CASE REPORTS

NEUROSYPHILIS - A CASE STUDY

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REZUMAT

În ciuda scăderii numărului de cazuri de sifilis în ultimii ani, acesta rămâne o problemă a societății contemporane. Prezentăm cazul unui bărbat în vârstă de 56 de ani, care a fost admis în clinica noastră prezentând un declin cognitiv rapid progresiv. După anamneză, examenul clinic și neurologic, studiile de laborator și neuroimagistice, a fost stabilit diagnosticul de neurosifilis.

Cuvinte cheie: neurosifilis, Treponema pallidum, tulburări cognitive

ABSTRACT

Syphilis remains a disease of contemporary society despite the decrease of the case numbers in the latest years. We present a case of a 56 years old male who was admitted to our clinic presenting a rapidly progressive cognitive decline. Based on the illness history, clinical and neurological examination, laboratory studies and neuroimaging, the diagnosis of neurosyphilis was established.

Key Words: neurosyphilis, Treponema pallidum, cognitive disturbances

BACKGROUND

The word “sypphis” comes from the Greek “syphlos” that means crippled or maimed. The disease was first described as a clinical entity at the turn of the 15th century, Francisco Lopez Villalobos publishing the first book on the illness in 1498. Shortly after its clinical recognition, its sexual transmission was identified. In 1905, Schaudinn and Hofmann identified the pathogen agent as being Spirocheta pallida (Treponema pallidum), an almost transparent, thin, delicate, spiral-shaped organism. The infection with Treponema pallidum is divided into several stages, syphilis being classified as primary, secondary and tertiary. Primary syphilis presents as a painless chancre, usually appearing three weeks after the inoculation. Secondary syphilis consists in a macular, maculopapular or pustular rash involving often the palms and soles and alopecia, fever, lymphadenopaty and central nervous system (CNS) disturbances, appearing within weeks to months after untreated primary infection. Tertiary syphilis presents from one to 30 years after primary infection, being characterized by skin, osseous, cardiovascular and neurological complications.

Neurosypilis or the neurologic complications due to infection with Treponema pallidum have a broad spectrum and some authors entered the clinical and laboratory features into templates for six diagnostic categories:

1. Neuropsychiatric disorders, including psychosis, delirium and dementia;
2. Cerebro-vascular accidents: acute, focal neurologic deficits compatible with cerebro-vascular accident or imagistic evidence of stroke;
3. Ocular disorders: uveitis, visual loss or optic nerve dysfunctions;
4. Myelopathy: acute, subacute or chronic dysfunction of the spinal cord (including tabs dorsalis);
5. Seizures: partial seizures, with or without secondary generalization, or myoclonus;
6. Brain stem or cranial nerves impairments: signs restricted to brain stem or cranial nerves.
A manifestation of parenchymatous neurosyphilis is the general paresis (sometimes referred as dementia paralytica), which was accounted for a substantial percentage of psychiatric illness in the preantibiotic era, the patients displaying a progressive dementia and a variety of psychiatric disturbances.³

CASE REPORT

We present the case of a 56 years old male, who was admitted to our clinic presenting a rapidly progressive cognitive decline. His history revealed that he was a heavy drinker (for 30 years, approximately 10 beers per day), abstinent from five months, when he presented an insomnia which wasn't treatable with any sleeping pills. Short time after that, he presented weight loss (15 kg) despite increased appetite, physical, psychical and sexual asthenia and memory disturbances. The onset of the memory impairments was slow, observed firstly by his wife, with affected short term memory and preserved long term memory. The wife described hypomaniacal behavioral disturbances that appeared in the same time, with euphoria and logorrhea of the moriatic type, the patient's previous personality being usually sober and reserved. The patient himself considered that he had lost a lot of his previous professional efficiency, becoming slow and erratic. Nevertheless, he had the tendency to deny some of the moriatic symptoms. Additionally, he also complained of an old headache that had become more frequent and more intense in the past months. Affirmatively, the patient did not have sexual relationships with his wife since 1999, but he had sporadic short-term relations with many promiscuous sexual partners. He was not tested before for syphilis.

The neurological examination was completely normal, with no neurological signs.

