Clinical case
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Myasthenia gravis and intrathoracic goiter presenting as a combined cause of dysphagia.

Miastenia gravis y bocio intratorácico como causa combinada de disfagia

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Abstract

BACKGROUND: Dysphagia is common among general population. Nevertheless, it is more common among patients with thyroid neoplasms or neurologic disease, presenting as one of the first complaints. Dysphagia characteristics classify and dichotomize its management, often requiring a thorough assessment excluding organic disease.

CLINICAL CASE: A 46-year-old male patient with dysphagia produced by extraesophageal compression due to goiter with a neurological spectrum due to myasthenia gravis.

CONCLUSIONS: With this case, we highlight the difference between the clinical spectrum of both entities and the characteristics both share.

KEYWORDS: Dysphagia; Myasthenia gravis; Retrosternal goiter; Esophageal dysphagia.

Resumen

ANTECEDENTES: La disfagia es común en la población general. Sin embargo, es más común entre los pacientes con neoplasias tiroideas o enfermedades neurológicas, manifestándose como una de las primeras molestias. Las características de la disfagia clasifican y dicotomizan su manejo, frecuentemente requiriendo un estudio minucioso excluyendo enfermedad orgánica.

CASO CLÍNICO: Paciente masculino de 46 años de edad con disfagia producida por compresión extraesofágica debido a bocio con un espectro neurológico debido a miastenia gravis.

CONCLUSIONES: Con este caso resaltamos la diferencia entre el espectro clínico de ambas afecciones y las características que comparten.

PALABRAS CLAVE: Disfagia; miastenia gravis; bocio retrosternal; disfagia esofágica.

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BACKGROUND

Dysphagia is a common complaint in patients, with variable prevalence in studies due to differences in assessment[1] and its prevalence has been reported as 3% of the adult population with more than one episode per week.[2] Dysphagia is defined as the subjective awareness of impaired swallowing. The main symptom in patients with dysphagia is globus pharyngeus and frequently this symptom is followed by retrosternal pain.[1,3]

Dysphagia can be broadly classified as mechanical or functional and anatomically as oropharyngeal or esophageal.[3] However, both anatomical locations may coexist in progressive neurological, infectious and collagen vascular disorders.[4,5] As of oropharyngeal dysphagia, it is often a product of neurologic dysfunction.[6]

Thyroid nodules can cause compressive symptoms, being dysphagia the most frequent, followed by neck fullness, choking and dyspnea; these symptoms seem to be related to nodule size and overall lobe diameter.[7] Although it is reported benign pathology, it is more amenable to improve with surgery.[8]

In this case, we report a clinical scenario in which the dysphagia symptom resulted from two different, yet pathophysiologically related conditions in a patient with a thymoma-associated myasthenia gravis and a large, intrathoracic, benign hyperplastic goiter.

CASE REPORT

A 46-year-old male, with a past medical history of smoking, diabetes and right peripheral facial nerve palsy, was referred to our tertiary care center for evaluation of dysphagia. Four months prior to admission, an anterior mediastinal mass had been incidentally diagnosed on a chest x-ray, which was not evaluated further.

Dysphagia began eight months prior, with difficulty in swallowing solid food, rapidly progressing into an inability to swallow liquids. He had a hard time maintaining gaze because of bilateral ptosis and complained of hoarseness and voice failure. He reported a 14 kg weight loss since the beginning of symptoms. A few weeks prior to presentation he had noticed a slowly growing, non-painful left suprasternal mass.

On physical examination, vital signs were normal and the only remarkable finding was an ill-defined right supraclavicular mass of approximately 6 x 6 cm. Neurological exam revealed left ptosis, with the trachea deviated to the right side, without other neck anomaly associated. Laryngoscopy was uncharacteristic. Upon edrophonium administration, upper extremities claudication and dysarthria appeared within 30 seconds, whereas left eye ptosis worsening and supraversion were evident within 60 seconds. Nerve conduction evoked potentials revealed a post-synaptic abnormality of the left facial nerve, and bilateral upper extremities claudication within thirty seconds of evaluation.

Laboratory work up (**Table 1**) was remarkable only for a mildly suppressed TSH with normal free T4 levels as well as high anti-thyroglobulin antibodies but negative antinuclear antibodies.

