Advances in Ophthalmology Practice and Research 1 (2021) 100025

Contents lists available at ScienceDirect

Advances in Ophthalmology Practice and Research

journal homepage: www.journals.elsevier.com/advances-in-ophthalmology-practice-and-research

Case Report

Myelin oligodendrocyte glycoprotein antibody-associated disease following DTaP vaccination: A case report

Xin Zhang

Department of Ophthalmology, The First Affiliated Hospital of Zhejiang Chinese Medical University (Zhejiang Provincial Hospital of Traditional Chinese Medicine), Hangzhou, China

Lessons

The discovery of MOG antibody (MOG-Ab) remarkably refined our thinking about inflammatory demyelinating disorders of the CNS. It is obvious that they comprise a diverse range disease spectrum. The research of MOGAD, which has rapidly advanced clinical and pathological in recent years, is a proof of that MOGAD represent a distinct disease entity different from other neuroinflammatory and demyelinating diseases, such as multiple sclerosis (MS) or aquaporin-4 (AQP4) IgG-positive neuromyelitis optica spectrum disorder (NMOSD).

1. Background

Unlike aquaporin-4(AQP4) which is an astrocytic protein1, myelin oligodendrocyte glycoprotein (MOG) is a mydlin protein exclusively expressed at the outer surface of the myelin sheath and oligodendrocyte membranes in the central nervous system(CNS).[2] Thus, immune-medicated attacks against MOG appear to be more demyelinating compared with AQP4 neuromyelitis optica spectrum disorder (NMOSD).[1] Optic neuritis (ON)is the most frequent clinical presentation in the positive result of MOG Immunoglobulin (Ig)G test.[3] When MOG antibody disease involves the brain, the phenotype is similar to acute disseminated encephalomyelitis (ADEM). It usually, affects pediatric population and most cases occur 1–2 weeks after a viral or bacterial infection or, in rare cases, after a vaccination.[4–6] The case presents a study of a pediatric patient diagnoses with Myelin oligodendrocyte glycoprotein-antibody-associated disease (MOGAD) following a diphtheria and tetanus toxoids and acellular pertussis (DTaP) vaccination. I obtained written informed consent from the patient's parents, and subsequently used the collected data.

2. Case presentation

Medical history: A previously healthy 6-year-old female arrived at the emergency room 1 week after receiving a DPT vaccination. Following the DTaP vaccination, she developed a high-fever and complained of headache, weakness, and severe bilateral visual loss. During the week, her parents found that she had difficulty writing. The patient had a cold 3 days before the vaccination, although she had not experienced febrile illness, diarrhea, vomiting in the recent past. There was no family history suggestive of psychiatric illness or demyelinating disease.

Physical examination: Visual acuity was 20/200 and light perception in the right and left eye respective, ophthalmic examination revealed relative afferent papillary defect and swollen optic disc in the left eye, normal in the right eye (Fig. 1 A1∼A2). Binocular abduction movement was limited. A neurological examination revealed: that the patient was positive for Babinski sign bilaterally, and meningeal stimulation of the neck revealed resistance.

Laboratory findings: No obvious abnormalities were found in routine blood, liver, and kidney function tests, and the patient was positive for Serum Epstein-Barr viral capsid IgG. Examination of the cerebral spinal fluid (CSF) yielded the following results: pressure, 170mm H2O; white blood cell count, $42*10^6$/L; protein, 572.3 mg/L; glucose, 1.6mmol/L; immunoglobulin IgA, 0.675mg/dL; IgG, 6.83mg/dL; IgM,0.158mg/dL. The patient was administered a titer of serum anti-MOG-antibody (1:32). The detailed clinical examination, laboratory, and imaging results are presented shown in Table 1.

An examination of the magnetic resonance imaging (MRI) revealed multiple abnormal signal lesions in the subcortical white matter, frontal lobe, parietal lobe, temporal lobe, occipital lobe, basal ganglia and thalamus, as well as some space-occupying lesions. The lesions also involved optic nerve, optic nerve sheath, optic chiasma and peribulbar fat (Fig. 1B∼G).