The psychological examination revealed diffuse general disturbances, with short term memory, attention and reasoning impairments and frequent mental blocks. Raven Intelligence Test score was 104. He was extroverted, logorrheic and very irascible.

The blood cells count, the chemistry profile and the transaminase levels were normal, except an increased erythrocyte sedimentation rate (55 mm/h).

On lumbar puncture, the cerebro spinal fluid (CSF) analysis revealed a moderate cellularity, with small lymphocytes and rare neutrophyl granulocytes. The Venereal Disease Research Laboratory (VDRL) serology was positive (titer 1/512). THPA was also positive (titer 1/20,480), the diagnosis of neurosyphilis being confirmed.

Tests for Borrelia, Cysticercosis and human immunodeficiency virus (HIV), were also were performed with negative results.

The Magnetic Resonance Imaging (MRI) native scan revealed multiple lesions of variable dimensions (up to 1-1.5 cm), moderately hyperintense in Flair and T2 - weighted images and iso- hypo-intense in T1 weighted images, without contrast enhancing, situated in the periventricular (around the frontal horns) and subcortical white matter and in the semiolateral centres bilaterally. Also, there was hyperintensity of the splenium of corpus callosum on Flair sequences. After the administration of contrast substance, at the level of the lesions described in frontal lobes, in the T1-weighted images there were visible liquid microcistic structures, hypointense. There were no lacunary lesions in the territory of the perforant arteries, no subtentorial or cervical lesions. Also, there was a marked diffuse cortical atrophy, more accentuated fronto-temporo-insular, with the enlargement of the sulci, of the anterior interemispheric fissure and of the insular cisterns. The Virchow-Robin spaces were prominent (liquid aspect in all sequences) in the fronto-parieto-temporal cortex and white matter bilaterally, in the basal ganglia, insular cortex and hippocampus bilaterally, secondary to the external cortical atrophy. The ventricular system was slightly increased in volume, secondary to the internal cerebral atrophy.

Based on the illness history, clinical and neurological examination, laboratory studies and neuroimaging, the diagnosis of neurosyphilis was established and the patient received a treatment with intravenous Penicillin.
(4,000,000 UI at 4 hours) for 10 days, continuing with Benzathine Penicillin (2,400,000 UI intramuscular at seven days for three weeks) and Doxicycline (100 mg po for 30 days).

Figure 2. Ventriculomegaly.

DISCUSSION

Our patient presented an accelerated progressive decline of the mental status, being consistent with parenchymatous neurosyphilis. In the late stages of syphilis infection, the central nervous system involvement includes the meningoovascular neurosyphilis and the parenchymatous neurosyphilis. The meningoovascular syphilis typically occurs six to seven years after the infection, the nature of the clinical signs depending on the affected brain areas; therefore the neurologic findings include a wide range of manifestations such as hemiparesis, hemianesthesia, aphasia, seizures and brain stem syndromes. The parenchymatous syphilis develops 10 to 20 years after the initial infection, including tabes dorsalis and general paresis. The onset of the psychiatric symptoms of the general paresis is usually insidious, firstly noticed by family or friends. They consist in emotional lability, irritability, memory loss, a decline of attention. Later, the patients present cognitive changes including euphoric mania, paranoia, delusions and hallucinations, with inappropriate behavior. After approximately five years of the onset of the symptoms, almost all patients are demented, with convulsions and progressive vegetative degeneration. The cognitive disturbances of our patient are consistent with the early signs of parenchymatous neurosyphilis.

The diagnostic workup of syphilis is dependent on the serologic studies. There are two categories of serological studies: nontreponemal tests (flocculation

tests using cardiolipin, lecithin and cholesterol as antigen – such as VDRL) and treponemal tests (relying on specific treponemal cellular components as antigens - such as THPA).

A positive VDRL in the CSF is specific, being rarely reported to be false positive, but a negative study cannot exclude the neurosyphilis. Sometimes the falsely negative VDRL can be due to a "prozone phenomenon", in which large amounts of antibody impair the formation of antigen-antibody lattice that is needed to visualize a positive flocculation test, its presence in asymptomatic neurosyphilis being lower than in the symptomatic forms. The VDRL can be used for the initial screening and for the follow-up; in tertiary syphilis it remains positive indefinitely, but the response to therapy can be assessed quantitatively by the titers of dilution.

