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Case Report

A rare presentation of toxoplasma encephalitis in systemic lupus erythematous patient: case report and review of literature

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ABSTRACT

We present a patient with systemic lupus erythematous (SLE) and visited emergency department, due to the progressive incoherent speech and disoriented to time in these few days. There were no obvious contact history or symptoms of infection. Due to the focal seizure, the brain magnetic resonance imaging (MRI) with gadolinium enhanced was arranged and revealed multiple ring enhancement picture and the brain abscess were suspected. The initial pathology suspected the lupus cerebritis, due to the vasculitis characteristic. Finally, according to the Immunohistochemistry study, the rare CNS infection of SLE patients– cerebral toxoplasmosis was confirmed the diagnosis.

Keywords: Toxoplasma encephalitis, Systemic lupus erythematous

INTRODUCTION

In the immunocompromised host, toxoplasmosis is an important cause of morbidity and mortality. Few reports of toxoplasmosis complicating systemic lupus erythematous (SLE) have been reported in the medical literature, and this emphasizes the difficulty in establishing the diagnosis, because of most report confirmed the diagnosis after autopsy. Moreover, a patient with SLE and neurologic manifestation is naturally suspected to lupus cerebritis. We present a patient with SLE and visited emergency department, due to the progressive incoherent speech and disoriented to time in these few days.

CASE REPORT

This 47-year-old male had the history of SLE, first diagnosis in 2001, since that, he takes oral medication of Prednisolone 5 mg 1tab three times per day and hydroxychloroquine 200 mg 1 tab twice per day. Due to the severe nephritis, he received the cyclophosphamide treatment since 2004. His past medical history included chronic glomerulonephritis, traumatic brain injury associated intracranial hemorrhage stat post craniotomy in 2002, alcoholism and hypertension.

The patient suffered the progressive incoherent speech and disoriented to time in recent days. Personality changed and wide-base gait were noted during initial evaluation. The further neurologic examination revealed the decline of cogitative function, impairment of recent and immediate memory without nuchal rigidity. Initial laboratory examination revealed the leukopenia (leukocyte count 2.5 x 10^9/L), chronic renal failure stage II (creatinine 1.22 mg/dl, estimated glomerular filtration rate: 66 mL/min/1.73m^2), hyperlipidemia (Triglyceride 191 mg/dl) without electrolyte imbalance. Computed tomography with contrast enhancement revealed multiple hypodense lesions in the bilateral cerebral hemispheres with perifocal edema and the metastases were suspected. The further evaluation of tumor survey, such as tumor marker of alpha-feto protein, carbohydrate antigen 19-9,

carcinoembryonic antigen, squamous cell ccarcinoma antigen and serum tissue polypeptide antigen all revealed the negative finding.

Three days later, the fever and focal seizure of left side limbs were founded. The brain magnetic resonance imaging (MRI) with gadolinium enhanced revealed the multiple well defined lesion involved bilateral cerebral hemispheres, right cerebellar hemisphere and pons. The lesions involved the gray white junction and were hypointense on T1W1 and hyperintense on T2W1 and fluid attenuated inversion recovery (FLAIR) with perifocal edema. The lesions in left and right temporal lobes revealed a ring enhancement picture and the brain abscess were suspected (Figure 1a, 1b, 1c). The CNS infection pathogen of Amobea, crypococci neoformans, acid fast bacilli stain, polymerase chain reaction of Tuberculosis and fungus culture were all negative finding. The Cerebrospinal fluid (CSF) analysis revealed the lymphocyte predominate and the normal range of sugar (72 mg/dl) and protein (32 mg/dl). The blood examination were also negative of acquired immune deficiency syndrome and syphilis. The further surgical intervention was arranged to confirm the diagnosis.

