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Case Report

Extensive brainstem lesions in myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD): A case report ☆,☆☆

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ABSTRACT

Myelin oligodendrocyte glycoprotein antibody-associated disease is a group of central nervous system demyelinating disorders caused by autoantibodies. While myelin oligodendrocyte glycoprotein antibody-associated disease typically presents as optic neuritis and myelitis in adults, this case report details a patient with brainstem lesions. A 45-year-old male presented with episodes of vertigo, nystagmus, and diplopia in left lateral gaze, which had persisted for 2 months, accompanied by headache. Computed tomography showed hyperdensity extending from the left side of the pons to the middle cerebellar peduncle. Magnetic resonance imaging revealed lesions exhibiting heterogeneous diffusion restriction, with enhancement that included granular and linear patterns. ^{18}F-fluorodeoxyglucose positron emission tomography demonstrated increased uptake in these lesions. Following further evaluation, myelin oligodendrocyte glycoprotein antibody-associated disease was diagnosed. Treatment with high-dose corticosteroids initially alleviated symptoms, but symptoms flared upon reduction of the steroids. This case underscores the importance of considering myelin oligodendrocyte glycoprotein antibody-associated disease in the differential diagnosis of brainstem lesions and discusses distinguishing imaging features from similar conditions.

Abbreviations: MOG, myelin oligodendrocyte glycoprotein; MOGAD, myelin oligodendrocyte glycoprotein antibody-associated disease; CNS, central nervous system; ADEM, acute demyelinating encephalomyelitis; CSF, Cerebrospinal fluid; CLIPPERS, chronic lymphocytic inflammation with pontine perivascular enhancement responsive to steroids; H&E, hematoxylin and eosin; IVMP, intravenous methylprednisolone; ^{18}F-FDG PET, ^{18}F-fluorodeoxyglucose positron emission tomography.

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Introduction

Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) is a group of central nervous system (CNS) demyelinating disorders caused by autoantibodies against myelin oligodendrocyte glycoprotein (MOG), affecting the optic nerves, brain, and spinal cord [1]. There is no difference in prevalence between males and females, and it can potentially affect individuals of any age [2]. The typical symptoms of MOGAD vary by age. In children, it often presents as acute disseminated encephalomyelitis (ADEM) with disturbances of consciousness and behavioral changes, frequently following a monophasic course. When measured by the CBA method, the specificity of serum MOG antibodies in pediatric inflammatory demyelinating diseases is close to 100%, with about 40%-70% of cases diagnosed as pediatric ADEM being positive for MOG antibodies [3]. On the other hand, in adults, symptoms similar to ADEM are seen in only about 5% of cases, with optic neuritis and myelitis being more common [4–8]. Additionally, adults often experience recurrent episodes, with monophasic courses being less common. Involvement of the brainstem and cerebellum has been reported in up to 34% of MOGAD patients, typically occurring as part of multifocal central nervous system manifestations, with isolated brainstem and cerebellar presentations being rare [9,10]. This case report details an instance of MOGAD with brainstem lesions, highlighting the importance of early diagnosis and treatment to enhance clinical awareness.

Case presentation

A 45-year-old male presented with episodes of vertigo, nystagmus, and diplopia in left lateral gaze, which had persisted for 2 months, accompanied by headache. His medical and family histories were unremarkable. Neurological examination revealed clumsiness in the left upper limb, but no other significant abnormalities were observed. CT images revealed a hyperdense area extending from the left side of the pons to the middle cerebellar peduncle (Fig. 1). In MRI, this region exhibited heterogeneous diffusion restriction (minimum ADC value: 0.71×10^{-3} mm^2/s) and enhancement, including linear and granular patterns, accompanied by extensive hyperintensity on FLAIR (Fig. 2). Additionally, slight granular enhancement was observed adjacent to the lateral ventricles, but no abnormal findings were observed in the spinal cord or optic nerve. 18F-fluorodeoxyglucose positron emission tomography (^{18}F-FDG PET), performed with lymphoma as a differential consideration, demonstrated increased uptake (SUVmax: 14.5) in these areas (Fig. 3). Antinuclear antibodies, antineutrophil cytoplasmic antibodies, and antibodies against dsDNA, SS-A, SS-B, sIL-2, GAD, TPO, and thyroglobulin were all negative. Cerebrospinal fluid (CSF) analysis showed an elevated cell count (22 cells/mm^3), a mild increase in protein (52 mg/dL), and normal glucose levels. Oligoclonal bands were not detected. CSF cytology did not reveal any malignant cells.

