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Case Report

Striatal dominant lupus encephalitis–Is it vasculitis or an autoimmune process? Literature review & new case report with vessel wall imaging

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ABSTRACT

Neurological and psychiatric symptoms are highly prevalent in the initial manifestation of systemic lupus erythematosus (SLE) and is classified as neuropsychiatric systemic lupus erythematosus (NPSLE). Despite the high prevalence rate of this condition, it is still very poorly understood and often delayed in its diagnosis due to its variety in clinical manifestations. For our case, an eighteen-year-old male who was recently diagnosed with SLE presented with progressive confusion, visual and auditory hallucinations, in addition to high fevers, diarrhea, abdominal and flank pain. Upon initial presentation, he was treated for sepsis while trying to identify a source of infection. However, with the help of laboratory tests like CSF analysis and autoantibody serum studies as well as neuroradiologic imaging, we were able to rule out infectious causes and diagnose our patient with lupus induced striatal encephalitis. We present the first case of striatal encephalitis with vessel wall imaging to ultimately rule out lupus associated vasculitis. The importance of MRI imaging and identification of specific patterns associated with autoimmune encephalitis allowed rapid diagnosis and initiated immediate treatment in the hopes of reducing long term affects from neuroinflammation in our young patient.

Introduction

Systemic lupus erythematosus (SLE) is an autoimmune disease that commonly affects women of reproductive age. This autoimmune disorder affects multiple organs in the body, however, the effects of lupus on the brain are still unclear and thus difficult to diagnose in a timely manner [1]. Neuropsychiatric symptoms of SLE include but are not limited to depression, headache, psychosis, stroke, or seizures [2,3]. Neuropsychiatric systemic lupus erythematosus (NPSLE) is the inclusive term for any neuropsychiatric manifestations of lupus associated with this systemic autoimmune disorder [1]. NPSLE is one of the most prevalent presentations and at times the first manifestation of lupus, appearing in 50% of patients with SLE

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with a wide range in adults (14%–80%) and children (22%–95%) [1,4]. Despite its prevalence, it is difficult to diagnose NPSLE in a timely manner due to its various presentations and is a diagnosis of exclusion. In addition to clinical symptoms, laboratory tests to identify antibodies in serum and cerebrospinal fluid (CSF) and radiological imaging to demonstrate the effect of the antibodies are important to establish the diagnosis [2]. FLAIR and T2- weighted radiological imaging showed abnormal appearance of the striatum. The etiology of this abnormal appearance of the striatum in a patient with SLE has been debated in the literature and has been attributed to encephalitis by some and to vasculitis by others. We hereby report a case with novel MRI technique known as vessel wall imaging (VWI) which could help us in differentiating encephalitis from vasculitis. VWI depicts the enhancement of vessel walls as a surrogate for inflammation of the vessel wall as seen in vasculitis. The completely normal appearance of vessel walls without enhancement, lack of diffusion restriction, and abnormal appearance of the striatum on T2 and FLAIR as seen in our case supports the hypothesis of inflammation of the striatum. This is the first case report of striatal dominant lupus encephalitis with vessel wall imaging. The lack of enhancement of vessel wall on VWI supports encephalitis over vasculitis.

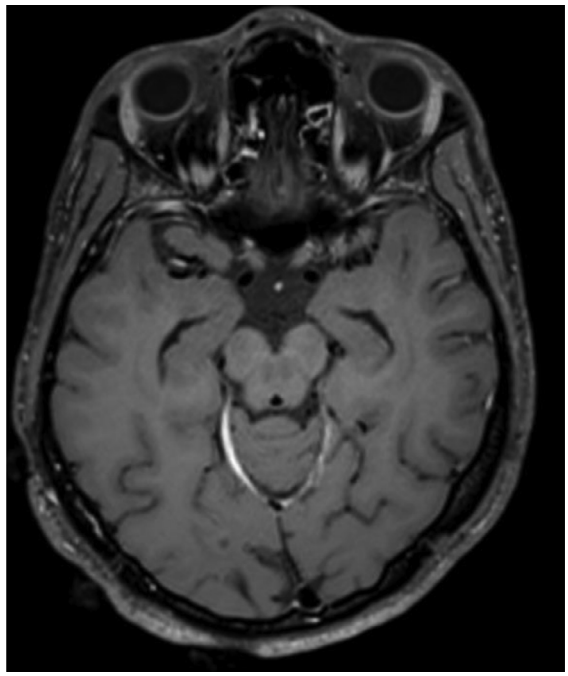

Fig. 1 – Axial Brain MRI with no vessel wall enhancement.

