

# The great imitator

## *Psychosis that responded to penicillin*

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**H**uman immunodeficiency virus infection has been associated with an increased incidence of syphilis and faster progression to later stages, namely neurosyphilis. Despite the well-known association of syphilis with psychiatric manifestations, it is often missed in the initial workup. We report a case of neurosyphilis, initially misdiagnosed and treated as schizoaffective disorder, that improved after penicillin therapy. This case emphasizes the importance of investigating for syphilis in patients with HIV infection or those at high risk of HIV who present with new-onset psychiatric symptoms.

### Case

A 44-year-old African American man was brought to our emergency department from an inpatient psychiatric facility for delirium, gait ataxia, and falls. Three months previously, he had presented to the outside clinic with agitation, paranoia, mania, and grandiose delusions, and was diagnosed with schizoaffective disorder. He was treated with haloperidol, citalopram, and clonazepam. However, his condition continued to deteriorate, and he became more delirious and combative, and started exhibiting a stumbling gait. On examination, he was delirious, combative, and unable to follow commands. His pupils were dilated to 6 mm bilaterally and were nonreactive to light; no accommodation of the eye was observed. Other findings included cogwheel rigidity in the lower extremities, symmetric hyperreflexia, and ankle clonus.

Screening results for HIV at the psychiatric facility had been positive, and these were confirmed by Western blot. His CD4 T-cell count was 66 cells/ $\mu$ L, which was consistent with a diagnosis of AIDS. He also had positive rapid plasma reagin test results (1:32) and positive test results for fluorescent treponemal antibody. Computed tomography of the brain did not show any acute process. Cerebrospinal fluid (CSF) examination showed elevated protein levels and lymphocytic pleocytosis, with 16 white blood cells/ $\mu$ L. Cerebrospinal fluid VDRL test results were positive (1:8) for syphilis, which confirmed the diagnosis of neurosyphilis. Cranial magnetic resonance imaging using subcortical fluid-attenuated inversion recovery showed ill-defined hyperintensity in the mesial temporal lobes and medial frontal lobes, which was suggestive of neurosyphilis (**Figure 1**). There was also a mixed lytic-sclerotic lesion with a

“worm-eaten” appearance on the left parietal bone owing to syphilitic osteitis (**Figure 2**).

He was treated with a 2-week course of aqueous penicillin G, with resolution of neuropsychiatric symptoms and signs. He became alert and oriented, with resolution of muscle rigidity and hyperreflexia. Accommodation of the eye was observed but light reflex remained absent (Argyll Robertson pupils).

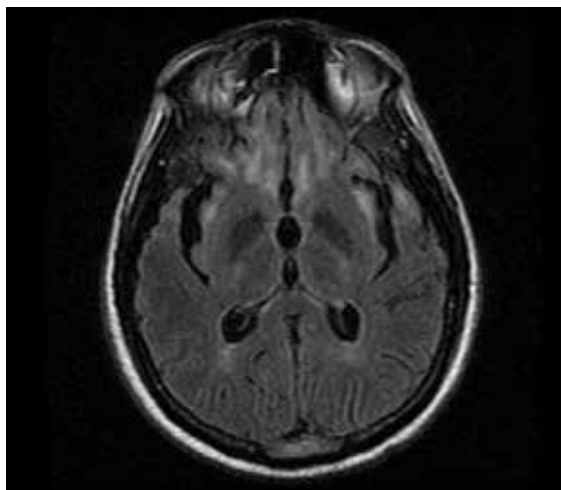
### EDITOR'S KEY POINTS

- The HIV pandemic has led to a resurgence of syphilis, with new diagnostic and treatment challenges. New-onset and treatment-resistant psychosis should be an indication to screen for both HIV and syphilis.
- The clinical, diagnostic, and treatment challenges presented by syphilis have changed, especially in the HIV era. Clinical features of neurosyphilis and HIV overlap in many respects, including acute or chronic meningitis, vasculitis, stroke, cranial neuropathies, myelopathy, and cognitive decline. The optimal antimicrobial regimen to treat neurosyphilis in patients co-infected with HIV is based on few objective data. This case illustrates the need for greater clinical and epidemiologic vigilance to decrease morbidity and mortality associated with syphilis.

