

# A Case of Subacute Headache and Fatigue in a Child (Acute Disseminated Encephalomyelitis)

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Diagnostic Radiology, RAD 4001

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# Clinical History

- 7yo F with no PMHx who presents with 2-3wks of headache followed by 2wks of progressive weakness and fatigue
- History of Present Illness:
  - HAs began 1 month ago as intermittent bifrontal pain (5-8/10) without radiation that occasionally woke her from her sleep and were of greater severity in the mornings
  - HAs subsided after 2-3 weeks at which point she developed anorexia, fatigue, and significant weakness in bilateral upper and lower extremities
    - Walking with stooped posture → unable to straighten her knees and trembling when standing/walking
- Physical Exam Findings:
  - Stable Vital Signs: T: 99.6F BP: 113/70 HR: 113 RR: 18 SPO2: 100 on RA
  - Significant exam findings: + neck stiffness with anterior flexion, strength 4/5 throughout, 2+ reflexes in UEs, 3+ reflexes in LEs (+ Cross adductor present in LEs), + Babinski, mildly unstable gait (most notable with tandem gait), waddles and unable to walk properly for heel or toe walking
- Initial Work-Up:
  - CBC, CMP
  - Infectious workup: + Group B Strep
  - LP: CSF with pleocytosis with lymphocytic predominance and high protein, Increased CSF IgG and serum IgG
  - EEG: Cortical slowing → mild encephalopathy. No epileptiform activity seen.

# ACR Appropriateness Criteria

Imaging was **appropriate** according to ACR appropriateness criteria

**Variant 3:** Ataxia. No history of trauma. Suspected intracranial process. Stroke intervention not a consideration. Initial imaging.

Procedure	Appropriateness Category	Relative Radiation Level
MRI head without and with IV contrast	Usually Appropriate	○
MRI head without IV contrast	Usually Appropriate	○
CT head with IV contrast	May Be Appropriate	☼☼☼
CT head without IV contrast	May Be Appropriate	☼☼☼
CT head without and with IV contrast	May Be Appropriate	☼☼☼
CTA head and neck with IV contrast	Usually Not Appropriate	☼☼☼
MRA head and neck without and with IV contrast	Usually Not Appropriate	○
MRA head and neck without IV contrast	Usually Not Appropriate	○
Arteriography cervicocerebral	Usually Not Appropriate	☼☼☼
CTV head with IV contrast	Usually Not Appropriate	☼☼☼
I-123 Ioflupane SPECT/CT brain	Usually Not Appropriate	☼☼☼
MRV head with IV contrast	Usually Not Appropriate	○
MRV head without IV contrast	Usually Not Appropriate	○
In-111 DTPA cisternography	Usually Not Appropriate	☼☼☼

**Variant 4:** Ataxia of any acuity. No history of trauma. Suspected spinal or spinal vascular process. Initial imaging.

Procedure	Appropriateness Category	Relative Radiation Level
MRI spine area of interest without and with IV contrast	Usually Appropriate	○
MRI spine area of interest without IV contrast	Usually Appropriate	○
MRA spine area of interest with IV contrast	May Be Appropriate	○
CTA spine area of interest with IV contrast	May Be Appropriate	Varies
MRA spine area of interest without IV contrast	May Be Appropriate	○
Arteriography spine area of interest	May Be Appropriate	Varies
CT myelography spine area of interest	May Be Appropriate	Varies
CT spine area of interest with IV contrast	May Be Appropriate	Varies
CT spine area of interest without IV contrast	May Be Appropriate	Varies
CT spine area of interest without and with IV contrast	Usually Not Appropriate	Varies
Radiography spine area of interest	Usually Not Appropriate	Varies

