CMEO
BriefCase

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

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CME OUTFITTERS

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Learning Objective

Develop a best practice protocol to triage patients who present to an emergency care setting for the likelihood of ARIA in association with ATT treatment.

Audience Response

A patient in the emergency department (ED) is being evaluated for possible amyloid-related imaging abnormalities (ARIA) that have been associated with new amyloid-targeting therapies (ATTs) for Alzheimer's disease (AD). The patient is experiencing stroke-like symptoms, and the team just identified that this patient was enrolled in a clinical trial studying AD and may be on an ATT. Your facility includes access to computed tomography (CT) and magnetic resonance imaging (MRI). How should brain imaging proceed to evaluate this patient most appropriately?

A. Perform CT to first rule out ARIA-H, then MRI to examine any ARIA with edema or effusion (ARIA-E)
B. Perform MRI to rule out ARIA-H (hemosiderin deposition), then CT to examine any ARIA-E
C. Prioritize starting high-dose glucocorticoids, and evaluate MRI as soon as it is feasible
D. Prioritize performing MRI to confirm or rule out ARIA
E. I don't know

Audience Response

In the ED, you are evaluating an adult patient who presents with some signs and symptoms that are consistent with ischemic stroke, and who also has a history of AD. Which of the following questions should you now prioritize with regard to the medical and medication history?

A. Has this patient ever had an infusion of any ATTs for AD?
B. When was the last time the patient presented for a neurological emergency?
C. Is this patient regularly taking acetylcholinesterase inhibitors for AD?
D. Has the patient had a recent major surgery?
E. I don't know

Patient Case: M.J.

- 68-year-old female is brought to the emergency department by ambulance following sudden speech impairment; time of arrival: ~ 15:00 hours (3:00 PM)
- Chief complaints:
  - Sudden and severe difficulty in speaking (dysphasia)
  - Mild confusion and disorientation
  - Unsteady gait observed by family members
- Vital signs on arrival:
  - Blood pressure: 160/90 mmHg
  - Heart rate: 88 beats per minute
  - Respiratory rate: 18 breaths per minute
  - Oxygen saturation: 94% on room air
  - Temperature: 36.8°C (98.2°F)

Patient Case: M.J.

Initial Observations

- Appearance: mildly distressed, responsive but having trouble articulating words
- Neurological: slight facial droop on the right side, no evident motor deficits
- Cardiovascular: regular heart rhythm, no murmurs or gallops

Medical History

- Chronic conditions: myasthenia gravis, obstructive sleep apnea, hypertension, dyslipidemia, etc.
- Surgical history: thymectomy, tubal ligation, appendectomy, etc.

Family History

- Alzheimer's disease in mother (onset at age ~70)
- Mixed dementia in father (onset at age ~75)

Audience Response

Based on the patient's initial presentation, which condition is most likely?

A. Hypertensive crisis
B. Acute ischemic stroke
C. Peripheral neuropathy
D. Myasthenic crisis
E. I don’t know

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Explanation: The patient's symptoms of sudden speech impairment, mild confusion, unsteady gait, and slight facial droop are classic signs that point toward a neurological event such as an acute ischemic stroke, making this the most likely diagnosis based on the initial presentation.

ED Stroke Alert Activation

Criticality of Prompt Response

- The presentation of symptoms consistent with a stroke necessitates immediate action; the “time is brain” principle underlines the urgency; every minute counts in mitigating potential neurological damage

Activation Protocol

- The stroke alert involves immediate notification of key departments—neurology, radiology, and the critical care team—to mobilize resources for rapid diagnostic imaging and potential intervention

Preparation for Urgent Interventions

- The team prepares for potential life-saving measures, including CT imaging and IV thrombolysis, aligning with standard protocols for acute stroke management

IV = intravenous

Powers WJ, et al. *Stroke*. 2019;50(12):e344-e418.

Audience Response

Which clinical trial/medication, relevant to the patient's case, is associated with an increased risk of developing ARIA?

