Neurosyphilis: A Monkey Among Men

Cameron Rowe DO  
*Cape Fear Valley Medical Center, cwrowedo@gmail.com*

Nathan Buckley DO  
*Cape Fear Valley Medical Center*

Bhaskar Chhetri MD  
*Cape Fear Valley Medical Center*

Suresh Paudel MD  
*Cape Fear Valley Medical Center*

Follow this and additional works at: [https://scholarlycommons.gbmc.org/jchimp](https://scholarlycommons.gbmc.org/jchimp)

Part of the [Bacteria Commons](https://scholarlycommons.gbmc.org/jchimp), [Infectious Disease Commons](https://scholarlycommons.gbmc.org/jchimp), [Internal Medicine Commons](https://scholarlycommons.gbmc.org/jchimp), [Neurology Commons](https://scholarlycommons.gbmc.org/jchimp), and the [Neurosciences Commons](https://scholarlycommons.gbmc.org/jchimp)

**Recommended Citation**
Rowe, Cameron DO; Buckley, Nathan DO; Chhetri, Bhaskar MD; and Paudel, Suresh MD (2022) "Neurosyphilis: A Monkey Among Men," *Journal of Community Hospital Internal Medicine Perspectives*: Vol. 12: Iss. 3, Article 10.
DOI: 10.55729/2000-9666.1055
Available at: [https://scholarlycommons.gbmc.org/jchimp/vol12/iss3/10](https://scholarlycommons.gbmc.org/jchimp/vol12/iss3/10)

This Case Report is brought to you for free and open access by the Journal at GBMC Healthcare Scholarly Commons. It has been accepted for inclusion in Journal of Community Hospital Internal Medicine Perspectives by an authorized editor of GBMC Healthcare Scholarly Commons. For more information, please contact GBMCcommons@gbmc.org.
Neurosyphilis: A Monkey Among Men

Cover Page Footnote
The authors have no conflicts of interest to declare and there is no financial interest to report. We certify that the submission is original work and is not under review at any other publication.
Neurosyphilis: A Monkey Among Men

Cameron Rowe*, Nathan Buckley, Bhaskar Chhetri, Suresh Paudel

Cape Fear Valley Medical Center, Fayetteville, NC

Abstract

Neurosyphilis is the progression of the untreated sexually transmitted infection caused by Treponema pallidum. When the initial infection is not adequately treated, progression of primary syphilis can lead to a wide variety of serious health sequelae. While neurosyphilis can appear up to 10–30 years after the initial infection, syphilis can invade the nervous system at any stage of infection and can imitate symptoms of many other diseases. This variety of symptoms is why syphilis has been called “The Great Pretender” or “The monkey among diseases” (Krämer et al., 2018). This is a case report of an 83-year-old female with a history of multiple TIA’s, dementia, and breast cancer who presented to the emergency department with complaints of her head “not feeling right” and intermittent ataxia (episodes of imbalance and difficulty ambulating) reported by patient and patients’ son. Physical exam only pertinent for chronic shuffling gait, but no ataxia. The patient underwent further work-up, demonstrating negative brain imaging for cerebral vascular accident and laboratory findings negative initially, for acute infection. An RPR was drawn as part of broadened altered mental status workup as the patient and family stated she was not back to baseline mental status and was positive with a quantitative titer of 1:8. Fluorescent treponemal antibody absorption (FTA-ab) was found to be positive as well. The patient was started on three million units intravenous Penicillin G every 4 h and was discharged with a peripherally inserted central catheter in order to receive two weeks of Rocephin at two grams daily. Patient returned to prior baseline following completion of treatment. Through this case, we hope to provide information on neurosyphilis and its differentiation from other disease processes and when neurosyphilis should be suspected during an evaluation of altered mental status.

Keywords: Neurosyphilis, Syphilis, Primary syphilis, Secondary syphilis, Tertiary syphilis, Treponema, Treponema pallidum, FTA-ab, Neurology

1. Hospital course

An 83-year-old woman presented to the emergency department with complaints of intermittent ataxia (episodes of imbalance and difficulty ambulating), not feeling well, and “head numbness.” The patient has a past medical history of multiple transient ischemic attacks (TIA), dementia, breast cancer, schizoaffective disorder, diabetes mellitus, hypertension, and iron deficiency anemia. Her pertinent current medications include Cefzil 10 mg daily, Furosemide 20 mg daily, Insulin Glargine 15 units nightly, Insulin Lispro on a sliding scale three times daily before meals, Lurasidone 80 mg daily, Quetiapine 400 mg daily, Vitamin B12 500 mcg daily, and Folic Acid 800 mg daily.

