The Silence of Neurosyphilis

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Introduction

Syphilis is a sexually transmitted infection. The infectious organism is a spirochete bacterium called *Treponema pallidum* subspecies *pallidum*. This organism also may transmit vertically in-utero from mother to fetus resulting in congenital syphilis. The following is a case report of tertiary syphilis in the form of tabes dorsalis. This case is of interest due to the rarity of late neurosyphilis in the immunocompetent host in the post-antibiotic era.[1]

Case Report

A 54-year-old African American male with no known medical problems presented to the emergency department during a snow storm, sitting and talking to himself in the waiting room. Dismissed by hospital security, he returned the next day and was evaluated. He denied the use of any medications except for acetaminophen. His social and family history was vague and non-contributory. He was afebrile, hemodynamically stable with laboratory results of leukocytosis and abnormal liver function tests. Computed tomography of the head without contrast (Figure 1) showed changes suggesting an acute stroke involving the left parietofrontal lobe with minimal extension into the posterolateral aspect of the temporal lobe. The patient was unable to provide a reliable history, appeared confused, and complained of dysgeusia, dizziness, blurred vision, headache, and right extremity weakness. He also complained of vague and poorly described lower extremity pain, dysuria, and orange-colored urine. He had nausea and vomiting for the previous three weeks.

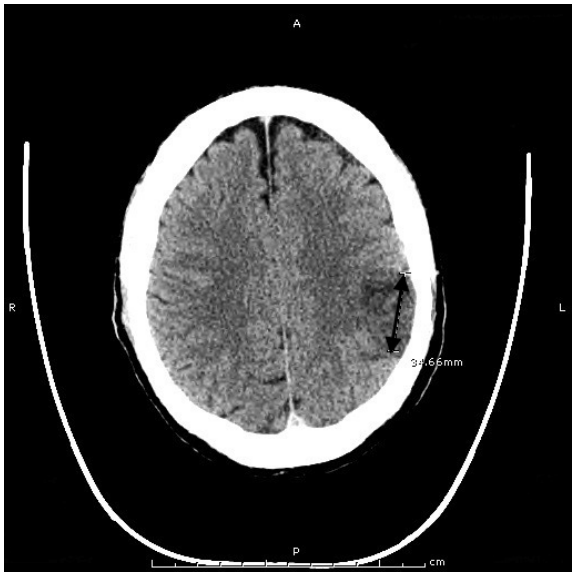

Figure 1. Abnormal geographic region of decreased attenuation in the left parietal frontal lobe. This may be reflective of an area of acute-to-subacute non-hemorrhagic infarct.

The patient was admitted to the hospital for a suspected stroke and further evaluation. The patient was alert with fluent speech but inappropriate word substitutions, neologisms, and moderate to severe

impairment of verbal comprehension. He manifested perseveration of verbal responses, anomia, dysgraphia, and he was unable to repeat sentences.

His pupils were equal, round, and reactive to light. Extraocular movements demonstrated an increase in horizontal nystagmus bilaterally and a few beats of vertical nystagmus with upward gaze. Visual fields were full and visual acuity was 20/100 O.S., 20/100 +1 O.D., without glasses using a pocket card. Facial sensation was normal with no facial weakness. Hearing for whispered numbers was normal. His tongue was at midline and no dysarthria was noted.

Strength in both upper and lower extremities and rapid alternating and fine motor movements were normal. He manifested mild postural tremor and intention tremor with finger-to-nose testing. The sensory examination was unreliable. Deep tendon reflexes were only trace in the upper extremities and at the knees but symmetrical. Plantar responses were equivocal bilaterally. His feet were swollen, firm, non-tender, and non-erythematous, with slight black discoloration of the pedal digits (Figure 2). The swelling extended above the ankles bilaterally.

