

## Three Episodes of Brain Stroke as a Manifestation of Neurosyphilis in an HIV-infected Man

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The clinical course of syphilis, particularly in cases of co-infection with HIV, has changed compared with the classic manifestations described in the past. HIV-infected patients develop neurosyphilis more frequently and in earlier stage of syphilis than do HIV-negative persons. The risk of neurosyphilis correlates with a low CD4<sup>+</sup> T-lymphocyte count (1). HIV-infected patients treated with combined antiretroviral therapy (cART) currently have a similar clinical course of syphilis to that of non-infected persons (2, 3). The clinical picture is not characteristic and is similar to other infections of the central nervous system (CNS) (mycobacterial, fungal and viral infections) and neurological disorders (i.e. vascular lesions, AIDS dementia complex, lymphoma) (4). We describe here a case of diagnostic difficulties in an HIV-infected man with neurosyphilis.

### CASE REPORT

A 41-year-old Caucasian man was admitted to the neurology department with symptoms of weakness of the left upper limb, which had been increasing for 2 weeks. On admission the patient was apathetic and showed sign of dementia. Mild brain stroke was diagnosed, confirmed by computed tomography (CT) scan. Arterial hypertension was diagnosed and treated. Cardiac ultrasound revealed moderate aortic insufficiency and haemodynamically insignificant muscular ventricular septal defect. Elevated levels of anticardiolipin antibodies immunoglobulin (Ig)G 8.79 GPL-E/ml and IgM 2.24 MPL-E/ml were also found. During hospitalization the focal neurological symptoms resolved completely.

After 4 weeks the patient was hospitalized again with subsequent brain stroke. Magnetic resonance imaging (MRI) revealed disseminated ischaemic lesions, corresponding with vasculitis (Fig. 1). Antiphospholipid syndrome and vascular lesions in the course of arterial hypertension were considered as a cause of brain strokes. Anti-coagulative treatment with acenocoumarol in international normalized ratio-guided doses was started. Moreover, HIV infection was diagnosed, with a CD4<sup>+</sup> count of 82 cells/ $\mu$ l and an HIV viral load of 44,578 copies/ml. Combined antiretroviral therapy was started. Due to persistent cognitive impairment and pathological cerebrospinal fluid (CSF) measurements (protein 165 mg/dl, glucose 36 mg/dl, pleocytosis 45 cells/ $\mu$ l with 95% of lymphocytes) the patient was referred to the department of infectious diseases for further investigation.

On admission, features of cachexy and symptoms of advanced dementia with significant psychomotor retardation and emotional indifference were observed. CSF examination revealed an increase in lymphocytic pleocytosis to 96 cells/ $\mu$ l, a slight decrease in CSF glucose to 32 mg/dl, and a similar level of protein concentration (157 mg/dl) to the previous results. Tuberculosis, syphilis, viral and fungal infections were considered in the differential diagnosis of neuroinfection. Advanced-stage HIV infection was also suspected as the reason for dementia.

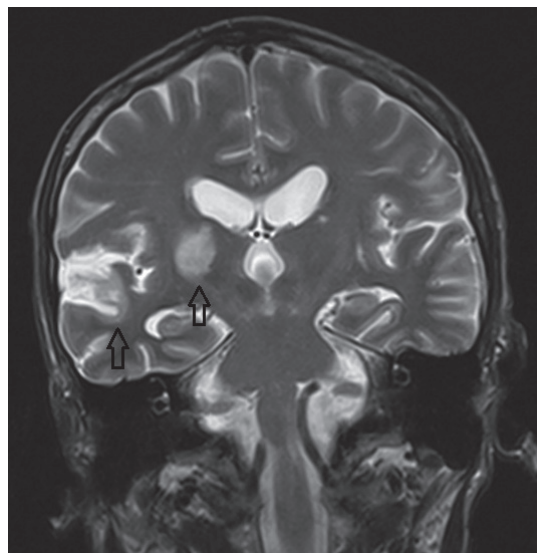


Fig. 1. Magnetic resonance imaging of the brain, disseminated lesions in the course of vasculitis – right temporo-parietal area (arrows).

During hospitalization symptoms of left-sided paresis appeared. A third ischaemic brain stroke was confirmed.

