Neurosyphilis in Newly Admitted Psychiatric Patients: Three Case Reports

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Background: Neurosyphilis, also known as "general paresis of the insane," at one time accounted for a large portion of admissions to state psychiatric facilities. With the introduction of antibiotics, neurosyphilis is now considered very rare.

Method: Chart review was performed on patients diagnosed with neurosyphilis who were admitted to a state psychiatric hospital in Raleigh, N.C., during 2002.

Results: We identified 3 cases of confirmed neurosyphilis, representing 0.1% of adult admissions, diagnosed in newly admitted psychiatric patients. None of the patients were immunocompromised. Response to antibiotic treatment was poor.

Conclusions: Given the increase in primary and secondary syphilis reported in the 1980s and early 1990s, routine screening of psychiatric patients for the presence of syphilis should be considered.

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Neurosyphilis, also known as "general paresis of the insane," was first described by Bayle in 1822 as a distinct syndrome consisting of severe mental dysfunction accompanied by motor and other neurologic symptoms.[1] The syndrome typically occurred 10 to 20 years after the initial symptoms of syphilis were observed and invariably led to death.[2] Neurosyphilis had previously accounted for a large proportion of mental asylum patients in both Europe (45% of the male patient population in the 1890s) and the United States (13% of admissions to California state hospitals in the 1930s).[3,4] Given the high prevalence and lethality of the disorder, it is understandable that Wagner-Jauregg was awarded the Nobel Prize for recognizing that patients with "general paresis of the insane" benefited from malaria therapy.[4,5] With the knowledge that syphilis is caused by infection of the spirochete *Treponema pallidum* came the development of efficacious antibiotic treatments. Neurosyphilis in nonimmunocompromised patients is now considered very rare in developed countries, though the actual prevalence is unknown.[6] In 2001, the rate of primary and secondary syphilis in the United States was 2.2 cases per 100,000 population.[7] This represented a slight increase from 2000, after rates had declined every year since 1990. We report here 3 cases of confirmed neurosyphilis diagnosed in patients newly admitted to a state psychiatric hospital during 2002.

METHOD

Patients described were diagnosed with neurosyphilis while inpatients at Dorothea Dix Hospital, a 360-bed state psychiatric hospital located in Raleigh, N.C., that serves patients 13 years or older who live in south-central North Carolina. The hospital's catchment area contains 16 counties with a total population of approximately 2 million. The hospital admits approximately 3000 adult patients per year. Summaries of clinical course and treatment were derived from chart review.

RESULTS

Case Reports

Case 1. This was the first psychiatric hospitalization for Ms. A, a 46-year-old African American woman with a history of diet-controlled diabetes mellitus and substance abuse. She initially presented as oriented to self only, unable to provide a coherent history, and lethargic with intermittent agitation. On physical examination, an intention tremor of both legs, ataxia, dysarthria, and bladder incontinence were reported. Laboratory analyses were remarkable for a reactive rapid plasma reagin (RPR) with a titer of 1:512, a negative human immunodeficiency virus (HIV) test, and normal brain magnetic resonance imaging results. To evaluate for neurosyphilis, a lumbar puncture was performed as a forced procedure. Cerebrospinal fluid (CSF) analysis revealed pleocytosis, elevated protein

level, and a positive Venereal Disease Research Laboratory (VDRL) assay. CSF microhemagglutination assay for *Treponema pallidum* was also positive, and the diagnosis of neurosyphilis was made. Intravenous penicillin G was started at a dose of 4 million units every 4 hours for 14 days. After 7 days of treatment the patient became alert and conversant. However, she was still oriented to self only and was occasionally combative. Although Ms. A's ataxia improved, other neurologic symptoms remained unchanged.

Case 2. Mr. B was a 47-year-old African American man with no prior psychiatric history who was transferred to our hospital after a brief admission to a local community hospital. He had lived independently until 2 years prior, when he began to experience a slow, steady cognitive decline. The month prior to his admission, Mr. B's confusion worsened and was now complicated by psychosis and violent behavior.

As a consequence of assaultive behavior, Mr. B was admitted to the community hospital. There, his medical evaluation was remarkable for a positive serum RPR at a titer of 1:2. His behavior became difficult to manage secondary to violent outbursts, and he was transferred to our hospital. A second RPR was positive with a titer of 1:128. HIV test results were negative. Analysis of CSF, obtained using a forced lumbar puncture, revealed a positive VDRL, confirming the diagnosis of neurosyphilis. He completed 2 weeks of treatment with 4 million units of intravenous penicillin G every 4 hours with subsequent improvement in cognition (Mini-Mental State Examination score of 20 vs. 6 on admission[8]). He did not, however, return to his premorbid baseline. Five months posttreatment, a follow-up serum RPR was positive with a titer of 1:256. He received another 2-week course of 4 million units of intravenous penicillin G, followed by intramuscular injections of benzathine penicillin once a week for 2 weeks. No further cognitive gains were evidenced.

