Meningovascular Syphilis in a Young Female: A Case Report

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Abstract

Background

Meningovascular syphilis is a rare manifestation of syphilis caused by an inflammatory endarteritis that leads to luminal obstruction (rarely aneurysm develops) of the blood vessels supplying the leptomeninges, brain and spinal cord resulting in infarction of distal neural tissues. This makes a combined syndrome of chronic syphilitic meningitis, cerebrovascular and/or myelovascular events.

Case Presentation

We present a case of 20-year-old unmarried female with prodromal symptoms followed by features of stroke, which was later diagnosed as meningovascular syphilis.

Conclusions

In the era of antibiotics, very few studies regarding meningovascular syphilis have been reported. Given the low incidence of MVS and the possibility of it being misdiagnosed as other causes of stroke, a high index of suspicion is crucial, particularly in young adult patients with CNS sign or symptoms and history of painless genital lesions.

Keywords: *neurosyphilis, infarction, stroke.*

Introduction

Luminal obstruction of the arteries supplying the leptomeninges, brain, and spinal cord causes distal neural tissue infarction in meningovascular syphilis (MVS).[1,2,3] This results in a mixed syndrome of chronic syphilitic meningitis, cerebrovascular, and/or myelovascular events.[2] Few studies highlighting meningovascular syphilis have been reported in the era of antibiotics. We present a case of a 20-year-old unmarried girl with prodromal symptoms and stroke-like characteristics who was ultimately found to have meningovascular syphilis.

Case Report

A 20-year-old unmarried female came to our hospital with sudden onset of dull headache, localized to the parietal area. The patient also complained about dizziness, nausea, vomiting, and orbital ache. She had a history of several episodes of vomiting which

was watery without bile or blood. The patient denied having a fever, blurring of vision or any history of trauma, diabetes or hypertension. According to the patient's mother, eight months prior, she had a painless lesion over her genitalia characterized as itchy which healed spontaneously after 2 months in the absence of treatment. She had visited emergency previously 2 weeks back with similar symptoms which was relieved with pain killer. The patient had altered sensorium as confusion, disorientation, amnesia, nervousness, personality changes, hostile attitudes, aggressive behaviors, hallucinations, and illusions. Her Temperature was 98.9 degrees Fahrenheit, pulse was 100 beats per minute, respiratory rate was 20 breaths per minute, blood pressure was 110/90 mm of Hg, and saturation was 94% in room air. Pupils were equal, dilated at 4mm, and reactive to light. She was disoriented to time, place and person. On motor examinations, bulk tone and power of both upper and lower limbs are within the limit. The plantar reflex and other reflexes were intact. Sensory examination could not be performed. Besides the neurological examination, the rest of the system examination yielded no significant findings.

Initial laboratory investigations included routine complete blood count (CBC), renal function test (RFT), liver function test (LFT) which were non-significant. Basic metabolic panel reports were within normal range. However, the patient's TSH was elevated to 16.28 mU/L (milliunits per liter). Her Vitamin B12 level was decreased to 143 ng/L (nanograms per liter). MRI Brain was performed which showed evidence of diffusion restriction at the posterolateral aspect of the left thalamus-likely to be an acute infarct [Figure 1]. MRI finding suggested an ischemic stroke. Serology tests for HBsAg, HCV and HIV were non-reactive. Since she gave history of genital lesion in the past, serum rapid plasma reagin (RPR) was sent which came out to be positive which was further confirmed by Treponema pallidum hemagglutination assay (TPHA). She underwent lumbar puncture and cerebrospinal fluid was collected for analysis. CSF Total count was 79 cell/cum with Lymphocytes predominant i.e., 100% which are illustrated in (Table 1).

Table 1. Cerebrospinal Fluid analysis.

Parameter	Result
Volume	1 ml
Color	watery
Transparency	Clear
Total WBC count	79 cells/cum
Differential counts	
Neutrophils	00
Lymphocytes	100
Monocytes	00
Eosinophils	00
Basophils	00

Biochemical and microbiological tests for CSF analysis showed remarkable protein level, prominently low glucose level with plenty of pus cells. No organisms were visualized on gram stain. Culture and sensitivity yielded no growth after 48 hours of incubation. Acid-fast Bacilli stain was negative. The Venereal Disease Research Laboratory (VDRL) test on CSF analysis was reactive. CSF PCR qualitative analysis were tested negative for HSV-1 DNA and HSV-2 DNA. The results are illustrated in (Table 2).

Table 2. Biochemical and Microbiological tests for CSF analysis.

