Geriatric Pearls: Cases from the Fellows’ Clinic: Malaise, Myoclonus, and Mental Status Changes

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Geriatric Update
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Case

• 76 year-old community dwelling and cognitively intact male admitted to the inpatient geriatric service with…
  • Generalized malaise
  • Loss of appetite
  • Subjective fevers
  • Lightheadedness
  • Loose stools
Case
Past medical history

• Pertinent past medical history:
  o CLL on current treatment with Ibrutinib
  o DM2 on oral medications
  o CKD stage 3
  o Atrial fibrillation on Rivaroxaban
  o Sick sinus syndrome s/p pacemaker placement
  o Hypertension
  o Hyperlipidemia
  o Hypothyroidism
  o Gout
  o OSA
Case

Social history

• Retired Catholic priest and psychologist
• Still saying mass on Sundays, including the week before admission
• 50 pack year smoking history (quit in 1980)
• One alcoholic drink per night
Case
Physical Exam

- General: Well-appearing male in no acute distress. Awake, alert, oriented, pleasant, cooperative, nontoxic.
- Lymph: No cervical, supraclavicular, or submandibular lymphadenopathy noted.
- Heart: Irregular rhythm. Normal S1 and S2.
- Lungs: Clear to auscultation
- Abdomen: Prominent hyperactive bowel sounds throughout. Abdomen is otherwise soft, nontender, nondistended. No appreciable masses or organomegaly.
- Neuro: Alert, oriented to person, place, and date. Cranial nerves II through XII were grossly intact. Upper and lower extremity strength is grossly intact and symmetric. No focal deficits.
Case
Initial Workup

- **WBC 22** (recent baseline 20) with neutrophilia and lymphocytosis, Hgb 13.6, platelets 186, **Na 130**, K 4.4, **Cr 2.6** (baseline 1.6), **lactate 2.2**, **AST 68**, **ALT 86**, ALP 54, bilirubin 0.8
- Chest x-ray, abdominal x-ray, urinalysis, and GI stool pathogen panel unremarkable
- Blood cultures negative
Case
Clinical Course

- Hospital Day 2: Develops high fevers
- Hospital Day 3: Fevers continue
  - CT chest negative for focal findings; decrease of lymphadenopathy that was noted in prior imaging
  - “More confused” with fluctuating mental status
- Hospital Day 4: Development of facial tremors, upper extremity myoclonus, and dysarthric speech. Mental status deteriorates even further
  - CT head obtained and negative for acute intracranial findings
  - ID and Neurology consult obtained
- Hospital Day 5-7: Fevers ongoing. Unable to follow any commands. Unable to sit up in bed or ambulate. Requiring 1:1 supervision
Case
Infectious Disease Workup

• Serum testing
  • EBV PCR
  • CMV PCR
  • Tick borne panel (Anaplasma, Ehrlichia, Lyme disease)
  • Fungal serology (Blastomycoses antibody, Cryptococcus antigen, and Histoplasmosis antigen)
  • HIV
  • Syphilis
  • St. Louis encephalitis IgG and IgM
  • West Nile Virus IgG and IgM
  • Heavy metal screen
  • QuantiFERON

• NEGATIVE
Case
Infectious Disease workup, continued

- Lumbar puncture
  - Cell count 33 with 68% lymphocytes
  - Glucose 90
  - Protein 113
  - Gram stain negative

- Testing
  - Arbovirus antibody panel
  - Herpes simplex PCR
  - West Nile antibody
  - West Nile PCR
  - VZV PCR
  - CMV PCR
  - EBV PCR
  - Lyme Disease PCR
  - JC virus PCR
  - Tropheryma whipplei PCR
  - Enterovirus PCR
  - Adenovirus PCR
  - HHV-6 PCR
  - Malignant cells
  - VDRL 0.2
  - AFB stain
  - Fungal smear
  - Cryptococcus antigen.
  - Bacterial culture
  - Powassan virus IgM
Case, continued

- WNV PCR in CSF positive!!!!

