A Case of Neurosyphilis and Review of Manifestations, Diagnosis, and Treatment

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ABSTRACT

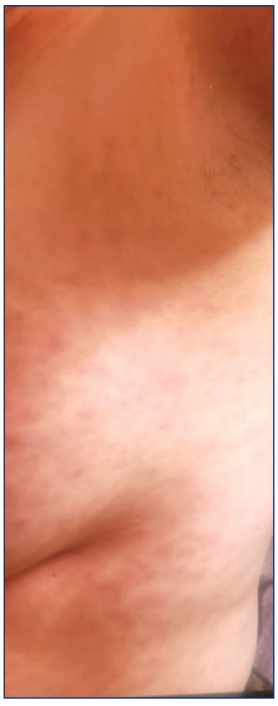
Diagnosis of neurosyphilis remains a challenge due to no existing standardized testing, but it is often made based on a combination of clinical and cerebrospinal fluid (CSF) analysis findings. Neurosyphilis is uncommon now compared to the era before the introduction of penicillin. Syphilis if left untreated may lead to debilitating complications including paresis, progressive dementia, and even death. Presence of ocular or hearing manifestations with positive serum treponemal and non-treponemal tests are diagnostic for neurosyphilis, regardless of presence or absence of CSF abnormalities. The preferred regimen for neurosyphilis is intravenous penicillin G for 2 weeks. Other regimens are not shown to be as effective as penicillin. Here we discuss an interesting case presenting with neurosyphilis along with manifestations consistent with primary and secondary stages of syphilis.

KEYWORDS: neurosyphilis, otosyphilis, ophthalmic syphilis

CASE REPORT

A 49-year-old female presented to the emergency department with 3 weeks of eye floaters followed by one week of bilateral leg cramping and sciatica. Her medical history was notable for rheumatoid arthritis (on methotrexate and Golimumab), benign paroxysmal positional vertigo, type-2 diabetes, and recurrent left thigh rash suggestive of HSV. Four weeks prior to her presentation, she experienced a non-blanching macular rash that started on the abdomen and extended to the upper extremities and back but spared the palms and soles (**Figure 1**). Skin biopsy taken from the left arm showed histiocytes, sparse lymphocytes, and hemorrhage, but the specimen lacked the epidermis, and no silver stain was applied. The rash resolved without medical treatment. One week later, she started to develop visual floaters. She was evaluated by an ophthalmologist, and had an unremarkable retinal exam, and was diagnosed with ophthalmic migraine. Later, the patient developed bilateral axillary lymphadenopathy and joint swelling mainly in the knees and ankles, and she was prescribed a course of prednisone for concern of a rheumatoid arthritis flare-up. Notably, the arthritis and visual floaters improved.

Figure 1.



Two weeks prior to presenting to the ED, the patient had neck stiffness, worsening vertigo that was unresponsive to meclizine, oral ulcers, decreased hearing, sore throat and a painful anal ulcer. One week prior to her presentation, she developed gradual onset but progressive shooting pain radiating from the buttocks to the toes, without relief with ibuprofen or acetaminophen.

The patient was monogamous with one male partner, who was ill at the same time with neurosyphilis. She admitted to vaginal, oral, and anal intercourse. She had no reported animal exposure or recent travel.

On presentation, the patient was afebrile, hypertensive at 201/86 mmHg, tachycardic at 107/min, saturating 100% on room air. She was mildly distressed, with conjunctival redness and throat erythema. Lower extremity strength was decreased in both legs (4/5), but otherwise neurological exam was unremarkable with intact cranial nerves and pupillary response to light and accommodation. Genitourinary exam was remarkable for an anal ulcer (0.5 x 0.5 cm) in the upper part of the anus; no vaginal discharge or ulcers were seen. Initial laboratory results are noted in **Table 1**.

A fourth-generation HIV antigen/antibody assay was negative. The cervical, rectal, and anal swabs were negative for Neisseria gonorrhea and chlamydia trachomatis. Rectal swab was negative for HSV with PCR and culture. Viral hepatitis panel was negative. Treponema pallidum antibody was reactive, (RPR) was positive 1:64. Lumbar puncture results are noted in **Table 2**.

Although CSF VDRL was negative, the patient was diagnosed with neurosyphilis. The rash and lymphadenopathy were suggestive of secondary syphilis which was overlapping with primary syphilis given the anal ulcer. The symptoms of otosyphilis,

Table 1. CBC and Comprehensive Metabolic Panel Laboratory Results

Hemoglobin	13.1 g/dL	AST	19 IU/L
WBC	10.9 x 10{3}/mcL	ALT	27 IU/L
Hematocrit	39.3%	ALP	82 IU/L
Platelets	381 x 10(3)/mcL	Calcium	9.5 g/dL
Sodium	133 mmol/L	Magnesium	1.8 g/dL
Potassium	3.5 mmol/L	Phosphorus	3.2 g/dL
Chloride	99 mmol/L	Total Bilirubin	0.7 g/dL
Carbon dioxide	25 mmol/L	Albumin	3.9 g/dL
BUN	10 mg/dL	Total protein	8.05 g/dL
Creatinine	0.8 mg/dL		
Glucose	211 mg/dL		

Table 2. Results of Lumbar Puncture

CSF analysis	
Color CSF	Colorless
Appearance SCF	Clear
RBC	33/mcL
WBC	46/mcL
Neutrophils	15%
Lymphocytes	61%
Monocytes	24%
Glucose	111 mg/dL
Total protein	93 mg/dL

ophthalmic syphilis, and radiculopathy with meningitis were all suggestive of neurosyphilis.

