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CASE REPORT

Transient isolated lesion of the splenium associated with clinically mild influenza encephalitis

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Abstract Transient isolated lesions of the splenium with restricted diffusion are rare in the pediatric population. We report two such cases with influenza-associated encephalitis/encephalopathy (IAEE). These reversible isolated central splenial lesions are not specific for IAEE, but the notable feature associated with this specific presentation is a comparatively milder form of encephalitis that resolves clinically and radiologically within a short time.

Keywords Influenza encephalitis · Reversible · Splenium · Diffusion · Child

Introduction

Influenza-associated encephalitis/encephalopathy (IAEE) is a complex clinical syndrome that includes lesions with a poorer prognosis or a relatively milder form associated with transient restricted diffusion of the splenium of the corpus callosum. In addition to IAEE, such lesions of the splenium have been reported secondary to various other infectious agents and in epilepsy patients who received antiepileptic medication. A case of influenza-associated encephalitis along with brief mention of a companion case with identical imaging findings is detailed.

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Case report

A 12-year-old boy presented with an acute onset of confusion and hallucinations that woke him from sleep. Some dramatic changes in the size of his pupils were also reportedly witnessed by his mother during this episode. There was a history of headache and low-grade fever for 5 days, starting about a week preceding this episode. A rapid 'flu test was negative, but influenza B virus was isolated from a nasal swab at that time. EEG obtained 2 days following the episode of confusion showed mild generalized slowing of the background and left temporal region, without epileptiform discharges. MRI performed the same day demonstrated an ovoid area of restricted diffusion and decreased ADC values in the central portion of the splenium of the corpus callosum (Fig. 1). Hyperintensity was seen in this lesion on T2-weighted images and FLAIR sequences and there was no enhancement with contrast agent. There were no other lesions seen on diffusion-weighted images or other sequences. CBC, urine for toxicology screen and hepatic function tests were negative. CSF examination revealed a glucose level of 66 mg/dl, protein of 31 mg/dl and no pleocytosis. No virus was detected by PCR in the CSF sample. No specific medication was started. A follow-up EEG after 3 weeks was normal and the boy remained symptom-free in the interval. A follow-up MRI after 5 weeks revealed resolution of the lesion on DWI as well as other sequences (Fig. 2).

Discussion

The transient lesion described could be attributed to IAEE given the history of prodromal illness preceding the mild CNS manifestations and isolation of the influenza virus