<https://acsearch.acr.org/>

# ACR Appropriateness Criteria

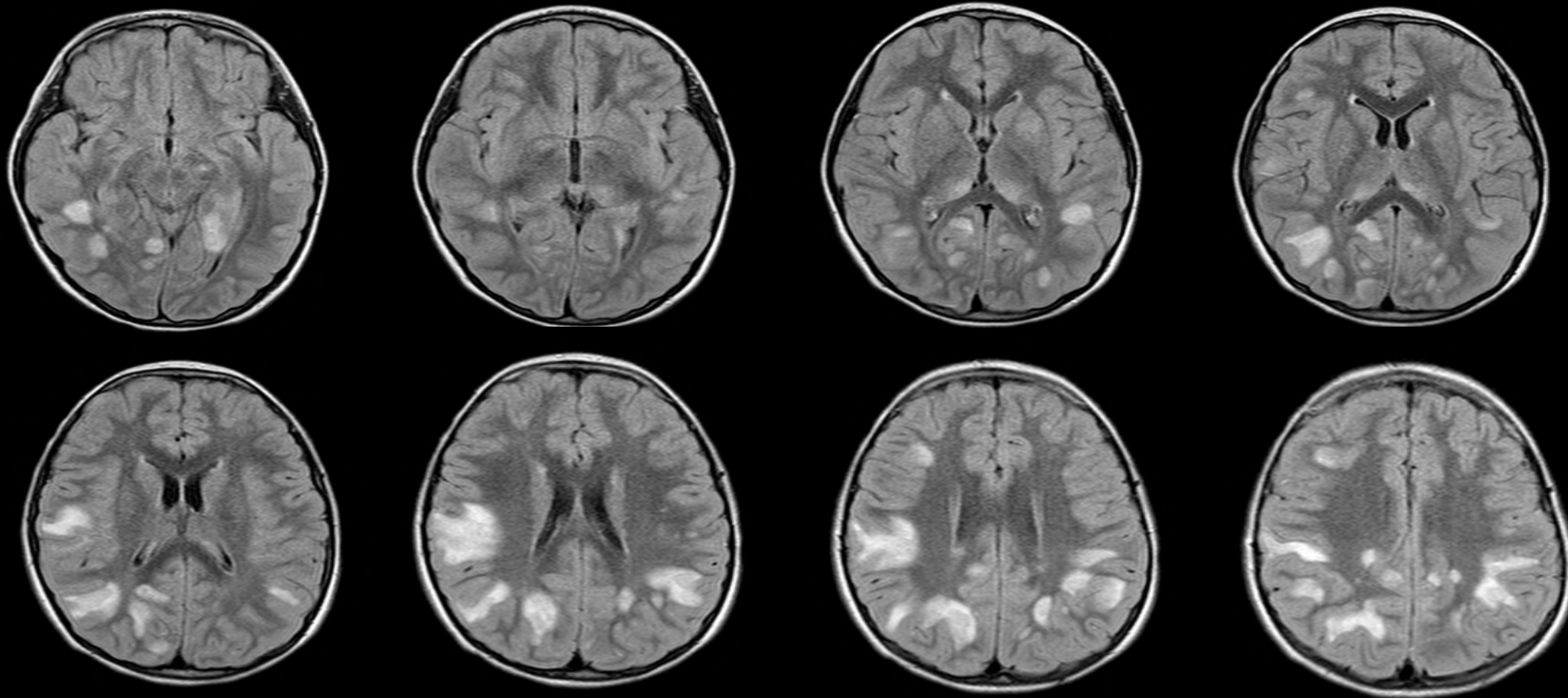
**Variant 2:** Child. Secondary headache. Initial imaging.

