Aquaporin-4 antibody Neuromyelitis optica spectrum disorder (AQP4-NMOSD) is a rare CNS autoimmune disease in adults and children classically characterised by myelitis, optic neuritis and/or area postrema syndrome. AQP4-NMOSD has been shown to be associated with a high frequency of organ and non-organ-specific autoantibodies which may be due to compromised central and peripheral B-cell tolerance checkpoints[1]. Although not typically considered a paraneoplastic syndrome, associated malignancies, particularly in older patients, have been reported[2] in addition to thymomas in patients with co-existing myasthenia gravis[3].

Tardo et al. describe a 14-year-old female patient with AQP4-NMOSD[4], presenting with area postrema syndrome and left optic neuritis who was found to an ovarian teratoma on abdominal imaging. Despite oophorectomy she had persistent neurological signs on examination and hyperintense T2 signal in the area postrema on neuroimaging. Her symptoms resolved after high dose intravenous methylprednisolone followed by steroid taper. Pathological specimens demonstrated prominent inflammatory infiltrate within neuroglial tissues and confirmed AQP4 antigen expression. Interestingly, the patient seroconverted to negative AQP4-Ab status one month after presentation with no clinical relapses at 1 year follow-up.

The case presented highlights two important issues. Firstly, as demonstrated by the inflammatory response on histopathology, the AQP4 expression within the teratoma is likely to have been an antigenic trigger for AQP4 antibody production. Furthermore, the fact that tumour removal coincided with seroconversion to negative AQP4-Ab status and the absence of further clinical relapses without maintenance immune therapy, suggests that the pathobiology of the paraneoplastic syndrome may be different to non-paraneoplastic forms of the disease; in the latter, patients often have frequent relapses without long-term immune therapies[5]. Secondly, as highlighted by the authors, there are clear parallels to the occurrence of ovarian teratomas in at least 50% of adolescent girls with anti-NMDAR

encephalitis. This may suggest a potential common pathogenesis of teratoma-associated CNS autoimmune diseases, which warrants further investigation.

This case and the additional recently reported AQP4-NMOSD associated with teratoma in 27-year-old Chinese woman[6], may support paraneoplastic screening in all patients, including children, as part of the standard of care of patients with AQP4-NMOSD.

## Declaration of Conflicting Interests

Omar Abdel-Mannan and Yael Hacohen have nothing to disclose


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## References


1. Kunchok A, Flanagan EP, Snyder M, et al. Coexisting systemic and organ-specific autoimmunity in MOG-IgG1-associated disorders versus AQP4-IgG+ NMOSD. Multiple Sclerosis Journal 2021;27:630-635.
2. Graus F, Vogrig A, Muñiz-Castrillo S, et al. Updated Diagnostic Criteria for Paraneoplastic Neurologic Syndromes. Neurology-Neuroimmunology Neuroinflammation 2021;8.
3. Leite M, Coutinho E, Lana-Peixoto M, et al. Myasthenia gravis and neuromyelitis optica spectrum disorder: a multicenter study of 16 patients. Neurology 2012;78:1601-1607.
4. Tardo L WC, Rajaram V, et al. Pediatric Paraneoplastic Neuromyelitis Optica Spectrum Disorder Associated with Ovarian Teratoma. Multiple Sclerosis Journal 2021 (in press).
5. Levy M, Fujihara K, Palace J. New therapies for neuromyelitis optica spectrum disorder. The Lancet Neurology 2020.
6. Ikeguchi R, Shimizu Y, Shimomura A, et al. Paraneoplastic AQP4-IgG–Seropositive Neuromyelitis Optica Spectrum Disorder Associated With Teratoma: A Case Report and Literature Review. Neurology-Neuroimmunology Neuroinflammation 2021;8.