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Myasthenia gravis (MG) with rheumatoid arthritis (RA): co-association and co-treatment In a Palestinian female patient

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Abstract

Introduction

Neuromuscular transmission disorders result from genetic, toxic, or immunological causes and can lead to muscle weakness and fatigue, especially after physical activity. Myasthenia gravis is the most commonly acquired disease caused by autoantibodies attacking signaling proteins at the neuromuscular junction. Other autoimmune diseases, such as autoimmune thyroiditis and systemic lupus erythematosus, are common in MG patients, and a small percentage may also have rheumatoid arthritis.

Case presentation

A 46-year-old woman was diagnosed with seropositive Rheumatoid Arthritis at 27 and later with Myasthenia Gravis due to muscle weakness. Despite multiple treatment regimens, including Prednisolone, Methotrexate, and etanercept, her disease was not well controlled. Thymectomy alleviates symptoms, followed by a current regimen of hydrocortisone and rituximab.

Discussion

Myasthenia gravis (MG) is a neuromuscular autoimmune disorder commonly linked to rheumatoid arthritis (RA). The incidence of RA in MG patients is between 1-4%, while RA patients have a higher prevalence of MG. Methotrexate is a primary treatment for RA, but its effectiveness on MG is limited. Some treatments like etanercept and tocilizumab have shown promise, but others like TNFi and Ipilimumab have caused worsening symptoms or development of MG. Rituximab has been successful in reducing disease symptoms in RA patients.

Conclusion

Myasthenia gravis linked to RA, methotrexate primary RA treatment, conflicting TNFi effectiveness in MG, tocilizumab, ipilimumab linked to MG onset, rituximab reduces RA symptoms.

Keywords: Rheumatology, Case report, rare cases, myasthenia gravis, Autoimmunity, Etanercept.

Introduction

Neuromuscular transmission disorders are uncommon and might have genetic, toxic, or immunological causes. The most prevalent acquired disease of these disorders is myasthenia gravis (MG), which is brought on by autoantibodies attaching to signaling proteins at the neuromuscular junction (NMJ). The nicotinic acetylcholine receptor is one of these proteins, as is the less frequently occurring muscle-specific tyrosine kinase (MuSK), which is essential in nicotinic acetylcholine receptor clustering. The symptoms of these disorders are brought on by a typical weakening of the affected muscles, which worsens after use. The extrinsic ocular muscles (EOMs) exhibit early symptoms in roughly two-thirds of individuals. Generalized MG (gMG) typically develops as the symptoms spread to other bulbar muscles and leg muscles. Ocular MG (OMG) is a disease where symptoms are exclusive to the EOM and affect roughly 10% of MG patients.**[1]**

A second autoimmune disease is more common in MG patients (around 13–22%), with autoimmune thyroiditis being the most prevalent (10–12%) and systemic lupus erythematosus being the second-most prevalent (1–8%).**[2]**

Rheumatoid arthritis (RA) is a systemic autoimmune disease characterized by a chronic inflammatory process that can result in irreversible joint destruction and severe disability. Less commonly, RA can induce inflammatory changes in extra-articular locations, such as the heart, kidney, lung, digestive system, eye, skin, and nervous system. Between (1-4%) of MG patients are reported to have rheumatoid arthritis (RA).**[3]**

Herein we present a case of an older woman with rheumatoid arthritis who later developed myasthenia gravis. At 27, she was diagnosed with rheumatoid arthritis 18 years later. She began complaining of palpebral ptosis and generalized muscle weakness, which led to the diagnosis of Myasthenia Gravis.

This work has been reported in line with the SCARE criteria used by authors, journal editors, and reviewers to increase the robustness and transparency in reporting surgical cases.

Case Presentation

Patient Information

- Age: 46
- Gender: Female
- Medical History: Diagnosed with seropositive Rheumatoid Arthritis (RA) at 27 years old
- Presenting Complaint: Joint pain and stiffness

History of Present Illness

At the age of 27, the patient presented with typical symptoms of joint pain and stiffness, predominantly affecting the wrist, metacarpophalangeal, and proximal interphalangeal joints. Diagnostic evaluation led to the diagnosis of seropositive RA. Notably, there was no prior significant medical history, and the patient had no family history of autoimmune diseases.

