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Case Report

Diagnosis and management of a mild case of cerebral amyloid angiopathy-related inflammation: A case report

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ABSTRACT

Background: Cerebral amyloid angiopathy (CAA) is a neurological condition characterized by the deposition of amyloid beta particles within the cerebral vasculature over time. A rare complication of CAA is an autoimmune inflammatory syndrome to cerebrovascular amyloid deposits. In this report, we present a case of CAA-related inflammation (CAA-RI) and discuss the diagnostic and management considerations when encountering this pathology.

Case Description: A 69-year-old man with a history of hypertension, hyperlipidemia, obstructive sleep apnea, benign prostatic hyperplasia, and major depressive disorder presented to the clinic with rapidly progressive cognitive impairment over the preceding 2 months. Magnetic resonance imaging (MRI) of the brain demonstrated white matter hyperintense lesions associated with innumerable microbleeds asymmetrically concentrated in the right parietal lobe, with subtle hyperattenuation of the sulci. These findings suggested a diagnosis of probable CAA-RI. The patient was started on intravenous methylprednisolone, one gram daily for 5 days, followed by a prolonged prednisone taper over the next 6 weeks.

Conclusion: Patients with CAA-RI typically present with cognitive decline, followed by focal neurologic deficits, seizures, and headaches. On MRI of the brain, T2/fluid-attenuated inversion recovery asymmetric hyperintense white matter lesions local to cerebral microbleeds are characteristic. Management of CAA-RI involves high-dose corticosteroids with emerging investigation of immunosuppressive therapies.

Keywords: Case report, Cerebral amyloid angiopathy, Cerebral amyloid angiopathy-related inflammation, Immunosuppressive therapies, Methylprednisolone

INTRODUCTION

Cerebral amyloid angiopathy (CAA) is a neurological condition characterized by the deposition of amyloid beta (Aß) particles within the cerebral vasculature over time.[1,4] This progressive damage to cerebral blood vessels impairs vascular compliance and is associated with microvascular disease and injury.[10] As a result, patients can experience transient neurologic episodes, permanent focal neurologic deficits, and progressive cognitive impairment.[3] A rare complication of CAA is an autoimmune inflammatory syndrome to cerebrovascular amyloid deposits. In this report, we present a case of CAA-related inflammation (CAA-RI) and discuss

the diagnostic and management considerations when encountering this pathology.

CASE DESCRIPTION

A 69-year-old man with a history of hypertension, hyperlipidemia, obstructive sleep apnea, benign prostatic hyperplasia, and major depressive disorder presented to the clinic with rapidly progressive cognitive impairment over the preceding 2 months. He scored 22/30 on the Montreal Cognitive Assessment (MoCA), with deficits in sustained attention, executive dysfunction, visuoconstruction, and semantic fluency. Per the Functional Activities Questionnaire and Barthel Index, he was independent with daily activities of living and had no changes in interpersonal conduct. The remainder of his neurologic examination was within normal limits. He was counseled on regular blood pressure monitoring and strict blood pressure control (goal blood pressure <120/80), lifestyle changes including increased physical activity, increased cognitively stimulating and social activities, dietary modifications, and proper sleep hygiene.

Laboratory assessment was unrevealing for a cause of the rapidly progressive cognitive decline. Magnetic resonance imaging (MRI) of the brain [Figure 1a-c] demonstrated white matter hyperintense lesions associated with innumerable microbleeds asymmetrically concentrated in the right parietal lobe, with subtle hyperattenuation of the sulci. There was a small focus on restricted diffusion in the right precentral gyrus. There was no evidence of neoplasm or infection. These findings suggested a diagnosis of probable CAA-RI. The patient was started on intravenous methylprednisolone, 1 g daily for 5 days, followed by a prolonged prednisone taper over the next 6 weeks.

During a follow-up appointment 2 months later, he scored 25/30 on repeat MoCA testing. A repeat MRI of the brain [Figure 1d] showed significant improvement in the right parietal inflammation. On longitudinal surveillance imaging over the next 2 years, he experienced no recurrent inflammation with associated microbleeds. His cognitive status has remained stable during this time.

DISCUSSION

CAA-RI is a rare complication of CAA in which Aß deposits into leptomeningeal and cortical blood vessels, leading to neuroinflammation.[4] CAA-RI has been described histologically as similar in appearance to a central nervous system vasculitis, where the inflammatory reaction occurs in proximity to amyloid-laden vasculature without angiodestructive features.[7] Patients typically present with a rapidly progressive cognitive decline or behavioral changes [8] followed by focal neurologic deficits, seizures, and/or headaches.[5] Due to the rapid functional and neurological decline seen in these patients, early clinical recognition is essential to ensure the most favorable patient outcomes possible. Magnetic resonance imaging is invaluable to diagnosis. T2/fluid-attenuated inversion recovery (FLAIR) hyperintense white matter lesions extending from the cortical to the subcortical white matter local to hemorrhagic lesions, including cerebral microbleeds and superficial siderosis, are most characteristic of CAA-RI.[5,8]

