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Anti-MuSK Antibody-Associated Myasthenia Gravis in Vasculitic Neuropathy on Rituximab Therapy

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Abstract

Background: Co-occurrence of multiple autoimmune diseases is common, but developing a second autoimmune condition during treatment for an existing one, particularly under immunosuppressive therapy, is rare. This case highlights the development of Muscle Specific Kinase (MuSK) positive Myasthenia Gravis (MG) in a patient with biopsy-proven non-systemic vasculitic neuropathy (NSVN) treated with rituximab. *Case Report*: A 74-year-old male initially presented with right foot drop, diagnosed as sensorimotor axonal neuropathy. He was treated with methylprednisolone and later rituximab for non-systemic vasculitic neuropathy. Despite some improvement, he developed progressive muscle weakness, bulbar symptoms, and respiratory failure. Anti-MuSK antibodies were positive, confirming MuSK-positive MG. A myositis panel showed borderline anti-Ro52 positivity, and systemic malignancy was excluded. Treatment with pyridostigmine and steroids led to significant recovery, including weaning off mechanical ventilation. *Conclusion*: The development of MuSK-positive MG during rituximab treatment for NSVN is a novel and paradoxical finding. This case highlights the complexity of diagnosing and managing co-existing autoimmune diseases, suggesting that genetic factors and immune dysregulation may contribute to such occurrences. The patient's response to pyridostigmine and steroids supports an immune-mediated origin for the MG.

Keywords: Autoimmune Diseases, Muscle Specific Kinase (MuSK), Myasthenia Gravis, Neuropathy, Steroids.

Introduction

The co-existence of many autoimmune diseases is not unusual. Patients who already have one autoimmune illness may later develop another one in as many as 25% of cases [1]. There have been earlier reports of up to five autoimmune diseases co-existing. However, it is extremely uncommon for a patient receiving treatment for one autoimmune illness to develop a second one. This case describes the previously unreported occurrence of Muscle Specific Kinase (MuSK) positive Myasthenia Gravis (MG) in a patient who was on second line immunosuppressant for biopsy proven non-systemic vasculitic neuropathy.

Case Report

A 74-year-old male in his usual state of health initially presented with an isolated right foot drop one year ago. Nerve conduction study showed sensorimotor axonal neuropathy involving the right common peroneal nerve. He was treated with methyl-prednisolone pulse as he was unwilling to undergo a nerve biopsy. His symptoms improved completely. After a span of four months, he developed weakness of his right lower limb, followed by right upper limb weakness. Nerve biopsy from right sural nerve revealed dense perivascular lymphocytic infiltrates around epineural vessels and acute axonal breakdown, implying an inflammatory neuropathy.

After thorough evaluation of systemic causes of vasculitis, a diagnosis of non-systemic vasculitic neuropathy (NSVN) was arrived at, and the patient was treated with one gram of methylprednisolone intravenously for five days followed by two doses of rituximab one week apart. Despite a brief improvement, his problems eventually got worse. He had gradual progression of weakness which involved his proximal limb muscles on the right. He had difficulty climbing stairs. Change in voice, nasal regurgitation, and exertional dyspnea were noticed by his family four months ago. A month ago, he was brought unresponsive to the emergency department. On examination, he was drowsy and had poor respiratory effort. Arterial blood gases showed CO_2 retention, confirming type 2 respiratory failure. The patient was intubated because of poor sensorium. Computed Tomography chest showed bilateral lower lobe consolidation. On regaining consciousness, he had difficulty moving his limbs. Power was grade 0 in proximal muscles, with grade 2 distally. Eye closure and extraocular movements were normal. Initially, confluent mononeuritis multiplex was considered. However, prominent bulbar symptoms with respiratory failure were very unusual in vasculitic neuropathy prompting evaluation for an alternate cause. 2 Hz and 50 Hz Repetitive Nerve Stimulation elicited normal responses. Intravenous immunoglobulin (400 mg/kg × 5 days) was initiated. Anti CD20 levels were zero and hence further doses of rituximab were not contemplated. The patient's clinical course was stormy, with waxing and waning of sensorium and need for mechanical ventilation and tracheostomy. Anti-MuSK levels returned positive after two weeks (anti-acetylcholine receptor antibody was negative on multiple occasions). Myositis panel showed borderline anti-Ro52 positivity. Patient was put on 180 mg of pyridostigmine per day and 0.5 mg/kg of steroids. There was a remarkable response over the next one week, with the patient coming off mechanical and later non-invasive ventilation. His motor response had also improved marginally during this period. Whole Body Positron Emission Tomography scan done to rule out systemic malignancies was negative.

Discussion

The probability of developing a second autoimmune illness in myasthenia gravis is 22%. The second immunological insult can be organ specific like thyroiditis, myositis, or myocarditis, or multisystemic like SLE or rheumatoid arthritis [2]. In MuSK positive MG, however, relatively few such instances have been observed. In one such report, a 53-year-old man on treatment for rheumatoid arthritis was diagnosed with MuSK-positive MG after 10 years [3]. An association with non-systemic vasculitic neuropathy has not been reported previously. Genetic factors like HLA association and CTLA4 gene polymorphisms may underlie the co-occurrence of these distinct immunological entities in the same patient [4,5]. When multiple autoimmune diseases co-exist with MG, the prognosis is typically dire because of the intensified immune response. In our patient there was emergence of a MuSK antibody mediated myasthenia while on rituximab which is a novel observation. This is paradoxical as the latter shows best response to rituximab in majority of cases although the clinical response to various immunological agents is very often inconsistent [6]. The response to IVIG and steroids albeit modest and too early to comment further lends support to the immune aetiology.

Another highlight of the present case is the atypical clinical scenario for MuSK antibody associated myasthenia. The clinical pitfalls in its diagnosis has received lot of interest in recent studies because of overlap with clinical features of other neurological entities like motor neuron disease, MNGIE (Mitochondrial neurogastrointestinal encephalopathy) and atypical parkinsonism [7].

Conclusion

This case presents a novel occurrence of MuSK-positive Myasthenia Gravis (MG) in a patient with non-systemic vasculitic neuropathy (NSVN), treated with rituximab. The development of MG during immunosuppressive therapy, particularly rituximab, is paradoxical given rituximab's established efficacy in MG treatment. This highlights the complex and unpredictable nature of autoimmune diseases and their treatments. Genetic factors and immune dysregulation may contribute to the co-occurrence of distinct autoimmune conditions, and the atypical presentation of MuSK-positive MG emphasizes the importance of considering alternative diagnoses in patients with unusual neurological symptoms. The patient's positive response to pyridostigmine and steroids further supports an immune-mediated etiology for MG.

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