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CASE REPORT **OLGU SUNUMU**

CEREBRAL AMYLOID ANGIOPATHY RELATED INFLAMMATION – TWO CASES

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ABSTRACT

Cerebral amyloid angiopathy-related inflammation is a rare but increasingly recognized subtype of cerebral amyloid angiopathy with distinctive clinical and imaging findings. Proposed diagnostic criteria depending on clinical and magnetic resonance imaging characteristics have excellent diagnostic accuracy. Patients with cerebral amyloid angiopathy-related inflammation should be treated with corticosteroids and/or immunosuppressives. In this paper, we report two cases with typical characteristics of cerebral amyloid angiopathy-related inflammation.
Keywords: Cerebral amyloid angiopathy, cerebral amyloid angiopathy-related inflammation, magnetic resonance imaging, treatment.

SEREBRAL AMYLOİD ANJİOPATİ İLİŞKİLİ İNFLAMASYON – İKİ OLGU

ÖZ

Serebral amyloid anjiopati ilişkili inflamasyon, serebral amyloid anjiopatinin nadir ancak gittikçe artan biçimde tanınan bir alt tipidir ve ayırt ettirici klinik ve görüntüleme özelliklerine sahiptir. Klinik ve manyetik rezonans görüntüleme bulgularına dayalı önerilmiş tanı kriterlerinin tanısal doğruluğu mükemmeldir. Serebral amyloid anjiopati ilişkili inflamasyonu olan hastalar kortikosteroidler ve / veya immünsüpresifler ile tedavi edilmelidir. Bu makalede serebral amyloid anjiopati ilişkili inflamasyonun tipik özelliklerine sahip olan iki olgu sunulmaktadır.
Anahtar Sözcükler: Serebral amyloid anjiopati, serebral amyloid anjiopati ilişkili inflamasyon, manyetik rezonans görüntüleme, tedavi.

INTRODUCTION

Cerebral amyloid angiopathy (CAA) is a cerebral small vessel disease characterized by amyloid beta (Aβ) accumulation in the media and adventitia of the small and medium-sized leptomeningeal and cortical blood vessels (1,2). Clinical spectrum is variable and includes symptomatic acute lobar hemorrhage, chronic progressive cognitive disturbances and transient focal neurological episodes (1,2). A minority of patients with CAA develop CAA-related inflammation (CAA-RI) which is characterized by acute or subacute onset cognitive and behavioral disturbances, headache and focal neurologic deficits, and caused by autoantibodies against Aβ in the leptomeningeal and cortical blood vessels (1,2). CAA-RI is a rare and aggressive subtype of CAA and has distinctive clinical presentations and characteristic imaging findings. In this paper, we report two patients with CAA-RI and emphasize the differential diagnosis and treatment response in CAA-RI. Of note, informed consent was signed by the patients.

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CASE 1

A 68-year-old female patient with a history of osteoporosis and intracerebral hemorrhage (ICH) presented with subacute onset confusion, speech disturbance and progressive left-sided weakness. Her medical records revealed that the patient had had transient focal sensorimotor dysfunction episode associated with non-traumatic cortical subarachnoid hemorrhage and lobar ICH. Neurological examination revealed the presence of a cognitive disorder including disorientation and memory disturbance (a Mini-Mental State Examination, MMSE, score of 16) and left hemiparesis (4/5 on Medical Research Council) with extensor plantar response.

Brain magnetic resonance images (MRI) showed cortico- subcortical hyperintense signal changes with a slight mass effect on T2-weighted and fluid attenuated inversion recovery (FLAIR) images in the right lateral temporal, parietal and the occipital lobes (Figure 1A and B). There was widespread leptomeningeal gadolinium enhancement on post-contrast T1-weighted images (Figure 2A and B). Widespread cortical and subcortical micro- and macro-hemorrhages and cortical superficial siderosis were seen on susceptibility weighted images (SWI) (Figure 3A and B). Brain MRI spectroscopy and perfusion images and digital subtraction angiography findings did not suggest an alternative diagnosis.

An electroencephalogram (EEG) showed focal background activity irregularity and intermittent sharp waves in the right frontotemporal electrodes. The protein level was increased in the cerebrospinal fluid (CSF, 69.5 mg/dl; normal range: 15-45 mg/dl).

