Introduction (100/100 words)

Cerebral amyloid angiopathy (CAA) is a common small vessel disease resulting from abnormal protein deposition within cerebral blood vessels. In the last 20 years, improved diagnostics have implicated CAA in the pathophysiology of intracerebral haemorrhage (ICH). CAA 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 population ageing, all general medics are likely to encounter CAA during their careers. This case highlights an important CAA-related cause of confusion in an older adult presenting on the general medical take.

Case report (400/400 words)

A 75-year-old retired publican with a background of benign prostatic hyperplasia, recurrent urinary tract infections (UTIs) and mild cognitive impairment presented to an urban teaching hospital with a five 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 UTI in view of fever (38.3°C) and microscopic haematuria. He denied infective symptoms, extremity weakness and sensory and 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 (CT) imaging of the head with and without contrast showed mild small vessel disease (SVD) 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 from SVD. The patient was started on high-dose aspirin and admitted under the general medical team.

In addition to SVD, subsequent magnetic resonance imaging (MRI) with blood-sensitive susceptibility weighted-imaging (Figure 2,2B) demonstrated innumerable cerebral microhaemorrhages in a peripheral (lobar) distribution, alongside generalised enlargement of the perivascular spaces. Focal areas of confluent T2w hyperintensity surrounding the frontotemporal microhaemorrhages in a distribution atypical for SVD were suggestive of cerebral amyloid angiopathy-related inflammation (CAA-ri). Cerebrospinal fluid was acellular, with negative Gram stain and viral polymerase-chain reaction screen, mildly raised protein (0.77) and oligoclonal bands suggesting intrathecal antibody synthesis due to inflammation. As our patient met the diagnostic criteria for probable CAA-ri, his aspirin was stopped and he was started on high dose intravenous methylprednisolone and transferred to our specialist neurology hospital.

Neuropsychological testing identified pronounced visuospatial and perceptual impairments and executive dysfunction. His confusion and stuttering improved with methylprednisolone and after five days of treatment he was switched to high-dose oral prednisolone with a taper over eight weeks. On review in outpatient clinic two months

later, he had returned to his premorbid baseline. Repeat MRI head showed complete resolution of vasogenic oedema but evidence 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.

Discussion (300/300 words)

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

CAA-ri is a rare subtype of CAA which often manifests as acute confusion. Other clinical sequelae include headaches, seizures and focal neurological deficits [Banerjee et al., 2017]. There is no consensus case definition, but our patient met the proposed clinicoradiological criteria for probable CAA-ri on grounds of age (over 40 years), altered behaviour and suggestive MRI findings [Auriel et al., 2016].

MRI Head is the investigation of choice. Imaging features of CAA include lobar micro- or macro-haemorrhages, cortical superficial siderosis, dilated perivascular spaces and subcortical T2w white matter hyperintensities [Charidimou et al., 2022]. CAA-ri shows, in addition, unifocal or multifocal areas of vasogenic oedema and occasional leptomeningeal enhancement [Greenberg S & Charidimou D, 2018]. CAA-ri may be under-diagnosed given poor awareness of the condition and limited access to MRI.

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 fail to respond to treatment. A proportion of patients relapse despite a steroid taper; long-term follow-up with serial neuroimaging and neuropsychometry is therefore recommended. [DiFrancesco et al., 2015]

CAA confers an increased risk of ICH and antiplatelet and anticoagulant medications should be avoided unless there is a compelling indication [DeSimone et al., 2017] Our patient received aspirin and while he did not come to harm this could have been avoided with earlier MRI. For general medics encountering patients with CAA 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.

Learning Points (5)

- Cerebral amyloid angiopathy is common in older adults, may mimic seizures and transient ischaemic attacks, and is an important cause of haemorrhagic stroke
- CAA-related inflammation is a rare subtype of CAA which can present with cognitive decline, behavioural changes such as confusion, seizures, transient focal neurological deficits and/or headaches

- MRI typically shows asymmetric areas of vasogenic oedema and occasional enhancement of the leptomeninges, in the context of radiological features of CAA such as lobar micro and macrohaemorrhages and cortical superficial siderosis
- The treatment of choice in suspected CAA-ri 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 CAA unless there is a compelling indication

MeSH Key Words (up to 50)

