Cerebral amyloid angiopathy-related inflammation: a rare but important cause of acute confusion on the general medical take

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Introduction

Cerebral amyloid angiopathy is a common small vessel disease caused by abnormal protein deposition within cerebral blood vessels. In the last 20 years, improved diagnostics have implicated cerebral amyloid angiopathy in the pathophysiology of intracerebral haemorrhage. Cerebral amyloid angiopathy is relevant to general medical doctors, as it can cause transient focal neurological episodes ('amyloid spells') which mimic seizures and transient ischaemic attacks; it also has a significant bearing on anticoagulation decisions. With the ageing population, general medics are more likely to encounter patients with cerebral amyloid angiopathy. This case highlights an important cause of confusion related to cerebral amyloid angiopathy in an older adult presenting on the general medical take.

Case report

A 75-year-old retired publican, with a history of benign prostatic hyperplasia, recurrent urinary tract infections and mild cognitive impairment, presented to an urban teaching hospital with a 5-day history of confusion, generalised headache and episodic stammering. Three days beforehand, he had been found wandering by his family and was prescribed oral antibiotics by a paramedic for a urinary tract infection in view of fever (38.3°C) and microscopic haematuria. He denied infective symptoms, extremity weakness, sensory or visual disturbance, and had no history of falls or head trauma. He lived alone and consumed 5 pints of beer each week.

Admission blood tests were unremarkable. Computed tomography imaging of the head with and without contrast showed mild small vessel disease and white matter hypodensities in the juxtacortical and periventricular white matter of both temporal lobes and anteroinferior frontal lobes, with no abnormal enhancement or underlying space-occupying lesion (Figure 1). An impression was formed of delirium secondary to possible stroke caused by small vessel disease. The patient was started on high-dose aspirin and admitted under the general medical team.

In addition to small vessel disease, subsequent magnetic resonance imaging with blood-sensitive susceptibility weighted-imaging (Figure 2b) demonstrated innumerable cerebral microhaemorrhages in a peripheral (lobar) distribution, alongside generalised enlargement of the perivascular spaces. Focal areas of confluent T2-weighted hyperintensity surrounding the frontotemporal microhaemorrhages in a distribution atypical for small vessel disease suggested cerebral amyloid angiopathy-related inflammation. CSF was acellular, with negative Gram stain and viral polymerase-chain reaction screen, mildly raised protein levels (0.77 g/litre; normal range 0.15–0.40 g/litre) and oligoclonal bands suggesting intrathecal antibody synthesis as a result of inflammation. This patient met the diagnostic criteria for probable cerebral amyloid angiopathy-related inflammation, so aspirin was stopped and he was started on high-dose intravenous methylprednisolone and transferred to the authors' specialist neurology hospital.

Neuropsychological testing identified pronounced visuospatial and perceptual impairments and executive dysfunction. His confusion and stuttering improved with methylprednisolone, and after 5 days of treatment he was switched to high-dose oral prednisolone with a taper over 8 weeks. On review in outpatient clinic 2 months later, he had returned to his premorbid baseline. Repeat magnetic resonance imaging of the head showed complete resolution of vasogenic oedema, but evidence was found of a new, small area of diffusion restriction in the left posterior corona radiata consistent with an acute infarct related to his underlying vasculopathy. However, he had no associated neurological deficit and, given his propensity to bleed with his high burden of microhaemorrhages, he was not started on antiplatelet therapy.

How to cite this article:
Coughlan C, Lim E, Chandratheva A, Jager R, Werring DJ. Cerebral amyloid angiopathy-related inflammation: a rare but important cause of acute confusion on the general medical take. Br J Hosp Med. 2023. https://doi.org/10.12968/hmed.2023.0102

