



Case Report

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Cerebral Amyloid Angiopathy Related Inflammation Presenting as Steroid Responsive Brain Mass

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ABSTRACT

Cerebral amyloid angiopathy (CAA) is a common but often asymptomatic disease, characterized by the deposition of amyloid proteins within brain parenchyma and leptomeningeal-cortical vessels. It can occur as a sporadic disorder or accompany Alzheimer disease (AD). The usual presentation of CAA is spontaneous lobar hemorrhage. Unlike CAA, cerebral amyloid angiopathy-related inflammation (CAA-ri), a subtype of CAA, can show various presentations and responds to steroid (or immuno suppressive) treatment. We report a patient with mixed dementia who showed subacute progression in cognitive impairment and had a mass lesion on brain magnetic resonance imaging (MRI). The lesion was identified as CAA related inflammation and the cognitive status of the patient improved significantly after steroid treatment. In this case report, we aimed to emphasize that CAA-ri is one of the possible diagnoses that should be considered in demented patients with rapid cognitive deterioration and showing brain lesions resembling neoplasms on the MRI. Therefore, steroids or other immunosuppressive treatments, which may lead to a dramatic clinical improvement, could be administered without delay.

KEYWORDS: Cerebral amyloid angiopathy, Steroid response, Brain mass, Inflammation

■ INTRODUCTION

Cerebral amyloid angiopathy (CAA) is a common pathology in the elderly caused by the deposition of amyloid-beta (Ab) in specific cerebral vessels and brain parenchyma (6). The prevalence of CAA is much higher in Alzheimer's disease (AD) and some other types of dementia (4). Although CAA is often asymptomatic, the most frequent presentation is spontaneous cerebral hemorrhage in non-hypertensive individuals (2).

CAA-related inflammation (CAA-ri) is a recently recognized phenomenon caused by an autoimmune response to Ab deposits (3). The clinical picture of CAA-ri includes encephalopathy, focal neurological signs, seizures and headaches (2,3,6).

Although CAA and CAA-ri are usually diffuse pathologies, mass lesions mimicking brain neoplasms, multifocal nonhemorrhagic lesions and leukoencephalopathy can be expected

on magnetic resonance imaging (MRI) (2,7). Unlike other Ab-depositing disorders (e.g., AD), both clinical and radiological symptoms of CAA-ri respond to immunosuppressive therapy (3). Therefore, the recognition and diagnosis of this treatable condition is important.

Herein, we describe a demented patient with CAA-ri presenting with subacute progression in cognitive impairment and brain lesions resembling brain neoplasm on the magnetic resonance imaging (MRI) which improved with low dose steroid therapy.

■ CASE REPORT

An 82-year-old male patient with mild degree mixed dementia was admitted to our outpatient clinic with rapid progression of cognitive decline, gait disturbance, new onset frontal headache and urinary incontinence in the last three weeks. The patient had diabetes mellitus, chronic kidney insufficiency and severe peripheral arterial disease as comorbidities.

His physical examination was not significant. He was disoriented, apathetic, speaking with a limited vocabulary, and walking in an ataxic manner. Blood tests showed no significant change in the routine laboratory tests. EEG and chest x-ray were normal.

Compared with his previous MRI which was performed one year ago, the current T2-weighted and fluid attenuated inversion-recovery (FLAIR) images showed progression of bilateral microangiopathic ischemic gliotic lesions in the cortico-subcortical area and deep white matter. Furthermore, new lesions were noted in the bilateral temporal lobes (more obvious on the right) and left occipital lobe together with some edema of nearby gyral regions (Figure 1). Three-dimensional susceptibility-weighted imaging (3D SWI) sequence demonstrated cortico-subcortical widespread resorbed punctate microhemorrhages mainly in the right frontotemporal and left parietal lobes (Figure 2). There was no restriction on diffusion-weighted MRI and the lesions were iso-hypoperfused on perfusion MRI. Although the lesion on the right hemisphere resembled neoplastic mass lesions, there was no significant enhancement on T1-weighted gadolinium (Gd)-enhanced images (Figure 3). MR spectroscopy was nonspecific and inconsistent with neoplasm. Consequently, the findings were considered as CAA-ri.

