Clinical features of MOG Ig-positive Optic Neuropathies

Le Guern G, Héron E, Benrabah R
Internal medicine, Centre Hospitalier National d'Ophtalmologie des Quinze-Vingts, Paris

Financial Interests : none

BACKGROUND

Neuromyelitis optica spectrum disorder (NMO SD) is an inflammatory CNS syndrome, defined by the association of uni or bilateral optic neuritis, and serum aquaporin-4 immunoglobulin G antibodies (AQP4-IgG) positivity and/or specific CNS lesions (including acute myelitis). Anti Myelin Oligodendrocyte Glycoprotein (MOG) antibodies have been identified in some patients diagnosed with optic neuritis and NMO SD. Our objective was to evaluate clinical features among patients with bilateral or recurrent optic neuropathy who are seropositive for MOG antibodies, and to compare them with patients with NMO SD.

PATIENTS AND METHODS

Observational retrospective study. Cases of recurrent or bilateral optic neuropathy with MOG antibodies seropositivity were included, and compared with cases of Aquaporin-4 seropositive NMO SD and seronegative NMO SD (*i. e.* NMO SD according to international criteria [1]). Patients underwent clinical evaluation (including visual acuity and fundus examination), visual fields, visual evoked potential, brain MRI.

RESULTS

Nine MOG + patients and 9 patients with NMO SD (7 with positive AQP4 antibodies and 2 seronegative with clinical or radiological criteria) were identified (Figure 1). In the MOG group, 66% of optic neuropathy were bilateral at onset and 56% of patients had several episodes. Vision loss were severe in both groups (counting finger or worse for at least one eye 88% of MOG + patients and in 77% of NMO, Figure 2). After IV corsticosteroids, visual recovery was excellent and quick for all MOG+ patients (recovery better than 0.6 in a 2 to 35 days period for 88% of MOG Abs+ patients, Figure 4).On the contrary, visual prognosis was poor for NMO SD patients (long term visual recovery worse than 0.6 for 88% of NMO SD patients). All the patients in this study were started on immunosuppressive therapy.

Figure 1. Demographic and clinical features of 9 MOG Abs+ patients and 9 NMOSD (AQP4 Abs+ or seronegative). All differences between groups were non significant, except visual recovery (p>0.003)

	MOG (n=9)	NMOSD (n=9)
Sex	3M/6F	5M/4F
Age	43 [26.8-59.2]	40 [26.5-53.3]
No of attacks	2.22 [0.7-3.7]	2 [0.3-3.7]
Myelitis	1 (11%)	5 (56%)
Bilateral ON at onset	6 (66%)	6 (66%)
Recurent ON	5 (56%)	3 (33%)
Visual recovery >0.6	**8 (88%)***	**2 (22%)***
Median delay to recovery	10 days	-
Follow up (months)	40	50
MRI caracteristics :		
- Chiasmatic lesions	0 (0%)	3 (33%)
- Cerebral T2 hypersignals	3 (33%)	3 (33%)

Figure 2. Clinical features, MRI and laboratory findings in patients with NMOSD with MOG Ab, AQP4 Ab, and seronegative patients

