




A Rare Case of Reversible Splenic Lesion Syndrome with Extracallosal Lesions in the Setting of Deep Anemia

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Dear Editor,

A 35-year-old female patient was admitted to our emergency department with impairment of consciousness, and somnolence. It was learned that the patient had been suffering from headache and anorexia over the last week. The clinic had begun abruptly, and the patient deteriorated over the last 5 hours before admission. The other medical history was unremarkable, and the patient had no history of recent drug use or an infection. The vital signs at admission to the emergency service were within normal limits. The neurological examination revealed that the patient was nonoriented and mildly cooperative. She could not cooperate properly with the examination and an increase in motor and psychological activity was apparent that was compatible with agitation. Other investigations including motor, sensory, and cerebellar tests were roughly within normal limits. The Kernig's and Brudzinski's signs were negative. The laboratory investigations revealed severe iron deficiency anemia (hemoglobin [Hb]: 5.3 mg/dL, serum ferritin: 30 µg/L), mild hyponatremia (131 mM/L [136–146 mM/L]), hyperkalemia (5.1 mM/L), neutrophilic leukocytosis (neutrophil: 89%), and increment of C-reactive protein (27.9 [0–0.8]). The results of the other investigations including liver-kidney functions, thyroid functions, vitamin B12, and folic acid were within normal limits. The initial cranial magnetic resonance imaging (MRI), performed on the 9th hour of the clinic, was normal (→Fig. 1). Lumbar puncture investigations revealed normal cerebrospinal fluid (CSF) biochemistry, microscopic examination, and the result of the CSF culture was negative. The infectious disease specialist did not consider an infectious etiology of the central nervous system to explain the clinic. Routine electroencepha-

logram showed mild slow background activity (7 Hz) without discharge and focal slow activity. At this point, the MRI was repeated the day after, which showed restricted diffusion in the splenium, bilateral corona radiata, and left hippocampus (→Fig. 1). Two-unit red blood cell (RBC) transfusion was administered for deep anemia (the follow-up test revealed Hb level of 8.3 mg/dL and Na level of 134 mM/L) and methylprednisolone 1 g intravenous treatment was initiated considering a possible underlying limbic encephalitis or autoimmune encephalitis. However, after the RBC transfusion, a marked and rapid clinical improvement was achieved, and the patient completely recovered after 2 days, and methylprednisolone was stopped at the second day of therapy. She was fully oriented and cooperative, and the Glasgow Coma Scale was evaluated as 15 points. The results of the screening tests for tumors including computed tomography (CT) thorax, CT abdomen, and pelvic ultrasound were unremarkable. Besides, the tumor markers were within normal limits. The anti-NMDAR antibody, anti-AMPA1 antibody, anti-AMPA2 antibody, CASPR2 antibody, GABAR1/B2 antibody, and LGI1 antibody tests results were negative. The follow-up MRI, performed 1 week later, showed total resolution of the diffusion-restricted lesions (→Fig. 2). The retrospective analyses of the results, in light of the related literature data, revealed the diagnosis of reversible splenic lesion syndrome (RESLES).

Discussion

RESLES has been reported secondary to several disorders, including acute or subacute encephalitis/encephalopathy, antiepileptic drug (AED) toxicity or withdrawal, high-

