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CASE REPORT

Cerebral amyloid angiopathy-related inflammation: A case report and literature review

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Abstract

Cerebral amyloid angiopathy (CAA) is a cerebral small vessel disease caused by the deposition of beta-amyloid in the small- and medium-sized blood vessels of the cerebral cortex and leptomeninges, leading to intracranial vascular amyloidosis. Herein, we report a case of CAA -related inflammation (CAA-ri), a rare clinical condition, focusing on the clinical manifestations, imaging characteristics, cerebrospinal fluid (CSF) findings, and treatment strategies. Key clinical manifestations included psychiatric abnormalities, cognitive impairment, and epilepsy. Brain magnetic resonance imaging revealed asymmetric white matter lesions, whereas susceptibility-weighted imaging demonstrated multiple microbleeds. CSF analysis indicated elevated total protein levels. Following corticosteroid pulse therapy, there was a marked improvement in both clinical symptoms and imaging findings. Given its rarity in clinical practice, early recognition and timely intervention of CAA-ri are crucial for optimizing patient outcomes and enhancing quality of life.

Keywords: Cerebral amyloid angiopathy-related inflammation; White matter degeneration; Multiple microbleeds; Diagnosis; Misdiagnosis

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1. Introduction

Cerebral amyloid angiopathy (CAA) is a common cerebral small vessel disease in the elderly, caused by the deposition of beta-amyloid (Aβ) in the small and medium-sized blood vessels of the cerebral cortex and leptomeninges, leading to intracranial vascular amyloidosis. CAA-related inflammation (CAA-ri) is a rare and treatable clinical subtype of CAA, which is considered to be related to Aβ deposition and immune inflammation.[1] Unlike typical CAA, CAA-ri is marked by extensive cortical and subcortical microbleeds, and its progression can be effectively managed with immunosuppressive therapy.[2] Given its atypical symptoms, CAA-ri is extremely easy to overlook clinically. Here, we report patients with diverse clinical manifestations of CAA-ri and review relevant literature to deepen clinicians' understanding of this disease and reduce misdiagnosis and missed diagnosis.

2. Case presentation

A 73-year-old male presented to the Department of Neurology, Suzhou Hospital Affiliated to Nanjing Medical University on July 15, 2023, due to "unsteady walking accompanied

by slow reaction for 2 months, with aggravation and abnormal behavior for 1 day." Two months before seeking medical consultation, the patient had developed unsteady walking and a slow reaction without apparent reasons. He visited the emergency department of our hospital, where a cranial computed tomography (CT) scan was conducted, showing multiple white matter lesions in the brain. When he was admitted to the hospital, biochemical tests indicated that creatinine was 158 μmol/L and serum potassium was 2.97 mmol/L. The results of blood routine, hepatitis B, treponema pallidum, human immunodeficiency virus, and immune tests were normal. Further cranial magnetic resonance imaging (MRI) showed multiple old hemorrhagic foci in the bilateral frontal lobes, accompanied by local brain tissue edema and demyelination, such as changes in the white matter of the bilateral occipital lobes (Figure 1). Total aortic CT angiography indicated severe stenosis of the left renal artery. Cerebrospinal fluid (CSF) tests showed that the total protein was 760 mg/L, and the results of CSF biochemistry, routine tests, and tests for autoimmune encephalitis were not significantly abnormal. During hospitalization, the patient's systolic blood pressure fluctuate around 180 – 200 mmHg, and renal function continued to deteriorate. Creatinine increased from 158 μmol/L at admission to 430 μmol/L. The initial diagnosis was reversible posterior leukoencephalopathy syndrome. Left renal artery stenting was performed. After the operation, the patient's blood pressure returned to normal, and the symptoms of unsteady walking and slow reaction improved slightly as compared to the condition at admission, and then he was discharged. Three weeks after discharge, that is, on July 14, 2023, the patient experienced uncontrolled bowel movement at home in the kitchen for undetermined reasons. After being discovered by his family, the patient was immediately sent to the emergency department of our hospital. While waiting for treatment, the patient developed a disturbance of consciousness accompanied by generalized tonic-clonic seizures. He was admitted to our department for further treatment.

