Case Report

Gastroparesis, Thymoma, and Asymptomatic Myasthenia: A Rare Clinical Scenario

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Abstract: Background: Paraneoplastic gastroparesis is a gastrointestinal syndrome that rarely precedes a tumor diagnosis. To increase awareness of this rare clinical entity, we present a case of severe gastroparesis, which was later proven to be associated with a thymoma. Case report: A 55-year old man had the sudden onset of severe abdominal cramps and abdominal distension, early satiety with postprandial nausea, acid regurgitation, belching, and flatulence. He lost about 20 pounds. The physical and imaging examination revealed stomach distension, gastroparesis, and the presence of a solid mass in the anterior mediastinum. Radical surgery was performed to remove the thymoma and, given the high value of Mib-1, the patient was submitted to postoperative chest radiation therapy. After thymectomy, a diagnosis of paraneoplastic myasthenia gravis with subacute autonomic failure was made. Conclusion: Autoimmune gastroparesis should be considered as a potential paraneoplastic syndrome in patients with thymoma, myasthenia gravis, and delayed gastric emptying in the absence of mechanical obstruction.

Keywords: thymoma; gastroparesis; paraneoplastic syndrome

1. Introduction

A diagnosis of thymoma is made in 10–15% of patients with myasthenia gravis (MG) [1]. Dysautonomia is not necessarily a feature of MG, the latter being associated with gastrointestinal autonomic failure only in some rare cases of thymoma. Such an association was the basis of gastroparesis in a patient described by Tabbaa et al. [2] who reported a slow recovery only after thymectomy. This surgery improved intestinal pseudo-obstruction in another case of thymoma reported by Tan et al. [3]. Thymoma-associated MG was considered the cause of intestinal pseudo-obstruction in two patients described by Anderson et al. [4]. Starting from their case series, Vernino et al. [5] assumed that paraneoplastic MG may trigger autonomic symptoms, such as autoimmune gastrointestinal dysmotility (AGID), by means of autoantibodies against ganglionic acetylcholine receptors (AChRs), as the symptom relief following the anticholinesterase (pyridostigmine) treatment suggested. Even in this experience, a case of gastroparesis as the clinical presentation of AGID faded with thymectomy. Due to the extreme rarity of gastroparesis in thymoma patients, here we updated the current literature with a further case of this kind of paraneoplastic disease.
2. Case Presentation

In October 2018, a 55-year-old man had the sudden onset of severe abdominal cramps and abdominal distension, early satiety with postprandial nausea, acid regurgitation, belching and flatulence. He lost about 20 pounds and three months later he was admitted to a general surgery department following the onset of intestinal pseudo-obstruction with rectum closed to feces and gas. Esophagogastroduodenoscopy revealed stomach distension and computed tomography (Figure 1) showed distension of some bowel loops with thickened walls, thickening of the mesenteric adipose tissue, slowing of the transit of iodine-based contrast agent and the presence of a 55 mm solid mass with sharp outlines in the anterior mediastinum. A radionuclide motility study (Figure 2) of the esophagus–gastroduodenal transit documented stagnation of the marked meal in the gastric lumen in the absence of signs of distal progression, the emptying time was extremely prolonged (no gastric empty after 2 h), and 18-F FDG PET/CT documented 18-F FDG uptake at the mediastinal mass (SUVmax 16.8). At this time, the recommendation was a surgical approach, and in April 2019 the patient was submitted to surgery to remove thymoma; histological examination showed a thymoma B1, Stage II-a, pT1a pNx; MIB-1 70%. Due to the high value of Mib-1, chest radiation therapy was delivered (50 Gy/25 fractions) using the daily image-guided intensity-modulated technique [6–10]. No treatment-related toxicity was observed. After thymectomy and during irradiation gastric symptoms persisted. In the suspicion of a paraneoplastic thymoma-related AGID, the following investigations were performed: serologic evaluation for paraneoplastic autoantibodies revealed ARAB (anti-acetylcholine receptor antibody) with a value of 1.20 nmol/L (normal range, <0.4 nmol/L) and single-fiber electromyography of the common extensor muscle of the fingers revealed increased jitter (mean consecutive difference, MCD = 51 μsec) with a defect of neuromuscular transmission. The diagnosis was of paraneoplastic MG with subacute autonomic failure. After starting pyridostigmine therapy, the patient improved, gradually showing weight gain and, to date (2021, December), he feeds regularly in the absence of recurrent disease. The patient has given written informed consent to publish his case, including the publication of images.