Optic neuropathy and other vascular, infiltrative, compressive, toxic, hereditary, and metabolic causes were excluded, and etiological ocular diseases that may cause vision loss were ruled out.[7] In addition to infectious causes, autoimmune and paraneoplastic conditions should also be used as differential diagnosis of clinical manifestations of subacute encephalopathy or behavioral disorders.

After treatment with methylprednisolone (500mg for 3 days, 240mg for 3 days, 120mg for 3 days), the patient's symptoms were greatly relieved. Then She received prednisolone tablets 0.8 mg/kg. These doses were gradually reduced by 5 mg twice a week.

E-mail address: jangwoohyukhot@163.com.

https://doi.org/10.1016/j.aopr.2022.100025
Received 12 December 2021; Received in revised form 18 January 2022; Accepted 19 January 2022
Available online 27 January 2022

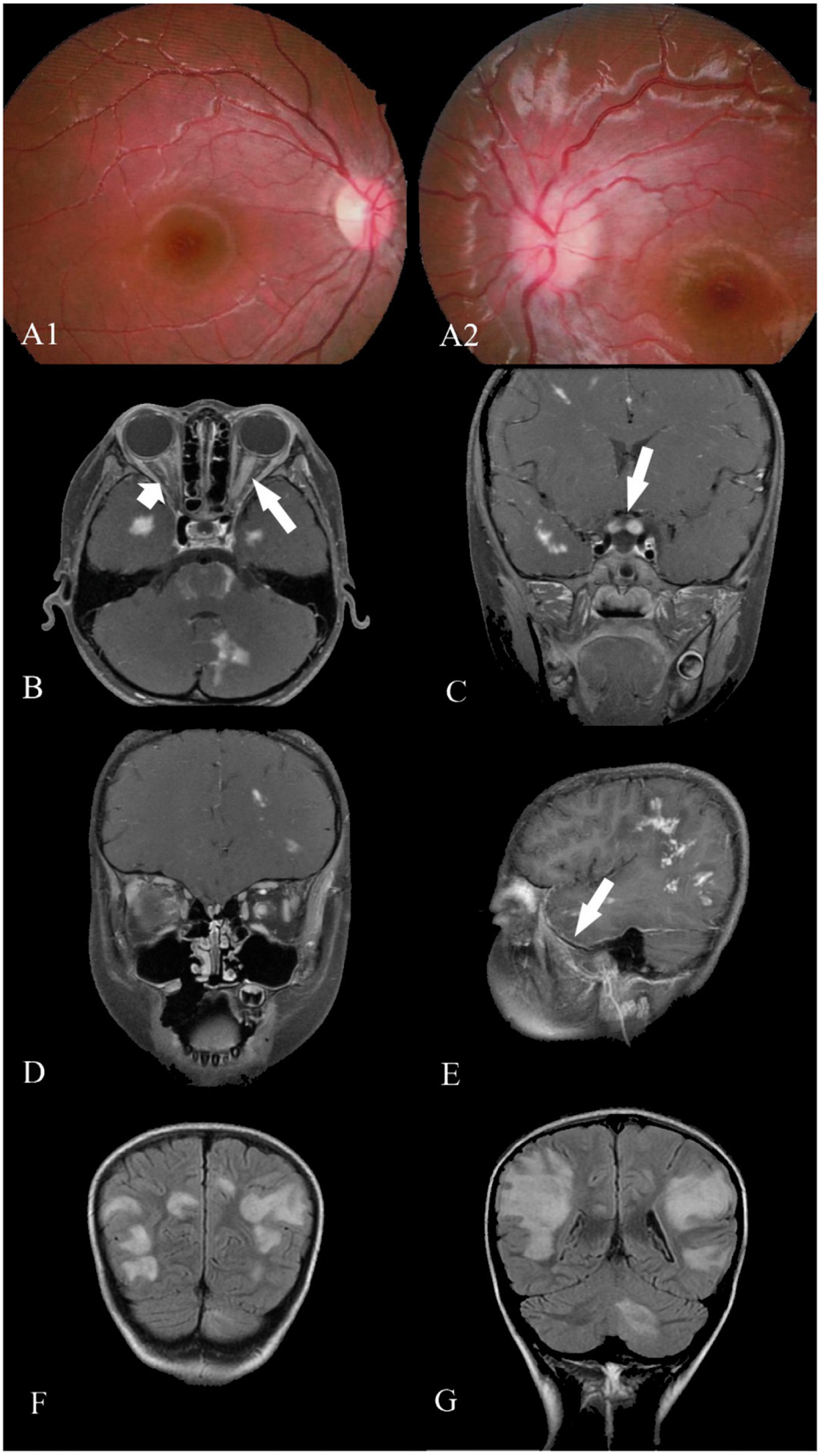

Fig. 1. Fundus pictures showed swollen optic disc in the left eye(A2) and normal optic disc in right eye(A1) at acute phase.
Orbital MRI images: B showed the enhancement of the right optic nerve sheath (arrow), the thickness and enhancement of the left optic nerve (Long arrow) in gadolinium-enhanced T1 at acute phase. C showed the thickness and enhancement of optic chiasma (Long arrow) in gadolinium-enhanced T1 at acute stage. D showed bilateral optic nerve enhancement that extends along the entire optic nerve and involves the optic nerve sheath and peribulbar fat.
Brain MRI images: E ~ G showed the multiple of abnormal signal lesions in subcortical structure, frontal lobe, parietal lobe, temporal lobe, occipital lobe, basal ganglia, thalamus and brainstem in different sequences. E showed the abnormal enhancement of lesions and dura mater (Long arrow) with gadolinium injection.

Table 1
Clinical, laboratory and MRI features of the patient associated MOG-antibody.

