May NMOSD be a paraneoplastic syndrome? Study of a case series

Juliana S. Amaral; Felipe B. Brunheroto; Luciana M. Rocha; Grazielle Fialho; Alice Horta; Mariana Fontanelle; Natália Talim; Hugo Brito; Clara C. Pinhati; Thales Ponsá; Paulo P. Christo; Marco A. Lana-Peixoto

CIEM MS Research Center, Federal University of Minas Gerais Medical School, Belo Horizonte, Brazil

Introduction:

Recent reports of the association of neuromyelitis optica spectrum disorder (NMOSD) with cancer have risen the hypothesis that it may have a paraneoplastic (PN) nature.

Objective:

To report the demographic and clinical features of a series of patients with NMOSD and cancer and discuss how these cases might be included in the group of the paraneoplastic syndromes.

Methods:

We selected patients who both met Wingerchuk 2015 diagnostic criteria for NMOSD and had a positive history of cancer. Demographic, clinical, laboratory and imaging features were obtained from medical records. Paraneoplastic syndrome was defined according to the PNS Euronetwork Criteria.

Results:

We identified six patients with NMOSD and history of cancer (5 women, 2/5 whites, 2/5 blacks and 1/5 mixed). Mean age at NMOSD onset was 47.7 [39-58] and at cancer diagnosis was 51 [40-61] years. Mean time interval between NMOSD onset and cancer was 33.3 [0-72] months. Three patients were AQP4-IgG seropositive and 2 seronegative. Relapses occurred in three patients. Presenting syndromes were myelitis in 4 (66%), area postrema syndrome in 2 (33.3%), optic neuritis in 2 (33.3%), and brainstem syndrome in 1 (16.7%) patient. Cerebral spinal fluid (CSF) was abnormal in 4 (66.7%) patients. Spinal MRI lesions were found in all patients, but only 2 had longitudinally extensive spinal cord lesions. Partial recovery after attacks occurred in 5/5 patients; at last follow-up the mean EDSS was 6.5. Five (83.3%) patients were in use of azathioprine. Two (33.3%) patients had breast cancer, 1 (16.7%) bladder cancer, 2 (33.3%) cervical cancer and 1 (16.7%) multiple myeloma.

Table 1. Patients' demographic and clinical characteristics.

Female	5 (83.3%)
Mean Age at NMOSD Onset (years)	47.7 [39-58]
Time between NMO and cancer (months)	33.3 [0-72]
AQP4-IgG Positive	3/5 tested (60%)
Changes in CSF	4 (66.7%)
Abnormal Spinal MRI	6 (100%)
Longitudinally Extensive Spinal Cord Lesion	2 (33.3%)
Mean EDSS at last follow-up	6.5

Table 2. Types of cancer developed by study patients. Bold text indicates Possible Paraneoplastic Syndrome, according to Euronetwork Criteria.

Cancer Type	N (%)
Breast	**2 (33.3)**
Bladder	1 (16.7)
Cervical*	**2 (33.3)**
Multiple Myeloma	1 (16.7)

*One of the cases can be classified as Possible Paraneoplastic Syndrome

Three (50%) patients met the current diagnostic criteria for paraneoplastic syndrome.

Conclusions:

The association of NMOSD with cancer is very rare. Half of our cases meet Euronetwork criteria for PNS. Collaborative studies may clear the frequency and pathophysiological mechanisms of this association.

References:

1. Wingerchuk DM, Banwell B, Bennett JL, et al. International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. Neurology 2015;85:177–189.

2. Lennon, V.A., D.M. Wingerchuk, T.J. Kryzer, S.J. Pittock, C.F. Lucchinetti, K. Fujihara, I. Nakashima, and B.G. Weinshenker. 2004. A serum autoantibody marker of neuromyelitis optica: distinction from multiple sclerosis. Lancet. 364:2106–2112.

3. Graus F, Delattre JY, Antoine JC, et al. Recommended diagnostic criteria for paraneoplastic neurological syndromes. J Neurol Neurosurg Psychiatry. 2004;75(8):1135-1140. doi:10.1136/jnnp.2003.034447

4. Shahmohammadi S, Doosti R, Shahmohammadi A, et al. Neuromyelitis optica spectrum disorder (NMOSD) associated with cancer: A systematic review. Mult Scler Relat Disord. 2021;56:103227. doi:10.1016/j.msard.2021.103227