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CASE REPORT

Neuropsychiatric Manifestations of Syphilis

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Abstract

Neurosyphilis is a condition characterized by insidious onset of encephalopathy and delirium. The infrequency with which it is encountered makes neurosyphilis a formidable diagnostic challenge. We present a rare case of a 71-year-old male with ischemic cardiomyopathy, chronic obstructive pulmonary disease (COPD), undifferentiated arthritis and alcohol use disorder who was brought to the emergency department after he was found altered, confused, and paranoid. His hospital stay was eventful for multiple episodes of agitation that were difficult to control despite benzodiazepines and high doses of antipsychotics. After an extensive workup, he was found to have neurosyphilis and his delirium resolved following a brief period of treatment.

This case illustrates the importance of early suspicion for neurosyphilis as a cause of delirium, especially in endemic areas and in patients with focal neurologic findings.

Keywords: Neurosyphilis, Syphilis, Delirium

1. Introduction

Neurosyphilis refers to infection of the central nervous system (CNS) by Treponema Pallidum, subspecies *pallidum* (hereafter termed *T. pallidum*), that can exhibit in a wide array of presentations. Early in the disease, the most common forms of neurosyphilis involve the cerebrospinal fluid (CSF), meninges, and vasculature, which present as asymptomatic meningitis, symptomatic meningitis, and meningovascular disease respectively.[1] However, late in the disease course, the brain and spinal cord parenchyma ("general paralysis of the insane"[2] and Tabes dorsalis) are involved. Each form has characteristic clinical findings, but in some cases, there can be an overlap between these findings.[3] Neurosyphilis can occur at any time after initial infection, and it is most often characterized by insidious onset of encephalopathy and delirium.[4] However, the infrequency with which it is encountered makes neurosyphilis a formidable diagnostic challenge.

2. Case presentation

A 71-year-old male with ischemic cardiomyopathy, chronic obstructive pulmonary disease (COPD), undifferentiated arthritis and alcohol use disorder was brought to the emergency department after he was found altered, confused, and paranoid. On presentation, he was hemodynamically stable with a temperature of 36.7 °C, a pulse rate of 62 bpm, an oxygen saturation of 99% on room air, but had a mildly elevated blood pressure of 189/76 mmHg. The physical exam was unremarkable except for a shuffling gait, without any focal deficits on a complete neurological exam. A mini mental state exam (MMSE) was done and was found to be 25 (above 24 is normal). His laboratory diagnostics demonstrated an elevated BUN 63 (normal range is <23), creatinine 1.61 (normal range is <1.2 mg/dL), elevated AST of 113 (normal range 20−40) with a normal ALT of 42, and an elevated creatinine kinase level of 1852 (normal range <100). He was also found to have a low platelet count of 124,000 (normal range is 145−400) and a borderline low Vitamin B12 level of 292 (normal range 211−911). His urinalysis was

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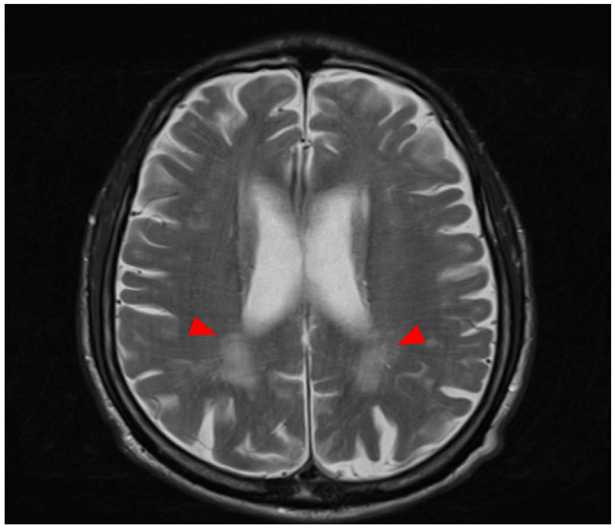

Fig. 1. FLAIR MR Images showing confluent and scattered foci of increased signaling within bilateral periventricular and subcortical white matter.

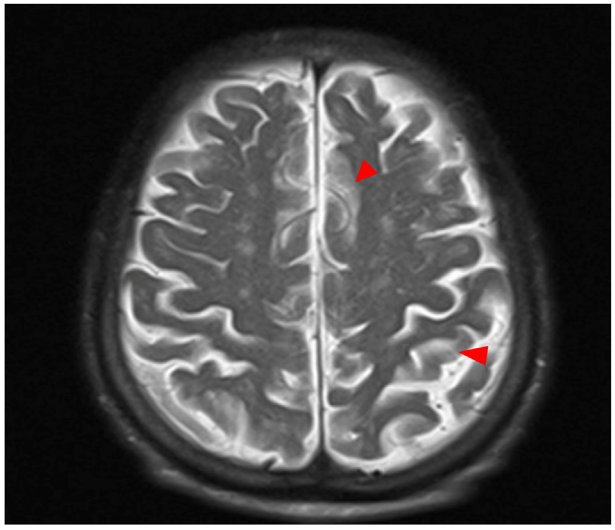

Fig. 2. FLAIR MR Images showing confluent and scattered foci of increased signaling within subcortical white matter.

significant for ketones. His ammonia level, ethanol level and blood sugars were unremarkable along with urine toxicology. His TSH level was 1.01 (normal range 0.4–4). HIV screening was found to be negative. Initial diagnostic imaging tests included a chest radiograph and unenhanced Computed Tomography (CT) of the head were both found to be normal. Additional imaging, including a magnetic resonance imaging (MRI) of the brain was also done and was found to be equally unremarkable (see Figs. 1 and 2). Given the concerns of subclinical seizures, an EEG was done and showed slowing rhythm without any epileptic activity, which was suggestive of nonspecific encephalopathy. During his hospital stay his revised Clinical Institute Withdrawal Assessment of Alcohol Scale (CIWA-Ar) scores remained unremarkable, yet his course was notable for multiple episodes of agitation, visual hallucinations, and multiple attempted elopements, for which he received intermittent high doses of lorazepam and haloperidol.