Clinical prodrome		1-week history of fever, headache, weakness, decreased vision in both the eyes
Encephalopathy		Yes
Presentation		Acute worsening of vision, behavioral change, cranial nerve sixth palsy
Physical examination		Visual acuity was 20/200 and light perception in the right and left eye respective, ophthalmic examination revealed relative afferent papillary defect and swollen optic disc in the left eye, normal in the right eye. Bilateral cranial nerve sixth nerve palsy. Babinski sign (+) bilaterally. Meningeal stimulation to neck resistance (+).
CSF	Pressure	170 mm H2O
	White blood cell	$42*10^6$/L
	Protein	↑ 572.3 mg/L
	Glucose	↑ 1.6 mmol/L
	immunoglobulin	↓ IgA:0.675 mg/dL, IgG:6.83 mg/dL, IgM:0.158 mg/dL
Anti-MOG antibody titer level at presentation (CBA)		↑ 1:32
Other antibodies	Anti-AQP4 antibody	Negative
	Anti-NMDA receptor antibody	Negative

MRI					
Brain			Orbit		
bilateral brain	+		Optic nerve	Orbital	+
				Tube	+ bilateral
				Sheath	+
Cerebellum	+		Optic chiasma		+
Basal ganglia	+				
Thalamus	+				
Brainstem	+				

Abbreviations.
CSF: cerebral spinal fluid.
MOG: myelin oligodendrocyte glycoprotein.
CBA: cell-based assay.
AQP4: aquaporin-4.
MRI: magnetic resonance imaging.
NMDA: N-methyl-D-aspartic acid.

At the patient's 1-month follow-up, her physical examination results were normal, her strength and deep tendon reflexes were normal, her vision gradually recovered, optic disc became pale (Fig. 2 A1∼A2) and a repeat brain MRI showed fewer signal abnormalities and no new lesions (Fig. 2 B ∼ E). Her best corrected visual acuity recovered to 20/30 and 20/40 in the right and left eye. Informing the parents of the patient that there is a possibility of recurrence of this type of disease, and immunosuppressive agents should be used if necessary. At her 3-month follow-up, her condition was stable.