The diagnosis of CAA-RI was made and the patient was treated with intravenous methylprednisolone (1 gr/d for 7 days) followed by 1 mg/kg/d oral prednisone for six months. After the treatment, the patient's clinical and imaging findings significantly improved (MMSE score of 26, Figure 4A and B).

CASE 2

A 63-year-old female patient with a history of diabetes mellitus, hypertension and hyperlipidemia was admitted to our outpatient clinic with the complaints of subacute onset headache and blurry vision on both eyes. She had left homonymous hemianopia. Her brain MRI showed cortico-subcortical hyperintense signal changes in the right parietooccipital lobes on FLAIR and T2-weighted images (Figure 5A and B). Leptomeningeal gadolinium enhancement in the right parietooccipital lobes on post-contrast T1-weighted images was noted (Figure 6). SWI images revealed widespread cortical and subcortical micro- and macro-hemorrhages (Figure 7). Brain MRI spectroscopy and perfusion images did not yield any abnormality. Her EEG and CSF findings were within normal limits. The patient had apolipoprotein E ε3/ε3 genotype.

The diagnosis of CAA-RI was made and intravenous methylprednisolone (1 gr/d for 7 days) followed by 1 mg/kg/d oral prednisone for six months was given to the patient. Her headache and visual field defect as well as brain MRI findings improved after the treatment (Figure 8).

DISCUSSION AND CONCLUSION

CAA-RI is a rare but increasingly recognized subtype of CAA. The prevalence of CAA-RI has been reported to be 0.13/100,000 (3). The mean age at onset is 67 years and males are affected more than females (4). The syndrome has two pathological subtypes: non-destructive perivascular inflammation (inflammatory CAA) and transmural or intramural inflammation (Aβ-related angiitis, ABRA) (5).

CAA-RI has distinctive clinical manifestations including acute or subacute onset mental status changes, headache, seizures and focal neurological deficits (4). One of our patients had subacute onset cognitive dysfunction and focal symptoms and the other had headache and visual field defect. A systematic analysis of 213 pathologically-confirmed patients with CAA-RI has reported the frequency of the neurological symptoms as follows: cognitive disturbance in 48%; seizures in 32%; headache in 32%; encephalopathy in 27%; paresis in 16%; aphasia in 14% and visual symptoms in 13% (4).

Making the diagnosis of CAA-RI in our cases could be possible depending on the clinical and the brain MRI findings showing typical imaging characteristics of CAA plus abnormal cortical and subcortical high signal areas on FLAIR images and leptomeningeal enhancement. Neuroimaging findings are important for diagnosis of CAA-RI.

