Focal Neurological Deficits due to a Contrast Enhancing Lesion in a Patient with Systemic Lupus Erythematosus
Case report and Review of Literature

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Abstract

Neuropsychiatric (NP) systemic lupus erythematosus (SLE) is a complex entity comprising 19 different discrete syndromes. We report a case of a 32-year-old female with SLE and new onset neurological symptoms and radiographic evidence of a contrast enhancing lesion on brain MRI. The lesion was successfully excised and found to be granulomatous in nature. Infection and malignant etiologies were ruled out suggesting that the lesion was due to SLE. Subsequently, the development of multiple reversible hyperintense signal abnormalities on brain MRI suggested the possibility of posterior reversible encephalopathy syndrome (PRES). The lesions resolved after the withdrawal of immunosuppression. This article reviews both the clinical and pathological complexity of PRES in SLE and the state of the current literature. We conclude that more data is required to understand the spectrum of PRES and its management in SLE patients.

Systemic lupus erythematosus (SLE) is a chronic, autoimmune disease characterized by multisystem inflammatory lesions that can affect any organ system in the body, including the central and peripheral nervous systems.1 Central nervous system (CNS) involvement in SLE occurs in 14% to 85% of patients. Neuropsychiatric SLE is a broad spectrum of 19 syndromes2 of which 12 involve the CNS: cognitive dysfunction, acute confusional state, cerebrovascular disease, movement disorder, demyelinating syndrome, seizure disorder, psychosis, mood disorder, anxiety disorder, headache, aseptic meningitis, and myelopathy.2 The other seven reflect peripheral nervous system involvement. The mediators of tissue damage in SLE such as antibodies, cytokines, and activated immune cells have direct access to most organs in the body but must penetrate the blood brain barrier to access brain tissue.

Hinchey and coworkers3 first described a clinicoradiological syndrome called reversible posterior leukoencephalopathy (RPLS). RPLS symptoms include headache, seizures, confusion, and visual changes with characteristic neuroimaging findings of posterior cerebral white matter edema. Two of the 15 patients in the initial case series had RPLS related to SLE.3 Imaging indicates presence of hyperpermeability of small vessels, one of the clinicopathological features of NP-SLE.3,4 A more recent study by Ishimori5 suggests that the use of the term posterior reversible encephalopathy syndrome (PRES) is more accurate since involvement of gray matter has been demonstrated with the advancement of MRI technologies. The posterior circulation is typically involved,3 but the anterior circulation may also be affected in some patients.5

MRI is sensitive in demonstrating CNS damage because of the excellent soft-tissue contrast and the ability to acquire multi-planar images, which provide higher quality anatomic descriptions. MRI white matter (WM) lesions have often described in SLE; 60% to 86% of patients have cerebral WM lesions. White matter lesions are considered non-specific in SLE patients, and they are also associated with hypertension and antiphospholipid antibodies.6,7

This article presents the case of a young woman with SLE and neurological symptoms and discusses the spectrum of complications and the complexity of the diagnosis of PRES.

Case Report

The patient is a 32-year-old African American female who first presented at the age of 16 with arthritis, discoid rash, autoimmune thrombocytopenia, positive antinuclear
antibody (ANA), and elevated double-stranded (ds) DNA titers. She was diagnosed with SLE. The patient had on and off episodes of arthritis and skin rashes treated adequately with prednisone; she has been off medications since 2003. In January 2010, she presented to our clinic with increased lupus activity. She had active arthritis and discoid rash. She had synovitis of wrist, MCP, PIP, and knee joints, and a rash on the back of her neck. Serologies were significant for positive ANA, dsDNA, anti-cardiolipin IgG, SSA and anti-RNP antibodies, and normal complement levels. Total IgA and IgG levels were high. She has a past history of exercise induced asthma and Raynaud’s phenomenon. She was started on hydroxychloroquine and responded well to treatment with gradual remission of her symptoms.