3. Discussion and conclusions

A majority of NMOSD cases have been found positive for the anti-AQP4 antibody. It was later realized that some of these anti-AQP4-antibody-negative NMOSD cases were in fact serpositive for anti-MOG antibody. A recent study reported the annual incidence of MOG-antibody diseases as 1.6/million population (children:3.1/million).[8] Isolated ON is the most common symptom at onset (55%–61%) of which almost half are bilateral.[9] Fifty percent of these patients had a history of precede infection or vaccination before onset.[10] Although this case had a history of cold before vaccination, however, according to the parents' complaint, cold symptoms have improved.

Following a DTaP vaccination, the patient presented with the typical systemic symptoms of fever, malaise, headache, and severe bilateral visual loss, which may occur shortly before the onset of neurological symptoms and signs. The clinical course progresses rapidly and maximum deficits develop within a few days. An increased level of white blood cells and protein in the patient's CSF reflects the clinical severity. The trigger for anti-MOG antibody production is unknown, but the autoimmune induction is thought to occur in the peripheral immune system. Potential mechanisms for autoimmunity, either in isolation or in combination.[11] Maybe a DTaP vaccination induce immune response. None of the clinical and neuroimaging finding is highly specific for MOGAD. The golden standard method for experts is the cell-based assay with full length human MOG as target antigen.[11]

Typical MRI findings of ON in MOGAD long lesions in the anterior part of optic nerve with periorbital enhancement,[12] but the lesions also involved the optic chiasma in this case. Brain MRI abnormalities are most common in the T2-weighted and fluid attenuation inversion recovery sequence, which manifests as patchy, unclear areas with increased signal intensity.

Perineural oedema is another radiological finding in up to half of patients with MOGAD with optic neuritis.[13] These features with swelling of the optic nerve head on fundoscopy can help discriminate MOGAD from optic neuritis in AQP4-IgG-positive NMOSD and MS[11](Table 2).

The research of MOGAD, which has rapidly advanced in recent years, it is now recognized as an autonomous, antibody-mediated inflammatory demyelinating disorder with a variety of clinical manifestations.[11] These pathological features are clearly different from MS or AQP4 antibody positive NMOSD.[14] The clinical is relapsing in approximately 34%–80% of cases.[9,15] Other advanced imaging techniques may help differential diagnosis and assess the exact degree of the disease.[16,17] There is no standardized treatment approved for MOGAD, current treatment strategies including immunomodulatory therapies (especially corticosteroids and intravenous injection immunoglobulin), and plasmapheresis has been successfully applied.[4,18,19]

