Introduction to ARIA

WHAT IS ARIA?

Amyloid-related imaging abnormalities, also known as “ARIA”, are MRI abnormalities typically associated with the use of monoclonal antibodies that remove amyloid plaque in patients with Alzheimer’s disease (AD)1-3.

ARIA is subdivided into ARIA-E (edema/effusion) or ARIA-H (hemosiderin/hemorrhage)2,3.

ARIA-E and -H may occur concurrently4 as shown here: parenchymal edema + microhemorrhages5.

ARIA MRI FINDINGS INCLUDE2-5:

- Parenchymal vasogenic edema (ARIA-E)
- Sulcal effusion (ARIA-E)
- Superficial siderosis (ARIA-H)
- Cerebral microhemorrhages (ARIA-H)
- Intracerebral hemorrhage (also termed macrohemorrhages)

ARIA-E (EDEMA/EFFUSION)

ARIA-H (HEMOSIDERIN/HEMORRHAGE)

MRI images data on file

Parenchymal edema or sulcal hyperintense abnormalities detected on FLAIR sequences3,5.

Microhemorrhages, superficial siderosis and/or rare lobar intracerebral hemorrhage observed as hypointense abnormalities detected on T2*GRE sequences3,5

HYPOTHESIZED PATHOPHYSIOLOGY OF ARIA

ARIA is a consequence of the presence of amyloid in cerebral blood vessel walls (cerebral amyloid angiopathy [CAA]), which can cause spontaneous ARIA.4 The increased occurrence of ARIA-E seen with treatments that remove amyloid plaques is thought to be due to the removal and disruption of amyloid in blood vessel walls.4 Other mechanisms are also hypothesized6.

Aggregation of toxic amyloid β (Aβ) species in the brain contributes to AD pathogenesis3.

After the introduction of monoclonal antibodies that removes amyloid plaques, amyloid deposits begin to clear leading to increased vascular permeability6.

This loss of vascular integrity may be thought of as a transient exacerbation of the effects of CAA5. The leakage of fluid could give rise to an increased signal detected on FLAIR images (ARIA-E), while leakage of red cells would result in ARIA-H4,6.

Limited evidence suggests that with repeated immunization and continued Aβ clearance, the integrity of vessels and efficiency of clearance can improve and risk of ARIA decreases7.
**REFERENCES:**


**ABBREVIATIONS:**

APOE ε4, ε4 allele of the Apolipoprotein E gene; Aβ, amyloid beta; AD, Alzheimer’s disease; ARIA, amyloid-related imaging abnormalities (includes ARIA-E and H); ARIA-E, ARIA-edema/effusion; ARIA-H, ARIA-hemosiderin/hemorrhage; FLAIR, fluid-attenuated inversion recovery; GRE, gradient recalled-echo; MRI, magnetic resonance imaging; SWI, susceptibility weighted imaging.

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**CLINICAL MANIFESTATIONS OF ARIA**

In most cases, ARIA-E and ARIA-H are **asymptomatic**.\(^1,^4,^6\)

The symptoms of **ARIA-E** are transient and nonspecific, and include headache, confusion, nausea, vomiting, visual disturbance, neuropsychiatric symptoms, dizziness, fatigue, or gait disturbances.\(^1,^4\) ARIA-H cases are generally asymptomatic.\(^1\)

Infrequently, severe neurological symptoms (e.g., encephalopathy, focal neurological symptoms, seizures, and status epilepticus) occur, and may require hospitalization and specific treatments (e.g., intensive care, corticosteroids, antiepileptics).\(^1,^4,^6\)

Most cases of ARIA-E occur early in the treatment course and decrease with increased duration of exposure.\(^1\)

**ARIA MAIN RISK FACTORS**

- **APOE ε4 carrier status**, treatment with monoclonal antibodies that remove amyloid plaque, and pretreatment history of microhemorrhages are risk factors for ARIA-E and ARIA-H.\(^4,^5\)

**TREATMENT-RELATED ARIA OVERVIEW**

- Most cases of ARIA-E and ARIA-H are **asymptomatic** and usually recognized as **incidental** ARIA during follow-up evaluation on MRI.\(^1,^6\)

- Most cases of ARIA-E occur **early in the treatment** course and decrease with increased duration of exposure.\(^1,^4\) ARIA-E and -H may occur concurrently.\(^2\)

- Most cases of ARIA-E resolve completely. Depending on the severity, treatment may continue, be interrupted or discontinued until resolution.\(^5,^10-12\) Some cases may require specific treatments and even hospitalization.\(^1\)

- In past clinical trials, ARIA-E resolved radiographically over time, whereas ARIA-H can remain visible on subsequent imaging.\(^4\)

For additional information on ARIA, scan here:

[www.UnderstandingARIA.com](http://www.UnderstandingARIA.com)