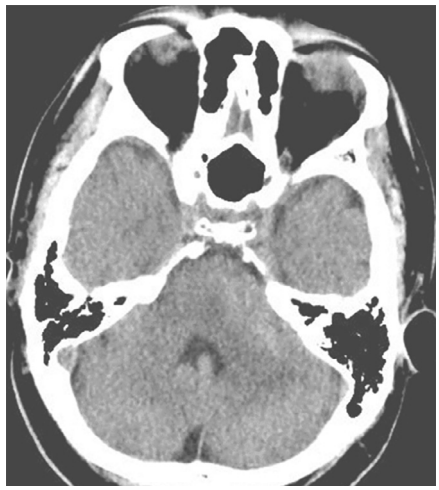

Fig. 1 – Brain CT images of a patient at the onset of the disease show an area on the left side of the pons extending to the left middle cerebellar peduncle that exhibits hyperdensity compared to the cortical gray matter. A slightly hypodense lesion is observed surrounding it, which is thought to reflect edema.

Imaging considered chronic lymphocytic inflammation with pontine perivascular enhancement responsive to steroids (CLIPPERS) due to the granular enhancement pattern primarily involving the pons. The fact that part of the lesion showed hyperdensity on CT, which is atypical for inflammatory or demyelinating diseases, and the same region showed enhancement on MRI, meant that the possibility of primary CNS lymphoma could not be ruled out, so a biopsy was performed on the lesion in the left middle cerebellar peduncle. Histopathology is shown in Fig. 4. Hematoxylin and eosin (H&E) staining revealed clusters of small lymphocytes, histiocytes, and plasma cells predominantly around blood vessels, with occasional hemorrhages, and no findings specific to malignant lymphoma were detected. Immunohistochemistry showed lymphocytic infiltration around blood vessels, including CD20-positive B cells and CD4-positive T cells. Klüver-Barrera staining identified demyelination patches and partial axonal loss corresponding to areas with significant inflammatory cell infiltration.

Subsequently, serum MOG-IgG was detected using a live cell-based assay. Serum aquaporin-4 antibody was negative. Based on clinical findings, positive MOG antibody results, and radiological evidence, a diagnosis of MOGAD was made [9]. Three courses of high-dose intravenous methylprednisolone (IVMP) (1 g for 3 days) followed by oral prednisolone (up to 30 mg) were administered, resulting in symptom relief and resolution of the enhancing brain lesions observed on MRI. Subsequent tapering of oral prednisolone led to a recurrence of symptoms, and the latest MRI showed expansion of the FLAIR hyperintense areas in the left side of the pons and left middle cerebellar peduncle, suggesting a relapse.

