Six Year Old With Chronic Headache: An Unexpected Meningitis Mimic

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ABSTRACT

The constellation of fevers accompanied by headache and vomiting is a red flag for clinicians that appropriately triggers evaluation for meningitis and other life-threatening diagnoses. When symptoms persist even after these conditions are ruled out, patient care becomes more challenging. We present the case of a 6-year-old male with a history of autism spectrum disorder who presented with 6 months of headaches and associated vomiting and intermittent fevers with negative infectious workup despite cerebrospinal fluid pleocytosis. Serial neuroimaging and laboratory evaluation ultimately led to a diagnosis of myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) presenting as aseptic meningitis. The clinical and radiographic findings of MOGAD are widely variable and overlap with several other inflammatory conditions, which makes diagnosis challenging. This case highlights the importance of recognizing this rare MOGAD presentation as an infectious meningitis mimic.

INTRODUCTION

The constellation of fevers accompanied by headache and vomiting is a red flag for clinicians that appropriately triggers evaluation for meningitis and other life-threatening diagnoses. When symptoms persist even after these conditions are ruled out, patient care becomes more challenging. We present the case of a 6-year-old male with a history of autism spectrum disorder who presented with 6 months of headaches and associated vomiting and intermittent fevers with negative infectious workup despite cerebrospinal fluid pleocytosis.

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CASE PRESENTATION

A 6-year-old male with a history of autism spectrum disorder presented with 6 months of headaches associated with nausea, vomiting, photophobia, phonophobia, and intermittent fevers. Ten days prior, he had been admitted to another institution for 48 hours. At that time, his vitals were normal except for intermittent fevers, and exam was unremarkable except for periods of "irritability." Infectious Disease service was consulted, and he had an extensive workup that was essentially unremarkable except for leukocytosis with a white blood cell count of 34.9 103/uL, elevated erythrocyte sedimentation rate (30 mm), and cerebrospinal fluid (CSF) pleocytosis (28 total nucleated cells) with an elevated opening pressure of >35 cm H_20. Brain magnetic resonance imaging (MRI) was remarkable for increased sulcal enhancement and foci of elevated T2/FLAIR signal within the right and left thalamus, suspicious for meningitis or other leptomeningeal process, although neoplastic process could not be excluded. He was diagnosed with viral meningitis and discharged home after blood and CSF cultures were negative and he demonstrated mild clinical improvement with scheduled outpatient follow-up and repeat brain imaging. Following discharge, his symptoms again worsened with ongoing fevers, headaches, and increasing sleepiness, weakness, and loss of appetite. The family reported no recent travel, trauma, or sick contacts. His immunizations were up-to-date, and he was on no current or recent medications.

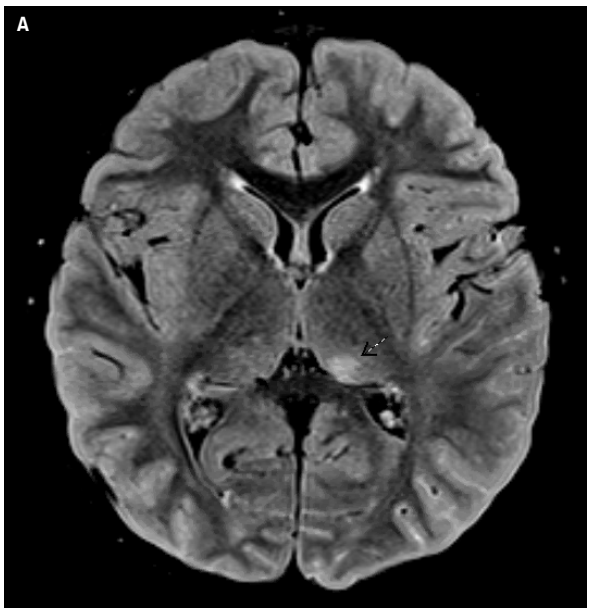
On presentation at our institution, the patient was uncomfortable appearing and lying stiffly in bed but answering questions appropriately. He was afebrile with a heart rate of 76 beats per minute, respiratory rate of 16 breaths per minute, and blood pres-

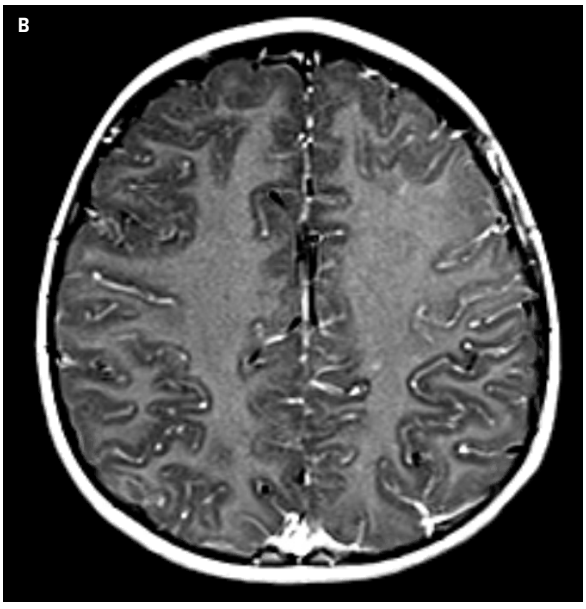
sure of 115/73 mm Hg. He had full range of motion when asked to move his neck, but he held his neck stiffly at rest and cried out in pain with neck flexion and palpation of the abdomen and along the spine. Neurological exam was notable for normal cranial nerves, no ataxia, and a plantar reflex that was up-going on the right and down-going on the left. He could follow commands appropriately for his age.