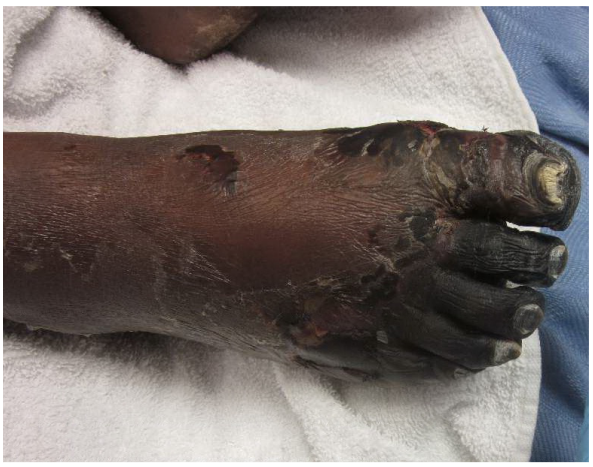

Figure 2. Gangrene of the right foot.

Laboratory results (Table 1) demonstrated an elevated white blood cell count, renal insufficiency, elevated creatine phosphokinase (CPK) consistent with acute rhabdomyolysis, and positive serology for syphilis. Emphysematous changes were noted on chest x-ray.

The patient developed a fever to 103.3^{o}F and became tachycardic and hypotensive, fulfilling Systemic Inflammatory Response Syndrome criteria.[2] The patient was transferred to the ICU and treated with IV fluids, vasopressors, and antibiotics after appropriate cultures were obtained. The CPK recovered with intravenous fluids and bicarbonate. An arterial ultrasound of the lower extremities showed absence of pedal pulses bilaterally. An orthopedic surgeon recommended pedal digit amputation secondary to wet gangrene as a complication of frost bite.

A magnetic resonance image (MRI) of the brain (Figure 3) displayed a subacute infarct in the distribution of the posterior division of the left middle cerebral artery. A magnetic resonance angiogram (MRA) showed mild distal carotid arterial atherosclerosis without other angiographic abnormality (Figure 4). Trans-esophageal echocardiogram and carotid ultrasound were unremarkable.

The patient was diagnosed with a stroke secondary to neurosyphilis-induced vasculitis and possible tabes dorsalis to explain the mostly painless nature of the wet gangrene of the toes. Therapy was initiated with penicillin G continuous infusion for three weeks with levofloxacin and metronidazole for the gangrene. The patient underwent bilateral pedal digit amputation with debridement and skin graft and was placed in a nursing home for physical rehabilitation. One-month after discharge, patient was readmitted for surgical debridement of his amputation. He had no improvement of his cognitive status.

Table 1. Laboratory results.

Complete Blood Count with Differential	
WBC	15.6 K/mcgL
Neutrophils	84%
Lymphocytes	7%
Monocytes	9%
Hemoglobin	14.3 g/dL
MCV	80.4 fL
Platelets	269,000 K/mcgL
Metabolic Panel	
Glucose	104 mg/dL
BUN	57 mg/dL
Creatinine	2.39 mg/dL
Calcium	8.6 mEq/L
Sodium	134 mEq/L
Potassium	3.8 mEq/
Chloride	98 mEq/L
CO2	22 mEq/L
Albumin	3.4 gm/dL
Total Bilirubin	1.8 mg/dL
ALK	88 U/L
ALT	182 U/L
AST	640 U/L
INR	1.3
AG	14

Specialty Tests	
Troponin	0.31 ng/mL
TSH	1.13 uIU/mL
CPK	CPK 26764U/L
Acetaminophen	<10 mcg/mL
Urine Drug Screen	Negative
ANA	Negative
Sexually Transmitted Infections	
HIV	Negative
Hepatitis Viral Panel	Negative
RPR	Reactive 1:64
Syphilis Ab IgG	Positive
Syphilis Ab IgM	Negative
Cerebrospinal Fluid	
Color	Clear
RBC	128 /mm3
WBC	2 /mm3
Neutrophils	32%
Lymphocytes	42%
Monocytes	26%
Gram stain	No organisms
Culture	No growth
VDRL	Positive 1:16
AFB	Negative
Protein	47 mg/dL
Glucose	66 mg/dL

