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Neurosyphilis presenting with a large vessel occlusion: A case report

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Abstract:

We describe a case of a 36-year-old man who presented with stroke in the right paramedian pons in the pontine perforator territory, manifesting as intermittent headache, slurred speech, left-sided weakness, and paresthesia. This case highlights the diagnostic challenge in identifying neurosyphilis as a cause of stroke in young individuals. Clinicians should maintain vigilance for this uncommon etiology through conducting a detailed history and investigation in susceptible patients with key risk factors. Once the diagnosis was confirmed in our case, a multidisciplinary approach was used for management with neurologists, infectious disease specialists, and the neurointerventional team. Our patient ultimately underwent successful therapy with mechanical thrombectomy for basilar artery thrombosis from meningovascular syphilis.

Keywords:

Infectious vasculitis, ischemic stroke, neurosyphilis, stroke in young adults

Introduction

Syphilis results from bacterial infection by *Treponema pallidum* (TP) and is a multisystem disease of individual and public health significance. The transmission mode is through sexual contact, transfusion of infected blood, and maternal-fetal passage in congenital infection. Risk factors for contracting the disease include men who have sex with men (MSM) and illicit drug use such as cocaine or methamphetamine.[1] The disease is progressive if untreated and divide into four stages: latent, primary, secondary, and tertiary syphilis.[2] Neurosyphilis is a form of central nervous system (CNS) infection seen on average in 1.5% of individuals with human immunodeficiency virus (HIV) infection, especially patients with low CD4+ T-cell counts and those not on antiretroviral therapy.[3] Lack of recognition and treatment may lead to various devastating neuropsychiatric complications ranging from symptomatic meningitis to general paresis and tabes dorsalis. While young patients admitted with ischemic stroke, clinicians should consider a high degree of suspicion for the rare entity of meningovascular syphilis (MVS) that can develop within a few months to years of initial infection.[4] An increased prevalence of HIV infection and noncompliance with highly active antiretroviral therapy (HAART) have led to the reemergence of syphilis in the past decade. However, prognosis is generally favorable with early detection through a detailed history, appropriate investigations, and timely management. In this case report, we present an HIV-positive young patient with focal neurologic deficit found to have MVS who underwent successful mechanical thrombectomy.

Case Report

A 36-year-old male with a past medical history of HIV/acquired immunodeficiency syndrome (AIDS) noncompliant with HAART presented with a 1-day history of

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left-sided weakness and slurred speech. In the morning preceding admission, he woke up with left-sided weakness and paresthesia that persisted, prompting him to visit the emergency department. He reported new-onset intermittent headaches that would awaken him from sleep during the preceding 3 months and an imbalance of 3 weeks' duration. There was no report of fever, head trauma, behavioral changes, bowel or bladder incontinence, or alteration of consciousness. He had no prior or family history of TIA or stroke. The patient had a male sexual partner and reported marijuana use but denied alcohol or tobacco use.

The patient was evaluated in the emergency room. Vitals signs were unremarkable, and the finger-stick glucose was 111. His National Institutes of Health Stroke Scale (NIHSS) was 3 for left leg drift, limb ataxia, and sensory loss. Computed tomography (CT) head was negative for acute intracranial hemorrhage or large territory infarction. He was not a candidate for any acute ischemic stroke therapy. On further history, he stated that he had stopped taking his HIV medication for approximately 2 months since he lost his provider.

During the hospitalization, he experienced rapid clinical deterioration in 12 h with NIHSS worsening to 6 for left upper extremity drift/sensory loss, left upper extremity dysmetria, dysarthria, and right lower facial weakness. CT angiography of head and neck demonstrated mid-basilar and left vertebral artery contrast nonopacification suggesting occlusion [Figure 1]. Magnetic resonance imaging noted acute infarction in right paramedian pons within the pontine perforator territory only [Figure 2]. Given the possibility of catastrophic brainstem infarction, basilar artery thrombectomy was pursued. The complete thrombolysis in cerebral infarction 3 was achieved using aspiration technique by selecting the basilar artery [Figure 3]. Blood work was notable for a slightly elevated D-dimer of 952, but otherwise showed normal hemoglobin A1c, lipid panel, inflammatory markers, and a negative hypercoagulable workup. Transthoracic echocardiogram was normal. His serum HIV-1 RNA was positive (viral load 45,700 copies/ml), absolute CD4 T cells were 9 (range: 535–1,451 cells/cu mm), and syphilis antibody was detected to 22.08 (ref range: <1.00) reflexed to TP particle agglutination (TP-PA) assay test was reactive with rapid plasma reagin (RPR) titer of 512 (ref range: nonreactive). This prompted a lumbar puncture and showed appearance: hazy, color: pale yellow, xanthochromia: present, nucleated cells: 568 (0–5/cu mm) (neutrophils: 73%, lymphocytes: 23%), red blood cell: 475 (0/cu mm), glucose: 18 (40–70 mg/dl), and protein: 122 (15–45 mg/dl).

