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CASE REPORT

Neurosyphilis Presenting as Psychiatric Symptoms at Younger Age: A Case Report

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Abstract: Neurosyphilis is a central nervous system infection caused by *Treponema pallidum* that imitates various neurological and mental disorders. Therefore, patients with this disease are prone to misdiagnoses. Here, we report a case of neurosyphilis with a psychotic disorder as the main manifestation. A young girl exhibited mental and behavioural abnormalities after a heartbreak, which manifested as alternating low mood, emotional irritability, and a lack of interest in social relations, followed by memory loss. The cerebrospinal fluid protein - Treponema pallidum particle agglutination test was positive, the toluidine red unheated serum test titre was 1:4, the white blood cell count was 5 × 10^6/L, the cerebrospinal fluid protein level was 0.97 g/L, and the brain CT was abnormal. After admission, the possibility of neurosyphilis was considered and the patient received intravenous penicillin G treatment. The patient's clinical symptom ms improved. This case emphasises that doctors should maintain clinical suspicion of *Treponema pallidum* infection in adolescent patients with mental abnormalities.

Keywords: neurosyphilis, case report, psychotic disorder, Treponema pallidum, syphilis

Introduction

Syphilis is a chronic infectious disease caused by *Treponema pallidum* (*T. pallidum*). In recent years, as the incidence of syphilis has increased worldwide, the incidence of neurosyphilis has also increased yearly.[1] The incidence of atypical neurosyphilis was 31% between 1965 and 1985 but increased to 86% between 1995 and 2005.[2] This disease entity, known as the "great imitator", may be easily overlooked or misdiagnosed without a high index of suspicion. After initial infection, *T. pallidum* could enter a latent stage where the *T. pallidum* remains in the body without causing symptoms. If untreated, syphilis could progress to the tertiary stage within a period of time after the initial infection. During the tertiary stage, the *T. pallidum* could invade the central nervous system, leading to neurosyphilis. This complication could manifest in various forms, including asymptomatic neurosyphilis, meningovascular syphilis and general paresis. Neuropsychiatric symptoms as the initial manifestation after *T. pallidum* infection have only been reported in a handful of cases.[3,4] Here, we present the case of an adolescent female who developed mental and behavioral disorders following a heartbreak. Initially diagnosed with emotional disorders secondary to heartbreak, she was ultimately found to have neurosyphilis through comprehensive laboratory and imaging examinations.

Case Presentation

A 16-year-old girl was admitted to the hospital because of abnormal mental behaviour for more than seven months, which had been aggravated for nine days. Seven months previously, the girl developed mental and behavioural abnormalities after a heartbreak, which manifested as alternating low mood and emotional irritability, a lack of interest in social relations, and memory loss. Her parents, brother, and sister were in good health and the parents were nonconsanguineous. There was no family history of genetic diseases. Her parents took her to the local hospital for consultation, but the general physical examination and laboratory test results were normal, and no treatment was administered. A few months later, the patient's

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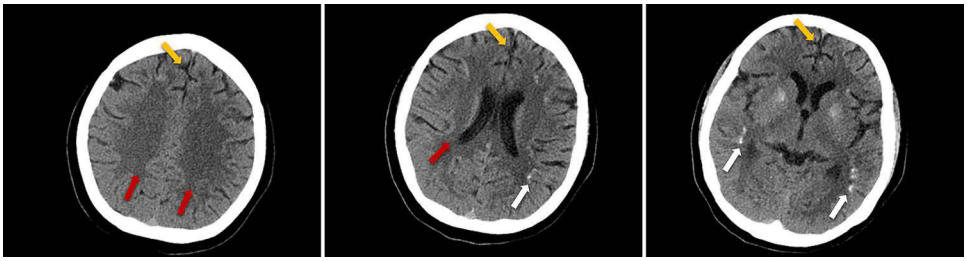

