SEEJPH Volume XXVI, S1, 2025, ISSN: 2197-5248; Posted:05-01-2025

Unveiling Neurosyphilis: A Case Report on Presentation, Diagnosis, and Therapeutic Approach to Neurosyphilis

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KEYWORDS
Neurosyphilis, Treponema pallidum, dementia, parkinsonism.

ABSTRACT
Neurosyphilis is a rare but serious complication of inadequately treated or untreated syphilis. It describes the infection of *Treponema pallidum* in the central nervous system (CNS), the bacterium responsible for syphilis. This condition can present at any stage of syphilis, but it most often occurs years after the initial infection, especially if left untreated. Neurosyphilis can mimic a range of psychiatric and neurological disorders, making it a diagnostic challenge. Despite the global decrease in syphilis cases following the advent of penicillin, there has been a resurgence in recent years, including cases of neurosyphilis, particularly among immunocompromised individuals such as those with HIV. This report discusses a case of neurosyphilis in a 48-year-old male with progressive cognitive decline, focusing on diagnostic, therapeutic, and management approaches.

1. Case Report

A 48-year-old male presented to the outpatient neurology clinic with complaints of cognitive impairment, difficulty walking, mood changes, and episodic confusion. The patient experienced subtle initial symptoms over a 12-month period, with a gradual worsening of his memory, particularly short-term recall. He also reported increased irritability, inappropriate behavior, and poor judgment in social interactions. His gait had become unsteady over the last three months, and he had suffered two minor falls. No notable prior medical history was present for the patient, but his sexual history revealed multiple unprotected sexual encounters with both male and female partners over the past decade. He did not recall any specific episode of genital sores or rashes, but he did report a previous sexually transmitted infection (STI) treated several years earlier, though he could not remember the details of the diagnosis or treatment. There was no history of visual disturbances, hearing loss, or any other focal neurological deficits. The patient did not have a history of cardiovascular disease, diabetes, or hypertension. He denied any history of substance abuse or alcohol misuse in the Initial Physical and Neurological Examination.

Upon physical examination, the patient seemed well-fed and not in any immediate pain. His vital signs remained consistent. However, the neurological exam revealed several abnormalities, Gait was ataxic, and the patient had difficulty maintaining balance during heel-to-toe walking. Romberg's sign was positive, indicating a sensory deficit in proprioception. Reflexes were brisk with bilateral hyperreflexia, particularly in the lower extremities. A positive Babinski sign was noted on both sides. Mild dysmetria was observed during finger-nose-finger testing. Cranial nerve examination was unremarkable, with no deficits in vision, hearing, or facial movement. Cognitive assessment using the Montreal Cognitive Assessment (MoCA) revealed moderate impairment, particularly in short-term memory, executive function, and attention. Given the cognitive and motor deficits, a broad differential diagnosis was considered, including neurodegenerative conditions such as Alzheimer's disease, vascular dementia, and parkinsonism. However, given the patient's sexual history and neurological findings, neurosyphilis was also suspected, and further investigations were planned.

2. Diagnostic Workup

2.1 Blood Work and Serology

A complete blood count, liver function tests, and a metabolic panel were among the initial laboratory tests that revealed unremarkable results. However, given the concern for syphilis, serological testing was ordered, which yielded the following results:

Fluorescent TreponemalAntibody-Absorption (FTA-ABS): Positive.

Rapid Plasma Reagin (RPR): Positive with a titer of 1:64.

These results indicated a previous or ongoing syphilis infection. Given the neurological symptoms, the next step was to confirm the diagnosis of neurosyphilis through cerebrospinal fluid (CSF) analysis.

2.2 Neuroimaging

A magnetic resonance imaging (MRI) scan of the brain has been done in order to rule out structural lesions or other pathologies. The MRI showed mild to moderate cortical atrophy, particularly in the frontal and parietal lobes, but no evidence of masses, infarcts, or demyelination. These findings were nonspecific but could be consistent with the chronic phase of neurosyphilis.

2.3 Lumbar Puncture and CSF Analysis

A lumbar puncture was performed to evaluate the CSF for infection or inflammation. The CSF analysis showed: Protein level: Elevated at 85 mg/dL (normal 15-45 mg/dL). White blood cell (WBC) count: 32 cells/μL (normal <5). CSF VDRL (Venereal Disease Research Laboratory) test: Positive. Glucose level: Normal. CSF FTA-ABS: Positive.The combination of a positive CSF VDRL, positive serum RPR, and elevated protein and WBC count in the CSF confirmed the diagnosis of neurosyphilis.

