NEUROSYPHILIS AS A CAUSE OF CONFUSION IN GERIATRICS

THE MYSTERIOUS CASE OF KG
OVERVIEW

CASE OF MRS. KG
NEUROSYPHILIS
PRESENTATION
DIAGNOSIS
TREATMENT
FOLLOW UP
THE CASE OF MS. KG

- 89yo female admitted on Aug. 10, 2011 with a C2 fracture
- RFR: Delirium since admission
- PMHx:
  - HTN, RA (extensive disease), OA, Hyponatremia 2° to HCTZ, L hip fracture 1 year ago, OP 2° long-term use of prednisone, A.fib
- Allergies: NKDA
- Social Hx:
  - Patient originally from India. Moved from India to Calgary with husband. Living with family - Son’s family and extended family. Family responsible taking care of all finances and medications for patient. Husband passed away in 1997 from esophageal cancer. No ETOH. No smoking. No illicit drug use
**Meds in Hospital**

- Acetaminophen 650mg PO TID
- Alendronate 70mg PO q7 days
- Bisoprolol 15mg PO daily
- Celebrex 200mg PO BID
- Enalapril 20 mg PO daily
- Hydromorphone 3 mg PO q12hr
- Hydroxychloroquine 200mg PO BID
- Nifedipine 30mg PO daily
- Pantoprazole 40mg PO daily
- Prednisone 5mg PO BID
- Warfarin 1mg PO daily

- Codeine 15-30mg PO q4-6hr PRN
- Dimenhydrinate PRN

**For delirium**

- Quietiapine 50mg PO q1700hr
- Quietiapine 12.5mg @ 0:00, 02:00, 22:00 for agitation overnight
History given by grandson as patient not answering questions appropriately.

- Aug 19 – Admission after fracture – No confusion
- Aug 27 – Started having hallucinations – Seeing relatives from India
- Grandson has noticed sundowning for approx. 3 nights

Yesterday:
- Increased agitation in the evening
- Patient found to be screaming for hours
- Patient given the regular quetiapine + all PRNs
- Finally nursing used lorazepam PRN → Patient has been drowsy all day

At home:
- Family describes as patient as “quite sharp”
- Relies more on family due to decreased mobility
- Daughter-in-law reports previous delirium after hip # and when changes to pain meds
PHYSICAL EXAM

- Vitals: T=36°C, HR=83, BP=145/82, RR=18, \( \text{SaO}_2 \)=96% on RA

MENTAL STATUS
- KG believes she is at her son’s house
- She is unable to give the date (grandson believes she wouldn’t be able to give date even at baseline)
- Answers to her name, unable to recognize grandson
- ++ Hallucinations –
  - Visual – Water leaking from the wall and snakes on her bed and surroundings
- No recollection of agitation last night

- CVS: Normal S1/S2, No S3/S4, No murmurs, Irreg. irreg HR
- ABDO: Soft, non-tender
- RESP: Decreased BS R> L, No adventitious sounds
- CNS: PERL, unable to test VF, Motor strength, Reflexes 1+ throughout, downgoing plantar reflexes, unsafe to walk
- Patient spoke only Punjabi and was difficult to understand
<table>
<thead>
<tr>
<th>Blood work</th>
<th>Electrolytes</th>
<th>Others:</th>
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<tbody>
<tr>
<td>Hgb: 123</td>
<td>Na: <strong>129</strong></td>
<td>Mg: 0.65</td>
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<tr>
<td>Plt: 262</td>
<td>K: 4.0</td>
<td>PO4: 0.93</td>
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<tr>
<td>WBC: 10.3</td>
<td>Cl: 93</td>
<td>Ca2: 2.29</td>
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<td></td>
<td>CO2: 27</td>
<td>INR: 2.4</td>
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<td></td>
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<td>Trops: Neg</td>
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<td></td>
<td></td>
<td><strong>TSH: 9.91</strong></td>
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<td></td>
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<td>Free T4: 22.9</td>
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<td></td>
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<td>CT head: N</td>
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<td>CT trauma: C2# through odontoid; generalized atrophy</td>
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OUR RECOMMENDATIONS

- **PAIN:**
  - Instead of using codeine, morphine and oxycodone, switch to long-acting hydromorphone and immediate release hydromorphone for PRN

- **DRUGS:**
  - Please stop dimenhydrinate. Avoid use of prednisone close to bed time.
  - Adjust BP meds when more stable. Hallucinations → Increased BP

- **DELIRIUM:**
  - May have underlying MCI as KG’s family is doing all finances and med control. Since she is so well looked after, there are no functional consequences
  - Meds: Avoid use of lorazepam → Increased sedation during the day. May use quetiapine. Use regular dosing during this acute state and switch to PRN when improvement.
  - Non-pharmacologic recommendations
What lab tests may need to be investigated?
Hospitalist ordered SYPHILIS SEROLOGY (Serum VDRL)

- REACTIVE

- More history given by family regarding sexual history
American Academy of Neurology (AAN) recommends screening for:

- B12
- TSH
- Depression screen

There are no clear data to support or refute ordering "routine" laboratory studies such as a complete blood count, electrolytes, glucose, and renal and liver function tests.