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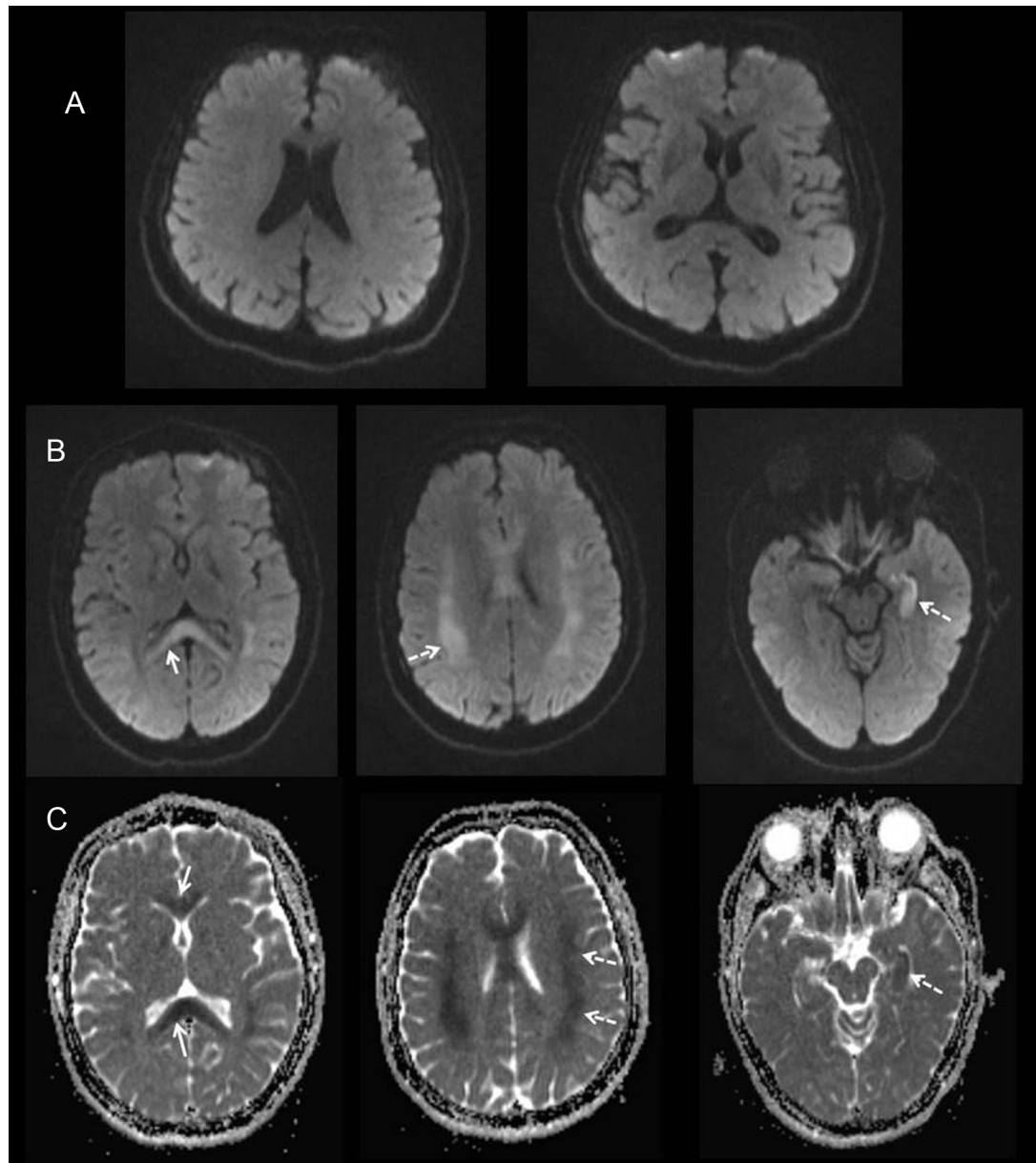


Fig. 1 (A) The cranial magnetic resonance imaging (MRI), performed at admission (9 hours after initiation of the clinic), shows a normal appearance. (B,C) The second cranial MRI (performed 1 day after the initiation of clinic) showing diffusion restriction in the corpus callosum, bilateral corona radiata, and left hippocampus (B represents the diffusion-weighted imaging [DWI] sequences; C represents the apparent diffusion coefficient [ADC] sequences).

altitude cerebral edema, hypoglycemia, or hypernatremia. Particularly, the refractory seizures, AED usage, and metabolic conditions constitute prominent etiological factors for RESLES.¹ Classically, RESLES has an excellent prognosis, resulting in complete recovery without neurological sequelae after the acute disease course.² Therefore, recognition of this entity may be important for predicting the clinical course and appropriate management of these patients. In our patient, the prominent metabolic impairment was deep anemia; however, mild hyponatremia was also present at admission. The RBC transfusion provided improvement of Hb to 8.3 mg/dL and the clinic markedly improved. Therefore, we did not continue the methylprednisolone 1g intravenous therapy which was initiated considering the possibility of an

underlying limbic encephalitis or autoimmune encephalitis. In addition to the clinical course, the results of the following investigations (limbic encephalitis antibodies and screening tests for malignancy) also excluded these diagnoses. The association between RESLES and various metabolic disturbances including endocrine disorders, hypernatremia and hypoglycemia, and multiple vitamin deficiencies have been well defined.^{3,4} However, up to our knowledge, our case with RESLES in association with deep anemia is unique expanding the spectrum of RESLES.

Another interesting point was that the diffusion-restricted lesions also involved bilateral corona radiata and hippocampus in addition to the splenium. Classically, the extracallosal lesions are not expected to occur in RESLES.⁵

