 DOI: https://doi.org/10.5114/ceji/214097

Epstein-Barr virus encephalitis complicated by glial fibrillary acidic protein astrocytopathy in a child: a case report

HONG LIANG, CHENYUAN LI

Department of Pediatrics, Hainan General Hospital (Hainan Affiliated Hospital of Hainan Medical University), Haikou, Hainan 570311, China

Abstract

Autoimmune glial fibrillary acidic protein (GFAP) astrocytopathy is an emerging autoimmune disorder of the central nervous system (CNS). Its potential association with Epstein-Barr virus (EBV) infection remains unclear, with only a few cases reported following CNS EBV infection. Here, we report a 6-year-old Chinese child who developed autoimmune GFAP astrocytopathy (GFAP-A) after EBV encephalitis. The patient presented with a 6-day history of headache and fever. Cerebrospinal fluid (CSF) analysis indicated viral encephalitis, and metagenomic next-generation sequencing confirmed EBV in the CSF. Brain imaging revealed cortical abnormalities, and elevated GFAP-immunoglobulin G titres were detected in both the CSF and serum. The patient showed marked clinical improvement following treatment with antivirals, corticosteroids and intravenous immunoglobulin. This case highlights the potential role of EBV as a trigger for autoimmune GFAP-A and underscores the importance of considering autoimmune mechanisms in paediatric CNS infections.

Key words: *autoimmune glial fibrillary acidic protein astrocytopathy, Epstein-Barr virus, encephalitis.*

(Cent Eur J Immunol 2026; 51 (2): 1-5)

Introduction

Autoimmune glial fibrillary acidic protein (GFAP) astrocytopathy is a central nervous system (CNS) disorder characterised by the presence of GFAP-immunoglobulin G (IgG) autoantibodies in the cerebrospinal fluid (CSF) [1]. Although its pathogenesis remains incompletely understood, viral infections such as Epstein-Barr virus (EBV) have been proposed as potential triggers. While EBV encephalitis is rare, it may provoke secondary autoimmune responses [2-4]. Here, we present a paediatric case of EBV encephalitis complicated by GFAP astrocytopathy (GFAP-A), highlighting key diagnostic and therapeutic considerations.

Case presentation

The patient was a 6-year-old girl with a 6-day history of fever and headache (Fig. 1A). Informed consent was obtained from the patient's guardians. On 15 September of last year, her initial head computed tomography and routine laboratory tests were unremarkable. Oral cefixime was prescribed due to concern for bacterial infection, but symptoms persisted. Other neural autoantibodies, including NMDAR, as well as paraneoplastic antibodies, were negative, and tumour markers with imaging showed no evidence of malignancy. Cerebrospinal fluid analysis revealed a white blood cell count of 148 × 10^6/l (57% polynuclear cells), and brain and spinal magnetic resonance imaging (MRI) showed no abnormalities. Metagenomic next-generation sequencing (mNGS) detected EBV DNA in the CSF, confirming EBV encephalitis. Acyclovir (0.25 g/8 h) led to temporary symptom improvement. On 8 October, brain MRI revealed left frontal cortical hyperintensity (Fig. 1B). On 12 October, fever recurred (39.2°C). Cerebrospinal fluid analysis showed lymphocytic pleocytosis (52 × 10^6/l, 98% mononuclear), with GFAP-IgG positive in both serum (1 : 320) and the CSF (1 : 100) (Fig. 1C). Intravenous immunoglobulin (IVIG, 1 g/kg × 2 d) and methylprednisolone (0.45 g/kg × 3 d) normalised body temperature. By 27 October, CSF leukocyte count and mNGS results had normalised, whereas GFAP-IgG remained positive in the CSF (titre 1 : 1) and negative in the serum (Fig. 1C). Following a 6-month prednisone taper (starting at 60 mg/day, reduced by 5 mg every 2 weeks), the patient's GFAP-IgG seroconverted to negative, MRI findings normalised and no neurological sequelae were observed.

Correspondence: Hong Liang, PhD, Department of Pediatrics, Hainan General Hospital (Hainan Affiliated Hospital of Hainan Medical University), No. 19, Xiuhua Road, Xiuying District, Haikou, Hainan 570311, China, phone: +86 0898-963399, e-mail: lianghong_lhlh@163.com
Submitted: 22.05.2025, Accepted: 09.11.2025