Procedure	Appropriateness Category	Relative Radiation Level
MRI head without IV contrast	Usually Appropriate	0
MRI head without and with IV contrast	Usually Appropriate	0
CT head without IV contrast	May Be Appropriate	⚠⚠⚠
MR venography head without IV contrast	May Be Appropriate	0
MRA head without IV contrast	May Be Appropriate	0
CT venography head with IV contrast	May Be Appropriate	⚠⚠⚠⚠
CTA head with IV contrast	May Be Appropriate	⚠⚠⚠⚠
MR venography head with IV contrast	Usually Not Appropriate	0
Arteriography cerebral	Usually Not Appropriate	⚠⚠⚠⚠
CT head with IV contrast	Usually Not Appropriate	⚠⚠⚠
CT head without and with IV contrast	Usually Not Appropriate	⚠⚠⚠⚠
X-ray skull	Usually Not Appropriate	⚠⚠

Imaging was **appropriate** according to ACR appropriateness criteria

<https://acsearch.acr.org/>

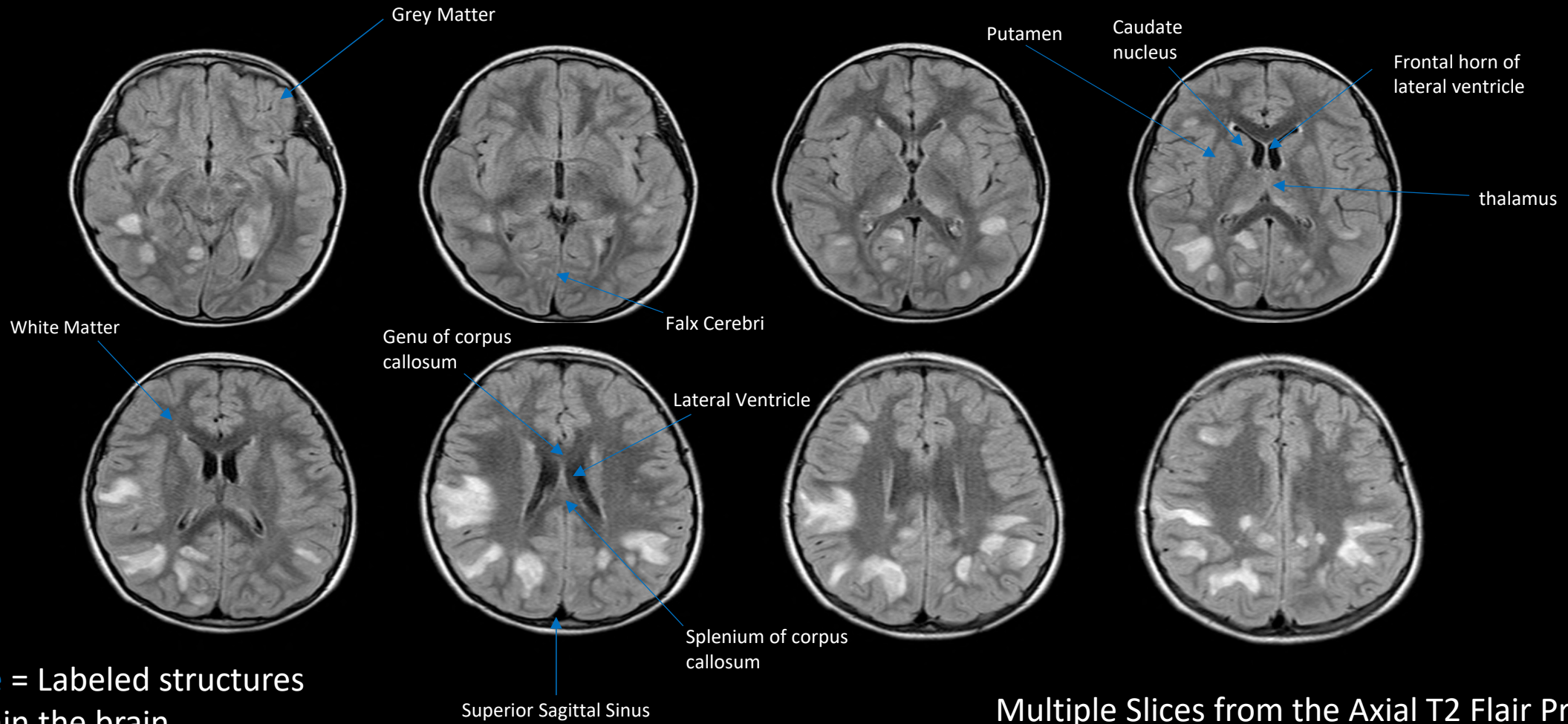
# Relevant Imaging



Multiple Slices from the Axial T2 Flair Pre-Contrast



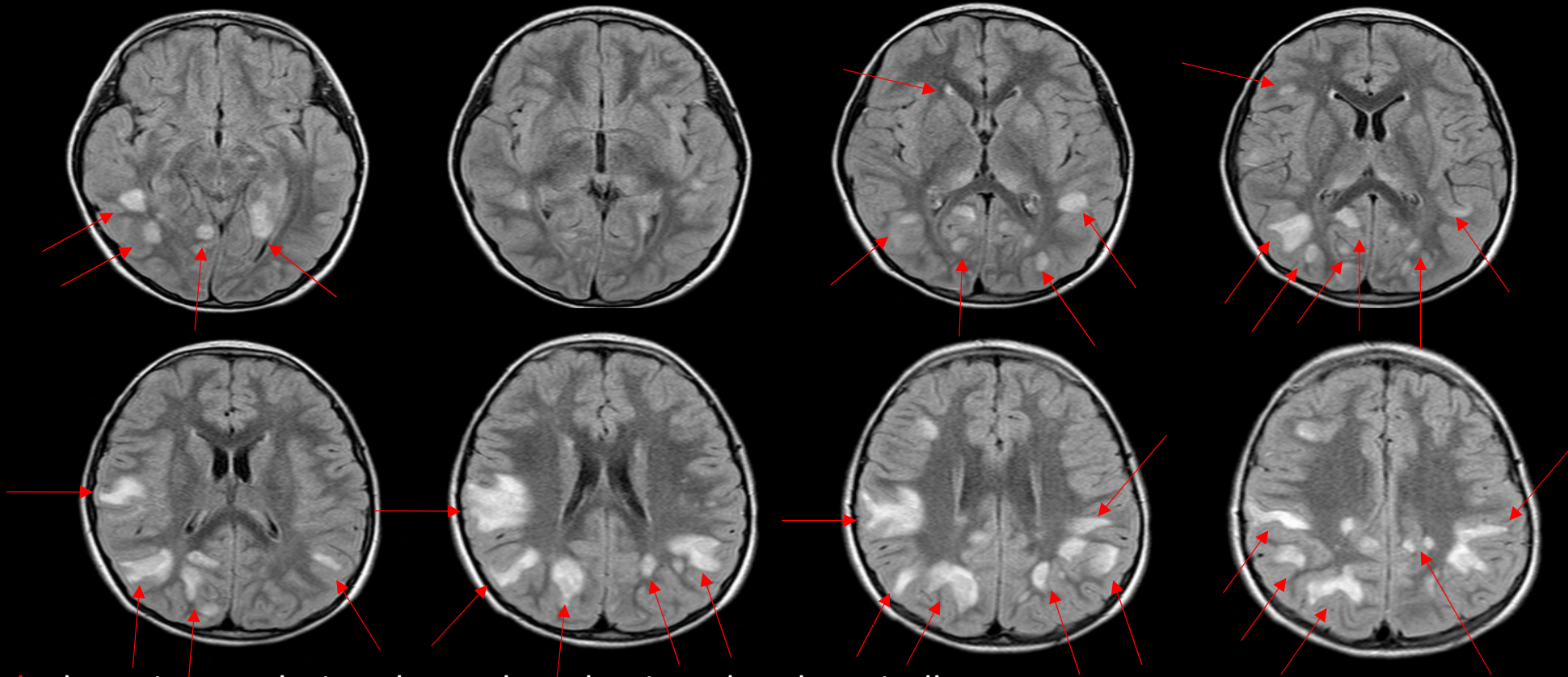
# Brain MRI



Blue = Labeled structures within the brain

Multiple Slices from the Axial T2 Flair Pre-Contrast

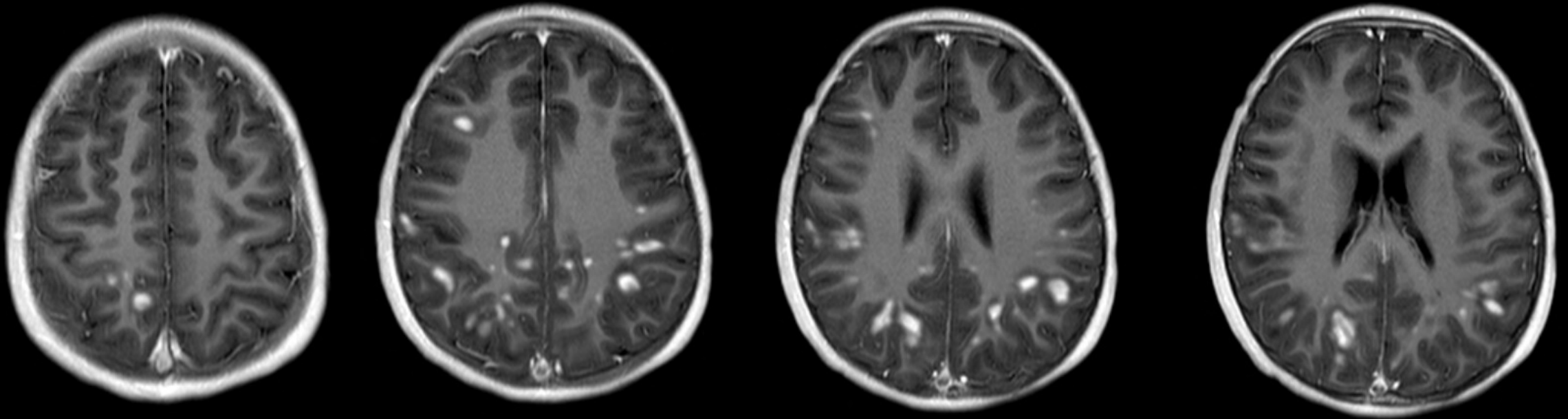
# Brain MRI



**Red** = hyperintense lesions located predominantly subcortically within all lobes