NEUROSYPHILIS - A CASE PRESENTATION

G.S. ŢIPLICA[1,2], Carmen SĂLĂVĂSTRU[1,2], Alina PÂRVU[1], Alina RUŞINOIU[1], Magdalena CONSTANTIN[1,2], Mihaela PANDURU[1], S.H. MORARIU[3]

1 - Second Clinic of Dermatology, Colentina Hospital Bucharest, 2 - „Carol Davila" University of Medicine and Pharmacy, 3 - University of Medicine and Pharmacy Targu Mures

Summary

Syphilis is representing a global health problem. More than 12 million people are infected each year. Treated as a public health problem by the Ministry of Pubic Health syphilis prevalence In Romania is showing a decrease: from 12,702 cases in 2002 to 5,657 syphilis cases in 2006. Some patients are diagnosed in advanced stages of the disease as neurosyphilis. A 38 years old male with generalized convulsive seizures and other neurological manifestations was spotted with *Treponema pallidum* infection. Benzyl penicillin in large doses was administered and Benzathine benzyl penicillin was sequent used. The neurological disorders improved.

Neurosyphilis is not a rare manifestation of *Treponema* infection and must be a differential diagnosis in all patients with seizures.

Key words: Neurosyphilis, Generalized seizures, Benzyl penicillin

Introduction

Syphilis has an impressive historical importance and has played a major role in medicine over many decades. Searching to understand syphilis emerged in important contributions to epidemiology, clinical practice, pharmacology, neurology, pathology, bioethics and history. As secret files are brought to light it is better understood that syphilis has had a prominent influence in history and literature for the last several hundred years. For example the presence of neurosyphilis can be explanatory for Lenin's important changes in attitude recorded during his public life. Whispers have circulated for decades that Lenin, founder of the Bolshevik Party, was afflicted with syphilis throughout his career. Lenin's illness at least mimicked the progression of syphilis, afflicting him for months with occasional seizures and excruciating headaches, as well as bouts of nausea, sleeplessness and partial paralysis. As Stalin plotted for control of the Communist Party, Lenin was alternately lucid and incapacitated. Sometimes, he was unable to walk without assistance or to speak. It is thought that Lenin was suffering from meningovascular syphilis on his deathbed [1].

Neurosyphilis refers to a site of infection involving the central nervous system. Neurosyphilis may occur at any stage of syphilis. Before the age of antibiotics, it was typically seen in 25-35% of patients with syphilis.

Case report

We present the case of 38 years old G. C. who was admitted in the Dermatology Clinic of Colentina Hospital for positive serology (VDRL and TPHA). The patient was transferred from the Neurology Clinic were he presented for generalized convulsive seizures, drowsiness and confusional state. The patient described another convulsive seizure in 2006, which was investigated at that time; the MRI from 2006, showed a small lacunar image in the right mesencephalon. In the recent past medical history the patient denied any cutaneous and/or mucous lesions. Social history revealed a married patient with apparently harmonious family environment and work place (he work as auto-mechanic).

Physical examination discovered a good general state, without fever, blood pressure of 100 / 70 mmHg, and heart rate of 82 b / min. No cutaneous or mucous lesions were identified and palpation did not identify any enlargements of peripheral lymph nodes.

The paraclinical investigations performed illustrated a mild inflammatory syndrome. The hemogram showed neutrophilia ($14,9x10^3$ μ/l) with lymphcytopenia ($0.43x10^3$ μ/l),: ESR=28 mm/h, negative HIV test (anti-HIV 1 antibodies, anti-HIV 2 antibodies were absent), serum VDRL was positive at a titer of 1/16, TPHA ++++. The cerebro-spinal-fluid (CSF) demonstrated VDRL ++, TPHA ++++. CSF further examination showed 45 lymphocytes / mm^3, no RBCs, no macroscopic sediment, slightly positive Pandy reaction.

A MRI examination was performed during the admission in the Clinic of Dermatology and there were identified bilateral temporal parenchymatous lesions. The differential diagnosis for these lesions was made between vascular lesions (secondary to microvascular damage possible due to cerebrovascular accident (CVA)), and edematous-inflammatory lesions (figure 1).