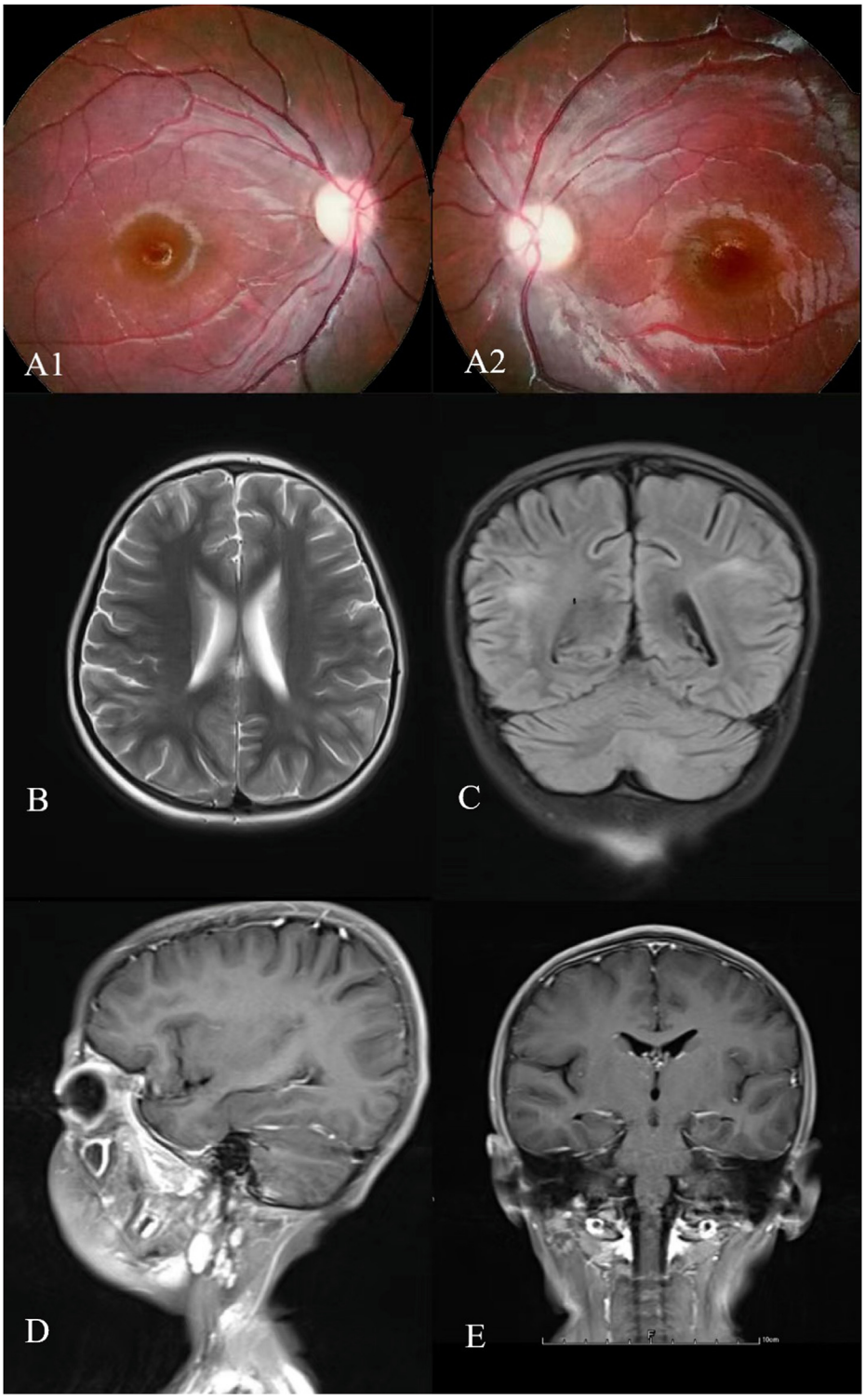

Fig. 2. Fundus pictures showed right (A1) and left (A2) optic disc pale. The repeat brain MRI images B ~ E showed subcortical structure, frontal lobe, parietal lobe, temporal lobe, occipital lobe, basal ganglia, thalamus and brainstem less signal abnormalities and no enhancement lesions in 1-month follow-up.

Table 2
Typical characteristics of optic neuritis in MOGAD compared with AQP4-IgG-positive NMOSD and MS.

Demographics and characteristics	MOGAD	AQP4-NMOSD	MS
Approx age at onset[20]	30's + children	40's	20's
Female: male[21]	1.3:1	9:1	3:1
Optic neuritis characteristics[20]			
Bilateral ON	Frequent	Frequent	Infrequent
Severe vision loss	Very frequent	Very frequent	Frequent
Risk of recurrent ON	Very frequent	Very frequent	Frequent
Steroid dependent	Frequent	Rare	Rare
Risk of blindness (<20/200)	Infrequent	Very frequent	Frequent
MRI optic nerve enhancement[19,20]			
Length and location	Long and anterior	Long and posterior	short
Perineural enhancement	Frequent	Rare	Rare
Optic chiasm involvement	Infrequent	Frequent	Rare

Study Approval

This study was approved by the First Affiliated Hospital of Zhejiang University of Traditional Chinese Medicine Ethics Committee and was conducted following the Declaration of Helsinki in its currently applicable version and applicable Chinese laws. And it was obtained from the patient's parents for publication of the case details.