of both cerebral hemispheres

Multiple Slices from the Axial T2 Flair Pre-Contrast

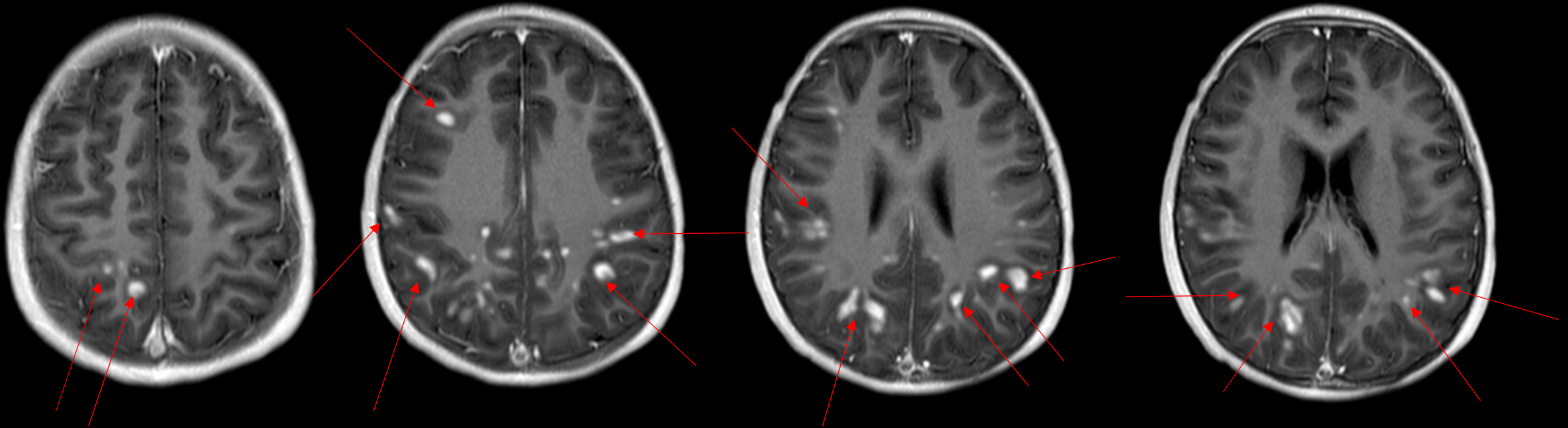
# Brain MRI



Multiple Slices from the Axial T1 Post-Contrast



# Brain MRI



**Red** = hyperintense lesions located predominantly subcortically within all lobes of both cerebral hemispheres

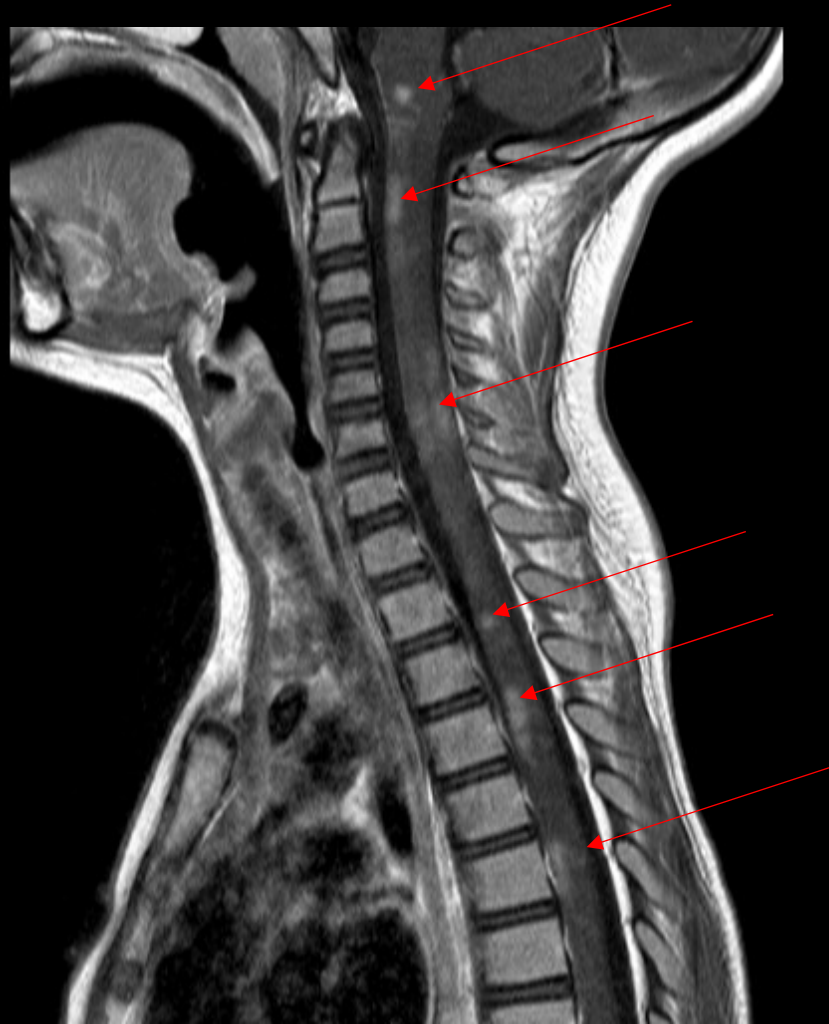
Multiple Slices from the Axial T1 Post-Contrast