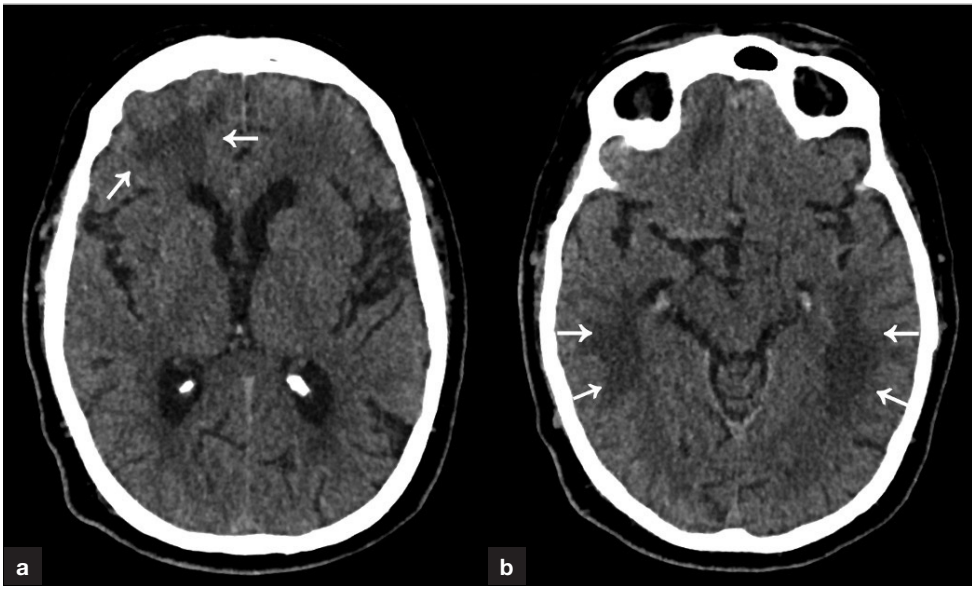

Figure 1. Axial unenhanced computed tomography images of the brain demonstrate (a) multiple large areas of hypodensity in the juxtacortical and deep white matter of the right frontal lobe and both temporal lobes (arrows), (b) in a distribution atypical for small vessel disease. No discrete mass lesion or pathological enhancement was evident on post-contrast imaging (not shown).

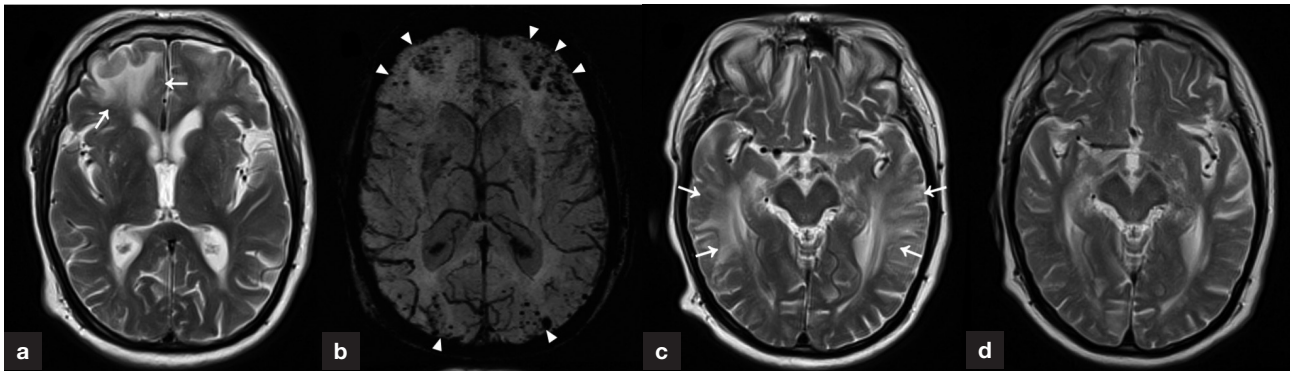

Figure 2. Axial T2 weighted images of the brain demonstrate multifocal areas of T2 hyperintense signal abnormality in the white matter of the (a) frontal and (c) temporal lobes, which involve the juxtacortical U fibres (arrows). b. Axial susceptibility-weighted imaging demonstrates innumerable peripherally located cerebral microhaemorrhages (arrowheads) in both cerebral hemispheres. d. Follow-up axial T2 weighted imaging after treatment shows resolution of the white matter signal abnormalities (arrows in c), with persistence of the cerebral microhaemorrhages on susceptibility-weighted imaging (not shown).

Discussion

Delirium is a common presentation on the general medical take. While most cases are a result of infection, constipation or electrolyte disturbance, clinicians should consider esoteric causes in patients with no clear precipitant or persistent confusion.