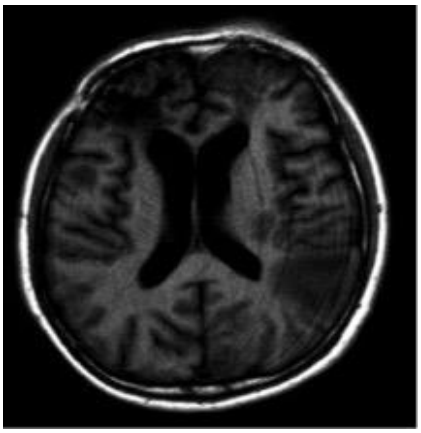

Figure 1a: T1 weighted MRI showed multiple hypointense lesion gray white junction on T1W1.

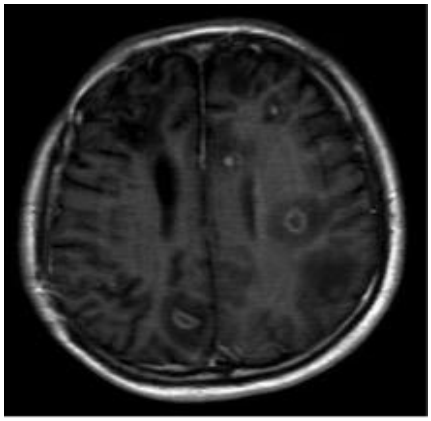

Figure 1b: T1 weighted MRI with enhancement showed the multiple ring-enhancing lesion.

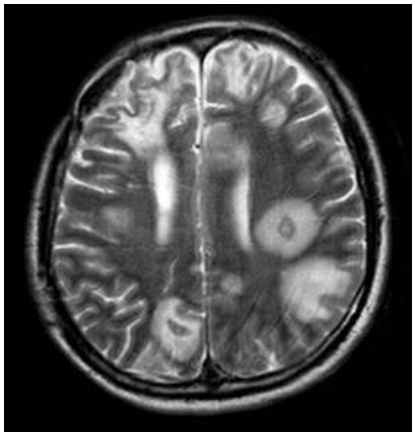

Figure 1c: T2 weighted MRI showed hyperintense picture and perilesional edema on FLAIR.

Microscopically, sections showed numerous necrosis forming abscesses with clusters of microglial cells and mixed inflammatory infiltrate, mainly lymphoplasmal cells and histiocytes. Proliferative vasculature with perivascular infiltrate, acute vascular injury, fibrinoid necrosis and vessel obliteration were also noted. No obvious tumor cell was seen (Figure 3a and 3b) and the CNS infection or lupus cerebritis were suspected. However, after few weeks antibiotics treatment, the drowsy of consciousness and no clinic improvement of infection condition. The repeated brain MRI with enhancement (Figure 2) revealed the markedly worsening of suspect granulomas/abscesses with perifocal edema in the bilateral cerebral hemispheres, midbrain, pons and cerebellar hemispheres and pons. After discussion with the pathologist, the review and further immunoreactive stain were arranged. In focal area, oval to crescent shaped micro-organisms with an ovoid basophilic nucleus and eosinophilic cytoplasm were identified. Cystic or ball-like micro-organisms with minute round basophilic organism were also noted.

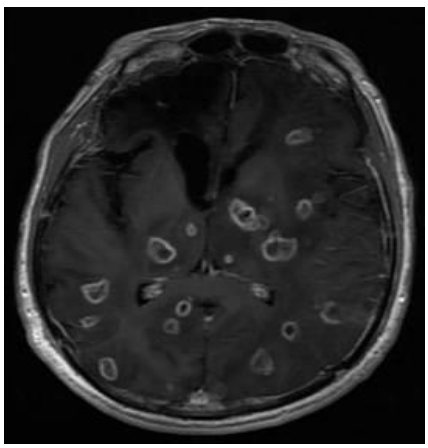

Figure 2: The obvious interval worsen of bilateral cerebral hemispheres, midbrain, pons and cerebellar hemispheres and pons.