In June 2010, she began experiencing frequent headaches and transient vision loss in the left temporal field. Focal seizures in the form of right hand tremors and right leg numbness were also reported. Her dsDNA (102 IU/mL) was elevated, and she had normal complements. Laboratory results are summarized in Table 1. Ophthalmological examination was normal. Neurological exam was non-focal. MRI brain demonstrated an ill-defined focal rounded abnormality of T2 FLAIR hyperintensity in the parafalcine left parietal lobe. A contrast enhanced MRI later demonstrated a more discrete rounded focus of abnormally increased signal with a central area of decreased signal intensity, which enhanced (4 mm) with contrast administration. Vasogenic edema in the surrounding regions was noted. The rounded nature and immediate subcortical location speak against a

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**Table 1** Laboratory Results

<table>
<thead>
<tr>
<th>Test</th>
<th>Ref. values</th>
<th>06/18/10</th>
<th>01/20/11</th>
<th>06/29/11</th>
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<tbody>
<tr>
<td>Hb%</td>
<td>12.0-15.5 g/dL</td>
<td>11.9</td>
<td>11.4</td>
<td>12.3</td>
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<tr>
<td>Hct</td>
<td>36.0-47.0 %</td>
<td>36.2</td>
<td>34.7</td>
<td>37.4</td>
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<td>RBC</td>
<td>4.10-5.70 x 10⁹/µL</td>
<td>4.69</td>
<td>4.44</td>
<td>4.85</td>
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<tr>
<td>MCV</td>
<td>82-100 fl</td>
<td>77.2</td>
<td>78.1</td>
<td>77</td>
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<tr>
<td>WBC Count</td>
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<td>5,100</td>
<td>3,900</td>
<td>5,700</td>
</tr>
<tr>
<td>ANC</td>
<td>1,800-9,000/µL</td>
<td>2,900</td>
<td>1,900</td>
<td>2,900</td>
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<tr>
<td>ALC</td>
<td>800-4,800/µL</td>
<td>1,500</td>
<td>1,400</td>
<td>2,000</td>
</tr>
<tr>
<td>Platelet Count</td>
<td>150-400 x 10⁹/µL</td>
<td>166</td>
<td>256</td>
<td>168</td>
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<tr>
<td>ESR</td>
<td>0-20 mm/hr</td>
<td>84</td>
<td>28</td>
<td>26</td>
</tr>
<tr>
<td>ANA</td>
<td>≤ 0.40</td>
<td>&gt; 160</td>
<td></td>
<td></td>
</tr>
<tr>
<td>dsDNA</td>
<td>&lt; 75 IU/mL</td>
<td>99</td>
<td>34</td>
<td>104</td>
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<td>C3</td>
<td>88-165 mg/dL</td>
<td>121</td>
<td>115</td>
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<td>C4</td>
<td>14-44 mg/dL</td>
<td>25</td>
<td>26</td>
<td>24</td>
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<tr>
<td>CRP</td>
<td>0-9 mg/L</td>
<td>6</td>
<td></td>
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</tr>
<tr>
<td>ACL IgG</td>
<td>&lt; 15.5 GPL</td>
<td></td>
<td></td>
<td>17</td>
</tr>
</tbody>
</table>

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MRI brain demonstrated an ill-defined focal rounded abnormality of T2 FLAIR hyperintensity in the parafalcine left parietal lobe. A contrast enhanced MRI later demonstrated a more discrete rounded focus of abnormally increased signal with a central area of decreased signal intensity, which enhanced (4 mm) with contrast administration. Vasogenic edema in the surrounding regions was noted. The rounded nature and immediate subcortical location speak against a
demyelinating disease; hence, it was suspected to be due to an infection, inflammation, or neoplasm (Fig. 1).

Extensive search for neoplasm was done with imaging of the abdomen, pelvis, and the chest. CT chest, abdomen, and pelvis showed non-specific diffuse lymphadenopathy. A lumbar puncture was performed and the cerebrospinal fluid (CSF) was evaluated for biochemical, cytological, and serological evidence of infection. All parameters were normal.

A microsurgical resection of the lesion was performed. The patient remained neurologically intact during and after the procedure. She was treated with high dose steroids after surgery and tapered over the next weeks. The biopsy showed a granulomatous lesion characterized by a necrotic center surrounded by a dense mixed inflammatory infiltrate, comprising plasma cells, lymphocytes, and macrophages. In addition, marked granulation tissue and gliosis were present. Immunostains for CD-3 (T-cell marker) and CD-68 (Histiocytic marker) showed abundant immunoreactivity within the inflammatory infiltrate. For further clinico-pathological correlation, the biopsy sample was sent to the Centers for Disease Control and Prevention (CDC). Immunohistochemical testing for Mycobacterium species (including *M. tuberculosis*, *M. avium*, and *M. marinum*), and a *Treponema pallidum* was negative. Multiple stains for acid-fast bacilli and bacterial pathogens were negative as well. PCR testing for HIV, *Brucella*, *Bartonella*, and *Toxoplasma* were also negative. In the absence of any evidence of infectious or malignant etiology, the CNS lesions were attributed to CNS lupus, and treatment with mycophenolate mofetil (MMF) was initiated.

