

# Diagnosis of Lupus Cerebritis with Balint Syndrome: A Unique Case Report

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DOI: <https://doi.org/10.58624/SVOANE.2023.04.097>

Received: June 19, 2023 Published: July 04, 2023

## Abstract

**Introduction:** Among the wide variety of clinical manifestations in Systemic Lupus Erythematosus (SLE), cognitive dysfunction (CD) is a subtle finding, where the reported prevalence ranges from 3-88% due to CD assessment inconsistencies and challenges with SLE correlations. Cognitive dysfunction may also be a cornerstone element for a diagnosis of Neuropsychiatric Systemic Lupus Erythematosus (NP-SLE). We present a case of Lupus Cerebritis displaying seizures and oculomotor dysfunctions referred to as Balint Syndrome. To our knowledge, no publications to date have shown a correlation between Lupus Cerebritis and Balint Syndrome.

**Case Report:** A 35-year-old female with a history of lupus, seizures, and migraines presented complaining of a severe headache associated with vomiting. The patient stated the onset of her symptoms was three days prior and had been worsening. While in the emergency room, the patient had a generalized tonic-clonic seizure lasting around 2 minutes at which point neurology was consulted for seizure management. The patient had been seen about a year prior for similar complaints and was started on Keppra to control her epilepsy. The patient was seizure free for about 6 months so Keppra was discontinued.

**Discussion:** A wide array of symptoms are associated with Lupus Cerebritis, which is a rare manifestation following a diagnosis of SLE. Our patient was having seizures and complaints of migraine with severe Balint Syndrome consisting of oculomotor apraxia, optic ataxia, and simultagnosia. Due to some patients' rapid decline following a diagnosis of SLE and the complex diversity of symptoms, it is crucial to prevent organ failure by treating them immediately, and furthermore, to equip and educate clinicians in identifying atypical presentations.

**Conclusion:** Due to the complexity of autoimmune diseases, patients may present with a plethora of symptomatology, ranging from mild to severe, making a thorough medical history and physical examination imperative elements of a complete workup. Since NP-SLE is a nuanced diagnosis requiring specific management, it is essential to have close follow-ups with neurology.

**Keywords:** Systemic Lupus Erythematosus, Lupus Cerebritis, autoimmune disease, seizures.

## Introduction

Systemic Lupus Erythematosus (SLE) is a chronic multisystemic autoimmune disease with intermittent relapsing and remitting course. It shows a higher prevalence in women of childbearing age, and predominance in females 9:1 [1]. The etiology is not well understood, but it has been shown that environmental and genetic factors interact to activate an excessive immune response [1]. It leads to a pathogenic production of autoantibodies by B cells and cytokine dysregulation causing organ damage [1]. SLE is mainly characterized by the presence of nuclear and cytoplasmic antibodies, such as anti-Scl-70 and Anti-Smith. This disease has a wide spectrum of clinical features ranging from mild cutaneous reactions to significant organ damage. The diagnosis of SLE is based on clinical findings and laboratory values, following the classification criteria by the American College of Rheumatology (ACR).

The global incidence and prevalence of SLE differ by geography with the highest incidence and prevalence in North America [1]. The current incidence rate in the Caucasian population is 6.73 cases per 100,000 and 31.4 cases per 100,000 in the African American population [1]. Because of the heterogenic manifestation of SLE, management varies according to disease severity and organ involvement.

Among the wide variety of clinical manifestations in SLE, cognitive dysfunction (CD) is a common but subtle finding, where the reported prevalence ranges from 3-88 % due to CD assessment inconsistencies and challenges with SLE correlations [2]. Neuropsychiatric (NP) manifestations in SLE have most commonly been referred to as Lupus Cerebritis and present with neurological and psychiatric dysfunctions, such as psychosis, stroke, mood disorders, and cognitive dysfunction. The reported prevalence of CD ranges from 3-88 % and up to 90% of patients with SLE experience nervous system disorders, which are defined in 19 syndromes by the ACR [2,3]. The recognition and diagnosis of NP symptoms in SLE patients is hindered by numerous factors including, the lack of standardized assessment, the heterogeneity of neurological findings, and the unreliability of biomarkers for diagnosing and monitoring the disease [4]. There is no biomarker that demonstrates significant ubiquitous or reproducible attribution for NP-SLE diagnosis [5]. Because of the challenging diagnosis and treatment of NP-SLE, studies have shown higher rates of morbidity and mortality in SLE patients with NP manifestations [4].

