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CASE REPORT

Antibody-Mediated Striatal Encephalitis and Aseptic Meningitis in A Child with Neuropsychiatric Lupus: A Case Report

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INTRODUCTION

Neuropsychiatric systemic lupus erythematosus (NPSLE) refers to the neurological and psychiatric symptoms that are thought to be related to systemic lupus erythematosus (SLE). NPSLE can be devastating, responsible for high rates of morbidity and mortality. It can occur any time in SLE. A recent large cohort study showed that NPSLE affects up to 25% of patients with juvenile-onset SLE.[1] The aetiology is thought to be multifactorial but vasculopathy, autoantibody production, and cytokine-induced neurotoxicity play a major role in the pathogenesis.[2]

Our clinical report highlights two infrequent subtypes of NPSLE–striatal encephalitis and aseptic meningitis, with substantial clinical and radiological response to immunosuppressants. The radiological features and treatment response of striatal encephalitis in our case are strikingly similar to those of the subset of anti–*N*-methyl-D-aspartate receptor (anti-NMDAR) autoimmune encephalitis involving the striatum.

CASE REPORT

An 11-year-old girl with known SLE presented to our hospital with a 1-week history of difficulty in passing urine, followed by acute-onset urinary retention. She was also suspected to have depersonalisation-derealisation syndrome for the last 1 year. She experienced progressive worsening with avolition, apathy, mental slowness, and insomnia 4 weeks prior to this acute presentation.

Urgent magnetic resonance imaging (MRI) brain examination demonstrated bilateral symmetrical T2 hyperintensity of the caudate nuclei, putamina, and globus pallidus without contrast enhancement or restricted diffusion. Bilateral thalami were spared (Figure 1a). Following intravenous gadolinium injection, scattered areas of leptomeningeal enhancement were present at bilateral frontal lobes and the right cerebellar hemisphere (Figure 1b and 1c). MRI of the spine demonstrated leptomeningeal enhancement along the lower thoracic cord and the conus medullaris (Figure 2).

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Ethics Approval: The patient was treated in accordance with the Declaration of Helsinki. Verbal consent for publication was obtained from the patient's parents.

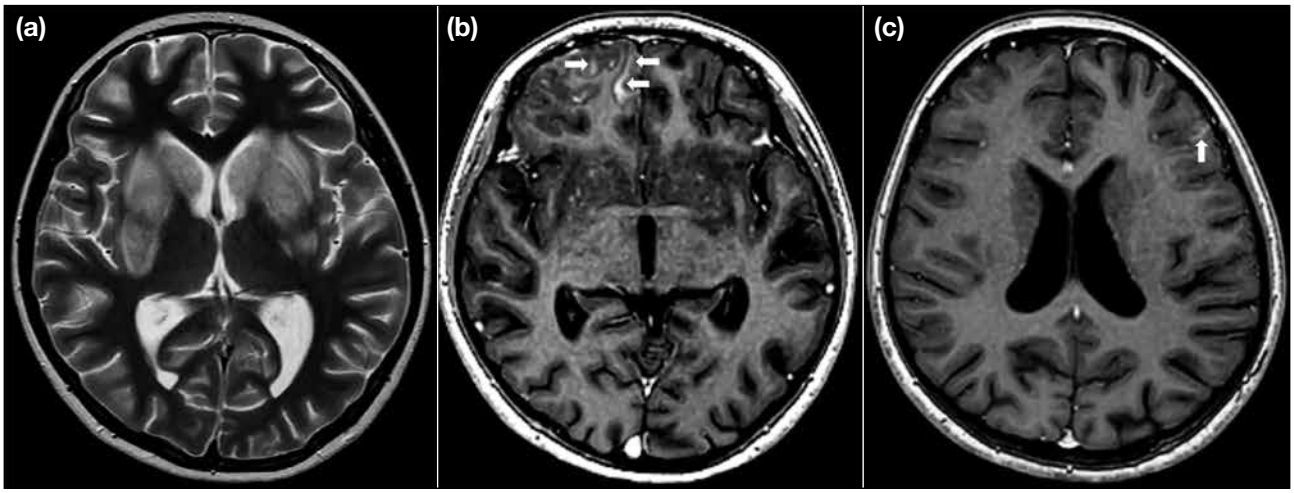

Figure 1. (a) Initial magnetic resonance imaging (MRI) of the brain. Axial T2-weighted image shows bilateral symmetric T2 hyperintensity of the caudate nuclei, putamina, and globus pallidi. Bilateral thalami are spared. (b and c) Axial T1-weighted post-gadolinium MRI of the brain show scattered areas of leptomeningeal enhancement at bilateral frontal lobes (arrows).

