CASE REPORT

Unveiling the uncommon: a captivating case of multiple autoimmune syndrome

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ABSTRACT

Multiple autoimmune syndrome (MAS) is characterized by the coexistence of three or more autoimmune diseases. We are reporting a unique case of MAS, presented as a Myasthenia Gravis exacerbation, found to have unexpected sero-abnormalities. A 39-year-old female presented with complaints of progressive difficulty swallowing of solids and liquids, droopy eyelids, and facial weakness. Physical examination revealed bilateral ptosis and proptosis, slow-muffled speech, loss of EOM, inability to smile, puff cheeks, clench teeth, or protrude tongue and an asymmetrical shoulder shrug. Motor tone was normal except $4/5$ in the left arm and $3/5$ in left hand with loss of flexion at left DIP joints. Acetylcholine receptor binding antibodies, ANA, Antithyroid peroxidase, antithyroglobulin and Anti SS-A were positive. MAS, while not a life-threatening condition, greatly degrades patients' quality of life. We recommend that when you encounter patients with one or more autoimmune disorder, you consider MAS in your differential.

KEYWORDS: multiple autoimmune syndrome; myasthenia gravis; thyroiditis

BACKGROUND

Incidence rate of autoimmune disease (AD) is around 80/100000 per year, and prevalence is higher in women than men [1]. Multiple autoimmune syndrome (MAS) is characterized by the coexistence of three or more autoimmune diseases and was first described in 1988 [2]. Combination of two autoimmune disorders is known as polyautoimmunity. Twenty Five percent of individuals with one autoimmune disease tend to develop other autoimmune disorders [3]. Additionally, coexistence of five or more conditions is rarely observed [4,5]. In MAS, one of the conditions typically affects the skin, like vitiligo, scleroderma, psoriasis, etc. [4,5]. The pathogenesis of MAS is unknown, but it is believed that familial or genetic, infectious, immunologic, and psychological factors have been implicated in the development of MAS [2,3]. Based upon their frequency of association, MAS has been classified into 3 types:

Type I: Myasthenia Gravis, Thymoma, Polymyositis and Giant cell myocarditis.

Type II: Sjogren's syndrome, Rheumatoid arthritis, Primary biliary cirrhosis, Scleroderma and Autoimmune thyroid disease (AITD).

Type III: Autoimmune thyroid disease, Myasthenia Gravis and/or Thymoma, Sjogren's syndrome, Pernicious anemia, Idiopathic thrombopenic purpura, Addison's disease, Type I Diabetes mellitus, Vitiligo, Autoimmune hemolytic anemia, Systemic lupus erythematosus, Dermatitis herpetiformis.

This classification helps to identify which condition is more likely to appear in a patient with preexisting two autoimmune conditions, which may provide a basis for underlying pathophysiology in autoimmune disorder [5]. Here in, we report a case of MAS, which presented as a Myasthenia Gravis exacerbation but was found to have unexpected sero-abnormalities on investigation.

CASE PRESENTATION

A female in her late 30s presented with complaints of progressive difficulty in swallowing for solids and liquids. Patient reported dysphagia for several months with coughing on swallowing and two days of inability to lie flat due to the same. Patient reports many years of droopy eye lids and progressive left facial weakness, left shoulder and arm weakness. She has a history of untreated Myasthenia Gravis without prior exacerbation, Syndrome-X, iron deficiency anemia (IDA), and polyarthralgia which was treated with Methotrexate and folate on an outpatient basis. Patient reported her Primary care physician (PCP) diagnosed her with Rheumatoid Arthritis, but no records found of outside investigations.

On admission vitals were: T-98°F (36.67°C), HR-102, BP-138/103, RR-18 and SpO2-99% on room air. On physical examination: Patient had bilateral ptosis and proptosis, slow-muffled speech with nasal tone, loss of extraocular movement (EOM), ability to smile, puff cheeks, clench teeth, protrude tongue and asymmetrical shoulder shrug.

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Sensation, taste, salivation, and lacrimation were intact. Motor tone was normal except 4/5 in the left arm and 3/5 in left hand with loss of flexion at left distal interphalangeal (DIP) joints. No joint destruction was observed on the left DIP on physical examination (Jaccoud's arthropathy).

Labs were notable for CRP (16.670 mg/L), ESR (80 mm/hr), Acetylcholine receptor (AchR) binding antibodies 4.97 nmol/L (normal <0.30 nmol/L). CT chest was only positive for a 2 cm left thyroid nodule. TSH (0.686 UIU/mL) and T4 (1.08 mg/dL) were WNLs but free T3 was decreased at 2.1 pg/ml. Patient was started on steroids, pyridostigmine and IVIG. She improved clinically. Later ANA titers were elevated at 1:160. Rheumatoid factor (RF) (<14 IU/mL), Anti SCL-70 (<0.1 AI), Anti-smith and anti-dsDNA (2 IU/mL) were negative. However, possibility of rheumatoid arthritis cannot be completely rule out as we did not get anti CCP titers. Antithyroid peroxidase antibody (46 IU/mL), antithyroglobulin antibody (124 IU/mL) and SS-A (3.4 AI) came back positive. FNAC of thyroid nodules under US guidance, showed benign follicular cells, colloids, macrophages, and scattered lymphocytes. She was discharged on pyridostigmine and tapering steroids, and advised close follow-up with PCP and rheumatologist.

