

## Cerebral Toxoplasmosis in a Patient with Systemic Lupus Erythematosus

Emily Ramasra, Naveen Parva, John Goldman and Vinod Nookala

PinnacleHealth Hospitals, Harrisburg PA, USA

### \*Corresponding author

Emily Ramasra, Pinnacle Health Hospitals, Harrisburg PA, USA

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### Introduction

*Toxoplasma gondii* is a globally distributed protozoan parasite that causes toxoplasmosis and is frequently associated with infections in the immune compromised and in neonates. On initial infection, the parasite enters the host through the intestinal epithelium, usually after oocysts are ingested. Additionally, vertical transmission from mother to fetus can occur as well as infection from organ transplantation. In immune competent hosts, presentation is commonly flu-like with fever, headache and lymphadenopathy. The host's immune response typically contains the infection, limiting it to tissue cysts comprised of slowly replicating bradyzoites. In immune deficient hosts, when tissue cysts containing bradyzoites rupture, the compromised immune system is unable to halt progression of the parasite. Bradyzoites differentiate into rapidly replicating tachyzoites and as the parasite proliferates, host cell death occurs and necrotic foci develop. Most commonly, immune deficient hosts present with encephalitis, pneumonitis, and chorioretinitis [1]. We report a case of cerebral toxoplasmosis in a female patient with systemic lupus erythematosus (SLE) being treated with hydroxy chloroquine, mycophenolate mofetil and prednisone.

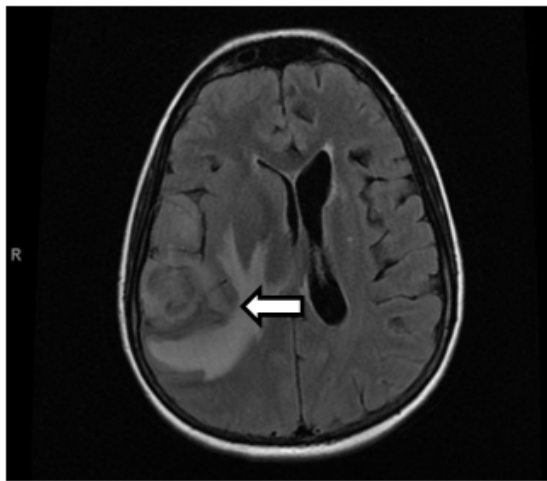
### Case

A 37 year old female, with a past medical history of SLE complicated by nephritis, previous lupus cerebritis, chronic kidney disease, hypertension and rheumatoid arthritis presented to the emergency department due to an excruciating frontal headache that had worsened over the last two weeks. She was afebrile and noted an unintentional weight loss of 15 lbs in six months and she denied seizures, stiff-neck and photophobia. Her lupus regimen at this point included mycophenolate mofetil 750 mg twice daily, prednisone 10 mg and hydroxyl chloroquine. Physical exam was unremarkable; the patient did not have any focal deficits. She was admitted and started to improve with supportive care. Initial labs showed hyponatremia with sodium 133 mEq/L, uremia, anemia and no leukocytosis. A differential diagnosis of lupus cerebritis, uremia and a reaction to the hydroxy chloroquine was considered. Computed tomography (CT) of the brain revealed multiple ring enhancing masses in the right cerebral hemisphere, with extensive surrounding vasogenic edema causing local mass effect. Magnetic resonance imaging (MRI) of the brain showed multiple bilateral brain masses and edema, most extensively in the right temporal lobe. The patient was started on dexamethasone. With these radiological findings the differential diagnosis was broadened to include metastatic disease and septic emboli, in addition to other

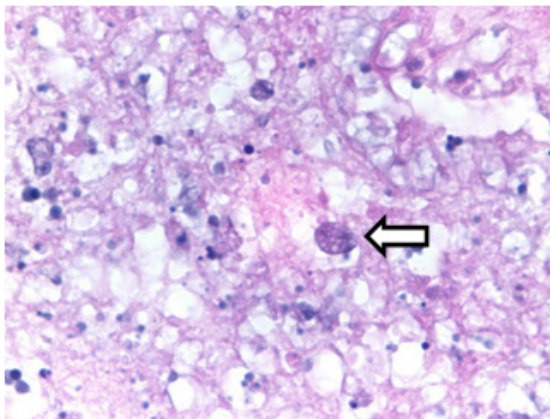
infectious etiologies. A trans esophageal echocardiogram ruled out vegetations. On day eight, the patient was taken for stealth guided biopsy and frozen section revealed only abnormal glial cells. A 1cm mass was sent for further pathology and microbiology studies. The patient remained stable, her headache improved and she was discharged home on day ten. The mycophenolate mofetil, prednisone, and hydroxychloroquine were stopped. The biopsy results revealed fragments of brain tissue showing gliosis, chronic inflammation and focal necrosis without malignancy. A circumscribed but unencapsulated mass lesion was present with necrosis surrounded by inflammatory infiltrate. PAS and GMS stain were negative for fungal organisms. Multiple organisms, largely tachyzoites were visualized by H&E staining and immune histochemistry confirmed toxoplasma. Toxoplasma IgG was greater than 400 IU/mL and IgM was negative. The patient was started on a six week course of pyrimethamine 100 mg daily, sulfadiazine 1 g daily and leucovorin 20 mg daily. MRI brain two months after the patient initially presented showed improvement in lesion in the right temporal lobe, and minimal sequela of other regions of toxoplasmosis in the lateral right occipital lobe and left basal ganglia. At the time this report was written, the patient remained on prophylactic treatment with atovaquone 750 mg twice daily. This regimen was chosen due to allergy and failure to desensitize to trimethoprim-sulfamethoxazole.