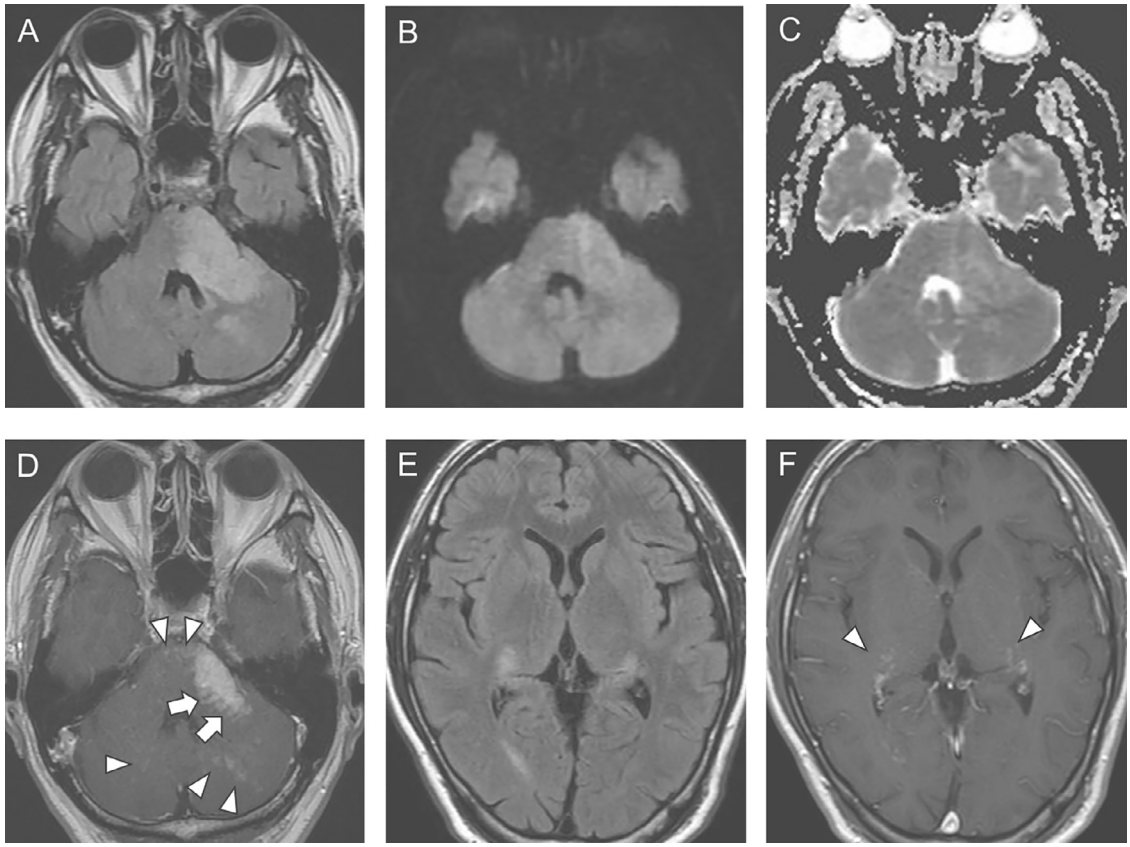

Fig. 2 – Brain MRI of a patient at disease onset (A-F). FLAIR image (A) reveals hyperintense lesions located from the pons to the left middle cerebellar peduncle, and parts of the left cerebellar hemisphere. Diffusion-weighted imaging (b = 1000 s/mm^2) (B) and apparent diffusion coefficient (ADC; C) demonstrate heterogeneous diffusion restriction of the lesion, with the minimum ADC of 0.71 x 10^{-3}mm^2/s. Contrast-enhanced T1-weighted image (D) shows enhancement of the lesion, accompanied by linear enhancement that appears to be located in the perivascular spaces (arrow), as well as granular enhancement observed in the pons and bilateral cerebellar hemispheres (arrowheads). FLAIR image (E) also shows hyperintense areas adjacent to the lateral ventricles, with granular enhancement similar to the lesions in the pons (F: arrowheads).

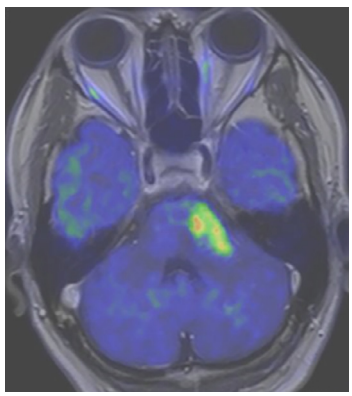

Fig. 3 – Axial ^{18}F-FDG PET/MRI fused image confirm focal ^{18}F-FDG uptake from the left side of the pons extending to the left middle cerebellar peduncle, with SUVmax of 14.5.

Discussion

Isolated brainstem and cerebellar episodes are rare in MOGAD patients, typically occurring as part of multifocal central nervous system manifestations. Approximately 60% of patients with brainstem lesions exhibit symptoms such as ataxia, diplopia, nausea, vomiting, cranial nerve palsies, or vertigo [9]. In this case, symptoms such as diplopia and vertigo were observed and brainstem lesions were identified on imaging, but there were no findings indicative of either optic neuritis or myelitis.