A. Solanezumab trial – solanezumab
B. ENGAGE trial – aducanumab
C. TRAILBLAZER-ALZ 2 trial – donanemab
D. CLARITY-AD trial – lecanemab
E. I don’t know

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Explanation: Donanemab is an investigational anti-amyloid beta antibody evaluated in the TRAILBLAZER-ALZ 2 trial for the treatment of Alzheimer's disease. One of the known complications of amyloid-targeting therapies, such as donanemab or lecanemab, is amyloid-related imaging abnormalities (ARIA), which includes ARIA-E (edema or effusion) and ARIA-H (hemosiderin deposition). This makes it a critical consideration in the emergency setting for patients presenting with neurological symptoms, as it could indicate ARIA rather than a typical ischemic stroke.

Sims JR, et al. *JAMA.* 2023;330(6):512-527.

ED Stroke Alert Activation

Initial Assessment and Stroke Alert Activation

- Description of the emergency medicine provider's initial assessment upon the patient's arrival, noting the sudden onset of speech impairment and potential stroke symptoms
- Decision to activate a stroke alert, emphasizing the criticality of prompt response in suspected stroke cases

Nursing Actions in Triage

- Rapid establishment of IV access to prepare for potential immediate interventions
- Urgent preparation for a CT scan to assess for possible ischemic or hemorrhagic stroke
- Continuous monitoring of vital signs and ensuring patient stability during the initial assessment

Pharmacist's Role in Triage

- Immediate review of the patient's medication list, brought by the patient's daughter, to identify potential blood thinners or medications that could influence stroke management
- Assessment of the patient's current medications for any that may contraindicate the use of thrombolytics or affect the treatment approach

Powers WJ, et al. *Stroke.* 2019;50(12):e344-e418.

Patient Case: M.J. (Continued)

- The patient is rushed to the CT scanner; neurology is to meet the team
- M.J.’s daughter brings a medication list and informs of a clinical trial that M.J. was recently involved in for AD
- The pharmacist reviews the medications and looks up whether the clinical trial would prohibit any therapies for management of acute ischemic stroke

Medication Review

Medication List

- Pyridostigmine 60 mg three times daily and 180 mg once daily (for myasthenia gravis)
- Aprovel (irbesartan) 75 mg (for hypertension)
- Mianserine 30 mg (antidepressant)
- Esomeprazole 40 mg (for gastroesophageal reflux disease [GERD])
- Simvastatin 10 mg (for dyslipidemia)
- Uvedose (vitamin D supplement)
- Risedronate 75 mg once a month (for osteoporosis)
- Participated in the TRAILBLAZER-ALZ 2 trial, started 5 months ago, last visit 2 weeks ago

Understanding Amyloid-Beta-Targeting Therapies

Overview of ATTs

- Lecanemab (BAN2401) and aducanumab are examples of novel FDA-approved beta-amyloid-targeting therapies for the treatment of AD; donanemab is under investigation, approval expected early 2024(?)

Mechanism of Action

- Amyloid-beta-targeting therapies bind with varying affinities to various stages of amyloid, on the amyloid-beta plaque formation timeline

Clinical Trials and Efficacy

- The results from trials of individuals with early AD have shown promise in reducing amyloid plaques in the brain and potentially slowing cognitive decline

Adverse Effects

- Infusion-related reactions
- Increased risk of hemorrhage from concomitant administration of thrombolytics
- Gastrointestinal symptoms
- ARIA

Van Dyck CH, et al. *N Engl J Med*. 2023;388:9-21. Cummings J, et al. *J Prev Alzheimers Dis*. 2023;10(3):362-377.

Understanding ARIA

- **ARIA in AD therapy**
  - Notable side effect of treatments such as lecanemab
  - Detected via brain imaging
- **Types of ARIA**
  - **ARIA-E:** brain edema (swelling/fluid)
  - **ARIA-H:** brain microhemorrhages (bleeding)
- **Why it matters**
  - Can resemble ischemic stroke
  - Accurate identification is crucial
- **Medications that can cause ARIA**
  - Lecanemab
  - Aducanumab
  - Donanemab
  - Gantenerumab

Barakos J, et al. *J Prev Alzheimers Dis*. 2022;9(2):211-220. Cummings J, et al. *J Prev Alzheimers Dis*. 2023;10(3):362-377.

