CASE REPORT

Neurosyphilis presenting with a stroke-like syndrome

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SUMMARY

Neurosyphilis results from infection of the central nervous system (CNS) by *Treponema pallidum*. Neurosyphilis can occur at any time after initial infection, particularly in immunocompromised patients. We describe a case of a 47-year-old man who presented with mixed dysphasia, right upper motor neuron facial palsy and right hemiparesis. Collateral history from the family revealed slowly progressive cognitive impairment and behavioural changes. Neuroimaging was unremarkable, suggesting a non-vascular aetiology. As there was no clear cause for the presentation, a lumbar puncture was performed and serum samples were sent for syphilis serology. The diagnosis of neurosyphilis was made on the basis of a positive RPR test in cerebrospinal fluid. The patient was treated with benzylpenicillin and made a full recovery, with restoration of cognitive function to baseline.

BACKGROUND

Diagnosis of neurosyphilis remains a challenge due to the frequent atypical presentations that are often indistinguishable from other diseases. The prognosis can be very good, with almost complete recovery if the appropriate therapy is started early.

CASE PRESENTATION

A right-handed 47-year-old man was brought to our facility by his neighbour. The neighbour found him wandering around the house, he was encephalopathic and was dysphasic with apraxia of speech. His medical history included depression for which he is on citalopram 20 mg daily, although he had several depressive episodes in the preceding year despite treatment. His family reported behavioural changes and slowly progressive cognitive impairment.

On further questioning, he had been in a monogamous relationship with a female partner for the past 20 years; however, he mentioned to the family that he had previously been sexually abused as a child.

At presentation he was encephalopathic and was not orientated in time or place. In addition, he was dysphasic, and had a right upper motor neuron facial palsy and right hemiparesis. The limb weakness resolved rapidly over the next 30 min with persistence of dysphasia and facial palsy. National Institutes of Health Stroke Scale (NIHSS) was 6 initially and improved to four on repeat assessment after 30 min. The patient was without fever and systemic examination was unremarkable.

INVESTIGATIONS

Initial laboratory studies were unremarkable except for elevated white cell count $13.6 \times 10^9/L$ (neutrophils 11.7) and marginally raised C reactive protein

at 37 mg/L. CT, MRI and MR angiography (MRA) of the brain were normal, no evidence of infarction was seen on diffusion-weighted imaging and the MRA did not support a diagnosis of cerebral vasculitis.

Investigations for a source of a suspected stroke included an echocardiogram, which showed normal left ventricular function with trace mitral regurgitation; a 24 h Holter monitor, with no arrhythmias found; ambulatory blood pressure, with no evidence of hypertension; and tests for serum glucose and cholesterol levels, both of which were within normal limits. Carotid Doppler ultrasound revealed bilateral extracranial carotid system atheromatous changes without haemodynamically significant stenosis.

As the aetiology of a suspected stroke could not be identified, further investigations for the cause of this stroke-like syndrome included a serum and cerebrospinal fluid (CSF) analysis of syphilis (table 1). The diagnosis of neurosyphilis was made on the basis of a reactive CSF rapid plasma regain (RPR). Serology for HIV was negative and auto-antibody screen did not reveal any abnormalities.

TREATMENT

As the patient presented with a stroke-like syndrome, he was given 300 mg of aspirin as haemorrhage had been excluded on a non-contrast axial CT brain. Thrombolysis was not considered due to rapid improvement in the neurological deficits.

On receipt of positive syphilis serology, treatment was initiated with intravenous benzylpenicillin (24 million units daily in six divided doses), for 17 days: as per UK National Syphilis Guidelines.¹

OUTCOME AND FOLLOW-UP

There was a slow improvement in the patient's functional and cognitive status. The patient was discharged home on completion of the course of antibiotics, with a plan to re-analyse the CSF after an interval of 6 months. However, he presented to the emergency department within 4 weeks with a sudden onset severe headache. As part of the evaluation of this the lumbar puncture was carried out.

The patient made an excellent recovery 6 months after treatment, had a score of 29/30 on the Mini-Mental State Examination (MMSE) and had no focal neurological deficits. CSF and serum samples were repeated and they showed evidence of successful treatment with resolution of the inflammatory markers in CSF. The serum RPR titre had fallen from 1 in 64 to 1 in 16.