# Spine MRI



Sagittal T1 Spine Post-Contrast

# Spine MRI



**Red** = hyperintense lesions located within the brainstem, cervical and thoracic spinal cord

Sagittal T1 Spine Post-Contrast

# Summary of Key Imaging Findings

- Patient CC: fatigue, weakness, ataxia, headache
- Notable Points from Workup: Subacute process (1mo), positive strep testing
- Imaging Findings:
  - Multiple predominantly subcortically located hyperintense lesions within all lobes of the both cerebral hemispheres, bilateral dorsal medial thalami, pons, medulla, dentate nuclei which demonstrate solid enhancement on postcontrast imaging.
  - No definite leptomeningeal enhancement is seen.
  - No significant mass effect, midline shift, obstructive hydrocephalus or intracranial hemorrhage is seen.
  - Extensive multifocal hyperintensities within the brainstem, cervical and thoracic spinal cord.
  - Minimal cord swelling.
- \$6,775 = the estimated cost of MRI brain wo contrast, MRI brain w/wo contrast, MRI spin wo contrast, MRI spin w/wo contrast)

<https://www.honorhealth.com/patients-visitors/average-pricing/mri-costs>

# Differential Diagnosis

- Acute Disseminated Encephalomyelitis
- Meningitis
- Infectious Encephalopathies (HSV encephalitis, HIV-associated encephalopathy)
- Autoimmune encephalitis
- Mitochondrial encephalopathies
  - MELAS
- Metabolic encephalopathies
  - Thiamine Transporter Deficiency

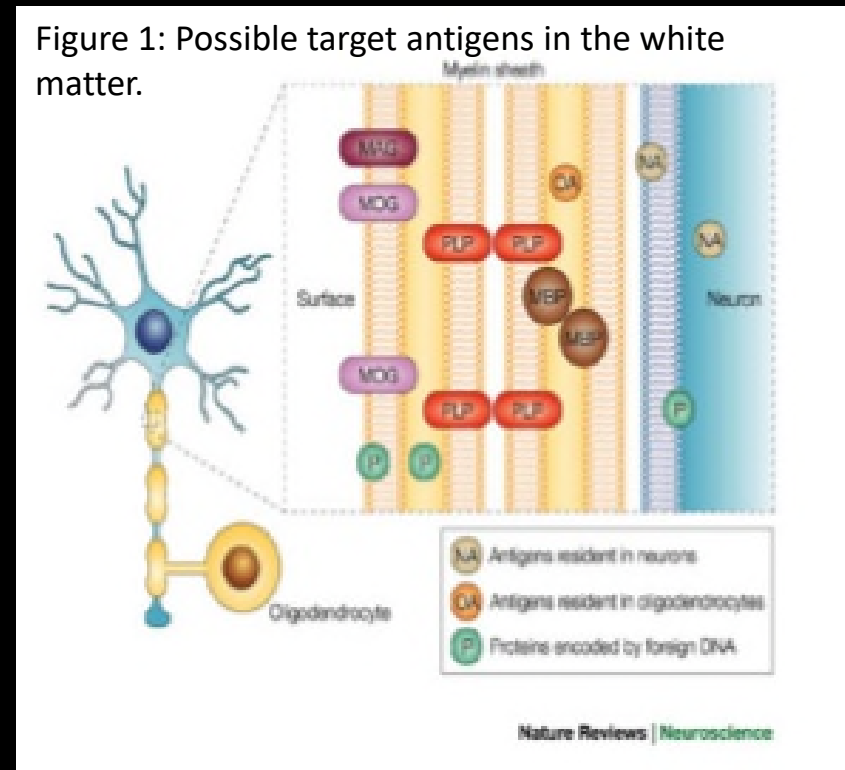


# Discussion: ADEM – The Basics

- Epidemiology:
  - Incidence: 0.2-0.8/100,000 children per year
  - Ethnicity: No specific ethnic distribution
  - Gender: Slight male predominance
  - Mean Age: 5 to 8 years old (in pediatric cohorts)
  - Geographic: ↑ incidence with ↑ distance from equator
- Classifications
  - Post-infectious: ~75% of all ADEM cases
    - Winter or spring
    - Within 1 month of infection
    - Viruses: Coronavirus, Coxsackie, Cytomegalovirus, EBV, HSV, HepA, HIV, Influenza, Measles, Rubella, VZV, West Nile
    - Other: Borrelia Burgdorferi, Chlamydia, Leptospira, Mycoplasma Pneumonia, Rickettsia, Beta Hemolytic Streptococcus
  - Post-vaccinial: <5% of all ADEM cases
    - MMR, Rabies, PCV, DTap, HPV, MNQ, Flu