A few cases of MOGAD, primarily localized to the pons and showing multiple granular enhancement, have been reported as mimicking CLIPPERS [11–13]. CLIPPERS, an inflammatory central nervous system disorder first proposed by Pittock et al. [14] in 2010, primarily presents with subacute symptoms such as diplopia, ataxia, and dysarthria. MRI features include punctate and nodular enhancement predominantly in the pons, middle cerebellar peduncles, and cerebellum. However, sim-

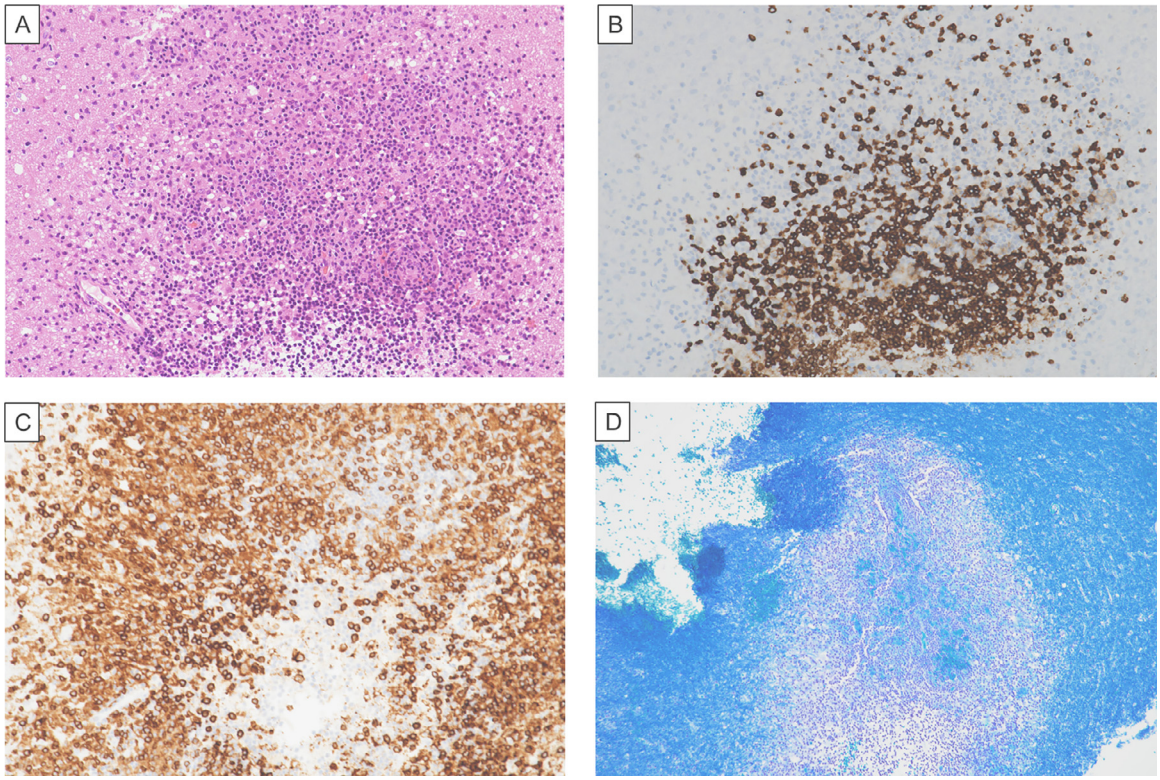

Fig. 4 – Hematoxylin and eosin (H&E) staining (A; low magnification) revealed clusters of small lymphocytes, histiocytes, and plasma cells predominantly surrounding blood vessels, with occasional hemorrhages observed. Immunostaining identified numerous B cells, primarily CD20-positive among others (B), and a significant presence of T cells around the vessels. It also showed that CD4-positive T cells (C) were more prevalent than CD8-positive T cells. No findings indicative of malignant lymphoma were detected. Klüver-Barrera staining (D) revealed demyelination patches corresponding to areas with significant inflammatory cell infiltration, and partial axonal loss was also noted.

