CASO CLÍNICO/CASE REPORT

Transient Ischemic Attack and Cerebral Amyloid Angiopathy-Related Inflammation: Similar Presentation, Different Entities

Acidente Isquémico Transitório e Angiopatia Amilóide Cerebral Associada a Inflamação: Apresentação Semelhante, Entidades Diferentes

Raquel Oliveira [1,*]; Raquel Batista [2]; Priscila Flores [3]; Ana Massano [4]; Sérgio Galo [5]; Isabel Martins [2]

1-Serviço de Medicina Física e de Reabilitação / Centro Hospitalar do Médio Tejo, Abrantes, Portugal
2-Serviço de Medicina Interna / Centro Hospitalar do Médio Tejo, Abrantes, Portugal
3-Serviço de Medicina Intensiva / Centro Hospitalar do Médio Tejo, Abrantes, Portugal
4-Serviço de Neurologia / Centro Hospitalar do Médio Tejo, Abrantes, Portugal
5-Serviço de Neuro-Radiologia / Centro Hospitalar do Médio Tejo, Abrantes, Portugal

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***Autor Correspondente / Corresponding Author:**
Raquel Oliveira
Largo Eng. Bioucas,
2200-202 Abrantes, Portugal
raqueloliv94@gmail.com

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Abstract

Cerebral amyloid angiopathy-related inflammation (CAA-ri) is a rare subtype of CAA characterized by a perivascular inflammatory response to amyloid deposition in the brain.

The authors detail the case of a 74-year-old man with aphasia, who was diagnosed with probable CAA-ri following brain magnetic resonance imaging. Treatment recommendations included a 5-day course of high-dose methylprednisolone.

CAA-ri may manifest with transient or permanent neurological symptoms resembling a transient ischemic attack or stroke, potentially leading to misdiagnosis and inadequate long-term treatment. Hence, our objective is to highlight the clinical and imaging findings of this case.

Resumo

A angiopatia amiloide cerebral associada a inflamação (AAC) é um subtipo raro de angiopatia amiloide cerebral e é caracterizada por uma resposta inflamatória perivascular à deposição de amiloide no cérebro.

Os autores descrevem o caso de um homem de 74 anos com afasia, que foi diagnosticado com AAC provável após realização de ressonância magnética cerebral. Foi realizado um ciclo de metilprednisolona em alta dose durante 5 dias.

AAC pode apresentar-se com sintomas neurológicos transitórios ou permanentes que mimetizam um acidente isquémico transitório (AIT) ou acidente vascular cerebral (AVC). Assim, pode conduzir a um diagnóstico e tratamento inadequados, pelo que os autores pretendem chamar à atenção para a apresentação e alterações imagiológicas neste caso clínico.

Introduction

Cerebral amyloid angiopathy (CAA) entails the deposition of amyloid-β in small to medium-sized vessels within the brain. In certain instances, this deposition leads to inflammation or edema, giving rise to CAA-related inflammation (CAA-ri). Unlike typical CAA presentations, which frequently involve acute intracerebral hemorrhage, CAA-ri is distinguished by alterations in memory, personality, consciousness, seizures, persistent headaches, and focal neurological deficits.[1-3]

The average age of presentation is 66 years.[4]

While a definitive diagnosis of CAA-ri necessitates brain and leptomeningeal biopsy, a probable diagnosis can often be inferred from clinical and radiological findings.[5,6] The most common imaging feature is the presence of asymmetric cortical or subcortical white matter hyperintense lesions, attributed to multiple microhemorrhages visible on T2-weighted or SWI sequences.

Immunosuppressive therapy with corticosteroids has been shown to impact the progression of the disease and is therefore the recommended treatment.

The authors intend to emphasize the clinical and radiological changes typically found in this disease due to its rarity, tendency to mimic other conditions, and the need for targeted treatment.

Case Report

A 74-year-old man presented to the Emergency Department (ED) experiencing aphasia with approximately 90 minutes of duration.

His medical history was remarkable for hypertension, diabetes mellitus type 2 and dyslipidemia. He was under daily pravastatin 40 mg, fenofibrate 160 mg, metformin 700 mg and telmisartan 80 mg. No allergies were recorded.