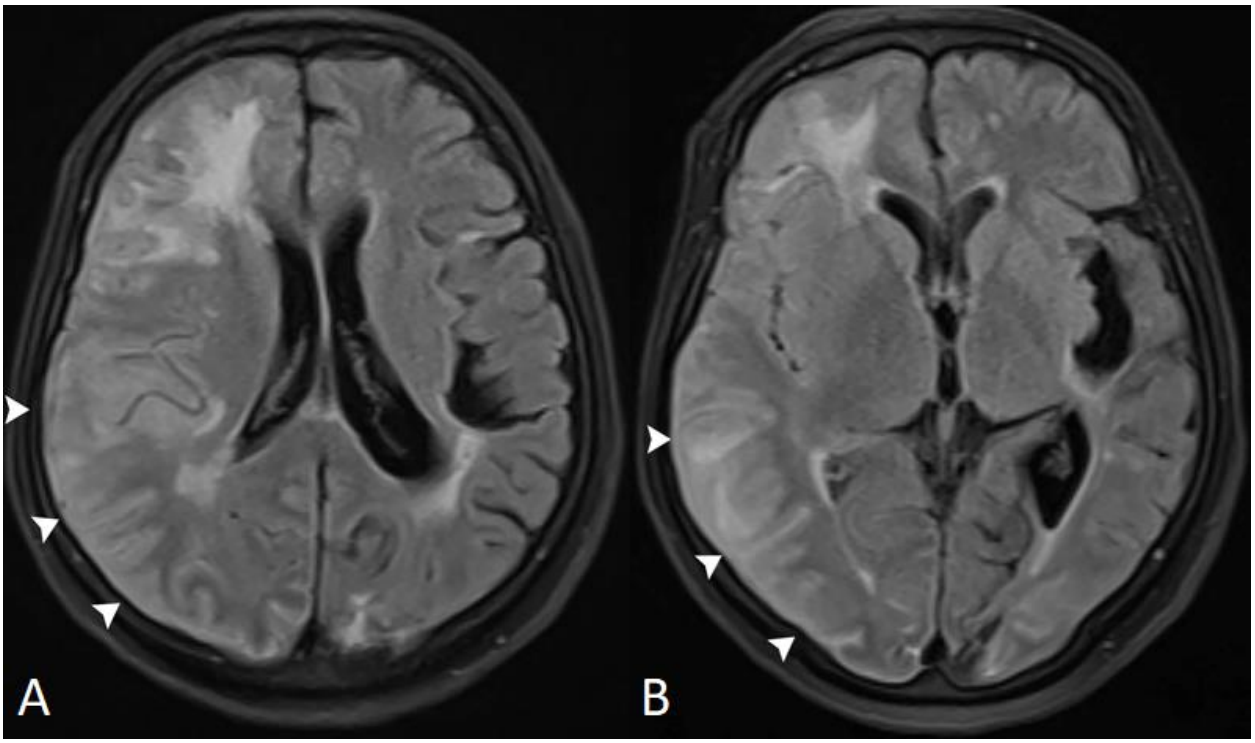

Figure 1. **A** and **B**. Brain MRI. Axial FLAIR images. Cortico-subcortical hyperintense signal changes with a slight mass effect on the right parietal and the occipital lobes (arrowheads).