Treatment History

- Initial Treatment: The patient was initiated on a treatment regimen consisting of Prednisolone 10 mg, leflunomide 10 mg, Methotrexate (20 mg once a week), and azathioprine 50 mg. However, despite treatment, minimal improvement was observed.
- Treatment Modification: Due to inadequate disease control, the treatment regimen was adjusted after three months. The revised regimen included Prednisolone (5 mg twice daily), Methotrexate (10 mg once a week), and Etanercept 50 mg.
- Response to Treatment: Although there was improvement in laboratory parameters such as CRP and ESR, the patient continued to experience joint pain and stiffness, indicating incomplete disease control.

Development of Myasthenia Gravis

- In 2010, the patient began experiencing palpebral ptosis and generalized muscle weakness, prompting further evaluation.
- Diagnosis: Myasthenia Gravis was confirmed based on clinical presentation and diagnostic tests.
- Treatment: Pyridostigmine was initiated, but the patient's symptoms persisted and worsened, impairing her ability to eat due to muscular weakness.
- Intervention: Thymectomy was performed one year after the diagnosis of Myasthenia Gravis, aiming to alleviate symptoms and improve disease management.

Follow-Up

- Despite the surgical intervention, ongoing monitoring and management are necessary to address both RA and Myasthenia Gravis symptoms comprehensively.
- Multidisciplinary Approach: Given the complexity of the patient's conditions, a collaborative approach involving rheumatologists, neurologists, and other specialists is crucial for optimizing treatment outcomes and enhancing quality of life.

Table. 1

Before Entanrecept	ESR: 150	CRP: 80
After Etanrecept	ESR: 30	CRP: 15

Discussion

The neuromuscular junction is affected by the autoimmune disease myasthenia gravis, which is frequently linked to other autoimmune conditions, including rheumatoid arthritis. Compared to the general population, myasthenia gravis is more common among rheumatoid arthritis patients. The prevalence of rheumatoid arthritis (RA) in MG patients is believed to be between 1 and 4 percent **[13,14]**. In contrast, RA patients had a higher prevalence of MG than the general population (84/100.000 versus 35.8/100.000) **[15]**. There are various treatment possibilities for both of these disorders, including rituximab, Methotrexate, and glucocorticoids.

There aren't many reports of people who have both RA and MG, but those who have MG and are being treated with anti-rheumatic medications may be able to provide more data. Because of that, we are reporting this case.

The primary treatment for RA is Methotrexate, despite not showing effectiveness on MG **[1]**, which is nevertheless recommended as a potential steroid-sparing treatment in MG that is refractory. **[2]**

While some findings indicate that etanercept may effectively decrease MG symptoms in some people, we discovered conflicting evidence regarding tumor necrosis factor Inhibitors (TNFi) **[4]**. Others connected patients who had TNFi medication for RA and psoriatic arthritis (PsA) with symptoms getting worse or developing MG **[5, 6, 7, 8]**. Interleukin-6 inhibitor tocilizumab has been used successfully in two patients with MG who had not responded to RTX **[9]**. A Nivolumab-induced MG in a cancer patient is responsive to abatacept, a recombinant Cytotoxic T-Lymphocyte Antigen 4 (CTLA4), a fusion molecule used in RA **[10]**. Ipilimumab, an anti-CTLA four

checkpoint inhibitor used to treat melanomatous skin cancer, shows an intriguing association with the onset or progression of MG **[11]**. In patients with active rheumatoid arthritis, despite methotrexate therapy, a single course of two infusions of rituximab, either alone or in combination with cyclophosphamide or continuing Methotrexate, significantly reduced disease symptoms at weeks 24 and 48 **[12]**.

Conclusion

Myasthenia gravis is an autoimmune disease that affects the neuromuscular junction and is linked to other autoimmune conditions, including rheumatoid arthritis. The primary treatment for RA is Methotrexate, but there are conflicting reports on the effectiveness of tumor necrosis factor inhibitors (TNFi) in decreasing MG symptoms. Interleukin-6 inhibitor tocilizumab and anti-CTLA4 checkpoint inhibitor ipilimumab have shown some association with the onset or progression of MG. Rituximab, either alone or in combination with other treatments, has successfully reduced disease symptoms in RA patients. Further research is needed to understand the relationship between RA and MG and the effectiveness of treatments for both conditions.

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