With these findings, the patient was classified as a Myasthenia Gravis IIIb.

Chest x-ray revealed the presence of an upper mediastinal mass with significant right tracheal displacement and what appeared to be an anterior mediastinal mass. **Figure 1**

Contrast cervical and chest CT scan confirmed the presence of a large intrathoracic goiter originating in the left thyroid lobe and compressing the trachea and esophagus (**Figure 2A**). An anterior mediastinal cystic mass was evident at the

Table 1. Laboratory test results

Free T4 (ng/dL)	0.980
TSH (mIU/L)	0.246
Thyroglobulin (ug/L)	5776
Thyroglobulin antibodies (UI/mL)	39.79
ANA	Negative
Alfa-fetoprotein	2.76
Carcinoembryonic antigen	1.62
CA-19.9	10.49
Glucose (mg/dL)	63
Creatinine (mmol/L)	0.64
AST (U/L)	51
ALT (U/L)	83
LDH (U/L)	176
GGT (U/L)	62
Sodium (mEq/L)	144
Potassium (mEq/L)	3.51
Chloride (mEq/L)	108
Calcium (mEq/L)	8.9
Phosphate (mEq/L)	3.9
Magnesium (mEq/L)	1.9
Leukocytes (x 10^3/µL)	6.87
Hemoglobin (g/L)	14.2
Hematocrit (%)	44.5
Platelels (x10 12/L)	221

level of the right pulmonary artery (**Figure 2B**). These findings were also confirmed by MRI. **Figure 3**

An ultrasound-guided fine needle aspiration biopsy was performed being benign (Bethesda II): **Figure 4**

Treatment and course

Given the compressive nature of the goiter and the likelihood that the lower mediastinal mass was a thymoma occurring in the context of myasthenia gravis, it was decided to proceed with

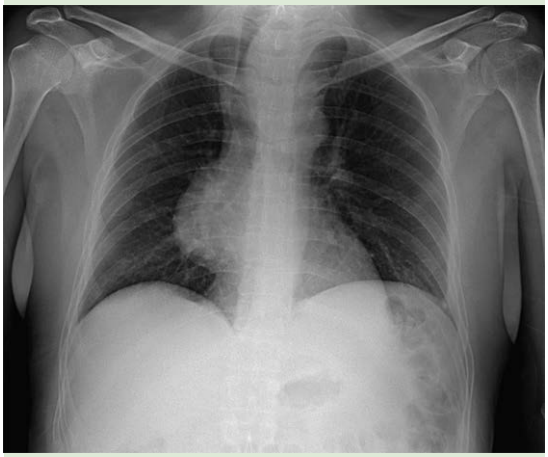

Figure 1. Tracheal deviation and compression to the right, mediastinal widening.

surgical treatment. The patient was treated with intravenous immunoglobulin and pyrdostigmine in preparation for surgery, which consisted of a left hemithyroidectomy and resection of the anterior mediastinal mass through a sternotomy approach. Postoperatively, dysphagia resolved almost completely. Despite an initial moderate improvement of the oculo-bulbar symptoms and peripheral muscle weakness, a few months post-operatively pharmacological treatment of this patient myasthenia gravis had to be escalated.

Histopathological findings

The left thyroid lobule was macroscopically nodular, weighted 180 g and measured 9.9 x 5.6 x 4.9 cm. **Figure 5**

Microscopically there was extensive hyperplasia of follicular cells and a few iron-laden macrophages indicative of hemorrhage, consistent with the diagnosis of benign hyperplastic goiter. The anterior mediastinal mass was a cystic lesion measuring 4.2 x 2.1 x 0.2 cm microscopically

