Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

Pediatric myelin oligodendrocyte antibody-associated disease presenting as eosinophilic meningoencephalitis: a diagnostic challenge

Vivien X. Xie Cherng

vivien.xie217@gmail.com

Children's National

Molly Moehlman

Cincinnati Children's Hospital Medical Center

Ilyse Genser

Children's National

Laura Tochen

Children's National

Ilana L. Kahn

Children's National

Alexandra B. Kornbluh

Children's National

Case Report

Keywords:

Posted Date: July 29th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-10195465/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License

Additional Declarations: No competing interests reported.

Abstract

Background

Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) is a neuroinflammatory disorder of the central nervous system that can present with a cerebrospinal fluid (CSF) pleocytosis. Eosinophils in the CSF are uncommonly identified in MOGAD and true eosinophilia of > 10 eosinophils/μL or > 10% of CSF leukocyte composition has not been previously reported.

Case Presentation:

We describe the case of a 4-year-old male who initially presented with headache and fever followed by a seizure one week later. Initial evaluations were suggestive of meningoencephalitis due to leptomeningeal enhancement on magnetic resonance imaging (MRI) and pleocytosis on CSF analysis. He subsequently developed encephalopathy and right leg weakness two weeks later. Repeat MRI demonstrated lesions in the basal ganglia and a longitudinally extensive thoracic spinal cord lesion. CSF analysis was significant for pleocytosis with 18% eosinophils. Comprehensive infectious workup initiated due to concern for a possible parasitic infection returned negative. He was presumptively treated for a neuroinflammatory disorder with pulse intravenous corticosteroids and intravenous immunoglobulin and returned to his neurologic baseline. Subsequent testing revealed positive serum MOG antibodies (titer 1:100), confirming a diagnosis of MOGAD with an acute disseminated encephalomyelitis (ADEM) core clinical event type.

Conclusions

This case demonstrates that MOGAD can present as true eosinophilic meningoencephalitis, expanding the recognized laboratory spectrum of the disorder. Clinicians should consider demyelinating etiologies like MOGAD in the differential diagnosis of CSF eosinophilia, particularly when infectious and neoplastic evaluations are negative. Identifying these atypical presentations is critical for the prompt initiation of appropriate immunotherapy.

Background

Eosinophilic meningoencephalitis, characterized as having > 10 eosinophils/μL or > 10% of cerebrospinal fluid (CSF) leukocyte composition [1, 2], represents a rare presentation of central nervous system (CNS) inflammation. CSF eosinophils necessitate careful evaluation of a broad differential diagnosis to establish appropriate treatment [3]. While parasitic infections and neoplastic etiologies are the most common triggers, eosinophils can also be present in the CSF during acute attacks of demyelinating conditions. We present a unique case of a 4-year-old male with who presented with an acute attack of

MOGAD with 18% CSF eosinophilia, highlighting key diagnostic challenges associated with its broad differential diagnosis and need for multidisciplinary evaluation.

Case Presentation

A 4-year-old male with a history of expressive speech delay presented to the emergency department with one week of severe headache and twenty-four hours of nausea and fever (Fig. 1). He had a diarrheal illness three weeks prior to presentation. Initial bloodwork obtained by his pediatrician was significant for a serum white blood cell count (WBC) of 22 cells/μL (cell differential not checked) and an erythrocyte sedimentation rate (ESR) of 15 mm/hr. In the emergency department, computed tomography of the head was normal. Repeat serum testing demonstrated WBC of 11 cells/μL with differential including 3.1% eosinophils. A lumbar puncture (LP) was performed showing mild pleocytosis (Table 1) with normal CSF glucose and protein. He was admitted for observation in the setting of presumed viral meningitis. His CSF culture remained without growth for twenty-four hours with resolution of fevers and headaches, and he was discharged home.

He returned to the emergency department two days later (Fig. 1) with concern for seizures followed by persistent encephalopathy. In the emergency department he had a focal seizure which resolved with lorazepam and a levetiracetam load. Repeat computed tomography of the head was normal, and a repeat LP was attempted with only sufficient CSF collected to test a viral meningoencephalitis panel, which returned negative. An electroencephalogram showed mild background slowing but no epileptiform discharges or ongoing seizures. Magnetic resonance imaging (MRI) brain with and without contrast demonstrated multifocal leptomeningeal enhancement with cortical and subcortical edema (Fig. 2A-C). After observation for thirty-six hours in the hospital, he had no further seizures and returned to his neurologic baseline. Serum myelin oligodendrocyte (MOG) and aquaporin-4 (AQP4) antibodies were sent but did not result due to inadequate sample quality.

