Case Report and Review of the Literature

Autoimmune Ganglionic Enteropathy Associated with Myasthenia Gravis and Thymoma

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ABSTRACT

Background: Autonomic neuropathies causing gastrointestinal complications are uncommon. Case Presentation: We report a case in which autoimmune autonomic enteric neuropathy was associated with myasthenia gravis and thymoma. Conclusion: Autoimmune autonomic enteric neuropathies are exceedingly rare, with only 10 cases reported in the literature to date. All have been associated with thymoma. We describe the prevalence of associated antibodies, summarise the previous cases and treatment received.

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1. Introduction

Gastrointestinal dysmotility may arise in inherited and degenerative neurological disorders, connective tissue diseases such as lupus and scleroderma, as a complication of various infections and as part of a more generalised autonomic neuropathy. Patients may present with symptoms due to gastroparesis, intestinal pseudo obstruction or colonic hypomobility. Early case reports noted an association between the disorder and cancer, leading to a supposition that the neuropathy was a paraneoplastic disorder; however, more recently, a relationship with other autoantibodies and autoimmune diseases has been identified. The disorder appears to be very rare, and this case adds to the literature and summarises our understanding of the pathogenesis and treatment to date.

2. Case Presentation

A 60-year-old lady presented with a three-month history of vomiting, gastric distension and weight loss, which had had a rather abrupt onset then progressively worsened. She was able to swallow well, but the food did not pass further, and she would then regurgitate. She underwent upper and lower gastrointestinal endoscopies with no abnormality seen. Ultimately her bowel failed altogether, and she passed neither flatus nor faeces. She was admitted to hospital where the general examination was normal and screening blood investigations unremarkable aside from low albumin. In hospital, her vomiting continued, and she developed abdominal distension. Three years previously, she had developed Grave’s disease, treated with carbimazole, and she had received regularly prescribed maintenance thyroxine since then. Pernicious anaemia had been diagnosed a year after.

During her initial investigations in hospital, she was noted to experience intermittently slurred speech and then difficulty with swallowing. At a neurological consultation, she was found to have facial weakness and weakness of eye closure, a nasal escape, slow tongue movements, dysphagia for solids and a symmetrical proximal fatiguing muscle weakness with retained reflexes and normal sensation. An MRI scan of the brain was normal. Neurophysiological investigations revealed evidence for a disorder of conduction at the neuromuscular junction (Figures 1 & 2). Large fibre conduction was normal, and the electromyogram showed no evidence for myopathy or myositis.

Endoscopic studies of the colon and stomach were unremarkable. Gastric emptying studies using technetium-99m sulphur colloid showed prolonged retention of the meal within the stomach with an estimated t½ of 231 minutes compatible with prominent gastroparesis. She was fed parenterally and improved. Acetylcholine receptor and striated muscle antibody levels were elevated. A CT scan of the chest was undertaken, which showed thymic enlargement. The thymus was removed, and a grade B3 thymoma was identified. She was found to have a3 ganglionic

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acetylcholine receptor antibodies. No other antibody (aside from that to intrinsic factor) was identified.

Figure 1: Single fibre electromyogram (SFEMG) of the left frontalis muscle showing significant abnormal jitter.

![Figure 1](image1)

She was treated with pyridostigmine at modest doses, and she made improvements over the course of the following six months. It was recommended that she undergo immunosuppression and treatment with intravenous immunoglobulin or plasma exchange in order to attempt to recover gastrointestinal function, but she chose to continue with total parenteral nutrition, preferring not to return to the disorder of abnormal gastric emptying.

3. Discussion

It has long been known that myasthenia gravis may complicate the development of thymoma; there are many fewer reports of the development of an autoimmune autonomic enteric neuropathy at the same time. All cases so far reported (which number only 10) have been associated with thymoma [1-3]. Patients with myasthenia may have more widespread autonomic dysfunction [4], including cardiovascular instability including postural hypotension and disturbances of cardiac rhythm, anhidrosis, pupillary disorders, the sicca syndrome, urinary and sexual dysfunction less common [5]. Enteric neuropathy may complicate other diseases, notably diabetes mellitus, and mitochondrial myopathies comprising the mitochondrial neurogastrointestinal encephalopathy (MNGIE) syndrome.

40% have α3 ganglionic acetylcholine receptor antibodies; these receptors mediate fast transmission within autonomic ganglia, and mice without these receptors have profound autonomic failure [6]. When exposed to sera containing the antibodies, whole-cell AChR current reduces, in keeping with antigenic modulation [7]. Antibody titre correlates with disease activity [6, 8, 9]. They are seen as paraneoplastic phenomena in small cell lung cancer, thymoma and malignant lymphoproliferative diseases. Patients may have other antibodies, such as ANNA-1, CRMP-5, Hu and GAD [8]. In a review of 24 patients with gastrointestinal dysmotility 11 had cancer, and there was a high prevalence in the remainder of organ-specific autoantibodies [10]. In these patients, the disorder was adjudged to be autoimmune.

Our case exemplifies the disorder clearly; the presentation was subacute with increasing symptoms of an enteric neuropathy culminating in cessation of intestinal function. A neurological assessment within the gastroenterology department revealed more widespread neuromuscular signs than had been recognised, allowing the correct further series of investigations to be undertaken, leading to the diagnosis. The subsequent identification of α3 ganglionic acetylcholine receptor antibodies confirms the association of the thymoma with the autonomic disorder. It is surely of relevance that she had previously been found to have other antibody-associated autoimmune diseases.

Patients respond to acetylcholinesterase inhibitors and metoclopramide, corticosteroids and immune suppression. There are reports of response to IVlg and apheresis, and in those with a subacute or acute onset, this form of therapy is recommended followed by steroid therapy and immunosuppression for 3-5 years [5, 11].

4. Conclusion

Autoimmune enteric neuropathy is a most uncommon condition, and when identified, requires a clear and successful search for the causative antigen. Treatment of the underlying disorder as well as the neuropathy is oftentimes highly successful.

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Conflicts of Interest

None.

Competing Interests

None.
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Data Availability Statement

The data are available in the Neurophysiology Department, Hertford County Hospital.

Author Contributions

Dr. Kanabar and Dr. Kidd were responsible for the study concept and design, acquisition of data and analysis and interpretation. Both authors were responsible for a critical revision of the manuscript for important intellectual content. Dr. Kidd was the study supervisor.

Consent

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

REFERENCES