Case 3. Mr. C was a 52-year-old African American man with a history of hypertension and alcohol abuse (but with no alcohol use in more than 8 months) who initially presented to another hospital with a chief complaint that he was "showing up for work" (he had actually worked at that hospital years ago). He had been hospitalized 3 times previously for alcohol detoxification, the last time being 10 years ago, and was treated briefly as an outpatient 2 years prior to his admission to Dorothea Dix Hospital for a first onset of psychotic symptoms. His current evaluation was remarkable for confusion, disorientation, and visual hallucinations. Vital signs of the patient were stable. Medical evaluation of the patient was remarkable for a reactive RPR with a titer of 1:64. He was HIV negative.

Upon transfer to our hospital, he was disoriented to place, time, and reason for admission; had short-term memory deficits; and complained of visual hallucinations. A diagnosis of neurosyphilis was considered. A forced lumbar puncture was performed, and CSF analysis revealed positive VDRL and fluorescent treponemal antibody absorption results, confirming the diagnosis of neurosyphilis. Mr. C received 2 weeks of intravenous penicillin G, 4 million units every 4 hours. His cognitive ability did not improve. His psychosis improved substantially with risperidone treatment. He was discharged home under the care of his family, with recommended follow-up assessment of serum RPR in 3, 6, 12, 18, and 24 months.

DISCUSSION

These 3 confirmed cases of neurosyphilis represented 0.1% of adult admissions to our state psychiatric facility in 2002. Three cases of neurosyphilis in nonimmunocompromised patients in 1 year was unexpected; however, it has been suggested that there may be an eventual upsurge in cases of tertiary syphilis given the resurgence in the 1980s and early 1990s of primary syphilis.[2,9] Several important points emerge when these cases are considered together. First, contact with medical professionals resulted from the expression of psychiatric symptoms, not other neurologic symptoms. Second, none of the patients were immunocompromised (e.g., all were HIV negative). Third, the use of a forced procedure (lumbar puncture) was required to confirm the diagnosis of neurosyphilis. In addition, for these cases, the only identified risk factor for syphilis infection was substance abuse, which is very common among psychiatric patients and is also highly prevalent in the general population.[10]

The chief presenting complaint in these cases was severe psychiatric symptomatology, including psychosis, aggressive behavior, and cognitive impairment. None of the patients evidenced classic neurologic signs of neurosyphilis (e.g., Argyll Robertson pupil). This type of presentation does support the observation that classic neurosyphilis, such as tabes dorsalis and general paresis, may now be less common than asymptomatic neurosyphilis.[11] The current cases are consistent with those reported by Roberts and Emsley,[12] whose retrospective review of 21 cases of probable neurosyphilis revealed that psychiatric symptomatology, in particular personality change, was the chief presenting complaint in most cases.

Immunocompromised status has been recognized as a significant risk factor for neurosyphilis, particularly acquired immune deficiency syndrome (AIDS) associated with HIV infection.[13] Importantly, in none of the cases did a patient have concurrent HIV infection. This observation highlights the need for consideration of neurosyphilis in the differential diagnosis of psychiatric patients, regardless of their immune status.

Interestingly, the 3 patients described here all required lumbar punctures to be obtained under guidelines for forced procedures due to both their inability to give in-

formed consent and their unwillingness to allow the procedure. These procedures allowed definitive diagnosis and appropriate treatment. Despite receiving treatment in accordance with current guidelines,[14] none of the 3 patients had a good recovery, with only limited improvement in some symptoms. Still, appropriate diagnosis and intervention prevented further decline.

Neurosyphilis has variable presentations, and these usually reflect the latency period. Earlier forms, such as syphilitic meningitis and meningovascular syphilis, are better candidates for response to antibiotic treatment. Longer latency leads to parenchymatous involvement (e.g., tabes dorsalis and general paresis). Parenchymatous disease is much less responsive to treatment, and the therapeutic goal is usually arrest of further disease progression as opposed to symptom abatement.[15] Our cases exhibited expected treatment outcomes of parenchymatous neurosyphilis: modest, if any, clinical improvement.

The detection of neurosyphilis in 3 psychiatric patients newly admitted to our hospital in a single year indicates that the routine screening of psychiatric patients for the presence of syphilis should be considered. It is possible that other cases of neurosyphilis were present in the patient population admitted in that year but went undetected. As primary syphilitic infection may be on the rise,[7] the use of standard screening tests (e.g., RPR) for all newly admitted psychiatric patients would hopefully result in earlier treatment and reduced morbidity.

Drug names: benzathine penicillin (Bicillin and Permapen), risperidone (Risperdal).

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