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Intestinal pseudo-obstruction in a myasthenia gravis patient after thymectomy: A case report and literature review

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Abstract

Intestinal pseudo-obstruction in patients with myasthenia gravis is a rare and poorly understood phenomenon. We report a case coexisting with intestinal pseudo-obstruction and myasthenia gravis. The patient was diagnosed to have myasthenia gravis and underwent thymectomy seven years ago. He was tested positive for anti-acetylcholine receptor antibody and was free of thymoma recurrence during the current illness. Despite being given gastrointestinal decompression and parenteral nutrition, the patient's gastrointestinal symptoms did not improve. Symptoms were rectified effectively by immunomodulatory therapy. This case adds intestinal pseudo-obstruction to the phenotypic profile of post-thymectomy myasthenia gravis. High titer of AChR antibody might play a role in the pathogenesis of myasthenia gravis with intestinal pseudo-obstruction.

Keywords: Intestinal pseudo-obstruction, myasthenia gravis, anti-acetylcholine receptor antibody, immunomodulatory therapy

INTRODUCTION

Intestinal pseudo-obstruction (IPO) is characterized by gastrointestinal dysmotility in the absence of mechanical obstruction. Myasthenia gravis (MG) is a well understood autoimmune disease. The common clinical features include ptosis (80–100%), limb weakness (25–100%), weakness of bulbar muscles (6–50%), weakness of axial muscles (50%), weakness of facial muscles (0–13%), and dyspnea (0.3%).[1] It is not difficult to diagnose patients with typical characteristics of MG. However, clinical presentations can vary significantly, with most patients experiencing weakness in the skeletal muscles while some patients having weakness in the smooth muscles. Here, we present a case of intestinal pseudo-obstruction in a MG patient after thymectomy. Further, we summarize cases of coexistent IPO and MG that have been reported previously. (Table 1)

CASE REPORT

A 25-year-old male visited the gastroenterology department due to abdominal distention, nausea, and constipation lasting seven days as of December 2022. Previously diagnosed with MG, he had undergone a thymectomy seven years prior. At the time of his MG diagnosis, pyridostigmine treatment was initiated and maintained for the first four years. Two years ago, the patient suffered an MG crisis characterized by a significant increase in anti-acetylcholine receptor (AChR) antibody levels to 8.00 nmol/L. Subsequent thymic computed tomography (CT) scans did not reveal any signs of thymic hyperplasia or thymoma. He was successfully treated with intravenous immunoglobulin (0.4 g/kg/day) for five days, along with pyridostigmine 240 mg/day. This treatment combination controlled his MG symptoms for nine months, enabling him to work as a driver without medication thereafter.

During the current hospital admission, a physical examination identified a distended abdomen with no bowel sounds and rectal examination revealed fecal impaction. Comprehensive laboratory tests including routine blood work, and assessments of liver, kidney, and thyroid functions, all returned results within normal ranges. Tests for antinuclear antibody, anti-double stranded DNA (dsDNA) antibody, anti-ribonucleoprotein (RNP) antibody, anti-histidyl transfer RNA synthetase (Jo-1) antibody, anti-neutrophil cytoplasmic antibody,

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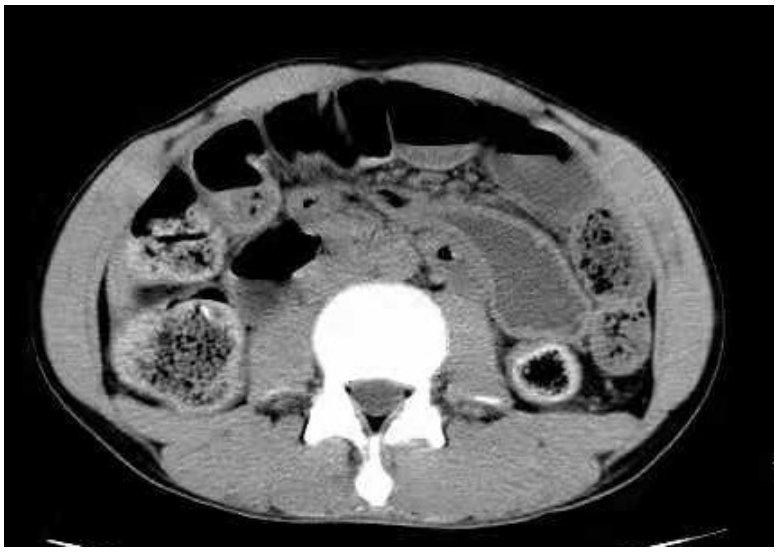

Figure 1. abdominal CT of patient showing distended loops with air-fluid levels.

and tumor markers were negative. Further imaging with enhanced thymic CT confirmed the absence of thymic hyperplasia or recurrent thymoma. Abdominal CT showed distended bowels but no obstructive intestinal lesions (Figure 1).

