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Research article

Five-year experience of neurosyphilis cases in a tertiary care hospital in Turkey

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ABSTRACT

Aim: To evaluate retrospectively the cases of syphilis who applied to different clinics of our hospital in the last 5 years and to emphasize the importance of admission screening tests in the diagnosis of neurosyphilis which is a rare but serious form of syphilis.

Methods: Sixty-one patients who admitted to different clinics of our hospital between 2013 and 2017 with different clinical manifestations and positive Venereal Disease Research Laboratory (VDRL) and Treponema pallidum microhemagglutination assay (TPHA) tests were recorded and analyzed retrospectively.

Results: Both VDRL and TPHA tests were positive in 44 males with a mean age of 57.4 ± 18.4 years and 17 females with a mean age of 65.3 ± 19.1 years. It was found that of the 61 patients who were examined for differential diagnosis of syphilis, 36 (%59) of them were referred from neurology clinic, 15 (25%) from infectious diseases clinic, 7 (12%) from dermatology clinic and 3 (4%) from gynecology clinic. The clinical presentation was venereal chancre in 15 cases, asymptomatic ischemic brain lesions in 17 cases, acute ischemic stroke in 13 cases, movement disorder in three cases, tabes dorsalis in two cases, tendinitis-arthritis in eight cases, Amyotrophic lateral sclerosis (ALS) in one case, Deep venous thrombosis (DVT) in one case, and pulmonary nodule in one case.

Conclusions: In conclusion, syphilis is often overlooked in the differential diagnosis in patient with neurological findings. Since neurosyphilis is an easily treatable disease, it should be considered in the differential diagnosis of patients presenting with neurological findings.

Keywords: Neurosyphilis, syphilis, tertiary syphilis, VDRL, TPHA.

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Introduction

Syphilis caused by Treponema pallidum is a sexually transmitted multisystemic disease that can be treated with early diagnosis [1, 2]. The widespread use of penicillin and other antibiotics has led to a decrease in the number of syphilis cases [3]. However, it remains important as one of the sexually transmitted

diseases in developing countries. On the other hand, the incidence of the disease increases with AIDS and HIV seropositivity [4].

Since the clinical symptomatology of the disease covers a wide spectrum and mimics many diseases, it is defined as “the great imitator" [5] Neurosyphilis develops in about 5% of cases infected with Treponema pallidum [6]. Central nervous system involvement of syphilis may occur early or late stage of the infection. Meningitis, vision and hearing loss, and stroke are common in early neurosyphilis. Cognitive involvement, hearing loss and gait disturbances are seen more frequently in the late period neurosyphilis [7].

The most common serological tests used for screening the infection are nontreponemal and treponemal tests. Nontreponemal tests such as Venereal Disease Research Laboratory (VDRL) or Rapid Plasma Reagin (RPR) show host immunoglobulin M (IgM) and IgG antibodies against lipoidal material released from damaged host cells and cardiolipin released from treponemas [8]. Nontreponemal tests are used qualitatively for screening in the diagnosis of infection or quantitatively in the follow-up of the treatment [9, 10]. Nontreponemal tests are easily accessible, inexpensive and easily applicable to the study of multiple samples [8]. The standard treponemal tests used today are the Microhemagglutination Assay (MHA-TP) or the Treponema pallidum microhemagglutination assay (TPHA) and the Flourescent Treponemal Antibody-Absorption (FTA-ABS) and 'FTAABS double staining' tests and are generally used to confirm positive results for nontreponemal tests [11, 12].

The aim of the present study was to evaluate retrospectively the cases of syphilis who applied to different clinics of our hospital in the last 5 years and to emphasize the importance of admission screening tests in the diagnosis of neurosyphilis which is a rare but serious form of syphilis.

Methods

After approval of the local ethics committee, the data of 61 patients who admitted to different clinics of Bolu Abant Izzet Baysal University Education and Research Hospital between 2013 and 2017 with different clinical manifestations and positive VDRL and TPHA tests were recorded and analyzed retrospectively. All patients underwent lumber puncture to rule out neurosyphilis. The diagnosis of neurosyphilis was based on clinical, laboratory and CSF findings. Age, gender and laboratory data of the patients were recorded. All patients were informed about the study and a written informed consent was obtained from each patient. All of the enrolled patients were HIV negative. The study was conducted in accordance with the Declaration of Helsinki. For all statistical analysis, statistical software package 18.0 for Windows (SPSS Inc., Chicago, IL, USA) was used. Descriptive statistics and frequency analysis were used. Data are presented as mean ± standard deviation for quantitative data, number (n) and percent (%) for categorical data.

