Approaching Amyloid-Related Imaging Abnormalities (ARIA) in the Emergency Department (ED)

In the ED, ARIA should be considered as a differential diagnosis in patients with Alzheimer's disease (AD) who are receiving anti-amyloid monoclonal antibody (mAb) therapy

What is ARIA?[1]

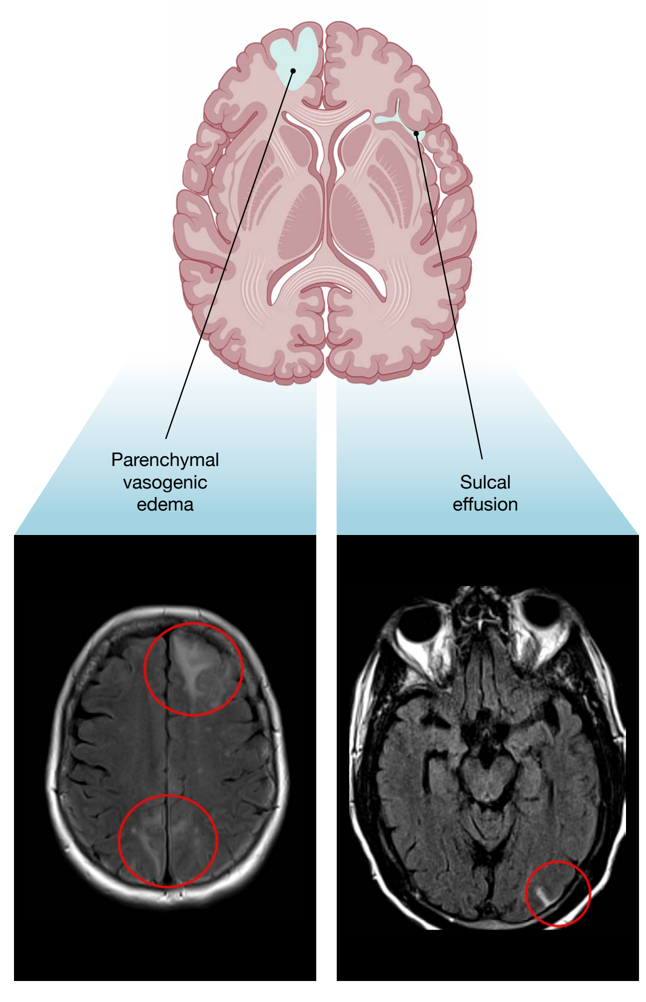
- ARIA are a consequence of **amyloid beta (Aβ) buildup in brain blood vessels**
- The mobilization of Aβ by **mAbs** is hypothesized to increase the permeability of blood vessels to fluid or blood products, leading to ARIA

THERE ARE TWO SUBTYPES OF ARIA

ARIA-edema, effusion (ARIA-E):

- A buildup of fluid on the brain due to damage to the blood–brain barrier[1]
- Brain swelling seen as **hyperintensities on FLAIR MRI sequences**[2]

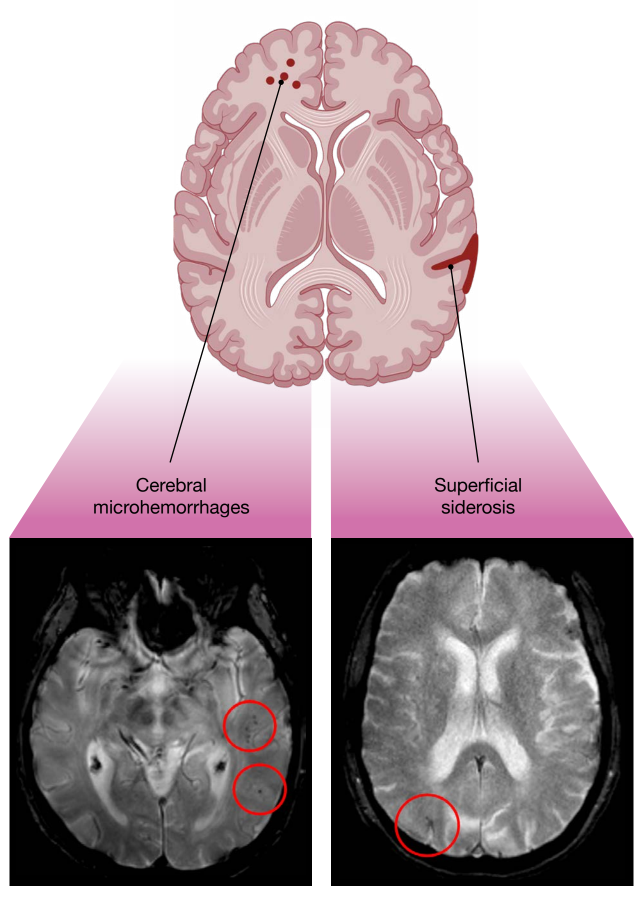
Hyperintense abnormalities on FLAIR sequences



