

Meningovascular neurosyphilis: a report of stroke in a young adult

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Key words: neurosyphilis; stroke; young adult.

Summary. A young adult patient with meningovascular neurosyphilis in the form of acute ischemic stroke with right hemiparesis and speech disturbance is reported. CT scan showed features of ischemic infarct and extensive laboratory studies were made before the diagnosis ultimately was revealed. Such cases could result in confusion for the clinician, and high index of clinical suspicion of this condition is required since syphilis is not routinely tested, as routine screening is seen to be of low diagnostic yield. As clinical practice indicates, it remains a difficult problem approaching diagnosis of neurosyphilis, and this is achieved through exclusion of neurosyphilis as a clinical possibility.

Introduction

Syphilis is a chronic multisystem infection caused by a thin, spiral, motile organism, *Treponema pallidum* spp. *pallidum*. Sexual contact with an infected individual is followed by an incubation period averaging about 3 weeks (1).

The infection, if untreated, passes through primary, secondary, latent, and tertiary stages (1, 2). Even though this illness is self-limited after the initial stage and may go undetected, some untreated individuals may suffer devastating consequences known as tertiary syphilis (3).

Late or tertiary neurosyphilis occurs in less than 10% of untreated individuals with syphilis, where meningovascular neurosyphilis comprises about 3% (1, 3). It is certainly true that neurosyphilis nowadays is a rare disorder in the developed world except in the context of human immunodeficiency virus infection and, in fact, may be overlooked as its prevalence has been drastically reduced with the advent of penicillin therapy (3–5). However, it is still a common illness in developing countries (4, 6). For example, according to the Lithuanian Health Information Center, the prevalence of syphilis in Lithuania decreased from 101.4 cases per 100 000 population in 1996 to 9.4 cases per 100 000 in 2008 (7). Unfortunately, prevalence data on neurosyphilis are unavailable. It should be emphasized that, actually, the resurgence of syphilis is being observed in many industrialized countries such as the United States, Canada, and United Kingdom, where outbreaks either have occurred recently or are currently occurring. This rise may be linked, in part, to individuals who are immunocompromised because of infection with HIV (5, 6). It has been suggested that HIV-infected individuals are more likely to develop

clinical neurosyphilis and this happens after shorter latent period compared to non-HIV-infected ones (1, 8). One may logically anticipate an increase in neurosyphilis prevalence (5, 9). Neurosyphilis can manifest as a stroke-like syndrome (10), intracranial space-occupying lesion (11), dementia (12) and psychosis, or as movement disorders and also can mimic amyotrophic lateral sclerosis, spinal cord compression, or transverse myelitis (13).

Many authors state that syphilis appears to be the “great imitator” of other diseases (3, 5), and in this case report, we present a case of meningovascular syphilis in the form of acute ischemic stroke in a young adult patient.

Case report

A previously healthy 30-year-old man was admitted to the hospital with a sudden onset of speech disturbance, right-sided weakness, and mild right facial weakness. A day before admission, the patient had experienced a slight disturbance of right arm movements. His medical history was remarkable with a tick bite around 6 months ago. There was no history of diabetes, hypertension, head injury, or intravenous drug abuse. The patient had spent two and a half years abroad before coming back home four months ago. On admission, he had been married for 6 years.

During general physical examination, the patient was subfebrile (body temperature, 37.1°C). His blood pressure was 120/80 mm Hg; the pulse was 86 beats per minute. Rest of his general examination was unremarkable. Neurologic examination revealed 2/5 muscle strength in the right arm, and muscle strength in right lower limb was 1/5. The patient showed a Babinski sign. There were no signs

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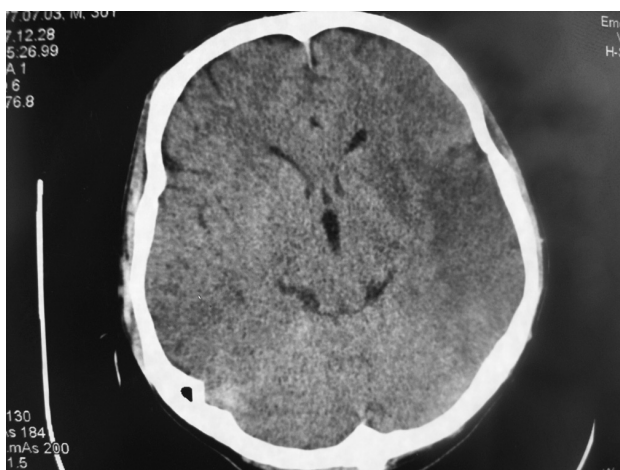