# Discussion: ADEM - Pathophysiology

- Autoimmune disorder of the CNS
  - Triggered by an environmental stimulus in genetically susceptible individuals
- A form of molecular mimicry
  - Myelin autoantigens (such as myelin basic protein, proteolipid protein, and myelin oligodendrocyte glycoprotein) share antigenic determinants with those of an infecting pathogen



<https://www.nature.com/articles/nrn784>

# Discussion: ADEM - Diagnosis

- Diagnosis is based on clinical and radiologic features
- Helpful diagnostic tools:
  - Neuroimaging
  - Lumbar Puncture
  - Laboratory Studies
  - EEG
- Alpha 2 macroglobulin

## Diagnostic criteria of acute disseminated encephalomyelitis (ADEM) in children

Clinical features (all are required)
A first polyfocal, clinical central nervous system event with presumed inflammatory demyelinating cause
Encephalopathy that cannot be explained by fever, systemic illness, or postictal symptoms
No new clinical and MRI findings emerge three months or more after the onset
Brain MRI is abnormal during the acute (three-month) phase
Lesion characteristics on brain MRI
Diffuse, poorly demarcated, large (>1 to 2 cm) lesions involving predominantly the cerebral white matter
Deep gray matter lesions (eg, involving the basal ganglia or thalamus) can be present
T1 hypointense lesions in the white matter are rare

The clinical features of ADEM typically follow a monophasic disease course, although they can fluctuate in severity and evolve in the first three months following disease onset. **Multiphasic ADEM** is defined as two episodes consistent with ADEM separated by three months but not followed by any further events. The second ADEM event can involve either new or a re-emergence of prior neurologic symptoms, signs and MRI findings.

<https://www.uptodate.com/contents/acute-disseminated-encephalomyelitis-adem-in-children-pathogenesis-clinical-features-and-diagnosis>

# Discussion: ADEM - Treatment

- Broad spectrum antibiotics and acyclovir until an infectious etiology is excluded
- High-dose IV glucocorticoids
  - Methylprednisolone (10-30mg/kg/day) or dexamethasone (1mg/kg/day) for 3-5 days
  - Followed by oral glucocorticoid taper over 4-6 weeks
- Alternate options: IVIG, plasma exchange (PLEX)
- Suggest obtaining 2+ additional MRIs after the first normal MRI, over a period of at least 5yrs from the initial episode of ADEM

# Take Home Points

- ADEM is usually a monophasic illness and symptoms can include fever, headache, decreased level of consciousness, seizure, and multifocal neurologic symptoms, behavioral changes.
- MRI is far more sensitive than CT and demonstrates lesions characteristic of demyelination.
- ADEM is thought to occur from a cross-reactivity in immunity to viral antigens, triggering a subsequent autoimmune attack on the CNS.
- In approximately half of confirmed cases, anti-MOG (myelin oligodendrocyte glycoprotein) immunoglobulin G antibodies can be identified.
- Treatment with steroids and complete recovery is seen in the majority of the cases.



# References

- <https://acsearch.acr.org/>
- <https://radiopaedia.org/articles/acute-disseminated-encephalomyelitis-adem-1?lang=us>
- <https://www.nature.com/articles/nrn784>
- <https://www.uptodate.com/contents/acute-disseminated-encephalomyelitis-adem-in-children-pathogenesis-clinical-features-and-diagnosis>



Questions?