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Table 1 Blood and CSF parameters before and after treatment with 17 days of intravenous benzylpenicillin

	June 2013	July 2013	December 2013
Blood			
TPHA	>10 240	>10 240	>10 240
RPR	1 in 64	1 in 32	1 in 16
Syphilis Antibody CMIA	Positive	Positive	Positive
Syphilis IgM EIA	Positive	Positive	Positive
CSF			
White cells (/μL)	56 (100% lymphocytes)	30 (100% lymphocytes)	<5
Red cells (/μL)	0	0	3
Glucose (mmol/L)	2.9	2.8	3.4
Protein (g/L)	0.68	0.60	0.45
TPPA	>1 in 80	>1 in 80	>1 in 80
RPR	1 in 2	1 in 2	Negative

CMIA, chemiluminescent microplate immunoassay; CSF, cerebrospinal fluid; EIA, enzyme immunoassay; RPR, rapid plasma reagin; TPHA, *Treponema pallidum* hemagglutination assay; TPPA, *Treponema pallidum* particle agglutination assay.

DISCUSSION

Syphilis is a sexually transmitted disease. It can be transmitted during primary or secondary stages with an efficiency of transmission of approximately 30%.²

Syphilis is often referred to as the Great Imitator, due to its frequent atypical presentation, which is often very similar to other diseases. When patients are untreated during the earlier stages of syphilis, they are at risk of serious complications involving the CNS, cardiovascular structures, skin or bone.

The neurological involvement occurs in less than 10% of untreated syphilis patients.³ Syphilis can affect the nervous system in many different ways. It may result in focal neurological deficits or global CNS dysfunction. The most common presentation is with neuropsychiatric manifestations.⁴ However, syphilis may also cause myelopathy, seizures, strokes, ocular disease and brain stem or cranial nerves abnormalities.

About 10% of patients with neurosyphilis and almost 3% of all syphilis patients present with a stroke.^{5–6} These patients tend to be younger than those with a stroke due to cardioembolism or atherosclerosis. In one study, up to 74% of this category of patients were under the age of 50.^{7–8} Therefore, neurosyphilis should be considered in the evaluation of a young patient with a cryptogenic stroke.

Inflammatory infiltration of medium to large arteries is thought to be the mechanism underlying cerebral infarction in these cases. The middle cerebral artery is affected most frequently in neurosyphilis, which may result in a typical stroke-syndrome. Less frequently, the posterior circulation may be involved.⁹ Compression of the left carotid artery by an enlarged thoracic aortic aneurysm has also been reported as a cause of stroke in patients with syphilis.¹⁰

The diagnosis of neurosyphilis requires a high degree of clinical suspicion. Lumbar puncture should be performed in suspected cases. A recently published Chinese study found comparable positive and negative predictive values between CSF Venereal Disease Research Laboratory (VDRL) tests, CSF-RPR tests and CSF toluidine red unheated serum tests (TRUST) among patients who are HIV negative. However, the specificity of CSF-VDRL (90.3%) test was lower than that of the other tests (92.7–93.4%).¹¹

A positive CSF VDRL or RPR test is considered diagnostic of neurosyphilis in the absence of substantial contamination of the CSF sample with blood. The number of red blood cells required to convert 1 mL of CSF is inversely related to the titre of VDRL in the blood. The amounts of red blood cells ranged between 202 000 (for 1:4 titred blood) to 12 000 (for 1:256 titred blood) per 1 mL.¹² The CSF VDRL test is very specific even in cases in which there are high serum VDRL or RPR titres (up to 1:256), and the results will be falsely positive only if blood contamination is sufficient to tinge CSF with blood.¹³

CSF examination should be repeated every 6 months after therapy if CSF pleocytosis is present on the initial sample. There is still controversy regarding the predictive value of serum RPR for prognosis of neurosyphilis.

PCR for detection of treponemal nucleic acids in the CSF has also been suggested to be useful and confirmatory.¹⁴ It has a sensitivity of 30–71% and a specificity of 93%.^{12–15–17}

Learning points

- ▶ Neurosyphilis has a diverse clinical presentation that often mimics other diseases, both clinically and radiologically.
- ▶ Reactive cerebrospinal fluid (CSF) rapid plasma regain or Venereal Disease Research Laboratory (VDRL) in the absence of substantial contamination with blood is considered diagnostic for neurosyphilis. CSF VDRL may be falsely positive if blood contamination is sufficient to tinge the CSF with blood.
- ▶ Physicians should be aware of the potential neurological complications of neurosyphilis in view of the increasing incidence of the disease.
- ▶ Syphilis screening should be considered in the diagnostic work-up of young patients with a cryptogenic stroke.

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Competing interests None.

Patient consent Obtained.

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