EFFICACY OF MYCOPHENOLATE MOFETIL IN TWO PATIENTS AFFECTED BY NEUROMYELITIS OPTICA

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Introduction

- Neuromyelitis Optica (NMO) is an inflammatory disease of the Central Nervous System (CNS).
- NMO is considered a different disease from multiple sclerosis (MS) because:
  - its course is usually more severe
  - the onset is delayed compared to MS
  - female/male ratio is 9:1 (2:1 in MS)
  - brain magnetic resonance imaging (MRI) is not typical for MS
  - spinal MRI shows spinal cord lesions which extend for 3 or more vertebral segments (longitudinally extensive transverse myelitis lesions, LETM)
  - oligoclonal bands are positive in no more than 40% of cases, compared to 90% in MS (1).
- Major changes in NMO nosology were brought about by the discovery of a serum marker, anti-aquaporina-4 antibody (AQP4-IgG), found in NMO patients with high specificity (about 90%), but not in MS patients, suggesting a different immunopathogenesis (2).
- NMO-IgG seropositivity became a supportive criteria for NMO diagnosis in the 2006 revised diagnostic criteria (3).
- Recently, the "International Panel for Neuromyelitis Optica Diagnosis" has proposed new diagnostic criteria which highlight AQP4-IgG status (4).
- Current MS treatments have poor efficacy in NMO (1).
- There are some retrospective and open-label studies with monoclonal antibody Rituximab (anti-CD20) which show a good efficacy and safety in NMO patients (5), but its use in NMO is currently off-label.
- One retrospective study on 24 NMO patients treated with Mycophenolate Mofetil also showed a good efficacy and safety profile (6).

Methods

we selected 2 female NMO patients, both positive for serum AQ-4 antibodies.
Patient 1: age 39, diagnosis of definite NMO according to diagnostic criteria (3) in July 2012, disease duration 20 years, pre-treatment EDSS 2.0.
Patient 2: age 76; diagnosis of LETM in NMO spectrum in January 2014, disease duration 18 months, pre-treatment EDSS 8.0 (due to severe paraparesis) (See **Table 1** and **Figures 1-4**).
We treated our patients with Mycophenolate Mofetil 2000 mg daily, 2 tablets of 500 mg twice a day every 12 hours.

Results

Treatment duration was 30 months for patient 1 and 16 months for patient 2. No relapses and no MRI activity occurred in both patients under Mycophenolate treatment. Mean yearly relapse rate in patient 1 was 1.5 before and 0 after Mycophenolate treatment. Patient 2 had only one episode of transverse myelitis, no relapses after Mycophenolate treatment occurred. EDSS improved from 2.0 to 1.5 in pt 1 and from 8.0 to 7.5 in pt 2 (**Table 2)**.
Treatment was safe and well tolerated and no serious infections occurred in both patients. Currently, our patients are still ongoing with Mycophenolate.

Table 1: Baseline Characteristics

Pts	Age	NMO Pattern	Disease Duration	MRI features	Pre-treatment EDSS
1	39	Definite NMO	20 years	LETM extending from C7 to D3; bulbar lesion	2.0
2	76	LETM–NMO spectrum	1.5 years	LETM extending from C5 to D4	8.0

Table 2: Results

Patients	Treatment Duration	Pre and post-treatment relapse rate		Current EDSS (improvement)
1	30 months	1.5	0	1.5 (0.5)
2	16 months	/	0	7.5 (0.5)

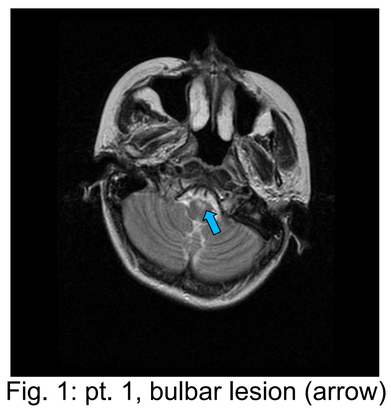


Fig. 1: pt. 1, bulbar lesion (arrow)