Figure 2. Initial magnetic resonance imaging of the spine. Sagittal T1-weighted post-gadolinium image shows leptomeningeal enhancement along the lower thoracic cord and the conus medullaris (black arrows).

The patient underwent extensive workup and was positive for antinuclear antibodies, anti–double-stranded DNA, anti-ribonucleoprotein, anti-extractable nuclear antigen antibodies including anti-Ro, anti-La and anti-Sm, as well as anti-ribosomal P antibodies; anti-NMDAR antibody was negative. Cerebrospinal fluid analysis revealed mildly elevated protein and normal leucocyte count. Cerebrospinal fluid gram stain, culture and virology were negative.

The patient was empirically treated with intravenous acyclovir, oral oseltamivir, and intravenous ciprofloxacin at the time of presentation for 2 days without any clinical improvement. Based on the clinical and characteristic MRI features, a working diagnosis was made of NPSLE with antibody-mediated striatal encephalitis and aseptic meningitis. Antiviral and antibiotic treatments were discontinued and immunosuppressive treatment was commenced. The patient received 5 days of pulse intravenous methylprednisolone and intravenous cyclophosphamide, followed by oral prednisolone and mycophenolate mofetil.

Follow-up MRI of the brain was performed 3 days later to guide clinical management. There was complete resolution of the leptomeningeal enhancement but persistent striatal T2 hyperintensity. With treatment, the clinical status of the patient gradually improved. Foley was weaned off successfully. Her mental state and sleep quality improved.

Another follow-up MRI of the brain 3 weeks from baseline demonstrated reduction in the extent of T2 signal abnormality but interval development of caudate and lentiform nuclei atrophy (Figure 3a). There was also novel T1 hyperintensity within the caudate and lentiform nuclei without associated susceptibility

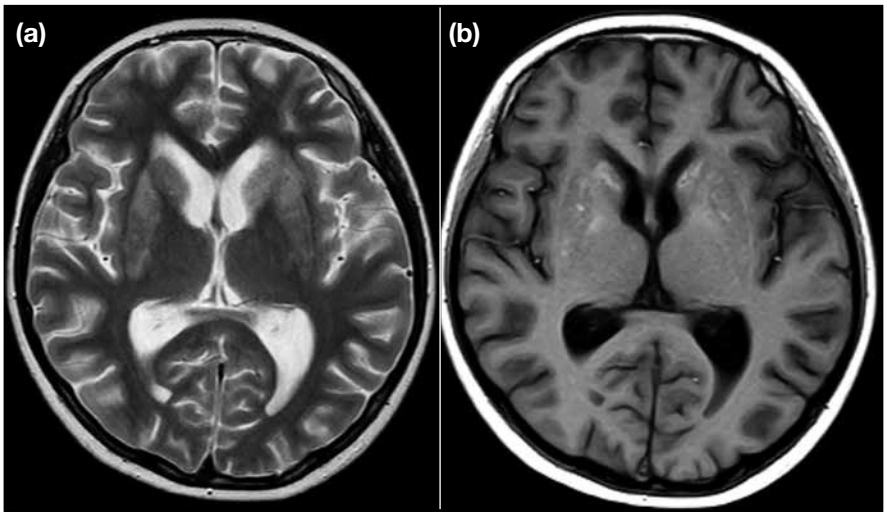

Figure 3. Follow-up magnetic resonance imaging of the brain at 3 weeks from baseline. (a) Axial T2-weighted image demonstrates markedly reduced T2 signal abnormality with atrophic change of the caudate and lentiform nuclei. Note that there is associated ex-vacuo dilatation of bilateral frontal horns relative to the baseline image. (b) Axial T1-weighted image shows new T1 hyperintense signals within caudate and lentiform nuclei without susceptibility artefacts, consistent with coagulative necrosis.

artefacts, consistent with coagulative necrosis (Figure 3b).