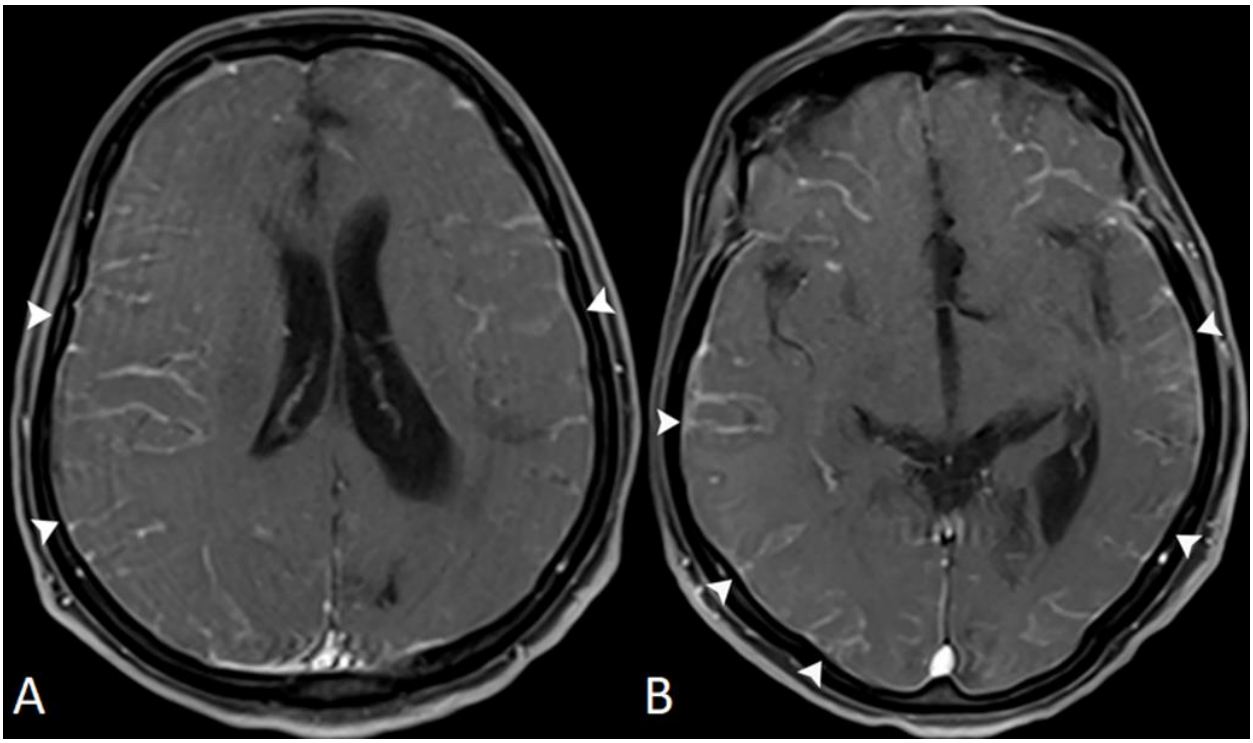

Figure 2. A and **B**. Brain MRI. Axial post-contrast T1-weighted images showing widespread leptomeningeal gadolinium enhancement in both of the cerebral hemispheres (arrowheads).

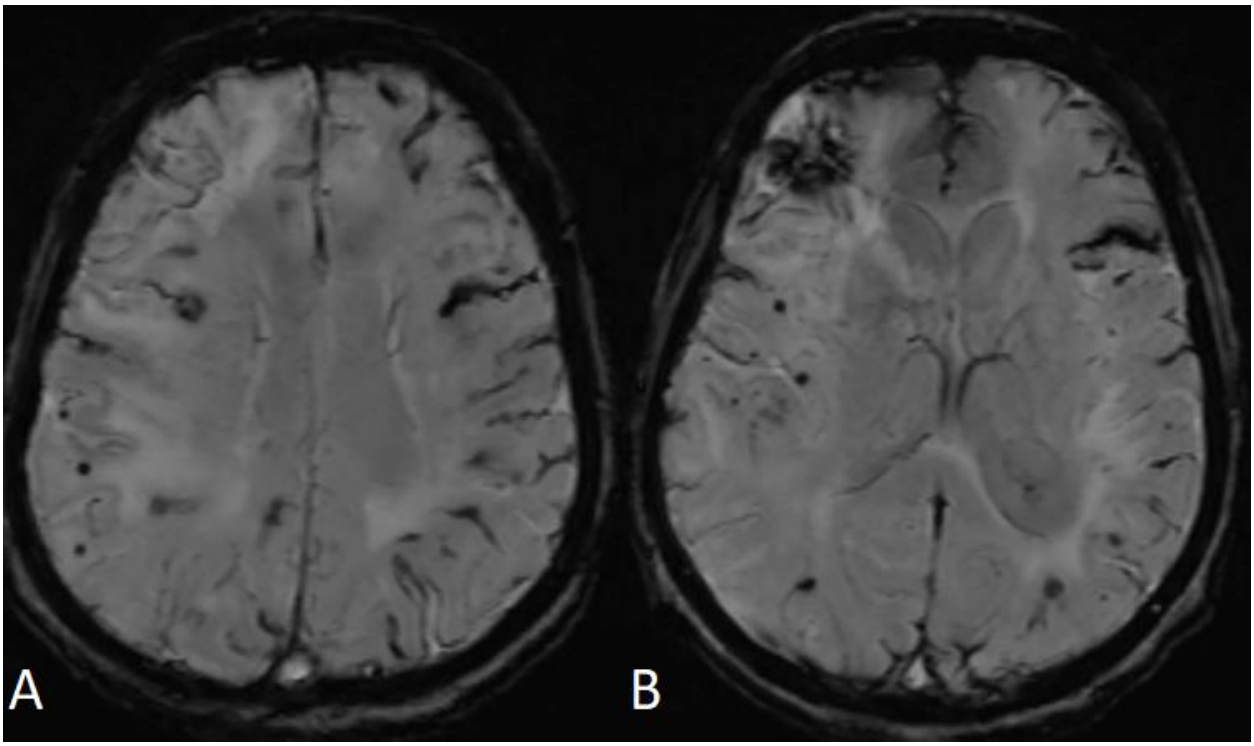

Figure 3. **A** and **B**. Brain MRI. Axial SWI. Widespread cortico-subcortical micro- and macro-hemorrhages and cortical superficial siderosis.