ARIA-hemosiderin, hemorrhage (ARIA-H):

- Hemosiderin deposition in the parenchyma (microhemorrhages) or leptomeningeal/subpial space (superficial siderosis)[1,2]
- Bleeds seen as **hypointensities** on T2* GRE or SWI MRI sequences[2,3]

Hypointense abnormalities on T2* GRE sequences



Rare lobar intracerebral hemorrhage, also termed macrohemorrhages, can also occur[4]

Figures created in Biorender.com. MRI images: data on file.

WHAT ARE COMMON CLINICAL SYMPTOMS OF ARIA?

Patients with symptomatic ARIA may present with varying symptoms, including:[1]

- Headache
- Confusion
- Dizziness, nausea, or vomiting
- Changes in vision
- Problems with walking or balance

ARIA can be serious and life-threatening

Approximately 80% of ARIA cases are asymptomatic and typically detected through routine MRI monitoring[1,5,6]

DIAGNOSING ARIA IN THE ED[2]

Medical history:

✓ Diagnosis of **AD**
✓ Recent or current **anti-amyloid treatment**
  ☐ Check for medication alert bracelet / medication card

CONSIDER A DIAGNOSIS OF ARIA!

USING MRI TO DETECT ARIA[6]

- **MRI** is key for the diagnosis and differential diagnosis of ARIA[7]
- The use of CT is limited by insensitivity to ARIA-H and milder forms of ARIA-E[7]
- It is essential to request the **right MRI sequences to detect ARIA**[7]
- If possible, request an MRI with similar characteristics as the baseline acquisition to facilitate comparisons[6]
- It is important to consider field strength, as this may affect visibility of microhemorrhages[6]

FIELD STRENGTH[6]

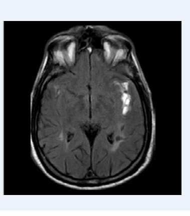
- 3T recommended
- ≥1.5T adequate
- <1.5T inadequate

Standardized consensus ARIA MRI protocol can be performed in <15 minutes[6]

ARIA are suspected

Order MRI sequences needed to detect ARIA (minimum T2 FLAIR, T2* GRE, and DWI)

- **ARIA-E** → 2D or 3D T2 FLAIR
- **ARIA-H** → T2* GRE or SWI
- **Differential diagnosis** → Other tests may be needed to confirm the differential diagnosis
  - **Stroke** → DWI
  - **SAH** → SAH may mimic ARIA-E effusion[2,9‡]
  - **Other** → E.g., PRES, infection[2]



- Ischemic stroke may mimic ARIA-E edema[2]
- DWI sequences can support differential diagnosis[2]