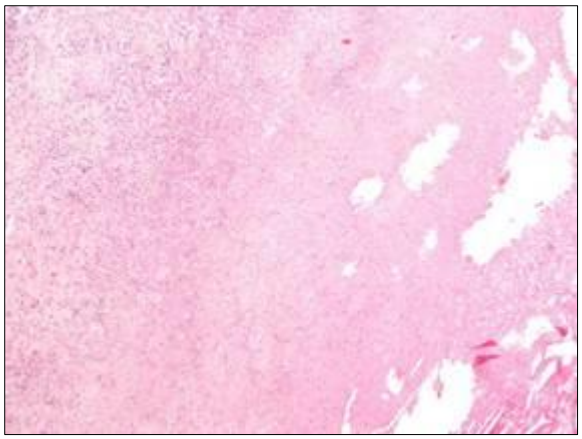

Figure 3a: Numerous necrosis forming abscesses without obvious capsular formation.

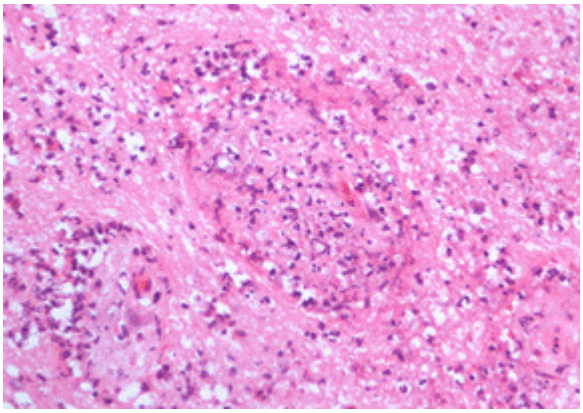

Figure 3b: It revealed cellular necrosis with mixed inflammatory infiltrate, mainly lymphoplasmal cells and histiocytes. Proliferative vasculature with acute vascular injury, fibrinoid necrosis and vessel obliteration were identified.

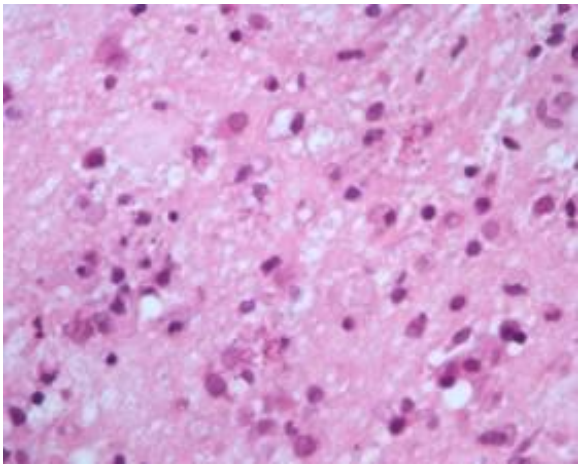

Figure 4a: Microscopically, sections showed oval to crescent shaped micro-organism with an ovoid basophilic nucleus and eosinophilic cytoplasm. Cystic or ball-like structure with minute round basophilic organisms was also identified.

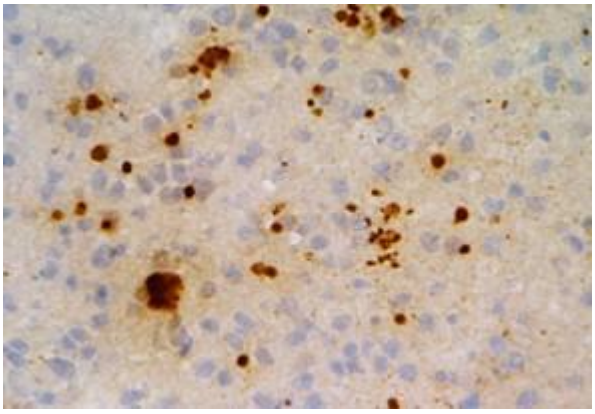

Figure 4b: The micro-organisms were immuo-positive for Toxoplasma antibody.

The Periodic Acid-Schiff (PAS), Gomori Methenamine Silver (GMS) and acid-fast stains were negative, but these micro-organisms were immunoreactive for Toxoplasma antibody, which suggested tachyzoites and bradyzoites forms of toxoplasma (Figure 4a and 4b). Moreover, the serum examination revealed the toxoplasmosis IgG positive. The final diagnosis of toxoplasma encephalitis was confirmed. The improved of Glasgow Coma Scale (GCS) to E4VtM5 and four limbs muscle power to 4 point were noted after 2 weeks antibiotics treatment with trimethoprim-sulfamethoxazole (TMP-SMX).