Case report

An 18-year-old male presented with high fevers, altered mental status with auditory and visual hallucinations, and altered gait to the emergency department. Prior to presentation, he had headaches, diarrhea, epigastric abdominal pain, and bilateral flank pain for 3 days. He was recently diagnosed with SLE and was discharged with a prolonged prednisone taper, which he failed to adhere to.

On initial presentation, the patient was found to be febrile, tachycardic, tachypneic, and lethargic and his treatment was managed along the lines of sepsis. He received 3 L of IV fluids and Vancomycin, Zosyn, and Ceftriaxone for sepsis. The patient was also started on 500 mg methylprednisolone and covered with Acyclovir for possible meningitis. In order to diagnose the cause of his altered mental status, ammonia, blood alcohol level, and urine toxicology were ordered to screen for any drug abuse, which all returned negative. Given his acute metabolic encephalopathy, the patient underwent CT scan of head, thorax, and abdomen as well, which also returned with normal findings. In addition, the patient underwent lumbar puncture and cerebrospinal fluid (CSF) analysis, which revealed an elevated RBC count at 36 mg/dl and an elevated protein count at 49 mg/dl, thus ruling out meningitis as a source of infection. The patient underwent testing for ESR and CRP, which were both significantly elevated with ESR at 49 and CRP at 24. As our patient was recently diagnosed with SLE, he also underwent testing for serum antinuclear antibodies (ANA), which revealed an elevation in the speckled pattern antinuclear antibody. Testing for ANA specificity demonstrated increased levels of SSA autoantibody, Smith autoantibody, and RNP autoantibody. Additional antibody testing associated with SLE showed increased levels of IgG and IgA B2 glycoprotein antibodies in the serum as well.

As the patient had no identifiable source of infection causing sepsis, he underwent magnetic resonance imaging (MRI) of the brain with and without contrast to determine the cause of his acute metabolic encephalopathy. The MRI of the brain without contrast revealed abnormal hyperintensity on T2 and FLAIR in the bilateral basal ganglia (Fig. 2). Upon further

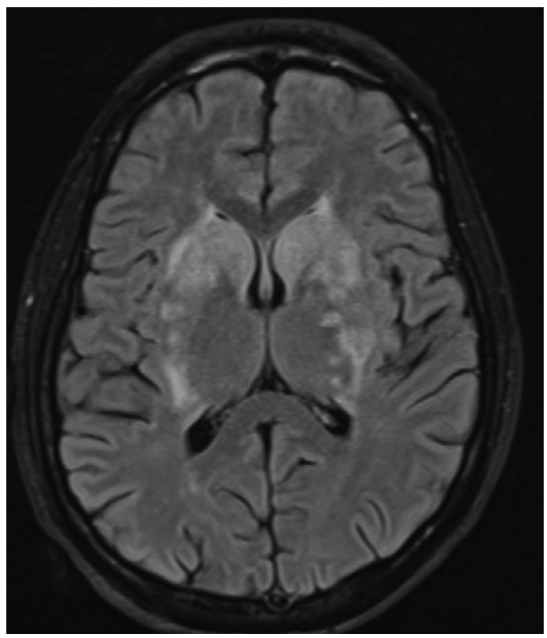

Fig. 2 – Axial Brain MRI with T2 FLAIR depicting hyperintense signal in bilateral basal ganglia.

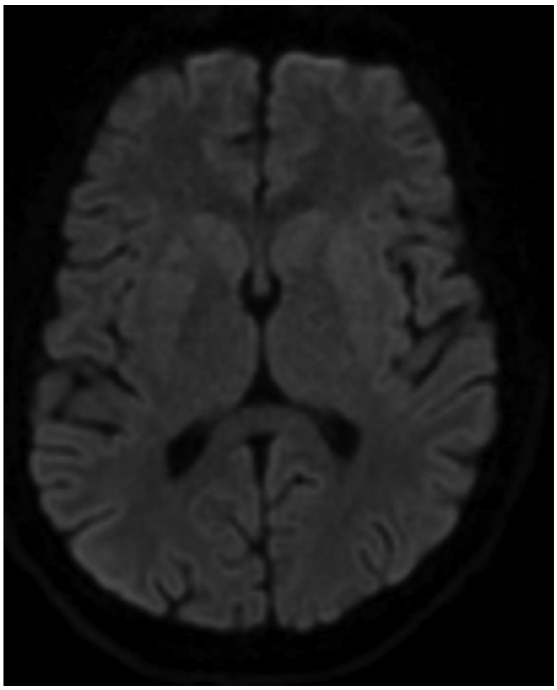

Fig. 3 – Axial Brain MRI with no DWI hyperintensity.