On physical examination at the ED, the patient exhibited elevated blood pressure reading at 180/110 mmHg and demonstrated anomic aphasia. However, no dysarthria or oculomotricity changes were noted. Moreover, there were no observed motor, sensitivity or coordination deficits. His NIHSS score was 2.

Routine laboratory analyses revealed no significant abnormalities. A brain computed tomography (CT) scan showed slight edematous hypodensity affecting the right parietal cortex and subcortex. Cervical CT angiography revealed atheromatous calcifications in the carotid bifurcations, with stenosis ranging from 50%-60% on the left and 40%-50% on the right.

Thrombolysis was not indicated, and the patient received labetalol.

The deficits resolved completely within 3 hours, and the patient remained under clinical observation for 24 hours.

Given the edematous appearance on the brain CT, a brain tumor was suspected. Due to the patient's stable condition and impossibility of performing a brain magnetic resonance imaging (MRI) at the ED, an appointment for MRI was scheduled for 4 days later, with a follow-up appointment set for the following week.

During an outpatient visit 7 days after the ED admission, echocardiography and Holter monitoring results were normal. The brain MRI revealed extensive lesional areas, predominantly affecting the bilateral temporal-occipito-parietal subcortical white matter, with a greater predominance on the right parietal side. These areas appeared hyperintense on FLAIR sequences **(Fig. 1)** and hypointense on T1-weighted sequences. There

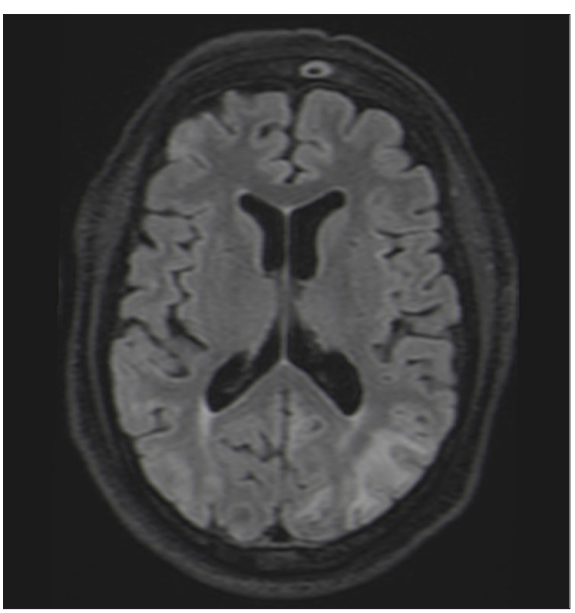

Figure 1. Extensive lesion areas with hyperintense expression on FLAIR sequences, predominantly involving the temporal-occipito-parietal subcortical white matter bilaterally, with greater parietal predominance on the right.

was no evidence of restricted proton diffusion or cortical, subcortical, or meningeal enhancement following intravenous contrast administration **(Fig. 2)**. However, numerous scattered areas of circumscribed hypointensity were observed in SWI throughout the juxtacortical white matter and bilaterally in the fronto-temporo-occipito-parietal cerebral cortex **(Fig. 3)**. The MRI an-

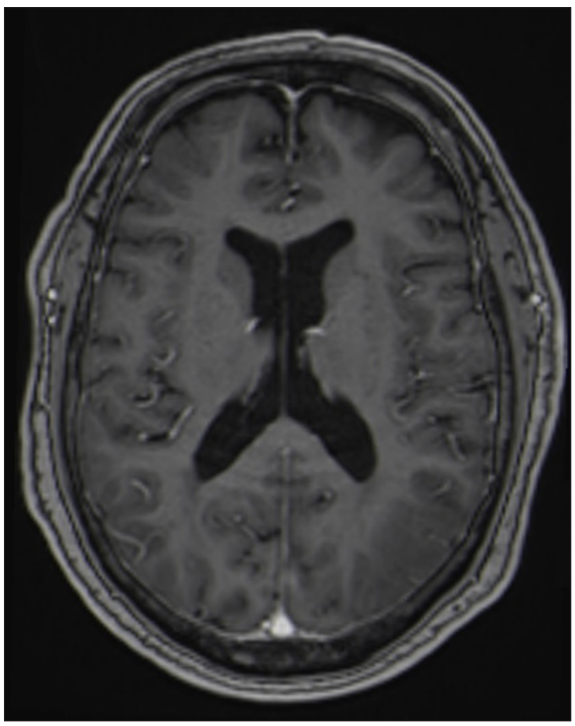

Figure 2. Demonstration of no cortical, subcortical or meningeal enhancement after intravenous constrast administration.