Meningitis/Encephalitis polymerase chain reaction panel detected Cytomegalovirus (CMV) IgM.

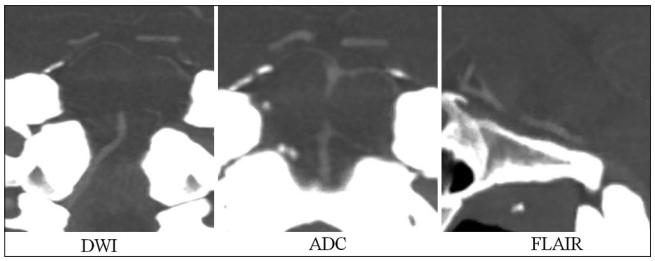

Figure 1: Computed tomography angiography revealing left vertebral artery occlusion in a proximal intradural segment without significant distal opacification. The midportion of the basilar artery demonstrates absent opacification across a 5.5 mm segment but opacified more distally from well-developed bilateral posterior communicating arteries

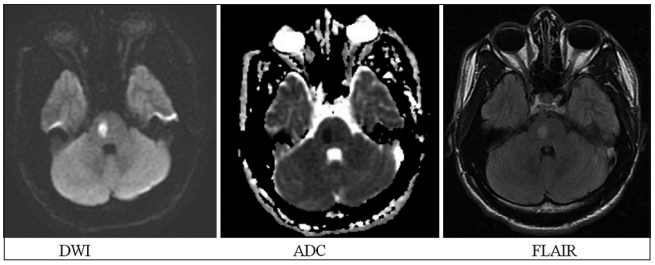

Figure 2: Magnetic resonance imaging image noting the absence of basilar artery flow void consistent with short segment occlusion and absent left vertebral artery flow void concerning for occlusion. Acute infarction demonstrated within right paramedian pons within pontine perforator territory

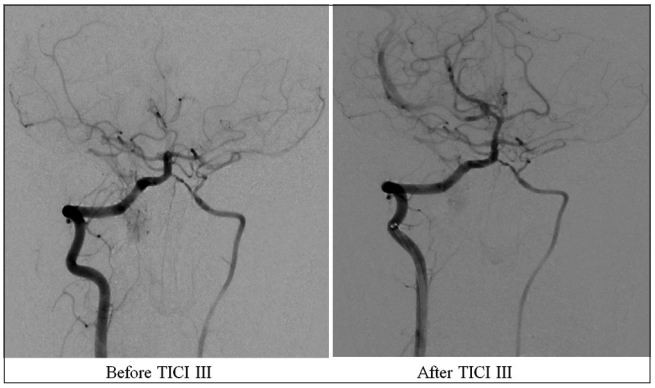

Figure 3: Complete recanalization (thrombolysis in cerebral infarction III) of the basilar artery vasculature was achieved following aspiration thrombectomy after two passes, using the thrombo-aspiration system

Cerebrospinal fluid (CSF) venereal disease research laboratory (VDRL) was reactive with a titer of 1:128 (ref range: nonreactive). This confirmed a diagnosis of MVS. Eventually, it was revealed that the patient had a history of latent syphilis treated with doxycycline 4 years before hospitalization due to penicillin allergy. HAART therapy was initiated, noting that his presentation was likely reinfection or unsuccessful treatment for syphilis during the past. He was started on IV ganciclovir for 14 days for CMV infection. He underwent successful penicillin desensitization and was commenced on IV penicillin G 4 million units every 4 h for 14 days. Treatment demonstrated a positive effect, and the

patient's strength and coordination improved clinically. As he refused a repeat lumbar puncture in the hospital, he was discharged with outpatient infectious disease and stroke clinic follow-up on aspirin 81 mg and atorvastatin 80 mg daily. At 3-month follow-up, his NIHSS was 1 for slight left upper extremity drift and the patient had returned to his baseline with no further neurologic symptoms.

