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CASE REPORT

An atypical presentation of a re-emerging disease

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ABSTRACT

Often referred to as 'The Great Mimicker', syphilis infections have been on the rise since 2000 including cases of primary and secondary syphilis where 19,999 were reported in the USA in 2014. The increase in cases has led the USPSTF to recommend screening for syphilis infection in persons who are at increased risk of infection. Changes in screening and re-emergence of the disease necessitates review of the multitude of circumstances a patient can present for care. Immunocompetent patients begin to show classic symptoms within 10–90 days following infection with the spirochete. In the immunocompromised patient, the presenting symptoms are often atypical and more complex. With the rise in HIV infections, syphilitic infections have become increasingly common worldwide and several atypical presentations have been observed. The following case is an atypical presentation of syphilis involving both central and peripheral nervous system findings in a patient without significant medical history.

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Syphilis; neurosyphilis; infectious disease; facial paralysis; meningitis

1. Case presentation

The patient is a 29-year-old male with no relevant past medical history presenting to the emergency department with a progressively intensifying headache of 10 days' duration. The headache is rated 10/10 in severity and associated with neck stiffness and photophobia. During the course of the headache, he presented to an outside emergency department, where he received a CT scan of his head without contrast and was given analgesics. The analgesia only mildly alleviated the pain, so the patient sought care at a second outside emergency department. At that time, right-sided facial paralysis was noted. The patient was diagnosed with Bell's palsy and was given ganciclovir and prednisolone. During this time the patient noted relapsing-remitting fever associated with chills and nausea. Upon noting these symptoms, the patient presented to a third emergency department. No further escalation in symptoms were noted at that time including vomiting, bowel, or urinary symptoms. The patient denied any sick contacts, recent travel outside of the USA and no close contacts with similar symptoms.

In addition, the patient reports no past medical or surgical history. The patient's only allergy is noted to be penicillin, to which he states that he had respiratory compromise as a child. No alcohol, tobacco or illicit drug use was elicited in the history. The patient states that he is heterosexual, uses condoms for contraception, has never been diagnosed with a sexually transmitted infection, and has been in a monogamous relationship for approximately one year. Prior to his current relationship, the patient had not been sexually active for 1.5 years. The patient reveals no pertinent family history.

On presentation, vital signs were BP 147/96, HR 93, temperature 98.8°F (31.7 C) (oral), respiration rate 18, height 5′11" (180 cm), weight 170 lbs (77.1kg). On physical examination, the patient is alert and cooperative. Head and neck exam revealed flattening of the right nasolabial fold, right-sided facial droop (including the forehead), and incomplete closure of the right eye lid (House-Brackmann grade V). Neurologic exam showed neck stiffness, positive Kernig's sign and a negative Brudzinski's sign. Deep tendon reflexes were 2+ and symmetrical. Strength was 5/5 and symmetric in both upper and lower extremities. The remainder of the exam including musculoskeletal, skin, and lymph node exams did not reveal any other abnormalities.

Initial laboratory tests included complete blood count (CBC), basic metabolic panel (BMP), chest X-ray and lumbar puncture. The CBC was negative for leukocytosis, anemia and thrombocytopenia (Hemoglobin: 12.8 mg dl^{-1}, white blood cells (Wbc): 4.9×10^3 cells ml^{-1}, platelets: 225). BMP was negative for any electrolyte disturbances (Na: 134 mmol l^{-1}, K: 4.0 mmol l^{-1}, Cl: 96 mmol l^{-1}, Co2: 26 mmol l^{-1}, BUN: 20 mg dl^{-1}, Cr: 1.0 mg dl^{-1}, glucose: 82 mg dl^{-1}, Ca: 9.7 mg dl^{-1}). Cerebrospinal fluid appeared clear, red blood cell count were 58 μl^{-1}, WBCs 580 μl^{-1} (73% lymphocytes), glucose 29 mg dl^{-1} and protein of 270 mg dl^{-1}. The infectious disease team was consulted. At this point a hepatitis panel, Lyme antibodies, Varicella zoster antibodies, Epstein Barr antibodies, herpes simplex virus (HSV) viral culture and polymerase chain reaction (PCR), enterovirus

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PCR, blood cultures and rapid plasma regain (RPR) were sent. The presumptive diagnosis was aseptic meningitis and the patient was admitted and started on vancomycin, acyclovir and ceftriaxone.

On day 3 of hospital stay, the RPR came back as reactive with a titer of 1:4 and the HIV test came back as positive. The RPR was confirmed by fluorscent treponema antigen antibodies. The Lyme, HSV, Varicella Zoster virus, blood cultures, enteroviral PCR, Ebstein Barr virus antibodies and hepatitis panel resulted as negative. A CD4 count was ordered and returned with a value of 358. The antibiotics were discontinued and penicillin desensitization was initiated. Once desensitization was completed, the patient was started on aqueous penicillin G 4 million units q 4 h for a total of 14 days of therapy based on the diagnosis of neurosyphilis.