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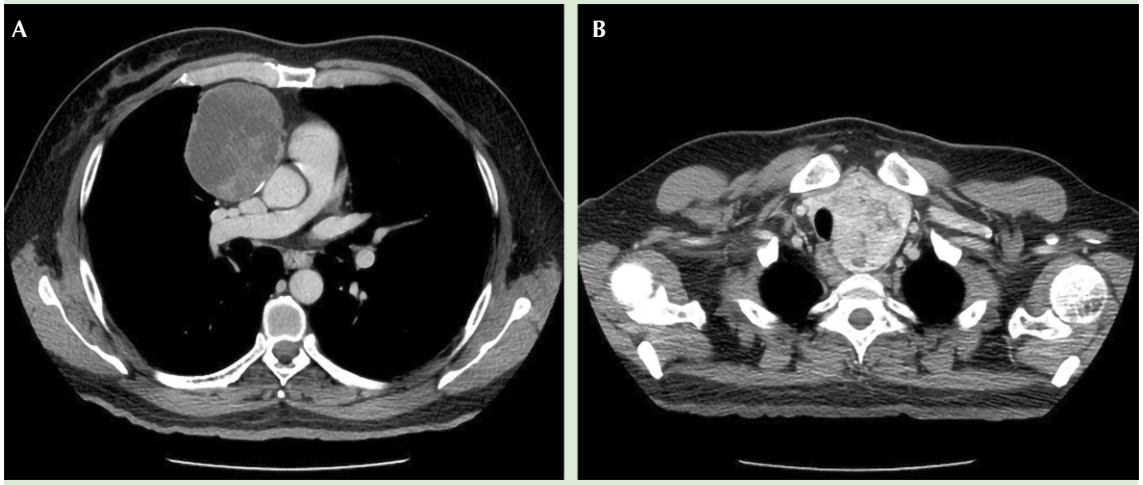

Figure 2. Contrast-enhanced axial computed tomography at right pulmonary artery level showcasing an anterior hypodense cystic mass without enhancement (**A**), left thyroid lobule producing external compression of esophago-tracheal structures (**B**).

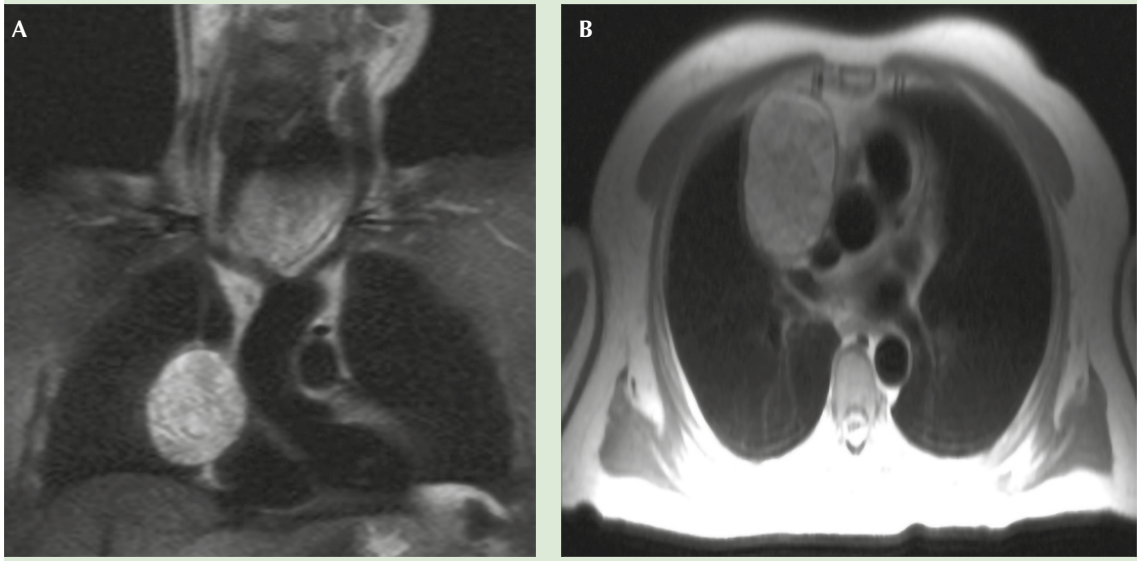

Figure 3. T2 weighted coronal section showcasing two independent masses: one hyperintense lateral to the great vessels, the other with a signal defect in left thyroid lobule (**A**), T1 weighted coronal section with an isodense image in the prevascular compartment (**B**).