The neurological consult showed a confuse, disoriented patient, without a stiff neck or bilateral pupillary reflexes. The patient hasn't presented any

motor deficit. The osteotendinous reflexes were diminished in the lower limbs. He had normal coordination, without sensory impairment, but he showed behavioral and mild memory impairment. There was also present an attention deficit (distruptability and inattention); without sleep disorders.

The ophthalmogyc examination didn't show any abnormalities.

The positive diagnosis was established based on the serology, the modifications in the CSF (positive VDRL, TPHA and the increased celularity) and the neurological manifestations (the clinical manifestations are not mandatory for the diagnosis).

The differential diagnosis included the various forms and stages of neurosyphilis. The differential diagnostic possibilities are broad. The first diagnosis that should be taken into consideration is CVA (all the causes of ischemic CVA). Other causes involved can be: meningitides (other basal meningitides should be considered if the presentation is that of cranial nerve paralysis), primary neoplasm's , metastasis, or other space occupying lesions (if gummata are present), psychiatric symptoms (delirium, dementia, mania, psychosis, personality change etc.) especially in general paresis, multiple sclerosis [2].

Adequate treatment of neurosyphilis is based largely on achieving treponemicidal levels of penicillin in the CSF. *Treponema pallidum* is highly susceptible to penicillin, which is the drug of choice for all stages of syphilis. Penicillin acts by interfering with the synthesis of cell walls and is active only against organisms that, like *Treponema pallidum*, synthesize their cell walls in growth and division. Penicillin has some ameliorative effect in every stage of neurosyphilis. Earlier forms of illness are better candidates for a response to antibiotic treatment. Meningovascular disease responds most dramatically.

The etiologic treatment was realized according to the Ministry of Public Health's Order 1070/25.08.2004 using Penicillin G at 3 million U/4 h, for 15 days achieving a total dose of 18 million U per day. During the hospitalization there was noticed an increase in the level of transaminases (SGPT= 89 UI/L and SGOT= 45UI/L) and a slight increase of potassium level (5.3 mmol/L). These modifications were interpreted in the context of penicillin treatment and did not pose special problems.

Other antibiotics have not been studied sufficiently, and their routine use is not recommended. Still either of the following is acceptable: Procaine PCN-G at 2.4 million U/day intramuscularly plus probenecid at 500 mg orally 4 times per day for 10-14 days (the regimen is not recommended if the patient has a history of allergy to sulfonamides). Ceftriaxone can be attempted at 1-2 g/day im or iv, for 10-14 days; if patients are allergic to PCN doxycycline can be another alternative as it is effective at a dose of 100 mg, bid, for 28-30 days.

The neurological treatment included Trileptal 600 mg, 2 tablets/day, Sermion 1 tablet/day and Piracetam 2 tablets/day.

After the release from the hospital the patient received Benzathine PNC G at 2.4 million U intramuscularly once a week for 3 weeks. The treatment was evaluated monitoring the CSF. A CSF examination 6 months following treatment should demonstrate a normal blood cell count and decreasing protein content. CSF examinations should be repeated every 6 months for 3 years or until the CSF is normal. A lack in the decrease of the protein content after 6 months or an abnormal CSF after 2 years is an indication for re-treatment.

Under the treatment the patient did not show an improvement of the neurological symptoms, the confusional syndrome was maintained, but the seizures did not appear anymore.

Discussion

Neurosyphilis is considered as positive diagnosis when the CSF WBC count is greater than 20 cells/mL or when CSF VDRL test gives a reactive result. Persons not treated for persistent CSF abnormalities are at risk of developing clinically apparent disease and are hereafter referred to as having contracted neurosyphilis. Neurosyphilis may occur at any stage of syphilis. Before the advent of antibiotics, it was typically seen in 25-35% of patients with syphilis. Neurosyphilis is now most common in patients with HIV infection. In 1999, the World Health Organization estimated that worldwide, approximately 12 million new cases of syphilis occurred among adults. Some degree of acute or subacute aseptic meningitis is present even in primary syphilis; therefore, neurosyphilis, in a broad sense, begins early. Approximately 35% to 40% of persons with secondary syphilis have asymptomatic central nervous system involvement. Syphilis is known as the great imitator, so the fact that symptoms of neurosyphilis are broad should come as no surprise.

