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LETTER TO THE EDITOR

Rheumatoid arthritis with aquaporin-4 antibody-positive neuromyelitis optica receiving rituximab therapy

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A spectrum of autoimmune diseases has been associated with optic neuritis or myelitis in the presence of aquaporin-4 (AQP4) antibody, creating a classification named neuromyelitis optica spectrum disorder (NMOSD).[1] Further studies have identified a pathogenic role of B cells,[2] and rituximab (RTX) is an effective and safe treatment in this disease.[3] Herein, we report a case of rheumatoid arthritis (RA) with anti-AQP4-positive optic neuritis. The RTX therapy resulted in absent autoantibody and clinical improvement.

A 58-year-old Han Chinese woman visited our hospital with a five-year history of polyarthritis and visual impairment. She was diagnosed to have RA with recent therapy including methotrexate (MTX) 10 mg/week and prednisolone 5 mg/day. For ocular presentations, there was retro-orbital pain with bilateral papillitis, followed by blurred vision with delayed responses/low amplitudes in visual evoked potential, leading to a diagnosis of optic neuritis. Nevertheless, she did not attend to the ophthalmological follow-up without taking medications, resulting in a progressive eyesight loss to a counting fingers vision (10/5 cm, right/left).

Physical examination at the rheumatology clinic showed swollen, tender joints over wrist, metacarpophalangeal, proximal interphalangeal, and knee areas. Conventional X-ray demonstrated erosion over the wrist. Erythrocyte sedimentation rates (ESR, 52 mm/h) and C-reactive protein (CRP, 11.9 mg/L) levels were elevated with a 5.88 Disease Activity Score-28 (DAS28). Autoantibody profiles had increased anti-AQP4 (11 U/mL, enzyme-linked immunosorbent assay, RSR Limited, UK), rheumatoid factor (RF, 105 IU/mL) and anti-cyclic citrullinated protein (anti-CCP, 28 U/mL) levels. Evaluation for systemic lupus erythematosus (SLE) showed normal hemogram and negative urine analysis, as well as anti-nuclear antibody negativity, anti-double-stranded deoxyribonucleic acid, and anti-Sm antibodies. Sjögren's syndrome survey revealed negative SSA/SSB antibodies and minor salivary gland biopsy. There was no demyelination on brain/spinal cord magnetic resonance imaging. The patient was

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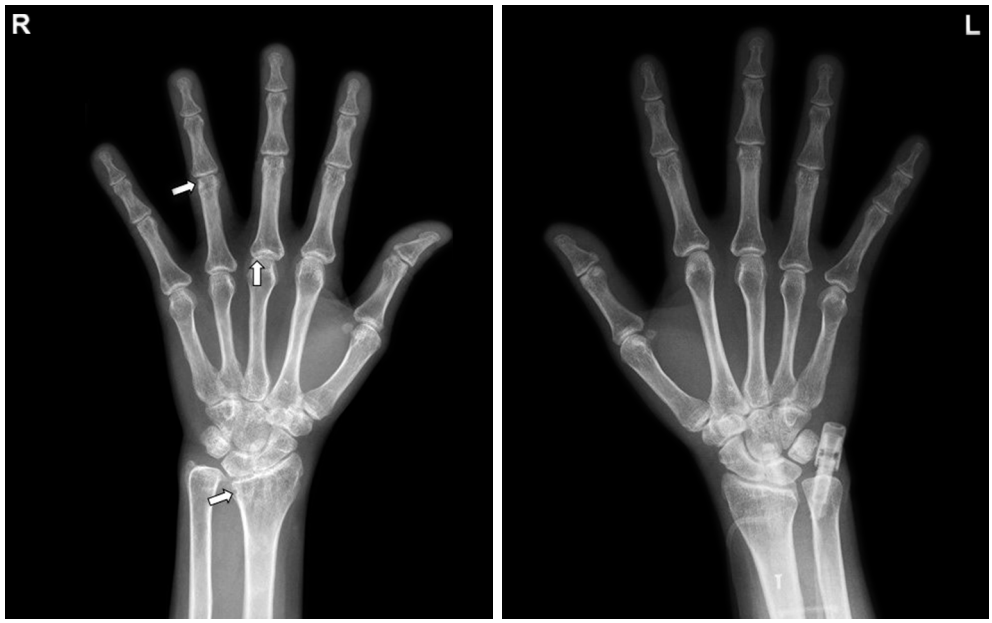

Figure 1. Conventional X-rays showing erosions (white arrows) over right wrist, 4th proximal interphalangeal, and 3rd metacarpophalangeal joints with joint space narrowing over wrists.

diagnosed with NMOSD associated with anti-AQP4-positive optic neuritis and an autoimmune disease RA.[4,5]

She had refractory RA activity under MTX 15 mg/week, prednisolone 5 mg/day, and sulfasalazine (SAZ) 2 g/day. Conventional X-rays demonstrated erosions over right wrist, proximal interphalangeal and metacarpophalangeal joint areas with joint space narrowing over wrists (Figure 1). The RTX therapy with a regimen of 1 g × two fortnightly infusions every six months was initiated from 2016, with a total of 20 infusions until the end of 2020. There were completely depleted circulating CD19-positive B cells (0/μL) after two infusions, normalized ESR/CRP levels with a reduced DAS28 to 2.99 after four infusions, followed by negative anti-AQP4 (1 U/mL, normal reference below 3 U/mL), anti-CCP (below 7 U/mL), and RF (below 20 IU/mL) levels. She had an improved ophthalmological vision to decimal visual acuity 0.06/0.04 (right/left) in 2019. After 20 infusions, the DAS28 further improved to 2.10 and MTX doses were tapered to 7.5 mg/week without using SAZ. Except for initial infusion-related reactions, no adverse effects were observed during RTX therapeutic period. A written informed consent was obtained from the patient for all diagnostic and therapeutic procedures.

Despite an extending spectrum of rheumatology disorders associated with NMO, including antiphospholipid syndrome, primary Sjögren's syndrome, SLE, and systemic sclerosis, there is no inclusion of RA.[5,6] An investigation of NMOSD identified juvenile RA as a coexistent autoimmune disorder,[7] and a survey on optic neuritis showed a poor visual outcome associated with RA.[8] Interestingly, a case with overlap syndrome involving RA and polymyositis was diagnosed to have NMOSD with the presence of anti-AQP4-positive longitudinal myelopathy.[9] Notably, in Han Chinese, genetic polymorphisms have been demonstrated to be shared among RA, NMOSD, and AQP4-seropositivity.[10]

In conclusion, in this report, we present an anti-AQP4-positive RA case with optic neuritis, which may raise a potential to incorporate RA into the autoimmunity spectrum in NMOSD.

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