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## An Atypical Cause of Potential Reversible Dementia

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### Abstract

**Background:** Neurosyphilis is defined as an infection of the central nervous system by spirochete bacterium, *Treponema pallidum* (*T. pallidum*). After infection by *T. pallidum*, symptoms may develop from weeks to months, most commonly within two years. The clinical manifestations of neurosyphilis are classified into two forms: early and late forms.

**Early Neurosyphilis:** Can be asymptomatic or symptomatic, and it involves the invasion of *T. pallidum* into the cerebrospinal fluid (CSF), meninges, and the vasculature. However, invasion of CSF does not always result in symptoms and that spontaneous resolution can occur.

**Late Neurosyphilis :** Occurs when the brain and spinal cord parenchyma are invaded. The two major manifestations are tabes dorsalis and general paresis. Tabes dorsalis is a disease of the posterior columns of the spinal cord and of the dorsal roots. Individuals with tabes dorsalis often have sensory ataxia and sudden, brief, stabbing pain affecting the face, back, or extremities [1]. They can also have paresthesia and severe nausea, vomiting, and epigastric pain. Another sign seen in patients with tabes dorsalis is the Argyll-Robertson pupils that accommodate but do not respond to light. General paresis usually develops about 20 years after infection and is associated with progressive dementia and personality change. Some individuals with general paresis may develop depression, mania, psychosis, and abnormal behaviors.

### Case

84-year-old male who presented to the adult specialty clinic because of forgetfulness in the past 5-10 years.

### History

An 84-year-old male with past medical history of type 2 diabetes mellitus with retinopathy, dementia, hyperlipidemia, colon polyps, CKD stage 3a who presented to the adult specialty clinic referred by his primary care physician due to forgetfulness and a possible diagnosis of dementia. His wife and daughter provided collateral history. His wife reported forgetfulness/short-term memory loss for more than 5 years, which worsened over the past year. She stated that patient forgets doctor's appointments, family members' names, directions, and keeps asking about the same things repeatedly. He cannot drive because he gets lost sometimes. He also wandered away from home and got lost many times in the neighborhood. As a result, his wife had to place locks on all the doors of their home. Nonetheless, his wife denied any other significant behavior disturbances. Patient scored 12/15 on the Geriatric Depression Scale. He was taking Sertraline 25 mg PO daily for major depressive

disorder. His wife and daughter believed he was depressed [2]. They did not think the medication was working well. They believed Sertraline was making him more agitated. During the last visit with his primary care physician, he was prescribed Memantine 5 mg PO BID for his short-term memory loss, which he tolerated without side effects. A cholinesterase inhibitor was not prescribed because patient had intermittent bradycardia. Because his PCP characterized his dementia as moderate to severe, Memantine was the appropriate treatment.

### Geriatric Assessment

Activities of Daily Living: Bathing, Dressing, Grooming, Toileting, Transfer, Eating – 6/6

Instrumental Activities of Daily Living: Shopping, Cooking, managing medications, Using the phone and looking up numbers, doing housework, doing laundry, Driving or using public transportation, Managing finances –0/8

Geriatric Depression Screening: 12/15

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Mini-Mental State Examination (MMSE): 10/30 (<24 abnormal)

### Physical exam

Vitals signs: Temp 98.4F, HR 76, RR 16, pulse ox 98% on room air. Caucasian male in nonapparent distress. No oral lesions. No throat erythema. No chest retractions. No crackles or wheezes. No heart murmurs appreciated. Abdomen soft, non-tender and non-distended. No lower extremity edema. No focal neurologic findings.

### Mental Status Exam

General appearance: 84-year-old male who appears stated age, calm, cooperative, in no acute distress, dressed in street clothes.

**Behavior:** evidence of psychomotor agitation, some PMR, good eye contact.

**Speech:** normal rate, normal rhythm and tone.

**Mood:** agitated. Affect: Blunted range and appropriate.

**Thought process:** Tangential and repetitive at times, but mostly linear and goal directed.

**Thought content:** Does not endorse suicidal or homicidal ideation, auditory or visual hallucinations or paranoia.

**Insight:** poor.

**Judgment:** poor.

**Decision Making Capacity:** no.

**Motor Vehicle Operation ability:** no.

**FAST scale:** Stage 4

**Mild Dementia Characteristics:** IADLs become affected, such as bill paying, cooking, cleaning, traveling.

### Assessment and Plan

Likely major neurocognitive disorder secondary to Alzheimer's disease versus vascular dementia.

