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Clinical Letter

Autoimmune Glial Fibrillary Acidic Protein Astrocytopathy Following Herpes Simplex Virus Encephalitis in a Pediatric Patient

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Introduction

Glial fibrillary acidic protein (GFAP) astrocytopathy is a novel form of autoimmune meningoencephalitis related to autoantibodies to GFAP.[1,2] A recent report described an adult patient developing GFAP astrocytopathy following herpes simplex encephalitis (HSE).[3] We present the first pediatric patient with history of HSE who developed acute cognitive and psychiatric symptoms and positive GFAP immunoglobulin G in the cerebrospinal fluid (CSF).

Patient description

This 12-year-old boy with attention-deficit/hyperactivity disorder presented with headache, fever, vomiting, decreased responsiveness, and seizures. His brain magnetic resonance imaging (MRI) revealed right greater than left temporal and frontal lobe swelling, suggestive of HSE. His CSF was positive for herpes simplex virus (HSV) by polymerase chain reaction (PCR). He completed 21 days of acyclovir and one week of rehabilitation. Clinically, he nearly returned to his baseline other than mild left-sided weakness and worsened attention-deficit/hyperactivity symptoms.

Over the next months, he had increasing memory deficits, impulsivity, and behavior problems. During this time, he was also diagnosed with migraines and started on topiramate. Around one year after his initial HSE, his symptoms acutely worsened and included disinhibition, impulsivity, hypersexuality, hypersomnia, hallucinations, aggression, and eventually suicidal ideation for which he was briefly admitted to an inpatient psychiatric facility. He had declines in multiple areas of neurocognitive functioning on neuropsychologic evaluation. Repeat brain MRI showed sequelae of HSE without acute findings. His CSF revealed elevated protein levels of 97, normal glucose and cell count, and negative HSV PCR. Autoimmune encephalopathy panels (Mayo Laboratories) in the serum and CSF were positive for anti-GFAP antibody in the CSF after reflexive testing. He received five days of intravenous methylprednisolone and intravenous immunoglobulins (IVIG). His symptoms minimally improved, and he experienced worsening psychiatric symptoms including auditory and visual hallucinations during his oral steroid taper. He was then started on monthly IVIG, mycophenolate mofetil, and extended oral steroid. Valproic acid and additional mood-stabilizing medications were started. Ten months after his diagnosis of GFAP astrocytopathy, he continues to

Conflicts of interest: None.

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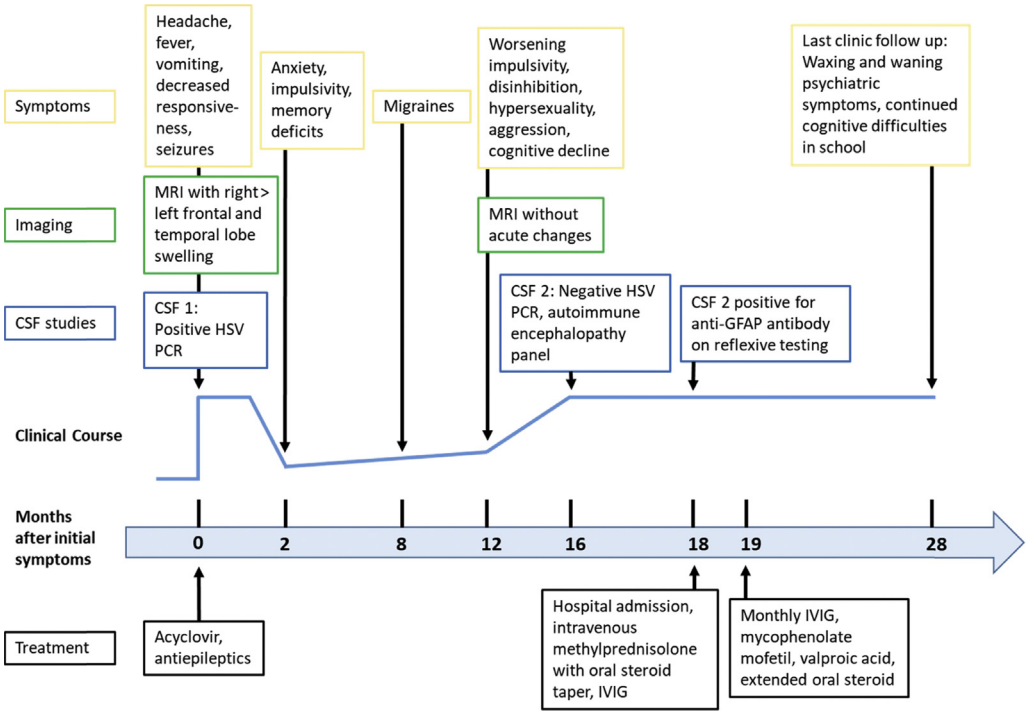

FIGURE. Timeline of clinical course. The color version of this figure is available in the online edition.

have waxing and waning neuropsychiatric symptoms. He has returned to school, but continues to struggle with cognitive deficits (Fig).

Discussion

Although damage to his bilateral frontal and temporal lobes from HSE may have contributed to this child's behavioral symptoms, his acute decline 12 months after initial HSE, inflammatory CSF profile, and positive CSF GFAP antibody with negative HSV PCR were consistent with acute encephalitis related to GFAP astrocytopathy. He presented with acute worsening of psychiatric symptoms, which is a common clinical feature of GFAP astrocytopathy.[4] Anti-GFAP antibody in the CSF is sensitive and specific for GFAP-related meningoencephalitis.[1,2] His repeat brain MRI revealed no acute findings, consistent with normal MRI in the majority of pediatric cases of GFAP astrocytopathy.[1] He did not respond to first-line immunotherapy with intravenous methylprednisolone and IVIG. Although the majority of reported patients with GFAP astrocytopathy improved with first-line immunotherapy, over 20% of patients were refractory to treatment.[1] He remains on prolonged immunosuppression with mycophenolate and monthly IVIG at 10-month follow-up, and additional second- or third-line agents are currently being considered. Longer follow-up is needed to determine his ultimate response to therapy and outcome.

This child suggests an observational link between HSE and autoimmune GFAP astrocytopathy in a pediatric patient. The association between HSE and anti-*N*-methyl-D-aspartate receptor encephalitis has been well recognized,[5,6] whereas few data are currently available on autoimmune GFAP astrocytopathy. Two adult patients have been documented with GFAP astrocytopathy following viral encephalitides—one following HSE[3] and the other following varicella zoster encephalitis.[1] It is reasonable to test for GFAP antibody along with other prevalent autoantibodies when autoimmune meningoencephalitis is suspected as a sequela of viral encephalitides.

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