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Coexistence of anti-synthetase syndrome, myasthenia and scleroderma: A scarce case report

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ABSTRACT

Introduction. Polyautoimmunity refers to the phenomenon where an individual is affected by multiple autoimmune diseases simultaneously. This condition underscores the complexity of autoimmune disorders and their interconnected nature, often resulting from shared genetic predispositions and overlapping immunological mechanisms. In this report, we present a case that exemplifies the coexistence of myasthenia gravis, scleroderma, and anti-synthetase syndrome in a female patient. The combination of these three distinct autoimmune conditions highlights the challenges faced by clinicians in diagnosis and management.
We herein report a case that illustrates the coexistence of myasthenia, scleroderma and anti-synthetase syndrome in a female patient.

Case description. A 45-year-old female patient was referred for systemic sclerosis, without respiratory or muscular involvement. Two years later, she presented with dyspnea and muscle fatigue. She had mechanic's hands and bilateral symmetric proximal muscle weakness. Laboratory investigations revealed CK levels at 995 IU/L and positive anti-PL7 antibodies. Thoracic CT showed diffuse interstitial lung disease. Spirometry demonstrated a restrictive lung disease. The electroneuromyogram (ENMG) showed a myopathic pattern. Diagnosis of anti-synthetase syndrome was established. Treatment was initiated with monthly cyclophosphamide infusions.
Seven months later, she presented with left ptosis and worsening dyspnea and muscle fatigue. An intravenous immunoglobulin infusion was administered, than the patient was commenced on mycophenolate mofetil. She showed a slight improvement, than she developed dysphagia. Brain MRI and cerebrospinal fluid were normal. Onconeuronal antibodies were negative. The ENMG did not reveal any decrement, but the acetylcholine receptor antibody level was positive at 1.12 nmol/L. Consequently, with the presence of ptosis, dysphonia and dysphagia, the diagnosis of myasthenia gravis was established. Imaging did not reveal a thymoma.
A favorable therapeutic response was achieved with intravenous immunoglobulins and pyridostigmine.

Conclusions. Patients with autoimmune diseases necessitate meticulous management and monitoring because they are at risk for developing multiple immune-mediated disorders, either simultaneously or in succession over the course of their illness. This phenomenon, known as polyautoimmunity, can complicate the clinical picture, as overlapping symptoms and disease manifestations may make diagnosis challenging.

Keywords: myasthenia, scleroderma, anti-synthetase syndrome, idiopathic inflammatory myopathies, multiple autoimmune syndrome

INTRODUCTION

Myasthenia gravis (MG) is a chronic condition that affects neuromuscular transmission, leading to significant muscle weakness and fatigue. This autoimmune disorder has been linked to idiopathic inflammatory myopathies (IIM), which also manifest with similar symptoms of muscle weakness. In this report, we present a unique case involving a female patient who was diagnosed with myasthenia gravis

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alongside anti-synthetase syndrome and scleroderma. The coexistence of these conditions is uncommon, highlighting the complexity of autoimmune disorders and their potential to overlap in clinical presentations. This case emphasizes the importance of careful diagnosis and management in patients exhibiting signs of multiple autoimmune diseases.

CASE PRESENTATION

A 45-year-old female patient was referred for systemic sclerosis, without respiratory or muscular involvement. Two years later, she presented with dyspnea and muscle fatigue. She had mechanic's hands and bilateral symmetric proximal muscle weakness. Laboratory investigations revealed CK levels at 995 IU/L and positive anti-PL7 antibodies. Thoracic CT showed diffuse interstitial lung disease. Spirometry demonstrated a restrictive lung disease. The electroneuromyogram (ENMG) showed a myopathic pattern. Diagnosis of anti-synthetase syndrome was established. Treatment was initiated with monthly cyclophosphamide infusions.

Seven months later, she presented with left ptosis, and worsening dyspnea and muscle fatigue. An intravenous immunoglobulin infusion was administered, than the patient was commenced on mycophenolate mofetil. She showed a slight improvement, than she developed dysphagia. Brain MRI and cerebrospinal fluid were normal. Onconeuronal antibodies were negative.

The ENMG did not reveal any decrement, but the acetylcholine receptor antibody level was positive at 1.12 nmol/L. Consequently, with the presence of ptosis, dysphonia and dysphagia, the diagnosis of MG was established. Imaging did not reveal a thymoma.

A favorable therapeutic response was achieved with intravenous immunoglobulins and pyridostigmine.

DISCUSSION

Myasthenia gravis (MG) is a relatively rare autoimmune neurological disorder characterized by impaired transmission at the neuromuscular junction [1,2]. This impairment is often mediated by antibodies that target the acetylcholine receptor (AChR) or other proteins integral to the neuromuscular junction, such as muscle-specific tyrosine kinase (MuSK). Notably, about 11% to 15% of MG patients are classified as double-seronegative [3,4], meaning they do not exhibit detectable antibodies against either AChR or MuSK, which was the case for our patient.