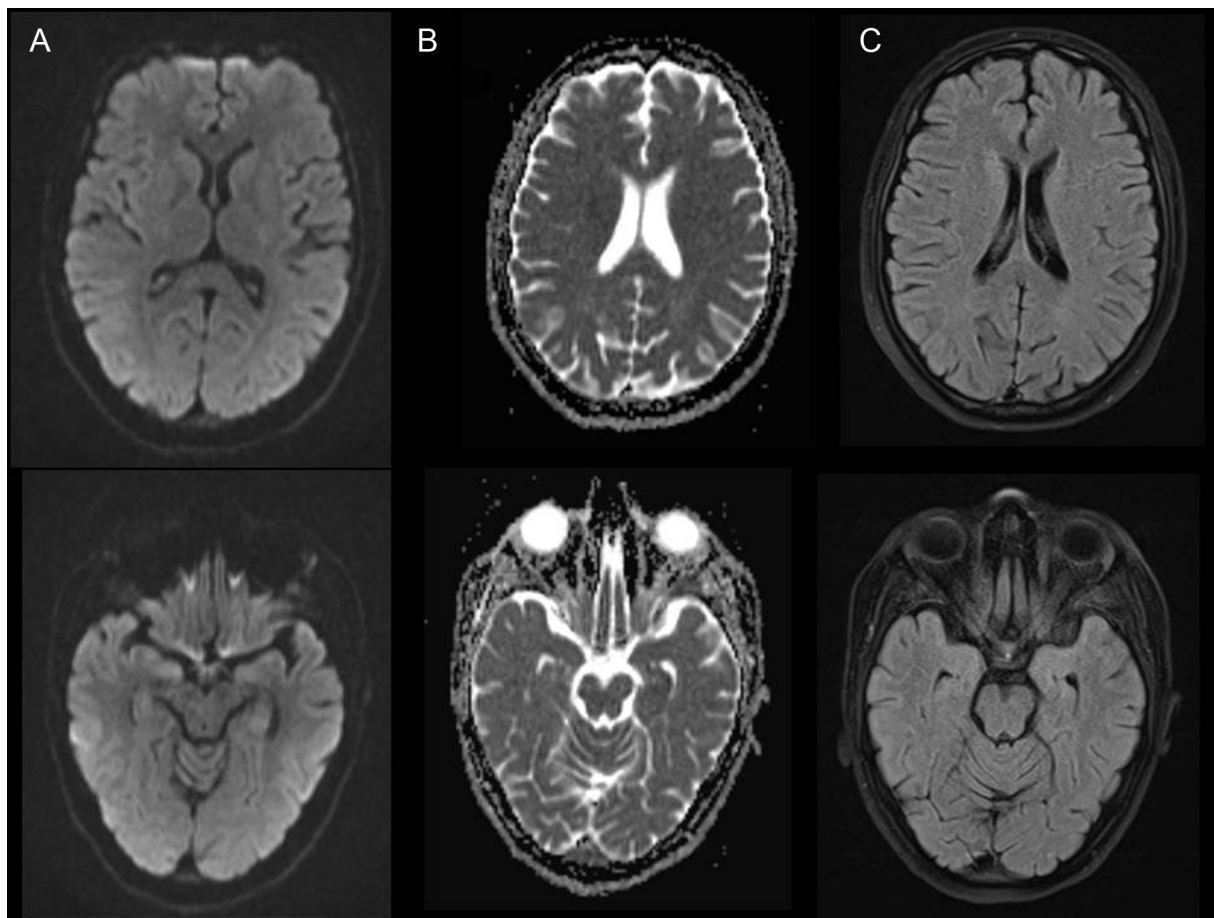


Fig. 2 The cranial magnetic resonance imaging (MRI) shows complete resolution of the diffusion-restricted lesions (A represents diffusion-weighted imaging [DWI] sequences, B represents apparent diffusion coefficient [ADC] sequences, C represents fluid-attenuated inversion recovery [FLAIR] sequences).

However, recent reports remark on the presence of extracallosal lesions frequently in patients with RESLES.^{4,6} Zhang et al reported extracallosal lesions in four of their eight patients with RESLES and they discussed that these lesions may be associated with unfavorable prognosis.⁴ Contrasting with this observation, the prognosis of our patient was excellent, such that she recovered completely in a few days following transfusion therapy.

A crucial hypothesis regarding the pathogenesis of a reversible diffusion-restricted lesion in RESLES is the excitotoxic mechanisms that do not lead to brain ischemia.⁷ In excitotoxic edema, glutamate is the main agent inducing edema and it occurs predominantly in glial cells and myelinic sheaths.⁷ This involvement pattern protects axons from intracellular edema and irreversible neuronal damage.⁷ The neuronal somata make up less than 1% of the corpus callosum whereas it is mainly composed of axons and glial cells⁸ which may be responsible from the specific vulnerability of this region in RESLES. The corona radiata also involve white matter connections without neuronal somata, however, we know that the hippocampus is comprised primarily of pyramidal cells. On the other hand, the pyramidal layers of the hippocampus are tightly packed with glutamatergic neurons that have a low firing thresh-

old⁹ supporting the view of glutamate-associated excitotoxic mechanisms. Of note, in our patient, the most probable etiological agent was deep iron deficiency anemia which is interestingly shown to lead marked functional alterations in both excitatory and inhibitory neurotransmitter receptors.¹⁰ However, these hypotheses are all warranted to be clarified in future studies including a large number of patients. We think that the illustration of these rare patients may provide contributions regarding our understanding of the mechanisms of RESLES also without extracallosal lesions. Finally, the clinical awareness of this entity is critical for optimal diagnosis and avoiding unnecessary interventions.

Authors' Contributions

HO contributed to the conception, organization, and execution of the paper, and the writing and review of the manuscript. SSC contributed to the conception and review of the paper.

Data Availability

The authors confirm that the data supporting the findings of this study are available within the article and its supplementary materials.

Informed Consent

A written informed consent was obtained from study participants. We confirm that we have read the journal's position on issues involved in ethical publication and affirm that this work is consistent with those guidelines.

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Conflict of Interest

None declared.

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