

Spontaneous and iatrogenic ARIA: Mechanistic insights from CAA-related inflammation

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Abstract

ARIA-E/H (amyloid-related imaging abnormalities-Edema/Hemorrhage) is an umbrella term that defines the radiographic appearance of MRI images abnormality during treatments with A β -lowering monoclonal antibodies (mAbs) for Alzheimer's disease immunotherapy.

Today, it is well-recognized that ARIA-E events can also occur spontaneously in patients with cerebral amyloid angiopathy-related inflammation (CAA-ri), a rare autoimmune encephalopathy associated with raised cerebrospinal fluid (CSF) concentrations of spontaneous auto-antibodies against A β (aAbs).

In this framework, the last years of research and experience of the iCAB international Network generated an increased consensus that therapy-induced ARIA is the iatrogenic manifestation of CAA-ri. Indeed, the natural history of CAA-ri, the response-to-corticosteroid therapy outcomes, the regional and temporal co-localization of radiographic ARIA-E with microglial activation (both on neuropathology and in vivo with TSPO-PET), the downstream negative effects on A β -clearance pathways and the related risks for an ARIA-H subsequent event, all provide remarkable supportive evidence that **ARIA-E associated with mAbs therapy is iatrogenic CAA-ri**.

In this talk, we will present and critically discuss the emerging new data supporting the potential of the assay for anti-A β (auto)antibody CSF testing as a companion diagnostic and early biomarker for CAA-ri and ARIA in real-world clinical practice and immunotherapy trials. In this framework, we will also present the recently launched "ARIAisCAArI NET" project; an international, prospective, longitudinal, observational Registry and Biobank of patients with ARIA and CAA-ri from the real-world clinical practice aimed at fostering a precision medicine approach and biomarker research collaborations between the AD and CAA community.

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