MRI Protocols for ARIA Detection

ARIA-E (ARIA with edema/effusion)

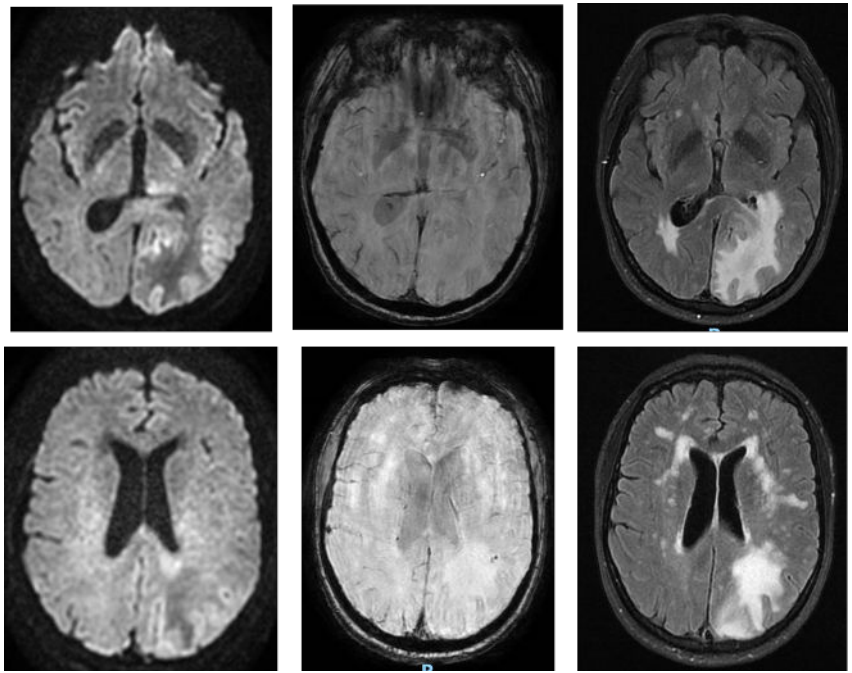
- MRI scans with T2-weighted FLAIR sequences are crucial for detecting vasogenic edema, a hallmark of ARIA-E

ARIA-H (ARIA with hemorrhage)

- Gradient echo (GRE) or susceptibility weighted imaging (SWI) sequences in MRI help in identifying microhemorrhages and hemosiderin deposits indicative of ARIA-H

Comprehensive Assessment

- MRI provides a detailed view of the brain, allowing for a comprehensive assessment of amyloid-related changes



FLAIR = fluid-attenuated inversion recovery

Barakos J, et al. *J Prev Alzheimers Dis*. 2022;9(2):211-220. Cummings J, et al. *J Prev Alzheimers Dis*. 2023;10(3):362-377.

Considerations for Head CT When MRI Is Unavailable

Initial Alternative to MRI

- Use head CT for initial assessment if MRI is not accessible
- Keep in mind the limitations in ARIA detection

Limitations in Detecting ARIA-E

- CT can show significant edema but may miss subtle ARIA-E changes

Challenges with ARIA-H

- Less effective in identifying ARIA-H, such as microhemorrhages

Interpreting CT Results

- Caution in interpretation; a negative CT does not exclude ARIA
- Plan for follow-up MRI for definitive assessment when possible

Integrating into Clinical Decision-Making

- Consider overall clinical context, symptoms, and treatment history
- Remain flexible in decision-making, prioritizing patient safety and accuracy

Barakos J, et al. *J Prev Alzheimers Dis*. 2022;9(2):211-220. Cummings J, et al. *J Prev Alzheimers Dis*. 2023;10(3):362-377.

