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Case Report

Simultaneous neurosyphilis and tuberculous meningitis in a patient with systemic lupus erythematosus: a case report

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Abstract: Background: Cooccurance of central nervous system (CNS) infection with neurosyphilis and tuberculosis meningitis (TBM) is very rare. Opportunistic infections due to listeria monocytogenes, mycobacterium tuberculosis, or fungi should be considered in the differential diagnosis of meningitis in patients with systemic lupus erythematosus (SLE) befor receiving immunosuppressive agents. Here we present a female diagnosed with SLE, with the cooccurance of neurosyphilis and TBM. Case presentation: A 49-year-old woman with history of SLE was admitted to the emergency department with the chief complaint of fever and altered mental state for 2 days. Cerebrospinal fluid (CSF) examination revealed white blood cell count of 189*10^6/l, elevated protein level (2.38 g/l), and depressed glucose level (1.24 mmol/l). Indian ink stain and direct observation of microorganizm were negative in random visual fields. The fever had not been subsided using isoniazid, rifampicin, streptomycin and pyrazinamide as anti-tuberculosis treatment. Later applying penicillin to treatment had relieved the fever, mental state and there was no neck rigidity. Discussion: Patients with SLE were prone to suffer from tuberculous meningitis when the immune system is supressed. As the patient's husband had infected with Treponema Pallidum (TP) 6 years ago and the patient's blood test of Treponema Pallidum antibody (TP-Ab) was positive, When the routine anti-tuberculosis treatment had not relieved TBM, there was a need to consider combined with neurosyphilis, and once confirmed, timely penicillin therapy may improve prognosis.

Keywords: Systemic lupus erythematosus, tuberculous meningitis, neurosyphilis, penicillin therapy

Background

Systemic lupus erythematosus (SLE) is an autoimmune disease that damages multisystem of the body. As patients receive long-term immunosuppressor treatments, they become immune-impaired. Tuberculosis infection is more commonly seen [1]. Neurosyphilis is a disease of the central nervous system caused by infection of Treponema Pallidum (TP). Neurosyphilis and tuberculosis meningitis (TBM) are both common in SLE, but very rarely comorbidity. Here we present a case of a 49-year-old woman admitted to our hospital with SLE, TBM and neurosyphilis.

Case presentation

A 49-year-old female of Han ethnicity was brought to the neurology emergency with a two-day history of altered mental status. The manifestations include refusal to eat, drink and lack of environmental interactivity with a rapid disease progression. No history of constipation or urinary incontinence, no spasm of the extremities seen. Patient had fever since 12 hours ago, with the highest fever at 38.5°C.

The patient was diagnosed with SLE for 5 years, and sustained long term treatment of methylprednisolone (10 mg/d). Her husband had a history of syphilis in 2010, and recovered after penicillin treatment with no relapse. There was no history of common risk factors of atherosclerosis, such as hypertension, diabetes mellitus, or coronary artery disease.

She was in poor spirit and the temperature was 38.5°C, the blood pressure was 121/66 mm Hg. Chest and cardiac examination suggested no positive sign. The neurological examination demonstrated severe neck rigidity. She

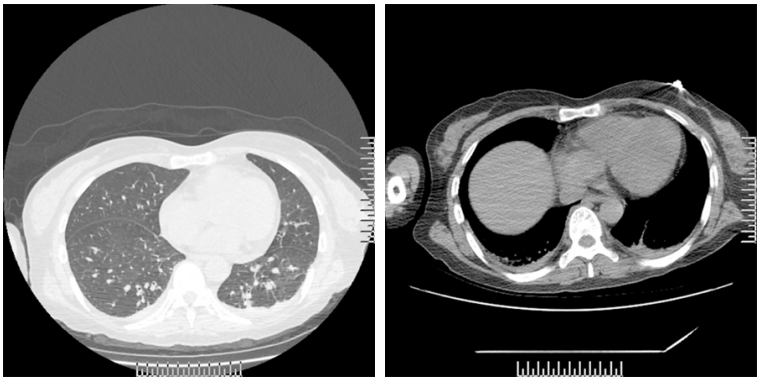

Figure 1. Chest CT showing the Pulmonary infection and bilateral pleural effusion.