Ab Positivity	Patient	age/sex	FU period (months)	Clinical caracteristics	No of attacks	Myelitis		Worst VA	VA 1 Month	VA 3 months	VA last FU	Papillary oedema	Brain MRI	Spinal MRI lesions	OCB	Treatment	Comments
MOG	1	41/M	22	Bilateral simultaneous ON	1	no	OD	0,3			1	yes	Bilateral intraorbital, intracanalicular and intracranial ON. Non specific subcortical WM lesions	no		CS, Mycophenolate mofetil	
							OS	0,2			1	yes					
MOG	2	36/F	21	Bilateral simultaneous ON	2	no	OD	CF	0,9		0,9	no	Bilateral intraorbital and intracanalicular ON. Normal brain MRI	no	no	CS, Azathioprine	
							OS	CF	0,9		0,9	no					
MOG	3	25/F	33	Unilateral recurent ON	3	no	OD	HM	0,3	1	1	yes	Left ON. Normal brain MRI	no	no	CS, Azathioprine	
							OS	1			1	no					
MOG	4	69/F	95	Bilateral ON	4	no	OD	LP+			0,8	no	Left intraorbital ON (first episode). Non specific WM lesions	ND		CS, Azathioprine	
							OS	LP+			0,7	yes					
MOG	5	59/M	17	Bilateral simultaneous ON	1	no	OD	0,2	0,9		0,9	no	Bilateral intraorbital and intracanalicular ON. Non specific subcortical WM lesions	ND		CS, Azathioprine	
							OS	LP-	0,7		0,7	no					
MOG	6	25/M	141	Bilateral ON	5	no	OD	LP+			1	no	Left ON. Normal brain MRI	no	no	CS, Azathioprine	
							OS	LP+			1	yes					
MOG	7	58/F	11	Bilateral simultaneous ON	1	no	OD	1	1		1	no	Bilateral ON (OS>OD). Normal brain MRI	no		CS, Azathioprine	
							OS	CF	1		1	no					
MOG	8	28/F	12	Bilateral ON	2	yes	OD	LP+			0,5	yes	Right Intracanalicular ON. Non specific WM lesions	C2 and C5 lesions	yes	CS, Azathioprine	
							OS	-			-	no					
MOG	9	46/F	7	Bilateral simultaneous ON	1	no	OD	HM	0,8	0,8	0,8	yes	Bilateral intraorbital ON. Normal brain MRI	no		CS, plasma exchange therapy, Mycophenolate mofetil	
							OS	CF	1	0,9	0,9	yes					
AQP4	10	23/M	28	Bilateral ON (chiasmatic lesion)	1	yes	OD	LP-			LP-	atrophy	Bilateral intracranial ON involving chiasma. Periventricular WM lesions	C2-C3 lesion		Mycophenolate mofetil	
							OS	LP-			LP-	atrophy					
AQP4	11	29/F	40	Bilateral ON (chiasmatic lesion)	1	no	OD	CF		0,2	0,6	yes	Right intraorbital, intracanalicular and intracranial ON involving chiasma. Normal brain MRI	no		CS, Azathioprine, Rituximab	Anti SSA +
							OS	0,9		0,6	1	no					
AQP4	12	28/F	57	Unilateral recurent ON	3	yes	OD	1			1,2	no	Left ON. Normal brain MRI	T6-T7 lesion	no	CS, Mycophenolate mofetil	
							OS	CF			1,2	no					
AQP4	13	29/F	40	Bilateral simultaneous ON	2	no	OD	HM	0,1		CF	no	Bilateral ON. Normal brain MRI	no	no	CS, Mycophenolate mofetil	
							OS	CF	1,6		LP+	no					
AQP4	14	54/M	40	Unilateral ON	1	yes	OD	0,9				no	Left ON. Normal brain MRI	T9-T10 lesion	no	CS, Mycophenolate mofetil	Anti SSA +
							OS	CF		CF		no					
AQP4	15	58/M	15	Unilateral ON	1	no	OD	CF		0,125		no	Right intraorbital ON. Normal brain MRI	no		CS, plasma exchange therapy, Azathioprine	
							OS	0,1		0,1		no					
AQP4	16	44/F	22	Bilateral simultaneous O N	1	yes	OD	0,3		0,2		no	Bilateral ON. Bulbopontic WM lesion	T3-T8 lesion		CS, Azathioprine	
							OS	0,2		0,1		no					
NEG	17	55/M	34	Bilateral ON (chiasmatic lesion)	1	no	OD	0,1		0,1		no	Right intracranial ON involving chiasma.Normal brain MRI	no	yes	CS, plasma exchange therapy, Mycophenolate mofetil	
							OS	0,8		0,7		no					
NEG	18	39/M	180	Bilateral simultaneous ON	6	yes	OD	CF			0,6	no	Bilateral intraorbital and intracanalicular ON. Subcortical and capsular VM lesions	C1-C2, C7-T4 and T5-T11 lesions	no	CS, Mycophenolate mofetil	
							OS	CF			0,2	no					

Abbreviations : Ab antibody, ON Optic neuropathy, VA Visual acuity, HM Hand motion, CF counting fingers, CS Corticosteroids, SSA Sjrogren syndrome A antibodies, WM White matter

Figure 3. Axial cerebral MRI (gadolinium enhanced T1 weighted sequence). Bilateral Optic nerve hypersignal in a MOG Abs+ patient (A). Right opticochiasmatic hypersignal in a AQP4+ patient (B)