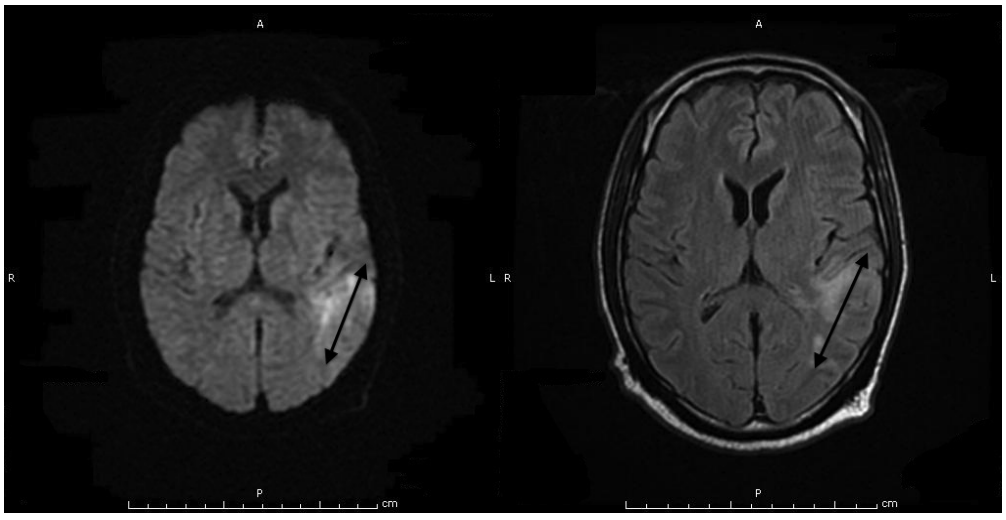

Figure 3. (Left) The T2 Flair demonstrates high signal in the left temporal parietal region and (Right) the diffusion study shows high signal on T2 Flair due to cytotoxic edema.

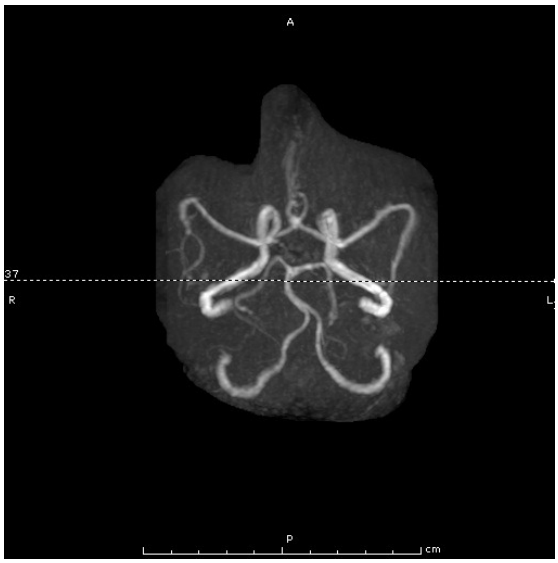

Figure 4. MRA showed no vascular occlusion in the posterior left middle cerebral artery distribution.

Discussion

Medical advancements during the 20th century have included antibiotics which have enabled physicians to provide potential cures for infections. *Treponema pallidum* subspecies *pallidum* is a bacterium under the spirochete family, taking its name from its microscopic appearance.[3,4] T. *pallidum* is a sexually transmitted infection that progresses through four stages: primary, secondary, tertiary, and latent. The former three stages usually occur within one year of inoculation. When transmitted in-utero, the infection is referred to as congenital syphilis.

Primary syphilis manifests after 2-3 weeks incubation after infection. A painless papule appears at the site which ruptures into a painless chancre ulcer with indurated margins and a non-exudative base.[3] Bilateral regional lymphadenopathy then develops. Patients tend not to address these lesions because they are painless and feel embarrassed to expose themselves. Chancres eventually heal within 3-6 weeks, while the spirochete disseminates freely.

