

Cerebral Toxoplasmosis in Systemic Lupus Erythematosus Following Intravenous Methylprednisolone

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SUMMARY

Cerebral toxoplasmosis is a rare complication of systemic lupus erythematosus (SLE). An 18 year old male student, newly diagnosed to have SLE, developed neurological symptoms two days after completing intravenous methylprednisolone. Computed tomography (CT) scan showed features consistent with a diagnosis of probable cerebral toxoplasmosis. He responded dramatically to anti-toxoplasma therapy. To our knowledge, this is the first case report in the literature that presents a newly diagnosed SLE patient who rapidly developed cerebral toxoplasmosis following administration of intravenous methylprednisolone. Our case illustrates that this drug is potentially fatal and the importance of differentiating cerebral infection from neuropsychiatric lupus.

KEY WORDS:

Systemic lupus erythematosus, Cerebral toxoplasmosis, Methylprednisolone, Lupus cerebritis, Neuropsychiatric lupus

INTRODUCTION

Toxoplasmosis is an opportunistic infection primarily affecting patients with immune deficiencies. It is commonly seen in patients with human immunodeficiency virus (HIV) and it is an important cause of morbidity and mortality. Toxoplasmosis complicating SLE has been reported in the literature and is a major cause of death. Furthermore, it is important to distinguish an infection of the central nervous system (CNS) from neuropsychiatric lupus, which can be a diagnostic challenge^{1,2}.

We report a case of a newly diagnosed SLE patient who rapidly developed cerebral toxoplasmosis following treatment with intravenous methylprednisolone.

CASE REPORT

An 18 year old male student was referred from a district hospital with one month history of low grade fever, oral ulcers, arthralgia and rashes over the face and body. On examination, patient had malar rash, photosensitivity, discoid rash and widespread cutaneous vasculitis. Investigations revealed mild cytopenia with haemoglobin of 10.3 g/dL, leukocyte count of 3 300/mm³ (with lymphopenia of 700/mm³) and platelet of 150, 000/mm³. Immunological

test showed a positive anti-nuclear antibody (ANA) 1: 1280 (speckled), anti double-stranded DNA antibody (11.58), anti-Sm and anti-SSA antibodies. Lupus anticoagulant and anti-cardiolipin antibodies were negative. The CRP level was 36.6 mg/L and ESR was 80 mm/hr with normal renal function. He was diagnosed to have Systemic Lupus Erythematosus (SLE).

In view of widespread vasculitis and cytopenia, he was treated with intravenous methylprednisolone 250mg daily for 3 days. His condition improved and the family requested to be discharged. He was discharged with oral prednisolone 30mg daily.

Two days later, he was readmitted with fever, poor oral intake and inability to talk. On examination, he had low grade fever with twitching of his right eyelid, without any signs of meningeal irritation. Orientation and attention were diminished and he was apraxic. Due to poor attention, we were unable to perform a full neurological assessment. Initial computed tomography (CT) scan of the brain showed ill defined hypodense area over the right thalamic and parieto-temporal region (adjacent to the ventricle) with no significant enhancement post contrast, suggesting an infection, infarct or ischemia (Figure 1). His CRP increased to 120.6 mg/L and he was treated with intravenous ceftriaxone 2g bd and metronidazole 500mg bd.

Four days later, the patient developed generalized tonic-clonic seizure. A repeat CT scan of the brain revealed worsening, multiple ill-defined ring enhancing lesions of varying size in both basal ganglia, right frontal and left parietal lobe (Figure 2). The rapid changes that occurred suggested a cerebral infection with the possibility of toxoplasmosis. Subsequently, his condition deteriorated with spiking fever of up to 40°C and decreasing consciousness, despite a switch of antibiotic to intravenous meropenam 2g tds. Examination of the cerebrospinal fluid (CSF) showed a raised white cell count of 27/mm³ (75% neutrophils), increased protein of 2.22 g/L and negative cryptococcal Ag.

All cultures including blood, urine and CSF were negative and an echocardiography did not reveal any vegetations. In-view of rapid deterioration of the radiological findings, he was started on anti-toxoplasma therapy with clindamycin 600mg qid and pyrimethamine 50mg od. Serum IgG antibodies, but not IgM antibodies for toxoplasma were positive, while HIV

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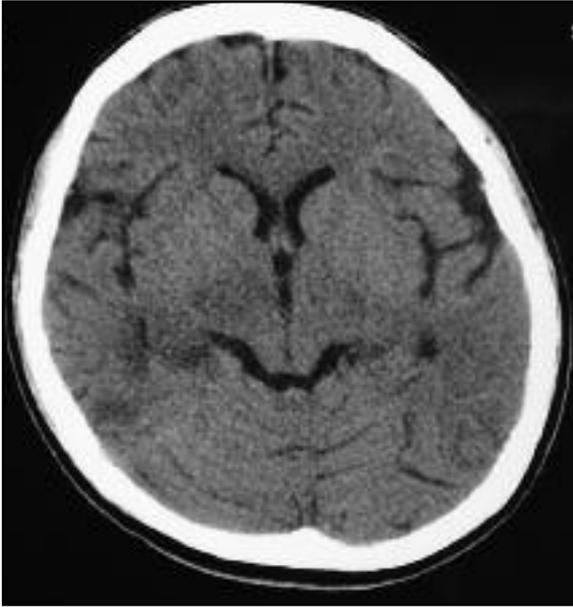


Fig. 1: Ill defined hypodense area over the right thalamic and parieto-temporal region (adjacent to the ventricle).