Sixteen days later (Fig. 1), he returned to the hospital with recurrent headaches, two days of intermittent back pain, right leg weakness, and unsteady gait. His teachers in school also noted word finding difficulties. He had no bowel or bladder dysfunction. On examination, he had 4/5 strength in his right leg and a wide-based gait with hyperreflexia in his bilateral lower extremities (presence of suprapatellar reflexes, crossed adductors, and 2 beats of ankle clonus bilaterally).

Repeat MRI brain with and without contrast showed new T2/fluid attenuation inversion recovery (FLAIR) enhancing lesions in the basal ganglia with resolution of prior lesions (Fig. 2D-2F). An MRI of the spine showed a longitudinally extensive gray matter-predominant thoracic cord lesion and mild enhancement of the cauda equina nerve roots (Fig. 2G-2I). A repeat CBC demonstrated progressive peripheral eosinophilia (14%) and a repeat LP showed CSF pleocytosis with elevated eosinophils and histiocytes (Table 1). His elevated CSF and serum eosinophils raised concern for a possible parasitic infection. He had no significant exposure or travel history, and after an infectious disease consult, workup was

expanded to include stool ova and parasites, *Coccidioides immitis* IgM/IgG, and *Toxacara* and *Toxoplasma gondii* IgG/IgM which all returned negative.

CSF autoimmune encephalopathy panel (Mayo Clinic Laboratories) and oligoclonal bands were negative. CSF cytokines showed elevated interleukin-6 (639, normal < 63 pg/mL) and interleukin-8 (229, normal < 181 pg/mL). He was treated empirically for presumed neuroinflammatory encephalomyelitis with intravenous (IV) immunoglobulin 2g/kg. Once infectious studies returned negative, he received a five-day course of pulse IV methylprednisolone and subsequently returned to his neurologic baseline by his initial clinic follow-up visit twenty days later. Serum aquaporin-4 IgG returned negative, and serum MOG-IgG returned positive with a titer of 1:100, consistent with a diagnosis of MOGAD with acute disseminated encephalomyelitis (ADEM) core clinical event type.

Table 1
Laboratory Findings

	Admission #1	**Admission #2**	**Admission #3**
CSF			
Total WBC Count (cells/mm^3)	**35**	N/A	**28**
%Lymphocyte	67	N/A	37
%Neutrophils	8	N/A	0
%Eosinophils	6	N/A	**18**
%Monocyte	19	N/A	14
%Histiocytes	0	N/A	**15**
SERUM			
Total WBC Count (cells/mm^3)	11	10.2	11.8
%Lymphocyte	40	42	39
%Neutrophils	47.2	43	39
%Eosinophils	3.1	5.5	14
%Monocyte	8.5	7.4	5

Table 1. Summary of cerebrospinal fluid (CSF) and serum white blood cell (WBC) count with differential from all hospital admissions. Admission 2 CSF cell counts were not analyzed due to insufficient quantity other than negative meningitis/encephalitis polymerase chain reaction panel.

Magnetic resonance imaging (MRI) demonstrating dynamic central nervous system lesions across the patient's clinical course. During the second admission (1 week from initial presentation), axial T2-

weighted post-contrast brain MRI revealed leptomeningeal enhancement (arrows, A, B) and cortical and subcortical T2/fluid attenuated inversion recovery (FLAIR) hyperintensities (arrows, A, C). During the third admission (4 weeks from initial presentation), axial T2-weighted post-contrast brain MRI showed new lesions in the basal ganglia (arrows, D), one of which demonstrated linear enhancement (arrow, E), with interval resolution of the previously identified cortical and subcortical T2 hyperintensities (F). Spinal MRI demonstrated a longitudinally extensive thoracic gray matter lesion (arrows) on sagittal (G) and axial (H) T2-weighted sequences, along with mild cauda equina enhancement on axial T1-weighted post-contrast imaging (arrow, I).