Repeat serial brain imaging revealed an enlarging left thalamic lesion, meningeal enhancement, and multifocal white matter and subcortical lesions with varying degrees of enhancement (Figure). Lumbar puncture revealed an elevated opening pressure of 45 cm H_2O, elevated protein at 52 mg/dl, and pleocytosis with 77 total nucleated cells. CSF analysis and serum immunologic studies were negative for viral, bacterial, and fungal infection. No unique oligoclonal bands were present in the CSF. Miscellaneous serum and spinal fluid immunologic studies were pending at the time of admission to the acute care floor. On hospital day 9, serum serology resulted positive for myelin oligodendrocyte glycoprotein (MOG) antibody with a titer of 1:100. He was diagnosed with MOG antibody-associated disease (MOGAD).

While the patient did not initially have papilledema, it developed on subsequent eye exams, and his headache was thought to be secondary to elevated intracranial pressure and autoimmune meningitis. He was treated with high dose intravenous (IV) methylprednisolone (30 mg/kg) for 5 days followed by a prolonged steroid taper and started acetazolamide for his increased intracranial pressure. He responded well to treatment with steady improvement in his symptoms. His last brain MRI and orbit 3 months posttreatment showed near complete resolution of previously seen lesions and leptomeningeal enhancement. Repeat serum MOG antibody testing 3 months posttreatment continued to be positive, but repeat testing at 10 months posttreatment was negative.

Figure. Magnetic Resonance Brain Axial Images Showing (A) FLAIR Hyperintensity in the Left Thalamus and (B) Diffuse Leptomeningeal Enhancement on T1-Weighted Post-Gadolinium Scan





DISCUSSION

This patient's constellation of chronic headache and systemic symptoms, including fevers, decreased appetite, and increased sleepiness, fits the pattern of aseptic or chronic meningitis. Viruses—particularly enterovirus—are the most common infectious cause of chronic meningitis; however, it can also be seen in Lyme disease, tuberculosis, and cryptococcosis. Autoimmune diseases, such as rheumatoid arthritis, lupus, and sarcoidosis, are also possible. The leptomeningeal enhancement seen on MRI can be found in cases of acute disseminated encephalomyelitis (ADEM) and other demyelinating syndromes. Neoplastic meningitis—either related to solid cancer metastasis, lymphoma, or leukemia—and drug-induced aseptic meningitis are also possible but are less likely given this patient's imaging results and history.

MOGAD is an acquired neuro-inflammatory demyelinating syndrome that causes inflammation in the brain, spinal cord, and optic nerve. MOGAD includes features of neuromyelitis optica (NMO), multiple sclerosis, optic neuritis, and ADEM.[1,2] The clinical and radiographic findings can vary among patients and overlap with several of the demyelinating conditions, which can make diagnosis challenging.[2] Typical signs and symptoms can include altered mental status, unilateral or bilateral visual disturbance, extremity weakness or paralysis, loss of sensation, bowel or bladder dysfunction, and seizures. MOGAD can also rarely present as aseptic meningitis, which was first reported in 2019 and has since been cited in a handful of pediatric case reports, as

well as prolonged fever of unknown origin.[1,3] MRI findings can be similar to patients with multiple sclerosis or non-MOGAD, NMO-spectrum disease, and ADEM. Typical CSF findings include pleocytosis (50% of patients), elevated protein (50% of patients), and absent oligoclonal bands (90% of patients).[4-6] MOG is a protein located on the surface of myelin sheaths in the central nervous system. Positive serum antibodies to MOG are a serum biomarker that is specific for MOGAD especially at high titers.[1] It is also recognized that NMDA receptor antibodies may also be positive in some patients with MOG antibodies; therefore anti-NMDA receptor encephalitis should be considered if clinically correlated.[7] ADEM is the most common initial pediatric presentation of MOGAD, occurring in up to almost 70% percent of all MOG-positive cases.[8] Children account for up to 50% percent of reported MOGAD cases with no sex predilection. In adults, the median age of onset is 20 to 30 years of age. Approximately 40% to 50% of individuals may have a relapsing course.[9-11]

Treatment/Management

The standard of care for acute attacks of MOGAD is a 5-day course of high-dose IV steroids, and in most cases the condition is responsive to therapy. A slow oral steroid taper is also recommended in some instances to reduce the risk of relapse.[10,12] Further treatment depends on clinical response and repeat MRI findings. Second line agents include IV immunoglobulin and plasma exchange, as well as immunosuppressants or immunomodulators for severe or refractory cases.[13,14]

CONCLUSIONS

MOGAD is a neuroinflammatory disorder that typically leads to CNS demyelination. In addition to common presentations like ADEM, optic neuritis, and transverse myelitis, MOGAD can also present as a meningitis mimic. These rare cases present initially with headaches, fever, and meningismus, CSF pleocytosis and leptomeningeal enhancement on imaging, then progress to have typical demyelinating lesions if left untreated. Recognition of atypical MOGAD presentations is important in order to provide timely treatment.

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