Symptoms of neurosyphilis include the following and are listed in order of frequency: personality change (including cognitive and/or behavioral impairment) 33%, ataxia 28%, stroke 23%, ophthalmic symptoms (e.g., blurred vision, reduced colour perception, impaired acuity, visual dimming,

photophobia) 17% , urinary symptoms (e.g., bladder incontinence) 17%, lightning pains 10%, headache 10%, dizziness 10% , hearing loss 10%, seizures 7% [3].

Signs of neurosyphilis, in order of decreasing frequency, include the following: hyporeflexia 50%, sensory impairment (e.g., decreased proprioception, loss of vibratory sense) 48%, pupillary changes (anisocoria, "Argyll Robertson pupils") 43%, cranial neuropathy 36%, dementia, mania, or paranoia 35%, Romberg sign 24%, Charcot joint 13%, hypotonia 10%, optic atrophy 7% [3].

According to Merrit classification the neurosyphilis implies these seven types [4]: (a) asymptomatic, (b) cerebromeningeal, (c) cerebral-vascular, (d) spinal meningovascular, (e) parenchimatous, (f) focal gummatous and (g) atypical presentation forms. The asymptomatic type is characterized by abnormal findings in the CSF and has two fases: early (0-5 years) and late (over 5 years). The cerebromeningeal type implies meningitis and cranial nerve palsies; in the cerebral-vascular type hemiparesis, aphasia and seizures can be encountered. General paresis, tabes dorsalis, optic atrophy are representative for the parenchymatous form and cerebral or spinal compression for the focal gummatous one. The atypical presentations include: tinnitus, deafness, dizziness, papillary changes, seizures, organic mental syndrome, pyramidal signs and other isolated or combined neurological abnormalities.

Although the cases of neurosyphilis are rare these days, they are not exceptional. In this case the patient eluded the epidemiologic network and developed symptoms that can be included in the cerebral-vascular type. The wife and daughter of the patient were investigated. The results showed that the wife had a positive serology (TPHA ++) as a sign of an old infection with *T.pallidum*. The daughter (3 years old) had a negative serology (VDRL - and TPHA-).

Conclusions

There is a need in strengthening of the public health component in the control and surveillance of STI and HIV/AIDS. The legal framework of epidemiologists has to improve reporting and to target vulnerable groups in prevention activities. Neurosyphilis can be clinically manifest in various signs and symptoms and CSF tests should routinely include TPHA and VDRL. Penicillin G is the gold standard in treating neurosyphilis.

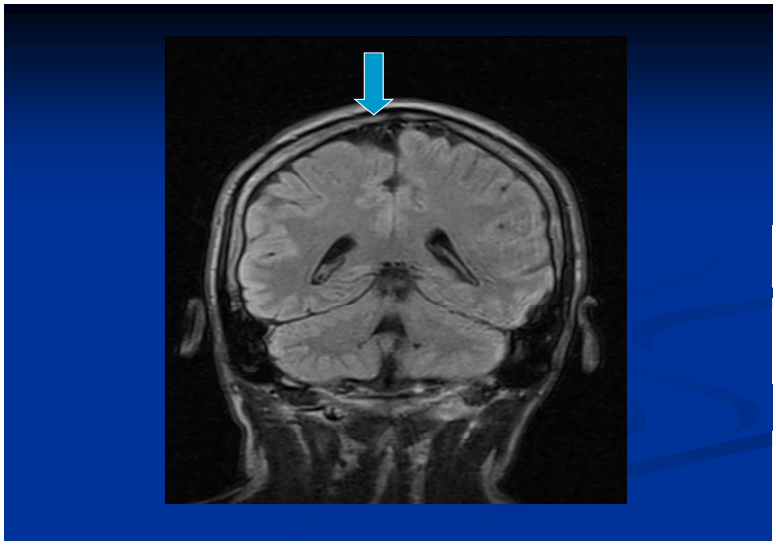

Figure no 1. Patient G.C. 38 years. Bilateral temporal parenchymatous lesions

Bibliography

1. Chivers C.J., "A retrospective diagnosis says that Lenin had syphilis", The New York Times, USA, 2004
2. Fitzpatrik Thomas B.,"Dermatology in general medicine", Vol. II, Forth Edition, McGraw-Hill, Inc., 2721, table 218-2.
3. Knudsen Richard P., De Menezes Marcio Soteres, Neurosyphilis, eMedicine, topic 684
4. Rowland, L.P. (Red.). (1989). Neurosyphilis. Meritt's Textbook of Neurology. Philadelphia: Lea and Flebiger.