## Case Presentation

We present a case of Lupus Cerebritis displaying seizures and oculomotor dysfunctions referred to as Balint Syndrome. Because of the modest number of cases, this report will increase awareness and clinical suspicion of NP-SLE during clinical practice.

### Patient Information

A 35-year-old female with a history of lupus, seizures, and migraines presented with complaints of a severe headache associated with vomiting. The patient had stated her onset of symptoms was three days prior to admission and had been worsening. While in the emergency room, the patient had a generalized tonic-clonic seizure episode that lasted around 2 minutes, at which point neurology was consulted for seizure management. Of note, the patient was seen about a year prior for a similar complaint when she had experienced two episodes of seizures and had subsequently been started on Keppra. The patient has been seizure free since then and Keppra was discontinued 6 months ago.

### PE and clinical findings

During the physical exam, the patient was lethargic, atraumatic, and normocephalic without any noticeable masses or swelling. The patient was stable with regular rate and rhythm, aerating well, and not in distress. The patient's abdomen was non-tender, and soft. The extremities had a normal inspection, normal temperature with a painless range of motion. The patient's neurological exam was unremarkable: PERRLA, reflexes equal bilateral, no motor deficits, and no sensory disturbances. The patient's skin was noted to be dry.

### Timeline

The patient was recently diagnosed with SLE one year prior, treated with a Medrol dose pack, and lost to follow-up. The patient had a previous history of witnessed seizures over one year that was controlled with Keppra and eventually weaned 6 months prior to admission. The presenting seizure was a generalized tonic-clonic seizure witnessed in the ED, lasting 2 minutes. The patient was treated with 1 gram of Keppra and placed on 500 mg BID for maintenance. On physical examination, the patient was following commands intermittently, appearing lethargic and post-ictal. Non-contrast CT Head showed no acute intracranial pathology. A routine EEG was negative for epileptiform discharges. MRI Brain without contrast showed patchy cortical/subcortical T2/FLAIR white matter hyperintensities without associated diffusion restriction or abnormal enhancement. The patient was treated with methylprednisolone 1 gram IV for 5 days, which was converted to prednisone 60 mg PO daily. On the second day of admission, the patient developed a new onset right gaze preference and left-side hemiparesis. Follow-up CTA Head and Neck and Rapid EEG were concerning for SAH vs cerebral edema and revealed some discharges with no status epilepticus, respectively. Consequently, the patient was loaded with 2 grams of Keppra and the maintenance dose was increased to 1000 mg BID. Given a concern for SAH, hypertonic saline was given along with Cardene with a systolic blood pressure goal of less than 140 mmHg. A repeat Non-contrast CT Head without contrast showed improved SAH. CT Venogram of the head was negative for venous sinus thrombosis. During the hospital course, the patient developed optic ataxia with oculomotor apraxia and simultagnosia as evidenced by poor target acquisition on finger-nose-finger testing, nystagmus on extraocular muscle testing, and an inability to adequately describe multiple objects when presented simultaneously. Additionally, the patient complained of intermittent severe headaches and musculoskeletal pain refractory to Acetaminophen.

Morphine sulfate and Topamax 25 mg BID were used for pain control. Cyclophosphamide 1365 mg was started for suspected Lupus nephritis and the patient was eventually stepped down from ICU due to improved mobilization and pain. MRI Brain was repeated, noting again focal areas of T2/FLAIR hyperintense signal in the bilateral frontal, parietal, and occipital lobes suspicious for Lupus Cerebritis vs PRES though the latter diagnosis was less likely.