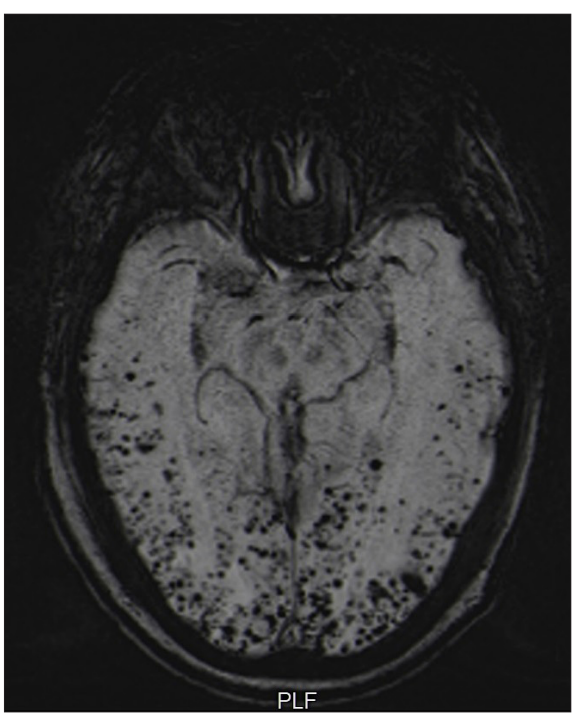

Figure 3. Numerous scattered areas of circumscribed hyposignal in SWI throughout the juxtacortical white matter and bilaterally fronto-temporo-occipito-parietal cerebral cortex.

giographic study showed regular permeability, contours, and intensity of the flow signal in the vessels of the carotid and vertebral-basilar circulations.

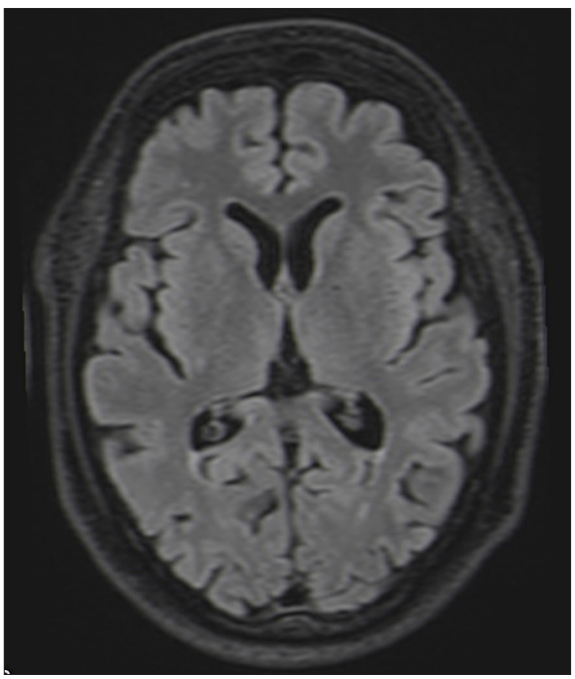

Figure 4. Reevaluating MRI showing reduction in signal intensity and the extent of edematous changes.

Due to these findings, the patient received a probable diagnosis of cerebral amyloid angiopathy-related inflammation (CAA-ri).

The patient was admitted for corticosteroid treatment with methylprednisolone 1000 mg/day IV for 5 days which was uneventful. He was discharged on prednisolone 1 mg/kg/day orally on a weaning schedule for 6 weeks.

During a 3-month follow-up, the patient remained free of new neurological symptoms. Reevaluating MRI showed a significant reduction in signal intensity and the extent of edematous changes **(Fig. 4)**. A discrete residual juxta-cortical right parietal hypersignal persisted, while the remaining hyperintense lesions in the subcortical white matter were nearly absent. Numerous microhemorrhagic foci scattered throughout the juxtacortical fronto-temporo-parietal regions were still evident.