Cerebral amyloid angiopathy

CAA-ri

Delirium

Amyloid spells

References (Harvard Style, <10)

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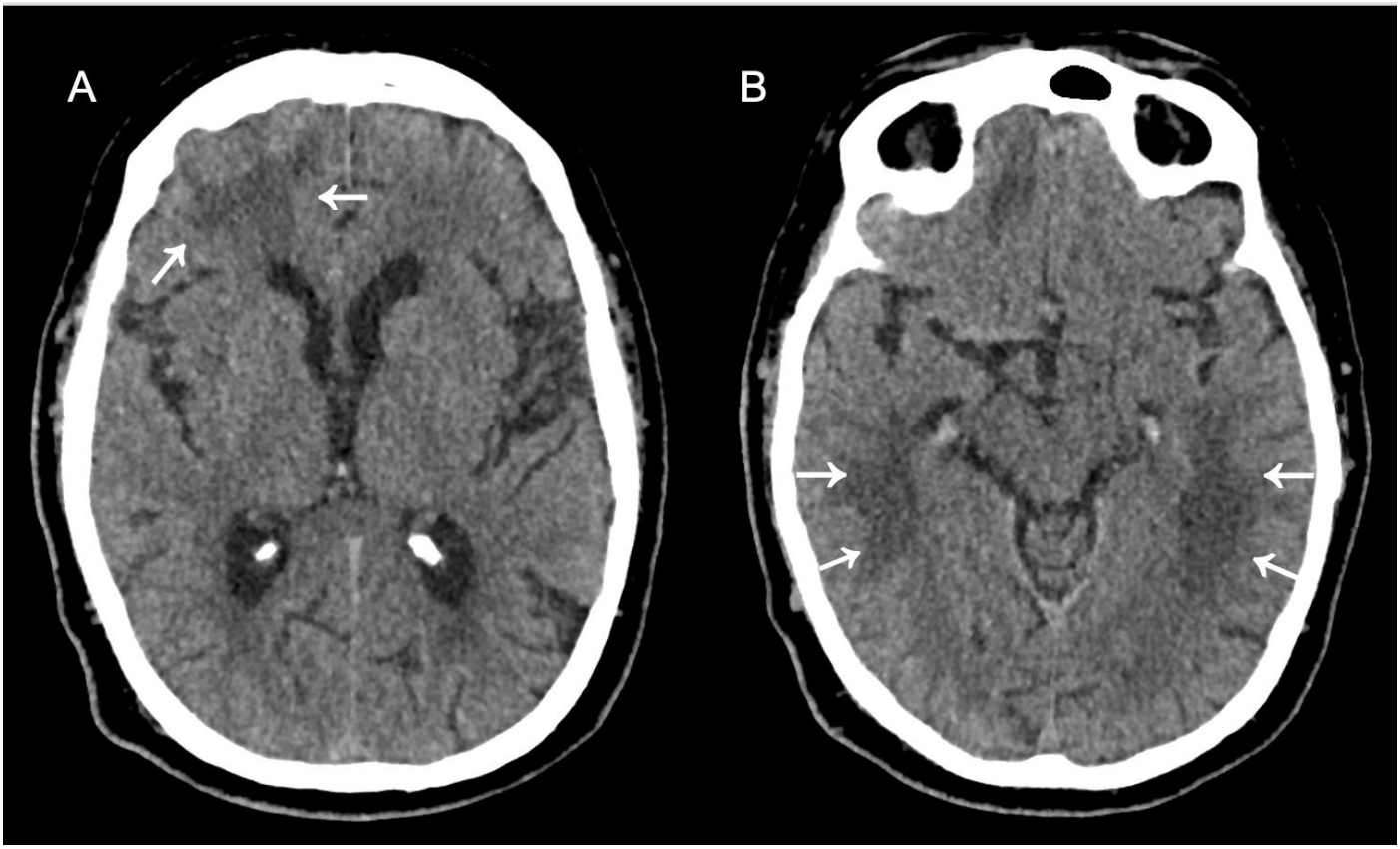

Figure 1. Axial unenhanced CT images of the brain demonstrate multiple large areas of hypodensity in the juxtacortical and deep white matter of the right frontal lobe and both temporal lobes (arrows), in a distribution atypical for small vessel disease. No discrete mass lesion or pathological enhancement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