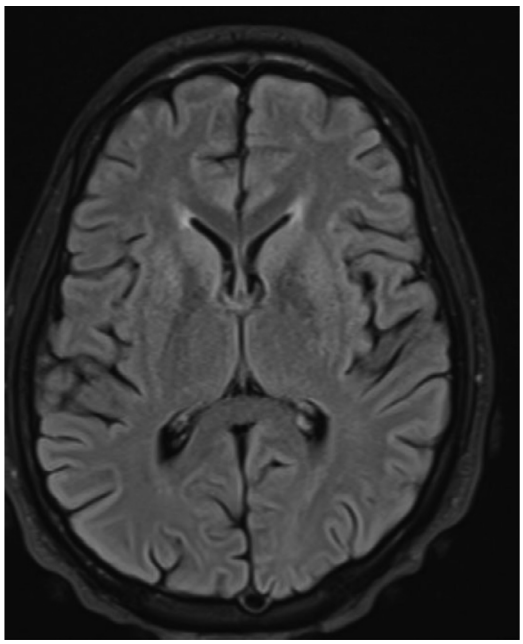

Fig. 5 – Follow up Axial Brain MRI 2 weeks after treatment with resolution of T2 FLAIR hyperintensity in bilateral basal ganglia.

examination of the brain MRI, there was no enhancement on post contrast MRI T1 sequence. The diffusion weighted images (DWI) were normal without any DWI hyperintensity or restricted diffusion (Figs. 3 and 4). The high resolution isotropic VWI was performed with 3.0 Tesla MRI (Siemens Vida) scanner with 20 channel head coil which enabled clear depiction of the vessel walls in our patient. There was no evidence of vessel wall enhancement to suggest vasculitis (Fig. 1).

Given the findings of the brain MRI with and without contrast, the patient was started on pulse dose steroids with methylprednisolone daily 1 gm for 5 days. As the patient's MRI findings indicate lupus induced encephalitis, the patient was also started on plasmapheresis for a total of 5 sessions, with treatments scheduled for every other day. As treatment proceeds, the patient may need to follow up with immunosuppression with rituximab or cyclophosphamide. After two weeks of treatment, the patient underwent follow up MRI of the brain and results show resolution of T2 FLAIR hyperintensity in the bilateral basal ganglia (Fig. 5).

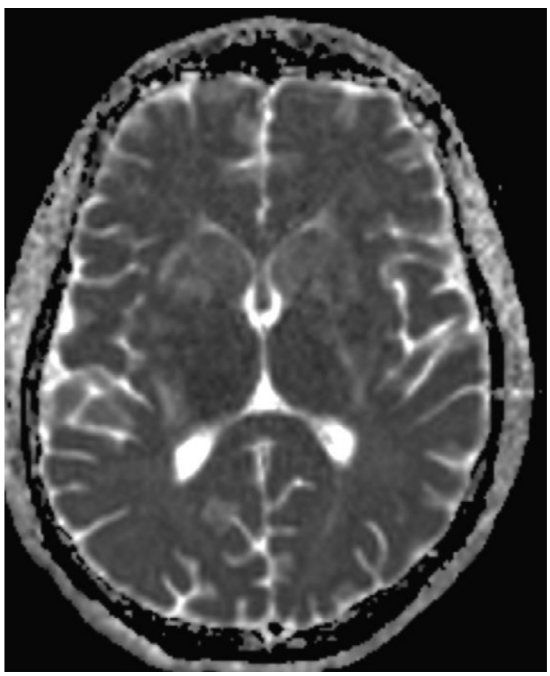

Fig. 4 – Axial Brain MRI with no restricted diffusion on ADC.

Discussion

The pathogenesis of NPSLE is a result of the numerous antibodies produced by patients with SLE [5]. These individuals produce large quantities of autoantibodies in the peripheral serum, which may pass the blood brain barrier (BBB) if the SLE flare causes a lesion in the BBB or if there were a prior injury to the BBB because of sepsis, trauma, or ischemia affecting the integrity of the BBB [6]. The antibody induced damage upon neurons ultimately results in the neuropsychiatric symptoms in patients with SLE[6].

