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Response to Penicillin for Presumed Neurosyphilis in a Patient with Human Immunodeficiency Virus (HIV), a Normal CD4 Count, and an Undetectable Viral Load: A Case Report

Authors' Contribution:

Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Conflict of interest: None declared

Patient: Female, 69-year-old
Final Diagnosis: Neurosyphilis
Symptoms: Altered mental status • unresponsiveness
Medication: —
Clinical Procedure: —
Specialty: Critical Care Medicine • Infectious Diseases • General and Internal Medicine • Neurology

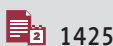
Objective: Unusual clinical course
Background: Neurosyphilis is a bacterial infection of the brain and the spinal cord, caused by *Treponema pallidum*. Its non-specific clinical presentation includes cognitive impairment and motor and/or sensory function compromise. Neurosyphilis infections in patients with HIV have increased over the past few years and many cases of neurosyphilis manifest in patients with HIV who have low CD4 T-cell counts and high viral loads (VL). However, there is extremely limited acknowledgement in the literature about neurosyphilis presentations in patients with HIV who have normal CD4 counts.

Case Report: We present a neurosyphilis and HIV coinfection in a patient with a normal CD4 count and an undetectable VL. A 69-year-old woman with a medical history of HIV was on a prescribed antiretroviral treatment regimen. She presented in the Emergency Room in an unresponsive state, although this had been preceded by a period of rapidly progressive cognitive decline. Her brain computed tomography scan without contrast was unremarkable. Laboratory test results were within normal limits, except for a positive result for the microhemagglutination assay for *Treponema pallidum* antibodies and rapid plasma regain (RPR) test, which was highly suggestive of neurosyphilis as a presumed diagnosis. She showed remarkable clinical improvement after the initiation of conventional treatment for neurosyphilis, which is a 14-day regimen of intravenous penicillin G.

Conclusions: Given the broad neurological manifestations of neurosyphilis and its increasing incidence in patients with HIV, it is important to consider neurosyphilis in the differential diagnosis after ruling out other causes of encephalopathy, especially in patients with an undetectable VL and a normal CD4 count.

Keywords: CD4 Lymphocyte Count • HIV Infections • Neurosyphilis

Full-text PDF: <https://www.amjcaserep.com/abstract/index/idArt/932467>



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Background

Neurosyphilis is an infection of the central nervous system, caused by *Treponema pallidum*. Regardless of the HIV infection status, untreated syphilis can develop into different stages (primary, secondary, latent, and tertiary syphilis). Tertiary syphilis is a result of untreated or misdiagnosed latent syphilis. Tertiary syphilis presents within 30 years from the onset of the primary infection and slowly manifests as neurosyphilis, which is further divided into early and late syphilis. The cerebrospinal fluid (CSF), meningeal layers, and intracranial vessels are affected in the early stages of neurosyphilis. Late-stage neurosyphilis attacks the cerebral structures and spinal cord, which is reflected in the diverse range of neurosyphilis symptoms seen in patients [1].

Syphilis-HIV coinfection is common in patients. Previous studies suggest an early neurologic deficit in syphilis-HIV coinfecting patients, although sometimes the patients with HIV can be asymptomatic, especially when they have a high syphilis serological titer and CD4 cell counts <350 cells/L [2].

In this case report, we present a unique clinical scenario of a suggested diagnosis of neurosyphilis with rapidly worsening cognitive function in a patient with HIV, who had an undetectable viral load (VL) and a normal CD4 count. She responded to the conventional treatment regimen for neurosyphilis.

Case Report

A 69-year-old woman had a medical history of HIV and was taking emtricitabine, dolutegravir, and tenofovir alafenamide for it. She was on benzotropine, risperidone, and valproic acid for controlled schizophrenia with tardive dyskinesia, and had a history of polysubstance abuse. She was brought to her local Emergency Department (ED) after being found unresponsive at a nursing home. According to a family member, at baseline she had normal cognitive function, ambulated using a rolling walker, and was partially independent in her activities of daily living. Over the past 1 month, she had gradually declined in her daily activities, and more recently had become non-verbal and bedbound. On the day she presented in the ED, she had been unresponsive for several hours. She was febrile (39.4°C), normotensive, and tachycardic. Her heart rate was 96 beats/min, respiratory rate was 40 breaths/min, and she had 99% oxygen saturation on room air. Her physical examination was unremarkable except for drowsiness, and she withdrew her lower extremities in response to pain, with a Glasgow Coma Scale of 8. She was intubated, placed on mechanical ventilation, and admitted to the Intensive Care Unit for higher-level care. The Infectious Diseases Team was consulted.