Screening for neurosyphilis is not recommended unless there is a high clinical suspicion.

Less than 1% in 1994 study showed reversible causes for dementia
Neurosyphilis = CNS by T. Pallidum

Early in course of syphilis – Involve CSP, meninges, and vasculature

Late in course of syphilis (TERTIARY SYPHILIS) – Involve brain, spinal cord parenchyma (general paresis and tabes dorsalis)

Pathogenesis:
- Invasion of CSF soon after acquisition
- “Asymptomatic neurosyphilis”
General Paresis:

- Rapidly progressive dementia due to destruction of the cerebral cortex by spirochetes → Psychotic features.
- Commonly encountered in individuals aged between 35 – 50
- Develops 10 to 20 years after occurrence of primary syphilis
- SPECT is more sensitive than MRI in detecting brain abnormalities
  - Demonstrated improvement in CBF determined by SPECT in affected patients after receiving antimicrobial treatment
- Brain atrophy may be irreversible

**Figure 3.** Fluid Attenuated Inversion Recovery (FLAIR) magnetic resonance imaging (MRI) after antibiotics treatment performed in May 2004 (A) and in January 2007 (B) revealed progressive right brain atrophy with persistent high signal and conspicuous dilated ventricle.
Clinical suspicion and spinal fluid examination

Unknown syphilis history:
• Confirmation of syphilis
  • Serum nontreponemal tests:
    ▪ VDRL
    ▪ RPR
  • Serum treponemal tests:
    ▪ FTA-ABS
    ▪ TPPA
    ▪ EIA

Known syphilis
• LP with CSF examination
  • Spinal fluid examination
    ▪ CSF-VDRL: Specific but not sensitive
    ▪ CSF FTA-ABS: Sensitive but not specific
NON-HIV patient with Nonreactive CSF VDRL
- CSF lymphocyte count > 5 cells/microL OR
- CSF protein concentration > 45 mg/dL
- * May also do CSF FTA-ABS
- → Consistent with diagnosis of neurosyphilis

HIV patient with nonreactive CSF VDRL
- Difficult to diagnose
  - HIV may cause mild CSF pleocytosis and protein concentration
  - One study [1] found that an HIV-induced CSF pleocytosis was independently and significantly associated with three factors [27]:
    - Lack of current antiretroviral use (OR 5.9, 95% CI 1.8-18.6)
    - CD4 count > 200/microL (OR 23.4, 95% CI 3.1-177.3)
    - Detectable plasma HIV RNA (OR 3.3, 95% CI 1.1-9.4)

DIAGNOSIS (CONT’D...)
GP has become rare in developed countries due to efficacy of penicillin treatment

- Results of the management of GP with penicillin are far from ideal. Penicillin therapy has a marked effect on both the clinical picture and cerebrospinal fluid abnormalities of GPI, but a large number of the patients treated are unable to regain their previous cognitive performance, whereby persisting cognitive and behavioral disturbances preclude a return to former professional activities.

- The treatment, to be completely efficient, must be accomplished before the cognitive and behavioral signs of GP have manifested. It is in the phase of early syphilis or in the latent period (asymptomatic neurosyphilis) or even when the first clinical signs of meningovascular neurosyphilis become noticeable, that penicillin therapy is highly efficient and prevents evolution to GP.
No available controlled clinical trial. Treatment based on clinical use, pharmacokinetics of the available drugs and the effect on T. pallidum in vitro

- **Intravenous penicillin G** (3 to 4 million units IV Q 4h or 18 to 24 million units per day by continuous infusion for 10 to 14 days) recommended by the Centers for Disease Control and Prevention (CDC)

- Other alternatives include **amoxicillin** (3 grams twice daily) plus **probenecid** (0.5 to 1 gram orally) for 14 days or **doxycycline** (200 mg orally twice daily) for 21 days. Not recommended by the CDC and are not considered standard-of-care.

- Penicillin skin testing can reliably identify persons at high risk for penicillin reactions. Patients with neurosyphilis who are allergic to penicillin should undergo **penicillin desensitization**, since this is clearly the optimal treatment for CNS infection.

- Alternative in patients with relatively mild manifestations of penicillin allergy is to administer ceftriaxone IV or IM (2 grams daily for 10 to 14 days), [possibility of cross-reactivity (approximately 5 percent) still exists]
No microbiological test for cure

Success of treatment based on resolution/stabilization of clinical symptoms and normalization of CSF abnormalities

Neuro exam and LP q3-6 months after treatment until CSF WBC is normal and CSF VDRL is nonreactive
  - Failure → Retreatment

Longitudinal study in patients showed that a decline in RPR titer predicted normal CSF WBC and non-reactive CSF VDRL in >90% patients
REFERENCES:


Ricardo N. The cure of one of the most frequent types of dementia: A historical parallel. Alzheimer Dis Assoc Disord 2005; 19(3): 156-158

UpToDate
ATTACK
OF THE
CURSED SYPHILIS
IT'S LURKING IN THE DEPTHS, WATCH OUT!

Starring
SYPHILIS - YOU - AND YOU - AND MAYBE YOU TOO