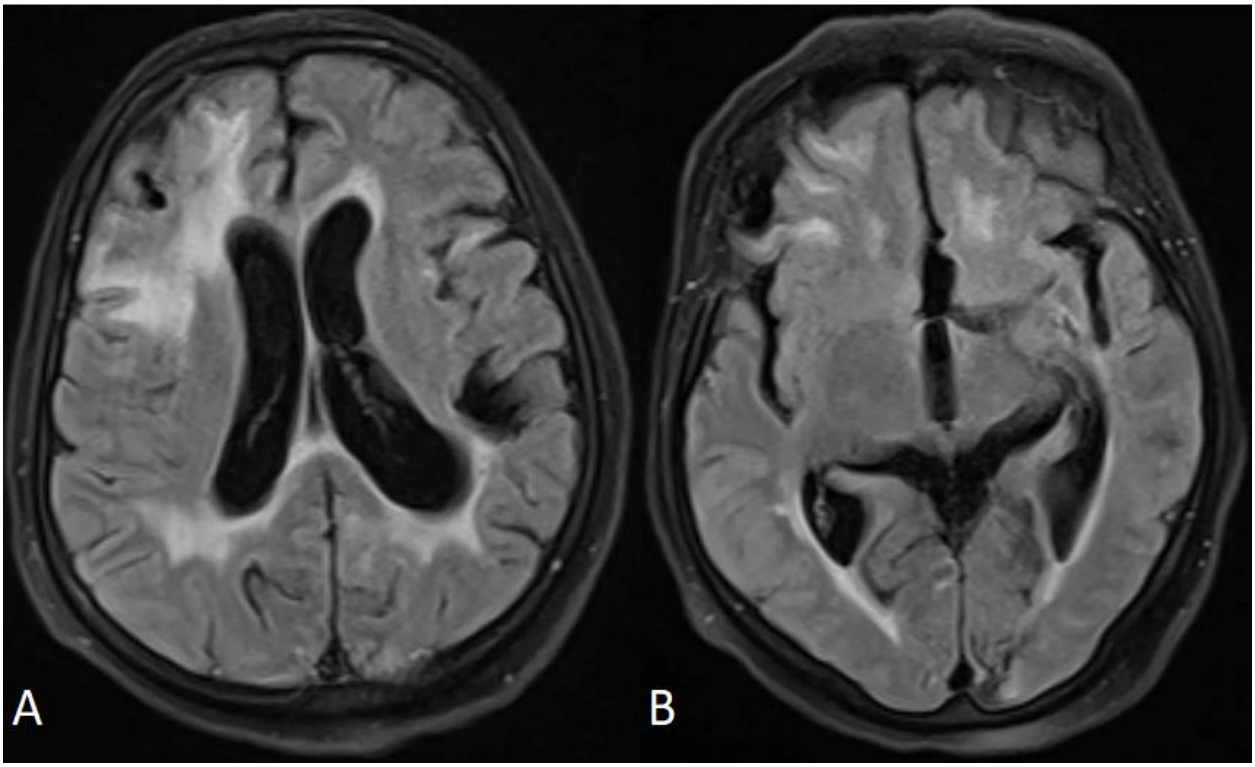

Figure 4. A and **B.** Brain MRI. Axial FLAIR images showing the resolution of the hyperintense signal changes seen on the previous MRI. There are gliotic hyperintense signals due to previous ICH.

