Neurosyphilis in a Patient with Psychotic Symptoms: Clinical Presentation in the Modern Era

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Neurosyphilis is a treatable condition which increasingly offers diagnostic challenges as it presents in atypical clinical patterns. We present a case that initially presented with paranoid psychosis refractory to treatment. Neurosyphilis was subsequently diagnosed during clinical evaluation. Blood serology was positive for rapid plasma reagin titres and fluorescent treponemal antibody absorption. Lumbar puncture was performed and cerebrospinal fluid analysis confirmed the diagnosis of neurosyphilis. Treatment was begun with a 2-week course of aqueous crystalline penicillin G. We suggest that the possibility of neurosyphilis should be included in the differential diagnosis of untreatable psychosis.

INTRODUCTION

Syphilis, although reduced after the introduction of penicillin in the 1940’s, has recently re-emerged as a prevalent and complex clinical problem. Although antibiotic availability has sharply decreased the complications of late-stage syphilis such as neurosyphilis, rates of syphilis in the US have been increasing since 2000. Moreover, the widespread use of antibiotics has drastically altered the clinical patterns of neurosyphilis; atypical forms with psychiatric symptoms such as psychosis, fury and depression are more frequently observed in the clinical setting. The resurgence of syphilis, especially in the population of patients with HIV, make it essential for clinicians to be aware of the challenges in diagnosing and treating this complex disease.

In this study we describe a case that initially presented with untreatable psychotic symptoms but was subsequently diagnosed as neurosyphilis during the clinical evaluation.

CASE REPORT

Three months prior to admission a 51-year-old single African-American male with a remote history of headaches and no prior psychiatric history developed paranoid ideation and aggressive behavior. The patient had been treated with olanzapine 10 mg once a day but reported little improvement and increased appetite. The patient was admitted to the psychiatric unit and initially received olanzapine 10 mg once a day, later replaced with ziprasidone 60 mg twice a day, without significant improvement of his symptoms. One day after hospitalization, the patient experienced a generalized tonic-clonic seizure with stool incontinence.

Physical examination on admission demonstrated +1 deep tendon reflexes but was otherwise unremarkable with no other motor, sensory or cerebellar findings on neurologic exam. He scored 14/30 on the Mini-Mental State Examination with deficits in orientation to time, place and short-term memory. Patient also exhibited slow speech, impaired judgement, limited insight, flat and guarded affect but reported no suicidal or homicidal ideation or hallucinations.

Standard laboratory workup was noted for hemoglobin of 13.9 g/dL but otherwise unremarkable. Magnetic resonance imaging (MRI) of the brain was
noted for mild microvascular changes but was negative for other pathologic findings. (Figure) Electroencephalogram was noted for diffuse slowing suggestive of encephalopathy. Blood serum analysis was negative for human immunodeficiency virus (HIV) 1 and 2 test but positive for rapid plasma regain (RPR) with a titer of 1:64 and positive for fluorescent treponemal antibody absorption (FTA-Abs). A lumbar puncture was performed and cerebrospinal fluid analysis was noted for protein level of 67.4 mg/dL, glucose level of 70.9 mg/dL, normal cell count and differential, and a positive VDRL test with a titer of 1:4 and positive FTA-Abs treponemal antibody absorption test.

The patient was started on 14 days of intravenous penicillin G infusion (24 million IU/day). After seven days of treatment the patient was still confused and somewhat paranoid but had no other complaints or symptoms. Physical examination was unremarkable and he scored 16/30 on the Mini-Mental State Examination with deficits in orientation to time and short-term memory. Patient was discharged to an extended-care facility to complete antibiotic therapy. At three months he did not show a full remission of psychotic symptoms but was reported to have improvement in short-term memory. Repeat lumbar puncture and CSF analysis demonstrated nonreactive VDRL and normal cell count and differential.

**DISCUSSION**

Syphilis is a chronic infection caused by the sexually transmitted spirochete *Treponema pallidum* that has been found to disseminate systemically within hours to days and invade the central nervous system early in the course of infection. The tertiary form of the disease, neurosyphilis, is uncommon and often perceived as a disease of “historic” interest. Classic presentations of parenchymal neurosyphilis included tabes dorsalis (ataxic gait, paresthesias, bladder disturbances, impotence, areflexia and loss of position, deep pain and temperature sensations) and general paresis (abnormalities in personality and affect, hyperactive reflexes, illusions, delusions, hallucinations, decrease in recent memory, orientation, judgment and insight). However, these patterns are relatively rare and a variety of more subtle and monosymptomatic atypical presentations now account for as many as 85.7% of cases. In contrast to the typical symptoms such as the Argyll Robertson pupil and tabetic symptoms, mental disorders and cognitive impairment have now become the most common expressions of neurosyphilis. This report is an addition to the small but growing body of neurosyphilis cases presenting as isolated psychosis.

Although there is no gold standard test to diagnose neurosyphilis, serum analysis for syphilis with nonspecific lipoidal tests (RPR and VDRL) and treponemal-specific tests (FTA-Abs) should be considered routine in patients presenting with and hospitalized for mental disorders. A CSF analysis for VDRL is used to define a “confirmed” case of neurosyphilis although this test has been found to be non-reactive in 43% of cases. The CSF RPR test is currently not recommended and studies have found it to be less specific. In summary, the CSF VDRL test is considered the test of choice in diagnosis of neurosyphilis and although a positive VDRL establishes a diagnosis, a negative VDRL does not exclude it.

Computed tomography and MRI used to evaluate series of patients with neurosyphilis most commonly found generalized cerebral atrophy and foci of increased signal intensity, but to date, there are no pathognomonic radiographic findings suggesting a diagnosis of neurosyphilis.

**TREATMENT**

Introduced in the 1940’s, penicillin remains the mainstay of therapy to treat neurosyphilis. This treatment regimen has been found to quickly resolve symptoms in patients with early meningeal neurosyphilis, but for late disease with parenchymal involvement, resolution of symptoms may not occur.

**CONCLUSION**

Far from an infection of historical significance, syphilis continues to be an important clinical problem which increases in prevalence and complexity. Progress in the study of syphilis has been limited by the inability to culture *Treponema pallidum*; HIV adds yet another layer of complexity. As
Figure. T1 weighted axial and sagittal projections obtained before and after administration of 15 mL IV contrast. Images are motion degraded. Subcortical and periventricular white matter hyperintensity consistent with mild to moderate microvascular change otherwise no pathologic findings.
clinical presentation and types of neurosyphilis can vary, diagnosis can become quite difficult. To appropriately identify and treat patients with neurosyphilis, physicians must broaden their differential diagnosis and be aware of atypical presentations.

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REFERENCES


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