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# Cerebellar alterations: an infrequent presentation of neurosyphilis☆

## Cerebelopatía por sífilis: una presentación infrecuente de neurolúes

*Dear Editor:*

With the era of antibiotics, the prevalence of syphilis decreased; however, it has increased in the past 10 years, with an estimated 18 million cases among people aged between 15 and 49 years.[1] Global incidence is 1.5 cases per 1000 population, with higher risk in homosexual men.[2] Neurosyphilis is the term used to refer to central nervous system involvement, which may develop at any stage, even in the early phase. Its manifestations include asymptomatic neurosyphilis, meningitis, meningovascular syphilis, general paresis, and tabes dorsalis, although there are also ''atypical'' forms, which do not meet clinical criteria for classic forms.[3]

We present the case of a 52-year-old homosexual man with a history of secondary syphilis 7 years before. Diagnosis was clinical and results from the non-treponemal (rapid plasma reagin [RPR] of 1:138) and treponemal tests were positive. We administered 2.4 million units of benzathine penicillin, and improvements were observed, with RPR titres decreasing to 1:2; however, at 3 years of follow-up, the same titre persisted and he voluntarily stopped attending his periodic follow-up consultations. The patient attended the emergency department due to a 3-month history of instability and gait disorder, which had worsened in the previous week, when he also developed language impairment. Physical examination revealed mild bulbar dysarthria and dysmetria in all 4 limbs (predominantly in the right side), as well as gait ataxia with tendency to drift, increased base of support, and Romberg sign, and even falls. Ocular motility showed no alterations, muscle balance was preserved in all 4 limbs, superficial and proprioceptive sensitivity were normal, and deep tendon reflexes were present and symmetrical in all 4 limbs. In the targeted medical history interview, the patient reported that he had not presented associated sphincter alterations or neuropathic pain. A cranial and spinal cord magnetic resonance imaging study revealed chronic small vessel disease in both brain hemispheres, without involvement of the cerebellar parenchyma or spinal cord or pathological contrast uptake. A subsequent spinal cord study with somatosensory evoked potentials yielded normal results. A basic blood analysis (blood count, biochemistry, vitamin $B_{12}$ and copper levels) revealed no alterations; in the syphilis serological test, RPR titre was 1:128 and VDRL titre was 1:64; the HIV serology test was negative. A lumbar puncture revealed predominantly lymphocytic pleocytosis (157 cells/$mm^3$), high protein levels (57 mg/dL), positive VDRL of 1:4, and positive PCR findings for *Treponema pallidum*. Differential diagnosis of rapidly progressive cerebellar syndrome should include structural cerebellar lesions (ischaemic, inflammatory, or tumour), infectious causes (HIV, Epstein-Barr virus, or cytomegalovirus), autoimmune

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disease, and paraneoplastic symptoms, which were ruled out in our patient. With the diagnostic suspicion of neurosyphilis of atypical presentation (due to clinical signs suggestive of cerebellar involvement with no parenchymal lesions in the cerebellum and normal spinal cord findings), we started treatment with intravenous crystalline penicillin for 14 days. One week after treatment onset, the patient's clinical symptoms improved and he was able to walk; Romberg test was negative.

The decrease in the mortality associated with HIV, due to the effectiveness of antiretroviral treatment, has caused an increase in the incidence of sexually transmitted infections, including syphilis. This has led to the reappearance of neurological manifestations (neurosyphilis).[2] Untreated syphilis may result in neurological impairment in 4%-10% of patients, but cases have also been described in immunocompetent patients receiving appropriate antibiotic treatment of the primary infection.[4]

To our knowledge, there are no previous reports of neurosyphilis with cerebellar alterations, although the wide spectrum of clinical manifestations of syphilis is widely known; syphilis was historically known as ''the great simulator.'' Classic forms of presentation include syphilitic meningitis, meningovascular variant, general paresis, and tabes dorsalis. However, there is an ''atypical'' form that may present with unusual manifestations, such as seizures, psychiatric symptoms, altered level of consciousness, and behavioural alterations similar to those of viral or autoimmune encephalitis.[3,5] In our case, we should mention the early clinical improvement with antibiotic treatment, which may suggest that progression time was shorter; in more chronic stages, such as tabes dorsalis or general paresis, the damage is irreversible.

Another controversial issue is the indication of lumbar puncture during diagnosis of syphilis; it is currently indicated in patients with neurological, ophthalmic, or ear signs and symptoms; tertiary syphilis in another part of the body; or treatment failure (including failure to decrease titres in non-treponemal blood tests).[6] However, a more controversial recommendation is that lumbar puncture should be performed in those patients with syphilis in any stage who present high titres in non-treponemal tests during the initial diagnosis (RPR $\geq$ 1:32), regardless of whether the patient presents neurological symptoms or is HIV-positive, since in these patients, the risk of presenting asymptomatic neurosyphilis is 11 times higher than among those with lower titres.[7] Our patient presented high titres during the first diagnosis of secondary syphilis (RPR 1:134). Twenty percent of patients with asymptomatic neurosyphilis develop the symptomatic form during the first 10 years, especially when they present high pleocytosis or high cerebrospinal fluid protein levels. In this scenario, there is controversy regarding the actions to be taken in daily practice, as more studies are needed to assess whether it is necessary to actively screen for and treat asymptomatic neurosyphilis.[8]

In conclusion, the incidence of syphilis is increasing both in immunosuppressed and in immunocompetent patients. This leads to a higher incidence of central nervous system infection due to syphilis (neurosyphilis). Neurological symptoms may vary greatly, from the classic form to atypical manifestations. Healthcare professionals should be aware of this increasing incidence and the possibility of unusual neurological symptoms in neurosyphilis, as early treatment may prevent sequelae and improve survival, as in our patient.

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