DISCUSSION

The protozoan parasite Toxoplasma gondii can infect a variety of warm-blooded hosts including humans although the sexual life cycle only occurs in members of the feline family.[1-3] Toxoplasma gondii can infect humans in 3 different ways: ingestion of tissue cysts, ingestion of oocysts, or congenital infection with tachyzoites.[4] Within a short period of time the tachyzoite form of the parasite actively crosses the gastrointestinal barrier by penetrating enterocytic cells in the small intestine and entering submucosal tissue.[5,6] Intracellular tachyzoites form a parasitophorous vacuole that ruptures following multiple cycles of replication. From there tachyzoites disseminate throughout the body and reach immunologically protected sites including brain, retina and fetus.[7-9] Latent infection with T. gondii involves an elaborate interplay between the parasite and the host in which the parasite ensures its survival and proliferation but avoids fatal damage to the host at the same time.[10]

By definition, latent infections involve a complex interplay between parasite and host, producing some degree of harmony. In humans, T. gondii performs a delicate balancing act that involves, on the one hand, modification of its proximal (and perhaps distal) environment in ways to promote its survival and transmission and, on the other hand, avoidance of overt tissue damage (directly from the parasite or indirectly from the immune response) that would lead to the demise

of its host. Latent chronic infection in immunocompetent (healthy) adult persons was thought to be benign. However, recent evidence has challenged this assumption. Within healthy immunocompetent populations, there have been increasing numbers of reported associations between T. gondii seropositivity and suicide, schizophrenia, psychiatric hospitalizations, depression, personality changes, and even, in very preliminary investigations, Alzheimer's disease.[11]

On the other hand, immunosuppression of the host may lead to the uncontrolled release of parasites during rupture of tissue cysts in the brain of latently infected individuals. Subsequently, released bradyzoites converting into rapidly proliferating tachyzoites may cause reactivated toxoplasmosis and lethal encephalitis.[12] In this case with SLE, the long-term treatment of prednisolone, hydroxychloroquine, & cyclophosphamide may suppress the patient's immune system and then reactivated toxoplasmosis encephalitis.

In the immunocompromised host, toxoplasmosis is an important cause of morbidity and mortality. Few reports of toxoplasmosis complicating SLE have been reported in the medical literature, and this emphasizes the difficulty in establishing the diagnosis, because of most report confirmed the diagnosis after autopsy. Moreover, a patient with SLE and neurologic manifestation is naturally suspected to lupus cerebritis.

The brain MRI with gadolinium enhanced revealed the multiple well defined lesion involved bilateral cerebral hemispheres, right cerebellar hemisphere and pons. The lesions involved the gray white junction and were hypointense on T1W1 and hyperintense on T2W1 and FLAIR with perilesional edema. The lesions in left and right temporal lobes revealed a ring enhancing eccentric target sign on post contrast T1 weighted spin echo imaging (Figure 5).[13] On axial T2WI (Figure 6), the lesions involving bilateral temporal and parietal gray white junction had "concentric target like" appearance with alternate hypo- and hyperintensities (target sign) and central hypointensity.[14]

Cerebral toxoplasmosis produces multifocal lesions, frequently affecting the basal ganglia, cerebral cortex, brain stem and cerebellum. The 'eccentric target sign' - a ring shaped zone of peripheral enhancement with a small eccentric nodule along the wall on post contrast T1W1 with 95% specificity and 25% sensitivity.[15]

The "concentric target sign" is a recently described MRI sign on T2-weighted imaging of cerebral toxoplasmosis that has concentric alternating zones of hypo- and hyperintensities.[16] The concentric target sign, seen in deep parenchymal lesions, is distinct from the surface-based cortical "eccentric" target sign. It is believed to be more specific than the well-known "eccentric target sign" in the diagnosis of cerebral toxoplasmosis.

