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Cerebral Amyloid Angiopathy and Transient Focal Neurological Episodes

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We read with interest the paper by Paterson et al. [1] sharing their clinical experience on the intriguing topic of transient focal neurological episodes (TFNEs) in cerebral amyloid angiopathy (CAA). Sporadic CAA is a common, yet under-recognised, small vessel disease caused by amyloid- β deposition in the wall of cortical and leptomeningeal arterioles [2]. Although the most widely recognised clinical presentation of CAA is with symptomatic lobar intracerebral haemorrhage (ICH) in older individuals (typically over 55 years), TFNEs, sometimes called 'amyloid spells' [3] are increasingly recognised as another characteristic presentation of CAA, and have been described as recurrent, stereotyped, spreading paraesthesias, usually lasting several minutes [4, 5].

Our recent European multicentre cohort study of TFNEs in CAA patients [6] found evidence of such spells in 14% (25/172) of patients (including cases without previous ICH), making them the

next most common clinical presentation of CAA after ICH. TFNEs were recurrent, stereotyped, brief (usually <30 min) but had a very wide clinical spectrum: although about half were positive ('aura-like') spreading somatosensory or visual symptoms, the other half were predominantly negative symptoms, resembling 'classic' TIAs (e.g. hemiparesis or dysphasia), in keeping with the observations by Paterson et al. [1]. Most crucially, about half of the patients with CAA-related TFNEs went on to suffer symptomatic lobar ICH after 3 months' follow-up [6].

What are the potential mechanisms of CAA-related TFNEs, and how could they be related to the high risk of future ICH? In our study, we found that TFNEs were strongly associated with cortical superficial siderosis on T2*-weighted gradient-recalled echo MRI. This finding may reflect active CAA in cortical and leptomeningeal vessels, likely to result in repeated bleeding into the subarachnoid space, with subsequent deposition of haemosiderin in the very superficial (subpial) cortical layers. Active CAA, with an ongoing tendency to bleed from superficial small vessels may in part explain the high risk of future ICH after TFNEs (fig. 1) [7]. Cortical superficial siderosis could cause TFNEs by mechanisms including seizure-like activity or 'cortical spreading depression' (CSD). Indeed, Paterson et al. [1] raise the interesting idea that 'migraine prophylaxis' may be efficient in symptomatic treatment of CAA-related TFNEs, which would support the hypothesis that some of these attacks might reflect CSD as seen in migraine aura [8]. Like others, we found that anticonvulsant medications may also be helpful for symptomatic treatment of TFNEs, consistent with a contribution from seizure-like activity, but attacks may also cease spontaneously

Fig. 1. **a** T2*-weighted gradient-recalled echo MRI of an elderly patient with a 3-year history of multiple, stereotyped, brief recurrent episodes of numbness and paraesthesias in the left face and arm with associated dysarthria (presumed to be TIAs). MRI scan shows multiple areas of superficial cortical siderosis in the right hemisphere including the right pre-central sulcus; multiple strictly lobar microbleeds were also detected. **b** One month later, the patient presented with a large symptomatic right frontal ICH.

[6]. It remains unclear whether TFNEs in CAA are related to CSD, to an epileptic process, to both together or sequentially, or if these two mechanisms are operational in different subtypes of TFNEs.

A key implication of the paper by Paterson et al. [1] and our recent work is that MRI, including blood-sensitive sequences, is essential in the investigation of patients with unexplained TFNEs or TIA-like episodes to clarify the diagnosis and future ICH risk. In turn, clinicians should generally avoid administering antiplatelets or anticoagulants in cases of TFNEs with imaging evidence of CAA (especially cortical superficial siderosis), even if the episodes seem clinically likely to be ischaemic.

References

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