3. Discussion

Neurosyphilis is a result of the invasion of the CNS by Treponema pallidum, occurring in untreated or inadequately treated syphilis infections. While historically thought of as a late-stage manifestation, neurosyphilis might manifest at any point during the illness. The clinical presentation of neurosyphilis is highly variable, depending on which part of the CNS is affected. It can be broadly classified into five forms: asymptomatic, meningeal, meningovascular, parenchymal (general paresis and tabes dorsalis), and gummatous neurosyphilis.

Asymptomatic Neurosyphilis: Often identified through abnormal CSF findings in the absence of symptoms. This can occur in the early stages of infection.

Meningeal Neurosyphilis: Typically occurs within the first few years of infection, presenting with symptoms of meningeal irritation such as headache, nausea, vomiting, neck stiffness, and cranial nerve abnormalities.

Meningovascular Neurosyphilis: A form that affects the blood vessels of the spinal cord and the brain, often leading to stroke-like symptoms due to vasculitis or small-vessel inflammation.

Parenchymal Neurosyphilis: Includes general paresis and tabes dorsalis.

Tabes dorsalis: Characterized by demyelination of the posterior columns of the spinal cord, resulting in lightning pains, sensory ataxia, and a loss of proprioception.

General paresis: Involves widespread cortical damage, leading to psychiatric manifestations, memory loss, personality changes, and progressive dementia.

Gummatous Neurosyphilis: A rare manifestation involving granulomatous lesions that can occur in the spinal cord or brain.

In this case, the patient presented with features most consistent with general paresis, one of the parenchymal forms of neurosyphilis. General paresis results from chronic inflammation and atrophy of the cerebral cortex, leading to progressive cognitive decline, personality changes, and psychiatric symptoms. This form of neurosyphilis can easily be misdiagnosed as a primary neurodegenerative condition like Alzheimer's disease, frontotemporal dementia, or other psychiatric disorders, which makes early diagnosis challenging but crucial for treatment.

3.1 Pathophysiology of Neurosyphilis

Treponema pallidum infects the central nervous system, resulting in neurosyphilis. Early in the course of syphilis the bacteria can cross the blood-brain barrier and invade the parenchyma and meninges of the brain and spinal cord. However, neurosyphilis does not always develop in infected individuals. Certain factors, such as untreated syphilis, immunosuppression (especially in patients with HIV), and genetic susceptibility, increase the risk of CNS involvement.

In general paresis T. pallidum infection leads to a chronic meningoencephalitis that causes neuronal loss, gliosis, and cerebral atrophy, particularly in the frontal and temporal lobes. This results in a wide range of neuropsychiatric symptoms, including memory impairment, mood disturbances, and behavioral changes. Pathological examination of brain tissue from patients with general paresis reveals spirochetes in the brain parenchyma and chronic inflammatory changes.

The damage in neurosyphilis is primarily driven by the host immune response to the bacteria, which causes local inflammation, tissue damage, and vascular injury. This results in progressive loss of neurons and glial cells, leading to the characteristic cognitive and motor symptoms seen in advanced disease.

4. Differential Diagnosis

The clinical presentation of neurosyphilis, especially in its parenchymal forms, often mimics other neurological and psychiatric conditions, making differential diagnosis essential. The most common conditions to be ruled out in a case like this include:

Alzheimer's Disease Both neurosyphilis and Alzheimer's can present with progressive memory loss and cognitive decline. However, the presence of ataxia, hyperreflexia, and other neurological signs in neurosyphilis may help distinguish it from Alzheimer's.

Vascular Dementia Given the stroke-like presentation in meningovascular syphilis, it can be mistaken for vascular dementia or other cerebrovascular conditions. A detailed history, imaging, and serological testing can help differentiate the two.

Multiple Sclerosis (MS)MS can present with neurological deficits, ataxia, and cognitive dysfunction, similar to neurosyphilis. However, MS is usually characterized by relapsing-remitting episodes, and MRI findings typically show demyelinating lesions.