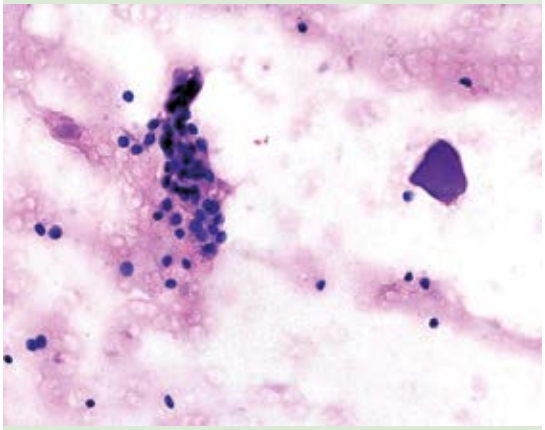

Figure 4. Fine needle aspiration biopsy Bethesda II, showing numerous follicular cells forming a microfollicular arrangement.

consisting of lymphocytes at different maturational stages and some cortical-epithelial cells, without lymphovascular invasion and was categorized as a benign cystic thymoma (WHO B2). **Figure 6**

DISCUSSION

Mediastinal masses encompass a wide spectrum of diagnoses, which can be modified by the age of the patient. In adults, primary thymic neoplasms, thyroid neoplasms and lymphomas are the most common masses encountered.[9] They can be classified according to localization in superior, anterior, middle or posterior compartments; or prevascular, visceral and paravertebral compartments.[10] In the prevascular compartment, the most common masses are thymic lesions, germ

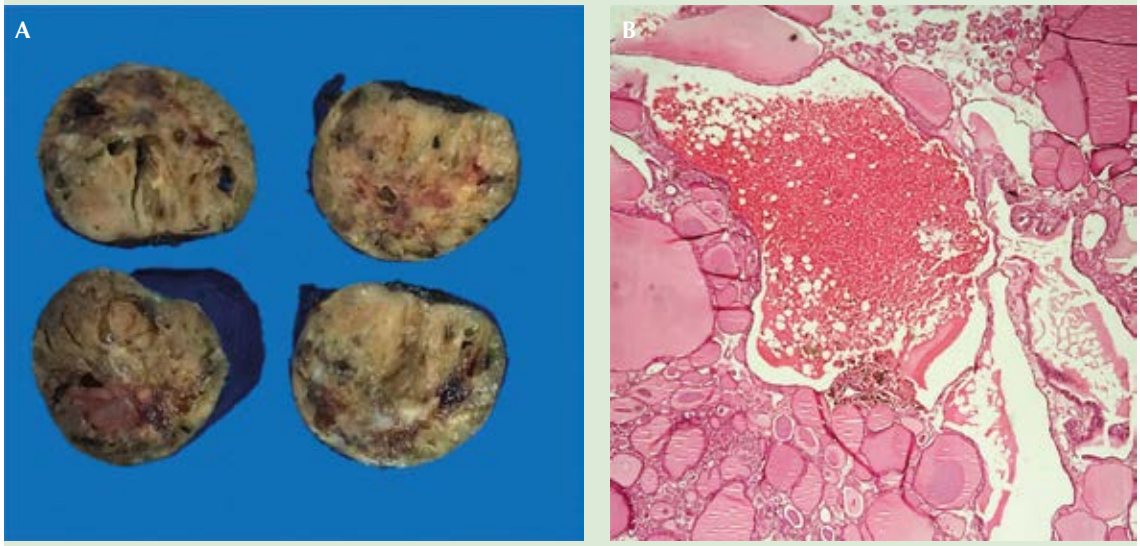

Figure 5. Cross-section of left thyroid lobule **(A)**, histological section showing nodular hyperplasia **(B)**.