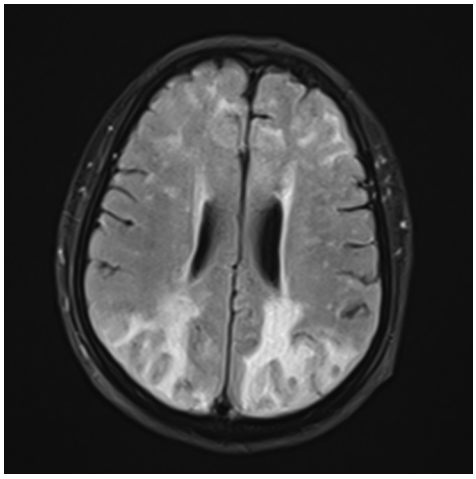

Figure 1. Fluid-attenuated inversion recovery shows abnormally high signals mainly in the posterior part of the brain

The patient had a history of hypertension and had undergone abdominal aortic aneurysm stenting and renal artery stenting. At admission, his body temperature was 36.5°C, pulse rate was 72 beats/min, and blood pressure was 166/78 mmHg. The patient was conscious but listless and was wheeled into the ward on a stretcher. At this point, he had a slow reaction, poor memory of recent events, and decreased calculation and execution abilities, but normal orientation and remote memory. He became less cooperative during the body examination and was not able to correctly respond to all questions asked. At this point, he had a slow reaction, poor memory of recent events, and decreased calculation and execution abilities, but normal orientation and remote memory. He became less cooperative during the body examination and was not able to correctly respond to all questions asked. The examination of cranial nerves showed no obvious abnormalities. The muscle tone of the four limbs was normal, the muscle strength of the four limbs was grade 4, and the tendon reflexes of the four limbs were symmetrical. The patient was uncooperative during the examination of deep and superficial sensations, and also uncooperative in the finger-nose test and heel-knee-shin test. He was not able to walk in a straight line and cooperate well in the Romberg test. The bilateral pathological signs were negative, and the meningeal irritation sign was negative.

Regarding the laboratory tests and auxiliary examinations, his red blood cell count was 2.93×10^{12}/L, high-sensitivity C-reactive protein was 36 mg/L, creatinine was 304.3 μmol/L, uric acid was 528.4 μmol/L, potassium was 3.49 mmol/L, albumin was 34.7 g/L, progastrin-releasing peptide was 132 pg/mL, and the test results of other tumor markers, rheumatological and immunological indexes were normal. According to the lumbar puncture examination, CSF pressure was 150 mmH_2O, the Pandy test was positive, total CSF protein was 969 mg/L, and the results of other CSF routine tests, paraneoplastic neurological syndrome antibody spectrum and metagenomic detection of pathogenic microorganisms were normal. In cranial MRI, asymmetric leukoencephalopathy was visible in the whole brain on T2 fluid-attenuated inversion recovery (FLAIR) sequence (Figure 2A and B), whereas multiple microhemorrhagic foci were visible on susceptibility-weighted imaging (SWI) sequence (Figure 3A and B). CT of the chest, abdomen, and pelvis showed scattered chronic inflammation in both lungs without malignant manifestations, and tumor markers were also negative. Immunological-related

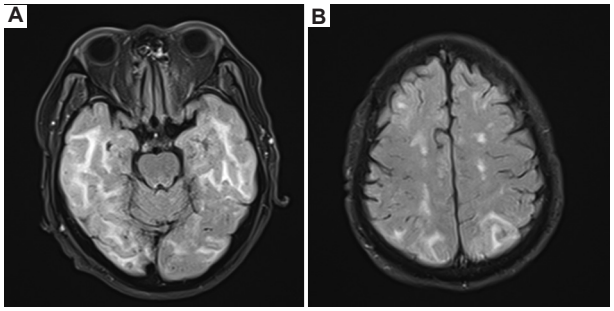

Figure 2. Fluid-attenuated inversion recovery shows asymmetrical high signals in both sides of the brain. (A) A substantial amount of subcortical white matter degeneration. (B) High signal intensity in the white matter of the parietal cortex.