The results of serological syphilis tests of the serum and CSF showed that, in the serum: Venereal Disease Research Laboratory (VDRL) titre was 1/16 (extremely positive), fluorescent treponemal antibody (FTA) was 1/4000 (positive), fluorescent treponemal antibody-absorption (FTA-ABS) – positive, *Treponema pallidum* haemagglutination assay (TPHA) titre was 1/2560 (extremely positive); and, in the CSF: VDRL – negative, FTA titre was 1/80 (positive), FTA-ABS – positive, and TPHA titre was 1/2560 (extremely positive).

The total clinical picture, results of imaging and laboratory tests led to a definite diagnosis of meningovascular syphilis, resulting in 3 brain strokes in the course of syphilitic vasculitis. The patient denied having any signs of primary or secondary syphilis in the past. He reported having engaged in unprotected heterosexual activity several years previously, but the exact time of infection was not defined.

Treatment with crystalline penicillin, 6 million IU every 8 h intravenously (i.v.) was introduced and patient's condition improved significantly; cognitive impairment and apathy withdrew, and the left-sided paresis was relieved. CSF examination after 10 days of penicillin treatment revealed significant improvement, with pleocytosis of 19 cells/ $\mu$ l, and protein concentration 73 mg/dl. Penicillin therapy was maintained for 4 weeks, according to Polish recommendations. The results of a control test for antiphospholipid antibodies (IgG and IgM anticardiolipin antibodies, IgG and IgM B2-glycoprotein antibodies and lupus anticoagulant) were negative. Chest CT revealed widening of the ascending aorta as a probable vascular complication of syphilis.

At follow-up, one year after diagnosis of, and treatment for, neurosyphilis, CSF parameters were within the normal limits, except for a slight elevation in protein concentration; 68 mg/dl.

The patient's cognitive and emotional functions had returned to normal and neurological examination revealed only mild left-sided weakness.

## DISCUSSION

Neurosyphilis is a rare manifestation of syphilis that usually occurs within the first 12 months of infection, but involvement of the CNS is possible at any stage of the disease (1). Most neurological symptoms of early neurosyphilis result from acute or subacute meningitis, abnormalities in cranial nerve function, and inflammatory vasculitis leading to obliterative endarteritis affecting the blood vessels, resulting in brain stroke in some cases.

In HIV-infected patients, particularly those who have not been treated with cART, the typical clinical course of syphilis is affected by concomitant immunosuppression (5). Early meningovascular syphilis, requiring detailed differentiation from other opportunistic infections of the CNS, is more frequent than other late manifestations, such as tabes dorsalis and general paresis.

The CSF abnormalities occurring in neurosyphilis include pleocytosis, elevated protein and low glucose (6). In order to confirm the diagnosis of neurosyphilis the Centers for Disease Control and Prevention (CDC) recommends reactive serological tests and elevated CSF protein or cell count or a positive CSF VDRL (7). However, a negative VDRL in CSF does not exclude neurosyphilis (8), as it is less sensitive than FTA-ABS in this condition (9).

Syphilis is often described as "the great imitator", and knowledge among doctors of the diverse clinical manifestations of syphilis is inadequate. Neurosyphilis is rarely taken into account in the differential diagnosis of brain stroke. A low number of cases of brain stroke as manifestation of neurosyphilis in HIV-infected patients have been reported (10–12). In the case described here the initial incorrect recognition of antiphospholipid syndrome was the reason for the delayed diagnosis. The presence of antiphospholipid antibodies has been described in both HIV and *Treponema pallidum* infections (13, 14) and their significance is unclear. The reactive treponemal tests for the CSF enabled a diagnosis of neurosyphilis, followed by appropriate treatment, which had good results.

We conclude that syphilis remains a challenge for clinicians. This easily forgotten, but now re-emerging, chronic infection has many clinical manifestations that mimic multiple non-infective diseases, among them brain stroke as a vascular complication. Doctors, especially

dermato-venereologists and neurologists, who deal with syphilis patients should consider neurosyphilis in the differential diagnosis of all cases of brain stroke of undetermined aetiology, particularly in young patients. The detection of antiphospholipid antibodies should always raise the suspicion of syphilis. Neurosyphilis should also be suspected in HIV-positive patients with unexplained neurological symptoms and CSF abnormalities.

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