### Diagnostic Assessment

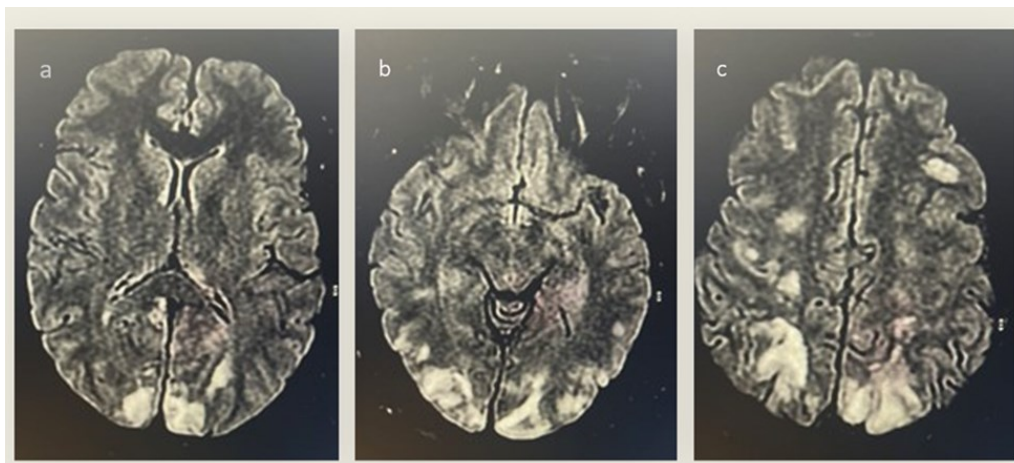
Several imaging studies were performed including vessel imaging CTA and CTV of the head and neck, MRI Head and Neck, and Non-contrast CT Head. CT Head showed no acute intracranial pathology. EEG was negative for epileptiform discharges. MRI Brain showed patchy cortical/subcortical T2/FLAIR white matter hyperintensities without associated diffusion restriction or abnormal enhancement. CTA Head and Neck performed was significant for SAH vs cerebral edema, with a repeat CT showing improvement. MRI Brain was repeated, showing focal areas of T2/FLAIR hyperintense signal in the bilateral frontal, parietal and occipital lobes suspicious for Lupus Cerebritis vs PRES.

### Therapeutic Intervention

The patient was treated with rescue dosages of 1-2 grams of Keppra and a maintenance dose of 1000 mg BID for seizures and monitored to avoid medications that will lower seizure threshold. Topamax 25 mg BID for headaches. SLE was treated with an initial dose of methylprednisolone 1 gram IV for 5 days and later converted to prednisone 60 mg orally to taper down over several weeks. Additionally, Cytoxan 1365 mg was given for Lupus Nephritis. Acetaminophen and Morphine sulfate were given as needed for musculoskeletal pain. Hypertonic saline and Cardene drip were used to treat subarachnoid hemorrhage.

### Follow-up and Outcomes

The patient was discharged to follow-up outpatient for further SLE management. Recommended supportive care for acute anemia and to avoid medications that lower the seizure threshold. Advised for physical and occupational therapy.



**Figure 1:** Axial Images of Magnetic Resonance of the Brain with bilateral patchy cortical/subcortical T2/FLAIR white matter hyperintensities without associated diffusion restriction or abnormal enhancement in parietal (a) and occipital areas (b)(c).

### Discussion

A wide array of symptoms are associated with Lupus Cerebritis, which is a rare manifestation following a diagnosis of SLE [6]. Such symptoms include but are not limited to altered mental status, seizures, oculomotor dysfunction, anxiety, and depression [6]. Our patient's symptoms were seizures and complaints of a severe headache associated with vomiting as well as severe Balint Syndrome as optic ataxia, oculomotor apraxia, and simultagnosia were present. To our knowledge, no publications to date have shown a correlation between Lupus Cerebritis and Balint Syndrome. Since Balint Syndrome is not well understood, this case report highlights this rare finding.