Laboratory results showed a normal white blood cell count with 22% bandemia, an absolute neutrophil count of 6500/uL, and elevated C-reactive protein (13.92 mg/dL). At the time of hospital admission, her sodium and chloride levels were 154 mEq/L and 126 mEq/L, respectively, and they improved after resuscitating her body volume status with intravenous fluids. The other results of her blood tests, including glucose levels, renal and liver function tests, vitamin B12, red blood cell folate levels, and thyroid function tests, were normal. The initial blood cultures and 2 repeat sets were negative. Serological tests were unremarkable for *Cryptococcus*, *Histoplasma*, *Mycoplasma*, *Legionella*, *Aspergillus* infections, and Lyme disease. The markers for vasculitis and urine drug-screening (UDS) tests were negative. The HIV-1 quantitative RNA level was <30 copies/mL (using the quantitative assay with an HIV viral detectable range between 30 copies/mL and 10⁷ copies/mL) with an absolute CD4 count of 755 cells/mL. She continued to be unresponsive despite having stable vital signs, electrolyte correction, and routine daily laboratory tests until the syphilis serology test results showed a reactive microhemagglutination assay for *Treponema pallidum* antibodies (MHA-TP) and rapid plasma regain (RPR) test (titer 1: 2). The initial and serial computed tomography (CT) scans without contrast did not show any acute intracranial events. An electroencephalogram (EEG) ruled out seizures. Based on these findings and observations, the Infectious Diseases Team's opinion was high suspicion for a diagnosis of neurosyphilis. Subsequent to this hospital admission, there was a concern for sexual assault.

Treatment with a daily continuous drip of penicillin G (24 million units) was initiated for 14 days and her mental status improved dramatically. She gradually became more awake, alert, able to follow commands and respond to questions. A magnetic resonance imaging of the brain with and without contrast showed no acute or subacute ischemic changes, and no abnormal, intracranial enhancing mass lesion was observed. She failed the continuous positive airway pressure ventilation mode trial in the extubation process due to frequent apneic episodes; therefore, she underwent a tracheostomy. Eventually, she was weaned to an automatic tube compensation trial with a tracheostomy collar. A brain CT scan without contrast before her discharge to the nursing home was unremarkable. She was clinically stable after completion of the treatment for neurosyphilis and was discharged to the nursing home. She remained clinically stable for over a year, and recently died from COVID-19 complications. Informed consent was obtained from her family for the publication of this case report.

Discussion

The incidence of syphilis has declined since the introduction of penicillin. In early the 2000s the US rate of reported cases

of diagnosed primary and secondary syphilis was 2.1 cases/100 000 people, which was the lowest rate since reporting began in 1941. Since then, the reported cases of syphilis in the US have increased almost every year in African Americans, Hispanics, and men who have sexual intercourse with men [3,4]. In developed countries, the increasing number of new cases are due to the occurrence of syphilis in patients with HIV. Neurosyphilis causes diverse clinical manifestations, including mood disorders, psychotic behaviors, emotional instability with the loss of social awareness, poor judgement, and different forms of memory deficits [1].

Our patient's mental status began a progressive decline over a 1-month period; however, her medical history and clinical presentation were not suggestive of primary or secondary syphilis. She was treated for HIV with emtricitabine, dolutegravir, and tenofovir alafenamide, and her recent CD4 count was above 350 cells/mL with an undetectable HIV VL. This was in addition to a medical history of controlled schizophrenia with tardive dyskinesia treated with benztropine, risperidone, and valproic acid.

Primary dementia was ruled out as she had a rapid decline in mental function from the baseline of being independent in activities of daily living. The brain CT and EEG suggested that her altered mentation was not likely to be secondary to a space-occupying lesion, seizures, cerebral edema, other forms of oncotic cerebral damage, or acute ischemic changes. The results of the initial and repeated routine blood tests, hepatitis panel, and UDS test were unremarkable and not suggestive of metabolic or infectious encephalopathy. In the literature, many case reports discuss patients with HIV who have early syphilis and are at increased risk for neurologic complications that range from mild cognitive impairment to psychosis and worsened altered mental status [1]. To date, there are no discrete studies or case reports discussing diagnosed neurosyphilis in patients with HIV and normal CD4 counts. The syphilis serology test of our patient showed a reactive MHA-TP and RPR test, low levels of HIV-1 RNA VL, and a normal CD4 count.

References:

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It is clearly stated in the literature that a lumbar puncture is essential for the diagnosis of neurosyphilis in patients with a syphilis-HIV coinfection, regardless of the patient's CD4 count [5]. We were not able to obtain consent for a lumbar puncture. Given our patient's worsening mental status and her medical history of HIV, upon the recommendation of the Infectious Diseases Team, she was started on intravenous penicillin G (24 mU over a 24-h period) for 14 days as treatment for presumed neurosyphilis. A few days after initiating the treatment, our patient's mental status improved significantly. Her routine laboratory results did not reflect any sign of infection, renal or liver injury, and/or electrolyte imbalance during the hospitalization. Despite the lack of a lumbar puncture and CSF analysis, the above results strongly support the theory that neurosyphilis was a contributing factor to the patient's clinical presentation in the ED. Our patient's serial CT imaging continued to be unremarkable.

Conclusions

As neurosyphilis occurs in various clinical manifestations, it must always be considered in the differential diagnosis of any neurological and psychiatric illness, after ruling out other etiologies of encephalopathy, including infection, electrolyte abnormalities, a brain mass or lesion. Neurosyphilis should be considered even in the absence of a confirmatory neurosyphilis-CSF analysis. This case report highlights the immediate clinical improvement and successful outcome from initiating a standard penicillin G treatment regimen for a presumed neurosyphilis diagnosis in a patient with HIV who had a normal CD4 count.

Department and Institution Where Work Was Done

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Conflicts of Interest

None.