Despite gastrointestinal decompression and parenteral nutrition, the patient's IPO condition did not improve. On the 10th day of hospitalization, he developed ptosis of the left eye and diplopia. Additional laboratory tests confirmed elevated levels of anti-acetylcholine receptor (AChR) antibody (13.00 nmol/L), while tests for anti-muscle-specific kinase (MuSK) antibody, anti-voltage-gated potassium channel Kv1.4 antibody, and anti-titin antibody returned negative results. Immunological screenings for paraneoplastic neurological syndromes, including tests for anti-CV2/collapsin response mediator protein 5 (CRMP5) antibody, anti-glutamic acid decarboxylase 65 (GAD65) antibody, anti-SRY-related HMG-box gene 1 (SOX1) antibody, anti-amphiphysin antibody, anti-Hu antibody, and anti-Yo antibody were also negative. Consequently, a coexisting diagnosis of IPO and MG was established. Treatment with pyridostigmine was initiated at 180 mg/day. The patient's overall condition continued to decline, marked by persistent abdominal pain, constipation, and a weight loss of 10 kg. By the 23rd day of hospitalization, he was treated with intravenous immunoglobulin (0.4 g/kg/day) and prednisone (50 mg/day) for five days, during which his pyridostigmine dosage was increased to 240 mg/day. Six days following the commencement of immunomodulatory therapy, notable improvements were observed in his symptoms of abdominal distention, nausea, and constipation. However, his ptosis and diplopia persisted unchanged. A month later, his symptoms were completely resolved with ongoing pyridostigmine and prednisone treatment (Figure 2). At the 12-month follow-up, the patient remained recurrence-free.

DISCUSSION

Intestinal pseudo-obstruction in patients with MG remains a poorly understood condition. Intestinal motility is regulated by complex mechanisms involving extrinsic autonomic nerves, the enteric nervous system, and smooth muscle function. Acetylcholine, nitric oxide, and neuropeptides are key neurotransmitters implicated in this control system.[2] Typically, the primary manifestation of neurological diseases affecting the gastrointestinal tract is altered motor function. Common gastrointestinal symptoms and syndromes associated with neurological disorders include dysphagia, gastroparesis, IPO, constipation, and fecal incontinence.[2] Various mechanisms underlying neurological disorders related to the gastrointestinal tract lead to diverse symptoms. Inflammatory cell infiltrates within the intestinal plexus were observed in an IPO patient with MG.[3] IPO related to MG is characterized as a motility disorder of the intestine that mimics the clinical and radiological features of intestinal obstruction without a mechanical cause.[4] Sporadically, MG has been implicated in predisposing patients to

Figure 2. Weight changes are shown in the blue line. QMGS changes are shown in the yellow line. QMGS quantitative myasthenia gravis scale

disturbances in intestinal motility, suggesting it as a potential cause of IPO.[5]

To the best of our knowledge, in all but one case (Table 1), MG coexisted with thymomas, thus raising concerns regarding the potential paraneoplastic nature of this clinical manifestation from the gastrointestinal tract.[6-8] Our patient was unique in that he exhibited no recurrence of thymoma during an episode of intestinal pseudo-obstruction, and the antibodies related to paraneoplastic neurological syndromes were all negative except for the AChR antibody. The patient presented with IPO, MG, and a history of thymectomy performed seven years earlier. Notably, the gastrointestinal symptoms preceded the appearance of typical MG symptoms, a sequence similar to those reported in previous studies.[6-8] Among the 13 cases, seven reported improvement in gastrointestinal symptoms following thymectomy (Table 1). However, our patient developed gastrointestinal symptoms seven years post-thymectomy, and imaging studies revealed no evidence of thymoma recurrence. Additionally, while pyridostigmine was reported effective in four cases for treating gastrointestinal symptoms, it was not effective for our patient. Interestingly, other autoimmune antibodies associated with MG were not reported in patients with IPO.