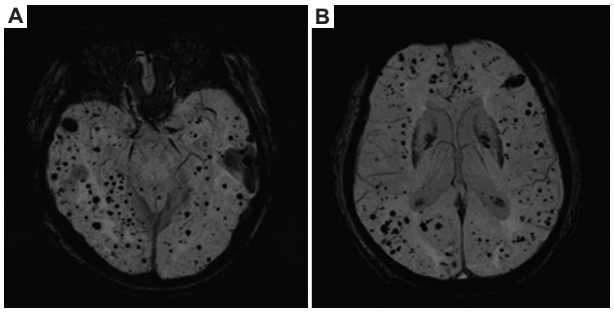

Figure 3. Susceptibility-weighted imaging shows extensive punctate and patchy microbleeds in the cortex and subcortex. (A) Numerous microhemorrhages were observable, and they were more pronounced in the temporal lobe. (B) Multiple bilateral occipital lobe microhemorrhages.

antibodies were all negative. Based on the clinical manifestations and auxiliary examinations, a diagnosis of CAA-ri was considered. The patient was advised to receive complete genetic testing and receive hormone treatment, but the patient's family refused genetic testing. Therefore, intravenous infusion of methylprednisolone sodium succinate at a dose of 1000 mg/day was given as shock therapy (the dose was reduced every 3 days, decreasing to 500 mg/day, 240 mg/day, 80 mg/day, and 40 mg/day); then oral prednisone acetate tablets at a dose of 50 mg/day were administered. After 2 weeks of treatment, the patient exhibited significant improvement in memory decline compared to baseline and was able to walk independently. A follow-up head MRI revealed a slight improvement in white matter degeneration. Prednisone acetate was continued at a dose of 45 mg/day, with a weekly taper of 5 mg initiated post-discharge. One month later, the patient was readmitted due to a lung infection. Upon neurological examination, there was no evidence of cognitive dysfunction or limb weakness. A repeat head MRI showed that SWI microbleeds had not progressed compared to the MRI on July 18, 2024 (Figure 4), and the abnormally high signals in the white matter on T2-weighted imaging FLAIR had significantly decreased

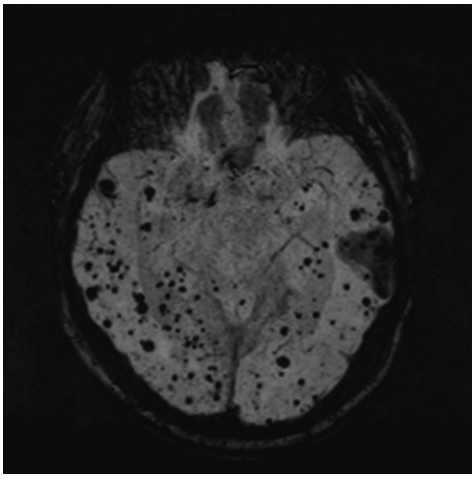

Figure 4. There is no significant change in susceptibility-weighted imaging microbleeds compared to before treatment.

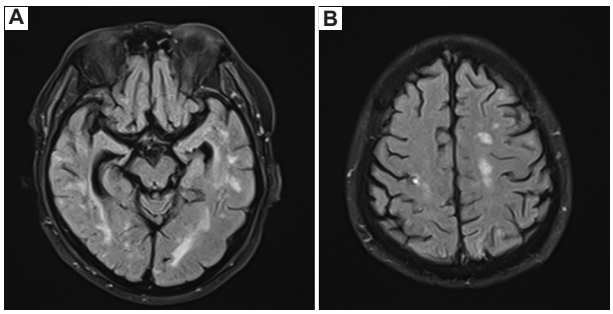

Figure 5. The white matter hyperintensity on T2 fluid-attenuated inversion recovery is significantly reduced compared to before treatment. (A) The high-signal intensity in the temporal lobe white matter has shown improvement compared with the previous findings. (B) The abnormal signals in the cerebral cortex have decreased as compared to the previous examination.

