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Case Report

The big imitator strikes again: a case report of neurosyphilis in a patient with newly diagnosed HIV

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Background: Neurosyphilis is the result of an infection of the central nervous system caused by the spirochete *Treponema pallidum*. Its clinical presentation includes meningovascular syphilis, tabes dorsalis, and dementia paralytica, resulting in a wide range of symptoms such as psychosis, Parkinsonism, and depression.

Case report: A 49-year-old male was admitted to a psychiatric hospital because of social withdrawal and self-neglect, indicative of a major depression. A routine HIV-test was positive and resulted in an admission to the Antwerp University Hospital. Clinical examination showed Argyll Robertson pupils, a wide-based gait, absence of vibration sense in the lower limbs, and a MMSE-score of 25/30. Blood analysis revealed a CD4+ count of 99 cells/μL and a HIV viral load of $2{,}13 \times 10^5$ copies/mL plasma. A serum TPHA (*T. pallidum* hemagglutination assay) titre of 1/20480 and RPR (rapid plasma reagin) titre of 1/128 were detected. TPHA and RPR titre in the cerebrospinal fluid were, respectively, 1/10240 and 1/4. A brain MRI showed diffuse cortical atrophy and lesions in the white matter compatible with HIV-encephalopathy. The diagnoses of advanced HIV-infection and late neurosyphilis were made. HAART (highly active antiretroviral therapy) and high-dose IV penicillin G were started.

Conclusion: In all patients with new-onset dementia or untreatable psychosis, neurosyphilis should always be considered. Argyll Robertson pupils are regarded as pathognomonic of neurosyphilis. The management of neurosyphilis includes high-dose IV benzyl penicillin for 10 to 14 days. Close follow-up including a lumbar puncture after 6 months is warranted to ensure treatment recovery.

Keywords: Neurosyphilis, HIV-encephalopathy, Treponema pallidum hemagglutination assay, Rapid plasma reagin, Argyll Robertson pupils

Case report

We present a case of a 49-year-old male admitted to a psychiatric hospital because of general deterioration, social withdrawal and self-neglect for two years noticed by his relatives. Because of conflicts on the work floor and a history of major depression, the general practitioner and his parents assumed a relapse that warranted a psychiatric admission. As part of a routine medical work-up at the psychiatric hospital, a rapid HIV (human immunodeficiency virus)-test was performed, which turned out to be positive. No other serological tests were investigated. He was therefore transferred to the Infectious Diseases department of the Antwerp University Hospital for a full medical work-up. During the anamnesis, we discovered that the man was homosexual and in the past few years he regularly had unsafe sexual contacts with other men.

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On clinical examination, we noted a cachectic man, facial seborrheic dermatitis, Argyll Robertson pupils, an unstable gait pattern with wide base and absence of vibration sense of the lower limbs. We noticed also cognitive problems, especially the short-term memory caused difficulties objectified by a MMSE (mini-mental state examination)-score of 25/30. He lost two points on orientation in place and time and three points on delayed recall (Figure 1).

Blood analysis revealed a CD4+ T-lymphocyte count of 99 cells/μL and a HIV viral load of $2{,}13 \times 10^5$ copies/mL plasma. Blood serology showed a positive TPHA (*Treponema pallidum* hemagglutination assay) titre of 1/20480 and a positive RPR (rapid plasma reagin) test of 1/128. Other serological tests, such as Epstein-Barr-virus (EBV), cytomegalovirus (CMV), hepatitis B and C, Cryptococcus neoformans antigen, Toxoplasma gondii and Herpes simplex (HSV), were negative. The cerebrospinal fluid (CSF) revealed the following: lactate (2.8 mmol/L) and protein level (0.85 g/L) were elevated, while the glucose level was decreased (34 mg/dL)