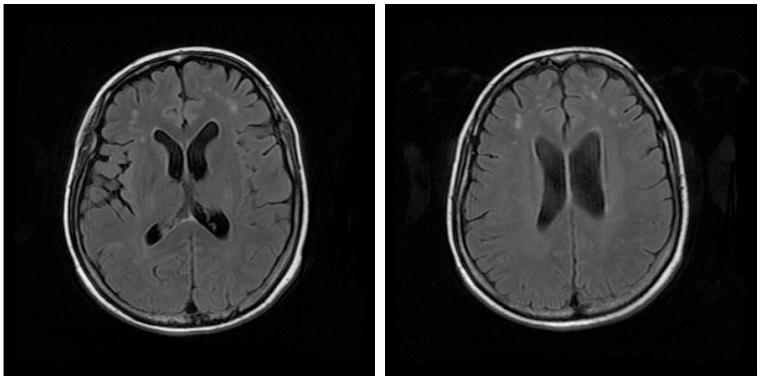

Figure 2. Cerebral MRI (T2 FLAIR sequence) showing multiple ischemic foci of infract in bilateral corona radiata and frontal regions.

did not cooperate with the other physical examinations. Routine blood test revealed white blood cell count of 8.74*10^9/l (neutrophils 7.33*10^9/l, accounts for 83.90%, lymphocytes 13.5%), the CRP was 177.04 mg/l. The lupus anticoagulation factor was 49.9 SEC, routine urine test revealed albuminous urine. The total protein in 24 hours urinary was 0.61 g. The C_3 complement was 30.564 g/l and the double-stranded DNA antibody was positive. Serum syphilis serology was strongly positive. The T-Spot test was also positive. A computed tomography (CT) scan of the chest showed pulmonary infection (**Figure 1**). Cerebral MRI scan found multiple ischemic foci of infract were located in bilateral corona radiata and frontal regions (**Figure 2**).

Diagnostic lumbar puncture was performed, the CSF examination revealed a mononuclear pleocytosis 189*10^6/l, (the neutrophil accounted for 27%, lymphocytes 72%, endothelial cells 1%), an elevated protein level (2.38 g/l), and a depressed glucose level (1.24 mmol/l). Indian ink stain and direct observation of microorganizm were negative in random visual fields. With a history of SLE and the serum lupus anticoagulation factor was higher than the normal, possibility of tuberculosis meningitis was considered, and then we began to use glucocorticoid (dexamethasone 10 mg/d) and Anti-TB treatment, including Isoniazid (12 ml/d), rifampicin (0.45 g/d), pyrazinamide (1 g/d), and streptomycin (0.75 g/d). At the same time, we used cephalosporins to treat lung infections. Within few days, patient gradually regained consciousness, but the fever repeated, mainly started from 11 am to 3 pm, then the temperature dropped to normal again, the highest temperature was 40.5°C.

With the husband provided history of syphilis, as well as current serology result, we had evidence to suspect neurosyphilis to cause intermittent fever. Two weeks after the initial lumbar puncture, the procedure was repeated, the CSF examination revealed a mononuclear pleocytosis of 19*10^6/l and an elevated protein level (1.26 g/l) and a depressed glucose level (2.71 mmol/l), no organisms were found and Indian ink stain was negative. This time, TP-Ab was tested positive in CSF. With all these test results, patient was diagnosed as TBM and neurosyphilis and started to treat with penicillin (400 IU q4h). On the second day of the treatment, the patient had a fever as high as 39.6°C, which we considered to be Jarisch-Herxheimer reaction [2]. Latter combined with the anti-TB drugs and the antibiotics, the patient had no fever anymore. TWO weeks later, we had the third lumbar puncture, compared to the last CSF examination, it showed a depressed mononuclear pleocytosis level (15*10^6/l), a depressed protein level (0.88 g/l), and a

depressed glucose level (2.4 mmol/l). After a month of therapy, the patient recovered.

Discussion

To our knowledge, a clinical case of CNS damage due to tuberculosis and syphilis has not been reported.In this case, neither tuberculosis nor syphilis could explain the clinical findings exclusively. The patient sustained hyperpyrexia, which was incompatible with TBM. As the patient's serum and CSF syphilis serology were both strongly positive, there were reasons to believe that the hyperpyrexia was caused by the neurosyphilis.