Discussion

This is a unique case of pediatric MOGAD presenting as ADEM with initial fluctuating course associated with CSF eosinophilia. The laboratory findings in this case expand the recognized spectrum of laboratory abnormalities associated with MOGAD. The marked peripheral and CSF eosinophilia initially shifted diagnostic suspicion towards infectious etiologies and thus presented a diagnostic and therapeutic challenge. Recognizing that MOGAD can present with eosinophilic meningoencephalitis is crucial to initiating appropriate and timely immunotherapy.

Within the literature, CSF eosinophil positivity is infrequently identified in MOGAD and is typically found in lower percentages of total CSF WBC if present. In a cohort of 36 pediatric MOGAD patients, 12 (33%) had CSF eosinophils present, and 11/12 (92%) had a CSF eosinophil percentage of 4% or less [4]. Our patient expands on these prior reports by demonstrating that demyelinating disorders can rarely present with true eosinophilic meningoencephalitis, defined as > 10 eosinophils/μL or > 10% of CSF leukocyte composition [1, 2].

This laboratory finding creates significant diagnostic overlap with alternative pathologies, most commonly with parasitic infections with central nervous system (CNS) involvement and a smaller proportion attributed to neoplastic, other demyelinating, and iatrogenic etiologies [3, 5]. There is a preponderance of eosinophilic meningoencephalitis in helminthic parasitic infections as well as a large spectrum of non-parasitic infections [3, 6–8]. Because many infectious causes of eosinophilic meningoencephalitis are endemic to specific geographic regions, obtaining a detailed travel, environmental, and exposure history is essential to identify epidemiologic clues that may guide diagnostic evaluation. The patient described here had no identifiable environmental or epidemiologic risk factors to suggest an infectious etiology, and thorough parasitic screening tailored to his geographic region guided by infections disease consult was negative.

A variety of malignancies are also associated with eosinophilic meningoencephalitis, regardless of the primary cell lineage involved. This is documented in Hodgkin lymphoma [9, 10], CNS neoplasms [11], and myeloproliferative disorders [12]. Specifically in pediatric patients, acute lymphoblastic leukemia is associated with eosinophilic infiltration into the CSF and theorized to be a result of a cytokine-mediated inflammatory response [13]. Drugs and medical devices can also be associated with eosinophilic

meningitis due to an immune-mediated hypersensitivity reaction. Ibuprofen is the most frequent cause of drug-induced eosinophilic meningitis, although this may be more likely to occur in individuals with underlying autoimmune disorders [5, 14, 15]. Implantation of intracranial devices, such as ventriculostomy catheters, have also been followed by eosinophilic meningitis, either due to hypersensitivity to antibiotics impregnated in the device or the device material itself [3, 5, 16, 17].

Overall, the time course of this case argued against these alternative etiologies. Having complete resolution of symptoms and return to neurologic baseline in between admissions is inconsistent with the typically progressive nature of an untreated parasitic infection or malignancy. In contrast, MOGAD attacks have been shown to fluctuate during an acute event; this is acknowledged in diagnostic guidelines that MOGAD symptoms can be considered one index event if they occur within 30 days of initial symptoms [18].

Aligned with this case, CSF eosinophil positivity in demyelinating and other neuroinflammatory disorders is becoming increasingly recognized. This has been identified in small percentages of patients with aquaporin-4 antibody positive neuromyelitis optic spectrum disorder (NMOSD) and MOGAD, and much more rarely in multiple sclerosis (MS) [19–22]. Among these disorders, CNS eosinophils are most frequently observed in NMOSD, with their presence reported in 10% of a large adult cohort [19]. Compared to NMOSD, the role of eosinophils in MOGAD demyelinating pathology is less well understood. In MOGAD, CSF eosinophils have been reported in case reports[23, 24] and identified in 2.6–33% of MOGAD cohorts [4, 20, 21]. The presence of eosinophils has also been identified in autopsy analysis of cortical MOGAD lesions, although eosinophilic-rich infiltrates are more of an established pathological feature in NMOSD [25]. Further study of eosinophil presence in both disorders may help advance understanding of the pathogenic role eosinophils play in CNS demyelination and could reveal future potential therapeutic targets.