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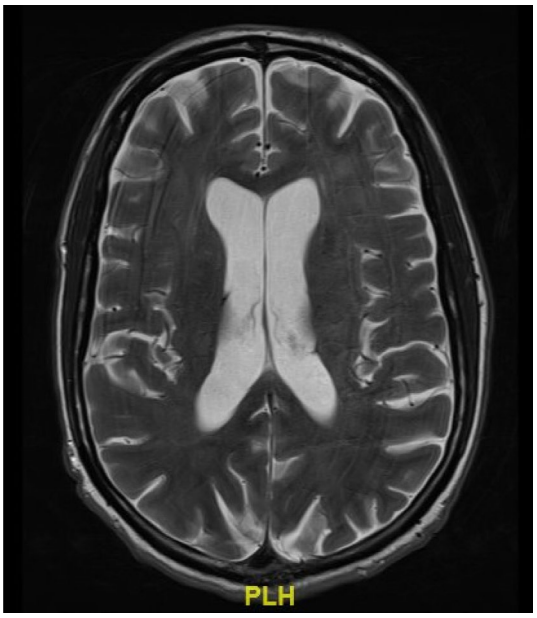

Figure 1 Brain MRI (T2 imaging) showed diffuse cortical atrophy compatible with HIV-encephalopathy.

and the white blood count (WBC) was normal (4 cells/mm³). Serology tests (TPHA and RPR) on the CSF showed a titre of, respectively, 1/10240 and 1/4. PCR (Polymerase Chain Reaction) for CMV, HSV, Toxoplasma, polyomavirus, Varicella-Zoster-virus and tuberculosis were negative. An MRI of the total spine showed no abnormalities indicative of tabes dorsalis. The chest X-ray showed an extensive consolidation in both lungs indicative of *Pneumocystis jirovecii* pneumonia (PJP). Diffuse ground-glass opacification and air bronchograms were found on a chest CT, compatible with an infection by *P. jirovecii*. A bronchoscopy with bronchoalveolar lavage was performed and the diagnosis of PJP was confirmed on immunofluorescence. A brain MRI showed diffuse cortical atrophy and lesions in the white matter compatible with HIV-encephalopathy (picture 1). The diagnoses of advanced HIV-infection complicated with an infection by the opportunistic yeast *P. jirovecii* and late neurosyphilis were made.

HAART (highly active antiretroviral therapy) including dolutegravir, emtricitabine and tenofovir disoproxil fumarate, co-trimoxazole and high-dose intravenous (IV) penicillin G (24 million units daily) was started. Unfortunately, we were forced to switch the benzyl penicillin to ceftriaxone after nine days of treatment because of lethargy, a decreased MMSE-score of 19/30, hypertonia of the upper limbs and torticollis. A penicillin-medicated encephalopathy was suspected to be responsible for his new symptoms. After four weeks of hospitalization, the neurocognitive symptoms improved somewhat (MMSE-score of 24/30).

Discussion

Neurosyphilis is the result of an infection of the central nervous system (CNS) caused by the sexually transmitted spirochete *T. pallidum*. Each year 10.6 million cases of syphilis are reported worldwide, and the rates of primary and secondary syphilis have increased in the past decade both in the developing and developed countries.[1,2] In developed countries, this increase was mainly observed in men who have sex with men (MSM).[3] In Belgium, the number of reported syphilis cases rose from 114 in 2002 to 1.532 in 2014, compatible with an incidence of 13.7 to 100.000 people in 2014[4] (Figure 2).

The clinical presentations of neurosyphilis include meningovascular syphilis, tabes dorsalis, ocular disturbances, syphilitic otitis and dementia paralytica.[5,6] Argyll Robertson pupils are considered by many to be pathognomonic of neurosyphilis.[1] Although tabes dorsalis was the most common manifestation of neurosyphilis in the pre- antibiotic era, it is rare nowadays.[7] Because of possible damage to several parts of the CNS, the infection can express itself with a wide range of (atypical) symptoms, such as psychosis, Parkinsonism and depression (picture 2). In the pre-antibiotic era, approximately 25–30% of admitted psychiatric patients tested positive for syphilis, and about 60% of the psychiatric patients with neurosyphilis suffered from marked dementia.[8,9] In all patients with newly onset dementia or untreatable psychosis, particularly