An MRI was done to determine the degree of intracranial involvement of the disease. The MRI showed areas of hyper-intensity scattered throughout the white matter in both cerebral hemispheres suggestive of vasculitis or demyelination. No masses or hemorrhages were noted (Figure 1(a–c)).

The patient received a right sided peripherally inserted central catheter for long term antibiotic treatment. He subsequently developed a non-occlusive thrombus in the right axillary vein extending into the right brachial and cephalic veins. The patient was started on anticoagulants for the DVT and the peripherally inserted central catheter (PICC) line was removed. The patient finished his 14-day course of penicillin G (4 million units every 4 h) and was discharged home. On discharge, the patient's headache had fully resolved and the right sided facial paralysis showed minor improvements, with slight improvement in his ability to move his right eye. Within six months, the patient's facial paralysis was almost fully resolved.

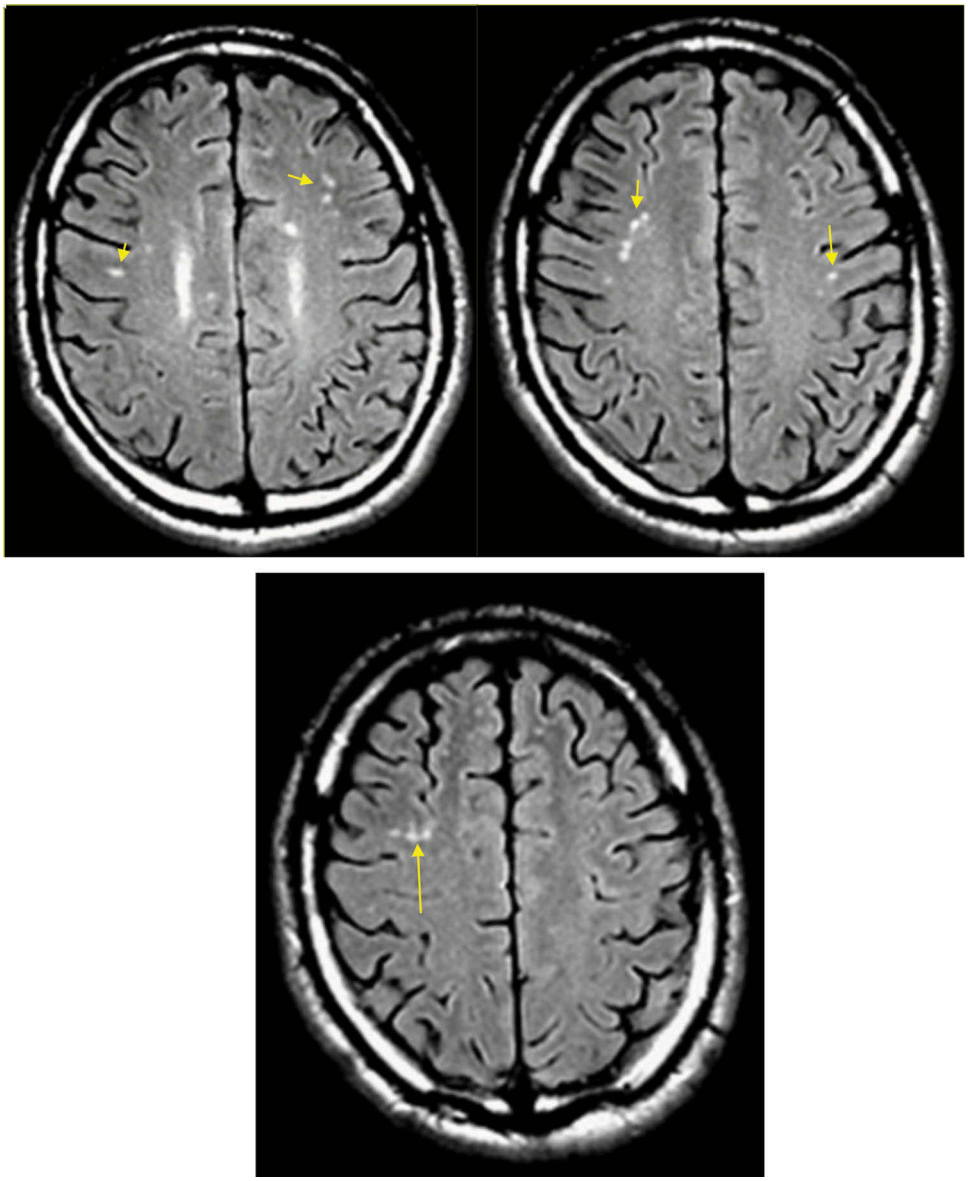

Figure 1. (a–c) T2 weighted images showing multiple hyper intense lesions in both cortical hemispheres. Initial differential included of demyelinating process and cerebral vasculitis.

On follow-up with his newly established PCP, the patient did admit that he was sexually active with both men and women.

2. Discussion

Syphilitic infection can be a difficult diagnosis to make due to the wide variation of clinical symptoms that are associated with the disease. Neurosyphilis is typically a late manifestation of syphilitic infection and is caused by invasion of the causative organism into the meninges and cerebral arteries. The neurologic complications of syphilitic infections are varied and are listed in Table 1.