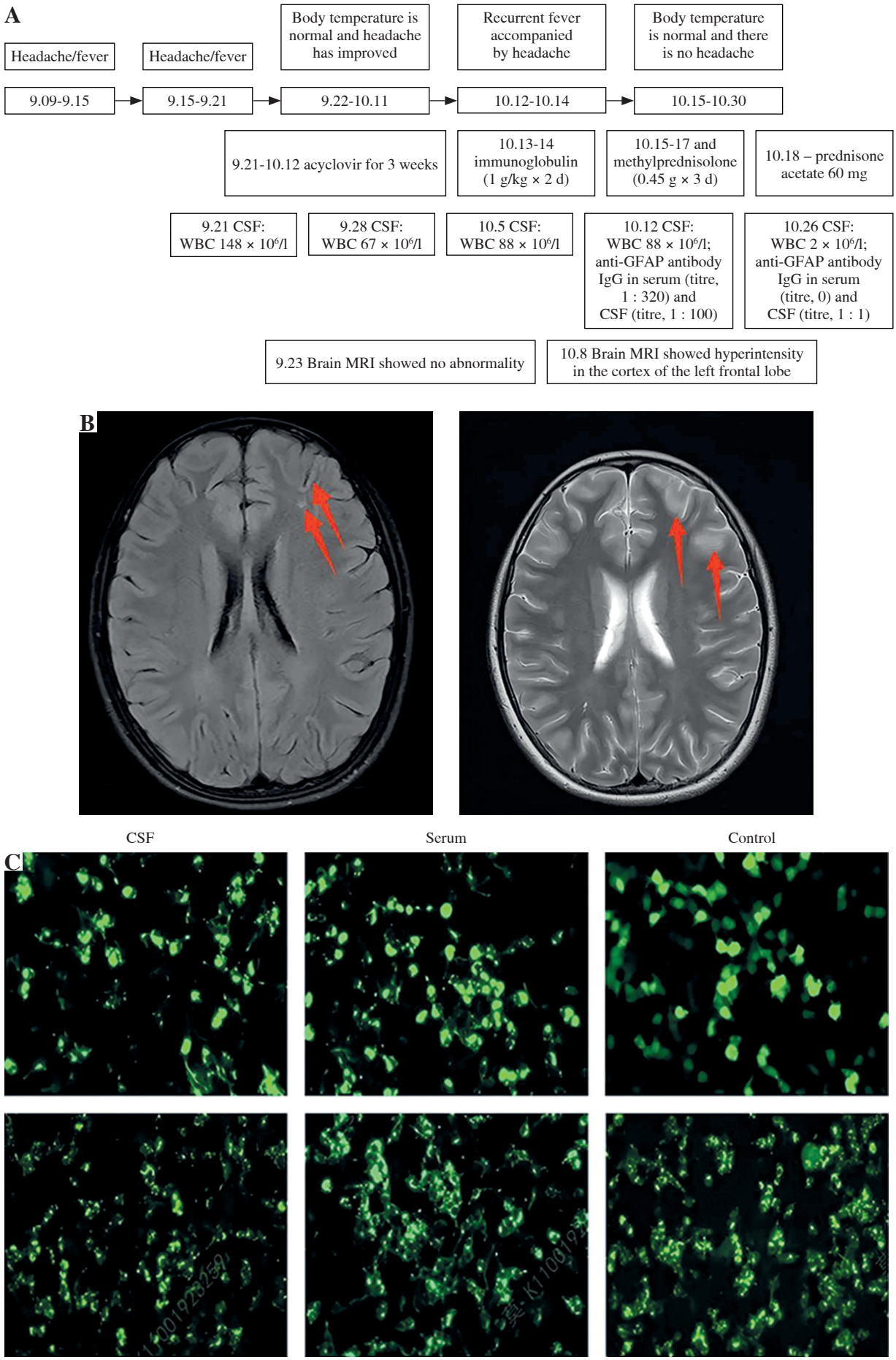

Fig. 1. Diagnosis and treatment of the patient. **A**) Timeline of the patient's diagnosis and treatment. **B**) Brain MRI showing abnormal signals in the left frontal cortex on both T1- and T2-weighted sequences. **C**) GFAP-IgG antibodies detected by cell-based assay (CBA) in cerebrospinal fluid (CSF) and serum. Before treatment, GFAP-IgG was strongly positive in CSF (1 : 100) and serum (1 : 320). After treatment, GFAP-IgG became weakly positive in CSF (1 : 1) and negative in serum

Table 1. Clinical data of patients with Epstein-Barr virus (EBV) infection complicated by glial fibrillary acidic protein astrocytopathy