DISCUSSION

NPSLE describes a wide spectrum of peripheral and central nervous system manifestations. The widely quoted classification of NPSLE, made by an American College of Rheumatology expert committee in 1999, comprised 12 central and seven peripheral nervous system manifestations.[3] Case definitions including diagnostic criteria, exclusions, and methods of ascertainment were developed for each specific neuropsychiatric syndrome.[3] Among these, headache, mood disorders, cognitive dysfunction, seizures, movement disorders, and cerebrovascular disease are the most common NPSLE manifestations.[1,4,5]

Neuroimaging plays a vital role in the diagnosis of NPSLE and MRI is the preferred imaging modality for assessment of neurological manifestations although a negative scan does not exclude the presence of active NPSLE. A wide range of radiological abnormalities has been described but are often non-specific. In a single-centre retrospective study by Al-Obaidi et al,[5] the major MRI findings in juvenile-onset NPSLE were focal T2-weighted white matter hyperintensities (33%), brain atrophy (18.5%), cortical grey matter lesions (3%), and basilar artery territory infarction (3%), although a majority of patients (59%) showed no MRI abnormalities despite clinically active NPSLE. Striatal encephalitis and aseptic meningitis have rarely been described as characteristic manifestations of neuropsychiatric lupus,[6-8] although they were coexistent in our patient.

Antibody-mediated striatal encephalitis is a rare but characteristic manifestation of NPSLE.[6,7] The radiological features and clinical course of lupus-related antibody-mediated striatal encephalitis closely resemble those of anti-NMDAR striatal encephalitis. It is suggested that peripheral anti–double-stranded DNA antibodies, a specific serum autoantibody in SLE, may enter the central nervous system to cross-react with NMDAR antigens[6,7] and mediate a non-thrombotic and non-vasculitic pathology with features of neuronal excitotoxicity.[6] Other autoantibodies thought to cause NPSLE include anti-neuronal, anti-NMDAR2, anti-ribosomal P, and anti-endothelial antibodies.[9]

The radiological pattern of bilateral symmetrical T2 hyperintensity involving lentiform and caudate nuclei typically suggests systemic or metabolic causes. The characteristic sparing of bilateral thalami and lack of restricted diffusion and contrast enhancement provide important clues for excluding multiple conditions in the differential list including hypoglycaemia, hypoxic ischaemic encephalopathy, extrapontine myelinolysis, arterial occlusion, venous thrombosis, and Creutzfeldt–Jakob disease. Other differentials including organophosphate or methanol poisoning can be excluded by clinical presentation and toxicology.

In an appropriate clinical setting, such as in our patient, the presence of bilateral symmetrical T2 hyperintense signal changes within the caudate and putamen without evidence of restricted diffusion or contrast enhancement was strongly suggestive of autoimmune encephalitis of the striatum.[7] Intrinsic T1 hyperintensity within the

striatum, also evident in our patient, may indicate a poor prognosis. This has been proposed to be related to the development of coagulative necrosis secondary to prolonged antibody-mediated inflammation and excitatory glutamate neurotoxicity.[7]

Aseptic meningitis is another manifestation of NPSLE. It is possibly mediated by a combination of mechanisms such as anti-neuronal antibodies, antiphospholipid antibodies, immune complex–mediated vasculitis, and cytokines. Due to the non-specific radiological findings, more common causes of leptomeningeal enhancement, including infection and malignancy, must be excluded before establishing the diagnosis.[4] Compared with pyogenic meningitis, cerebrospinal fluid leucocytes and proteins are usually lower in cases of lupus-related aseptic meningitis.

In children with SLE, neuropsychiatric manifestation is frequently associated with high overall SLE activity. Aggressive treatment, including systemic corticosteroid and immunosuppressants, is often required to control the autoimmune process and avoid further damage.[4] Close collaboration between the radiologist, paediatric rheumatologist and neurologist is crucial to reach a prompt diagnosis and maximise clinical outcomes in these patients with NPSLE.

CONCLUSION

We present a patient with NPSLE presenting as striatal encephalitis and aseptic meningitis who demonstrated a good clinical and radiological response to immunosuppressive therapy. The clinical course and imaging features of antibody-mediated striated encephalitis in our patient closely resemble those of a striatal variant of anti-NMDAR encephalitis.

Neuroimaging plays an important role in diagnosis, monitoring treatment response and prognostication by identifying complications such as brain atrophy or intrinsic basal ganglionic T1 hyperintensity. Prompt diagnosis and early treatment facilitates optimisation of clinical outcomes.

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