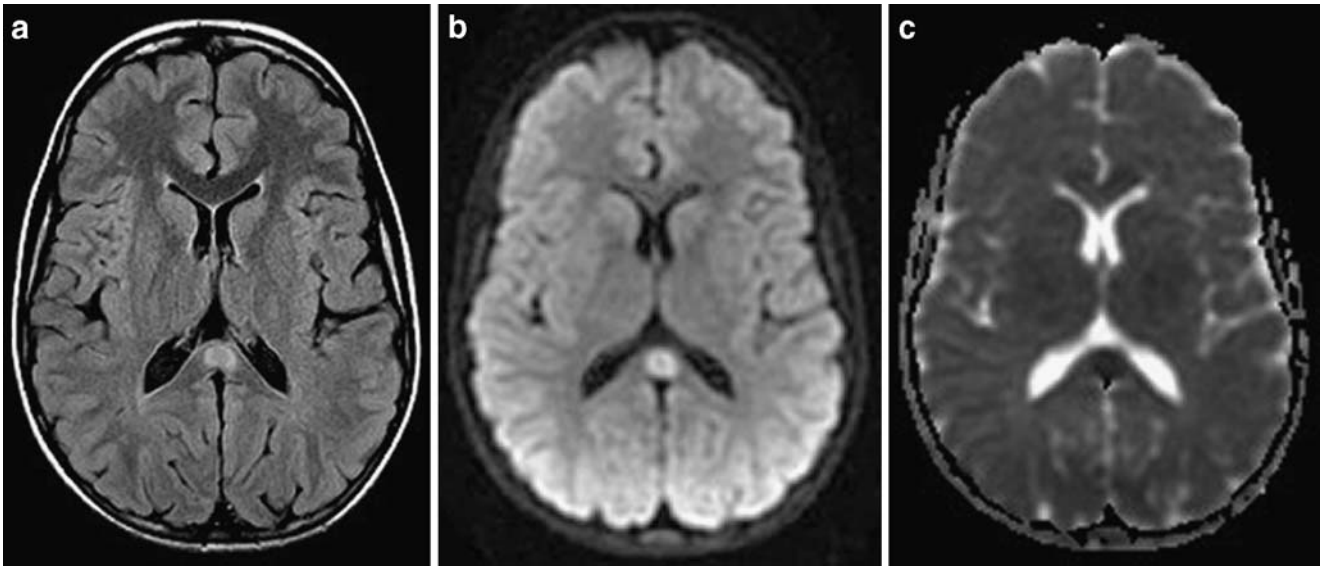

Fig. 1 MR image at onset of symptoms. Axial FLAIR image (**a**), axial diffusion-weighted image (**b**), and ADC map (**c**) reveal a hyperintense lesion in the central splenium that shows restricted diffusion

from the respiratory tract during the episodes. The CSF analysis of patients with IAEE often reveals normal protein and glucose with lack of pleocytosis [1, 2]. Positive CSF virus isolation is very rare and is postulated to be caused by either the disappearance of the virus during sampling or undetectably low amounts of virus in the CSF [1]. To our knowledge, there are fewer than ten reported cases of reversible splenial lesions in the literature where influenza virus was isolated, mostly from Japan. The virus was not detected by PCR in CSF samples in any of those patients and was instead isolated from the respiratory tract, as in our patients [1–4]. Influenza B virus was isolated in both of our patients, as in two previously reported patients.

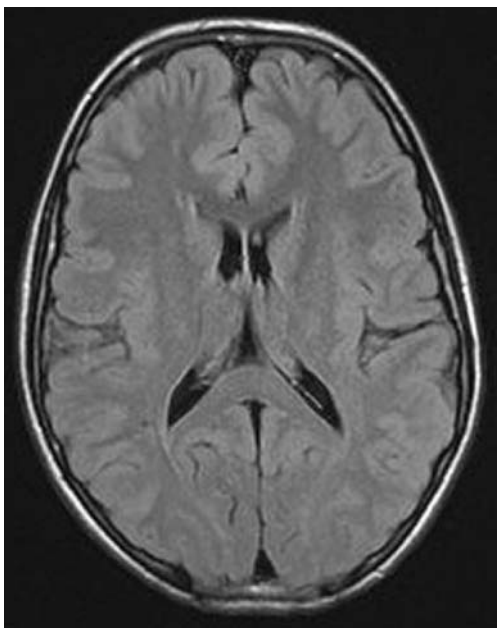

Fig. 2 MR FLAIR image shows resolution of the lesion on follow-up after 5 weeks

Homogeneous diffusion restriction and decreased ADC, which had resolved on follow-up imaging after 5–6 weeks, was observed. A follow-up EEG at 3 weeks was normal and hence it is possible that the lesion resolved radiologically earlier than we observed. The companion case that illustrates similar findings occurred during the same period as in the first case. A 13-year-old child presented with a 2-day history of fever, sore throat, petechiae, gross hematuria, disorientation and hallucinations (Fig. 3). Again, the clinical course lasting a few days was mild and the lesion had resolved on follow-up imaging after a few weeks. These reversible splenial lesions have been described with other causative agents such as rotavirus, measles, herpesvirus 6, salmonella organisms, mumps, varicella zoster virus, adenovirus, 0157 *Escherichia coli*-associated hemolytic uremic syndrome and unknown pathogens [5, 6]. The clinical features are nearly identical to those in our patients, with relatively mild CNS manifestations and complete recovery within a month.

Brain lesions other than splenial lesions have also been described with IAEE, and these include restricted diffusion involving cerebral cortex and subcortical white matter in various locations, symmetric involvement of the thalamus, brainstem and cerebellum with or without brain edema (acute necrotizing leukoencephalopathy-type) and brain edema. These other lesions can have a poorer prognosis and higher mortality [2].