We could not get approval for further invasive procedures such as cerebrospinal fluid (CSF) examination and brain biopsy.

The apolipoprotein E (APOE) gene analysis determined that the patient was homozygous for the APOE $\epsilon 4/\epsilon 4$ allele.

Because the patient has serious co-morbid conditions, a relatively low dose of methylprednisolone (32mg/day) was administered for three weeks. A remarkable clinical improvement in the following days and a dramatic regression of the cerebral lesion in the first month follow-up MRI were observed (Figure 4).

DISCUSSION

CAA-ri is postulated as an autoimmune vasculitic and perivasculitic response mediated by autoantibodies to vascular Ab deposits, and generally presents with subacute cognitive decline, headache, seizures, behavioral changes and focal stroke-like deficits (3,6). Our case, consistent with the usual presentation of CAA-ri, showed subacute cognitive decline, headache and ataxic gait.

CAA-ri patients show a higher percentage of homozygous APOE $\epsilon 4/\epsilon 4$ allele than non-inflammatory CAA. This allele is critical for vascular deposition of Ab and activation of inflammation (6,8). Consistent with the literature, our patient was homozygous for the APOE $\epsilon 4/\epsilon 4$ allele.

Although brain biopsy is the gold standard, the diagnosis can be established based on clinical features and MRI findings as well (3). Moreover, the presence of the APOE $\epsilon 4/\epsilon 4$ genotype, elevated anti-Ab autoantibodies (above 32ng/mL) in the CSF and a positive response to steroid therapy are supportive for the diagnosis (3,6,8).

The characteristic MRI appearance is large, confluent and asymmetrical multiple T2-hyperintense lesions extending through the subcortical white matter and cortical gray matter with signal characteristics of vasogenic edema and deterioration of the blood-brain barrier (7,8). Gradient echo (GRE) sequences showing multiple scattered cortical or subcortical microhemorrhages and hemosiderin depositions (evidence of prior subclinical hemorrhages at different ages) are important indicators for the diagnosis (7). CAA-ri can also show a mass effect mimicking brain neoplasms, particularly similar to low-grade gliomas (6,7). On these MRI images,

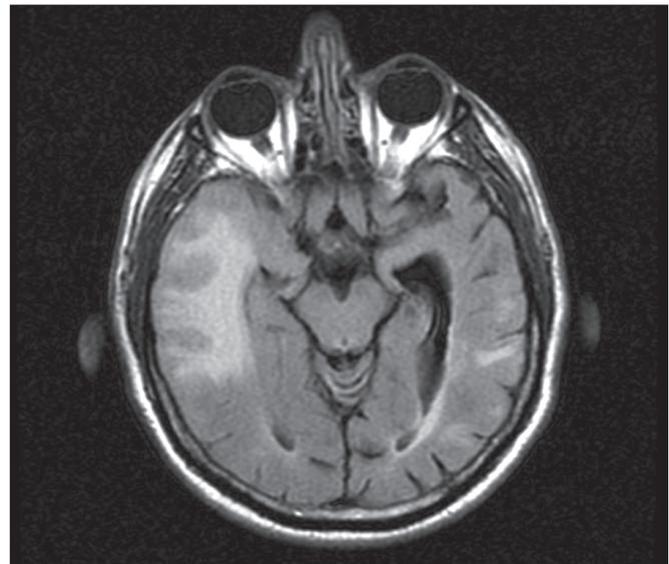


Figure 1: Axial MR Image, FLAIR sequence, obtained at the time of CAA-ri attack. Note the lesion in the right temporal lobe mimicking brain neoplasm.