In the era of the HIV pandemic, syphilis infection has become more complex. Many rare presentations of syphilitic infections are seen in patients with HIV, as is the case with our patient. Though syphilitic ocular manifestations are relatively rare (2.25% of patients with ocular inflammation), the median age of the presentation of ocular syphilitic infection was found to be significantly lower (66 years in HIV negative patients and 37 years in HIV positive patients).[3]

One study found a rate of co-infection with syphilis of 46.5% of HIV infected men and 37.5% of total men followed exhibited RPR titers of greater than or equal to 1:4.[4] Another found that 31.47% of patients were concomitantly diagnosed with both HIV and syphilis on initial presentation with 68.53% of patient studied being diagnosed with syphilis within the first year of HIV diagnosis.[5] The average CD4 counts of those men positive for syphilis and those negative for syphilitic infection showed no significant difference ($p = 0.06$).[4] Venereal Disease Research Laboratory (VDRL) test titers of >1:32 were associated with a statistically significant rate of neurosyphilis.[5]

It has also been shown that syphilis infection can lower CD4 counts in HIV infected patients and that treatment of syphilis can raise CD4 counts.[6,7] A significantly higher rate of serologic failure in the treatment of syphilis was also seen in HIV positive patients versus HIV negative patients (17% vs. 5%, $p < 0.001$).[8] Serologic failure was significantly associated with CD4 count of less than 200 cells mm^{-3} and lack of HAART; serologic failure was not associated with HIV RNA or HAART use >6 months.[9]

Our patient presented with meningeal signs which can be attributed to early neurosyphilis, more specifically, acute syphilitic meningitis. This presentation of syphilis represents a rare, but growing presentation of neurosyphilis. Merrit et al. [10] found only 80 cases of early neurosyphilis from three hospital centers over a 15 year period (1920–1945) and reported a prevalence of neurosyphilis in 1.4% of during that time. This study did not define what proportion of the cases presented as acute syphilitic meningitis. However, a later study (1985–1992) showed 38 patients with early neurosyphilis out of 117 confirmed syphilis patients, i.e. 33%. Of these patients, 34 out of 38 were confirmed to be HIV positive or had documented behaviors that confer high risk for HIV infection.[11] Of the patients with early neurosyphilis, 19 were confirmed to have acute syphilitic meningitis, and of those, five had cranial nerve deficits (26%).[11] The authors of this study documented an incidence rate of 0.3–1.25 cases/year/100,000 population for symptomatic early neurosyphilis, suggesting that it is incredibly rare even in high risk communities.

Smith and Anderson presented a case report of a 51-year-old patient presenting with mild vertigo for several weeks, bilateral facial weakness and severe headache. Exam showed multiple central nerve deficits including bilateral central facial weakness and profound sensorineural hearing loss on the right.[12] This patient also exhibited MRI hyperintensities at the verebrobasilar junction, involving the intracanalicular, labyrinthine, geniculate, and tympanic segments of the seventh cranial nerve and the cisternal segment of the right seventh and eighth cranial nerves.[12] Thirty-one percent of patients with documented neurosyphilis have no abnormalities on neuroimaging with CT or MRI.[12] Our patient is distinct in from this patient in that he showed a single peripheral facial nerve palsy without central nerve palsy in the setting of meningismus.

3. Conclusions

Syphilis has varied presenting symptoms and has been shown to be increasing in prevalence with the HIV pandemic. Concomitant infections with both HIV and syphilis have also been shown to be increasing as are atypical presentations of syphilitic infection. Based on the data presented above, the threshold to test for both HIV and syphilis in patients presenting with atypical neurologic symptoms,

Table 1. The possible symptoms of tertiary syphilis. Phases of syphilitic infection often co-exist and tertiary syphilis is caused primarily by infiltrative small vessel endartitis, such as the vasa vasorum and the vasa nervorum.

Central neurologic	Meningismus, Headache, uveitis, vision loss, Argyll-Robertson pupil, hearing changes, tabes dorsalis,[3] seizures, neuropsychiatric, generalized paresis
Peripheral neurologic	Mononeuritis, hypotonia, hyporeflexia, sensory loss, paresthesias
Vascular	Stroke, aortic root dilatation

meningitis, ocular abnormalities, or newly diagnosed infections suggestive of immunosuppression should be low. Testing should include a VDRL and a lumbar puncture is indicated if the VDRL >1:32 to rule out neurosyphilis in the absence of symptoms. Atypical neurologic symptoms and a positive RPR should also prompt consideration for a lumbar puncture. CD4 counts may be helpful in determining the response to treatment but are typically not useful in determining co-infection. Syphilis may also independently lower the CD4 counts, with successful treatment leading to improvement of CD4 counts. Even in the HIV era, early neurosyphilis is a rare but real concern that warrants consideration in persons with unknown or high risk and atypical neurologic symptoms.

Disclosure statement

No potential conflict of interest was reported by the authors.

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