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Letter to the Editor: New Observation

Gastrointestinal Dysmotility as the First Manifestation of Myasthenia Gravis

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Gastrointestinal involvement in myasthenia gravis (MG) and thymoma is rare but has been described previously[1,2]. Symptoms include abdominal pain, recurrent vomiting, weight loss, and constipation secondary to intestinal pseudo-obstruction.

Acetylcholine receptor antibodies (AChRAb) directed at the α1 subunit of the acetylcholine receptors (AChR) in skeletal muscle impair neuromuscular transmission in MG. AChR in autonomic ganglia are structurally similar to muscle AChR, but contain the α3 subunit[3]. Autonomic ganglia AchR located on myenteric neurons are implicated in the regulation of gastrointestinal motility[3].

Vernino et al.[4] described the presence of ganglionic AChRAb in patients with autoimmune autonomic neuropathies such as idiopathic gastrointestinal dysmotility. In a case series of 24 patients with autoimmune gastrointestinal dysmotility, 15 patients had AChRAb (11 ganglionic type and 4 muscle type)[5].

Here, we report a patient with autoimmune gastrointestinal dysmotility with thymoma who had muscle-type AChRAbs and abnormal neuromuscular transmission.

A 38-year-old man had the insidious onset of nausea along with early satiety, epigastric abdominal discomfort, constipation, generalized fatigue, and a weight loss of 24 lb. He did not have ocular, bulbar, or limb weakness. The neurological examination was normal. CT scan of the abdomen demonstrated bowel wall thickening indicating bowel obstruction. Diverticulitis causing his obstruction was considered and he was prescribed antibiotics for 6 weeks. He did not respond and his symptoms and clinical status worsened steadily. Exploratory laparotomy excluded mechanical reasons for obstruction. He underwent a repeat CT scan of the abdomen and on cuts showing the lower thoracic area, a mass in his pleura was evident. A CT scan of his chest showed an anterior mediastinal mass, 3.4 cm in diameter, and multiple left pleural deposits, the largest being 5.8 cm in diameter. He had a biopsy of the pleural deposits that showed B2 malignant thymoma. He had AChRAb >8.0, and the anti-ganglionic AChR-specific antibody assay was negative. Repetitive nerve stimulation studies of the right facial nerve were normal. A single fiber electromyography (SFEMG) study of the right frontalis muscle showed increased jitter of 83.5 μs, 60% abnormal pairs and 40% blocking pairs indicating impaired neuromuscular transmission. His bowel obstruction was felt to be paraneoplastic in origin, and he was treated with an intravenous immunoglobulin (IVIG) loading dose of 2g/kg given over 2 days followed by 1 g/kg every 4–6 weeks and six cycles of chemotherapy (CISPLATIN and ETOPOSIDE) plus prednisone 75 mg daily for 1 month tapered gradually. He then had an extended pleurectomy and decortication. The pathology report revealed type B2 thymoma (WHO) involving the lung with pleural drop metastases (Masaoka stage IV). Thereafter, he was treated on an outpatient basis, with low-dose prednisone at 10 mg daily and dose adjustments according to his gastrointestinal symptoms. These symptoms resolved and the patient continued to be monitored closely for 7 years. He remained on a low dose of prednisone at 10 mg three times a week without clinical evidence of MG or gastrointestinal symptoms. The prednisone was discontinued and 10 months later the patient developed swallowing difficulties and nasal speech. He did not have ocular or limb weakness. He had a repeat CT scan chest that showed no evidence of progression. He was restarted on prednisone 75 mg daily for 1 month and this has been tapered gradually to a dose of 50 mg daily followed by IVIG 1 g/kg every 4 weeks and his myasthenic symptoms improved. His gastrointestinal symptoms had resolved previously and did not recur.

In summary, we report a patient who presented with intestinal pseudo-obstruction as the first manifestation of a metastatic thymoma. He had elevated skeletal muscle AChRAb, normal anti-ganglionic AChRAb, and an abnormal SFEMG but remained neurologically asymptomatic except for generalized fatigue, consistent with the diagnosis of subclinical paraneoplastic MG. This patient had a good response to thymectomy, chemotherapy, and steroids for both the thymoma and the gastrointestinal dysmotility syndrome. He developed clinical MG 7 years after the gastrointestinal presentation.

An autoimmune autonomic neuropathy with gastrointestinal dysmotility has been described in patients with thymoma and was associated with autonomic ganglia acetylcholine receptors (Table 1).[4] In addition, a co-occurrence of myasthenic syndrome and autonomic dysfunction in patients with thymoma showing both muscular and ganglionic AChRAb has been described.[6]. Our patient presented with gastrointestinal autonomic dysfunction with positive muscle AChRAb and negative ganglionic AChRAb. Considering that ganglionic AChRAb is 60% identical

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Table 1: Antibody status and clinical presentations in different case reports of AChR (skeletal muscle-type) and AChR (ganglionic-type) antibodies

	Gastrointestinal dysmotility syndrome	MG Syndrome	MG Syndrome + Gastrointestinal dysmotility syndrome
AChR (skeletal muscle type)	Current case	Typical autoimmune MG phenotype	7 cases,[9–11]
AChR (ganglionic type)	4 cases[12–15]	Not reported	Not reported
AChR (muscle type) + (ganglionic type)	Not reported	2 cases[16]	4 cases[2,6,17]

in amino acid sequence to the muscle type AchRAb,[7] cross-reactivity might be a possible explanation for the gastrointestinal autonomic dysfunction in our patient despite the negative ganglionic AChRAb status.

MG is an autoimmune disease that affects the postsynaptic membrane at the neuromuscular junction affecting the voluntary muscles of the body and the skeletal muscle AchRAb are frequently positive[8]. Gastrointestinal autonomic symptoms in myasthenic syndrome have a differential diagnosis including Lambert–Eaton myasthenic syndrome or medication side effects. Considering our patient and previous reports, it seems that autoimmune autonomic disorders such as gastrointestinal dysmotility in a myasthenic patient might be explained as a paraneoplastic syndrome in the context of thymoma or as a phenomenon caused by muscle and ganglionic AChRAb cross-reactivity, in addition to medication side effects or a diagnosis of Lambert–Eaton mysathenic syndrome.

This unusual case joins the list of reports about cancer patients with unexpected paraneoplastic events delayed a long time after treatment of the tumor and alerts clinicians who are involved in the diagnosis and treatment of such patients[9–11].

Conflicts of Interest. The authors have no conflict of interest to declare.

Statement of Authorship. SA: writing, review, and editing. JI: writing, review, and editing. DF: review and editing. GL: review and supervision. VB: writing, review, editing, and supervision.

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