(Figure 5A and B). On January 23, 2024, the patient was admitted for a follow-up examination of the renal stent. At this time, the patient exhibited no significant cognitive impairment and no recurrence of behavioral abnormalities. An MRI was performed, revealing demyelinating changes on the T2 sequence similar to those observed in September 2023, with a slight reduction in high signals near the frontal and parietal cortex (Figure 6A and B).

3. Discussion

CAA-ri is a rare autoimmune encephalopathy in which Aβ deposition triggers a vascular inflammatory response. As early as 1979, from the biopsies of three CAA patients' brain tissues, some scholars found that amyloid deposits (showing orange-red in Congo red staining) were widespread in the leptomeningeal and cerebral cortical blood vessels. Moreover, lymphocyte infiltration was detected in and around these deposits.[3] Through

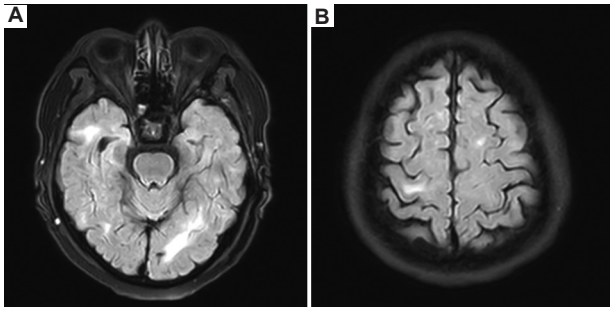

Figure 6. The abnormally high signal detected by fluid-attenuated inversion recovery imaging resembles those observed in September 2023 but with a reduction of the signal near the cortex. (A) No progression of white matter degeneration was noted compared to the previous assessment. (B) No significant white matter degeneration was noted in the cortex.

further exploration in subsequent research, CAA-ri has been divided into two subtypes: Aβ-related angiitis with granulomatous inflammation damaging the blood vessel wall (angiodestructive inflammation and amyloid β-related angiitis) and non-destructive perivascular inflammation with only lymphocyte and macrophage infiltration (inflammatory CAA [ICAA]).[4] At present, the etiology and pathophysiological mechanisms of CAA-ri remain unclear. Two plausible pathogenesis mechanisms are that Aβ deposition in the blood vessel wall promotes vasculitis or that the inflammatory response promotes Aβ deposition.[1]

This patient was an elderly male with an acute onset. The clinical manifestations included cognitive decline, abnormal behavior, and epileptic seizures. Cranial MRI indicated multiple asymmetric leukoencephalopathy and cerebral microhemorrhages. The modified diagnostic criteria proposed by Theodorou *et al.*[5] include the following: (i) Age ≥ 40 years old; (ii) presence of ≥1 of the following clinical features: Headache, decreased consciousness, behavioral changes, or focal neurological signs and epileptic seizures, and this manifestation cannot be directly attributed to acute intracranial hemorrhage; (iii) presence of ≥1 of the following subcortical hemorrhagic lesions: Cerebral macrohemorrhage, cerebral microhemorrhage, or cortical superficial siderosis; and (iv) no tumors, infections, or other causes. To diagnose CAA-ri, imaging should also show single or multiple asymmetric white matter hyperintense lesions (and the asymmetry is not due to previous intracranial hemorrhage). The 73-year-old patient described in this article exhibited clinical manifestations including behavioral changes and focal neurological signs. MRI revealed abnormal white matter degeneration and extensive microbleeds, fulfilling the criteria for probable CAA-ri. At present, brain pathological biopsy remains the gold standard for the diagnosis of CAA-ri. Considering the risks of bleeding, infection, and aggravation of the condition caused by invasive examinations, as well as the poor acceptance of patients, the current utilization rate of brain biopsy is only 0.5 – 1%.[6] In terms of genes, being a homozygous ε4/ε4 in the ApoE-ε4 allele is considered the only definite risk factor for CAA-ri.[7] The carriage rate of ε4/ε4 in CAA-ri patients is 76.9%, whereas only 5.1% of non-ICAA patients carry the homozygous gene.[8] Nevertheless, this patient did not undergo complete genetic testing. In addition, high-titer anti-Aβ autoantibodies can be detected in the CSF of CAA-ri patients in the acute phase, and the antibody level decreases after treatment. This suggests anti-Aβ autoantibody level as a biomarker for the diagnosis of CAA-ri and the monitoring of treatment effects.[9] Due to the progression of the condition, we resorted to adopting diagnostic treatment after considering CAA-ri. In future diagnoses of CAA-ri, genetic testing, and CSF antibody testing are indispensable.