The treponemal tests are very sensitive and specific for syphilis infection, confirming the diagnosis, remaining positive indefinitely after the seroconversion, despite adequate treatment. Our patient was VDRL and THPA positive in CSF and blood, the diagnosis of neurosyphilis being definite.

Due the fact that syphilis and HIV infection have the same epidemiologic factors and can be frequently associated, our patient was also tested for HIV, but showed to be negative. In concomitant infections, the patients have a higher protein level and pleiocytosis in CSF and the response to therapy is lower.

The neuroimaging studies can be suggestive for neurosyphilis and can help to exclude other possible pathologies, but they are not diagnostic. Some studies report 31% normal brain images, 31% brain infarctions, 20% non-specific findings, 6% cerebral gummas and extra-axial enhancement indicating meningitis in the patients with neurosyphilis.

The radiological findings in neurosyphilis include meningeal and CSF enhancement, hydrocephalus, ischemic lesions (with typically lacunar or middle cerebral artery distribution) or gummas. On MRI scans, the gummas are avascular, dural-based masses with a variable degree of surrounding edema, hypo or isointense on T1-weighted images and hyperintense on T2-weighted images, usually with contrast enhancement. In patients with general paresis (parenchymatous syphilis), MRI scans appear to correlate with the psychiatric and cognitive disorders, being described cerebral atrophy (in the frontoparietal and temporal regions bilaterally), disseminated frontal high signal lesions, mesiotemporal T2 hyperintensity, diffuse white matter T2 hyperintensity (which
is supposed to be due to edema and gliosis), ventricular enlargement and T2 hypointensity in the globus pallidum, putamen, caudate and thalamus.7-9

The MRI scan of the patient that we have described showed multiple supratentorial, periventricular and subcortical lesions, apparently inflammatory (but also possible to be present due to a cerebral parasitosis, accordingly with the microcystic aspect). There were no vascular lesions (that could suggest a possible small vessels disease), but he presented severe cortical atrophy, with prominent Virchow-Robin spaces and ventriculomegaly.

Figure 3. Cortical atrophy.

Figure 4. Microcystic lesions.

As concerning the treatment, Treponema pallidum is highly sensitive to Penicillin, the treponemical level being 0.03 µg/ml. Penicillin acts by interfering with the synthesis of cell walls; the serum levels must be maintained for many days because the Treponema divides slowly. It is used in all stages of syphilis. The optimal treatment regimes in neurosyphilis are still questionable, because there are no controlled, randomized, prospective studies. The most authors recommend crystalline Penicillin G, 2-4 million UI intravenously every four hours for 10-14 days, some consider adding oral penicillin to supplement levels. The Centers for Disease Control and Prevention recommends 18 to 24 million UI of penicillin intravenously each day for 10 to 14 days.10 The potential adverse reactions of the penicillin treatment can be the Jarisch-Herxheimer reaction (particularly in early syphilis), allergic reactions and anaphylactic shock. The Jarisch-Herxheimer reaction is an inflammatory response to the destruction of Treponemas, occurring within hours of treatment and consists in fever, headache, hypotension and myalgias, but it is rare in late syphilis.11

Our patient received one of the recommended dosages of Penicillin. Within about six months after therapy, the CSF leukocyte count should decrease, but the protein levels should decrease more slowly, with normalization within approximately two years. However, only a minority of patients with late syphilis (such as with general paresis) show improvements with Penicillin therapy. There are studies that suggest that medial temporal atrophy is a particularly poor prognostic factor.12 In the case of our patient, stabilization of the progressive disorder can be expected, but the improvement has a low probability.

CONCLUSIONS

Despite the decrease of the cases of syphilis in the latest years, it still remains a disease of the contemporary society. Asymptomatic syphilis is more frequent lately, the American Health Department reporting 2.5 cases of late or late-latent syphilis for each case of primary or secondary syphilis.13 Our patient was difficult to diagnose, because of the lack of history of primary or secondary syphilis. His drinking problems made the diagnosis more difficult, because there also can be cognitive deterioration due to alcohol abuse. An early diagnosis is very important, the patients with early neurosyphilis responding better to therapy.

REFERENCES


