A Tangled Autoimmune Trio: Multiple Sclerosis, Systemic Lupus Erythematosus and Antineutrophil Cytoplasmic Antibody Vasculitis

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Abstract

The coexistence of multiple autoimmune diseases in the same individual is unusual and has received little attention in the literature. We present a young female patient with multiple sclerosis, systemic lupus erythematosus, and biopsy-proven renal proteinase 3 antineutrophil cytoplasmic antibody-associated vasculitis who responded well to intravenous rituximab clinically and serologically.

Keywords: Multiple sclerosis, systemic lupus erythematosus, ANCA-associated vasculitis

Introduction and Case Presentation

After the birth of healthy twins in 2016, a 36-year-old Emirati female presented with an established diagnosis of relapsing-remitting multiple sclerosis (MS) diagnosed in 2009 after presenting with blurry vision and painful eye movements. She began experiencing excruciating joint pain associated with early morning stiffness involving the hands in 2016. She was assessed by a rheumatologist at an outside facility for recurring malar rash, photosensitivity, recurrent oral ulcers, and polyarthralgia. She had additional autoimmune testing, which revealed a positive lupus profile, including a positive immunofluorescence antinuclear antibody 1:160 homogeneous pattern, positive double-stranded DNA antibodies by enzyme-linked immunosorbent assay and C3 antibodies, and positive anti-Ro antibodies. She was commenced on hydroxychloroquine 200 mg twice a day, along with a titration dose of oral prednisolone. Dimethyl fumarate was prescribed for her MS.

She established care with rheumatology and neurology at our facility in 2019 for SLE and MS, respectively, and was then referred to nephrology due to new onset proteinuria and microscopic hematuria in the setting of active lupus serologies and positive PR3 antibody found on her initial laboratory workup at our facility. Her serum creatinine was normal at 70 μmol/L. Her repeat laboratory tests at our facility included positive PR3 antibody of 5.7 antibody index (AI) (0.0-0.9 AI), an elevated erythrocyte sedimentation rate of 50 mm/h (0-10 mm/h), and a positive extractable nuclear antibody panel with positive double-stranded DNA antibodies at 34 IU/mL (<5 IU/mL), positive chromatin antibodies at 46 AI (0.0-0.9 AI), and positive anti-Ro antibodies >8 AI (0.0-0.9 AI). Her initial physical examination revealed intact extraocular movements without nystagmus, bilateral equal pupils reactive to light, no facial asymmetry, mild decreased sensation over the right side of the face, hyperreflexia in all extremities with bilateral plantar responses, decreased sensation over the right arm and leg, and dystaxia on heel-to-shin testing bilaterally. There were no skin rashes, including vasculitic lesions, joint tenderness, or joint swelling. A renal biopsy was performed in 2019 and revealed pauci-immune necrotizing crescentic glomerulonephritis, which is consistent with acute PR3-ANCA-associated vasculitis rather than lupus nephritis (Figure 1). Due to the overlap syndrome, it was determined that she required additional immunosuppression, and she was started on intravenous rituximab in September 2019, which was administered every 6 months. She had an excellent response, with resolution of her previously reported joint pain, rashes, microscopic hematuria, and proteinuria, as well as clinical and radiological evidence of MS stability. On her routine magnetic resonance imaging (MRI) of the body 1:160 homogeneous pattern, positive double-stranded DNA antibodies by enzyme-linked immunosorbent assay and C3 antibodies, and positive anti-Ro antibodies. She was commenced on hydroxychloroquine 200 mg twice a day, along with a titration dose of oral prednisolone. Dimethyl fumarate was prescribed for her MS. There was no family history of connective tissue disease. She is the mother of 2 healthy children and has no history of miscarriage or arterial or venous thrombosis. She continued to receive care at an outside hospital for MS and systemic lupus erythematosus (SLE) with relative stability of her SLE but did have infrequent flares of MS requiring courses of IVIG and as needed prednisolone.
right superior midbrain. This progression was thought to be due to her CD19 count reaching 2% or above on multiple occasions prior to receiving her rituximab dose, due to patient’s poor compliance. Her next rituximab dose was administered in June 2022, and her most recent MRI in June 2022 revealed stable findings with no new or enhancing demyelinat ing lesions (Figures 2 and 3). Written informed consent for the article was obtained from the patient.

Discussion

To the best of our knowledge, this is the first case of an individual having MS, SLE, and ANCA-associated vasculitis all at the same time. Generally, clustering of autoimmune diseases is well illustrated in families, either as coexistences or as overlaps.1 In a Greek study,2 it was found that approximately 1% of SLE patients also met MS criteria, but neither was associated with severe phenotypes. Furthermore, 9 patients were identified in the literature who met the criteria for SLE-MS overlap, and it was discovered that the coexistence of SLE and MS was uncommon.3 Our PubMed literature search yielded no results for case reports of patients with MS, SLE, or vasculitis. To that end, we included cases of similar overlap from 2 diseases out of 3 (MS and SLE, MS and ANCA vasculitis, and SLE and ANCA vasculitis). There were 2 case reports of MS and SLE, both of which began with optic neuritis.4,5 The first patient4 developed right foot paresis and numbness, urinary retention, and hemolytic anemia as a result of SLE, which responded well to methylprednisolone, INF-beta-1a, and rituximab. The second patient5 experienced bilateral wrist pain and a malar rash that improved with prednisolone and hydroxychloroquine. There was 1 case report of SLE and granulomatosis with polyangiitis6 with a complicated course with multiple relapses after being treated with prednisolone, cyclophosphamide, and rituximab, which resulted in remission of her symptoms. There was an early case of MS and eosinophilic granulomatosis with polyangiitis7 of an unfortunate gentleman who had recurrent relapses of both MS and vasculitis that were treated with prednisolone alone. The final case report was of a woman with mixed connective tissue disease and EGPA8,9 who was diagnosed after developing constitutional symptoms such as polyarthrits, pleuritis, and Raynaud’s phenomenon. She was given methylprednisolone first, followed by prednisolone maintenance. Corticosteroids were used in the treatment plans of many of the cases mentioned above. Our patient was treated with intravenous rituximab and achieved clinical and biochemical remission as early as 6 months following induction, which was maintained up to 2 years later.

Conclusion

This case highlights the complexity of overlap syndromes, which occur when more than 2 autoimmune diseases cluster in the same

**Main Points**

- This case is an example of an extremely rare presentation of overlap syndrome with a favorable outcome.
- Although systemic lupus erythematosus, antineutrophil cytoplasmic antibodies, and multiple sclerosis overlap syndrome is a very rare entity, this case highlights the importance of performing a kidney biopsy as soon as possible in a patient with new-onset proteinuria and hematuria.
- A multidisciplinary approach with rheumatology, neurology, and nephrology is warranted in the setting of such autoimmune overlap.
individual, that often require a multidisciplinary approach for early diagnosis and guidance for the most appropriate immunosuppressive therapy. Furthermore, determining which disease entity is more prominent at presentation and which entity may recur after remission is a challenge when dealing with such complex conditions, requiring a keen clinical eye and close monitoring.

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References