Case	Author, year	Age, sex	Clinical features	Imaging features	GFAP-IgG CSF/serum	Main treatment
1	Wang, 2022 [2]	37, M	Fever, headache	Bilateral cortical & white matter T2/FLAIR hyperintensity; C2-5 patchy enhancement; meninges	+ / Not mentioned	Antiviral, IVIG
2	Lan, 2023 [3]	14, M	Fever, headache, tremor, urinary & bowel dysfunction, ataxia, psychiatric symptoms, seizures	Perivascular radial enhancement; hippocampus, thalamus, midbrain hyperintensity; cervical cord & meninges enhancement	+ / +	Antiviral, antibiotics, IVIG, IVMP
3	Lan, 2023 [3]	14, F	Similar to #2	Mild pia mater thickening; possible MERS	+ / –	Antiviral, antibiotics, IVIG, steroids
4	Lan, 2023 [3]	27, M	Fever, vomiting, pain, urinary/bowel dysfunction, ataxia	Normal	+ / +	Antibiotics
5	Lan, 2023 [3]	30, M	Fever, headache, ataxia, seizures	Splenium & thoracic cord signal abnormalities	+ / –	Antibiotics, antiviral, low-dose steroids, IVIG
6	Lan, 2023 [3]	47, F	Fever, headache, altered consciousness	Right occipital, corona radiata, cerebellar nodules	+ / –	Antibiotics, antiviral, antitubercular
7	Lan, 2023 [3]	50, M	Fever, headache, urinary/bowel dysfunction, ataxia	Normal	+ / +	Antiviral, antibiotics, dexamethasone
8	Lan, 2023 [3]	65, M	Fever, headache, psychiatric symptoms, seizures	Splenium signal abnormalities	+ / +	Antibiotics, antiviral, antitubercular, low-dose steroids, IVIG
9	Lan, 2023 [3]	65, M	Fever, headache, limb weakness	Normal	+ / +	Antiviral, antibiotics
10	Lan, 2023 [3]	86, M	Headache, numbness, ataxia, seizures	Not available	+ / +	Antiviral, antibiotics, IVIG, steroids
11	Zhang, 2023 [4]	54, M	Fever, tremor, coma, urinary dysfunction, paralysis	Perivascular radial enhancement; mild basal ganglia & corona radiata hyperintensity; spondylitis	+ / –	Antiviral, IVMP, IVIG
12	Zhang, 2023 [4]	59, M	Fever, tremor, coma, lower limb weakness	Bilateral cerebral white matter, basal ganglia, cerebellum T2/FLAIR lesions	+ / +	Antiviral, IVMP, IVIG
13	Zhang, 2023 [4]	62, M	Fever, headache, tremor, GI bleeding	Left frontal lobe patchy hyperintensity	+ / +	Antiviral, IVMP, IVIG
14	Li, 2023 [5]	33, F	Fever, headache, cognitive decline, limb weakness	Radial periventricular linear enhancement; meningitis	+ / –	Steroids, MMF
15	Li, 2023 [5]	60, M	Fever, abdominal pain, limb weakness, urinary retention	Radial periventricular enhancement; meningoencephalomyelitis	+ / +	Steroids, MMF
16	Li, 2023 [5]	71, M	Fever, urinary retention, cognitive dysfunction	Similar to #15	+ / –	Steroids, MMF

Table 1. Cont.

Case	Author, year	Age, sex	Clinical features	Imaging features	GFAP-IgG CSF/serum	Main treatment
17	An, 2025 [5]	36, M	Fever, ataxia, cognitive decline, hiccups, urinary/bowel dysfunction	Bilateral basal ganglia, corona radiata, thalamus patchy hyperintensity; cervical cord; perivascular radial enhancement	+ / –	Acyclovir, high-dose corticosteroid
18	Yu, 2025 [7]	36, M	Headache, fever, dysuria, weakness, ataxia	Bilateral corona radiata, basal ganglia, thalamus low signal; thoracic/lumbar cord normal	+ / +	Antiviral
19	Yu, 2025 [7]	37, M	Headache, fever, dysuria, left eye blindness, tremor	Brain and cervical cord enhancement; PET-CT hypermetabolism	+ / –	Not mentioned
20	Yu, 2025 [7]	37, M	Headache, fever, radiculalgia, ataxia	Brain and spinal cord pia mater enhancement; C4-5 T2 high signal; PET-CT hypermetabolism	+ / –	Not mentioned
21	Yu, 2025 [7]	40, M	Headache, fever, limb weakness, dysuria	Diffuse brain membrane thickening	+ / +	Not mentioned
22	Yu, 2025 [7]	44, M	Headache, fever, dysuria, limb numbness	Brain T2/FLAIR high signal; spinal cord linear enhancement; PET-CT negative after recovery	+ / +	Not mentioned
23	Yu, 2025 [7]	47, M	Headache, fever, weight loss, ataxia, dysuria	Lateral ventricle radial vessel enhancement; diffuse PET-CT hypermetabolism	+ / –	Not mentioned

Discussion

Epstein-Barr virus (human herpesvirus 4) can directly invade the CNS, causing encephalitis, meningitis or, less commonly, myelitis [1-3]. Patients typically present acutely with fever, headache, limb weakness or muscle spasms. Our patient displayed these features, with mNGS confirming EBV DNA in the CSF and MRI revealing left frontal lobe abnormalities. Initial improvement with antiviral therapy supported the diagnosis of EBV encephalitis. However, persistent fever suggested a secondary autoimmune process. Strongly positive GFAP-IgG in the CSF (1 : 100) and serum (1 : 320) confirmed autoimmune GFAP-A. Treatment with antivirals, IVIG and corticosteroids resulted in full recovery.

Most reported cases of EBV-associated GFAP-A have involved adults, with heterogeneous clinical manifestations and imaging findings (Table 1). The majority demonstrated CSF GFAP-IgG positivity and were treated with antivirals in combination with immunotherapy, highlighting the novelty of our paediatric case [2-7]. The underlying aetiology remains uncertain. Experimental evidence indicates that the activation of EBV-inducible gene 2 in astrocytes can modulate extracellular signal-regulated kinase phosphorylation and calcium signalling, potentially promoting astrocyte migration [8]. Epstein-Barr virus-inducible gene 2 may also influence astrocytic receptors involved in CNS infection pathogenesis and therapeutic responses. Epstein-Barr virus infection could induce neuronal injury, exposing antigens and disrupting immune tolerance, thereby facilitating autoimmune responses. Additionally, nonspecific B-cell activation or molecular mimicry may contribute, as structural similarities between EBV antigens and GFAP epitopes could trigger cross-reactive antibody production, leading to autoimmune encephalitis. In the present case, GFAP-IgG positivity may have been initiated by EBV infection. However, early antibody testing was declined by the patient's family, limiting the determination of the precise onset of autoimmunity and the temporal relationship between EBV infection and GFAP-A. These mechanisms remain speculative, underscoring the need for further research to clarify EBV's role in triggering GFAP autoimmunity.

In this case, the patient was diagnosed with autoimmune GFAP-A secondary to EBV infection. No standardised international diagnostic criteria currently exist for GFAP-A, and diagnosis relies on clinical presentation, neuroimaging and GFAP antibody detection. Key features include acute-onset neurological symptoms (e.g. fever, headache), positive GFAP antibodies in serum or the CSF and MRI findings such as perivascular radial enhancement in the periventricular white matter or longitudinally extensive spinal cord lesions. Differential diagnosis remains challenging and requires careful, comprehensive clinical evaluation.

Conclusions

Most EBV-associated GFAP-A cases occur in adults. This first paediatric case highlights the uncertain link between EBV encephalomyelitis and GFAP-A and the need for further research on optimal treatments.

Funding

This research received no external funding.

Disclosures

This study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Hainan General Hospital (Hainan Affiliated Hospital of Hainan Medical University) (ID: YLY2025No.118). Written informed consent was obtained from all parents/local guardians.

The authors declare no conflict of interest.

References

1. Shetty D, Brahmbhatt S, Desai A, et al. (2024): Glial fibrillary acidic protein astrocytopathy: Review of pathogenesis, imaging features, and radiographic mimics. AJNR Am J Neuroradiol 45: 1394-1402.
2. Wang L, Dong L, Zhao M, et al. (2022): A case of EBV encephalomyelitis with positive anti-GFAP-IgG antibody with recurrent fever and dysuresia as the main symptoms: Case report and retrospective analysis. Medicine (Baltimore) 101: e31995.
3. Lan W, Li J, Ai P, Luo W (2023): Autoimmune glial fibrillary acidic protein astrocytopathy: clinical analysis and review of 15 cases. Acta Neurol Belg 123: 1465-1479.
4. Zhang JR, Zhuang S, Xu XD, et al. (2023): Overlapping Epstein-Barr virus encephalitis and autoimmune glial fibrillary acidic protein astrocytopathy. J Neuroimmunol 382: 578174.
5. Li XL, Wang JY, Li LK, et al. (2023): Epstein-Barr virus: To be a trigger of autoimmune glial fibrillary acidic protein astrocytopathy? CNS Neurosci Ther 29: 4139-4146.
6. An Q, Liu L (2025): A case report of autoimmune glial fibrillary acidic protein astrocytopathy combined with Epstein-Barr virus infection. BMC Neurol 25: 347.
7. Yu X, Zou Y, Li M, et al. (2025): Auto-immune glial fibrillary acidic protein astrocytopathy with active intrathecal Epstein-Barr virus: a single-center case series report. Neuropsychiatr Dis Treat 21: 1119-1130.
8. Li D, Liu X, Liu T, et al. (2020): Neurochemical regulation of the expression and function of glial fibrillary acidic protein in astrocytes. Glia 68: 878-897.