Secondary syphilis may develop in 25% of those infected and usually is seen 3-6 months after the resolution of the chancre.[4] It most commonly presents as diffuse symmetric maculopapular lesions that occur non-sparingly over the body, including palms and soles.[5] There is also systemic constitutional symptoms and diffuse lymphadenopathy as well other skin, gastrointestinal, hepatic, musculoskeletal, renal, and ocular manifestations. It is during secondary syphilis where the cerebrospinal fluid is infiltrated.[3]

Tertiary syphilis, also known as late syphilis, includes neurosyphilis which presents with gummas, described as ulcers or an aggregation of granulomas that may occur anywhere in the body, from skin to bone.[6] Heart manifestations are usually dilatation and calcification of the aortic root and arch in addition to coronary artery narrowing with potential thrombosis.[7]

Neurosyphilis presents depending on the affected region of the nervous system.[8] Early neurosyphilis usually involves the cerebrospinal fluid (CSF), meninges, and vasculature and may either be asymptomatic or symptomatic. Late neurosyphilis usually affects the brain and spinal cord. Asymptomatic neurosyphilis may occur any time after infection but usually within

months and may be diagnosed if the CSF white blood count is more than 5 cells/μL or protein more than 45 mg/dL.

Symptomatic neurosyphilis usually occurs within the first year after infection and may present with typical meningitis-like symptoms, such as headache, nausea, vomiting, altered mental status or confusion, audiovisual impairments, and stiff neck.[8] Patients also may develop arteritis with small, medium, or large vessel disease potentially causing ischemia or infarction of brain and/or spinal parenchyma and gummas that may induce seizures.

Late neurosyphilis may present with general paresis and tabes dorsalis.[8] General paresis may have a normal neurologic examination but common abnormal findings include dysarthria, intention tremors of the face, tongue, and hands, as well as reflex abnormalities. Cerebrospinal fluid will show a reactive Venereal Disease Research Laboratory (VDRL) result of 25 to 75 cells/μL lymphocytes and 50 to 100 mg/dL protein. Atrophy is seen on neuroimaging.

Tabes dorsalis is a process that usually does not manifest until 20 years post infection and involves the dorsal columns and dorsal roots of the spinal cord.[8] Patients present with sensory abnormalities and/or lancinating pains affecting the face, back or limbs. Patients also may develop paresthesias, absent lower extremity reflexes, depressed vibratory and position sensation, attenuated touch and pain, and gastric crises which manifest as recurrent nausea, vomiting with severe epigastric pain. Argyll-Robertson pupils is one of the most common presentation in tabes dorsalis, and less so in general paresis. CSF may be normal or show 10 to 50 cells/μL lymphocytes and 45 to 75 mg/dL protein.

Our patient had a positive rapid plasma reagin with positive IgG and negative IgM syphilis antibodies representing active or recently treated syphilis. CSF findings also supported a diagnosis of late neurosyphilis. Clinically, the patient had a stroke secondary to a vascular occlusion to the left middle cerebral artery. The etiology of the vaso-occlusion is uncertain but most likely leans towards a vasculitis secondary to syphilis. The T. *pallidum* aggregate around any subarachnoid vessel, surrounding the brain or spinal cord, causes an influx of lymphocytes and plasma cells which infiltrate the arterial wall and perivascular tissue.[8] As the infectious inflammation progresses, the potential cascade of vasoconstriction complicated with vascular obliteration occurs after the release of pro-thrombotic reactants by the damaged vascular endothelium (Figure 3).

Our patient had peripheral neuropathy described as paresthesia, absent lower extremity reflexes with decreased sensation. His depressed level of sensorium did not allow him to recognize that he had suffered from frostbite and gangrene. He also complained of food tasting awful associated with nausea and vomiting. The constellation of symptoms manifested by our patient may fall under the umbrella of tabes dorsalis, amongst other possible diagnoses. A reliable history from this patient was difficult to ascertain, especially regarding how recently he had been infected with syphilis. Therefore, the possible diagnosis of tabes dorsalis cannot be ruled out.

Conclusion

Meningosyphilis is an uncommon cause of stroke in the post-antibiotic era. In untreated neurosyphilis, meningosyphilis is found in 10% of cases.[9] Its pathophysiology involves vasculitis of any vessel in the subarachnoid space with extension into the perivascular tissue resulting with ischemia and infarct. Diagnosis is made with a positive CSF-VDRL test and treatment is 18-24 million units of penicillin G infused daily for two weeks.[3]

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