Author Contributions

Conception and design of study: ZX; Data collection: ZX; Drafting the manuscript: ZX. The author reviewed the results and approved the final version of the manuscript.

Acknowledgments

I would like to thank the patient and her family for supplying the data.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Abbreviations

MOG	myelin oligodendrocyte glycoprotein
MOGAD	myelin oligodendrocytes glycoprotein associated disease
CNS	central nervous system
ADEM	acute disseminated encephalomyelitis
ON	optic neuritis
DTaP	diphtheria and tetanus toxoids and acellular pertussis
MS	multiple sclerosis
AQP4	aquaporin-4
IgG	immunoglobulin G
NMOSD	neuromyelitis optica spectrum disorder
CSF	cerebral spinal fluid
MRI	magnetic resonance imaging
IVIG	intravenous injection immunoglobulin

References

1. Salama S, Khan M, Pardo S, et al. MOG antibody-associated encephalomyelitis/encephalitis. *Mult Scler*. 2019 Oct;25(11):1427–1433. https://doi.org/10.1177/1352458519837705. PubMed PMID: 30907249; PubMed Central PMCID: PMCPMC6751007. eng.
2. Johns TG, Bernard CC. The structure and function of myelin oligodendrocyte glycoprotein. *J Neurochem*. 1999 Jan;72(1):1–9. https://doi.org/10.1046/j.1471-4159.1999.0720001.x. PubMed PMID: 9886048; eng.
3. Ambrosius W, Michalak S, Kozubski W, et al. Myelin oligodendrocyte glycoprotein antibody-associated disease: current insights into the disease pathophysiology, diagnosis and management. *Int J Mol Sci*. 2020 Dec 24;(1):22. https://doi.org/10.3390/ijms22010100. PubMed PMID: 33374173; PubMed Central PMCID: PMCPMC7795410. eng.
4. Tenembaum S, Chitnis T, Ness J, et al. Acute disseminated encephalomyelitis. *Neurology*. 2007 Apr 17;68(16 Suppl 2):S23–S36. https://doi.org/10.1212/01.wnl.0000259404.51352.7f. PubMed PMID: 17438235; eng.
5. Tenembaum S, Chamoles N, Fejerman N. Acute disseminated encephalomyelitis: a long-term follow-up study of 84 pediatric patients. *Neurology*. 2002 Oct 22;59(8):1224–1231. https://doi.org/10.1212/wnl.59.8.1224. PubMed PMID: 12391351; eng.
6. Esposito S, Di Pietro GM, Madini B, et al. A spectrum of inflammation and demyelination in acute disseminated encephalomyelitis (ADEM) of children. *Autoimmun Rev*. 2015 Oct;14(10):923–929. https://doi.org/10.1016/j.autrev.2015.06.002. PubMed PMID: 26079482; PubMed Central PMCID: PMCPMC7105213. eng.
7. Xu Q, Du W, Zhou H, et al. Distinct clinical characteristics of paraneoplastic optic neuropathy. *The British journal of ophthalmology*. 2019 Jun;103(6):797–801. https://doi.org/10.1136/bjophthalmol-2018-312046. PubMed PMID: 30021813; eng.
8. Hor JY, Asgari N, Nakashima I, et al. Epidemiology of neuromyelitis optica spectrum disorder and its prevalence and incidence worldwide. *Front Neurol*. 2020;11:501. https://doi.org/10.3389/fneur.2020.00501. PubMed PMID: 32670177; PubMed Central PMCID: PMCPMC7332882. eng.
9. Jurynczyk M, Messina S, Woodhall MR, et al. Clinical presentation and prognosis in MOG-antibody disease: a UK study. *Brain : J Neurol*. 2017 Dec 1;140(12):3128–3138. https://doi.org/10.1093/brain/awx276. PubMed PMID: 29136091; eng.