Figure 1 The images of Brain CT (axial view). Yellow arrow: this arrow reveals the slightly widened and deepened sulcus, and slightly narrowed frontal parietal gyrus. Red arrow: this arrow reveals the bilateral semioval centre and lateral ventricle brain white matter region low-density changes. White arrow: this arrow reveals the scattered calcifications.

symptoms worsened; she refused to eat, drink, sleep, or communicate, exhibited slowness in movement, and was finally transferred to our hospital. The physical examination showed the following results: clear consciousness; able to answer simple questions; and no redness, ulcers or vegetation in the perianal skin. The bilateral Babinski sign and the right Oppenheim sign were positive. No obvious abnormalities were observed on cardiopulmonary or abdominal physical examinations. Tests for hepatitis B, hepatitis C, and human immunodeficiency virus were negative. The treponemal serological test result was positive and the toluidine red unheated serum test (TRUST) titre was 1:128. The results of cerebrospinal fluid (CSF) testing results are as follows: White blood cells: 5.0 ×106/L, Red blood cells: 2.5×106/L, Glucose:3.41 mmol/L, Cl-:128.3 mmol/L, Total protein:970.0 mg/L, Treponema pallidum particle agglutination test (TPPA): positive. Brain computed tomography (CT) showed a bilateral cerebral hemisphere gray matter junction area, scattered calcification in the bilateral lenticular nucleus and thalamus, bilateral semioval centre, lateral ventricle brain white matter region, a slightly widened and deepened sulcus, and a slightly narrowed frontal parietal gyrus (Figure 1). After admission, the possibility of neurosyphilis infection was considered. The patient was administered an intravenous penicillin G solution, oral olanzapine, and depakin for 12 days. After treatment, the patient's clinical symptoms improved, and she was discharged with her parents. We informed the patient to continue penicillin G treatment at a hospital near their home.

Discussion

Neurosyphilis is a group of clinical syndromes caused by *T. pallidum* invading the central nervous system, including the meninges, blood vessels, and brain or spinal cord parenchymal damage. Patients may present with dorsal muscular atrophy, Argyll Robertson's pupils, tingling, and rare psychiatric symptoms (including psychosis, mood changes, and dementia).[5] Currently, most patients infected with *T. pallidum* do not develop neurosyphilis because they are diagnosed early and treated effectively with penicillin. Furthermore, owing to the widespread use of antibiotics for infectious diseases, the clinical manifestations and stages of syphilis seem to have changed considerably. The proportion of patients with neurosyphilis and atypical or asymptomatic manifestations has gradually increased.[3] Atypical neurosyphilis refers to cases where the clinical manifestations do not match the classic symptoms of neurosyphilis. Patients may exhibit non-classical neurological symptoms such as mild memory impairment, headaches, fatigue, or mild psychotic symptoms instead of classic signs like meningitis, tabes dorsalis, or general paresis. This increases the difficulty for clinicians to diagnose neurosyphilis accurately and is prone to missed diagnosis and misdiagnosis. Relevant studies have shown that middle-aged men have a higher risk for neurosyphilis.[6,7] The prevalence of syphilis in men is higher than that in women, which may be related to the higher levels of sexual activity and unsafe sex among men, especially homosexual men.

In this case, the patient was a 16-year-old girl who exhibited mental and behavioural abnormalities after loss of love. Without performing the syphilis antibody test and TRUST, the patient's age and sex would make it more likely that heartbreak was the cause of the mental and behavioural abnormalities. Therefore, the patient was admitted to a local hospital without syphilis screening, to exclude the possibility of *T. pallidum* infection. Physical and mental development in adolescents is immature, and they lack sexual health knowledge and self-protection awareness of sexual behaviours, which leads to a higher incidence of unsafe sexual behaviours. This case revealed that the sexual behaviour history of

both male and female adolescent patients with mental abnormalities should be collected by doctors. If necessary, syphilis screening should be performed to exclude neurosyphilis.