Fig. 2: Multiple ill-defined ring enhancing lesions of varying size in both basal ganglia, right frontal and left parietal lobe.



Fig. 3: Six weeks post treatment.

was negative. Serum galactomanan antibody was also negative. His condition improved dramatically within the next few days and a repeat CT scan at 2 weeks and 6 weeks later (Figure 3) showed marked improvement. He was discharged 2 months after admission with prednisolone 30mg od and hydroxychloroquine 200mg od. He completed 2 months of anti-toxoplasma treatment and was continued on trimethoprim-sulphamethoxazole (TMP-SMX) prophylaxis.

DISCUSSION

Our case illustrates some important points in the management of SLE patients. This young teenager presented with sufficient criteria for a diagnosis of SLE. Intravenous methylprednisolone was given in view of widespread cutaneous vasculitis and cytopenia. Two days later he presented with neurological symptoms. Initial computed tomography (CT) scan of the brain was inconclusive but a repeat scan 4 days later showed multiple ring enhancing lesions which may represent metastasis, abscess/infections, or demyelinating lesions. In our patient, the presence of fever, rapid clinical deterioration and 3-fold increase in CRP suggested disseminated infection secondary to immunosuppression with methylprednisolone, as the likely cause. The pathogen that causes brain abscess in immunocompromised patients differs from that of a normal population and the organisms that need to be considered are *Toxoplasma gondii*, *Cryptococcus neoformans*, *Aspergillus* and tuberculosis³.

The site of the lesions in the brain which is predominantly over the basal ganglia and the rapid worsening of the lesions prompted us to make the diagnosis of probable cerebral toxoplasmosis. Furthermore, the negative blood and CSF cultures, the absence of vegetations in the heart valves and lack of response to antibiotics supported the fact that a normal bacterial pathogen is rather unlikely. In toxoplasmosis, neuroimaging usually reveals nodular or ring-enhancing lesions of brain with edema and mass effect. A study showed that in majority of patients, there were multiple enhancing lesions with most lesions occurring in the basal ganglia and the frontal and parietal lobes⁴. Failure of response to therapy in 2 weeks may suggest an alternative diagnosis. We used the second line anti-toxoplasma

treatment (clindamycin plus pyrimethamine) as sulfadiazine is not available in our hospital's formulary. Since the patient responded dramatically to this treatment, tuberculosis is rather unlikely.

There is a possibility that this patient had a latent infection with toxoplasmosis, as suggested by the presence of IgG antibodies. However, serum toxoplasma serology alone may not be useful in patients with SLE. It has been shown that seropositivity for toxoplasma is more common in SLE patients than healthy controls, and some may even have particularly high antibody titer⁵. A brain biopsy is probably the best method to confirm the diagnosis. However, due to lack of facilities and refusal of the family members, this procedure was not performed. Newer modality of diagnosis such as real-time PCR of CSF is not available at our center. The prompt response of this patient to anti-toxoplasma treatment and the characteristic radiological appearance were evident enough to conclude that this is indeed cerebral toxoplasmosis.

Firstly, our case demonstrates the importance of distinguishing CNS infection from lupus cerebritis. He had generalized convulsions with organic brain disease such as impairment of orientation and apraxia which is consistent with CNS disease in SLE, known commonly as "neuropsychiatric lupus". In lupus patients, one should always look for a secondary cause of CNS manifestations. This case illustrates the importance of this exclusion. Because the clinical manifestations of toxoplasma infection may be protean and nonspecific, it must be carefully considered in the differential diagnosis of lupus cerebritis¹. Furthermore, the initial inconclusive CT scan findings could have been interpreted as lupus cerebritis. A wrong diagnosis and treatment can be fatal.

Secondly, methylprednisolone is a synthetic corticosteroid with potent anti-inflammatory properties. It decreases

inflammation by suppression of polymorph nuclear leucocytes and reversal of increased capillary permeability. The relative potency of methylprednisolone (Solu-Medrol) and hydrocortisone sodium succinate, as indicated by depression of eosinophil count following intravenous administration, is at least four to one. Masking of infections, reactivation of latent infections and opportunistic infections are among the known complications of methylprednisolone. Our patient received only 250mg of methylprednisolone daily for 3 days, rather than the usual 500mg. Thus, we have shown that this drug can be potentially fatal even with minimal dose with the development of opportunistic infections. We suggest extreme caution in using methylprednisolone except in cases with clear clinical indications.

Lastly, in immunosuppressed patients, although rare and uncommonly reported, cerebral toxoplasmosis is a possible complication and this case shows how rapid the complication can occur. We would recommend TMP-SMX prophylaxis to be given to patients who need high doses of corticosteroids to prevent toxoplasmosis, especially if there is serologic evidence of latent infection. TMP-SMX has been proven efficacious for the prevention of toxoplasmosis in HIV infected and solid organ transplant patients.

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