After three months of treatment with MMF, a follow-up MRI (Fig. 2) showed evidence of two new CNS lesions larger than the original one with discrete contrast enhancement in the areas of T2 abnormality. Her neurological status was intact. She did not experience any headaches or subsequent visual symptoms and had no motor or sensory symptoms. Mental status testing was normal. Cranial nerve evaluation, motor testing, sensory testing, coordination, and gait were intact. Her reflexes were normal and her toes were downgoing. A repeat spinal tap was ordered to check for encephalitis panel and neurocysticercosis. Again, the results were negative. Due to lack of response to MMF, we advised the patient to start cyclophosphamide and prednisone. She refused to take cyclophosphamide and, against our advice, discontinued MMF.

**Figure 2** February 8, 2011.
Surprisingly, during the next months, she did not experience any neurological deterioration. A repeat MRI (Fig. 3) revealed complete resolution of the previously identified areas of abnormal enhancement in the absence of any specific treatment. This suggested the possibility of PRES. Review of the MRI showed characteristic subcortical foci of FLAIR abnormality involving the mesial left frontal lobe as well as the right superior frontal convolution.

Discussion

SLE can involve the central and peripheral nervous systems. Due to the immune suppressed state, patients are also at risk for infections. Published case reports suggest that a wide variety of infectious, neoplastic, and inflammatory diseases can produce contrast enhancing brain lesions. The most common infections are tuberculosis, neurocysticercosis, toxoplasmosis, cryptococcal meningitis, brain abscess, and HIV. Neoplastic etiology is the most common non-infective etiology.8

Our patient presented with a single contrast enhancing lesion which was excised and found to be granulomatous. The granulomatous nature of the lesion also raised the possibility of granulomatous amoebic encephalitis due to *Acanthamoeba* species. The diagnosis is challenging, since *Acanthamoeba* species are rarely isolated from cerebrospinal fluid and serological testing is not useful. The amoebas in biopsy specimens can be easily mistaken for histiocytes. In most cases, *Acanthamoeba* encephalitis is fatal. In rare cases, patients with granulomatous encephalitis have survived, usually when a single brain lesion could be excised. Our patient did not have any direct water exposure, which excludes amoeba transmission.9

It is unclear whether SLE patients develop reversible focal deficits, which respond to steroid therapy. There are six major reversible NP-SLE lesions: 1. reversible posterior leukoencephalopathy syndrome (RPLS) or posterior reversible encephalopathy syndrome (PRES), usually associated with active SLE, hypertension, glomerulonephritis, and isolated generalized seizures (not epilepsy); 2. reversible lesions associated with isolated seizures without hypertension and especially with status epilepticus in SLE; 3. reversible edema associated with focal infarct; 4. reversible lesions of acute myelopathy, usually resulting in a reversible or irreversible cord or brain stem syndrome; 5. reversible leukoencephalopathy associated with withdrawal of immunosuppression; and 6. reversible brain lesions associated with TTP or cardiac lesions.10

The profound similarities in the clinical manifestations between PRES, NP-SLE, and lupus-related CNS complications, such as CNS infection and psychiatric conditions, often pose a major diagnostic and therapeutic challenge. Neuroimaging is the major diagnostic tool for PRES. The recognizable MRI features of PRES are diffuse hyperintensities on T2-weighted and fluid-attenuated inversion recovery (FLAIR) images in the white matter in the posterior areas of cerebral hemispheres.11

A recent study by Barber and associates12 identified 66 adult cases of PRES in SLE till date. Complete resolution of the MRI lesions was demonstrated after treatment with corticosteroids, prompt control of blood pressure, and cessation of immunosuppressive agents.12 In all these cases, the CNS involvement was focal and not diffuse.

Our patient also had active SLE, focal (not generalized) seizures and radiological findings suggesting the possibility of PRES. Complete clinical and radiological resolution of the lesions strongly supports PRES. Lowering of immunosuppression is integral to the treatment as there is a possible link between the induction of PRES and medications like MMF and cyclophosphamide. We propose that the possible pathology in PRES can be of granulomatous nature. The lack of adequate literature on the biopsy findings of the earlier patients limits our proposal. Further studies into understanding PRES in SLE are needed. In patients with SLE who present with neurological manifestations, careful review and observation of the patient’s clinical course may help diagnose PRES.

Disclosure Statement

The authors have no financial or proprietary interest in the subject matter or materials discussed, including, but not limited to, employment, consultancies, stock ownership, honoraria, and paid expert testimony.

References:


