



# Clastrum sign in febrile infection-related epilepsy syndrome (FIRES)

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## Neuro-images

A previously healthy 19-year-old woman presented with acute encephalopathy and status epilepticus 5 days after a febrile illness with flu-like symptoms. On admission, the patient was drowsy. Neurological examination revealed memory loss. She had focal motor evolving into bilateral convulsive status epilepticus. Ictal electroencephalogram revealed bilateral multifocal epileptiform discharges, predominant in the left hemisphere. After the failure of repeated intravenous benzodiazepines, we added levetiracetam and successfully controlled the status epilepticus, and it no longer recurred 3 days after the treatment was initiated. However, she still had daily focal seizures. Cerebrospinal fluid (CSF) examination revealed lymphocytic pleocytosis of 13 WBC/ $\mu$ L. Brain MRI 2 weeks after the status epilepticus onset revealed isolated bilateral claustrum lesions, the so-called “claustrum sign” (Fig. 1). Extensive diagnostic workups, including viral tests using PCR, bacterial and fungal culture, onconeural antibodies, and autoimmune encephalitis antibodies tested in serum and CSF were negative. The diagnosis of febrile infection-related epilepsy syndrome (FIRES) was made. She then received high-dose corticosteroid pulse therapy (1000 mg/day) for 5 days and was kept on levetiracetam and oxcarbazepine to control her seizures. At the follow-up 3 months later, the patient reported approximately one focal seizure a week with no further sequela.

FIRES is a rare subcategory of new-onset status epilepticus arguably triggered by cytokine storm, occurring in previously healthy patients [1, 2]. The etiology of FIRES remains uncertain despite the speculative consideration of the role of immune system-mediated mechanisms in the pathophysiology base on circumstantial evidence [3]. Patients had a prodromal phase of fever that preceded the onset of neurologic symptoms by 6 days on average [3]. Symmetric or asymmetric T2/FLAIR hyperintensity in the bilateral claustrum (the “claustrum sign”) is the characteristic neuroimaging feature of FIRES, appearing 10 days after status epilepticus onset on average [3]. The “claustrum sign” can occur isolated to the bilateral claustrum or together with hyperintensity extending to the insula, the mesial-temporal lobes, and other more diffuse cortical areas [3]. Interestingly, besides hyperintensity on T2/FLAIR images and diffusion-weighted imaging in the bilateral claustrum, which agrees with the previous research [4], we also observed hypointensity on apparent diffusion coefficient images that suggest diffusion restriction in the present case. We presumed that this finding might be related to the different timing of the MRI examination. Recently, the “claustrum sign” also has been described in other diseases, including COVID-19-related encephalopathy and acute necrotizing encephalopathy [5]. The treatment of FIRES includes anti-seizure medication, anesthetic therapy, and immunotherapy [1]. Although status epilepticus was responsive in approximately one-quarter of patients with FIRES, it was refractory in most cases. Among survivors, most of them developed chronic drug-resistance epilepsy [3].

In conclusion, the “claustrum sign” is a neuroradiological hallmark of FIRES and possibly of other cytokine-mediated disorders.

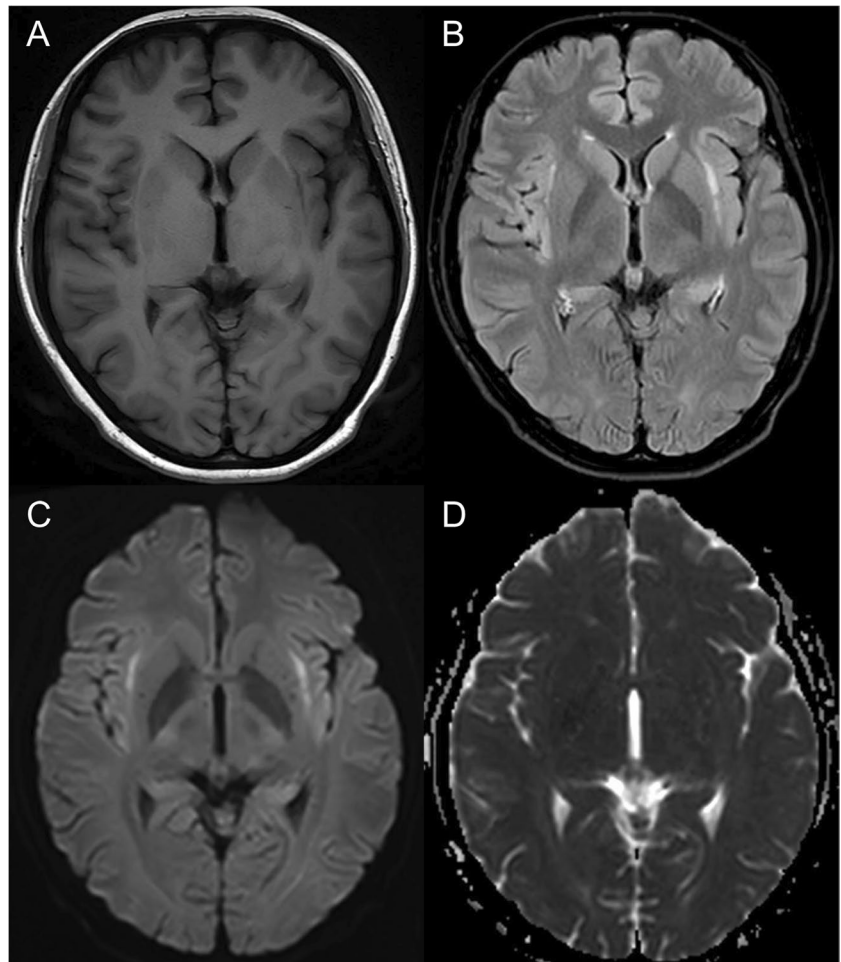
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**Fig. 1** The “claustrum sign”. Brain MRI shows bilateral claustrum hypointensity on T1-weighted images (A) and hyperintensity on fluid-attenuated inversion recovery images (B). Diffusion-weighted imaging (C) and apparent diffusion coefficient images (D) reveal restrictive diffusion of the bilateral claustrum



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**Authors' contributions** K.G. and Z.H. contributed to the conception and design of the study. K.G. contributed to the acquisition and analysis of data, drafting the manuscript, and preparing the figures. Z.H. revised the manuscript for intellectual content. All authors read and approved the final manuscript.

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**Data availability** Further anonymized data can be made available to qualified investigators upon request to the corresponding author.

## Declarations

**Ethics approval** Ethics approval was not required for the publication of the case.

**Consent to participate** Written informed consent was obtained from the patient.

**Competing interests** The authors declare that they have no competing interests.

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