Results

Both VDRL and TPHA tests were positive in 44 males with a mean age of 57.4 ± 18.4 years and 17 females with a mean age of 65.3 ± 19.1 years. It was found that of the 61 patients who were examined for differential diagnosis of syphilis, 36 (%59) of them were referred from neurology clinic, 15 (25%) from infectious diseases clinic, 7 (12%) from dermatology clinic and 3 (4%) from gynecology clinic. Of the 13 patients who underwent ear nose throat (ENT) and audiometric examination, three of them were normal and 10 patients had sensorineural hearing loss, and 48 patients had no audiometric

examination. The clinical presentation was venereal chancre in 15 cases, asymptomatic ischemic brain lesions in 17 cases, acute ischemic stroke in 13 cases, movement disorder in three cases, tabes dorsalis in two cases, tendinitis-arthritis in eight cases, Amyotrophic lateral sclerosis (ALS) in one case, Deep venous thrombosis (DVT) in one case, and pulmonary nodule in one case. All patients were found to be HIV negative (Table 1).

Table 1. Clinical characteristics of the patients.

Parameters	Male (n=44)	Female (n=17)
Age, years ± SD	57.4 ±18.4	65.3 ±19.1
Venereal chancre, n (%)	11 (18%)	4 (6.6%)
Asymptomatic ischemic brain lesions, n (%)	12 (19.7%)	5 (8.2%)
Acute ischemic stroke, n (%)	10 (16.4%)	3 (4.9%)
Movement disorder, n (%)	1 (1.6%)	2 (3.3%)
Tabes dorsalis, n (%)	-	2 (3.3%)
Tendinitis-arthritis, n (%)	6 (9.8%)	2 (3.3%)
ALS, n (%)	1 (1.6%)	-
DVT, n (%)	1 (1.6%)	-
Pulmonary nodules, n (%)	-	1 (1.6%)
Admission Clinic		
Neurology, n (%)	36 (59%)	
Infectious diseases, n (%)	15 (25%)	
Dermatology, n (%)	7 (12%)	
Gynecology, n (%)	3 (4%)	

SD: Standard deviation, ALS: Amyotrophic lateral sclerosis, DVT: Deep venous thrombosis.

Discussion

In our study, in the last 5 years 31% of the cases diagnosed with syphilis in our hospital were diagnosed by infectious diseases, dermatology and gynecology clinic and the most common complaint was venereal chancre. Fifty-nine percent of the patients were diagnosed with syphilis by the referral of neurology and these patients were evaluated as late stage neurosyphilis. The most common clinical signs of neurosyphilis are dementia, stroke, tabes dorsalis, vasculitis, and parkinsonism [13]. In the present study, the most common clinical presentation was acute ischemic stroke in patients diagnosed with neurosyphilis.

Syphilis caused by Treponema pallidum is an infectious disease that is widely reported all over the world [14]. The organism can invade the central nervous system in the early period. The disease spreads by "neuroinvasion" during the pre-clinical primary syphilis. Neurological involvement is one of the most important manifestations of syphilis. Typically, neurosyphilis is defined as a late finding, but neuroinvasion and neurological disease are seen in both early and late syphilis, and Treponema pallidum is often detected in cerebrospinal fluid (CSF) in early stage syphilis patients [15, 16]. Neurosyphilis is most commonly asymptomatic, other forms of neurosyphilis include meningeal, meningovascular and parenchymal

involvement including general paresis and tabes dorsalis [17]. Asymptomatic neurosyphilis poses a risk of developing subsequent neurological symptoms in the partially treated patients. In asymptomatic neurosyphilis, treatment can be significantly delayed. Early neurosyphilis was common in this cohort. It has been shown that highly active antiretroviral therapy to reverse immunosuppression may alleviate neurological complications of syphilis [18, 19]. With the widespread use of antibiotics, atypical forms in which symptoms are intertwined instead of classical neurosyphilis forms have started to be seen more frequently, which makes diagnosis difficult [20]. In a multivariate regression analysis, headache was a protective factor in NS patients, whereas double vision was significantly associated with poor outcomes. They concluded that double opinion gave negative results for NS patients. In addition, they suggested that a high clinical suspicion is needed for the diagnosis of NS, and that the presence of headache in syphilitic patients may help in the early diagnosis of central nervous system disease [21].

In recent years, there have been studies on neurological involvement in HIV-negative syphilis patients in addition to HIV-positive patients [22, 23]. All patients with the neurological findings in the current study were found to be HIV negative.

In this study, we aimed to draw attention to neurosyphilis in the differential diagnosis of the patients with ischemic cerebrovascular disease, parkinsonism, dementia and neuropsychiatric findings. Syphilis is often overlooked in the differential diagnosis in these patient groups which are very common in daily clinical practice. Therefore, many patients may be deprived of the treatment. It also should be kept in mind that syphilis positive patients should be asked about their partners and if necessary, the partners may be treated.

Conclusion

In conclusion, neurosyphilis, an easily treatable disease, should be considered in the differential diagnosis of patients presenting with such neurological findings.

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