Neurosyphilis exhibits several clinical manifestations. However, no laboratory test can be used to diagnose neurosyphilis. CSF testing, an important indicator, can be used to assist in the diagnosis of neurosyphilis. CSF testing included routine CSF tests, biochemical tests, and *T. pallidum*-related testing. Currently, CSF treponemal tests include the highly sensitive fluorescent treponemal antibody absorption test, TPPA, and *T. pallidum* haemagglutination test. However, IgG antibodies against *T. pallidum* have relatively low molecular weights and can easily penetrate the blood-brain barrier, causing false-positive results in treponemal tests. Therefore, these tests are commonly used to exclude neurosyphilis.[8] Non-treponemal tests mainly include the Venereal Disease Research Laboratory (VDRL) test, rapid plasma reagin (RPR) test, and TRUST. The United States Centers for Disease Control and Prevention guidelines emphasise that CSF-VDRL positivity can be used as an important diagnostic criterion for symptomatic neurosyphilis.[9] CSF-VDRL test abnormalities have been included in the diagnostic criteria for neurosyphilis in Chinese Guidelines. However, because of the low sensitivity of the VDRL test and high cost of its reagents, many hospitals do not perform VDRL tests. Therefore, Chinese and European guidelines suggest that CSF-RPR/TRUST can be used to replace the CSF-VDRL test under these conditions.[10,11] Meanwhile, a white blood cell count $\geq 5 \times 10^6$/L and/or protein level > 500 mg/L in the CSF are important criteria for the diagnosis.[10] In this case, the CSF-TPPA was positive, the TRUST titre was 1:4, the CSF white blood cell count was 5×10^6/L, and the CSF protein was 0.97 g/L, which met the laboratory diagnostic criteria for neurosyphilis. Recent research has shown that serum UCH-L1, GFAP, and NF-L are good entry points and biomarker candidates that are comparable to or even superior to CSF, and allow patients to avoid lumbar puncture.[12]

The role of imaging in diagnosing neurosyphilis is also critical. CT and magnetic resonance imaging (MRI) could reveal abnormalities associated with neurosyphilis, such as cerebral atrophy, stroke, or white matter lesions. In the presented case, imaging findings included the widened and deepened sulcus, brain white matter region low-density changes and the scattered calcifications, which are consistent with neurosyphilis. The likely cause of these imaging findings is the inflammatory and ischemic damage caused by T. pallidum to the brain parenchyma and blood vessels. Imaging plays a pivotal role in the diagnosis and management of neurosyphilis, providing valuable information on the extent and nature of central nervous system involvement. A recent review highlights the importance of advanced imaging techniques in identifying neurosyphilis-related abnormalities, suggesting that imaging should be an integral part of the diagnostic workup for patients suspected of having neurosyphilis.[13]

Conclusion

The case presented in this article was that of a 16-year-old girl with mental and behavioural abnormalities as the main manifestations, who was finally diagnosed as atypical neurosyphilis and improved after treatment. The clinical manifestations of neurosyphilis are diverse, vary greatly, and lack specificity. However, adolescents are not a high-risk group for syphilis, especially for neurosyphilis. Clinicians must keep this diagnosis in mind when adolescent patients with mental disorders visit hospitals. If necessary, syphilis screening should be performed to exclude *T. pallidum* infection. This could minimise the adverse effects of syphilis in adolescents.

Abbreviations

T. pallidum, Treponema pallidum; TRUST, toluidine red unheated serum test; CSF, cerebrospinal fluid; TPPA, Treponema pallidum particle agglutination test; CT, Computed tomography, MRI, magnetic resonance imaging; VDRL, Venereal Disease Research Laboratory test, RPR, rapid plasma regain.

Ethical Approval and Consent for Publication

We have obtained the informed consent from the patient's parents for publication of this case report and any accompanying images. No institutional approval is required to publish case details.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically

reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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