- WNV encephalitis
West Nile Virus (WNV)

- An arbovirus transmitted via mosquito bites
- Seasonal epidemic in US since 1999

- 80% asymptomatic
- 20% acute febrile illness
- <1% develop neuroinvasive disease
  - Meningitis
  - Encephalitis
  - Acute flaccid paralysis
WNV Infection
In the US and MN

- In the United States, 1352 cases of West Nile virus disease have been reported to CDC this year (as of 10/18/16)
  - 692 (51%) were classified as neuroinvasive
- In Minnesota, 41 total cases reported this year
  - 17 (41%) classified as neuroinvasive
WNV Encephalitis

Clinical presentation

- Fever
- Encephalopathy
- Weakness
- Tremors
- Myoclonus (typically upper extremities)*
- Parkinsonian features (rigidity, postural instability, bradykinesia)
- Headache
- Cranial neuropathies
WNV Encephalitis
Risk Factors

• Elderly
• Immunocompromised
• Malignancy
• Male gender
• Diabetes
• Cardiovascular disease
• Kidney disease
• Alcohol
WNV Encephalitis

Diagnosis: What to look for if suspect WNV

- Serum WNV IgM antibody (MAC-ELISA) and WNV PCR

- For neuroinvasive disease, obtain CSF and send for WNV IgM antibody and WNV PCR
  - CSF pleocytosis and elevated protein

- Plaque reduction neutralization test (PRNT): Most specific antibody test and only available through CDC and some state departments. Done to rule out cross-reactions
**WNV Encephalitis**

**Diagnosis: CDC diagnostic criteria**

- **Confirmed case** = clinically compatible disease and
  - Isolation of virus from, or demonstration of specific viral antigen or nucleic acid in, tissue, blood, CSF, or other body fluid, **OR**
  - Fourfold or greater change in virus-specific quantitative antibody titers (PRNT) in paired sera, **OR**
  - Virus-specific IgM antibodies in serum with confirmatory virus-specific neutralizing antibodies (PRNT) in the same or a later specimen, **OR**
  - Virus-specific IgM antibodies in the CSF and negative IgM in the CSF for other arboviruses endemic to the region where the exposure occurred

- **Probable case** = clinically compatible disease and
  - Virus-specific IgM antibodies are present in CSF or serum but no other testing (i.e., PRNT, PCR) is performed

- For routine clinical purposes, a diagnosis of probable disease is sufficient for the vast majority of patients
WNV Encephalitis
Diagnosis: Other supportive evidence

- EEG with generalized slowing with anterior or temporal prominence
- Elevated WBC, hyponatremia, and elevated liver enzymes
- Head imaging is often normal
  - CT nearly always normal
  - MRI can be abnormal (20-70% of cases) with T2-weighted hyperintensities in basal ganglia, thalami, caudate nuclei, brainstem, and cerebellum. If abnormalities are seen, can predict outcome
WNV Encephalitis
Treatment

• SUPPORTIVE
• Several therapeutic agents have been tried (ribavirin, interferon, intravenous immunoglobulin) without promising results

• Prevention relies on protection from mosquitoes, no vaccines currently available
WNV Infection
Prognosis

• Sequelae for many months to years after WNV infection.
  • Physical: muscle weakness, fatigue, myalgia
  • Functional: Trouble performing ADLs
  • Cognitive: Memory loss, depression, difficulty concentrating
• Disposition:
  • In one series of 221 patients with WNV encephalitis…
    • 18% of patients died
    • 46% discharged to rehabilitation or long-term care
    • 15% returned home with assistance
    • 20% returned home independently
  • In another series of 15 patients with WNV neuroinvasive disease at 8 months
    • 73% returned to independence
    • 20% returned home but required assistance
    • 7% remained in rehabilitation
  • In a review article that summarized 14 studies, 45% did not achieve full
    recovery (did not return home to independence)
WNV Infection
Prognosis

• Patients admitted to acute rehabilitation after WNV encephalitis with neuropsychological testing had persistent cognitive deficits and neuropsychiatric symptoms resembling frontal subcortical dementias
  • Language/communication deficits
  • Memory impairments
  • Executive dysfunction
  • Defects in concentration
  • Emotional dysregulation
  • Apathy and agitation
Case Resolution

• Hospitalized for 2 weeks
• MRI: Suggestion of patchy bilateral T2/FLAIR hyperintensities in the bilateral thalami, basal ganglia, and possibly central brainstem, although significantly degraded by motion artifact
• Fevers, facial tremor, and myoclonus all resolved
• Encephalopathy slowly improving but not back to baseline
• Discharged to inpatient rehabilitation
References

Questions & Discussion