HIV-Associated Neurocognitive Disorders (HAND) HIV infection can lead to cognitive decline, especially in advanced stages. Co-infection with syphilis is common in high-risk populations, and distinguishing HAND from neurosyphilis requires careful assessment of clinical history, serological testing, and CSF analysis.

Other, bipolar disorders, psychiatric disorders Schizophrenia and major depressive disorder can present with mood changes, cognitive impairment, and behavioral disturbances, similar to neurosyphilis. A thorough neuropsychiatric assessment and appropriate syphilis testing are needed to rule out psychiatric conditions in these cases.

5. Management

Once neurosyphilis is diagnosed, penicillin remains the cornerstone of treatment. The primary goal of therapy is to eradicate the bacteria and halt the progression of neurological damage. The recommended regimen for neurosyphilis, as in this case, is aqueous crystalline penicillin G, 18 to 24 million units daily, administered intravenously for 10 to 14 days. This high-dose regimen is necessary to achieve adequate penetration of the drug into the CNS and ensure the clearance of the infection from the brain and spinal cord.

If the patient has a history of penicillin allergy, desensitization to penicillin should be considered, as penicillin is the only antibiotic with proven efficacy in treating neurosyphilis. Alternatives, such as ceftriaxone, can be considered in cases where desensitization is not possible, though they are less well-studied.

5.1 Monitoring Response to Treatment

Following treatment, patients with neurosyphilis require close follow-up to assess their response to therapy. The most important markers of treatment success are:

Clinical improvement: A reduction in cognitive, motor, or psychiatric symptoms over time.

CSF normalization: CSF anomalies include high protein levels and white blood cell counts should progressively go away over the course of several months to years after treatment.

A repeat lumbar puncture to assess CSF parameters is typically performed at 6 months and again at 12 months. If CSF abnormalities persist or worsen, re-treatment may be necessary.

In this instance, the patient received intravenous penicillin G treatment for 14 days. At his 6-month follow-up, he showed modest improvement in gait and cognitive function. Repeat CSF analysis revealed a decrease in the protein levels and white blood cell count, though they were not yet fully within the normal range. A continued improvement was anticipated with time.

5.2 Prognosis and Long-Term Outcomes

The prognosis of neurosyphilis largely depends on the stage of the disease at the time of diagnosis and the extent of CNS damage that has occurred. Early neurosyphilis, especially the meningeal form, responds well to treatment, and patients can experience full recovery if therapy is initiated promptly.

However, in cases of general paresis and tabes dorsalis, as seen in this patient, the prognosis is more guarded. Significant neurocognitive and motor impairments may persist even after successful eradication of the infection. While further neurological deterioration can be prevented, many patients do not regain full cognitive or motor function due to irreversible damage to the spinal cord and the brain.

The patient in this case was referred to a neurorehabilitation program to help manage his cognitive and motor deficits. He continued to show slow but steady improvement in his balance, coordination, and memory. Long-term follow-up was arranged to monitor for any recurrence of symptoms or evidence of relapse.

5.3 Prevention and Public Health Implications

Early primary stage syphilis diagnosis and treatment are necessary to prevent neurosyphilis. Reducing the occurrence of neurosyphilis requires routine syphilis screening, particularly in high-risk groups like men who have sex with men (MSM) and those living with HIV. Public health initiatives aimed at increasing awareness, promoting safe sexual practices, and ensuring access to healthcare can help prevent the resurgence of this once-rare condition.

Furthermore, HIV-infected individuals are at higher risk of developing neurosyphilis, and regular syphilis screening in this population is recommended. Early treatment with penicillin in HIV-positive patients can prevent syphilis complications, particularly CNS involvement, can occur both early and late.

6. Conclusion

This case report highlights the clinical presentation, diagnosis, and management of neurosyphilis, a rare but serious complication of syphilis. The patient’s insidious onset of cognitive decline, gait abnormalities, and behavioral changes were consistent with general paresis, a form of late-stage neurosyphilis. Prompt recognition and treatment with intravenous penicillin led to stabilization and modest improvement, though full recovery was not achieved.

The case underscores the importance of considering neurosyphilis in the differential diagnosis of unexplained neurological and psychiatric symptoms, particularly in patients with a history of risky sexual behavior or syphilis infection. In order to prevent irreversible CNS injury, early detection and treatment are crucial and improve outcomes in affected individuals.

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