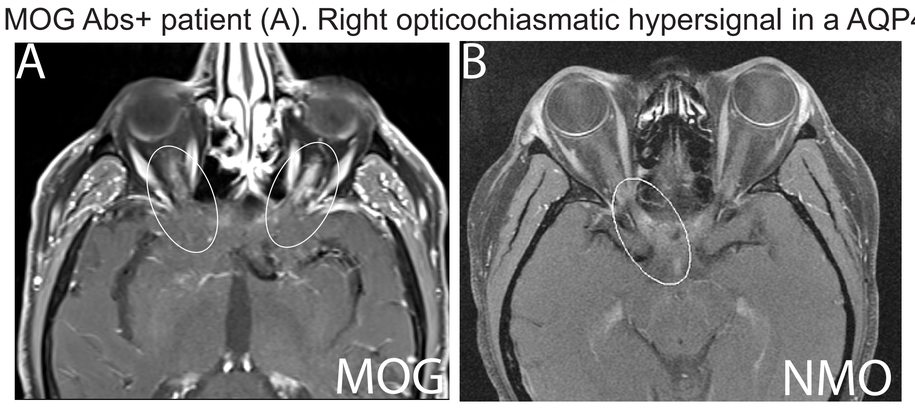
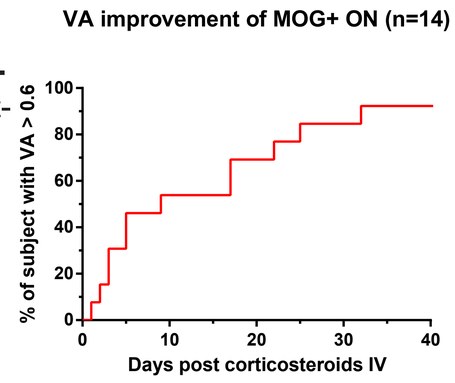


Figure 4. Visual acuity improvement of 14 MOG Abs+ optic neuropathy. All the patients were started on treatment with VA between no light perception and 0.3. At day 10 post corticosteroids IV, more than 50% of the patients had a visual acuity better than 0.6.



COMMENTS

Our study suggest that MOG Abs seropositive optic neuropathy have a better prognosis and a quicker recovery than AQP4 Abs positive NMO SD and seronegative NMO SD. Several studies are consistent with this observation [2-4]. Anti MOG Abs and anti AQP4 Abs target two different cell populations [5]. Anti MOG Abs presumably bind to myelin-forming oligodendrocytes and myelin, causing acute demyelinating lesions. On the other hand, anti AQP4 Abs binds to AQP4 water channels on astrocytes, causing blood brain barrier disruption and astrocytic dysfunction, which may explain a worse prognosis in AQP4 Abs+ patients. There is no consensual treatment of MOG Abs positive NMO SD. However, acute myelitis is reported in the litterature in MOG Abs positive patients, and one of our MOG Abs positive patient developped an acute myelitis. For this reason, all patients in this study were started on immunosuppressive therapy.

CONCLUSION

Anti MOG Abs seropositive optic neuropathies have a better visual prognosis than AQP4 Abs positive and seronegative NMO SD. Testing for anti MOG antibodies may be useful in bilateral or recurrent optic neuropathy to evaluate the prognosis.

REFERENCES

[1] Wingerchuk DM, Banwell B, Bennett JL, Cabre P, Carroll W , Chitnis T, et al. International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. Neurology. 2015.
[2] Sato DK, Callegaro D, Lana-Peixoto MA, W aters PJ, de Haidar Jorge FM, Takahashi T, et al. Distinction between MOG antibody-positive and AQP4 antibody-positive NMO spectrum d orders. Neurology. 2014.
[3] Van Pelt ED, Wong YY, Ketelslegers IA, Hamann D, Hintzen RQ. Neuromyelitis optica spectrum disorders : comparison of clinical and magnetic resonance imaging characteristics of AQP4-IgG versus MOG-IgG seropositive cases in the Netherlands. Eur J Neurol. 2016
[4] Chalmoukou K, Alexopoulos H, Akrivou S, Stathopoulos P, Reindl M, Dalakas MC. Anti-MOG antibodies are frequently associated with steroid-sensitive recurrent optic neuritis. Neurol Neuroimmunol. 2015
[5] Zamvil SS, Slavin AJ. Does MOG Ig-positive AQP4-seronegative opticospinal inflammatory disease justify a diagnosis of NMO spectrum disorder? Neurol Neuroimmunol Neuroinflamm. 2015.