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Case Report

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Thymic Epithelial Tumour Size Reduction after Steroid Therapy without Chemotherapy: A Possible Tumour Treatment? Case Report and Literature Review

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Abstract

Myasthenia Gravis (MG) is a neuromuscular junction disorder characterised by antibodies directed against postsynaptic antigens (mainly the Acetylcholine Receptors (AChR)). The management of MG symptoms relies on the utilization of anticholinesterases (such as Pyridostigmine), immunosuppressive and immunomodulatory therapies, including therapeutic plasmapheresis or high-dose human immunoglobulin. The removal of thymoma presents an oncological "urgency», in the context of myasthenic patients, it is crucial to undertake the operation solely when myasthenic symptoms are effectively controlled by pharmacological therapy. A literature review was conducted on Pubmed with the terms "thymoma" and "steroid" to explore the role of steroids, administrated for MG treatment in tumor dimension reduction. To date, only a limited number of studies have investigated the effect of steroids on tumour size, particularly in the context of thymoma, which is relatively rare. Finally we presented the case of a 53-year-old male patient affected of a severe form of MG and a thymoma with suspicious infiltration of anonymous vein, who was treated with high doses of steroids, with final control on MG symptoms and tumor dimension reduction. The patients was at the end operated successfully with a robot assisted technique.

To further solidify and expand our understanding of this phenomenon, studies involving larger cohorts would be invaluable to gain to a more comprehensive consolidation of knowledge regarding the therapeutic role of corticosteroids in managing thymic epithelial tumors.

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Introduction

Myasthenia Gravis (MG) is a neuromuscular junction disorder characterised by antibodies directed against postsynaptic antigens (mainly the Acetylcholine Receptors (AChR)). One-half of cortical thymoma patients develop Myasthenia Gravis (MG), while 15% of MG patients have thymomas [1].

In thymomatous patients, whether with or without MG, elective thymectomy is mandatory with the dual aim of, firstly, ensuring oncological control of the neoplastic condition, and, secondly, ameliorating or resolving myasthenic symptoms exhibited in MG patients. While the removal of thymoma presents an oncological "urgency», in the context of myasthenic patients, it is crucial to undertake the operation solely when myasthenic symptoms are effectively controlled by pharmacological therapy.

The management of MG symptoms relies on the utilization of anticholinesterases (such as Pyridostigmine), immunosuppressive and immunomodulatory therapies, including therapeutic plasmapheresis or high-dose human immunoglobulin. The adoption of innovative and biological drugs remains in the experimental phase.

Methods

In our investigation, a literature review was conducted on Pubmed using the Advanced tool, employing the keywords "thymoma" and "Steroid", resulting in a total of 201 relevant works. We specifically selected studies published in English from 1980 to 2024, with no restrictions on the number of included patients or type of study. Ultimately, six studies met out inclusion criteria and were selected (Table 1).

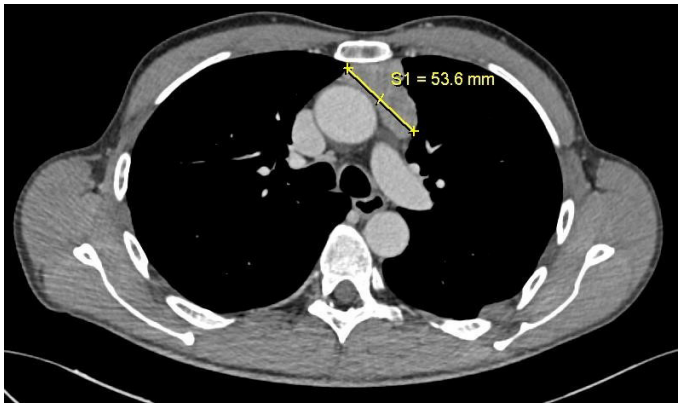

Figure 1: Viability assay in Hela cell cultures. *Arracacia xanthorrhiza Bancr* (AXB) cytotoxic effect on HeLa cells was evaluated by MTT assay. Cells were seeded at $1x10^4$ per well and treated with increased doses of AXB from 10^{-11} mg/ml to 10^{-1} mg/ml. Experiments were performed in triplicate to evaluate half-maximal inhibitory concentration for AXB.

