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Dual Benefit of Methotrexate in Psoriatic Arthritis and Myasthenia Gravis: A Case Report

Shrushti Dalal[1,*], Freya Shah[2], Aditya Parekh[3], Dan Olson[4]

[1]PGY Internal Medicine, Western Reserve Health Education, Warren, Ohio, USA

[2]PGY Landmark Medical Center, USA

[3]MD Internal Medicine, Summa Health, USA

[4]MD Internal Medicine, Trumbull Mahoning Medical Group, USA

[*]Correspondence should be addressed to Shrushti Dalal, shrushtidalal97@gmail.com

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Abstract

Psoriatic arthritis (PsA) is a chronic inflammatory condition affecting approximately 30% of individuals with psoriasis, while myasthenia gravis (MG) is an autoimmune neuromuscular disorder caused by antibodies targeting acetylcholine receptors, leading to progressive muscle weakness. Although autoimmune diseases often coexist, concurrent presentation of PsA and MG is exceedingly rare and poorly documented. We describe a 66-year-old male with a longstanding history of psoriasis and PsA, previously well controlled on methotrexate, who developed seropositive generalized MG after discontinuation of his methotrexate therapy. When methotrexate was reintroduced for PsA management, he demonstrated marked and sustained clinical improvement in both his psoriatic disease and neuromuscular symptoms. This case highlights the challenges of managing coexisting autoimmune conditions and emphasizes the need for further investigation and clearer guidance for such complex clinical scenarios.

Keywords: Methotrexate, Psoriatic arthritis, Myasthenia gravis

Background

Psoriatic arthritis is an immune-mediated inflammatory condition that affects approximately 30% of individuals with psoriasis [1]. It typically manifests either before, at the same time as, or—most commonly—several years following the onset of skin lesions. The underlying factors that determine why only a subset of psoriasis patients develop psoriatic arthritis remain poorly understood.

Myasthenia gravis (MG) is an antibody-mediated autoimmune disorder in which pathogenic antibodies target acetylcholine receptors, impairing neuromuscular transmission and leading to fluctuating muscle weakness. This weakness classically worsens with sustained or repetitive activity. Based on 35 studies published up to 2007, the incidence of MG ranges from 1.7 to 21.3 per million person-years, with an estimated global incidence of approximately 5.3 per million person-years [2].

While substantial progress has been made in understanding each condition individually, research on the management of patients with coexisting inflammatory arthritis and myasthenia gravis remains limited. Autoimmune diseases are known to often coexist, with the presence of one increasing the likelihood of developing others. However, cases involving the simultaneous occurrence of inflammatory arthritis and myasthenia gravis are rarely documented in the literature. This highlights the necessity for continued research and the development of clear, evidence-based management guidelines for these complex clinical scenarios.

We present the case of a 66-year-old male patient, treated with methotrexate for psoriatic arthritis, who also achieved symptom control for concurrent myasthenia gravis.

Case Presentation

A 66-year-old male presented to the emergency department with a two-month history of progressively worsening proximal muscle weakness in both upper extremities, dysphagia, diplopia, and dysarthria. These symptoms had notably worsened over the past week. His past medical history included well-controlled gout treated with allopurinol, hypertension, hyperlipidemia, type 2 diabetes mellitus, psoriasis, and psoriatic arthritis, for which he had been prescribed methotrexate 7.5 mg weekly.

Upon admission, the patient's vital signs were stable. Neurological examination revealed difficulty swallowing liquids and bilateral ptosis that worsened with sustained upward gaze. Motor testing showed a strength of 4/5 in the upper limbs with noticeable fatigability, and the patient had difficulty rising from a chair without arm support. Sensory and cerebellar examinations were unremarkable.

Initial laboratory investigations, including complete blood count (CBC), comprehensive metabolic panel (CMP), and urinalysis, were within normal limits. Creatine kinase was 77 U/L, aldolase 4.1 U/L, thyroid-stimulating hormone (TSH) 5 µU/mL, lactate dehydrogenase (LDH) 236 U/L, and myoglobin 65 ng/mL. A CT scan of the head ruled out acute stroke, hemorrhage, or mass lesions. Given the presentation of fatigable weakness, myasthenia gravis was suspected. A contrast-enhanced CT scan of the chest revealed no evidence of mediastinal masses or thymoma.