Tests	Result	Reference Range
Protein CSF	155 mg/dl	Adult < 60 years: 15-45; Adult >60 years: 30-60;
Sugar, CSF	10 mg/dl	40.0 - 80.0
ADA	9 U/L	Serum: < 18.0 Pleural fluid: <33.0 Ascitic Fluid: < 30.0 CSF: <10.0
Gram Stain	Pus cells have plenty/ no microorganisms	
Culture and Sensitivity Report	No growth after 48 hours of incubation at 37 degrees Celsius	
AFB Stain	No Acid-fast bacilli seen	
VDRL	Reactive	
CSF HSV- 1 and HSV-2 DNA PCR	Negative	

Patient was admitted in ICU with provisional diagnosis of acute ischemic infarct with meningoencephalitis. On the day of admission, Empirical antibiotics regimens were commenced. She was given ceftriaxone, Acyclovir and vancomycin and the next day ampicillin was added to the existing antibiotic regimen. She was managed with aspirin along with atorvastatin on view of acute ischemic infarct. She was managed with Levothyroxine

75 milligram for hypothyroidism and supplemented with methyl cobalamin 1000mcg for Vitamin B12 deficiency. Patient was managed with above mentioned drugs. However, after CSF reports, antiviral and other antibiotics were held except ceftriaxone. In view of stroke at a young age, other investigations like RA factor, ANA, Serology for HIV, HCV, hepatitis B, natural anticoagulant level and vasculitis markers were sent (Table 3).

After VDRL and TPHA reports, the patient was diagnosed with neurosyphilis particularly meningovascular neurosyphilis.

Table 3. Biochemical and Microbiological tests for Serum analysis.

Parameters	Patient's value	Reference
RA factor	Negative	
ANA	Negative	
HIV	Non-reactive	
Hepatitis B	Non-reactive	
HCV	Non-reactive	
Protein S Functional/ Activity	22	55-123
Protein C, Functional	>155	70-140
Homocysteine	6.90	4.44-13.56
c-ANCA	Negative	
p-ANCA	Negative	

Despite our best efforts, we were unable to provide our patient with crystalline penicillin because it was not readily available in our country. Patient initially showed some improvement with ceftriaxone and steroids but eventually her condition deteriorated. The patient's condition deteriorated on day 14 after admission. Following a generalized tonic-clonic seizure, the patient's GCS score was E2V3M2. The seizure was treated with midazolam, and the patient was immediately intubated and managed with medications. A repeat MRI was planned, but unfortunately, it could not be performed on the same day. Her pupil was dilated to 4.5mm. Babinski's sign was positive. One day after intubation, a brain MRI with MRA contrast was done which demonstrated tonsillar herniation, effacement of visualized sulci and cisterns and diffuse high signal intensity in cerebral and cerebellar cortex consistent with diffuse brain oedema (Figure 2). The patient's vitals and GCS got deteriorated. In time, she passed away.

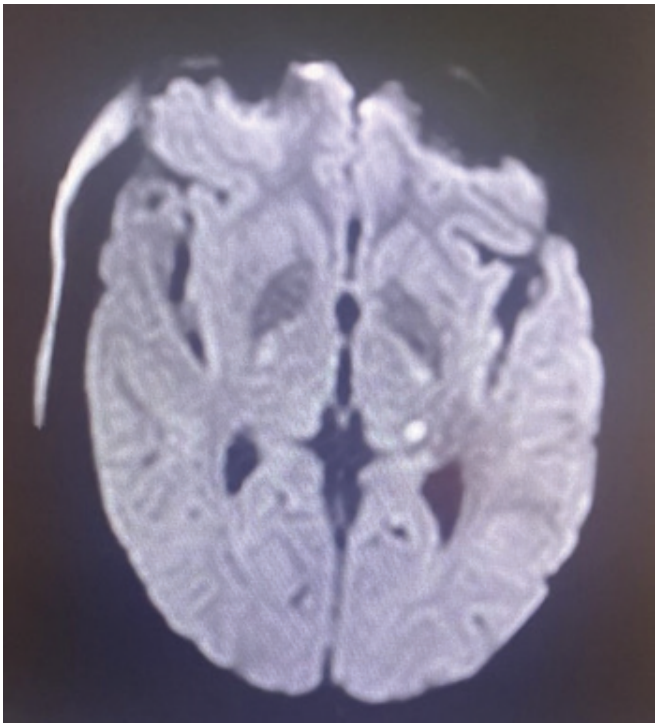

Figure 1. *Axial DWI image shows diffusion restriction at posterolateral aspect of left thalamus s/o infarct.*