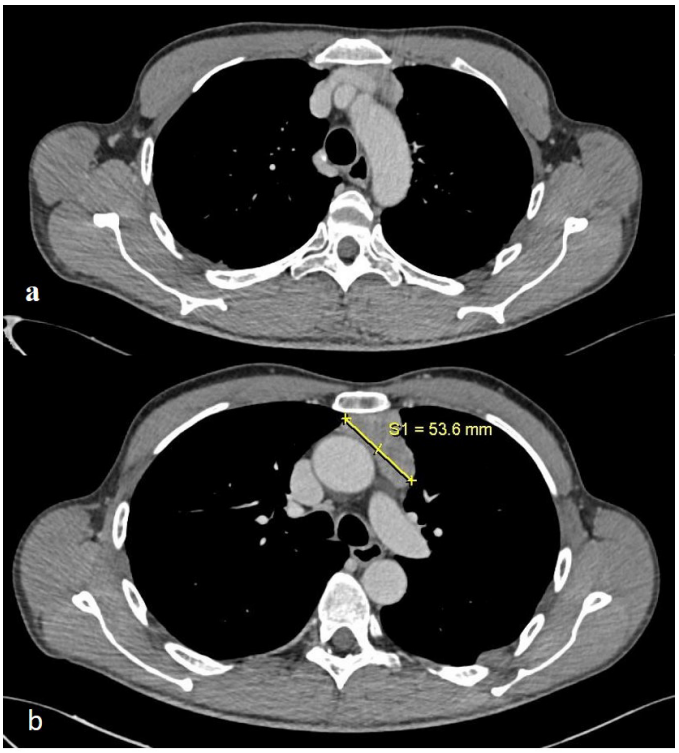

Figure 2(a-b): CT scan (August 2023), showing extension of the lesion to the anonymous vein.

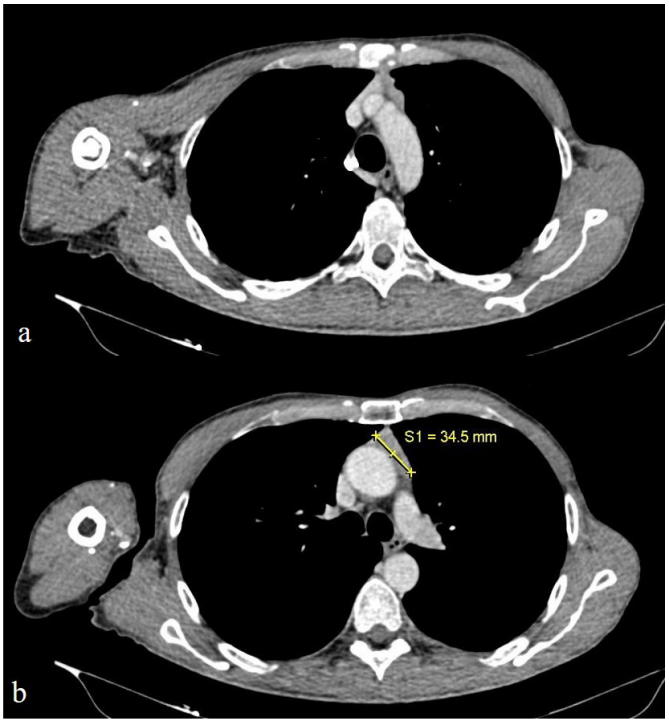

Figure 3(a-b): PET-CT showing increased SUV max.

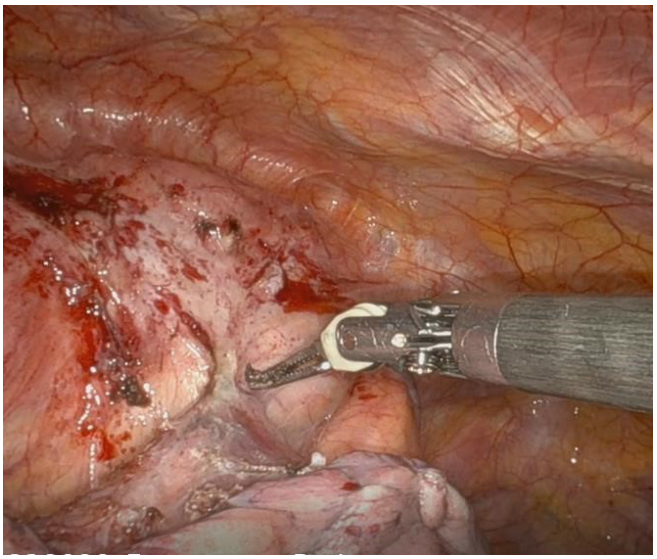

Figure 4a: Intraoperative findings.

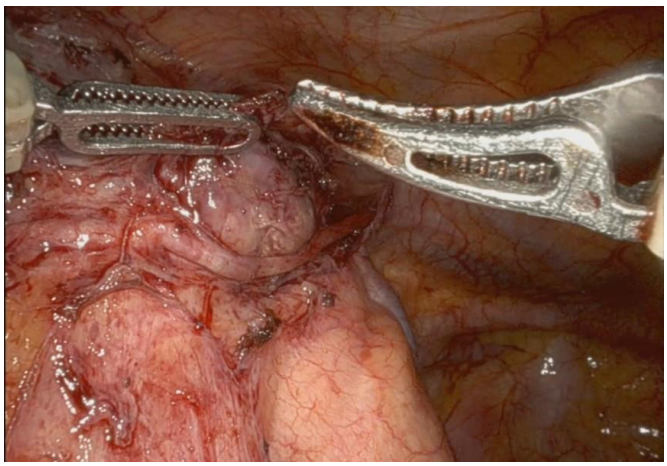

Figure 4b: Phrenic nerve involvement.

Table 1: Literature review.

