Acute Necrotizing Encephalopathy (ANE)

Clinical Practice Guidelines

Patient with Suspected ANE:
Known or suspected viral infection, *AND*
Clinical encephalopathy *AND/OR*
Glasgow coma scale (GCS) score < 14

Definition: ***Acute necrotizing encephalopathy (ANE)*** *is a rare and severe form of acute encephalopathy, usually preceded by a virus-associated (commonly influenza) febrile illness and characterized by rapid clinical deterioration and high risk of morbidity and mortality. Given severity and rapid progression, early identification and timely treatment is imperative.*

Initial Evaluation

STAT head CT

Laboratory studies:

CBC, CMP, PT/PTT/INR, type & screen, CRP, procalcitonin

If no contraindication (i.e. evidence of acute obstructive hydrocephalus or posterior fossa mass effect) perform **lumbar puncture** with opening pressure, CSF culture, cell count/diff, protein, glucose, MEP, and separate tube for CSF cytokines

CT Consistent with ANE?
*(see Imaging Findings Associated with ANE)

Yes / No

Obtain STAT MRI
Flu Imaging Protocol, "FLIP"

MRI Consistent with ANE?
*(see Imaging Findings Associated with ANE)

Yes / No

End of protocol.
Continue managing patient as clinically indicated

Consultations

ED to place STAT consults to:
Neurology, ID, Rheumatology, and PICU (for admission)

PICU to consult Nephrology pending confirmation of plasma exchange in treatment plan (see Treatment, below)

Initiate Acute Treatment: (DO NOT DELAY)

1. ***STAT*** antiviral (oseltamivir preferred. *I.V. Peramivir may be used if there is absolute contraindication to enteral medication*
   -*Order one-time peeramivir dose and contact ID for additional doses*)
   First dose should be given without delay, in ED or PICU
2. ***STAT*** Methylprednisolone 30mg/kg (max 1 g) daily x 5 days
   First dose should be given without delay, in ED or PICU
3. Consider initiating empiric broad-spectrum antibiotic therapies for alternative diagnoses (i.e. bacterial meningitis)
4. Tocilizumab (weight <30 kg: 12 mg/kg; weight ≥30 kg: 8 mg/kg) on day 0
   -*Requires approval of consulting Rheumatology attending*
   (See additional considerations on page 2)
   -Administer one dose prior to plasma exchange therapy but do not delay plasma exchange
   -Further doses post plasma exchange to be determined by Rheumatology team
5. PICU to provide urgent placement of vascular access for plasma exchange

Additional Management

PICU Early Mobility Consult for PT/OT/SLP evaluation

Genetics consult during business hours (non-urgent) to discuss testing for *RANBP2* and other mutations associated with ANE.

a. Genetic testing strategy to be determined based on clinical presentation and severity of illness. Testing may include *RANBP2* testing or rapid genome.
b. *RANBP2* testing may be informative in
   i. Patients with recurrent ANE or family history.
   ii. MRI findings can be delayed in some cases

Imaging Findings Associated with ANE

CT

·Bithalamic hypodensity and swelling +/- hemorrhage, cavitation

MRI (*any of the following*)

·**Trilaminar thalamic necrosis:** a three-layered appearance on the apparent diffusion coefficient (ADC) maps, whereby there is an outer high signal ring, a middle low signal ring, and a central high signal region

·**Abnormal susceptibility-weighted imaging (SWI):** foci of susceptibility in the thalami

·There may also be involvement of the brainstem and cerebral and cerebellar white matter, but ***bithalamic involvement is invariable and tends to be a distinctive finding***

References:

https://radiopaedia.org/articles/acute-necrotising-encephalopathy?lang=us

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Additional Considerations Before Starting Tocilizumab:

- Tocilizumab requires approval from an attending Rheumatologist

- Obtain history and physical examination to confirm low risk of tuberculosis

- Tuberculosis testing (i.e. quantiferon gold) *NOT* necessary if benefit of early administration outweighs risk of infection

- Patients with high risk of tuberculosis exposure or known exposure should undergo chest X-ray and discussion with ID and Rheumatology prior to initiating tocilizumab

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