The early presentation of NPSLE is often misdiagnosed because it presents like many other diseases, leading to a significant delay in the correct diagnosis. Symptoms range from less complicated afflictions like headaches and depression to more complex manifestations like stroke and seizures [2,3]. Furthermore, there is no conclusive test to correctly diagnose NPSLE as it depends on the clinical features of the patient in addition to the presence of antibodies in the serum and CSF [2]. To further differentiate the various neuropsychiatric presentations of lupus, it is important to obtain serum and CSF antibody studies and MRI imaging.

Some commonly seen conditions related to NPSLE are associated with antiphospholipid antibody syndrome [1]. A subset of patients with lupus develop antiphospholipid antibody syndrome (APS) and may present acutely with symptoms due to ischemic stroke or dural venous sinus thrombosis as a result of coagulopathy from specifically the anticardiolipin, lupus anticoagulant, or B2 glycoprotein antibodies [1,2]. Recent literature suggests when examining causes of neuropsychiatric symptoms in SLE, the focus should not only be limited to the specific type of antibody but also to the location of injury in the BBB allowing these antibodies to trespass and induce neuronal damage [6]. In patients with NPSLE with autoimmune encephalitis, laboratory findings show peripheral anti-dsDNA antibodies specifically interacting with N-methyl-D-aspartate receptor (NMDAr) antigens after crossing the BBB [1]. The interaction between the anti-dsDNA antibodies and NMDAr antigens induces neuronal excitotoxicity that presents as a nonthrombotic, nonvasculitic presentation of NPSLE, categorizing this presentation as lupus encephalitis in contrast to the vasculitis seen with the antibodies of antiphospholipid antibody syndrome [1]. In the striatum, neurons are regulated by glutaminergic and dopaminergic input, which lends support to the association between anti-NMDAr antibodies and anti-dopamine D2 receptor antibodies seen in patients with striatal autoimmune encephalitis [1,7].

However, the presence of such specific antibodies is not sufficient for diagnosis as individuals with SLE will have these antibodies without the neuropsychiatric symptoms; these specific antibodies have even been found in healthy individuals without lupus [1]. Diagnosis must be supported with the corresponding neuroimaging for patients with lupus induced striatal encephalitis: the presence of bilateral symmetric hyperintensities within the caudate and putamen on FLAIR and T2-weighted imaging, in combination with the clinical symptoms, is highly indicative of lupus induced striatal encephalitis [1].

The presence of bilateral basal ganglia hyperintensity could occur from other pathologies rising from intoxication or infectious conditions. Carbon monoxide poisoning classically presents with bilateral hyperintensity in the globus pallidus with restricted diffusion as the high metabolic activity of the basal ganglia is compromised [8]. However, his recent presentation and diagnosis of SLE as well as bloodwork results and no restricted diffusion on DWI did not support this differential diagnosis. Our patient could also have presented with bilateral basal ganglia hyperintensity due to an infectious cause given his high fevers and altered mental status. Patients with Flavivirus encephalitis or cerebral toxoplasmosis present with bilateral hyperintensities in the posteromedial thalamus or multiple ring-enhancing lesions in the basal ganglia, respectively [8]. However, our patient has not been exposed to environments where he could contract Flavivirus encephalitis nor is he immunocompromised to contract cerebral toxoplasmosis. The normal metabolic profile, bloodwork, and CSF analysis support the diagnosis of an inflammatory cause of encephalitis as opposed to an infectious one.

For this patient and his symptoms, FLAIR imaging is ideal as it is highly sensitive in identifying lesions in white matter in contrast to CSF and normal brain tissue [9]. The use of diffusion weighted imaging (DWI) helped determine whether symptoms could be from acute infarction, which would present as a bright signal from limited diffusion of water molecules [10]. However, our patient's imaging revealed no hyperintensity on DWI imaging and no evidence of restricted diffusion on ADC (Figs. 3 and 4). The high resolution VWI we obtained with high field spatial strength demonstrated no vessel wall enhancement and makes this patient the first case with encephalitis with detailed vessel wall imaging that rules out vasculitis.

From the literature review, similar cases of NPSLE have been described as vasculitis rather than encephalitis (Table 1). While it is difficult to define exactly what pathophysiological processes cause the display of these symptoms in each patient, there is significant evidence to classify our case as striatal encephalitis rather than vasculitis [11]. The hypothesis known as "cerebral vasculitis" is uncommon in patients with SLE [11]. Patients presenting with NPSLE do not present with evidence of inflammatory infiltrate in their vessel walls and similarly, our patient did not present with vessel wall enhancement [11]. This supports our decision to describe this case as striatal encephalitis due to an autoimmune process, which clinically impacts many different organ systems, including brain function in patients [11].