Considerations in the Acute Care Setting

Reviewing Medication History

- Thorough evaluation of current medications, especially those related to AD treatment and anticoagulants

Assessing Recent Neurology Notes

- Examining notes for any recent changes in neurological condition

Imaging Review and Decision-Making

- Prioritize reviewing any recent imaging, particularly MRI, for insights into the patient's current neurological status
- In the absence of recent imaging, prioritize arranging an MRI

Risk-vs-Benefit Analysis of Fibrinolytics/Anticoagulants

- Careful consideration of the risks and benefits of fibrinolytics or anticoagulants, especially in the context of potential ARIA
- Decision to withhold these medications should be based on a thorough clinical assessment

Cummings J, et al. *J Prev Alzheimers Dis*. 2023;10(3):362-377.

Potential Triage Protocol for ARIA

Step 1: Initial Patient Assessment
- Assess chief complaints and vital signs
- Perform initial neurological examination

Step 2: Medication History Review
- Note any anticoagulants or antiplatelet agents
- Review current medications, focusing on amyloid-targeting therapies

Step 3: Detailed Clinical History
- Inquire about past medical history, especially neurological conditions

Step 4: Comprehensive Physical and Neurological Exam
- Conduct a thorough physical and neurological examination
- Identify signs that may indicate ARIA or stroke

Step 5: Decision Point: Imaging and Treatment
- Consult specialist (neurology)
- If findings suggest ARIA, prioritize MRI
- Consider withholding fibrinolytics until ARIA is ruled out

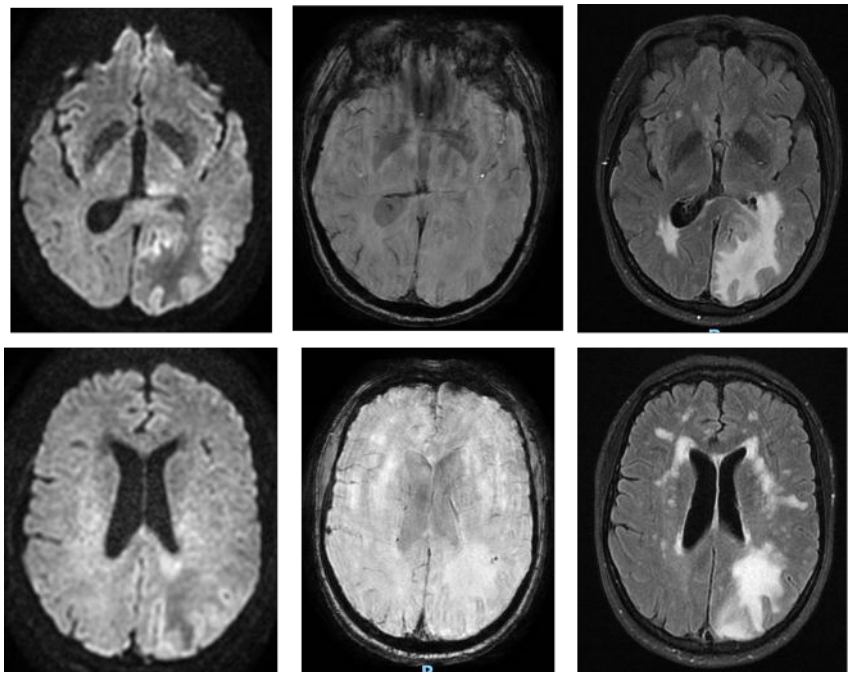
Step 6A: MRI Available
- Perform MRI to confirm/rule out ARIA
- Proceed based on MRI findings

Step 6B: MRI Unavailable
- Use CT as initial imaging but note its limitations
- Plan for MRI as soon as feasible

Step 7
- Consider holding or discontinuing treatment
- Hold fibrinolytics
- Consider supportive care

Patient Case: M.J. (Continued)