The patient was afebrile, tachypneic at 22 breaths per minute at an SpO2 of 96%, but otherwise hemodynamically stable. She had no history of fall or injury prior to the onset of her symptoms. The patient was alert and oriented x3 and denied any other complaints other than chronic intermittent face numbness which was stable since her last TIA. She denied any chest pain, shortness of breath, or urinary complaints. Her physical exam was unremarkable and notably the patient was without ataxia upon physical exam other than shuffling gait which is present at patients’ baseline.

The initial laboratory evaluation demonstrated a complete blood count without leukocytosis, slight anemia with a hemoglobin of 10.7 g per deciliter, a complete metabolic panel significant for hypokalemia of 3.2 milliequivalents per liter and a slightly elevated BUN of 19 mg per deciliter. She was also hyperglycemic at 319. Urinalysis was questionable for UTI. Her ECG was unremarkable rate of 78 beats per minute with left axis deviation and no

Received 9 June 2021; revised 21 December 2021; accepted 23 December 2021.
Available online 2 May 2022.

* Corresponding author at:
E-mail address: cwrowedo@gmail.com (C. Rowe).

https://doi.org/10.55729/2000-9666.1055
2000-9666/© 2022 Greater Baltimore Medical Center. This is an open access article under the CC BY-NC license (http://creativecommons.org/licenses/by-nc/4.0/).
significant ST segment changes. Her chest x-ray was unremarkable. Computerized tomography of the head without contrast demonstrated stable chronic findings without evidence of acute intracranial abnormality. The patient was admitted to the hospitalist service with a diagnosis of altered mental status likely secondary to urinary tract infection (UTI).

The patient was started on Ceftriaxone one gram daily for UTI. Notably, in her history the patient had had a UTI six months prior to this visit secondary to pan-sensitive *E. coli*. She had also undergone an evaluation for TIA two months prior to her current visit. At that time her magnetic resonance imaging demonstrated mild chronic findings with chronic microvascular ischemic change at supratentorial white matter without evidence for hemorrhage, mass lesion, mass-effect, hydrocephalus or evolving ischemia. During this current visit the patient’s urine culture returned as mixed organisms and antibiotics were stopped due to likely contamination. A broadened medical evaluation of the patient’s altered mental status was obtained, including a rapid plasma reagin (RPR) for evaluation of syphilis. This performed as a result of the patient/family stating they felt the patient was not at her baseline mental status.

On the patient’s second day of hospitalization her RPR was found to be positive. A syphilis confirmatory test was ordered. Patient was discharged home with home health with physical therapy prior to the final result of the confirmatory test. Patient’s RPR quantitative was found to be 1:8 and FTA-Ab was reactive. The patient was diagnosed with neurosyphilis and notified with referral to follow-up with infectious disease as an outpatient.

Before the patient’s appointment with infectious disease she was readmitted to the hospital for hyperosmolar hyperglycemic state. Infectious disease was consulted and the patient was started on IV penicillin G 3,000,000 units every 4 h. Lumbar puncture was attempted, but unable to be performed secondary to the patient’s inability to lie still. A PICC line was placed and IV penicillin G every 4 h was transitioned to ceftriaxone 2 g IV daily for ease of administration after discharge. The patient completed 2 weeks of antibiotics for neurosyphilis at home with home health. Patient returned to prior baseline following completion of treatment.

2. Discussion

The purpose of this case was to demonstrate an example of atypical presentation of neurosyphilis and stresses the need to include neurosyphilis in a differential diagnosis of altered mental status, not only for high-risk populations such as HIV positive individuals, but also in the general population. Those who present to the emergency department or outpatient office with signs and symptoms of TIA, stroke, and/or other neuropsychiatric manifestations may have a confounding disorder like neurosyphilis. While syphilis is a reportable disease in the United States, neurosyphilis is not, which makes tracing incidence and prevalence challenging. The most common symptoms of neurosyphilis include headache, confusion, seizures, nausea, vomiting, stiff neck, uveitis, vitritis, retinitis, optic neuropathy, facial/cranial neurupathies, vestibulococchlear abnormalities, and other psychological abnormalities. On average 1 in 10 patients with neurosyphilis present with a stroke and, although the majority of these are patients under the age of 50, there are still a significant amount who are older patients. Even before CVA occurs, prodromal symptoms such as headaches, vertigo, insomnia, emotional lability, and personality changes can occur for several months. Thrombosis of affected arteries leading to cerebral infarction occurs secondary to meningovascular pathology leading to arteritis and is not due to the CNS invasion of *Treponema pallidum*. Cerebral infarcts most commonly occur in the territory of the middle cerebral artery and are typically lacunar in nature. Movement disorders such as sensory ataxia, parkinsonism, myoclonus, chorea, dystonia, hyper-reflexia can result from ischemic lesions in a variety of areas including the midbrain, cerebellum, and basal ganglia as well.