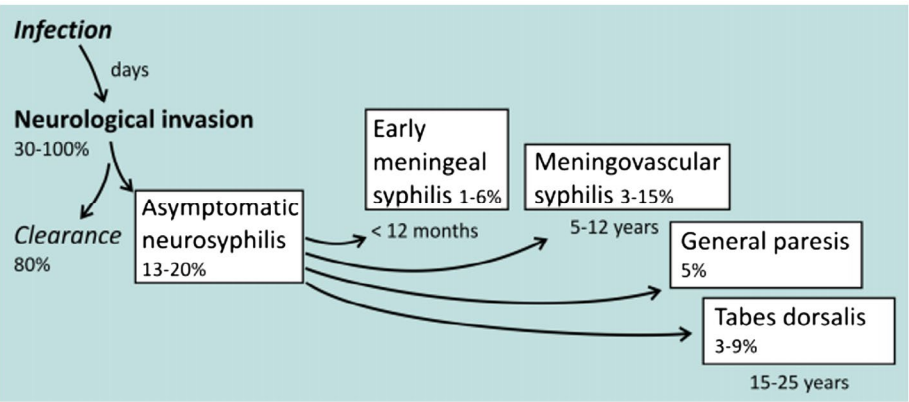

Figure 2 Wide spectrum of clinical presentation in neurosyphilis with the probability of progressing to each stage and average time to progression; data copied from Ghanem et al.

those with abnormal neurological examination, neurosyphilis should therefore always be considered.[8,10–12]

Abnormalities in the CSF, for example, an elevated WBC (pleocytosis) and protein level, may be the first laboratory clue of the diagnosis, although pleocytosis was not seen in our patient.[3] The CSF VDRL (Venereal Disease Research Laboratory) test has only a moderate sensitivity of approximately 30–70%, but its high specificity of 99.8% makes it a very useful test to rule in the diagnosis of neurosyphilis. The VDRL is more sensitive than the RPR for the diagnosis of neurosyphilis. The TPHA or FTA-Abs (Fluorescent Treponemal antibody-absorbed) is sensitive but less specific tests for the diagnosis of neurosyphilis.[8,13]

The optimal management of (neuro)syphilis continues to be high-dose (24 million units/day) intravenous benzyl penicillin for 10 to 14 days.[2,14] Intramuscular procaine penicillin G combined with oral probenecid offers an alternative. Another acceptable alternative treatment in patients allergic to penicillin is ceftriaxone administered either IM or IV daily, but penicillin desensitization for these patients is preferred.[3] Penicillin encephalopathy, as seen in this patient, is a rare and potentially reversible complication of penicillin-induced neurotoxicity, which normally presents with myoclonic jerking.[15] Close follow-up, with a lumbar puncture every 6 months until the CSF parameters normalize, is warranted to ensure complete treatment recovery.[1,9] A decline in the CSF pleocytosis is generally the first measure of improvement, but in patients co-infected with HIV the normalization of all CSF parameters occurs more slowly.[3,13,14]

HIV-infected patients have higher rates of syphilis with an up to 77-fold greater reported incidence compared to the general population.[3] In this population, one should be vigilant for this CNS infection and making this diagnosis can be challenging. HIV-infection itself is associated with mild elevation of CSF protein and mild CSF pleocytosis. Because of the diagnostic problems in HIV-infected patients and the insensitive CSF-VDRL assay, it is proposed to treat HIV-patients, even with a negative CSF-VDRL test, when they have a CSF WBC count between 6×10^6 and 20×10^6/L and those who have a high risk for neurosyphilis.[13] HIV-infected patients are not only at increased risk of developing neurosyphilis, some case reports suggest that they have a more fulminant course, to have higher viral loads in their CSF and to be more resistant to treatment, resulting in potentially higher rates of treatment failure.[7,16–18]

Conclusion

The diagnosis of neurosyphilis remains a challenge, especially in individuals infected with HIV. A good clinical neurological examination may give a clue to this diagnosis. Irreversible damage to the CNS in late neurosyphilis is not rare and sometimes can be partially prevented by starting the appropriate treatment on time.

Disclosure statement

Contributors

SB, CK and EV worked on the acquisition of data. CK was involved in the conception and design of study. SB, CK, and EV were involved in the analysis and/or interpretation of data. SB, CK, NL and EV drafted the manuscript; CK, NL and EV revised the manuscript critically for important intellectual content. SB, CK, NL and EV approved the version of the manuscript to be published.

Conflict of interest

No potential conflict of interest was reported by the authors.

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