The hallmark symptoms of myasthenia gravis include muscle weakness and fatigue, which can fluctuate in severity and may worsen with exertion. While MG can occur independently, its association with other autoimmune diseases is considered relatively uncommon, with reports indicating a co-occurrence rate of approximately 11.6% to 13% [3,5]. Understanding these associations is crucial for clinicians, as the presence of multiple autoimmune conditions can complicate diagnosis and treatment, necessitating a comprehensive approach to patient management.

Idiopathic inflammatory myopathies (IMs) encompass a diverse group of muscle disorders, including polymyositis (PM), dermatomyositis (DM) — which also includes amyopathic dermatomyositis — as well as inclusion body myositis, immune-mediated necrotizing myopathy, antisynthetase syndrome, and overlap myositis [6,7]. The simultaneous occurrence of myasthenia gravis (MG) and IMs, referred to as MG-IM, is relatively uncommon but has been documented in several case series.

In a literature review conducted by Ying Zhu et al., a total of 69 cases of MG-IM were identified [8]. The findings from this review indicated that over 60% of individuals diagnosed with this combination had an underlying thymoma, suggesting a significant relationship between thymus pathology and the development of these overlapping conditions. Among the cases of MG-IM, polymyositis with thymoma was noted as the most frequently associated disorder. Additionally, a specific case report described the coexistence of MG with inclusion body myositis in a 75-year-old man [9]. This underscores the need for heightened clinical awareness and investigation when managing patients with myasthenia gravis, particularly for the potential presence of other inflammatory myopathies and related conditions

The association of MG and anti-synthetase syndrome is exceptional. To our knowledge, the first case was reported in 2004 [10].

Polyautoimmunity refers to the phenomenon in which an individual is affected by more than one autoimmune disease simultaneously. This complex interplay can complicate both diagnosis and treatment, as the presence of multiple autoimmune conditions can lead to overlapping symptoms and varied disease manifestations. When a patient presents with three or more distinct autoimmune diseases at the same time, this condition is specifically termed multiple autoimmune syndrome (MAS) [11,12].

The concept of MAS was first introduced by Humbert and Dupond in 1988, highlighting the need for a framework to understand the coexistence of these disorders [13]. This classification has important implications for clinical practice, as it emphasizes the necessity for comprehensive evaluation and management strategies tailored to patients with multiple autoimmune diseases. Recognizing MAS can aid healthcare providers in anticipating complications and optimizing treatment plans to address the unique

challenges posed by this syndrome.

We herein report a case of MAS. It illustrates, to our knowledge, the second reported case of coexistence of MG, IM and scleroderma, and the first case where IM is anti-synthetase syndrome.

The initial case of polyautoimmunity involving myasthenia gravis and other autoimmune disorders was documented in 1993 in Poland [4]. This particular case involved a 58-year-old female patient who tested positive for PM-Scl antibodies, which served as an important immune marker. Unlike our patient, she had a persistent thymus and also exhibited acetylcholine receptor antibodies. Her treatment regimen included corticosteroids at a daily dose of 30 mg, along with Mestinon (pyridostigmine) administered three times daily, to manage her symptoms effectively.

Similar to our patient's presentation, a study examining the characteristics of patients diagnosed with myasthenia gravis in conjunction with other autoimmune disorders found that these patients were predominantly female. Furthermore, this study noted a lower incidence of thymoma among these individuals compared to other MG patients. The clinical manifestations of myasthenia gravis in this cohort tended to be milder, indicating that the presence of additional autoimmune conditions may influence the severity and expression of MG. This highlights the complexity of autoimmune diseases and the need for personalized treatment approaches based on individual patient profiles.

CONCLUSIONS

The mechanisms that contribute to the development of autoimmune diseases, as well as their coexistence, remain largely unclear. This phenomenon may be linked to shared immunological pathways that involve different autoimmune targets, yet originate from a common genetic predisposition. Various factors, such as environmental triggers, infections, and dysregulation of the immune system, may also play significant roles in this complex interplay.

Although the coexistence of myasthenia gravis (MG) and idiopathic inflammatory myopathies (IMs) has been documented in numerous studies, the association with scleroderma is notably rare. This rarity suggests that while overlapping autoimmune mechanisms may exist, the specific pathways leading to each condition may differ significantly. The unique characteristics of scleroderma, including its effects on connective tissue and vascular systems, further complicate the potential for coexistence with MG and IMs.

Understanding these underlying mechanisms is crucial for developing effective management strategies and treatment protocols for patients presenting with multiple autoimmune conditions. Further research is needed to elucidate the interactions among these diseases and to identify potential therapeutic targets that can address the complexities of polyautoimmunity.

Learning points:

- The coexistence of three or more autoimmune diseases in a patient constitutes multiple autoimmune syndrome.
- Patients suffering from autoimmune diseases necessitate special consideration, given the potential coexistence of various immune-mediated disorders throughout the disease progression.

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Ethics approval:
Ethics committee approval was deemed not necessary in our institutions for case reports.

Conflict of interest: nothing to disclose

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