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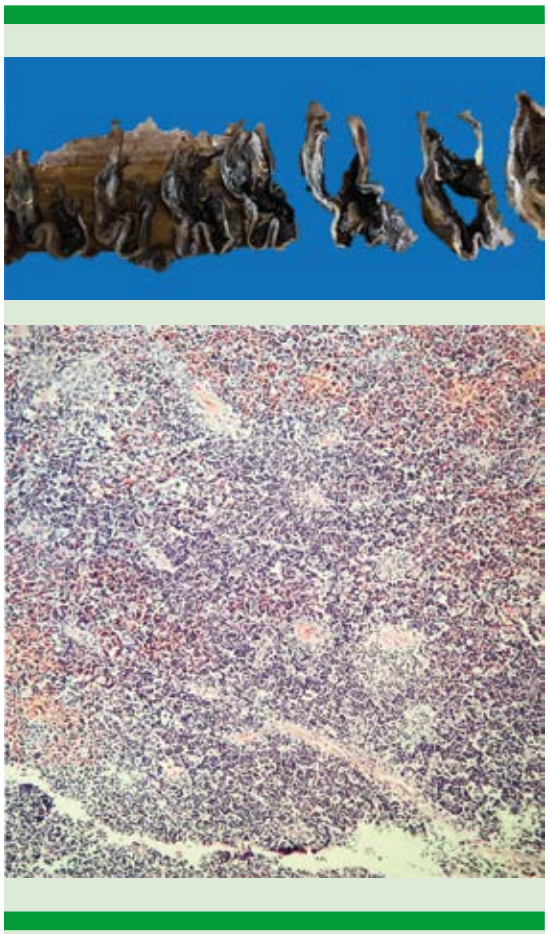

Figure 6. Fragmented thymoma WHO B2, showing a lymphocyte background in different maturation stages and cortical epithelial cells, without lymphovascular involvement.

cell neoplasms, lymphoma, metastatic lymphadenopathies and intrathoracic goiter; in the case of hypodense lesions, magnetic resonance imaging can help in identifying a thymic cyst.[10]

Intrathoracic, retrosternal or substernal goiter was initially described by Haller in 1749[11] it is defined as a thyroid mass 50% or more below the thoracic inlet[12] or 50% or more retrosternal.[11] Furthermore, it can be classified as incomplete if there is a cervical component or complete/true if it exists completely within mediastinum.[12] Most of the cases can be resected only with a neck incision, the need to perform a sternotomy has been estimated to be between 0-13%.[13] This type of goiter constitutes 5% of mediastinal masses, many of them localized in the superior-anterior compartment; and only 20% having a retro-tracheal component.[10,14,15] The prevalence of transient complications (hypoparathyroidism and damage to recurrent laryngeal nerve) seems to be increased, but without a difference in permanent damage.[16]

Compressive symptoms seem to be similar between cervical and intrathoracic goiters, the only difference being chest discomfort.[16] Malignancy rates are also similar among intrathoracic goiters compared to cervical ones.[17]

Myasthenia gravis has been associated in 10-20% to thymomas, and thymectomy is considered part of treatment in patients with an early presentation or with acetyl-choline receptor antibodies.[18] Thymic neoplasms are the most common primary tumor in the anterior mediastinum, comprising at least 50% of them, and 20% of all mediastinal tumors. They have three different clinical scenarios: an incidental finding on a computed tomography scan, presenting with compressive symptoms or presenting with a paraneoplastic or autoimmune disease; myasthenia gravis being present in at least 50% of the group, with oculo-bulbar symptoms the most common presentation.[19,20]

Both entities share compressive symptoms, however thymoma presents with additional bulbar symptoms associated with myasthenia gravis. Our patient had ptosis, dysarthria and dysphagia, the latter presenting the clinical challenge of inferring if it was due to the important extrinsic compression or the functional compromise due to myasthenia gravis. We performed surgery based on the patient's clear indication of thymectomy given the mediastinal mass and myasthenic

syndrome and the extrinsic compression of both masses.

However, in this case even though the patient had an initial recovery of dysphagia, he later had further exacerbation due to late diagnosis of myasthenia gravis.

CONCLUSIONS

Mediastinal masses present the challenge of deciding surgical approach and excluding ample differential diagnoses. Patients with dysphagia in this region may be not only affected by the size of the mass, but by antibodies produced in the case of thymic tumors.

We consider the diffusion of this case important, to study the impact of compressive symptoms versus functional symptoms; the former having an initial recovery instead of the latter which could also improve with surgical management but tend to have an insidious course of exacerbations.

Ethics statement and conflict of interest disclosures

Conflicts of interest: All authors have declared that no financial support was received from any organization for the submitted work. Financial relationships: All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. Other relationships: All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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