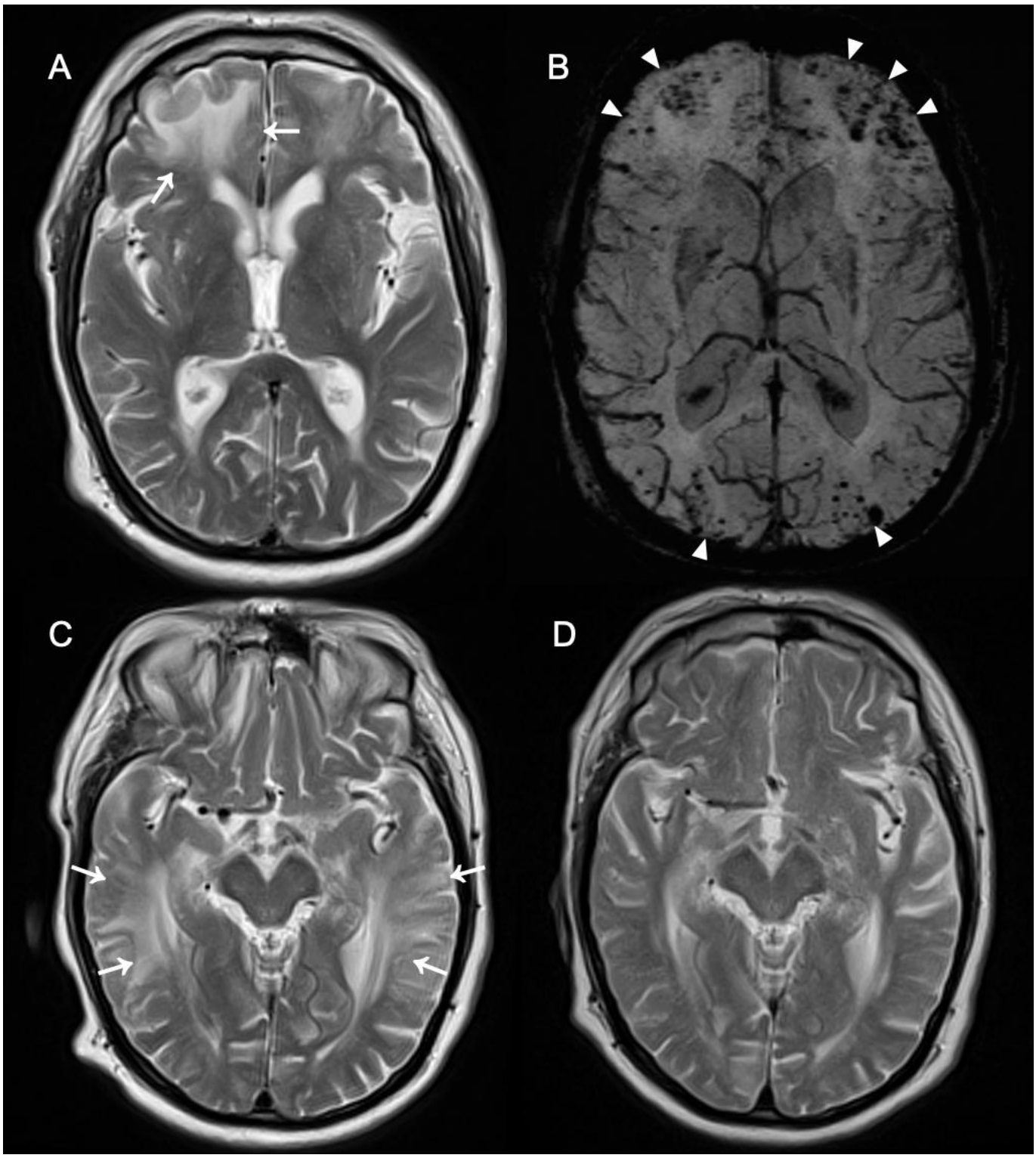

Figure 2. Axial T2 weighted (A + C) images of the brain demonstrate multifocal areas of T2 hyperintense signal abnormality in the white matter of the frontal and temporal lobes which involve the juxtacortical U fibres (arrows). Axial susceptibility weighted imaging (B) demonstrates innumerable peripherally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