CSF composition during an acute MOGAD attack is generally variable, ranging from normal findings to a pleocytosis (> 5 white blood cells (WBC)/mm^3), typically with a lymphocytic or monocytic predominance [20, 21]. About half of MOGAD patients present with a CSF pleocytosis of < 50 WBC/mm^3, however pleocytosis has been shown to exceed 100 WBC/mm^3 in 6–10% of cohorts [20, 21, 26–28]. As the CSF composition of MOGAD patients is further studied in larger cohorts, the role of eosinophils as a CSF marker may provide further prognostic information regarding disease severity, relapse risk, and neurologic sequelae given their roles in mediating cell death and secondary effects on collateral CNS damage [29]. Additionally, our patient had histiocytes identified in the CSF later in the clinical course. Histiocytes, or tissue-resident macrophages, arise from monocytes and can represent nonspecific inflammation due to a variety of etiologies when reported within CSF analysis [30]. Histiocytes are not normally reported in CSF analysis of MOGAD patients but may have served as a proxy of active inflammation from demyelination in our case.

In conclusion, we present a unique case of ADEM due to MOGAD with an associated eosinophilic meningoencephalitis, which expands the growing clinical spectrum of MOGAD clinical and laboratory

phenotypes. If an eosinophilic meningoencephalitis is identified during initial diagnostic evaluation, careful consideration of demyelinating, infectious, neoplastic, and iatrogenic etiologies is required to inform prompt initiation of therapies.

Abbreviations

• **ADEM**
Acute disseminated encephalomyelitis
• **AQP4**
Aquaporin-4
• **CBC**
Complete blood count
• **CNS**
Central nervous system
• **CSF**
Cerebrospinal fluid
• **FLAIR**
Fluid attenuation inversion recovery
• **IVIg**
Intravenous immunoglobulin
• **LP**
Lumbar puncture
• **MOGAD**
Myelin oligodendrocyte glycoprotein antibody-associated disease
• **MRI**
Magnetic resonance imaging
• **MS**
Multiple sclerosis
• **NMOSD**
Neuromyelitis optica spectrum disorder

Declarations

Ethics approval and consent to participate:

The authors' institution does not require ethical approval for the publication of a single case report. Written informed consent to participate was obtained from the patient’s parents.

Consent for publication:

Written informed consent for publication of clinical details and accompanying images was obtained from the patient's parents. A copy of the signed consent form is available for review by the Editor of this

journal.

Availability of data and materials:

Not applicable.

Competing interests:

The authors declare that they have no competing interests

Funding

This work was completed with philanthropic support from the Global Autoimmune Institute.

Authors' contributions:

VXC, **MM**, and **IG** drafted the manuscript. **LT** and **ILK** critically reviewed and revised the manuscript for intellectual content. **ABK** supervised the case report and reviewed and edited the manuscript. All authors read and approved the final manuscript.

Acknowledgements:

Not applicable

References

1. Höftberger R, Guo Y, Flanagan EP, et al. The pathology of central nervous system inflammatory demyelinating disease accompanying myelin oligodendrocyte glycoprotein autoantibody. Acta Neuropathol. 2020;139:875–92.
2. Kuberski T. Eosinophils in cerebrospinal fluid: criteria for eosinophilic meningitis. Hawaii Med J. 1981;40:97–8.
3. Graeff-Teixeira C, da Silva ACA, Yoshimura K. Update on eosinophilic meningoencephalitis and its clinical relevance. Clin Microbiol Rev. 2009;22:322–48. Table of Contents.
4. Jarius S, Lechner C, Wendel EM, et al. Cerebrospinal fluid findings in patients with myelin oligodendrocyte glycoprotein (MOG) antibodies. Part 2: Results from 108 lumbar punctures in 80 pediatric patients. J Neuroinflammation. 2020;17:262.
5. Kornbluh AB, Campano VM, Har C, et al. Cerebrospinal fluid eosinophils in pediatric myelin oligodendrocyte glycoprotein antibody-associated disease. Mult Scler Relat Disord. 2024;85:105526.
6. Lo Re V, Gluckman SJ. Eosinophilic meningitis. Am J Med. 2003;114:217–23.
7. Taylor MG, Ankar A, Meoded A, Jarjour IT, Risen S, McNeil JC. Eosinophilic Meningitis: Eleven-Year Experience at Texas Children's Hospital. J Pediatr. 2022;251:202–e2081.