Many lab tests may have unclear significance which can further complicate a quick and accurate diagnosis. Clinicians may struggle to confidently confirm or exclude neurosyphilis because existing definitions of neurosyphilis require evidence of invasion into the CNS but there is no available test that is sensitive and specific enough to confirm *T. pallidum* invasion. The “gold standard” test for neurosyphilis is the venereal disease research laboratory test (CSF-VDRL) and although specific, the sensitivity is 30–70%. In comparison, The CSF FTA-Ab test, while more sensitive than the former test, lacks the same level of specificity. For example, CSF pleocytosis may be more specific for diagnosing neurosyphilis compared to increased CSF protein concentration. In immunocompetent asymptomatic individuals, CSF lymphocyte counts greater than 5 per liter or a concentration protein greater than 45 mg/dL is highly indicative of asymptomatic neurosyphilis. MRI findings such as global cortical atrophy, temporal horn widening, or dural thickening
may be seen when evaluating a patient with CVA.\textsuperscript{3,4,14,21} Cerebral gummas, or dural based lesions that look similar to meningiomas and medial temporal lobe changes that mimic herpes encephalitis are two neuroimaging patterns that should raise suspicion for neurosyphilis rather than CVA.\textsuperscript{13} When looking at the MRA meningovascular syphilis specifically more often involves the supraclinoid portion of the internal carotid artery where atherosclerotic disease affects the common carotid bifurcation and cavernous portion of the carotid.\textsuperscript{6} Syphilitic plaques are long and smooth while atherosclerotic plaques are typically shorter and irregular.\textsuperscript{6}

Increased diligence of both clinical and epidemiological findings is necessary to reduce the morbidity and mortality of neurosyphilis in patients with neurological and cognitive symptoms along with shortening the lengthy diagnosis time.\textsuperscript{7} Due to the variety of symptoms surrounding syphilis including dementia, personality changes, neurological impairments such as loss of peripheral reflexes and impaired vibration sense, hallucinations, depression, and others a comprehensive interdisciplinary approach may help lead to an earlier diagnosis and less misdiagnoses.\textsuperscript{3,7,5,11,14}

Early identification of neurosyphilis is critical as the prognosis is favorable with early treatment of patients especially with meningeval neurosyphilis or gummas.\textsuperscript{10} It is also imperative to select a treatment that will ensure full compliance on the patients’ part because the risk of neurosyphilis is increased nearly ten-fold in those who were inadequately treated compared to those without any treatment at all.\textsuperscript{20}

The RPR titer can be linked to disease activity and a four-time reduction in the titer does demonstrate completed treatment.\textsuperscript{1} Partial immunity to \textit{T. pallidum} is developed by the human host following initial infection, but this is insufficient to fully eliminate the organism which leads to future neurological infection.\textsuperscript{10} Treatment for neurosyphilis is aimed at increasing and maintaining the antibiotic levels in the CNS during the period of bacterial reproduction.\textsuperscript{4} Treatment was typically with IV penicillin G 2.4 million units for 10–14 days.\textsuperscript{3,5} If patients have anaphylaxis as an allergic reaction to penicillin and desensitization is not an option, they may receive ceftriaxone 2 g daily for 10–14 days in replacement of penicillin.\textsuperscript{4} Other antibiotics with varying activity against syphilis include doxycycline 100 mg twice daily for 21–30 days or macrolides 500 mg four times daily for 30 days.\textsuperscript{4} Although the above two substitutions still need further studies and trials to show similar efficacy as penicillin or ceftriaxone. Following treatment with penicillin or ceftriaxone clinical cure was more common than serological cure demonstrating the need for further research into other tests to gauge for objective treatment success.\textsuperscript{4}

It is of the utmost importance to keep a broad diagnosis when patients present with stroke-like symptoms after TIA and strokes are ruled out in order not to miss a life changing diagnosis or treatment of neurosyphilis. Neurosyphilis should be kept in the differential diagnosis when patients present with neurological symptoms like cerebellar ataxia since it is easily treatable.\textsuperscript{10}

Conflict of interest

There is no conflict of interest.

References

1. Abkur TM, Ahmed GS, Alfaki NO, O’Connor M. Neurosyphilis presenting with a stroke-like syndrome. BMJ Case Rep. 2015;2015, bcr201406988. Published 2015 Mar 4. https://doi.org/10.1136/bcr-2014-206988.

