

LETTER TO THE EDITOR**TO THE EDITOR****Location, Location: The Clue to Aetiology in Cerebellar Bleeds**

A 62-year-old man with no cardiovascular risk factors presented with acute onset of ataxia and nausea. Computed tomography (CT) of the brain revealed a vermian haemorrhage (Figure 1 A arrow). Clinically and radiologically, he deteriorated with expansion of the visualised haemorrhage evident on repeat CT (Figure 1B), so the decision was made to proceed to surgical evacuation.

Given the location of the bleed and an absence of hypertension on history and exam, a clinician-initiated neuropathological review was requested (Figure 2, magnified bars 200 μ m). Sections through the haemorrhage are shown (Figure 2A). Morphologically normal arterioles that contained beta-amyloid (Figure 2B arrows) on staining were seen, confirming the clinical suspicion that the bleed was related to underlying amyloid angiopathy. Magnetic resonance imaging scanning went on to show susceptibility in the right temporal, occipital and frontoparietal cortices (Figure 1C and D). This led to a diagnosis of *probable cerebral amyloid angiopathy (CAA) with supporting pathology* as per the modified Boston criteria.

The modified Boston criteria for CAA include cerebellar haemorrhage as a location but do not distinguish superficial from

deep locations.¹ Recently, superficial cerebellar haemorrhages (including the vermis) were associated with strictly lobar microbleeds – a marker of CAA.² Thus, superficial locations of cerebellar haemorrhage may help distinguish CAA from hypertensive bleeds and should arouse this suspicion in the treating physician.

Furthermore, in a very recently published case series, Gavriluc et al.³ describe that 34% of 41 patients with CAA-related intracerebral haemorrhage had cerebellar involvement. Cerebellar microbleeds were more frequently superficial than deep (11/14 patients – superficial, 1/14 – mixed superficial/deep, compared to 2/14 – deep). Additionally, CAA-related cerebellar involvement had significantly higher numbers of lobar cortical microbleeds compared to patients without cerebellar involvement (37.8 ± 39.5 vs. 2.8 ± 8.5 ; $p < 0.00001$). Thus, patients with CAA-related cerebellar involvement had a higher burden of lobar microbleeds and additionally worse white matter disease potentially portending a more severe disease course. An alternative possibility is that cerebellar microbleeds might reflect a more advanced stage of the natural history of CAA.

Taken together, these papers suggest that cerebellar involvement in CAA is not rare and, when it occurs, it is more likely to be superficial rather than deep. This suggests accumulation of amyloid occurs in cerebellar cortical areas similar to the observation in hemispheric cortical CAA.

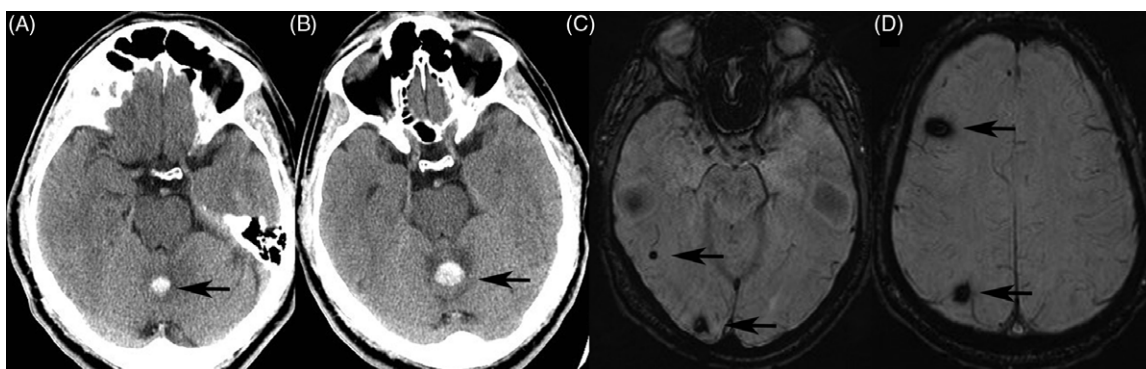


Figure 1: Serial head CTs showing expanding vermian haemorrhage (A/B). Post-operative susceptibility-weighted magnetic resonance imaging showing susceptibility in the right temporal, occipital and frontoparietal cortices (C/D).