The uniqueness of this case is that SLE rarely presents with seizures, as seen with our patient. This rare complication requires further research [6]. Due to the rapid decline following diagnosis of SLE among these patients, it is crucial to prevent organ failure by providing immediate care in order to reduce hospitalization rates, mortality, and disabilities [6]. The diverse clinical presentations as well as the absence of distinct anatomical and functional cerebral features make the diagnosis of NP-SLE difficult [7].

The present patient's previous history of SLE allowed to correlate the neurological symptoms; however, it has been shown that neuropsychiatric symptoms can be the initial finding for SLE, therefore, NP-SLE should be always included in the differential diagnosis [7]. The complex evolution of our patient demonstrates potential overlapping pathologies that can affect SLE patients. Zimmermann et al. demonstrated a decreased cerebral volume and cortical thickness among NP-SLE patients as compared to non-neuropsychiatric SLE patients [8]. Similarly, the anatomical changes seen in our patient due to SLE immunoinflammatory effects led to vascular changes as presented by SAH. Cerebrovascular disease appears in about 20% of all SLE cases that may be attributed to age, hypertension, comorbid disease-related factors in early stages, or corticosteroid use in late stages [7]. In Figure 1, focal hyperintensities in the posterior and parietal lobes may explain the visual abnormalities observed in our patient. Balint Syndrome, as observed in our patient, includes altered perception, interpretation and optic apraxia in response to convoluted images [9]. It has been proposed that bilateral lesions at the occipito-parietal areas seen in Balint Syndrome are due to connection disruption between the posterior visual association areas and the motor areas of the prefrontal cortex [10]. Despite the evidence of damage in biparietal areas in Balint Syndrome, visual symptoms can develop through different combinations of lesions [11]. In our case, we review the wide possible pathologies from SLE, which can further lead to complex neuroanatomical changes. Diagnostic misinterpretation arises due to the broad variety of symptoms of NP-SLE, their unfounded time life, and the use of objective and subjective criteria [7]. Similarly, the unprecedented findings of Balint Syndrome in our patient demonstrates the importance of a thorough neurological examination. Due to the infrequency of Balint Syndrome and the low specificity of standard tools, the literature is vastly based on case reports [11]. Further research is needed to properly assess the central and peripheral neurological lesions caused by SLE.

Treatments for Lupus Cerebritis include immunosuppressants, corticosteroids, immunomodulators such as abatacept or rituximab, and finally pain control [12]. As seizure activity may be a sequela of Lupus Cerebritis, anti-epileptic medications, such as Levetiracetam, are given symptomatically, as dependent on both patient presentation and the clinical judgment of the physician [13]. In most serious SLE involvements, chemotherapy medications such as cyclophosphamide are used intermittently [14]. In the present case, the early intervention with a high dose of Cyclophosphamide allowed for proper management and stabilization of our patient. It is worth noting that common side effects of cyclophosphamide may include nausea, vomiting, and bone marrow depression [14].

Lupus Cerebritis is a rare complication of SLE and should be in the differential diagnosis of all patients presenting with NP-SLE. This case demonstrates the importance of ordering laboratory tests as well as diagnostic imaging regardless of the initial severity of the symptoms as dictated not only by the initial patient presentation but also by a thorough clinical history in order to prevent the rapid progression to fatal consequences.

## Conclusion

The present case of Lupus Cerebritis is interesting and uncommon with seizures and oculomotor dysfunction, known as Balint Syndrome. Because of the modest number of cases, this report will increase awareness and clinical suspicion of NP-SLE during clinical practice. Due to the complexity of autoimmune diseases, there could be patients presenting with a range of mild to severe symptoms, which emphasizes the cruciality of a thorough medical history and physical examination for a complete workup. Since NP-SLE could lead to fatal conditions, it is essential to have close follow-ups.

## Conflict of Interest

The authors declare no conflict of interest.

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**Citation:** Cazzaniga J, Silva CEJ, Nittala S, Filippi D. Diagnosis of Lupus Cerebritis with Balint Syndrome: A Unique Case Report. *SVOA Neurology* 2023, 4:4, 89-93.

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