Fig. 1. Noncontrast computed tomography of the brain revealing a region of hypodensity on the left, around sylvian fissure that involves white and gray matter, consistent with infarction

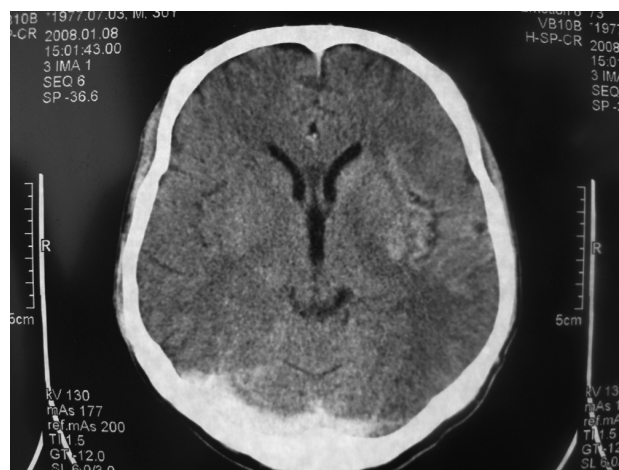


Fig. 2. The contrast-enhanced image showing decreased hypodensity regions

of meningeal irritation. The mental state was normal. Both computed tomography (CT) of the head obtained on admission and contrast-enhanced CT, which was performed later, showed hypodensity consistent with infarction (Figs. 1 and 2). Investigations revealed normal hemoglobin level and total leukocyte count. Serum biochemical parameters were normal. C-reactive protein (CRP) was 2.5 mg/L; however, erythrocyte sedimentation rate (ESR) was elevated – 37 mm/h. Other parameters were as follows: cholesterol level, 3.08 mmol/L; low-density lipoproteins (LDLP), 2.03 mmol/L; high-density lipoproteins (HDLP), 0.89 mmol/L; and triglycerides (TG), 1.79 mmol/L. Coagulation profile was as follows: SPA, 55%; partial thromboplastin time (PTT), 37 s; and international normalized ratio (INR), 1.36. The findings from electrocardiography and chest radiography were normal. Echocardiography (transthoracic) was performed. No pathology was found. Neuro-ophthalmologic examination showed normal findings. Transcranial Doppler (TCD) revealed inadequate segments of cerebrovascular circulation of the left middle cerebral artery. Carotid duplex scanning showed no abnormalities. Results of specific blood tests were as follows: herpes simplex virus DNA, –; anti-neutrophil cytoplasmic antibodies (ANCA, 1:20), –; antinuclear antibodies (ANA, 1:40), 1+; antiphospholipid antibodies (APLAs), >112.0 GPLU/mL (normal ratio, <19 GPLU/mL); anti-TBE IgM and IgG (tick-borne encephalitis), –. Antibodies against *Borrelia burgdorferi* were not detected. Results of cerebrospinal fluid (CSF) analysis showed a prominent lymphocytic pleocytosis (47 cells, 78% lymphocytes per mm³) with markedly elevated protein levels (1.26 g/L). The results of serum rapid plasma reagin (RPR) test were positive (1:1024), confirmed by a *Treponema pallidum* hemagglutination assay (TPHA), 4+. The results of

Venereal Disease Research Laboratory (VDRL) test of CSF were positive (1:16). The patient was human immunodeficiency virus negative. The wife of the patient was tested as well with serum RPR and TPHA; the results came back negative.

The patient was treated with penicillin intravenously at a dose of 4 million units 6 times a day for two weeks together with prednisolone to prevent the occurrence of Jarisch-Herxheimer reaction. Treatment showed a positive effect. Clinically, the patient became afebrile and his condition slowly improved. He did not show up for repeat examination.

Discussion

Neurosyphilis is seen in the tertiary and occasionally in the secondary stages of the infectious syphilis and has a diverse clinical presentation (1). Treponemes usually invade the CNS within 3 to 18 months of inoculation with the organism (9). Inflammation due to infection leads to endothelial swelling, and lymphocyte- and plasma cell-predominant tissue response. In the CNS, lymphocytic pleocytosis involving lymphocytes, plasma cells, and occasional polymorphonuclear leukocytes occurs predominantly. The humoral immune response to syphilis predominates only in the first several weeks of infection and later is transformed into a T-cell predominant cellular response. T helper-stimulated macrophages play a crucial role in the eradication of spirochetes (1).

Our patient was considered as having neurosyphilis in the tertiary stage as cutaneous lesions, which are characteristic of the secondary stage of the disease, were not observed, and there was no sexual transmission of the infection to the wife of the patient. Diagnosis was disclosed in close collaboration with a dermatovenerologist.

The major forms of neurosyphilis are syphilitic

meningitis, meningovascular syphilis, parenchymatous syphilis, and gummatous syphilis (1, 3). With the advent of penicillin therapy, neurosyphilis more frequently manifests as meningeal and vascular syndromes, not as abnormalities of the CNS parenchyma (4). Meningovascular syphilis comprises up to 30% of all cases of neurosyphilis, and the middle cerebral artery is the most commonly involved (1, 9). Meningovascular neurosyphilis is an inflammatory process that results from the development of typical endarteritis obliterans in small blood vessels of the meninges, brain, and spinal cord and leads to multiple small areas of infarction (5). It may result in focal neurologic deficits or global CNS dysfunction. The symptoms, which include hemiplegia, insomnia, personality changes, and dementia, may appear from months to a decade after the primary infection (14). Diagnosis of neurosyphilis could be established if there is a syndrome consistent with neurosyphilis, investigations of CSF cell count and protein concentration, and test of nontreponemal antibody as well as serologic treponemal antibody testing are made (3, 14). Suspicion of the underlying chronic infection was due to elevated body temperature and increased ESR. CSF analysis showed lymphocytic pleocytosis with elevated protein concentration. It is considered that CSF cell count best reflects neuro-

syphilitic activity (15). Results of serologic TPHA, RPR, and CSF VDRL tests performed in our patient were positive. Even though it is widely assumed that CSF VDRL test is sufficient to diagnose neurosyphilis, there is no gold standard for such diagnosis (4). Many authors are reluctant to rely only on the CSF VDRL tests for diagnosing active neurosyphilis (1). This test has a high specificity; however, the reported sensitivity of the test for diagnosing neurosyphilis is between 30% and 70% (1, 5). Our patient had elevated antiphospholipid antibodies, and it is known that this condition may be associated with false-positive VDRL results (16); however, the role of syphilis in such neurological manifestation was supported by positive serum serology in addition to specific results of CSF analysis. The elevated antiphospholipid antibody titers could be the result of an underlying chronic infectious disease where syphilis is the most common one (17).

Neurosyphilis is a treatable disease with a favorable outcome. However, the diagnosis of neurosyphilis remains a challenge, as it requires a high index of suspicion. In conclusion, we underscore again the importance of considering such diagnosis in young patients presenting with stroke, and syphilis screening tests should be reincorporated into the diagnostic workup if clinical features are outlined.

Meningovaskulinis neurosifilis: insultas, įvykęs jauno amžiaus pacientui

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Raktažodžiai: neurosifilis, insultas, jaunas amžius.

Santrauka. Straipsnyje aprašomas klinikinis meningovaskulinio neurosifilio atvejis, kai jauno amžiaus pacientui buvo diagnozuotas ūminis išeminis insultas su dešinės pusės hemipareze ir kalbos sutrikimu. Išeminis insultas buvo patvirtintas kompiuterinės tomografijos duomenimis. Atlikta daug ir įvairių laboratorinių tyrimų siekiant nustatyti jo priežastį. Tyrimai dėl sifilio panašių klinikinių atvejų metu jau nebedaromi dėl minimalios jų diagnostinės vertės. Tokios situacijos dažnai kelia daugybę klausimų ir dvejonių gydytojams, todėl klinikinis įtarimas yra vienas svarbiausių aspektų, pagreitinančių neurosifilio diagnostiką. Klinikinė praktika rodo, kad tokiems įtarimams paprastai nėra pagrindo, todėl dažniausiai neurosifilio diagnozė nustatoma atmetimo būdu atsižvelgiant ir į tokią klinikinę galimybę.

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Received 4 September 2008, accepted 6 April 2010
Straipsnis gautas 2008 09 04, priimtas 2010 04 06