Figure 1. Computed tomography shows distension of some loops of the small bowel, stomach distension, and the presence of a solid mass in the anterior mediastinum on the left, in the paracardiac area.
Figure 2. Scintigraphic study shows no gastric empty after 2 h.

3. Discussion

We report a rare case of thymoma associated with MG and paraneoplastic AGID, which remained long after thymectomy (Figure 3). Despite being one of the most common mediastinal tumors (47% of tumors in the anterior mediastinum) [11], thymoma has a low global incidence ranging from 1.3 to 1.7 cases per million people [12] and a 5-year survival varying from 30% to 100% according to the disease stage, which has gone through many changes during the years, as well as the histologic classification [13,14]. The rarity of thymoma-associated MG makes any related gastrointestinal dysfunctions hard to be suspected even further. The thymus is a primary lymphoid organ whose main function is T-cell maturation and differentiation by means of positive and negative selection; the first ensures the functionality of major histocompatibility complex (MHC) for a competent immune system, while the second prevents the development of autoimmunity by turning off any T cells that would be able to react against self-antigens. When the latter mechanism is disrupted due to the presence of neoplastic thymic epithelial cells, immune-mediated paraneoplastic syndromes may develop [15]; if negative selection does not work, the immune system is not prevented from cross-reacting against self-antigens [16]. Moreover, auto-reactive T lymphocytes are characterized by a slow post-thymectomy clearance from peripheral blood and this could explain the delayed symptom relief following surgery, as reported by our patient.

Figure 3. Computed tomography shows persistence of stomach distension three months after thymectomy.
The most common thymoma-associated paraneoplastic syndrome is myasthenia gravis, the symptoms of which follow the antibodies-mediated inactivation of the postsynaptic AChR in the neuromuscular junction [17]. Acetylcholinesterase inhibitors increase the synaptic availability of acetylcholine, which, by displacing autoantibodies from its receptors, restore neuromuscular transmission, while thymectomy stops the production of autoreactive T-cells and related antibodies. This is why thymectomy represents a cornerstone in the treatment of thymoma-associated MG [18–20].

In addition to MG, other thymoma-associated paraneoplastic autoimmune disorders are described in the literature, mostly affecting the nervous system, such as neuromyotonia, psychosis, and polymyositis [21]. Outside the nervous system, autoimmune thyroid diseases (both Grave’s disease and Hashimoto’s thyroiditis), bone marrow aplasia, cutaneous syndromes (pemphigous, vitiligo), systemic lupus erythematosus and glomerulonephritis are possible.

Indeed, our literature review found few reports of AGID with gastroparesis secondary to a thymoma [2,4,22,23]. Among 507 patients with thymoma-associated paraneoplastic syndromes (PNS) reviewed by Zhao et al. [24], only nine patients had a generic diagnosis of “intestinal pseudo-obstruction”, without specifying whether gastroparesis coexists. The latter is more commonly associated with non-autoimmune pathologies and is characterized by a delayed gastric emptying in the absence of a mechanical obstruction; clinically, this manifests as early satiety, nausea, vomiting, postprandial fullness, bloating and epigastric or abdominal pain [25,26]. When gastrointestinal disorders arise in patients with thymoma, they are likely a consequence of an autoimmune autonomic ganglionopathy following AChR blockade by autoantibodies in the context of a full-blown MG [5].

What characterizes our patient is the fact that AGID with gastroparesis and its related symptoms were the only initial findings of a subclinical thymoma-associated MG. Indeed, the latter usually starts with classic skeletal muscle symptoms such as weakness, fatigue, drooping of eyelids, swallowing difficulty, etc. In this case, the diagnosis of gastroparesis preceded that of thymoma-associated MG and not vice versa.

So, this case report has the merit of alerting insiders about such a possibility, particularly the radiation oncologists who are used to facing far more common gastrointestinal disorders in their daily clinical practice (e.g., emesis, diarrhea, proctitis [27–29]). Gastroparesis occurrence is possible among patients with thymoma and latent myasthenia gravis.

4. Conclusions

Gastroenteric neuropathies are not typical of MG, and AGID has been also associated with some cancers such as lung adenocarcinoma, small cell lung cancer and ovarian cancer. However, autoimmune autonomic failure should be suspected in patients with thymoma-associated MG and gastrointestinal disorders. Autoimmune AGID with gastroparesis should be considered as a potential paraneoplastic syndrome in patients with thymoma, lung cancers and ovarian cancer, myasthenia gravis and delayed gastric emptying in the absence of mechanical obstruction. The presence of one of these (thymoma cancers, myasthenia gravis, gastroparesis in AGID) in any order should prompt a search for the signs and symptoms of the others.

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References