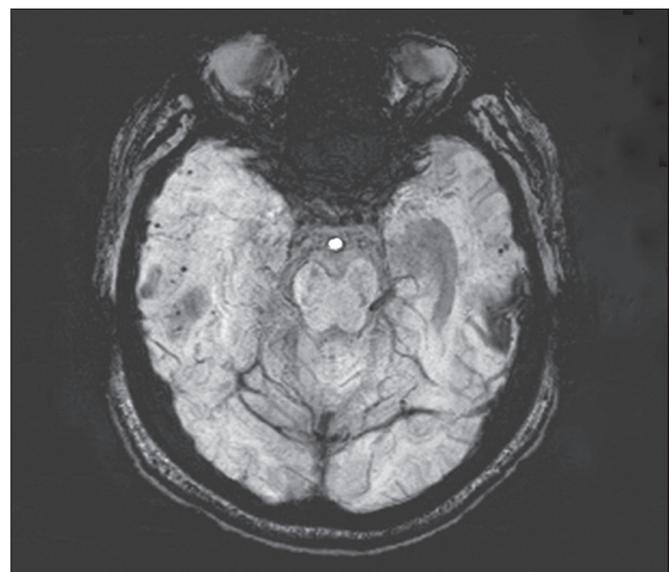


Figure 2: Axial MR Image, 3D SWI sequence, demonstrates cortico-subcortical widespread resorbed punctate microhemorrhages.

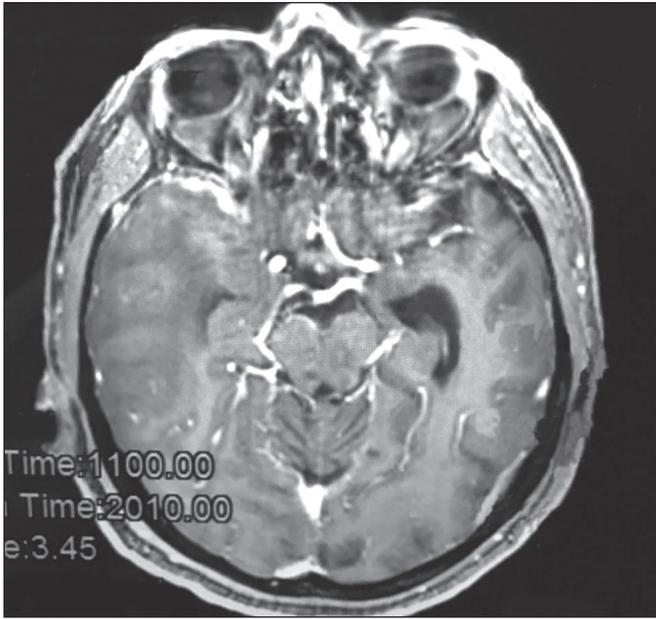


Figure 3: Contrast enhanced, T1-weighted sequence shows no significant enhancement.

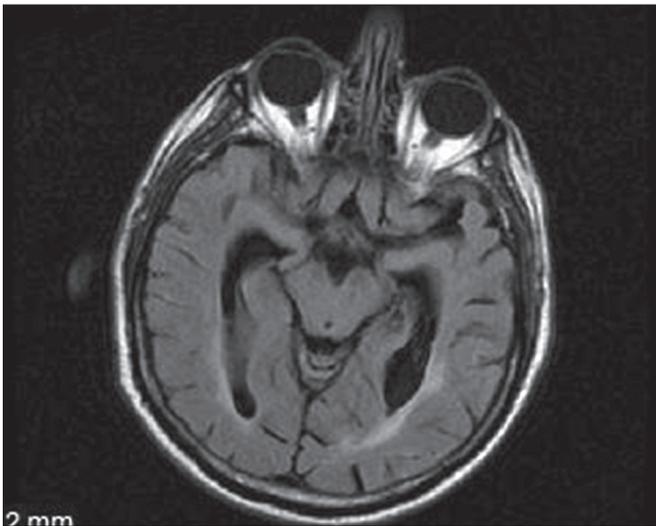


Figure 4: Control MRI (FLAIR sequence) on the first month following three weeks of steroid treatment shows dramatic regression in the right temporal lobe.