Cerebral amyloid angiopathy-related inflammation is a rare subtype of cerebral amyloid angiopathy which often manifests as acute confusion. Other clinical sequalae include headaches, seizures and focal neurological deficits (Banerjee et al, 2017). There is no consensus case definition, but this patient met the proposed clinicoradiological criteria for probable cerebral amyloid angiopathy-related inflammation on grounds of age (over 40 years), altered behaviour and suggestive magnetic resonance imaging findings (Auriel et al, 2016).

Magnetic resonance imaging of the head is the investigation of choice. Imaging features of cerebral amyloid angiopathy include lobar micro- or macro-haemorrhages, cortical superficial siderosis, dilated perivascular spaces and subcortical T2-weighted white matter hyperintensities (Charidimou et al, 2022). Cerebral amyloid angiopathy-related inflammation also shows unifocal or multifocal areas of vasogenic oedema and occasional leptomeningeal

Learning points

- Cerebral amyloid angiopathy is common in older adults, may mimic seizures and transient ischaemic attacks, and is an important cause of haemorrhagic stroke.
- Cerebral amyloid angiopathy-related inflammation is a rare subtype of cerebral amyloid angiopathy which can present with cognitive decline, behavioural changes such as confusion, seizures, transient focal neurological deficits and/or headaches.
- Magnetic resonance imaging typically shows asymmetric areas of vasogenic oedema and occasional enhancement of the leptomeninges, in the context of radiological features of cerebral amyloid angiopathy, such as lobar micro- and macrohaemorrhages and cortical superficial siderosis.
- The treatment of choice in suspected cases is high-dose intravenous methylprednisolone followed by a prolonged oral steroid taper to reduce the risk of relapse.
- Avoid antiplatelets and anticoagulants in patients with confirmed cerebral amyloid angiopathy unless there is a compelling indication.

enhancement (Greenberg and Charidimou, 2018). It may be under-diagnosed, given poor awareness of the condition and limited access to magnetic resonance imaging.

CSF analysis for cell count and cytology is a useful discriminating test. Early treatment of probable cases with high-dose steroids results in improved outcomes, with confirmatory brain biopsies reserved for patients who do not respond to treatment. A proportion of patients relapse despite a steroid taper, so long-term follow up with serial neuroimaging and neuropsychometry is recommended (DiFrancesco et al, 2015).

Cerebral amyloid angiopathy confers an increased risk of intracerebral haemorrhage and antiplatelet and anticoagulant medications should be avoided unless there is a compelling indication (DeSimone et al, 2017). This patient received aspirin, and while he did not come to harm this could have been avoided with earlier magnetic resonance imaging. For general medics encountering patients with cerebral amyloid angiopathy in a hospital setting, other important aspects of care which mitigate the risk of intracerebral haemorrhage include abstention from alcohol and tight blood pressure control.

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References

Auriel EA, Charidimou A, Edip Gurol M et al. Validation of clinicoradiological criteria for the diagnosis of cerebral amyloid angiopathy-related inflammation. JAMA Neurol. 2016;73(2):197–202. https://doi.org/10.1001/jamaneurol.2015.4078

Banerjee G, Carare R, Cordonnier C et al. The increasing impact of cerebral amyloid angiopathy: essential new insights for clinical practice. J Neurol Neurosurg Psychiatry. 2017;88(11):982–994. https://doi.org/10.1136/jnnp-2016-314697

Charidimou A, Boulouis G, Frosch MP et al. The Boston criteria version 2.0 for cerebral amyloid angiopathy: a multicentre, retrospective, MRI-neuropathology diagnostic accuracy study. Lancet Neurol. 2022;21(8):714–725. https://doi.org/10.1016/S1474-4422(22)00208-3

DeSimone CV, Graff-Radford J, El-Harasis MA et al. Cerebral amyloid angiopathy and implications for atrial fibrillation management. Lancet. 2017;390(10089):9–11. https://doi.org/10.1016/S0140-6736(17)31326-0

DiFrancesco JC, Touat M, Caulo M et al. Recurrence of cerebral amyloid angiopathy-related inflammation: a report of two cases from the iCAβ international network. J Alzheimers Dis. 2015;46(4):1071–1077. https://doi.org/10.3233/JAD-150070

Greenberg SM, Charidimou A. Diagnosis of cerebral amyloid angiopathy: evolution of the Boston criteria. Stroke. 2018;49(2):491–497. https://doi.org/10.1161/STROKEAHA.117.016990