8. Park S, Jung J, Chong YP, et al. Infectious Causes of Eosinophilic Meningitis in Korean Patients: A Single-Institution Retrospective Chart Review from 2004 to 2018. Korean J Parasitol. 2021;59:227–33.
9. Vinayan KP, Dudipala SC, Roy AG, Anand V. Clinical Characteristics and Treatment Outcome of Eosinophilic Meningoencephalitis in South Indian Children: Experience From a Prospective Registry. Pediatr Neurol. 2023;147:9–13.
10. Patchell R, Perry MC. Eosinophilic meningitis in Hodgkin disease. Neurology. 1981;31:887–8.
11. Hollister D, Clements M, Coleman M, Petito F. Eosinophilic meningitis in Hodgkin's disease. Report of a case and review of the literature. Arch Intern Med. 1983;143:590–2.
12. Defendini R, Hunter SB, Schlesinger EB, Leifer E, Rowland LP. Eosinophilic meningitis in a case of disseminated glioblastoma. Arch Neurol. 1981;38:52–3.
13. Jaffe JP, Loprinzi CL. Basophilic-eosinophilic meningitis in an undifferentiated myeloproliferative disorder. JAMA. 1983;249:73–4.
14. Fasipe F, Bestak M, Green NS. Recurrent central nervous system acute lymphoblastic leukemia associated with cerebrospinal fluid eosinophilia and basophilia: a proposed cytokine-mediated mechanism. Pediatr Hematol Oncol. 2003;20:31–7.
15. Quinn JP, Weinstein RA, Caplan LR. Eosinophilic meningitis and ibuprofen therapy. Neurology. 1984;34:108–108.
16. Bansal S, Gupta M, Sharma D, Bansal S. A rare case of Ibuprofen-induced eosinophilic meningitis in a 13-year-old girl. Clin Med Insights Pediatr. 2014;8:3–4.
17. Saito K, Yamasaki K, Yokogami K, et al. Eosinophilic meningitis triggered by implanted Gliadel wafers: case report. J Neurosurg. 2017;126:1783–7.
18. Bell RS, Vo AH, Cooper PB, Schmitt CL, Rosner MK. Eosinophilic meningitis after implantation of a rifampin and minocycline-impregnated ventriculostomy catheter in a child. Case report. J Neurosurg. 2006;104:50–4.
19. Banwell B, Bennett JL, Marignier R, et al. Diagnosis of myelin oligodendrocyte glycoprotein antibody-associated disease: International MOGAD Panel proposed criteria. Lancet Neurol. 2023;22:268–82.
20. Jarius S, Paul F, Franciotta D, et al. Cerebrospinal fluid findings in aquaporin-4 antibody positive neuromyelitis optica: results from 211 lumbar punctures. J Neurol Sci. 2011;306:82–90.
21. Jarius S, Pellkofer H, Siebert N, et al. Cerebrospinal fluid findings in patients with myelin oligodendrocyte glycoprotein (MOG) antibodies. Part 1: Results from 163 lumbar punctures in 100 adult patients. J Neuroinflammation. 2020;17:261.
22. Li Z, Liu Y, Jia A, Cui Y, Feng J. Cerebrospinal fluid cells immune landscape in multiple sclerosis. J Transl Med. 2021;19:125.
23. Ataka T, Kimura N, Matsubara E. A case of myelin oligodendrocyte glycoprotein-antibody-associated disease presenting with tumefactive demyelinating lesion. Mult Scler Relat Disord. 2020;43:102191.

24. Narayan RN, Wang C, Sguigna P, Husari K, Greenberg B. Atypical Anti-MOG syndrome with aseptic meningoencephalitis and pseudotumor cerebri-like presentations. Mult Scler Relat Disord. 2019;27:30–3.
25. Fadda G, Armangue T, Hacohen Y, Chitnis T, Banwell B. Paediatric multiple sclerosis and antibody-associated demyelination: clinical, imaging, and biological considerations for diagnosis and care. Lancet Neurol. 2021;20:136–49.
26. Cobo-Calvo A, Ruiz A, Maillart E et al. Clinical spectrum and prognostic value of CNS MOG autoimmunity in adults. Neurology. 2018;90.
27. Jurynczyk M, Messina S, Woodhall MR, et al. Clinical presentation and prognosis in MOG-antibody disease: a UK study. Brain. 2017;140:3128–38.
28. Sechi E, Buciuc M, Flanagan EP, et al. Variability of cerebrospinal fluid findings by attack phenotype in myelin oligodendrocyte glycoprotein-IgG-associated disorder. Mult Scler Relat Disord. 2021;47:102638.
29. Zhang H, Verkman AS. Eosinophil pathogenicity mechanisms and therapeutics in neuromyelitis optica. J Clin Invest. 2013;123:2306–16.
30. Ali SZ, Cibas ES. Serous Cavity Fluid and Cerebrospinal Fluid Cytopathology. Boston, MA: Springer US; 2012.