Ordered Syphilis total, TSH with reflex FT4, vitamin B12, folic acid levels, HIV, MRI brain without contrast.

Stop sertraline and start citalopram 10 mg PO daily. Continue memantine 5 MG BID, titrate up weekly to 10mg BID, instructions given verbal and written instructions [3].

Follow up in 1-2 months or PRN.

Follow up with primary care within 3 weeks.

Patient/Caregiver understands the recommendations.

### Follow up

### Labs Results

CMP, TSH within normal limits. Vitamin B12 >2000, Folate >20, A1c 6.6%, HIV negative. Syphilis T 1.3, Syphilis Ab IgG reactive, RPR Ab Titer 1 non-reactive, Syphilis Ab by TP-PA positive. Results suggested infection with T. Pallidum at some time in the past but does not distinguish between treated and untreated syphilis as Treponemal antibodies can remain elevated despite proper treatment. RPR testing was recommended to distinguish between treated and untreated syphilis.

### Imaging

MRI brain without contrast

**History:** 84-year-old M with Alzheimer's disease.

**Comparison:** 1/22/2016

**Findings:** There is mild sulcal and ventricular prominence. There is mild interval increase in periventricular and subcortical white matter confluent T2 hyperintensity. The brain otherwise shows normal morphology and signal characteristics. No abnormal diffusion restriction, or susceptibility hypointensity is present. There is a partial empty sella. The major intracranial flow voids are present. The aerated spaces are normal. The orbital contents and extracranial soft tissues appear normal.

**Impression:** Mild cerebral atrophy with mild progression mild to moderate nonspecific white matter changes compared to 1/22/2016.

After reviewing results with patient and wife, they both agreed to proceed with a lumbar puncture to rule out neurosyphilis.

### Differential Diagnosis

Alzheimer dementia, Lewy body dementia, vascular dementia, frontotemporal dementia, and possibly dementia related to neurosyphilis.

### Discussion

When there is clinical suspicion of neurosyphilis, CSF analysis should be done to make the diagnosis. In individuals with suspected asymptomatic neurosyphilis (who do not have HIV infection), the diagnosis based on CSF abnormalities including lymphocytic pleocytosis between 5-100 cells/microL, an elevated protein concentration between 45-100mg/dL, or a reactive CSF-Venereal Disease Research Laboratory (VDRL) test. CSF abnormalities in symptomatic meningitis include lymphocytic pleocytosis to 200-400 cells/microL, an elevated protein concentration

between 100-200 mg/dL, and CSF-VDRL is almost reactive. Neuroimaging often shows enhancement of the spinal fluid, cranial nerves, spinal roots, or the meninges. If the infection leads to arteritis (meningovascular syphilis), the affected individuals may present with a stroke. The CSF abnormalities accompanying meningovascular neurosyphilis include lymphocytic pleocytosis between 10-100 cells/microL, a protein concentration of 100-200mg/dL, and CSF-VDRL is usually but not always reactive. Neuroimaging may show area(s) of infarction.

### Treatment and Surveillance

This patient's CSF analysis was pending at the time of submission of this case report. However, if his CSF shows abnormalities consistent with neurosyphilis, the treatment will be:

1. Aqueous crystalline penicillin G 3-4 million units IV every 4 hours or 18-24 million units continuous IV infusion for 10-14 days, or
2. Procaine penicillin G 2.4 million units IM once daily plus probenecid 500mg PO 4 times daily for 10-14 days.
3. For those with mild penicillin allergy, an alternative

treatment based on limited data is ceftriaxone 2g IV or IM daily for 10 to 14 days. High dose of doxycycline 200 mg PO BID for 21 to 28 days is another alternative.

Neurologic examination and lumbar puncture should be repeated at 3 to 6 months after treatment and every 6 months thereafter until CSF white blood cell (WBC) count is normal and CSF-VDRL is non-reactive. The individual will need to be retreated if the CSF WBC count does not decline by 6 months and all other CSF abnormalities are not normalized by 2 years. Re-treatment is also indicated if any subsequent CSF samples show an increase in CSF WBC count or a fourfold increase in CSF-VDRL titers.

Dementia related to neurosyphilis is one of the possibly reversible forms of dementia. Therefore, patients who present for evaluation of dementia should always be tested for syphilis, even if their history does not suggest exposure to syphilis.

### References

1. Marra CM (2020) Neurosyphilis.
2. Syphilis (2015) STD Treatment Guidelines
3. Tuddenham SG, Ghanem KG (2018) Neurosyphilis: Knowledge Gaps and Controversies. Sexually Transmitted Diseases 45(3): 147-151.

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