10. Li XJ, Hou C, Qiu W, et al. [Clinical features and prognosis of pediatric myelin oligodendrocyte glycoprotein antibody associated acute disseminated encephalomyelitis]. *Zhonghua Yixue Zazhi*. 2020 Feb 11;100(5):339–344. https://doi.org/10.3760/cma.j.issn.0376-2491.2020.05.005. PubMed PMID: 32074776; chi.
11. Marignier R, Hacohen Y, Cobo-Calvo A, et al. Myelin-oligodendrocyte glycoprotein antibody-associated disease. *Lancet Neurol*. 2021 Sep;20(9):762–772. https://doi.org/10.1016/s1474-4422(21)00218-0. PubMed PMID: 34418402; eng.
12. Bartels F, Lu A, Oertel FC, et al. Clinical and neuroimaging findings in MOGAD-MRI and OCT. *Clin Exp Immunol*. 2021 Dec;206(3):266–281. https://doi.org/10.1111/cei.13641. PubMed PMID: 34152000; PubMed Central PMCID: PMCPMC8561692. eng.
13. Liu H, Zhou H, Wang J, et al. The prevalence and prognostic value of myelin oligodendrocyte glycoprotein antibody in adult optic neuritis. *J Neurol Sci*. 2019 Jan 15;396:225–231. https://doi.org/10.1016/j.jns.2018.11.029. PubMed PMID: 30522039; eng.
14. Takai Y, Misu T, Kaneko K, et al. Myelin oligodendrocyte glycoprotein antibody-associated disease: an immunopathological study. *Brain : J Neurol*. 2020 May 1;143(5):1431–1446. https://doi.org/10.1093/brain/awaa102. PubMed PMID: 32412053; eng.
15. Hennes EM, Baumann M, Schanda K, et al. Prognostic relevance of MOG antibodies in children with an acquired demyelinating syndrome. *Neurology*. 2017 Aug 29;89(9):900–908. https://doi.org/10.1212/wnl.0000000000004312. PubMed PMID: 28768844; eng.
16. Bennetto L, Scolding N. Inflammatory/post-infectious encephalomyelitis. *J Neurol Neurosurg Psychiatry*. 2004 Mar;75(Suppl 1):i22–i28. https://doi.org/10.1136/jnnp.2003.034256. PubMed PMID: 14978147; PubMed Central PMCID: PMCPMC1765651. eng.
17. Küker W, Ruff J, Gaertner S, et al. Modern MRI tools for the characterization of acute demyelinating lesions: value of chemical shift and diffusion-weighted imaging. *Neuroradiology*. 2004 Jun;46(6):421–426. https://doi.org/10.1007/s00234-004-1203-5. PubMed PMID: 15114427; eng.
18. Berzero G, Cortese A, Ravaglia S, et al. Diagnosis and therapy of acute disseminated encephalomyelitis and its variants. *Expert Rev Neurother*. 2016;16(1):83–101. https://doi.org/10.1586/14737175.2015.1126510. PubMed PMID: 26620160; eng.
19. Sahlas DJ, Miller SP, Guerin M, et al. Treatment of acute disseminated encephalomyelitis with intravenous immunoglobulin. *Neurology*. 2000 Mar 28;54(6):1370–1372. https://doi.org/10.1212/wnl.54.6.1370. PubMed PMID: 10746613; eng.
20. Tajfirouz DA, Bhatti MT, Chen JJ. Clinical characteristics and treatment of MOG-IgG-associated optic neuritis. *Curr Neurol Neurosci Rep*. 2019 Nov 26;19(12):100. https://doi.org/10.1007/s11910-019-1014-z. PubMed PMID: 31773369; eng.
21. Chen JJ, Bhatti MT. Clinical phenotype, radiological features, and treatment of myelin oligodendrocyte glycoprotein-immunoglobulin G (MOG-IgG) optic neuritis. *Curr Opin Neurol*. 2020 Feb;33(1):47–54. https://doi.org/10.1097/wco.0000000000000766. PubMed PMID: 31743235; eng.