The patient was treated for neurosyphilis with two weeks of intravenous (IV) penicillin G after penicillin desensitization, with an additional dose of intramuscular (IM) benzathine penicillin G (2.4 MU). All the symptoms improved at the end of the treatment.

DISCUSSION

Cases of primary and secondary syphilis have increased in the United States every year since 2000, with 11.9 cases per 100,000 persons in 2019. Neurosyphilis is uncommon now compared to the era before the introduction of penicillin. In the United States, prevalence of neurosyphilis was 1.8% among persons with early syphilis.[1]

Early neurosyphilis usually goes unnoticed causing asymptomatic meningitis, but can be symptomatic with headache, cranial-nerves palsies, meningismus, blindness or deafness. Late neurosyphilis, which develops decades after the primary infection, has been reported in 10%-20% of the cases, according to data obtained before penicillin introduction.[1,2]

Our patient had multiple forms of early neurosyphilis. The hearing loss was due to involvement of the VIII cranial nerve (CN), while the vertigo was due to involvement of the VIII CN and adjacent vestibular system.[3] Syphilis-induced radiculopathy is also reported, and her sciatica pain resolved with treatment.[4] Floaters as a manifestation of ophthalmic syphilis are rare but reported.[5] Our patient had an overlapping primary and secondary stages of syphilis with the anal ulcer indicating primary syphilis and rash with lymphadenopathy suggesting secondary syphilis. The anal ulcer was most likely due to syphilis despite pain, but syphilis ulcers can be painful in 30% of the cases.[6] Additionally, HSV tests on the ulcer were negative.

Diagnosis of neurosyphilis remains a challenge due to no existing standardized testing, but it is often made based on a combination of clinical and CSF analysis findings. The CSF abnormalities in primary and secondary syphilis are common; however, unless neurological signs and symptoms are present, a CSF analysis is not recommended as there has been no proven benefit or a better outcome.[7] Patients suspected to have neurosyphilis should, however, undergo CSF analysis before treatment and should receive a neurosyphilis regimen if abnormal.[8]

CSF VDRL is highly specific and is generally accepted as the diagnostic test of neurosyphilis. However, sensitivity only reaches 30–70%.[9] If the CSF VDRL test is negative in patients with symptoms highly suggestive for neurosyphilis, CSF treponemal tests are advised.[10] CSF protein may aid in the diagnosis, but their presence is neither sensitive nor specific for neurosyphilis.[11]

Ocular syphilis and otosyphilis are treated with the same regimen used for neurosyphilis, regardless of the presence or absence of CSF abnormalities.[12] Treatment with oral or topical glucocorticoids for ocular syphilis and oral glucocorticoids for otosyphilis is controversial. In a retrospective study that included 85 patients with otosyphilis, adding steroids to the neurosyphilis regimens tended to improve and stabilize hearing, but the results were not statistically significant among treatment modalities.[13]

Our patient was treated with the recommended regimen for neurosyphilis and was desensitized to penicillin in the ICU. She received IV penicillin G for 14 days followed by an additional dose of IM Benzathine penicillin because the neurosyphilis regimen is shorter than the regimen used for latent syphilis.[14] Other antibiotics options are not shown to be as effective as penicillin.

For monitoring after treatment, neurological examination and serum RPR should be monitored; however, the new 2021 guidelines do not recommend lumbar puncture in immunocompetent patients or controlled HIV patients if there was concomitant clinical and serological improvement.[14] Repeat lumbar puncture remains recommended for immunocompromised patients; it should be performed at three to six months after treatment and every six months thereafter until the CSF white blood cell count is normal and the CSF VDRL is nonreactive.[15]

Normalization of RPR titer may predict successful

neurosyphilis treatment. Supporting evidence comes from a longitudinal study of 110 patients with neurosyphilis, most with HIV coinfection, who were treated for neurosyphilis.[14]

CONCLUSION

If left undiagnosed or untreated, syphilis may lead to debilitating complications including paresis, progressive dementia, and even death. Presence of ocular or hearing manifestations with positive serum treponemal and non-treponemal tests are diagnostic for neurosyphilis, regardless of presence or absence of CSF abnormalities. The preferred regimen for neurosyphilis is penicillin; patients with allergy should undergo desensitization in the ICU setting. Steroid use for otosyphilis and ocular syphilis is controversial; although improvement in some cases is reported, no clinical significance was found in most of the cases.

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