While there is not currently a standard treatment protocol for CAA-RI, there are medications that have proven to be highly effective. In several retrospective studies, the early use of high-dose corticosteroids or other immunosuppressive agents has been identified as a cornerstone of management. Regenhardt *et al*. determined in their retrospective cohort study that

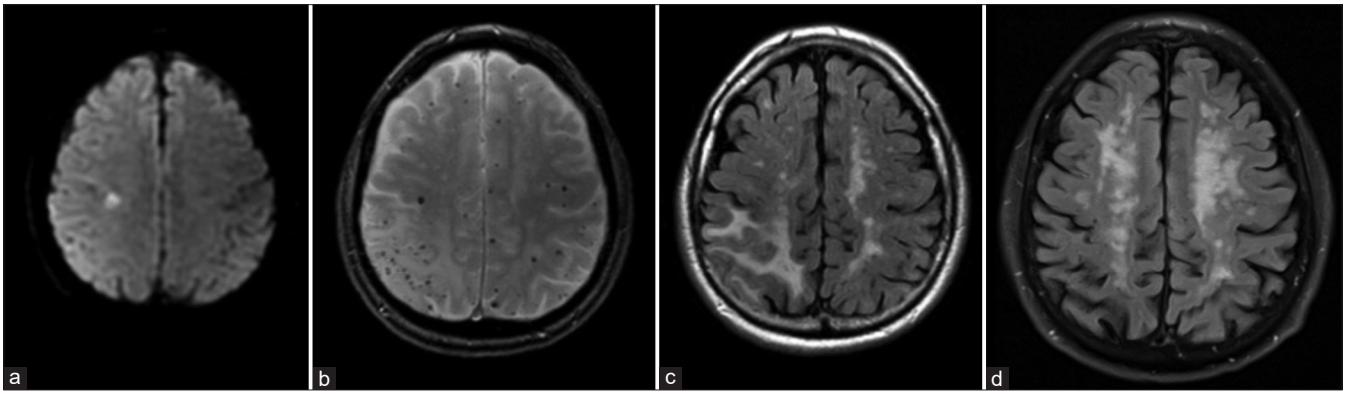

Figure 1: MRI brain with and without contrast of a 69-year-old male with CAA-RI before and after corticosteroid therapy. (a-c) Initial brain MRI. Diffusion-weighted imaging with right frontal infarct. (a) Gradient echo imaging demonstrated multifocal cerebral microbleeds with predominance in the right parietal lobe. (b) T2-FLAIR sequence with asymmetric white matter hyperintensities with predominance in the right parietal lobe and background moderate burden of chronic microvascular disease. (c) Repeat imaging with resolution of right parietal white matter hyperintensities with the progression of chronic microvascular disease. (d) Repeat brain MRI 2 months after initial presentation and corticosteroid therapy. MRI: Magnetic resonance imaging, CAA-RI: Cerebral amyloid angiopathy-related inflammation, FLAIR: Fluid-attenuated inversion recovery.

CAA-RI patients had a statistically significant likelihood of improved clinical and radiographic findings when treated with corticosteroids or other immunosuppressive agents (cyclophosphamide and mycophenolate), as compared to their counterparts who received no therapies.[6] Likewise, Theodorou *et al*. had similar results from their study, finding that CAA-RI patients with early diagnosis and corticosteroid pulse therapy had rapid resolution of symptoms, improved radiographic findings, and a lower likelihood of disease and symptom recurrence.[8] In addition, there is evidence that using empirical immunosuppressive therapy in patients meeting the criteria for probable CAA-RI could avoid brain biopsy, the current gold standard for diagnosis.[9] Finally, while there is less data on the usefulness of intravenous immunoglobulins in CAA-RI, some cases have found it helpful; similar to immunosuppressants, in cases where corticosteroids failed, immunoglobulins have demonstrated symptomatic and radiologic improvement.[2]

In our patient, intravenous high-dose methylprednisolone prescribed for a 5-day course followed by a prolonged steroid wean resulted in cognitive improvement over 2 years. It is important to emphasize that in patients with a suspected CAA-RI diagnosis, the current literature recommends the early use of anti-inflammatory agents, such as corticosteroids, to achieve the most favorable patient outcomes possible. Further, large-scale studies are needed to outline treatment criteria for patients with CAA-RI, specifically for therapeutic regimens, initial treatment duration, and episodes of recurrence.

CONCLUSION

CAA-RI is caused by Aß depositing into cortical and leptomeningeal blood vessels. Patients with CAA-RI typically present with cognitive decline, followed by focal neurologic deficits, seizures, and headaches. On MRI of the brain, T2/FLAIR asymmetric hyperintense white matter lesions local to cerebral microbleeds are characteristic. Management of CAA-RI involves high-dose corticosteroids with emerging investigation of immunosuppressive therapies.

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