- The pharmacist, upon reviewing the patient's medication history, immediately identifies the ongoing donanemab therapy and alerts the emergency medicine physician
- The neurologist conducts a detailed review of the patient's previous imaging studies and is highly suspicious of ARIA-E
- The patient underwent an initial MRI scan (shown to the right)



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Summary

ARIA Essentials

- Key in AD therapy
- ARIA-E (edema) and ARIA-H (bleeding)

Diagnosis Priority

- Differentiate ARIA from stroke
- MRI over CT for detection

Triage Steps

- Review medications, especially amyloid drugs
- Neuro evaluation; prioritize MRI

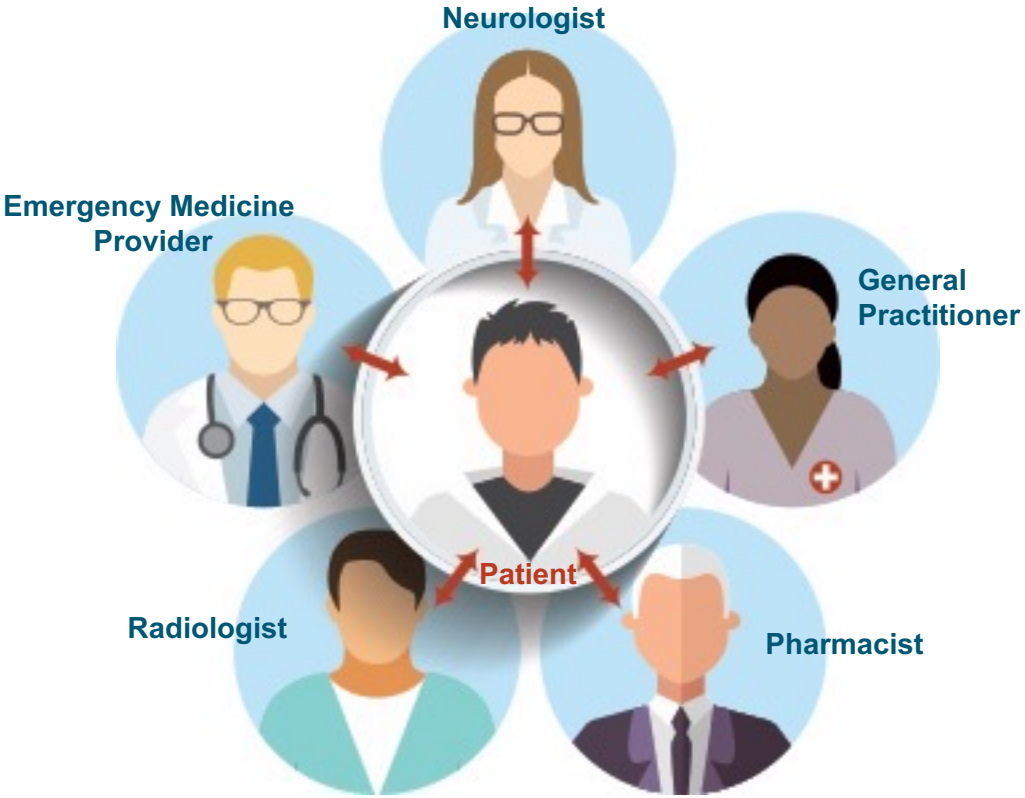
Medication Caution

- Be wary of fibrinolytics/anticoagulants
- Withhold amyloid drugs if needed

Team Approach

- Cross-specialty collaboration

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



SMART Goals

Specific, Measurable, Attainable, Relevant, Timely

- Initiate appropriate care for patients with suspected ARIA, focusing on the use of MRI over CT and cautious use of fibrinolytics
- Identify novel amyloid-targeting therapies when considering a patient's medication history (these may be part of a clinical trial, or the patient may not think of these as a medication they take regularly as these are infused periodically)

CMEO BriefCase 1

Throwing ARIA Alert:
Timely Recognition in the Emergency Department

CMEO BriefCase 3

How to Treat ARIA in Emergency Settings:
Timely Communication with Multi-Disciplinary Colleagues

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