**Figure 1:** CT Brain without contrast showing low-attenuation edema, without definite focal mass, involving the right temporal/frontal/parietal regions. Effacement of the adjacent right lateral ventricle and there is 4 mm associated right to left midline shift



**Figure 2:** Multiple bilateral brain masses with surrounding vasogenic edema, most extensive in the right temporal lobe. Mass effect on the right lateral ventricle with uncal herniation on the right.



**Figure 3:** Right Temporal Brain biopsy showing H and E stain at 100 x magnification demonstrating intracellular toxoplasma within macrophages. Background has areas of abscess and necrosis with increased inflammatory response and gliosis.

### Discussion

Cerebral toxoplasmosis is not commonly reported in patients with SLE, though multiple case reports document the infection in patients being treated with immunosuppressive agents including prednisone, anti-TNF alpha, methotrexate, infliximab, adalimumab and mycophenolate mofetil [2-5]. Our patient was being treated with prednisone, hydroxy chloroquine, and mycophenolate mofetil. Her progression to cerebral toxoplasmosis likely represented a reactivation of the disease as she did not have immediately obvious risk factors such as exposure to cats or undercooked meat and toxoplasma IgM was negative.

In general, the immunosuppressive medications mentioned above lead to down-regulation of the immune response at multiple cell levels. The medications that our patient was on alter T-cell function, dendritic cells and antigen presentation in addition to a multitude of effects on other immune cell lines [6]. Furthermore, it has been suggested that CD4+ and CD8+ T cells may be decreased

or present in different ratios in patients with SLE [7]. Given the changes in the immune system associated with SLE and standard pharmacological treatments, it is reasonable to consider these patients as immune compromised.

Our patient presented with a persistent headache and no focal deficits, and was found to have bilateral lesions on MRI brain. A broad differential was considered including lupus cerebritis, metastatic disease, and septic emboli, and infection with *Toxoplasma gondii* was confirmed on biopsy of the right temporal lobe. Cerebral toxoplasmosis is rarely reported in SLE and of the cases that have been documented, there were cases with rapid disease progression and mortality [8-10]. The authors believe that severe neurologic symptoms with positive radiologic imaging should trigger early inclusion of cerebral toxoplasmosis in the differential diagnosis. Moreover, view in treated SLE patients as immunodeficient on presentation may lead to more timely diagnosis, possible prophylaxis and better outcomes.

### References

1. Kim K, Kasper LH (2014) *Toxoplasma* Infections. Harrison's Principles of Internal Medicine, 19e New York, NY: McGraw-Hill.
2. Pulivarthi S, Reshi RA, McGary CT, Gurram MK (2015) Cerebral toxoplasmosis in a patient on methotrexate and infliximab for rheumatoid arthritis. *Intern Med* 54: 1433-1436.
3. Pistacchi M, Gioulis M, Mazzon D, Marsala SZ (2016) Cerebral toxoplasmosis in undifferentiated connective disease treated with mycophenolate mofetil: an unusual case report. *Acta Neurol Belg* 116: 633-636.
4. Nardone R, Zuccoli G, Bringio F, Golaszewski S (2014) Cerebral toxoplasmosis following adalimumab treatment in rheumatoid arthritis. *Rheumatology (Oxford)* 53: 284.
5. Young JD, McGwire BS (2005) Infliximab and reactivation of cerebral toxoplasmosis. *N Engl J Med* 353: 1530-1.
6. Sacre Karim, Criswell Lindsey A, McCune Joseph M (2012) Hydroxychloroquine is associated with impaired interferon-alpha and tumor necrosis factor-alpha production by plasmacytoid dendritic cells in systemic lupus erythematosus. *Arthritis Research & Therapy* 14: 155.
7. Tsokos G (2011) Systemic Lupus Erythematosus. *N Engl J Med* 365: 2110-2121.
8. Zamir D, Amir M, Groisman G, Weiner P (1990) *Toxoplasma* infection in systemic lupus erythematosus mimicking lupus cerebritis. *Mayo Clin Proc* 74: 575-578.
9. Pagalavan L, Kan FK (2011) Cerebral toxoplasmosis in systemic lupus erythematosus following intravenous methylprednisolone. *Med J Malaysia*. Mar 66: 68-70.
10. Murro D, Novo J, Arvanitis L (2016) Asymptomatic diffuse "encephalitic" cerebral toxoplasmosis in a woman with systemic lupus erythematosus. *Case Reports/Journal of Clinical Neuroscience* 29: 196-198.

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