During his hospitalization, the patient demonstrated clinical improvement with corticosteroid therapy and was discharged with a prescription for pyridostigmine. Follow-up electrodiagnostic testing, including repetitive nerve stimulation electromyography (EMG), showed findings consistent with myasthenia gravis. Serologic tests confirmed elevated acetylcholine receptor antibodies, both blocking and binding, leading to a diagnosis of seropositive myasthenia gravis.

At a one-month follow-up with neurology, the patient reported persistent symptoms with minimal relief from pyridostigmine. While initially beneficial, the medication had since become less effective. It was hypothesized that the patient's prior immunosuppressive therapy with methotrexate may have masked the earlier manifestations of myasthenia gravis. A review of his medical history revealed that methotrexate had been discontinued a year before symptom onset to facilitate healing of a chronic right foot ulcer.

Considering the timeline, methotrexate was reinitiated, and prednisone was gradually tapered. The patient subsequently showed significant improvement in his myasthenia gravis symptoms. Eight years later, he remains in clinical remission from myasthenia gravis while continuing treatment with methotrexate monotherapy.

Discussion

Myasthenia Gravis (MG) is an autoimmune disorder characterized by the production of autoantibodies against acetylcholine receptors (AChR antibodies) located on the postsynaptic membrane of the neuromuscular junction (NMJ), leading to impaired receptor function and disrupted neuromuscular transmission. This results in progressive muscle weakness, with a hallmark feature being that muscle strength improves with rest and worsens with exertion. Several other autoantibodies targeting proteins of NMJ like muscle-specific tyrosine kinase (MuSK) and lipoprotein receptor-related protein 4 (LRP-4) antibodies have also been found in patients with MG. MG is classified into ocular MG, which involves the extraocular muscles and presents with symptoms such as ptosis, diplopia, or both, and generalized MG, where any voluntary muscle may be affected [3]. MG is also known to be associated with various other autoimmune conditions, including systemic lupus erythematosus, autoimmune thyroiditis, rheumatoid arthritis, psoriasis, and hypothyroidism. While the literature documents an increased risk for patients with MG to develop secondary autoimmune diseases, the exact pathophysiological mechanisms remain poorly understood. One retrospective study observed that psoriasis was present in approximately 4% of patients with MG in the cohort. This study also noted that the clinical presentation of MG tended to be milder when accompanied by other autoimmune diseases, a finding consistent with the clinical course observed in our case [4].

Psoriatic arthritis is a chronic inflammatory arthritis associated with psoriasis and influenced by a combination of genetic, environmental, and immunologic factors. Clinical manifestations commonly include joint swelling, tenderness, stiffness, and pain. A distinguishing feature is dactylitis—sausage-like swelling of the digits—resulting from inflammation of joints, tendons, ligaments, and surrounding soft tissue in the hands and feet [5]. Pharmacologic management typically begins with nonsteroidal anti-inflammatory drugs (NSAIDs) for mild symptoms. However, early initiation of conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs) is critical to slowing disease progression, with methotrexate (MTX) being the most commonly prescribed csDMARD. In addition, biologic agents such as anti-TNF, anti-IL-17/23 agents, and PDE-4 inhibitors have been approved for use. More recently, Janus kinase (JAK) inhibitors have also been introduced as effective treatment options for psoriatic arthritis.

Methotrexate, a dihydrofolate reductase inhibitor, is well-established as a first-line DMARD for inflammatory arthritis. While its role in the treatment of myasthenia gravis (MG) remains less defined, MTX has been explored as a potential immunosuppressive agent, particularly as a steroid-sparing option in cases of generalized MG that are refractory to first-line therapies [6,7]. Our case highlights the potential utility of methotrexate in achieving disease control in patients with coexisting generalized myasthenia gravis and psoriatic arthritis. This observation supports further consideration of methotrexate as a dual-purpose agent in managing overlapping autoimmune conditions and highlights the importance of early therapeutic intervention to achieve optimal disease remission.

Summary

Our case demonstrates that methotrexate (MTX) can be a safe and effective steroid-sparing agent in the management of myasthenia gravis. However, there is a lack of established clinical guidelines for the treatment of patients with concurrent psoriatic arthritis or inflammatory arthritis and myasthenia gravis, underscoring the need for further research to develop targeted management strategies for such cases.

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