2. Ahbeddou N, El Aloufi Taoussi K, Ibrahimi A, et al. Stroke and syphilis: a retrospective study of 53 patients. Rev Neurol (Paris). 2018;174(5):313–318. https://doi.org/10.1016/j.neuro.2017.07.014.

3. Blazeković A, Ozretić D, Habek M, Bilić E, Borovečki F. Neurosyphilis: the shape of a rising threat. Int J Infect Dis. 2018;76:1–3. https://doi.org/10.1016/j.ijid.2018.07.022.

4. Buitrago-García D, Martí-Carvajal AJ, Jimenez A, Conterno LO, Pardo R. Antibiotic therapy for adults with neurosyphilis. Cochrane Database Syst Rev. 2019;5(5):CD011399. Published 2019 May 27. https://doi.org/10.1002/14651858.CD011399.pub2.

5. Cdc.gov. STD facts - syphilis (detailed); 2021 [online] Available at: https://www.cdc.gov/std/syphilis/stdfact-syphilis-detailed.htm. Accessed January 10, 2021.

6. Chahine LM, Khoriaty RN, Tomford WJ, Hussain MS. The changing face of neurosyphilis. Int J Stroke. 2011;6(2):136–143. https://doi.org/10.1111/j.1747-4949.2010.00568.x.

7. Chrzapczak-Wlodarczyk A, Wlodarczyk A, Szarmach J. Different faces of neurosyphilis. Sex Transm Dis. 2018;45(7):e50. https://doi.org/10.1097/OLQ.0000000000000848.

8. Galindo J, Mier JF, Miranda CA, Rivas JC. Neurosyphilis: an old disease with new faces. Neurosyphilis. Continuum. 2015;21(6 Neurological Disease):1714–1728. https://doi.org/10.1212/CON.0000000000000250.

9. Ganesh A. Neurosyphilis is an easily missed cause of encephalopathy. CMAJ (Can Med Assoc J). 2017;189(45):E1401. https://doi.org/10.1503/cmaj.733535.

10. Garg D, Vibha D, Pandit AK, Srivastava AK. Neurosyphilis presenting as pure cerebral ataxia: an atypical manifestation. BMJ Case Rep. 2019;12(8), e251058. https://doi.org/10.1136/bcr-2019-231058. Published 2019 Aug 31.

11. Kato H, Ando T. Brain Nerve. 2016;68(4):309–316. https://doi.org/10.1007/mf.141620399.

12. Krämer S, Clark D, Ziegenein M. Chronischer Verlauf einer Neurourose [Classic course of neurosyphilis]. Nervenarzt. 2018; 89(5):386–388. https://doi.org/10.1007/s00115-017-0465-1.

13. Marra CM. Neurosyphilis. Continuum. 2015;21(6 Neuroinfectious Disease):1714–1728. https://doi.org/10.1212/CON.0000000000000250.

14. Mukku S, Safal SS, Pritam R, et al. Neurosyphilis presenting as rapidly progressive psychosis & dementia - a forgotten entity. Asian J Psychiatr. 2019;40:103–106. https://doi.org/10.1016/j.ajp.2019.02.010.
15. Ninds.nih.gov.; 2021. Neurosyphilis Information Page. [online] Available at: https://www.ninds.nih.gov/Disorders/All-Disorders/Neurosyphilis-Information-Page>. Accessed January 6, 2021.
16. Sabre L, Braschinsky M, Taba P. Neurosyphilis as a great imitator: a case report. BMC Res Notes. 2016;9:372. Published 2016 Jul 28. https://doi.org/10.1186/s13104-016-2176-2.
17. Shah BB, Lang AE. Acquired neurosyphilis presenting as movement disorders. Mov Disord. 2012;27(6):690–695. https://doi.org/10.1002/mds.24950.
18. Skalnaya A, Fominykh V, Ivashchenko R, et al. Neurosyphilis in the modern era: literature review and case series. J Clin Neurosci. 2019;69:67–73. https://doi.org/10.1016/j.jocn.2019.08.033.
19. Smibert OC, Jenney AW, Spelman DW. Management of neurosyphilis: time for a new approach? Intern Med J. 2018;48(2):204–206. https://doi.org/10.1111/imj.13703.
20. Tuddenham S, Ghanem KG. Neurosyphilis: knowledge gaps and controversies. Sex Transm Dis. 2018;45(3):147–151. https://doi.org/10.1097/OLQ.0000000000000723.
21. van Hoe K, Van den Ameele H, Vanopdenbosch L. Neurosyphilis: een historische ziekte met actueel belang [Neurosyphilis: a historical disease with current relevance]. Tijdschr Psychiatr. 2019;61(10):720–724.