA-RI could be divided in to three groups (7). The first "improved" group improved shortly after treatment and the second "relapsing" group initially improved but experienced subsequent symptoms of encephalopathy, seizure, headache. The last "stable/progressive" group had no clinical response to treatment (7).

Although the exact mechanism of how Aβ causes vasculitis is not known, the apolipoprotein E epsilon 4 (APOE e4) genotype has been identified as the only risk factor for CAA-RI (1). However, our case doesn't have genotype information.

CAA-RI is primarily treated with empirical high-dose corticosteroids, and if it does not respond to corticosteroids, immunosuppressants such as cyclophosphamide are used (2). However, a recent systematic review found that there was no statistical difference in outcome between the group treated with steroid alone and the group that used with combination corticosteroid with immunosuppressant (8).

In our case, follow-up MRI showed improvement in vasogenic edema in subcortical white matter despite not receiving corticosteroid treatment. Tetsuka and Hashimoto (9) reported a case of spontaneous remission of CAA-RI. In the case, a patient presented only mild neurologic symptoms (lightheadedness) and was diagnosed with probable CAA-RI based on the proposed criteria. The patient's symptoms and radiologic findings spontaneously resolved without any corticosteroid or immunosuppressant. Therefore, they suggested that in patients with mild symptoms, it would be better to monitor the clinical symptom and radiologic finding without starting immunosuppressive therapy.

An important differential diagnosis for CAA-RI is amyloid-related imaging abnormalities (ARIA). ARIA refers to imaging findings from adverse events associated with monoclonal antibody therapy for beta amyloid in Alzheimer disease. Although both CAA-RI and ARIA share similar imaging findings of sulcal effusion, edema involving gray and white matter, microhemorrhages, and siderosis, but the clinical setting is different. That is, ARIA occurs secondary to anti-amyloid therapy, whereas CAA-RI occurs spontaneously (10).

Another radiological differential diagnosis of CAA-RI may include hemorrhagic infarction, hemorrhagic tumor or primary CNS vasculitis. The characteristic imaging findings of CAA-RI, such as location of edematous change, pattern of microbleeds, and lack of contrast-enhancement, can be distinguish from hemorrhagic infarction, hemorrhagic tumor or primary CNS vasculitis.

In summary, MRI imaging findings are important in diagnosis of CAA-RI. When the accurate diagnosis of CAA-RI is made, unnecessary tests or incorrect treatment can be avoided. If radiologists know the typical MRI findings of CAA-RI, it will be of great help to diagnosis and improving prognosis of patient.

Supplementary Materials

The online-only Data Supplement is available with this article at http://doi.org/10.3348/jksr.2022.0113.

Author Contributions

Conceptualization, K.E.; data curation, P.C., K.E.; formal analysis, P.C., K.E.; investigation, P.C., K.E.; methodology, P.C., K.E.; writing—original draft, P.C., K.E.; and writing—review & editing, all authors.

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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대뇌 아밀로이드 혈관병증 연관 염증: 증례 보고와 문헌 고찰

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대뇌 아밀로이드 혈관병증 관련 염증은 베타 아밀로이드가 혈관에 침착되어 혈관 주위의 급성 염증성 반응으로 발생하는 뇌병증이다. 이 질환은 주로 고령자에게서 발생하는 드문 질환으로, 급격히 진행하는 치매, 두통, 발작, 국소 신경학적 결손을 동반한 증상으로 나타나며 특징적인 뇌자기공명영상 소견을 보인다. 또한 스테로이드 또는 기타 면역억제요법에 반응하는 가역적인 질병이다. 대뇌 아밀로이드 혈관병증 관련 염증을 처음에는 아급성 경색으로 오진하였다가 추적 관찰 중 뇌 자기공명영상 소견을 분석하면서 대뇌 아밀로이드 혈관병증 관련 염증이 진단되었고, 자연 관해가 이뤄진 대뇌 아밀로이드 혈관병증 관련 염증 증례를 보고한다.

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