Due to the long-term oral glucocorticoids and immune inhibitors, patients with SLE are easily misdiagnosed with SLE lupus activity when they have fever, headache or abnormal mental behaviors. these clinical manifestations make it difficult to identify SLE with lupus encephalopathy or with CNS infection, the most common CNS infection is TBM. In this case, CSF examination plays an important diagnostic value. The main features of lupus encephalopathy CSF are almost normal, just a small number of people have a midly elevated CSF pressure or a slight increase in white cell number (mainly the lymphocyte), most people have an elevated protein level, while the glucose level and the chloride level change little. The typical CSF examination of TBM has an obvious increase in white blood cell level, about 50-500*10^6/l, moderate increase in protein level (>1 g/l), a reduced glucose and chloride level [1]. The gold standard in diagnosing TBM is the founding of tuberculosis bacilli in CSF [3]. However, it is very difficult to find tuberculosis bacilli in CSF. Therefore, timely anti-tuberculosis treatment has a diagnosing value when the TBM cannot be excluded. Delayed treatment may lead to high morbidity and mortality [4].

Neurosyphilis is a chronic disease in central nervous system caused by TP, mainly damaging the nerve tissue and the blood vessel, which may occur at every stage of syphilis [5]. But it mainly happens in the third phase of syphilis, the incidence may increase by up to 30% [6]. Generally, neurosyphilis occurs decades after the first infection, but it may be shorter in immunosuppressed individuals [7]. It has been found that up to 4-10% of patients with untreated syphilis may develop neurosyphilis [8]. Clinical manifestations of neurosyphilis are diverse and complex, especially in immunocompetent individuals [9], almost can cause neurological, otorhinolaryngological, ophthalmological or psychiatric diseases related to similar clinical manifestations, it is called "the great imitator". In this case, the patient is mainly manifested as abnormal mental behaviors and hyperpyrexia, which need to be identified with the similar symptoms caused by other CNS infection. To diagnose the neurosyphilis, doctors should inquire about patients' medical history carefully and then make conclusions according to the results of the serum and CSF syphilis serology test. The imaging of neurosyphilis is not characteristic, while the serum and CSF syphilis serology test are most comonly applied in clinical setting. When doctors find TP-Ab in blood and CSF, they can almostly make a definite diagnosis of neurosyphilis, so the serum and CSF syphilis serology test of TP-Ab accounted for the first place [10]. There is still no gold standard at present in diagnosing neurosyphilis. So the diagnosis has to base on the personal histories, such as the TP infection of themselves or their spouses, the blood transfusion history or the sexual partner infection.

CNS infection with neurosyphilis and TBM is very rare, especially in patients with SLE. If we ignore the patient's history of TP infection, it is easy to cause misdiagnosis. When TBM and neurosyphilis cooccurs in patients with SLE, it can aggravate the patient's condition. Due to co-infection of neurosyphilis, the symptoms can not be relieved when only using the anti-tuberculosis treatment with a history of TP infection, when fever and headache occurs, in addition to the diagnosis of TBM, we should also consider the possibility of relapse of neurosyphilis. At this point, the detection of TP-Ab in CSF is particularly important. If the TP-Ab in CSF is found positive, the nerve syphilis infection cannot be excluded. Once diagnosed as the neurosyphilis, large doses of penicillin is important in addition to anti-tuberculosis drugs. Further investigations are necessary on patients with multiple infections, including tuberculosis, syphilis and SLE.

Conclusions

Timely diagnosis and treatment of neurosyphilis and tuberculous meningitis is very important for the prognosis of the disease.

Consent

Written informed consent was obtained from the patient for publication of this case report. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Acknowledgements

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Disclosure of conflict of interest

None.

Abbreviations

CNS, central nervous system; SLE, systemic lupus erythematosus; TBM, tuberculous meningitis; CSF, cerebrospinal fluid; JHR, Jarisch-Herxheimer Reaction; TP, Treponema Pallidum; TP-Ab, TP-antibody.

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