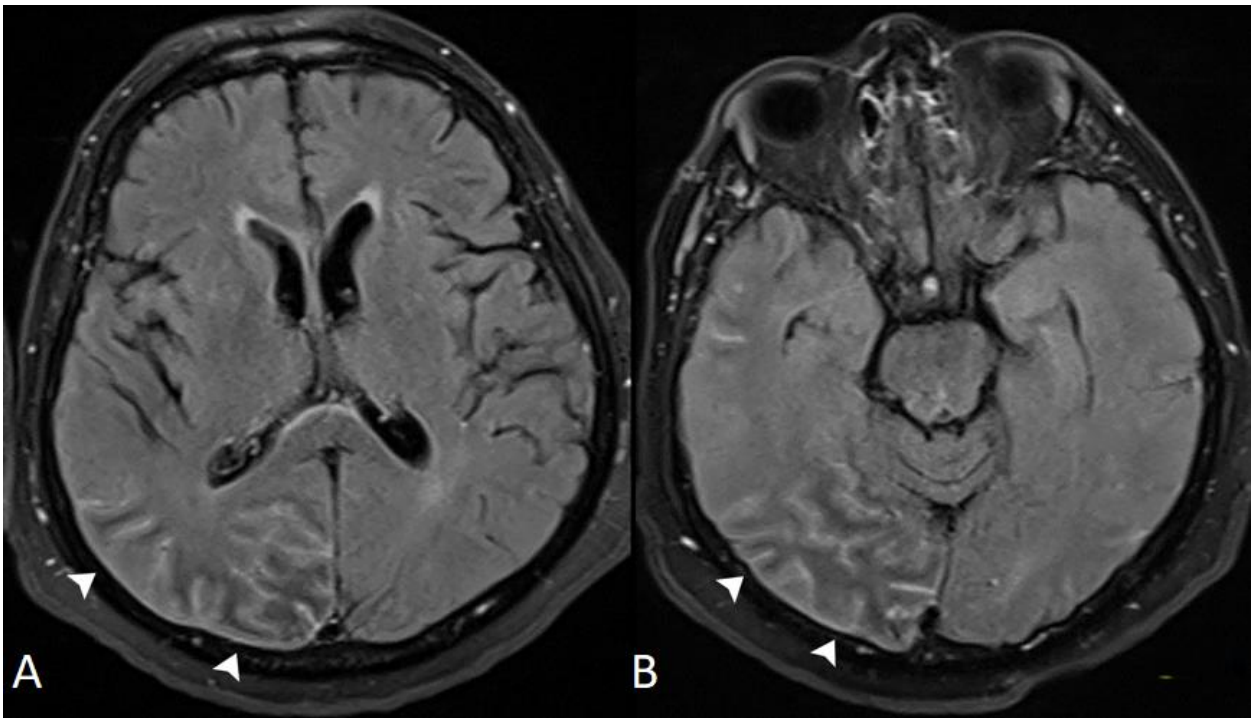

Figure 5. A and **B.** Brain MRI. Axial FLAIR images show cortico-subcortical hyperintense signal changes in the right parietooccipital lobes (arrowheads).

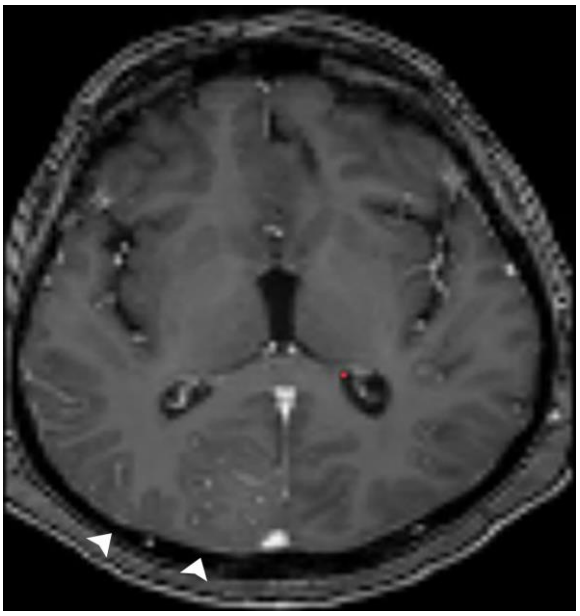

Figure 6. Brain MRI. Axial post-contrast T1-weighted image shows leptomeningeal gadolinium enhancement in the right parietooccipital lobes (arrowheads).