DISCUSSION

It is not uncommon to consider the presence of one autoimmune disorder as a potential risk factor for developing another. While the exact mechanisms behind the development of multiple autoimmune disorders remain elusive, it is widely believed that environmental factors can trigger these conditions in individuals with a genetic predisposition. For instance, research suggests that Cytomegalovirus infection may lead to the production of various autoantibodies, contributing to the onset of multi-organ autoimmune disorders. In our case report, we aim to underscore the importance of recognizing that the diagnosis of one autoimmune condition may increase the likelihood of developing additional ones. Therefore, it is advisable to conduct thorough evaluations for related autoimmune conditions, particularly those within the same group. For instance, in our case patient with MG, when we search for extensive autoimmune panel to see for MAS type 1 vs. type 3, abnormal value of ANA, antithyroid peroxidase, antithyroglobulin and anti SS-A, and normal CT scan for thymoma, normal value for anti-SCL 70 were obtained, which supports diagnosis of MAS type 3. We obtained AchR antibody titers as diagnosis was made in her childhood in her home country by her physician who told her verbally, but we never had any labs or documentation available supporting that; additionally, rare number of cases are available with seronegative AchR antibody MG, in whom first line of approach should be plasmapheresis than the anticholinesterase inhibitors.

Our case stood out due to the initial diagnosis of MG during childhood, followed by the development of additional autoimmune conditions. It is noteworthy to mention that a previous literature indicated that 15% of MG patients also experienced at least one other autoimmune disorder [6]. This may be attributed to the pronounced severity of MG symptoms, prompting patients to seek medical attention. Furthermore, the study highlighted that thyroid conditions were the most commonly associated autoimmune disorders with MG, a finding corroborated by Mao et al. in their research [7].

In our scenario, the patient exhibited antithyroid peroxidase antibody and antithyroid globulin antibody presence alongside a decreased T3 level, while TSH and T4 levels remained within normal ranges. These findings lend credence to the suggested link between autoimmune thyroid conditions and myasthenia gravis. Despite the absence of true hypo- or hyperthyroidism, it's important to consider the presence of proptosis as a potential feature. Additionally, Marino et al. and Chen et al. have independently highlighted in their research that the ocular variant of MG tends to be more commonly associated with autoimmune thyroid disease (AITD), particularly Graves' disease presenting with ophthalmological symptoms, and this association is notably prevalent among female patients [8,9]. In these particular groups, the occurrence of thymic hyperplasia was observed to be less common than other types of generalized MG. Moreover, according to Gilhus et al., females with MG, particularly those with early onset and generalized symptoms, exhibited a higher susceptibility to other autoimmune diseases compared to the general population [10].

After AITD, Rheumatoid arthritis (RA) is a common AD associated with MG [7,11]. SLE stands out as a prevalent autoimmune disorder, alongside Sjögren's syndrome, often linked with systemic connective tissue or organ-specific autoimmune ailments. Our case also showed presence of anti SS-A and elevated ANA titers, however subsequent RF, anti-DNase and anti-smith were negative. However, we could not be able to get anti CCP levels. The occurrence of Sjögren's syndrome can impact the manifestation of other autoimmune diseases, potentially heightening fatigue, and the risk of lymphoma. While the mechanisms driving this syndrome remain unclear, its prevalence might surpass current estimations [12].

Additionally, a heightened occurrence of neoplasms in Myasthenia Gravis and other autoimmune disorders is not uncommon. Beyond thymoma, the susceptibility to other tumors outside the thymus is also elevated in MG, with a prevalence rate ranging from 3% to 12% [13-16], This susceptibility could stem from both immune dysregulation and the use of immunosuppressive therapies. Additionally, AD is linked with conditions such as Diabetes Mellitus as well as hyperlipidemia (HLD), likely attributed to immune dysregulation and the administration of steroids. However, it is noteworthy that statins, although effective in managing HLD, may exacerbate symptoms of MG [17].

Additional conditions found in various combinations in MAS are: Type 1: pemphigus and autoimmune thyroid disease; Type 2: Chronic active hepatitis (CAH), SLE, pemphigus, bullous pemphigoid, AIHA, ITP, alopecia areata and Addison's disease; Type 3: Acquired primary hypogonadism, hypophysitis, RA, PBC, relapsing polychondritis, multiple sclerosis, CAH, ulcerative colitis, and scleroderma [18]. Other diseases seen in different combinations are ulcerative colitis, autoimmune hemolytic anemia, alopecia areata, scleroderma, multiple sclerosis.

CONCLUSION

In this case report, we emphasize the importance of closely monitoring patients with one or more autoimmune disorders to ensure their well-being and quality of life. While not typically life-threatening, multiple autoimmune syndrome significantly impacts daily life. It is essential to remain vigilant for the development of additional autoimmune disorders,

particularly those falling within the same category. Additionally, diligent surveillance is necessary for other associated health conditions and potential malignancies due to prolonged immunosuppressive therapy. Furthermore, educating patients is crucial to ensure their understanding and compliance with treatment regimens and close follow-up.

Disclosure

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Informed consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

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