Discussion

Syphilis has been recognized since the late 15th century. Still, the widespread use of antibiotics and the advent of public health measures in the past century led to a downward trend in the incidence of syphilis. After reaching a nadir in the late 1950s, rates of syphilis began to rise gradually. This marked resurgence was attributed to increased cases among MSM at the onset of the AIDS pandemic. A decrease in safe sex practices, increased recreational drug use, and a lack of adherence to HAART likely contributed to this pattern. The disease has a rapid and more aggressive course in patients with HIV infection, corresponding to atypical forms, including MVS. Neurosyphilis has been noted 7–10 years after initial infection with inadequate treatment.[5] Approximately 10% of the patients with neurosyphilis and 3% of all patients with syphilis present with ischemic stroke.[6] Stroke may be a complication of AIDS for a variety of other causes including infectious meningitides or vasculitides, altered coagulation, and cardioembolic events.[7] The rising incidence of stroke in young individuals leaves patients disabled in their most productive years and poses an increased risk of death relative to the general population. Primary and secondary prevention in conjunction with timely intervention is crucial for reducing disease burden.

In MVS, focal ischemia may lead to symptoms of stroke through the mechanism of vasculitis. Endarteritis obliterans affecting the brain's blood vessels, spinal cord, and meninges may lead to catastrophic ischemic injuries. Two categories of syphilitic vasculitis have been described in MVS. Huebner arteritis classically involves medium and large arteries with intimal fibroblastic proliferation, medial thinning, adventitial inflammation, and fibrosis.[8] A variant form known as Nissl-Alzheimer arteritis affects small vessels with intimal and adventitial thickening.[9] Both forms cause plasma cell and lymphocytic infiltration resulting in concentric narrowing and occlusion, which may induce cerebral infarction.[10] Cerebrovascular events in neurosyphilis frequently involve the anterior circulation such as the middle cerebral artery and its branches.[11] On occasion, the posterior circulation, including the basilar artery and branches, is impacted.

Preliminary workup includes nontreponemal testing with RPR and VDRL. These screening tests correlate with disease activity but lack sensitivity in early and late syphilis, often yielding false positives.[12] Serum RPR has a sensitivity of 78% and specificity of 85%, while VDRL has a sensitivity of 86% and specificity of 85%.[13] An RPR or VDRL titer of 1:8 or greater indicates syphilis.[13]

Confirmatory tests include fluorescent treponemal antibody absorption, which has the highest sensitivity for all stages, TP hemagglutination assays (TPHA and MHA-TP), and TP-PA. RPR or VDRL titer of 1:32 or > 1:8 with stroke or neurological symptoms indicates lumbar puncture and CSF analysis.[13] First-line therapy with penicillin G benzathine is recommended for all stages of syphilis with periodic follow-up CSF testing to ensure adequate treatment response. Ceftriaxone, which has good CSF penetration, has also been utilized as an alternate treatment for 10–14 days.[14]

Although MVS is a rare etiology of ischemic stroke, clinicians should maintain a high index of clinical suspicion in young individuals susceptible to syphilitic infection. A 2009 study by Feng *et al*. describes a case of MVS with vertebrobasilar occlusion and acute ischemic stroke.[15] The patient was managed with thrombolytic treatment and endovascular recanalization but ultimately succumbed to fatal pontine hemorrhage with transtentorial herniation.[15] Our case is a unique presentation of mechanical thrombectomy in treating MVS with a successful outcome. Acute stroke intervention with endovascular therapy demonstrated considerable benefit and improved outcomes in our patient promptly. However, it is important to note that mechanical thrombectomy may easily cause vessel rupture due to fragility from infection. In fact, there is limited data available regarding the safety of mechanical thrombectomy in infectious vasculitis. As there are no established safety guidelines on the use of intravenous tissue plasminogen activator and mechanical thrombectomy in the management of ischemic stroke caused by MVS, nevertheless this case would add valuable information to the existing current literature of infectious vasculitis.[16]

Conclusion

With the increasing incidence of neurosyphilis, young individuals presenting with ischemic strokes of unclear etiology should be tested for HIV and syphilis. A high index of suspicion should be reserved for patients who demonstrate the appropriate risk factor profile, including illicit drug use, and unsafe sexual practices. An incapacitating stroke is devastating to young adults in their most productive years and maybe easily averted with careful screening. It is crucial for clinicians to

consider MVS on the differential of CNS vasculitis as infectious etiologies maybe frequently overlooked. Due to similar radiographic features, MVS is sometimes misdiagnosed as primary CNS vasculitis. With timely detection and effective therapy with penicillin, physicians can prevent potentially disabling and fatal complications of untreated disease.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Patel had full access to all of the case report data and took responsibility for the integrity and accuracy of this case report.

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Conflicts of interest

There are no conflicts of interest.

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