LETTER TO THE EDITORS

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This Letter is accompanied by Response, see page 142

Cerebral amyloid angiopathy associated with Alzheimer's Disease: two pathologies from a single peptide?

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To the Editors

We read with interest the extensive and thorough ahead-of-print review article entitled 'Updates on pharmacological treatment for Alzheimer's Disease' [1]. This article addresses the compelling issue — not only medical/scientific, but also social and cost/benefit — of pharmacological therapies to slow/block the progressive organisation of β-amyloid peptide (Aβ) deposits in Alzheimer's Disease (AD), their specific molecular targets, and the major related phase III and IV clinical trials.

One aspect that is not addressed is the frequent coexistence of AD and other β-amyloid deposition pathologies, which could, at least hypothetically, benefit equally from the aforementioned anti-amyloid therapies.

Below, we briefly report a histological case arising in this context.

A 78-year-old woman presented with new-onset dementia and sudden loss of left-side motor skills. Radiology showed a haemorrhage with marked signal reduction in the right parietal lobe, with contrast enhancement of uncertain significance, whether inflammatory or neoplastic: for this reason, surgery was performed.

Microscopy revealed thickened and hyalinised vessels (Fig. 1a) that were positive for Congo red histological staining (Fig. 1b) and Aβ immunohistochemical staining (Fig. 1c), leading to the diagnosis of cerebral amyloid angiopathy (CAA). The surrounding tissue also showed microbleeds (Fig. 2a) and scattered so-called 'red motor neurons' (Fig. 2b), which are hypoxic consequences of CAA [2], and were likely to be the cause of the clinically observed motor impairment. However, the aforementioned Aβ immunohistochemistry also highlighted coexisting microscopic AD morphology with typical extravascular deposits, both diffuse and focal (Fig. 1c), justifying the neurological condition of dementia.

The accumulation of Aβ in the brain can lead to several diseases, including CAA and AD. Whereas in CAA Aβ is deposited in the vascular wall, in AD it accumulates at the extravascular parenchymal level or intracytoplasmically in neurons in the form of tangles. These different Aβ depositions would be the result of different pathways, but with common initial steps, which is why the two diseases often co-occur [3, 4]. It is estimated that c.48% of AD cases have co-existing CAA [5].

The coexistence of CAA and AD is often suspected clinically, and the fact that it can be documented histologically supports this thesis, as well as that of a common aetiopathogenesis. However, despite the existence of important data [2–5], it is still not fully understood why some individuals develop only CAA, some others only AD, and in still others, as in the present case, both CAA and AD coexist.

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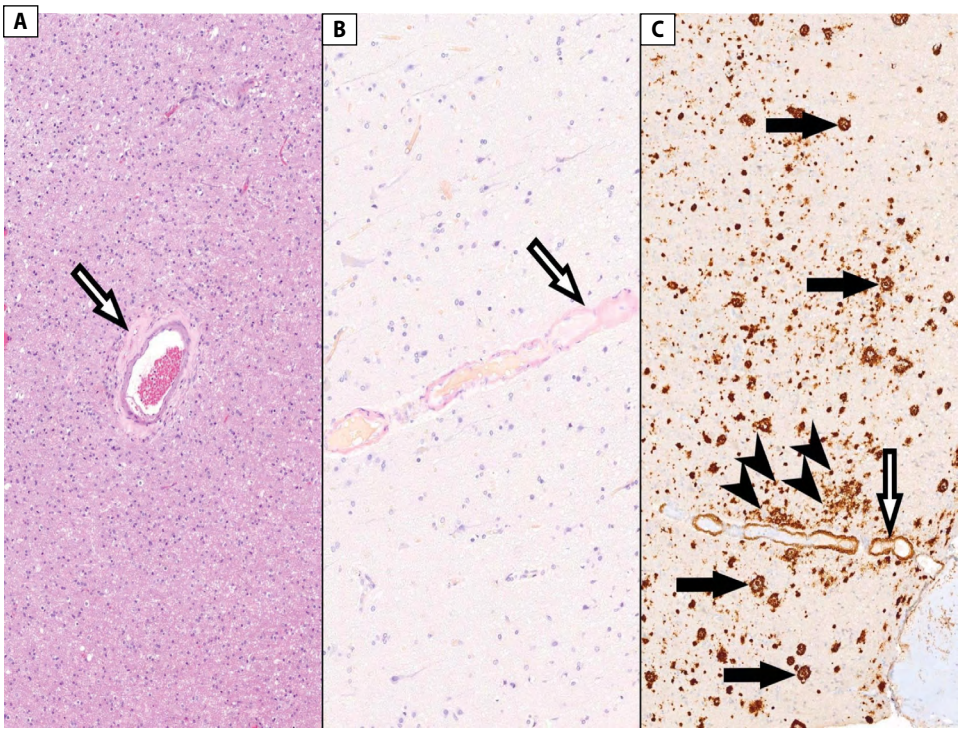