Table 1. Cerebrospinal fluid studies and VDRL testing.

CSF studies and VDRL testing	Results
Appearance	Slightly cloudy
Color	Pink (Abnormal)
Xanthochromia	Absent
WBC	2/mm^3 (0–5)
Segmented Neutrophils	Not performed (Given WBC<5)
Lymphocytes	Not performed (Given WBC<5)
Monocytes	Not performed (Given WBC<5)
RBC	3722/mm^3 (0–1)
Proteins	65 mg/dL (15–45)
Glucose	51 mg/dL (40–70)
Culture	Not done due to insufficient sampling
VDRL Screen	Positive
VDRL Titer	1:1 (Abnormal)

He was started on thiamine for suspicion of Wernicke's encephalopathy, multivitamin and folic acid for nutritional deficiencies, and B12 supplementation due to his borderline low level on testing. However, despite resolving azotemia and administering treatment, there was no improvement in his altered mental status after 3 days. For further evaluation, a serum Treponemal antibody was sent and came back positive. His non-treponemal antibody was positive with an elevated titer of 1:32. Upon questioning, the patient reported no prior history of syphilis, rashes or chancre. Lumbar puncture was subsequently performed (Table 1) and confirmed a positive CSF venereal disease research laboratory (VDRL) test screening test with a positive titer of 1:1, therefore, he was started on IV Penicillin G every 4 h for a total of a two-week course. After just a few doses, a significant improvement in his mentation was noted. The patient was subsequently discharged on IV Penicillin through a Peripherally Inserted Central Catheter (PICC) line to complete his therapeutic course of two weeks with instructions to follow up in the Infectious Disease clinic for re-evaluation of his titers in three to six months.

3. Discussion

Neurosyphilis is very difficult to diagnose because of its similar manifestations to many other diseases and syndromes. According to a new report from the Centers for Disease Control and Prevention (CDC), the number of syphilis cases in the U.S. are

increased by nearly 80% to more than 207,000 between 2018 and 2022.[5] A high index of suspicion and microbiological workup is essential for diagnosis, especially in areas that are historically endemic.[6] Having a multidisciplinary approach is always helpful in establishing a narrow differential and will ensure proper workup and management, especially in patients with non-focal deficits.

There is no gold standard test to diagnose neurosyphilis, the diagnosis must be based on a combination of laboratory tests and clinical findings. Although the CSF VDRL is helpful to confirm neurosyphilis, its absence does not rule it out.[1] Usually, determination of a reactive treponemal test is the first step to investigate prior history of exposure, or active disease, after which this can be confirmed by means of the VDRL test or the RPR titer in serum.[4,7]

When neurological or neuropsychiatric symptoms are present, a lumbar puncture is required. Even though our patient initially presented with a normal WBC count in the CSF, this did not exclude the possibility of syphilis, especially since the patient has a relatively elevated protein count.[3] If the VDRL test is positive, then the diagnosis of neurosyphilis is established.[4]

While imaging of the CNS can provide additional information to rule out more common and time sensitive diagnoses such as a stroke, tumor or bleeding, it is often non-specific, as was in this case.

According to the CDC, crystalline penicillin G 18–24 MIU/day is the mainstay of treatment for neurosyphilis. It is given intravenously at a rate of 3–5 MIU every 4 h or as a continuous infusion for 14 days.[8] There is a paucity of reports regarding management of neuropsychiatric manifestations, and limited research suggests prudent use of atypical antipsychotics. Some recommended doses were quetiapine 300–1200 mg/day, risperidone 6 mg/day, or olanzapine 20 mg/day.[4,9] However, it is important to note that these should be administered at the lowest effective dose based on a patient's specific situation. Furthermore, antipsychotics are useful when one has an early suspicion of neurosyphilis to help decrease hospital length of stay and complications.[10]

According to the previously mentioned guidelines, our patient started receiving intravenous crystalline penicillin 4 MIU every 4 h until he was discharged to skilled nursing facility where he completed treatment.

Ideally, follow-up of neurosyphilis is based on re-evaluation of CSF every six months. The cell count should decrease within six months, and the VDRL test and protein concentration should decrease within two years.[11] Otherwise, the patient must be retreated with intravenous penicillin. This follow-up could not be completed because the patient did not attend follow-up visits after he was discharged.

4. Conclusion

Neurosyphilis is often a missed cause of delirium.[12,13] Early suspicion is crucial, particularly in endemic areas, and in patients with non-focal neurologic findings. Syphilis remains an important public health threat, especially with the recent rise in the number of cases reported.

Disclaimers

None.

Ethics approval

Not applicable.

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Conflict of interest

The authors have no conflict of interest to declare.

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