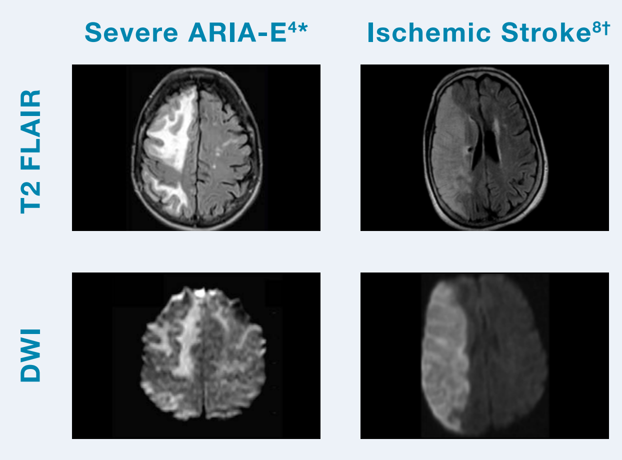
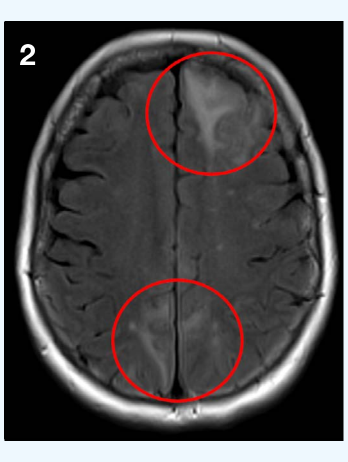
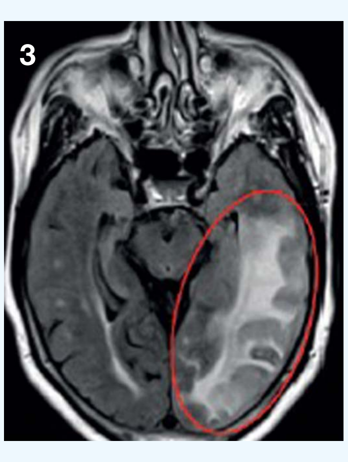
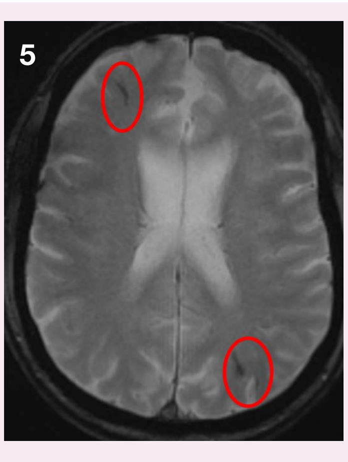
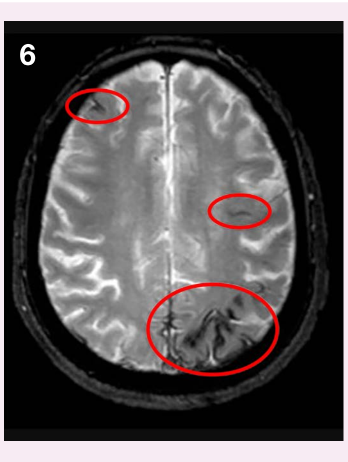
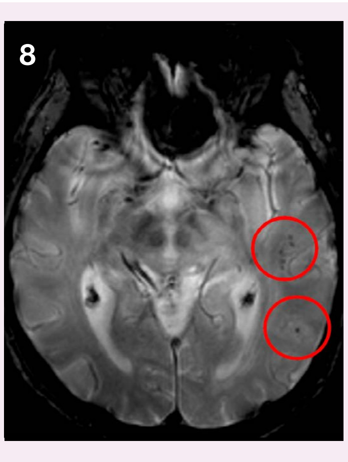


*Figure adapted with permission from Cogswell (2022)[4]; †Case courtesy of Balachandran G, Radiopaedia.org, rID-10704[8]; ‡Case courtesy of Abdrabou A, Radiopaedia.org, rID-22738.[9]

KNOWING IF A PATIENT IS ON AN ANTI-AMYLOID mAb THERAPY IS KEY FOR DIAGNOSIS[2]

It is essential to gather the appropriate information to support an accurate diagnosis. Inaccurate differential diagnosis of stroke may result in the administration of thrombolytic therapy, which may increase the risk of intracerebral hemorrhage in patients with ARIA[10]

GRADING THE SEVERITY OF ARIA[4]