Figure 1. Photomicrographs of cerebral tissue with amyloid angiopathy (CAA): (a) view of an intraparenchymal blood vessel with hyaline wall thickening (arrow) suspicious for amyloid deposition (haematoxylin and eosin, 10×); (b) Congo red staining showing pink amyloid deposition (arrow, 20×); (c) β-amyloid immunohistochemistry showing Alzheimer's Disease deposits: besides confirmed positivity in vessel wall (white arrow), further multiple intraparenchymal/extravascular positivities are highlighted, both in focal/targetoid form (black arrows) and as diffuse deposits (black arrowheads, 10×)

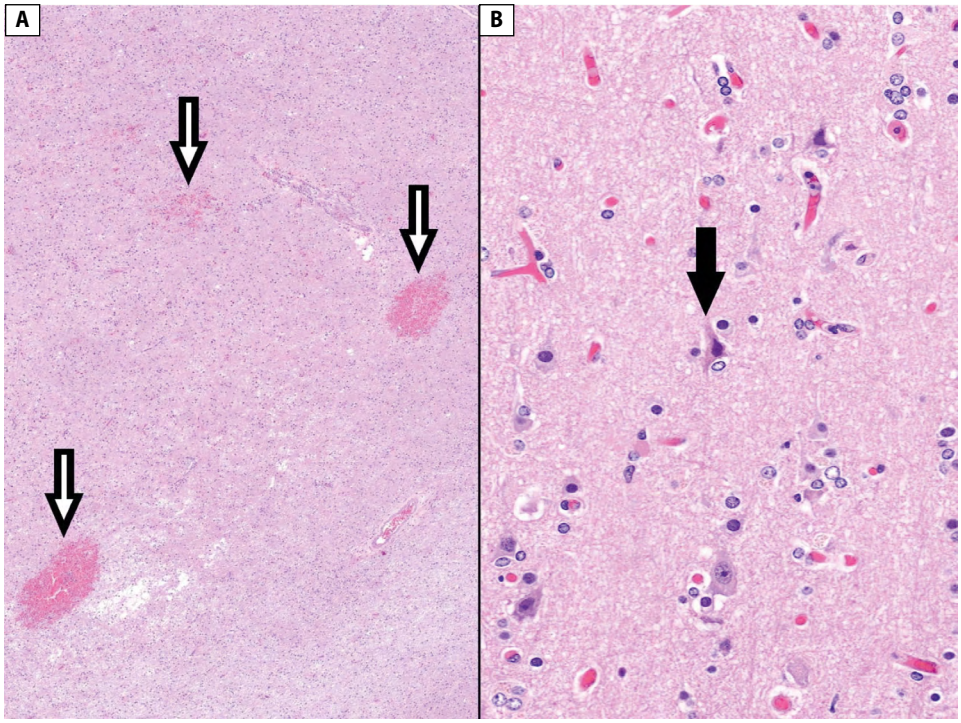

Figure 2. Photomicrographs of surrounding brain tissue: (a) intraparenchymal microbleeds (white arrows) (haematoxylin and eosin, 4×); (b) so-called 'red neurons' (black arrow), a morphological feature of neuronal hypoxic distress CAA-related (haematoxylin and eosin, 40×)

The case described does not represent a novelty of Aβ deposition brain lesions, but it helps to reflect, also in a histological/topographical sense, that the consideration of anti-amyloid therapies should be placed in a broader context than AD, although AD is certainly its most important chapter in terms of incidence, prevalence, morbidity, mortality, and cost to society.

Article information

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