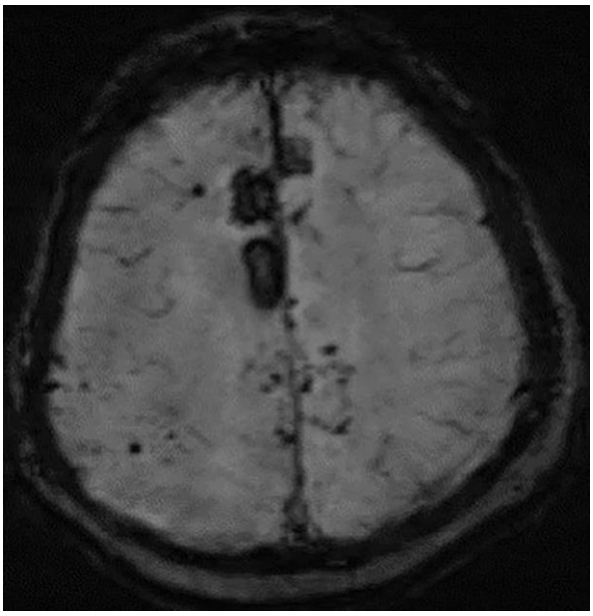

Figure 7. Brain MRI. Axial SWI. Multiple cortical and subcortical micro- and macro-hemorrhages.

The supportive findings are asymmetrical, patchy or confluent subcortical white matter hyperintense signal changes on T2-weighted/FLAIR images in addition to multiple cortico-subcortical microhemorrhages, lobar hemorrhages and cortical superficial siderosis on T2* or SWI images typical for CAA. These signal changes are characterized by vasogenic edema and

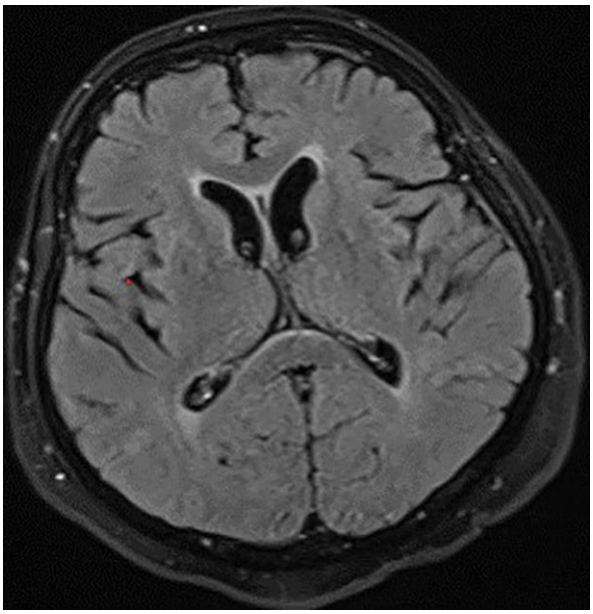

Figure 8. Brain MRI. Axial FLAIR images showing the resolution of the right parietoocipital lesion.

may have mass effect. There may be parenchymal and / or leptomeningeal gadolinium enhancement (2). Leptomeningeal enhancement has a sensitivity of 70.4% and a specificity of 92.6% for discriminating CAA-RI from CAA (6). As CAA and CAA-RI are small vessel diseases, angiography findings are normal, if the medium-sized vessels are affected, there may be nonspecific changes. Amyloid positron emission tomography showing regional increased amyloid accumulation, may be useful (2).

The gold-standard method for diagnosis is brain biopsy. Because of the invasiveness of brain biopsy, diagnostic criteria depending on clinical and imaging findings have been proposed. Boston Criteria proposed in 2011 have been revised in 2016 (7,8). The sensitivity and the specificity of the revised criteria for CAA-RI diagnosis are 82% and 97%, respectively (8). It is recommended that patients diagnosed as CAA-RI with these criteria should be given empirical immunosuppressive medications and brain biopsy should be considered if there is no response (8).

CAA-RI can be treated effectively. High dose corticosteroids and immunosuppressives, if necessary, are effective in most patients. Without treatment, the prognosis is poor (2).

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Ethics

Informed Consent: The authors declared that informed consent form was signed by the patients.

Copyright Transfer Form: Copyright Transfer Form was signed by the authors.

Peer-review: Internally peer-reviewed.

Authorship Contributions: Surgical and Medical Practices: ÖKY, SK, ÖNC. Concept: ÖKY, SK. Design: ÖKY, ÖNC. Data Collection or Processing: SK, ÖNC. Analysis or Interpretation: SK, ÖNC. Literature Search: ÖKY, SK. Writing: ÖKY, SK, ÖNC.

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