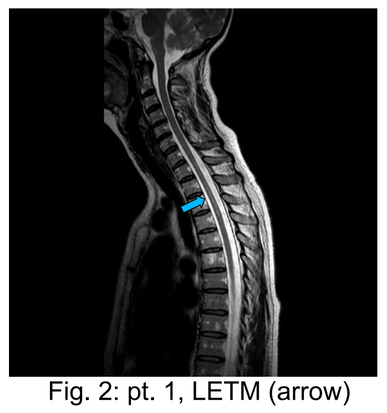
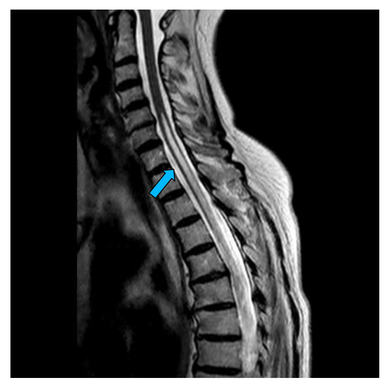
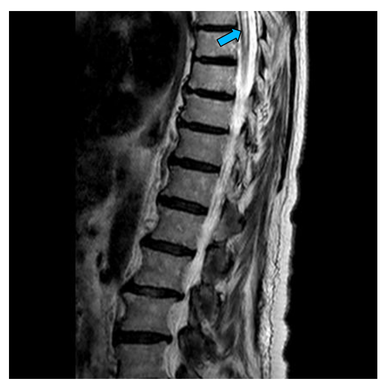


Fig. 2: pt. 1, LETM (arrow)





Figs. 3-4: Pt 2, LETM (arrows)

Discussion: our positive experience with Mycophenolate on only 2 NMO patients doesn't allow us to formulate definitive judgments about its efficacy. However, our results are consistent with previous published data (6). The use of Rituximab in NMO is supported by small open-label and retrospective studies, but it is important to remark some limitations to its use, above all in small, not academic, MS hospital centers. These limitations are its high costs as well as the management of potential serious adverse events, like infusion-related reactions and the occurrence of serious infections. In contrast, Mycophenolate didn't show any serious adverse event, above all no severe infections occurred (6).

Conclusions: *our results suggest that Mycophenolate Mofetil treatment is effective and safe in NMO patients and may represent a promising option other than Rituximab treatment.*

References

1.Corinna Trebst, Sven Jarius, Achim Berthele, Friedemann Paul, Sven Schippling, et al. Neuromyelitis Optica Study Group (NEMOS): Update on the diagnosis and treatment of neuromyelitis optica: Recommendations of the Neuromyelitis Optica Study Group. J Neurol (2014) 261:1–16.
2.Lennon VA, Wingerchuk DM, Cryzer et al: a serum autoantibody marker of neuromyelitis optica: distinction from multiple sclerosis. Lancet 2004; 364: 2106-2112.
3.Wingerchuk DM, Lennon VA, Pittock SJ, Lucchinetti CF, Weinshenker BG. Revised diagnostic criteria for neuromyelitisoptica. Neurology 2006;66: 1485–1489.
4.Wingerchuk DM, Banwell B, Bennett JL, et al: International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. Neurology, 2015; 85: 177-189.
5.Bedi GS, Brown AD, Delgado SR, Usmani N, Lam BL, Sheremata WA (2011) Impact of rituximab on relapse rate and disability in neuromyelitis optica. Mult Scler 17:1225–123.
6.Anu Jacob, MD; Marcelo Matiello, MD; Brian G. Weinshenker, MD; Dean M. Wingerchuk, MD; Claudia Lucchinetti, MD; Elizabeth Shuster, MD; Jonathan Carter, MD; B. Mark Keegan, MD; Orhun H. Kantarci, MD; Sean J. Pittock, MD: Treatment of Neuromyelitis Optica With Mycophenolate Mofetil: Retrospective Analysis of 24 Patients. Arch Neurol. 2009 Sep;66(9):1128-33

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