For our patient, the acute exacerbation of SLE with increased levels of autoantibodies coinciding with the neuropsychiatric symptoms strongly support the diagnosis of NPSLE. While the specific autoantibodies were not present to localize the NPSLE specifically to the striatum, after obtaining MRI imaging, we were able to specify based on the symmetric bilateral hyperintensities seen in the basal ganglia without vessel wall enhancement, our patient is affected with lupus induced striatal encephalitis. Treatment for autoimmune encephalitis consists of steroid therapy, IVIG, plasma exchange therapy, rituximab, and cyclophosphamide [12]. There are no randomized controlled trials to determine the appropriate duration and protocol of these various therapies, thus they are based off of expert recommendations, small, controlled trials, and case studies [5]. The most commonly used treatment for patients with severe presentations such as our patient is the use of high dose corticosteroids in "pulse therapy" for approximately 3–5 days followed up with oral therapy [5]. Plasma exchange therapy is supplemented to remove any autoantibodies currently circulating in the patient's sera and long-term management is provided with immunosuppressants like rituximab or cyclophosphamide to reduce the production of antibodies at the source.

Table 1 – Striatal dominant lupus encephalitis- Is it vasculitis or autoimmune process? Review of literature and report of a new case with vessel wall imaging.

	Nakamura[1]	Kelley[2]	Budhram[3]	Dale[4]	Rey[5]	Our Case
Striatal Involvement	Bilateral symmetric hyperintensity	Bilateral symmetric T2/FLAIR hyperintensity of the basal ganglia, thalami, and surrounding white matter	Pt A & B: Striatal T2-hyperintensity, as well as multifocal punctate hyperintensities on DWI	Normal or subtle generalized atrophy	Pt 1: small T2 hyperintense lesion in the right hippocampus Pt 2: slight medial temporal hyperintensity bilaterally on FLAIR sequences Pt 3: left medial temporal hyperintensity on FLAIR sequences	T2 FLAIR hyperintensities in bilateral basal ganglia
Symmetry Diffusion	Symmetric Hyperintensity of the basal ganglia and thalami without restricted diffusion	Symmetric Hyperintensity of the basal ganglia, thalami, and surrounding white matter without restricted diffusion	N/A Corresponding apparent diffusion coefficient (ADC) map hypointensities confirmed true diffusion restriction, compatible with infarctions	N/A N/A	Asymmetric N/A	Symmetric No restricted diffusion
Post contrast enhancement	No	No	N/A	N/A	No contrast enhancement	No enhancement
CT MR Angiogram	N/A	N/A	Pt A: Brain MRA normal Pt B: Multifocal arterial stenosis	Normal	N/A	Normal
Vessel Wall Imaging	N/A	N/A	N/A	N/A	N/A	No evidence of vessel wall enhancement
Autoimmune Panel	Antinuclear and anti-Sm antibodies positivity, lymphocytopenia, hypocomplementemia	Anti-dsDNA	Pt B: elevated ESR, elevated double-stranded DNA, low C3 and low C4	N/A	N/A	Increased levels of SSA autoantibody, Smith autoantibody, and RNP autoantibody increased levels of IgG and IgA B2 glycoprotein antibodies
Plasmapheresis	Not used as treatment	5-6 sessions	N/A	N/A	N/A	5 sessions

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Conclusion

Our case report highlights the additional benefit of vessel wall imaging in diagnosis of lupus induced encephalitis. In addition to laboratory tests to determine the various types of autoantibodies present during the NPSLE exacerbation, the use of FLAIR and DWI MRI imaging were very helpful in diagnosing the patient's condition. VWI ruled out vasculitis as an underlying cause of changes seen on routine MRI sequence and helped in the management of the patient. Furthermore, imaging displayed no restricted diffusion and allowed us to consider parenchymal autoimmune inflammatory etiology rather than basal ganglia infarction resulting in cytotoxic edema that can be related to thrombosis associated with lupus. The neuroradiological identification of bilateral symmetric T2/FLAIR hyperintensity in the basal ganglia of similar patients can tremendously benefit by rapid diagnosis and treatment initiation to limit the extent of antibody induced neuronal damage potentiating a more rapid recovery in such patients.

Patient consent

Consent was not obtained from the patient as all patient identifiers associated with this individual were removed.

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