The differential diagnoses for splenial lesions include ischemia, diffuse axonal injury, multiple sclerosis, lymphoma, Marchiafava-Bignami disease, and extrapontine myelinolysis. These other lesions are not usually isolated to the

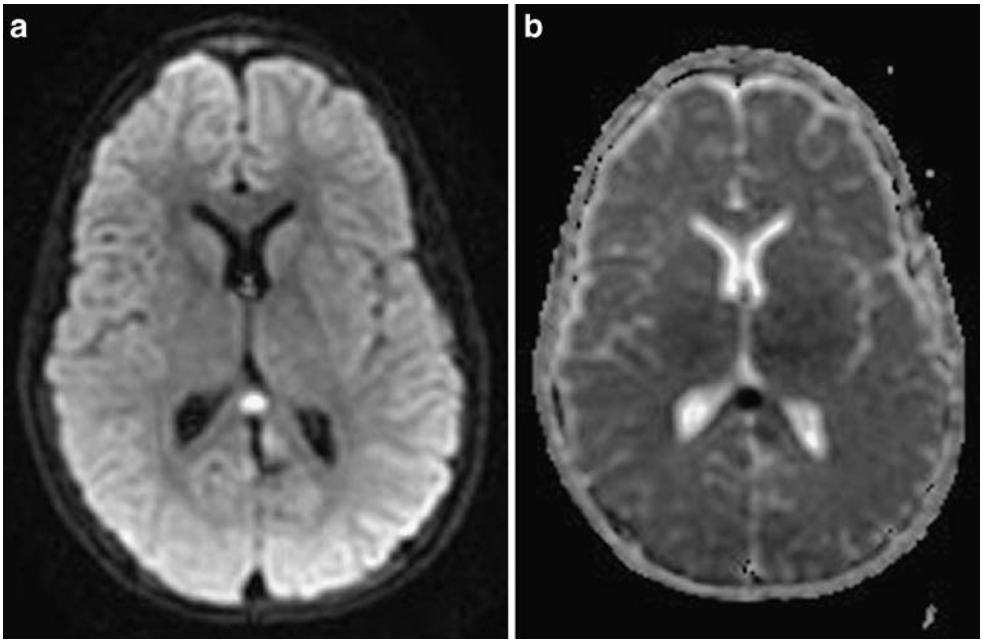

Fig. 3 MR images in a 13-year-old child with a similar presentation. Diffusion-weighted image (**a**) and ADC map (**b**) show a similar lesion with restricted diffusion in the splenium

splenium of the corpus callosum and do not usually resolve completely within a short period of time. Reversible splenial lesions have also been reported in patients with epilepsy receiving antiepileptic medication, where toxic levels or rapid drug withdrawal is the presumed cause [7]. Acute disseminated encephalomyelitis (ADEM) can be considered in the differential diagnosis of splenial lesions. There is, however, a clear distinction between these transient lesions and ADEM, which is characterized by multiple foci of asymmetric T2 prolongation that can evolve over weeks to months, rather than a unifocal transient splenial lesion.

There is no clear explanation regarding the pathogenesis of these transient lesions. Tada et al. [3] postulated that there are two possible mechanisms for the transiently decreased ADC of the lesions: intramyelinic edema caused by separation of myelin layers or an influx of inflammatory cells. The reversibility suggests that this finding is distinct from cytotoxic edema seen in cellular energy failure as in, for example, acute infarction, which is mostly irreversible. The predilection for the splenium is also poorly understood.

Establishing a causative agent in encephalitis remains a diagnostic challenge, and if clinicians are aware of this specific presentation, more expensive investigations and corticosteroid therapy can be avoided. The ramification of this report is that these isolated transient lesions of the central splenium have a mild clinical course and favorable prognosis and hence should be distinguished from ADEM and more serious demyelinating disorders [3, 8]. A causative agent can sometimes be isolated, but this will not necessarily add to the management because these lesions usually resolve without specific therapy.

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