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### Learning Objective

Manage ARIA in patients receiving ATTs according to best guidance, including communication with ATT-treating clinicians and radiologists.



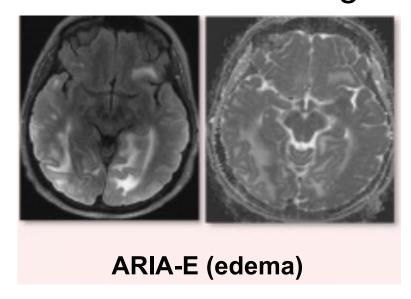
#### **Amyloid-Targeting Therapies (ATTs)**

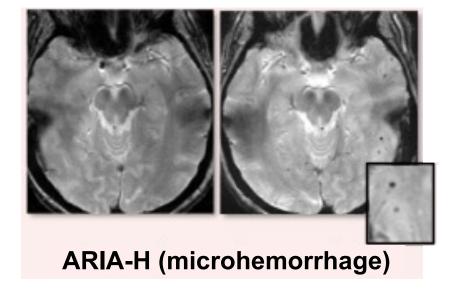
- Aducanumab: FDA approval June 2021
- Lecanemab: FDA approval January 2023 CLARITY AD trial
- Donanemab: FDA approval early 2024?
   TRAILBLAZER-ALZ 2 trial
- Drugs work by targeting beta-amyloid at different stages of plaque formation



## Amyloid-Related Imaging Abnormalities (ARIA)

- ARIA-E: edema
- ARIA-H: hemorrhage





#### **Patient Case 1**

- 65-year-old female presents 30 minutes after acute onset of aphasia and left gaze preference
- Blood pressure (BP): 163/84; glucose: 170
- CT of head/CT angiography: left temporal hypodensity, left middle cerebral artery distal M3 occlusion
- Platelets: 256; international normalized ratio (INR): 1.0



#### **Patient Case 1 (Continued)**

- Past medical history: early stages of cognitive decline, homozygous for APOE4 allele
- Medications: lecanemab infusions every 2 weeks; latest infusion 4 days prior; no antiplatelets or anticoagulants
- Prior imaging: MRI of brain 81 days prior showed mild small-vessel disease with no microhemorrhages, edema, or ARIA



#### **Audience Response**

# Is this patient a candidate for alteplase or tenecteplase at this time, and should alteplase or tenecteplase be given?

- A. Yes, the patient may be a candidate, but fibrinolytic therapy is not preferred
- B. Yes, the patient may be a candidate, and fibrinolytic therapy should be given
- C. Yes, the patient may be a candidate, but fibrinolytic therapy should only be administered within the first hour after symptom onset in this case
- D. No, the patient is not a candidate
- E. I don't know



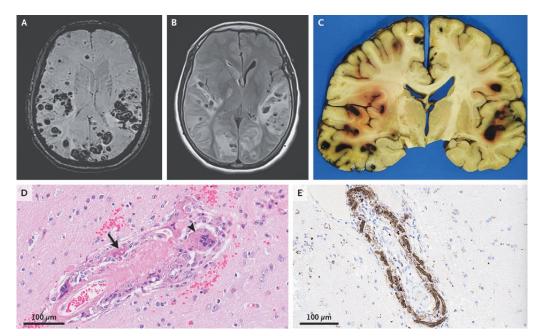
#### **Patient Case 1 (Continued)**

- Patient received alteplase
- 50 minutes after start of infusion, systolic BP rose from 160 to 250
- Infusion stopped; repeat CT showed extensive multifocal intraparenchymal hemorrhages; no systemic bleeding
- Reversal agents tranexamic acid and cryoprecipitate administered



#### **Patient Case 1 (Continued)**

- Patient with persistent global aphasia, agitation, and non-convulsive seizures; required intubation
- Ultimately made comfort care and died



#### **Audience Response**

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- E. I don't know



#### **Audience Response**



- A. Unfractionated heparin infusion
- B. Prophylactic loading dose of anti-seizure medication
- C. Early initiation of high-dose glucocorticoids
- D. No medications are recommended; only discontinue ATT
- E. I don't know



## Resources Needed for Medical Center to Manage Serious or Severe ARIA

- Neurologist experienced in managing seizures and status epilepticus
- Electroencephalogram (EEG) availability for inpatients
- Intensive care unit availability
- Hospital ward for management and monitoring
- Clinicians experienced in managing cerebral edema or ARIA
- MRI interpreters who have knowledge about and are proficient in detecting and interpreting ARIA
- MRI available for unscheduled scans of symptomatic patients
- Emergency department with the resources to assess for suspected or known ARIA



### Considerations for Management of Serious or Severe ARIA

- Written protocol for management of serious or severe ARIA should be developed before patients are treated with ATT
- Note the resources needed for a medical facility to manage patients with severe ARIA
- Serious cases of ARIA can resemble cerebral amyloid angiopathy
   related inflammation
- Encephalopathy, stupor, seizures, and status epileptics may occur
- Admission to hospital or critical care unit; experience in management of cerebral edema could be needed
- Early initiation of high-dose glucocorticoid treatment
  - For example, intravenous (IV) methyprednisolone 1 g per day for 5 days followed by oral steroid taper for several weeks
- Monitoring for seizures; treatment if they occur



#### **Audience Response**



A. Unfractionated heparin infusion

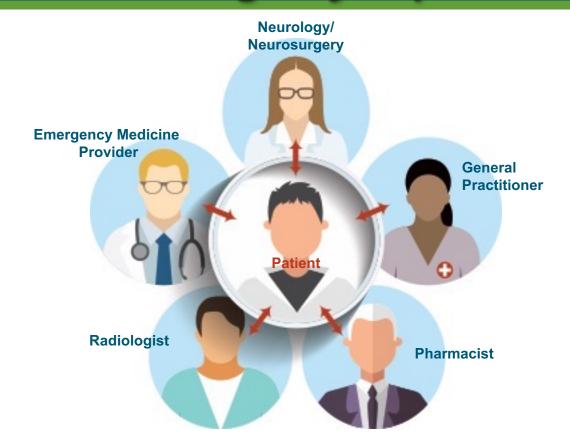
ARIA-E?

- B. Prophylactic loading dose of anti-seizure medication
- C. Early initiation of high-dose glucocorticoids
- D. No medications are recommended; only discontinue ATT

## Neurologic Emergency Medicine Perspective

- No official clinical guidelines yet for emergency department setting with regard to ATT use / possibility of ARIA
- Consider MRI as first-line imaging if possible
- For stroke, consider discussing early with neurology/neurosurgery if intervention candidate rather than IV fibrinolytic
- Beware of anticoagulation common presentations: ACS/Afib/DVT/MI/PE/etc.
- Ask for help early using a multidisciplinary approach: radiology, neurology, neurosurgery
- Low threshold to admit in unclear presentations

### Team-Based Approach for the Management of ARIA in the Emergency Department



### **SMART Goals**Specific, Measurable, Attainable, Relevant, Timely

- Find or participate in developing an institutional protocol for emergency management of serious or severe ARIA.
- When patients present to emergency care settings with ARIA, seek a multidisciplinary approach (including radiology, neurology, neurosurgery) for management.
- For patients with ARIA, depending upon severity and characteristics, consider admission to the hospital or critical care unit, seizure management, and initiation of high-dose glucocorticoids as part of management.



ARIA Alert:
Timely Recognition in the Emergency Department



What to Do: My Patient in the ED May Have ARIA

www.cmeoutfitters.com/practice/alzheimers-disease-hub/







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