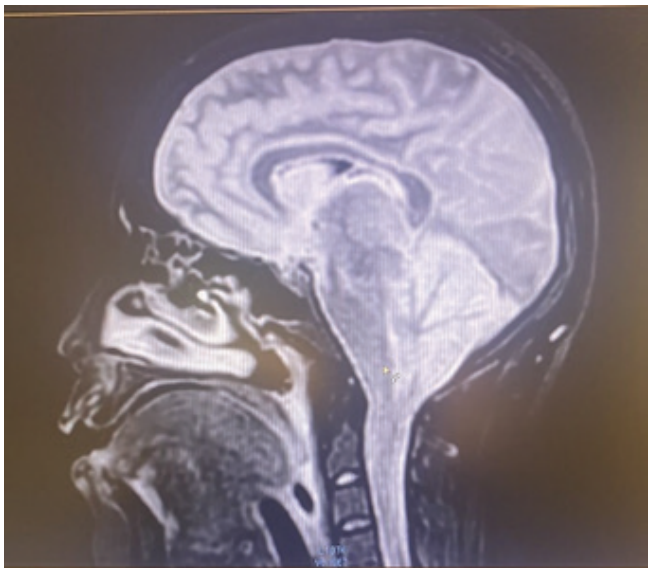

Figure 2. *Sagittal FLAIR image shows tonsillar herniation, effacement of visualized sulci and cisterns and diffuse high signal intensity in cerebral and cerebellar cortex consistent with diffuse brain oedema.*

Discussion

According to WHO, incidence and prevalence of syphilis were 19.9 million and 6.3 million respectively in adolescents and adults aged 15 to 49 years.[4] Treponema pallidum elicits innate and adaptive cellular immune responses with lesional infiltration of polymorphonuclear leukocytes which are replaced by T lymphocytes later.[5] The initial clinical manifestation of syphilis is a localized painless, indurated skin lesion called "chancre".[6] Our patient also had had a chancre

which was itchy on her genital before she developed neurosyphilis. Chancre usually heals on its own within three to six weeks even in the absence of treatment.[7] The exact mechanism of healing is unknown.[7] In our patient, the painless genital lesion got healed spontaneously in the absence of treatment.

Neurosyphilis begins when treponema invades cerebrospinal fluid (CSF).[8,9] The organism can be isolated from the CSF in nearly one-quarter of untreated patients with early syphilis.[8,9] The more abnormal the CSF in asymptomatic meningitis, the more likely that symptomatic neurosyphilis would develop.[10] Our patient also did have asymptomatic meningitis with abnormal CSF. Study of nonhuman primates infected with T. Pallidum showed that the number of CSF CD4+ T cells and the amount of gamma-interferon produced by CSF lymphocytes are consistent with a "Th-1-type" cellular immune response.[11] Neurosyphilis was common in the pre-antibiotic era wherein approximately one-third had asymptomatic neurosyphilis, one-third had tabes dorsalis, and at least 10 percent had meningovascular syphilis.[1,6]

Meningovascular syphilis(MVS) is caused by an inflammatory obliterating endarteritis and subsequent luminal obstruction(rarely aneurysm develops) of the blood vessels supplying the leptomeninges, brain and spinal cord leading to distal neural tissue infarction.[1,2,3] This makes a combined syndrome of chronic syphilitic meningitis, cerebrovascular and/or myelovascular events.[2] Around a quarter of patients with MVS have prodromal symptoms like intermittent headaches, vertigo, insomnia or behavioral changes prior to the ischemic event.[2,12] The patient presented to the emergency department on two occasions with symptoms of a headache, which were managed with painkillers (probably features of asymptomatic meningitis). Altered sensorium as confusion, disorientation, amnesia, nervousness, personality changes, hostile attitudes, aggressive behaviors, hallucinations, and illusions prior to ischemic events were also developed by our patient.

A reactive serologic test for syphilis with reactive VDRL in cerebrospinal fluid (CSF) is the definitive diagnosis of neurosyphilis.[13] Serum rapid plasma reagin (RPR) was positive in our patient which was further confirmed by Treponema pallidum hemagglutination assay (TPHA). Recommended regimen for primary lesion in adults is a single dose of 2.4 million units of IM injection of benzathine penicillin G.[14] Injection benzathine penicillin G, even at high dose, does not produce adequate CSF concentration for bactericidal effects.[15] Prospective multicentric randomized controlled clinical trial has been ongoing in China which is comparing injection aqueous crystalline penicillin G(ACPG) vs injection ceftriaxone for the treatment of neurosyphilis.[16] So, we cannot say whether ceftriaxone is superior to ACPG. However, patients treated with ceftriaxone have lesser hospital stay burden.[16] Good blood brain barrier penetration property of ceftriaxone makes it the best alternative to ACPG.[16] In our case due to unavailability of inj. ACPG in our institution, injection ceftriaxone was used for the treatment of neurosyphilis. With the commencement of the ceftriaxone therapy, the patient initially showed good response but later her condition deteriorated and she died. It's important to note that meningovascular syphilis is a rare disease, and proper diagnosis and treatment are essential to prevent serious complications.

Conclusion

In the era of antibiotics, very few studies highlighting MVS have been reported. Moreover, MVS may be misdiagnosed as other ischemic or hemorrhagic causes of stroke. So, when a young adult population with a prior history of painless lesion over genitals come with CNS manifestations following prodromal symptoms, possible diagnosis like meningovascular syphilis should not be missed out and antibiotic treatment should be started promptly to prevent serious complications.

Consent

Written informed consent was obtained ensuring patient's anonymity.

Declaration of competing interest

There are no conflicts of interest.

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