The clinical manifestations of CAA-ri are diverse and it is highly prone to misdiagnosis. Our patient had high blood pressure, combined with renal artery stenosis and continuous deterioration of renal function. Therefore, at the first diagnosis, it was difficult to completely distinguish it from posterior reversible encephalopathy syndrome (PRES). The clinical symptoms of PRES are similar to those of CAA-ri, including headache, focal neurological deficits, visual impairment, mental and behavioral abnormalities, epileptic seizures, etc. PRES is usually induced by hypertension, pregnancy-induced eclampsia, severe renal impairment, and the use of immunosuppressants.[10] The lesion is mostly located in the territory supplied by the posterior cerebral artery, and the imaging findings can be reversed after treatment. Although this patient had focal neurological deficits, hypertension, and renal function problems, the white matter lesions on CT and MRI were mainly in the posterior part of the brain. Since the patient's symptoms and imaging findings did not improve after antihypertensive treatment, his condition was not a match to PRES. Another differential diagnosis is intravascular lymphoma (IVL), a highly aggressive extranodal systemic malignant tumor caused by massive hyperplasia and abnormal aggregation of malignant B-cells in the lumen of small blood vessels. IVL can involve various organs throughout the body, with the central nervous system and skin being the most common. IVL is more common in middle-aged and elderly people, often presenting with headaches, epileptic seizures, and focal neurological deficits. On cranial MRI T2 and FLAIR sequences, multiple patchy hyperintense signals can be seen, with small patchy enhancement. In a few patients, lobar cerebral hemorrhage and SWI microhemorrhages can be observed.[11] This patient had epileptic seizures and

similar imaging manifestations, but the patient's condition improved after immunosuppressive treatment, which is inconsistent with the characteristics of IVL, such as rapid disease progression and poor prognosis. Clinically, there are CAA-ri patients presenting with stroke-like symptoms or epileptic seizures. These patients were only given cerebrovascular and inflammatory treatments, missing the chance of receiving immunotherapy at an early stage, thereby leading to a decline in their quality of life and even poor prognosis.

CAA-ri is potentially treatable. Clinically, short-term high-dose glucocorticoid shock therapy is the first choice. Baskaran *et al.*[12] demonstrated sustained cognitive improvement lasting over 24 months through a 5-day high-dose methylprednisolone pulse therapy followed by a long-term maintenance regimen.[12] The therapeutic effect of glucocorticoids on CAA-ri is also demonstrated in this patient. Glucocorticoid treatment can not only relieve the patient's clinical symptoms and improve imaging manifestations but also reduce the risk of recurrence. Some research indicates that the recurrence rate of CAA-ri can also be reduced in patients who only receive short-term corticosteroid treatment.[11] For long-term treatment, immunosuppressants such as azathioprine, methotrexate, and mycophenolate mofetil can be added to reduce the patient's dependence on hormones.[13] Experimental glucocorticoid treatment can reduce the necessity of brain biopsy for patients. The biopsy is only considered when there is no significant improvement in patients after 3 weeks of corticosteroid treatment.[8]

4. Conclusion

At present, there are relatively few reports of CAA-ri in China. The incidence of this pathological condition has been underestimated, and misdiagnosis is common among the affected patients. Therefore, CAA-ri should be considered for the elderly with symptoms such as cognitive impairment, headache, epileptic seizures, mental and behavioral abnormalities, and focal neurological damage, if MRI shows multiple asymmetric leukoencephalopathy and microhemorrhages. Further improvement of CSF antibody and genetic testing can be carried out for early identification, diagnosis, and treatment, so as to improve the quality of life of patients.

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Conflict of interest

The authors declare they have no competing interests.

