

An unusual presentation of neurosyphilis as a probable migraine

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Abstract We describe a case which initially presented as persistent and untreatable probable migraine, which was subsequently diagnosed as neurosyphilis during the clinical evaluation. All symptoms regressed after appropriate treatment. We suggest that the possibility of neurosyphilis should be taken into account in the differential diagnosis of a persistent headache which does not respond to medication.

Keywords Neurosyphilis · Migraine · CSF

Introduction

Syphilis, although significantly reduced in the period after World War II by means of penicillin, has reappeared as a worldwide problem, with approximately 12 million new cases annually [1]. The widespread and at times indiscriminate use of antibiotics in recent years has considerably modified the forms and stages of syphilis and, subsequently, the clinical features of neurosyphilis [2]. Headache is part of the clinical forms of neurosyphilis but its appearance as a single symptom is extremely rare, especially when, at least, the skin symptoms of syphilis have not developed and when there is total absence of the characteristic clinical picture [3, 4].

We describe a case that initially presented as persistent and untreatable migraine, which was subsequently diagnosed as neurosyphilis during the clinical evaluation.

Case presentation

A 38-year-old male, a sailor by profession, presented with a 6 years history of sustained undiagnosed headache. Initially, the pain was relatively mild, continuous, and diffuses into both hemispheres, but located primarily at the frontal region. At the time there were no other definite neurological signs and the whole incident was attributed to stress. There were some episodes of headache associated with symptoms of migraine such as nausea, vomiting, sensitivity to light and sound, but with mild frequency (every 12–15 days). He was treated with antidepressants, with no particular clinical response. The headaches gradually became daily and of longer duration and at the time acquired the characteristics of migraine, without aura. The pain located unilaterally, near the eye and the right temporal site and then spread to both the hemispheres, pulsating with moderate to severe intensity and associated with nausea, vomiting, phonophobia and photophobia. Brain CT and MRI were performed and there were no pathological findings.

Six years after the initiation of the headache the patient was admitted in the hospital presenting a severe episode of probable migraine with vertigo. The patient underwent a new brain MRI, ENT evaluation, auditory-evoked potentials and electronystagmograph and all results were normal. Detailed neurological examination was performed by two neurologist. Bradypsychism and mild impairment of cognitive function (MMSE: 25) were noted during hospitalization, without any other neurological signs. Visual field

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examination and direct ophthalmoscopy were normal. In laboratory testing, he was found positive for syphilis infection (VDRL+++, FTA+); and negative for HIV infection. Due to these laboratory results, a subsequent lumbar puncture took place and it yielded positive results for antibodies against spirochete *Treponema pallidum* (positive CSF FTA-abs and CSF VDRL tests, and TPHA was 1/2560). CSF color, protein, glucose and opening pressure were normal. There was a mild CSF pleocytosis (CSF WBC count was 22/ μ l). After this, the patient was treated with intravenous penicillin G, to which he responded very well with significant improvement of headaches [4].

Discussion

Syphilis is a chronic infection which is mainly sexually transmitted and which is caused by the spirochete *Treponema pallidum* [5]. The progress of the disease consists of different stages: primary, secondary, latency and tertiary. The first stage involves skin symptoms, with the primary lesion to develop at the site of inoculation 2–6 weeks after infection. The second stage is characterized by a wide range of clinical signs and symptoms, including malaise, low grade fever, headache, rash, generalized lymphadenopathy, etc., resulting from the multiplication and dissemination of treponemes throughout the body [1]. Syphilitic meningitis may occur at a rate of 1–2% alongside the classic symptoms even at the second stage. The typical manifestations will present mainly in the tertiary stage, during which treponemes invade the CNS, cardiovascular system, eyes, skin, and other internal organs, causing damage as a result of their invasive properties and inflammation. Replication of treponemes in the wall of the aorta may lead to aneurysm, aortitis or aortic endocarditis. Neurosyphilis includes syphilitic meningitis, meningovascular syphilis and parenchymal syphilis, which, in turn, are differentiated in tabes dorsalis and general paralysis neurosyphilis [6].

In recent years, the use of antibiotics and especially of penicillin has led to a significant decline in the incidence of neurosyphilis in Greece [2, 7]. Furthermore, the widespread use of antibiotics for any infection in conjunction with the inadequate treatment of syphilis in its early stages seems to have considerably changed the clinical picture of syphilis. The classic forms (general paralysis and tabes dorsalis) are rarely encountered in everyday clinical practice and they have been replaced by other atypical clinical forms, where the usual symptoms of syphilis are absent [7]. More specifically, the early and correct diagnosis of the second stage of syphilis, which simulates a wide range of infections and autoimmune diseases, is particularly challenging to the physician. However, a carefully taken medical and family history of the patient could provide useful pieces of

indications, such as immigration from high-prevalence country, infected family members, sexual orientation and sexual contacts with infected individuals. According to the international bibliography, there is a significant increase in the incidence of syphilis worldwide in the last years, not only in the developing countries, but also in the economically developed countries [7, 8]. Quite often, the indiscriminate use of antibiotics for all kinds of infections, together with the inefficient treatment of syphilis in its first stages, seems to have altered the clinical manifestation of neurosyphilis. On the other hand, male patients are affected at a higher rate than female patients (3.6 times more often). This fact can possibly be explained by the prevalence of primary infection in populations where men are more than women (homosexuals, seamen and drug addicts) [7, 9].

Headache is a common clinical finding in neurosyphilis, especially in the presence of syphilitic meningitis. The headache may be manifested in a variety of characteristics, thus preventing a clear clinical point indicative of neurosyphilis [5]. In the case described, the headache was originally the only symptom; moreover, it exhibited clear migraine characteristics, a fact that misled clinical thinking. Also, normal brain imaging and the normal laboratory monitoring until the last hospitalization supported the diagnosis of migraine. After 6 years of disease with no skin signs or other characteristic symptom of syphilis, the occurrence of mild bradypsychism and the deduction of cognitive function, considering his profession, led to the suspicion of syphilis. The positive laboratory control of peripheral blood and CSF confirmed the neurosyphilis diagnosis. The link between neurosyphilis and migraine was made due to the patient's response to the medication, the regression of bradypsychism and migraine, and the improvement of his cognitive functions. This is particularly interesting, because the brain imaging showed no evidence of meningeal infection which is the usual cause of headaches. In addition, the occurrence of neurosyphilis with the unique clinical manifestation of migraine is very rare. In the literature, there is only one corresponding case [10]. In conclusion, the possibility of neurosyphilis should be taken into account in the differential diagnosis of a persistent headache which does not respond to medication (even if it could easily be attributed to migraine), as the condition is fairly common in developing countries.

Conflict of interest None.

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