Discussion

CAA-ri poses a challenge for diagnosis despite its potential for treatment, as it can mimic other neurological conditions, resulting in inadequate patient care. Because ischemic stroke is much more prevalent than CAA-ri, the latter is rarely considered as an alternative diagnosis in clinical practice.

The primary differential diagnoses for edematous le-

sions on brain CT include traumatic lesions, extensive ischemic stroke, tumors, infections such as abscesses or meningitis, metabolic changes like hepatic encephalopathy or hyponatremia, and amyloid angiopathy.

In this case, the patient's initial presentation could have been mistaken for a transient ischemic attack (TIA), given his cardiovascular risk factors and changes observed in the CT angiography study. However, the presence of a small, uncommon edematous lesion on the brain CT scan did not support this diagnosis. Otherwise, considering the high-risk profile for TIA (ABCD2 score of 5), hospitalization would have been warranted. Ideally, the patient should have undergone an MRI in an emergency or inpatient setting. However, due to the impossibility to perform MRI at the ED, the low likelihood of ischemic injury based on imaging characteristics, and the patient's preference for waiting the MRI at home with family supervision, the patient was discharged with an MRI scheduled for the same day as if he had remained in the hospital.

Other potential causes such as traumatic injury, infection, and metabolic changes were ruled out based on clinical history and laboratory tests. A lumbar puncture and electroencephalogram were postponed to be considered after the MRI because the clinical temporal profile was very atypical for acute infectious causes or epileptic etiologies. Therefore, MRI was requested to provide further clarification, ultimately excluding the possibility of a tumor and confirming the absence of ischemic injury, as well as leading to the diagnosis of cerebral amyloidosis.

MRI is crucial in suspected cases of CAA-ri.

A probable diagnosis can be established through clinical and imaging criteria,6 including age ≥ 40 years, presence of one or more of the following symptoms: headache, altered consciousness, altered behavior, focal neurological deficits, or convulsive episodes; along with characteristic findings on MRI such as asymmetric focal or multifocal white matter hyperdensities extending to the subcortical, or presence of one or more cortico-subcortical hemorrhagic lesions, and absence of other causes. All criteria are required.

The response to immunosuppressive therapy further supports the diagnosis.[6] If patients with a probable diagnosis fail to respond to empiric high-dose corticosteroid therapy within three weeks, brain biopsy may be reconsidered.[5]

Current evidence supports treatment with immunosuppression, mainly with glucocorticoids (methylprednisolone 1000 mg/day IV for 5 days and then prednisolone 1 mg/ kg/day), given the likelihood of clinical and imaging improvement, and reduced symptom recurrence.[7] A percentage of 70%-80% of clinical improvement occur within 3-6 months,[5,8] and 84% of full recovery within 12 months.[8] Despite this, there is a 42% risk of relapse, particularly within the first year,[9] which may be higher if pulsed IV therapy is suddenly stopped rather than being followed by corticosteroid therapy orally.[10] The optimal duration of treatment remains uncertain but should be guided by clinical and radiological responses, often necessitating prolonged courses of immunosuppressants.[7,10]

When managing a patient with CAA-ri, clinicians must weigh the risk of bleeding, with cautious consideration of antiplatelet therapy and avoidance of anticoagulants. Patients with recurrent seizures may benefit from anticonvulsants.

CAA-ri is frequently overlooked by clinicians, leading to potential misdiagnosis and inappropriate treatment. Prompt management of the inflammatory process is crucial for clinical outcomes, while the administration of antithrombotics may elevate the risk of hemorrhagic stroke associated with CAA-ri.

A better understanding of CAA-ri may lead to improved clinical management and future therapeutic options. We then aim to contribute to a better understanding of the presentation, diagnosis process and imaging findings associated with this pathology. ■

Contributorship Statement / Declaração de Contribuição

RO, RB, AM and SG: Patient assessment, collection of clinical, imaging and laboratory data; revision of the manuscript.

RO, PF and IM: Preparation of the manuscript; revision of the manuscript.

All authors approved the final version to be published.

RO, RB, AM e SG: Avaliação dos doentes, recolha de dados clínicos, imagiológicos e laboratoriais; revisão do manuscrito;

RO, PF e IM; Preparação do manuscrito; revisão do manuscrito.

Todos os autores aprovaram a versão final a ser publicada.

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