A Patient with NMO and Ulcerative Colitis: Is it only Autoimmunity?

Ibtisam Al-Thubaiti1* and Farah Al-Eissa2

1Board certified Neurologist, Department of Neurology, King Fahad Specialist Hospital, Dammam, Saudi Arabia
2Neurology Resident, Department of Neurology, King Fahad Specialist Hospital, Dammam, Saudi Arabia

Abstract

We report a case of a patient who developed neuromyelitis optica one year after discontinuation of her immunosuppressive agent used to treat her ulcerative colitis. We highlight the association between the two diseases that their similarities may not be limited to their autoimmune etiology, but also due to abnormal water channels, or aquaporins, and briefly discuss the possible role of aquaporins in ulcerative colitis pathogenesis.

Keywords: NMO; Ulcerative colitis; Aquaporin

Case Report

A 35-year-old lady referred for recurrent bilateral severe optic neuritis. Her past medical history is significant for ulcerative colitis (UC) diagnosed in 2006 and treated successfully with azathioprine (AZA).

In August 2010, one year after AZA discontinuation, she had her first attack of severe right optic neuritis that caused blindness for which she received 5-day-course of intravenous methylprednisolone (IVMP) with complete recovery. Three months later, she had similar attack that was treated with another course of IVMP but with partial improvement. In May 2012 she had another episode of simultaneous bilateral severe optic neuritis not responding to 2 courses of IVMP. The MRI showed the enhancement of both optic nerves, chiasm, optic tracts, and lateral geniculate bodies (Figure 1a and 1b).

Upon presentation to our hospital 5 months after the last attack, she was blind and had no light perception. Her pupils were not reactive to light; she had pale optic discs, and otherwise normal neurological exam. A repeated MRI showed residual optic nerve atrophy with no brain or spinal cord lesions.

Patients’ serum sent for neuromyelitis optica (NMO) antibodies in Mayo clinic laboratories were positive with a titer of >1:160, and the diagnosis of NMO spectrum disorder (NMOSD) was confirmed. Other serological investigations showed negative rheumatoid factor, ANA, anti-DNA, anti-Ra, anti-La antibodies. A spinal tap showed normal abnormalities in the water channels or aquaporin (AQP).

While the patient was scheduled to receive rituximab infusion, she had another relapse in December 2012 causing left sided weakness and hemianesthesia. The repeated MRI showed a "longitudinally extensive" lesion involving the right inner capsule and right cerebral peduncle (Figures 1b-1h). Her spine MRI was normal. She received 5-day-course IVMP with good recovery, followed by rituximab infusion of 1000 mg biweekly (Table 1).

Six months after treatment, her neurological exam came back to baseline and she continued to receive rituximab 1000 mg biweekly every 6 months. She also remains in remission from her ulcerative colitis since 2006.

Discussion

Coexistence between NMO and both organ-specific and non-organ-specific systemic autoimmune diseases is not uncommon. In a cohort study of 153 patients with NMOSD, 4 (2.6%) patients diagnosed with ulcerative colitis, 26 (17.0%) with autoimmune thyroid disease, 5 (3.2%) with systemic lupus erythematosus or sjogren’s syndrome, 2 with idiopathic thrombocytopenic purpura (1.3%), 2 with rheumatoid arthritis (1.3%), 2 with myasthenia gravis (1.3%), one with Raynaud phenomenon (0.7%), one with polymyositis (0.7%), and one with celiac disease (0.7%) [1]. A recent multinational study highlighted the association with acetylcholine receptor antibody positive myasthenia gravis (AChR-MG) [2]. Sixteen patients had both disorders, and four out of five patients whom stored sera where available had AQP4-IgG present 4 to 16 years before NMOSD onset [2]. Another case series suggested that those who underwent thymectomy maybe at higher risk for developing NMO [3,4]. Because of the association of two rare autoimmune disorders, authors suggested that patients diagnosed with AChR-MG might be at risk of developing NMO, and vice versa [2].

The association between NMO and UC is more interesting as they are not only two rare autoimmune disorders, but they share abnormalities in the water channels or aquaporin (AQP).

In 1991 Preston and Agre discovered a channel specific for water transportation formally called “CHIP28” for channel-like integral membrane protein of 28 kDa [5]. AQP are highly selective channels allowing water movement in response to osmotic gradient [6]. To date there are 13 subtypes of the AQP family in mammals [6,7].

The role of AQP4 subtype is better understood in the CNS, as it is the most expressed water channel in the brain, spinal cord, and optic nerve. Its peculiar distribution on the astrocytic foot processes surrounds the endothelial cells and ependymal cells; i.e at the interface between brain parenchyma and perivascular space, and between brain and CSF has directed to the discovery of its critical role in maintaining the water homeostasis inside the CNS [8,9]. In 2004 the discovery of pathogenic IgG autoantibody against AQP4 in NMO has revolutionized the understanding of disease pathogenesis, aided in earlier identification, expanding its spectrum, and better targeted therapy [10]. The antibody demonstrated an excellent specificity (90%) and sensitivity (50%-90%) and was included in the 2006 revised diagnostic criteria for NMO [10,11].

*Corresponding author: Ibtisam Al-Thubaiti, Department of Neurology, King Fahad Specialist Hospital, Omar Bin Thabet Street, P.O. Box 15215, Dammam 31444, Saudi Arabia, Tel: +966505801270; Fax: +96638153315; E-mail: dr.althubaiti@gmail.com

Received August 22, 2013; Accepted December 24, 2013; Published December 26, 2013


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of UC; diarrhea [14]. Another study showed opposite results with increased AQP8 expression in intestinal epithelium of non-inflamed mucosa and a subset of lamina propria mononuclear cells [16]. The authors suggested that early diarrhea is due to downregulation of AQP8 and later it is upregulated as a compensatory mechanism. There was also increased expression of AQP1, 3, and 11 in patients with UC [16]. Though the role of AQP in UC is still under discovery, the coexistence of UC in patients with pathogenic auto-antibodies against AQP4 or NMO raises the question about water channelopathy or “aquarinopathy” disorders. Perhaps individuals with one “aquarinopathy” disease like NMO are susceptible to another “aquarinopathy” like UC, and if such susceptibility exists early screening or watchful follow up is warranted before clinical appearance.

Acknowledgement
The authors thank Dr Jameelah Al-Saaedi (Neurology department, King Fahad Medical City, Saudi Arabia) for her help revising the final manuscript.

No IRB approval was taken as this a case report and does not disclose any identifiable body parts of the patient (MRI Brain).

All authors report no disclosure.

References