Figures

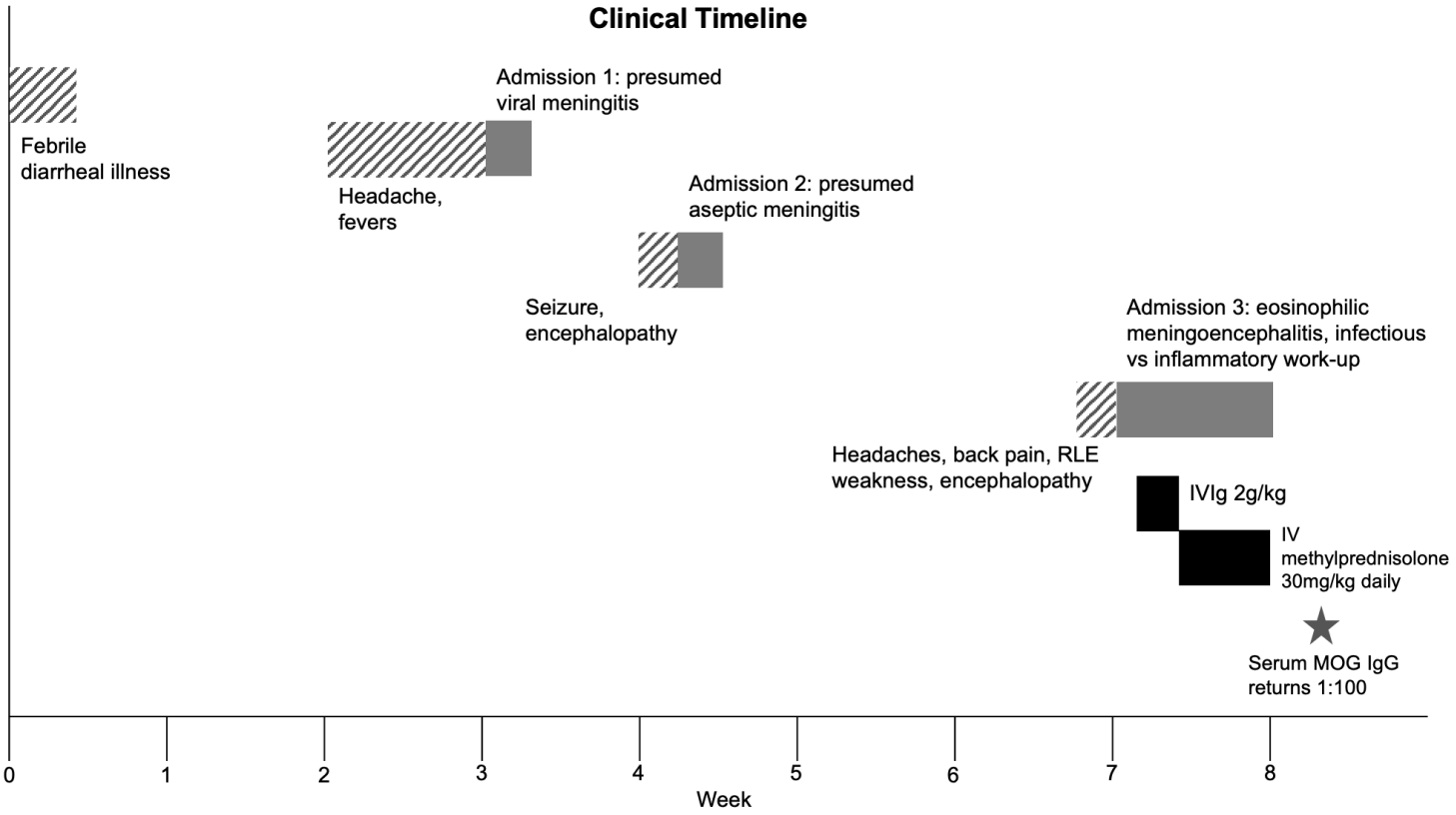


Figure 1

Graphical depiction of timeline of clinical symptoms, admission courses, and treatment. Dashed lines represent preceding symptoms, grey boxes represent hospital admissions, black boxes represent immunotherapy, and star represents diagnostic results.