Author contributions

Conceptualization: All authors
Investigation: Yue Zhang
Writing – original draft: Yue Zhang
Writing – review & editing: Zhong Zhao, Chen-hong Qiu

Ethics approval and consent to participate

Written informed consent was obtained from the patient following his participation.

Consent for publication

The patient consented to the publication of his data.

Availability of data

Not applicable.

Further disclosure

Part of the findings have been presented at the 26th Academic Conference on Neurology of Jiangsu Medical Association on December 28, 2023, at Xuzhou, Jiangsu, China.

References

1. Yiyuan X, Rong W, Xin G, *et al*. Research on the pathological characteristics and mechanism of inflammation associated with cerebral amyloid angiopathy. *Chin J Geriatr Heart Brain Vessels*. 2022;24(7):775-777.

   doi: 10.3969/j.issn.1009-0126.2022.07.028

2. Charidimou A. Cerebral amyloid angiopathy-related inflammation spectrum disorders: Introduction of a novel concept and diagnostic criteria. *Ann Neurol*. 2025;97(3):470-474.

   doi: 10.1002/ana.27162

3. Mandybur TI. Cerebral amyloid angiopathy: Possible relationship to rheumatoid vasculitis. *Neurology*. 1979;29(10):1336-1340.

   doi: 10.1212/wnl.29.10.1336

4. Wu JJ, Yao M, Ni J. Cerebral amyloid angiopathy-related inflammation: Current status and future implications. *Chin Med J (Engl)*. 2021;134(6):646-654.

   doi: 10.1097/CM9.0000000000001427

5. Theodorou A, Tsibonakis A, Pateras IS, *et al*. Multiple cerebral microinfarcts: An uncommon presentation of

cerebral amyloid angiopathy-related inflammation. *Neurol Res Pract*. 2023;5(1):28.

doi: 10.1186/s42466-023-00253-9

6. Singh B, Lavezo J, Gavito-Higueroa J, *et al*. Updated outlook of cerebral amyloid angiopathy and inflammatory subtypes: Pathophysiology, clinical manifestations, diagnosis and management. *J Alzheimers Dis Rep.* 2022;6(1):627-639.

   doi: 10.3233/ADR-220055

7. Theodorou A, Palaiodimou L, Malhotra K, *et al*. Clinical, neuroimaging, and genetic markers in cerebral amyloid angiopathy-related inflammation: A systematic review and meta-analysis. *Stroke*. 2023;54(1):178-188.

   doi: 10.1161/STROKEAHA.122.040671

8. Regenhardt RW, Thon JM, Das AS, *et al*. Association between immunosuppressive treatment and outcomes of cerebral amyloid angiopathy-related inflammation. *JAMA Neurol*. 2020;77(10):1261-1269.

   doi: 10.1001/jamaneurol.2020.1782

9. Piazza F, Caminiti SP, Zedde M, *et al*. Association of microglial activation with spontaneous ARIA-E and CSF levels of anti-Aβ autoantibodies. *Neurology*. 2022;99(12):e1265-e1277.

   doi: 10.1212/WNL.0000000000200892

10. Li L, Zheng W, Juan D, *et al*. Clinical and imaging characteristics of reversible posterior leukoencephalopathy syndrome. *Chin J Stroke*. 2016;11(3):179-183.

    doi: 10.3969/j.issn.1673-5765.2016.03.004

11. Richie MB, Guterman EL, Shah MP, *et al*. Susceptibility-weighted imaging of intravascular lymphoma of the central nervous system. *JAMA Neurol*. 2022;79(1):86-87.

    doi: 10.1001/jamaneurol.2021.4391

12. Baskaran AB, Kozel OA, Jhaveri A, *et al*. Diagnosis and management of a mild case of cerebral amyloid angiopathy-related inflammation: A case report. *Surg Neurol Int*. 2025;16:37.

    doi: 10.25259/SNI_1097_2024

13. Chwalisz BK. Cerebral amyloid angiopathy and related inflammatory disorders. *J Neurol Sci*. 2021;424:117425.

    doi: 10.1016/j.jns.2021.117425