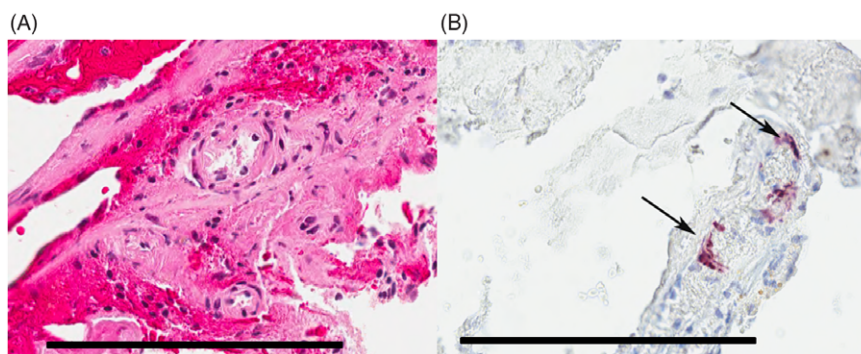


Figure 2: Haemorrhage and morphologically normal arterioles on H&E (A) that contain beta-amyloid (B) on immunostaining (A β Dako, 1/100, Mach4 detection system). Magnified, bars 200 μ m.

Unfortunately, there is a paucity of confirmatory pathological data in this regard. In the only recent relevant meta-analysis that we could identify through a comprehensive literature search, Samarasekera et al.⁴ include six cases of cerebellar involvement and cerebellar lesion location was not discussed in most. In a single case where location was outlined, the bleed was centred in the left cerebellar hemisphere and vermis with extension into the third and fourth ventricles causing obstructive hydrocephalus. Treatment with warfarin was a complicating factor.

Itoh et al.⁵ looked at 1000 consecutive autopsied cases of intracerebral haemorrhage in the elderly in order to understand the burden of CAA-related bleeds. They found 14 cerebellar cases of haemorrhage, and of these, CAA accounted for 14.3% ($n = 2$). These two cases with cerebellar CAA bleeds demonstrated severe CAA in the cerebral and cerebellar cortex and were free from hypertension. This series further showed that CAA-related bleeds, both lobar and cerebellar, were located near the cortical surface (i.e., superficial) and ruptured into the subarachnoid space without exception. In contrast, hypertensive bleeds were deeper and only ruptured into the subarachnoid space when large.

Until more comprehensive pathological data sets are available, it is prudent for physicians treating patients presenting with cerebellar bleeds to be cognizant of the possibility of underlying CAA pathology. This is especially true in settings like our case, where there was no history of hypertension and the cerebellar bleed location was superficial. Since many older patients have common cerebrovascular risk factors, such as atrial fibrillation, hypertension, diabetes and dyslipidaemia, the identification of CAA is important when selecting treatment options which may include anticoagulants and antiplatelets. Furthermore, it is known that the presence of microbleeds is associated with accelerated cognitive decline and dementia,⁶ so these patients would likely benefit from being followed from a cognitive perspective with modifiable vascular risk factors addressed where possible.

Cerebellar haemorrhages are divided into lobar, and deep, with lobar haemorrhages raising suspicion for CAA and deep haemorrhages suggesting hypertension. It is quite possible that the distinction also holds in the case of the cerebellum as suggested by these recent studies. Our case is unusual, as it is rare to have a pathologically confirmed diagnosis ante-mortem and it supports recently emerging literature that superficial cerebellar haemorrhages are more likely to relate to CAA than hypertensive.

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