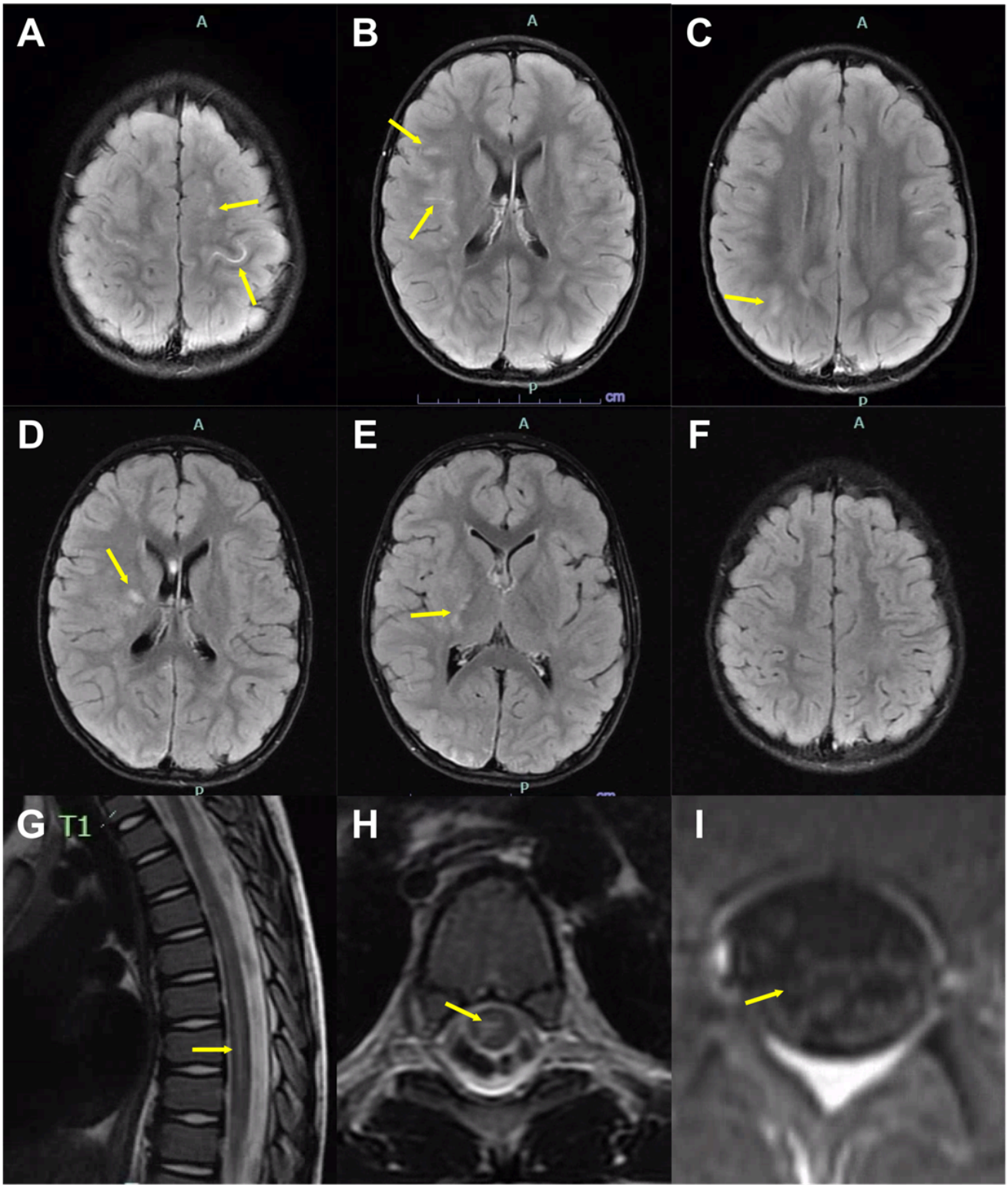


Figure 2

MRI findings in the brain and spine