It is noteworthy that AChR antibody was the only antibody reported in the previous cases, and the titer of AChR antibodies was high in four seropositive patients. Gastrointestinal dysmotility may result from autoimmune autonomic dysfunction. Recently, there has been an increased focus on the interaction between autonomic nerves and the immune system. The autonomic nervous system can either be a part of systemic autoimmune disorders or the primary target of autoimmunity. Approximately 70% of patients with autoimmune autonomic disorders experience gastrointestinal symptoms.[14] Ganglionic AChR antibodies are associated with autoimmune autonomic dysfunction. Vernino *et al*.[13] reported that autoantibodies to AChRs in ganglionic neurons were found in patients with subacute autonomic neuropathy and MG. In a case series of seven patients with MG and dysautonomia, all had AChR antibodies (three ganglionic-type + muscle-type and four muscle-type).[13] The high titer of ganglionic-receptor autoantibodies correlates with the severity of autonomic dysfunction.[15,16] Dhamija *et al*.[17] conducted a serologic evaluation of autoimmune gastrointestinal dysmotility, finding AChR antibodies (11 ganglionic-type and four muscle-type) in 15 out of 23 patients. While ganglionic AChR antibody was not tested in our case, a high titer of muscle-type AChR antibody was observed. The amino acid sequence of the ganglionic AChR antibody is approximately 60% identical to that of the muscle-type AChR antibody.[18] It is postulated that this close resemblance may lead to cross-reactivity. Given the unnecessary surgery, we hypothesized that our patient's persistent gastrointestinal symptoms could have been caused by autoimmune autonomic neuropathy associated with AChR antibodies. His gastrointestinal symptoms responded positively

Table 1: Summary of patients with intestinal pseudo-obstruction and myasthenia gravis

Author (reference)	Age/ Sex	Clinical manifestations	AchR (nmol/L)	gAchR (pmol/L)	IPO precedes MG	Thymoma	Thymectomy effective	PRY effective	Immune modulate effective	Surgery on IPO effective
Rakocevic *et al*.[3]	28/M	Severe bilateral ptosis and facial weakness	16.5	NA	Y	NT	N	N	N	Y
Anderson *et al*. [5]	48/M	Mild left ptosis, bilateral slow adduction saccades,	18	NA	N	NT	N	Y	NA	N
Anderson *et al*.[5]	70/F	Bilateral ophthalmoparesis, weakness of neck flexion	2.2	NA	Y	NT	Y	Y	NA	N
Pande *et al*.[6]	64/M	Bilateral ptosis, bilateral complete ophthalmoplegia, pupillary involvement	1.7	255	N	IT	Y	N	N	N
Malhotra *et al*.[7]	53/M	Bilateral ptosis, ophthalmoplegia	negative	NA	Y	IT	N	N	NA	N
Greenburg *et al*.[8]	36/M	Intermittent diplopia, dysgeusia, and sicca symptoms	negative	NA	N	NT	N	N	Y	N
Musthafa *et al*.[9]	45/M	Ptosis, ophthalmoparesis	NA	NA	Y	NT	Y	NA	NA	N
Kidher *et al*.[10]	41/M	Bilateral, limb weakness	25.2	NA	Y	IT	Y	N	NA	N
Seretis *et al*.[11]	34/F	Mild, bilateral ptosis, ophthalmoplegia	NA	NA	N	NA	NA	N	NA	Y
Alnajjar *et al*.[12]	38/M	Generalized fatigue	>8	negative	Y	IT	Y	NA	Y	N
Vernino *et al*.[13]	29/M	Diplopia, left ptosis, mild dysarthria	2.42	negative	Y	IT	Y	Y	NA	NA
Vernino *et al*.[13]	12/M	Generalized fatigue	0.2	negative	N	NT	Y	Y	NA	NA
Vernino *et al*.[13]	64/M	Severe bilateral ptosis, complete ophthalmoplegia	1.7	255	Y	IT	N	NA	NA	NA

F, female; M, male; IT, invasive thymoma; NT, noninvasive thymoma; N, No; Y, yes; NA, not available; PRY, Pyridostigmine

to immunomodulatory therapy, suggesting that his rapid recovery was due to the accelerated clearance of pathogenic autoantibodies by the therapy.

In conclusion, our report extends the phenotypic profile of post-thymectomy MG to include intestinal pseudo-obstruction. A high titer of AChR antibody might play a role in the pathogenesis of MG associated with intestinal pseudo-obstruction. Immunomodulatory therapy can be considered a viable treatment option for patients with MG that involves intestinal pseudo-obstruction.

DISCLOSURE

Ethics: Informed consent was obtained from the patient for publication of this case report.

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Conflict of interest: None

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