ilar findings can also be seen in other diseases, underscoring the importance of considering differential diagnosis [15]. In 2017, Tobin et al. reported several clinical and radiological features that distinguish CLIPPERS from its mimics [15,16]. Brain biopsy is recommended when (a) gadolinium-enhancing lesions are unilateral, or (b) the lesions are large (>3 mm) [17]. In this case, granular contrast enhancement in the pons and cerebellar hemispheres suggested CLIPPERS, but the unilateral and extensive nature of the enhancement led to the consideration of other diseases that mimic CLIPPERS. Previous reports have indicated that MOGAD mimicking CLIPPERS often presents with asymmetric distribution, in contrast to the more symmetric distribution typically seen in CLIPPERS, serving as a distinguishing feature [11,18]. There are few reports of other demyelinating diseases such as multiple sclerosis (MS), neuromyelitis optica spectrum disorder (NMOSD), or ADEM mimicking CLIPPERS.

There are few reported cases of CT and 18F-FDG PET imaging findings in associated with MOGAD. In this case, the lesions exhibited hyperdensity on CT compared to the cortical gray matter, making it crucial to differentiate from lymphoma [19]. Additionally, this case showed linear enhancement, thought to be perivascular spaces, similar to those observed in lymphoma, complicating their differentiation [20]. Pathological features of MOGAD include demyelination and reactive gliosis, along with infiltration by predominantly CD4-positive T cells and granulocytes. The increase in inflammatory cells may explain the observed hyperdensity on CT [2]. The ADC values in lymphoma are typically between 0.40 and 0.60 $\times$ 10^{-3} mm^2/s [19], and the minimum ADC value in this case was 0.71 $\times$ 10^{-3} mm^2/s, suggesting that differences in ADC values may be a point of distinction between MOGAD and lymphoma on imaging. However, another study on lymphoma's ADC values has reported mean ADC 0.73 $\pm$ 0.13 (0.57-1.04) and min ADC 0.57 $\pm$ 0.12 (0.40-0.82), indicating that the cases in this study cannot rule out malignant lymphoma based solely on ADC values [21]. Additionally, the same region showed increased uptake on ^{18}F-FDG-PET, suggesting that MOGAD may involve heightened glucose uptake due to inflammation. However, caution is necessary as increased uptake is also observed in conditions such as CLIPPERS and lymphoma [22,23].

Treatment for acute MOGAD includes corticosteroids, intravenous immunoglobulins, or plasma exchange. For patients with a high risk of relapse, long-term immunomodulatory therapy may involve intravenous immunoglobulins, rituximab, azathioprine, or mycophenolate mofetil [4,24,25]. Approximately 40% to 50% of MOGAD patients exhibit a monophasic course, with MRI of the brain and/or spinal cord returning completely to normal [2]. This represents a signifi-

cant distinction from NMOSD and MS, where complete resolution of lesions is exceedingly rare. Meanwhile, 50% to 60% of cases experience a relapse of the disease [2]. In the current case, the patient responded well to IVMP and steroid treatment, but symptoms flared and lesion enlargement was observed on imaging following steroid tapering. Careful monitoring with gradual reduction of steroids is necessary to prevent relapses in MOGAD, but the duration of immunotherapy to prevent episodes and recurrence is not clearly defined and requires further study.

Conclusion

This case report highlights the significance of considering MOGAD in the differential diagnosis when enhanced lesions similar to those seen in CLIPPERS or lymphoma are observed in the brainstem. MOGAD can exhibit hyperdensity on CT and increased uptake on ^{18}F-FDG-PET, which are characteristics also common in lymphoma. Since MOGAD can occur with isolated brainstem lesions without accompanying optic neuritis or myelitis, it is crucial to consider MOGAD as a diagnostic option when such imaging findings are present in the brainstem, to facilitate early diagnosis and treatment.

Compliance with ethical standards

Guarantor

The scientific guarantor of this publication is Yasuyuki Kojita.

Statistics and biometry

No complex statistical methods were necessary for this paper.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Declaration of generative AI and AI-assisted technologies in the writing process

During the preparation of this work the authors used ChatGPT (https://openai.com/chatgpt) in order to improve readability and language. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

Patient consent

Written, informed consent was obtained from the patient for publication of this case.

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