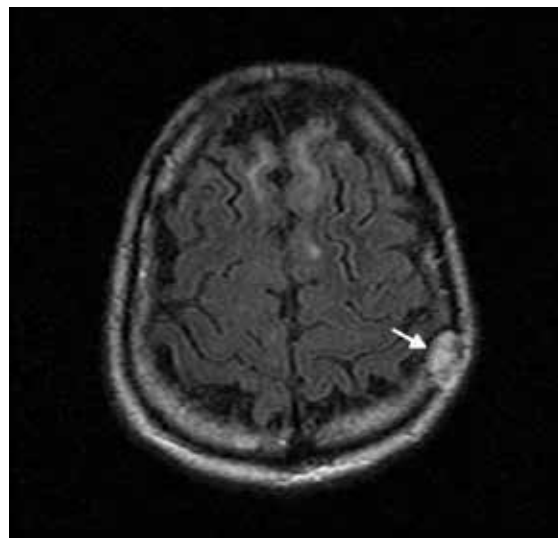
### POINTS DE REPÈRE DU RÉDACTEUR

- La pandémie du VIH a entraîné une résurgence de la syphilis ainsi que de nouveaux défis sur les plans du diagnostic et du traitement. L'apparition d'une psychose résistante au traitement devrait être une indication qu'il faut faire un dépistage à la fois du VIH et de la syphilis.
- Les défis cliniques, diagnostiques et thérapeutiques que présente la syphilis ont changé, en particulier à l'ère du VIH. Les caractéristiques cliniques de la neurosyphilis se chevauchent à de nombreux égards, y compris la méningite aiguë ou chronique, la vascularite, l'AVC, les neuropathies crâniennes, la myélopathie et le déclin cognitif. Le régime antimicrobien optimal pour traiter la neurosyphilis chez les patients infectés en même temps par le VIH se fonde sur très peu de données objectives. Ce cas démontre la nécessité d'exercer une plus grande vigilance clinique et épidémiologique pour réduire la morbidité et la mortalité associées à la syphilis.

**Figure 1.** Cranial magnetic resonance imaging illustrates mesial temporal and frontal hyperintensities on fluid-attenuated inversion recovery images



**Figure 2.** Cranial magnetic resonance imaging illustrates syphilitic osteitis affecting the left parietal bone (arrow)



## Discussion

In the past 2 decades, there has been a resurgence in reported cases of both early and late syphilis with concurrent HIV infection. Psychiatric symptoms usually start with personality changes and amnesia, but gradually mood changes, psychotic symptoms, and cognitive decline might occur, with more crippling paralytic symptoms occurring in later stages.<sup>1</sup>

Human immunodeficiency virus-induced breakdown in cell-mediated and humoral immunity and functional defects in macrophages can alter the course of syphilis.<sup>1,2</sup> Clinical features of neurosyphilis and HIV overlap in many respects, including acute or chronic meningitis, vasculitis, stroke, cranial neuropathies, myelopathy, and cognitive decline.<sup>3</sup>

All symptomatic patients and asymptomatic HIV patients with CD4 cell counts of fewer than 350 cells/ $\mu$ L and rapid plasma reagin test results of greater than 1:32 should be considered for CSF evaluation for neurosyphilis.<sup>4,5</sup> In some instances of asymptomatic neurosyphilis, CSF VDRL test results might be negative, and diagnosing pleocytosis (ie, more than 20 cells/ $\mu$ L in the CSF) might be helpful in diagnosing syphilis. Co-infection with HIV can result in diagnostic difficulties, as HIV itself can cause CSF pleocytosis. The CSF VDRL test is highly specific for neurosyphilis. Negative test results should be verified by CSF fluorescent treponemal antibody tests and by determining the percentage of CSF B cells.<sup>6</sup>

Imaging studies have little role in diagnosing neurosyphilis but can be used to rule out other intracranial

lesions. Neurosyphilis can be associated with a range of imaging findings, depending on the stage of disease, such as meningeal enhancement, vascular lesions, cortical atrophy, and hyperintensities in the frontal and mesial temporal regions on fluid-attenuated inversion recovery imaging.<sup>7</sup>

The optimal antimicrobial regimen to treat neurosyphilis in patients co-infected with HIV is based on few objective data.<sup>8</sup> Current guidelines suggest treatment with 18 to 24 million units per day of aqueous crystalline penicillin for 10 to 14 days, regardless of HIV status. Highly active antiretroviral therapy to reverse immunosuppression might help mitigate neurologic complications of syphilis.<sup>9</sup> Success of therapy is based on neurologic improvement and resolution of CSF pleocytosis and positive VDRL test results. However, HIV patients can have slow serologic resolution and persistent baseline CSF pleocytosis secondary to HIV infection itself.<sup>10</sup>

## Conclusion

Human immunodeficiency virus has unveiled a new face of syphilis. Instead of being a disease of historical importance, syphilis continues to create new diagnostic and treatment challenges. New-onset and treatment-resistant psychosis should be an indication to screen for both HIV and syphilis. Early labeling of psychiatric symptoms with a primary psychiatric diagnosis without investigating for potential secondary causes can be detrimental. The clinical, diagnostic, and treatment challenges presented by syphilis have changed, especially in the HIV era. This case illustrates the need for greater clinical and epidemiologic vigilance to decrease morbidity and mortality associated with syphilis. 🌿

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**Competing interests**  
None declared

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