	MILD	MODERATE	SEVERE
ARIA-E **New** sulcal and/or cortical/subcortical FLAIR hyperintensity	 1 1 location <5 cm	 2 1 location 5–10 cm OR >1 location each <10 cm	 3 ≥1 location >10 cm
ARIA-H **New** superficial siderosis	 4 1 focal area	 5 2 focal areas	 6 >2 focal areas[11]
ARIA-H Number of **new** microhemorrhages	 7 ≤4 microhemorrhages	 8 5–9 microhemorrhages	 9 ≥10 microhemorrhages

ARIA are graded on the basis of treatment-emergent events. For ARIA-H, this count includes cumulative new microhemorrhages or regions of siderosis compared with the baseline, pretreatment examination.[4]
MRI images 1 to 5 and 7 to 9: data on file.
MRI image 6 adapted with permission from Kate et al. (2018)[11] CC BY 4.0: http://creativecommons.org/licenses/by/4.0/

RISK FACTORS FOR ARIA[1]

CORE RISK FACTORS

- Exposure to anti-amyloid mAb therapy
- Anti-amyloid mAb therapy characteristics (e.g., dose, schedule, antibody, treatment duration)
- Presence of *APOE ε4* allele
- Presence of bleeds before anti-amyloid mAb therapy

Additional risk factors:

- Amount of Aβ plaques in the brain tissue
- Level of Aβ in the cerebral blood vessel walls (CAA)
- Antithrombotic treatment

MANAGING ARIA IN THE ED

In Canada and in the US, there are currently **no evidence-based clinical guidelines** for the management of ARIA in the ER[5]

Management of ARIA and stroke are time-sensitive – **timely action and appropriate treatment** are essential to ensure optimal patient outcomes[5]

Communication about suspected ARIA with patient's neurologist/physician is crucial[6]

Refer to the anti-amyloid mAb prescribing information for guidance. Careful clinical evaluation should be performed prior to continuing anti-amyloid mAb therapy[12]

Scan the QR code for ARIA MRI protocols and additional resources from the **American Society of Neuroradiology**

Scan the QR code for additional information on ARIA from **www.UnderstandingARIA.ca**

REFERENCES

1. Hampel H, et al. Neur odegener Dis Manag. 2024;14(3):51–62.
2. Barakos J, et al. AJNR AM J Neuroradiol. 2013;34(10):1958–1965.
3. Hampel H, et al. Brain. 2023;146(11):4414–4424.
4. Cogswell PM, et al. AJNR Am J Neuroradiol. 2022;43(9):E19–E35.
5. Lo AX, et al. J Am Geriatr Soc. 2024;72(12):3945–3949.
6. Cogswell PM, et al. AJNR Am J Neuroradiol. 2025;46(1):24–32.
7. Barakos J, et al. J Prev Alzheimers Dis. 2022;9(2):211–220.
8. Balachandran G. Radiopaedia.org. https://doi.org/10.53347/rID-10704 (Accessed January 2025).
9. Abdrabou A. Radiopaedia.org. https://doi.org/10.53347/rID-22738 (Accessed January 2025).
10. Reish NJ, et al. N Engl J Med. 2023;388(5):478–479.
11. Kate MT, et al. Alzheimers Res Ther. 2018;10(1):112.
12. Ramanan VK, Day GS. Mol Neurodegener. 2023;18(1):42.
13. Duchesne S, et al. Can J Neurol Sci. https://doi:10.1017/cjn.2024.338 (Accessed January 2025)

ABBREVIATIONS

Aβ, amyloid beta; AD, Alzheimer's disease; ARIA, amyloid-related imaging abnormalities; ARIA-E, amyloid-related imaging abnormalities – edema, effusion; ARIA-H, amyloid-related imaging abnormalities – hemosiderin, hemorrhage; CAA, cerebral amyloid angiopathy; CT, computerized tomography; DWI, diffusion weighted imaging; ED, emergency department; FLAIR, fluid-attenuated inversion recovery; GRE, gradient recalled echo; mAb, monoclonal antibody; MRI, magnetic resonance imaging; PRES, posterior reversible encephalopathy syndrome; SAH, subarachnoid hemorrhage; SWI, susceptibility weighted imaging; T, Tesla.

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