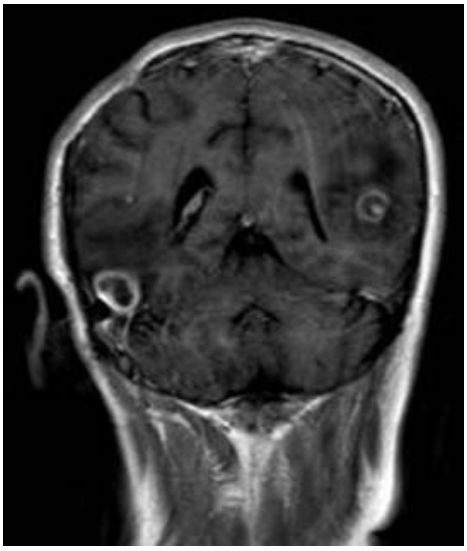

Figure 5: The ring enhancing eccentric target sign on post contrast T1 weighted MRI.

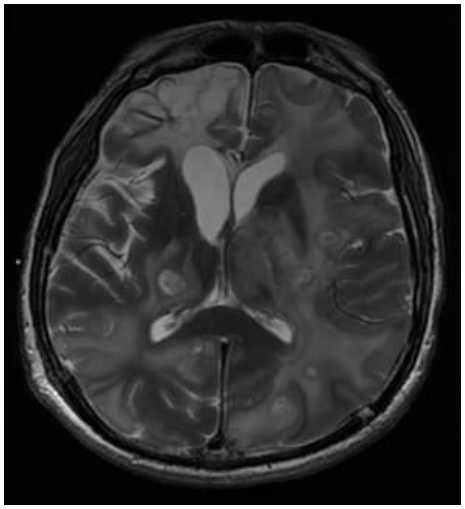

Figure 6: The hypo- and hyperintense zones of concentric sign on T2 weighted MRI.

The diagnosis of Toxoplasmic Encephalitis (TE) is clinically defined by the following 3 criteria: a) the recent onset of a focal neurologic abnormality that is consistent with intracranial disease or an impaired level of consciousness; b) lesions presenting with a mass effect or a radiographic appearance that is enhanced by the injection of a contrast medium in brain imaging [Computed Tomography (CT) or nuclear magnetic resonance]; and c) the presence of T. gondii–specific serum antibody or a successful response to specific therapeutics for toxoplasmosis. However, serology is not a sufficiently sensitive marker for the diagnosis of TE because a rise in the titer of IgG antibody occurs in only approximately 30% of cases and IgM antibody is seldom found. Even the intrathecal production of antibody to T. gondii is found in only 50% of TE presenting AIDS patients.[17] The diagnosis is mostly according to the clinic information and the contact history.

However, there were no obvious contact history, or acute factor to suppress the immune system in this case. The lupus cerebritis or CNS infection were the first impression, before the Immunohistochemistry for Toxoplasma report. The differential diagnosis includes tumor, vasculitis and infectious process. The clinical picture of abscess may be similar with biopsy error leading to glioma mimicking infection but cytological atypia and hyperchromasia of tumor cells should be identified. Our case showed no pleomorphic cell and IDH-1 negative. Lupus cerebritis is another diagnosis considered but vasculitis is a rare manifestation and rare progress into abscess, most in male with cyclophosphamide or prednisolone usage. However, CNS vasculitis also presents with systemic SLE activity. Cryptococcus, histoplasmosis, microsporidium, leishmaniasis, trypanosomiasis and toxoplasma are opportunistic infection in immunocompromised patients. The PAS and GMS stains can disclose fungal micro-organism but our case was no immunoreactivity. Besides, the patient denied any traveling history and Taiwan is not an epidemic infectious area of leishmaniasis or trypanosomiasis. The patient is not only an immunocompromised patient but also a cat owner. Tachyzoite and bradyzoite form micro-organisms were also seen microscopically.

In this case, the long term treatment of steroid and alkylating agent to treat lupus nephritis may destroyed the balance between host immunity and parasite invasion, even without obvious contact history or high risk group.

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Conflict of interest: None declared
Ethical approval: Not required

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