lobar white matter signal abnormalities extending out to subcortical U fibers, consistent with edema, are seen without evident gadolinium enhancement (7,8). In our case, MRI images showed multiple T2 hyperintense cortico-subcortical and deep white matter lesions besides bilateral temporal and left occipital lesions mimicking a brain mass together with some edema of nearby gyral regions without gadolinium enhancement. Also, 3D SWI sequence demonstrated cortico-subcortical widespread resorbed punctate microhemorrhages mainly in the right frontotemporal and left parietal lobes.

MR spectroscopy can be helpful to distinguish abnormal amyloid deposition from tumors. CAA-ri, as seen in our case,

shows a normal N-acetylaspartate to creatine (NAA/Cr) ratio and no increase in the cerebral choline/creatin (Cho/Cr) ratio revealing the normal metabolic state of the underlying brain tissue (7).

CAA-ri patients show varying degrees of improvement with corticosteroid and/or immunosuppressive treatment, unlike other Ab-depositing disorders (3,5,6,8). The success of the treatment may vary depending on the pathological subtype of CAA-ri (6). Corticosteroids, such as methylprednisolone and dexamethasone, are the most commonly used drugs (5). Although the treatment response is generally seen within weeks after treatment onset, the improvement can occur over the following months (1,3,5,8). In our case, in view of the many co-morbid diseases of the patient, we administered low dose methylprednisolone (32 mg/day) for three weeks and the patient showed a relevant improvement with steroid therapy.

Our report emphasizes that CAA-ri is one of the possible diagnoses which should be considered in the cognitive and clinical deterioration of demented patients showing brain lesions resembling neoplasms on the MRI. Therefore, steroids or other immunosuppressive treatments, which may lead to a dramatic clinical improvement, could be administered without delay.

REFERENCES

1. Bekkelund SI, Midtbo CE, Arvola L, Eldevik OP, Lindal S: Good outcome in a patient treated for cerebral amyloid angiopathy presenting as an expansive process with inflammation and contrast enhancement. *AJNR Am J Neuroradiol* 32(4): E75, 2011
2. Caulo M, Tampieri D, Brassard R, Christine Guiot M, Melanson D: Cerebral amyloid angiopathy presenting as nonhemorrhagic diffuse encephalopathy: Neuropathologic and neuroradiologic manifestations in one case. *AJNR Am J Neuroradiol* 22(6):1072-1076, 2001
3. Crosta F, Orlandi B, De Santis F, Passalacqua G, DiFrancesco JC, Piazza F, Catalucci A, Desideri G, Marini C: Cerebral amyloid angiopathy-related inflammation: Report of a case with very difficult therapeutic management. *Case Rep Neurol Med* 2015:483020, 2015
4. Jellinger KA: Alzheimer disease and cerebrovascular pathology: An update. *J Neural Transm* 109:813-836, 2002
5. Kimura A, Sakurai T, Yoshikura N, Hayashi Y, Takemura M, Takahashi H, Inuzuka T: Corticosteroid therapy in a patient with cerebral amyloid angiopathy-related inflammation. *J Neuroinflammation* 16:10:39, 2013
6. Kloppenborg RP, Richard E, Sprengers ME, Troost D, Eikelenboom P, Nederkoorn PJ: Steroid responsive encephalopathy in cerebral amyloid angiopathy: A case report and review of evidence for immunosuppressive treatment. *J Neuroinflammation* 9:7-18, 2010
7. Safriel Y, Sze G, Westmark K, Baehring J: MR spectroscopy in the diagnosis of cerebral amyloid angiopathy presenting as a brain tumor. *AJNR Am J Neuroradiol* 25(10):1705-1708, 2004
8. Weiss SA, Pisapia D, Mayer SA, Willey JZ, Lee K: Amyloid β -related angiitis causing coma responsive to immunosuppression. *Case Rep Pathol* 2012:678746, 2012