Author	Year	Country	Kind of study	N of patients	Histology	Kind of treatment	Dimension reduction
Wrona et al. [7]	2021	Poland	Case report	1	B1	low dose prednisone (0.5/kg a day)	75 to 30 mm
Kobayashi et al. [8]	2005	Japan	Prospective	17	B1, B2, B3, AB	1 g metilprednis olone	Reduction rate 2 to 85%
Qi et al. [9]	2016	China	Retrospective	12	B2, B3, B1, AB	Pulse therapy	Basic remission or marked improvement
Fujuwara et al. [10]	2015	Japan	Case report	1	B1	Pulse therapy	Improved reduction
Yoshida et al. [11]	2012	Japan	Case report	1	B2	Prednisone	Hyalinization
Kodama et al. [12]	1997	Japan	Case report	1		Pulse therapy	Complete remission

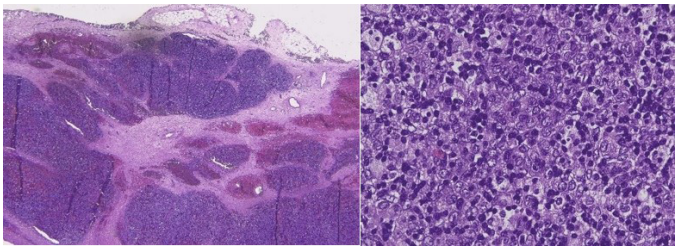

Figure 5: Histological findings of thymoma type B2. At low power (left), an invasive thymoma is shown, extending beyond the capsule near the surface, where adipose tissue is present. At high power (right), thymoma consists in a predominant epithelial lesion, with a significant amount (uncountable) of lymphocytes.

Discussion

Thymic epithelial tumours represent the most common neoplastic lesions found in the anterior mediastinum, originating from thymic epithelial cells. Over 90% of patients with thymoma develop autoimmune diseases, with Myasthenia Gravis (MG) being the most prevalent among them [2]. It has been reported that approximately 30-50% of patients with thymoma develop MG, whereas 10-20% of MG patients are found to have thymoma [1,3]. In terms of therapeutic approaches, steroids and pyridostigmine have generally been used as mainstays for the control of MG [4,5].

Kumagai and colleagues have described the use of immunosuppressive agents, such as azathioprine and methylprednisolone, in the treatment of thymomaassociated MG, demonstrating notable improvement in clinical symptoms and reduction in tumour volumes [6].

Literature review

Among these, four were case reports, while one was a prospective study and another a retrospective one.

Wrona and colleagues [7] documented the impact of steroid therapy on a patient affected by thymoma and autoimmune disorder. They observed a reduction in maximal tumour dimensions after implementing steroid therapy (from 64x30x76 mm to 30x17 mm) and remission in infiltration on VCS, rendering the patient eligible for surgery.

Kobayashi and colleagues [8] conducted a prospective study to evaluate the efficacy of intravenous high-dose glucocorticoid (steroid pulse) therapy in 17 previously untreated advanced thymoma patients. They found that preoperative steroid pulse therapy was most effective in type B1 thymoma, probably due to the its specific effect on GR-rich CD4+8+ double-positive immature lymphocytes.

A retrospective study from Qi and colleagues [9] analysed the effect of steroid Pulse Therapy Plus Immunosuppressive Agent for thymoma associated with MG in 12 patients. Their findings suggested that steroid pulse therapy combined with immunosuppressive agents were effective and well-tolerated in treating both metastatic thymoma and MG.

In the case described by Fujiwara and co-workers [10], the Authors report a case of a woman with an anterior mediastinal mass, 4.3 cm in diameter, with suspected invasion to the pericardium and left brachiocephalic vein, along with multiple disseminations to the mediastinal pleura and diaphragm, as well as pleural effusion. Following the first line of chemotherapy which included cisplatin (30 mg/m^2, day 1), vincristine (1 mg/m^2, day 1), doxorubicin (40 mg/m^2, day 1), and etoposide (80 mg/m^2, days 1 to 3) administered over a 7-day cycle, the patient exhibited stable disease. Consequently, as a second-line treatment, CAMP chemotherapy was initiated, comprising cisplatin (20 mg/m^2, days 1 to 4), doxorubicin (40 mg/m^2, day 1), and methylprednisolone (1,000 mg/body weight, days 1 to 4 and 500 mg/body weight, days 5 to 6). Additionally, due to respiratory failure attributed to MG, the patient underwent two courses of methylprednisolone pulse therapy, followed by oral administration of prednisolone. After seven months from the initial diagnosis, the patient became eligible for surgery, as evidenced by a significant reduction in tumor size observed on CT scan.

Yoshida and colleagues [11] analysed the pathological findings showing that prednisolone triggered a reduction in a B2 thymoma by inducing apoptosis in both epithelial neoplastic cells and lymphocytic non neoplastic component of the thymoma.

In the case report by Kodama et al. [12], steroids were employed to treat the lung recurrence of a thymoma that had been surgically resected 6 years prior. Remarkably, the patient exhibited a positive response both on lung nodules and on the newly developed MG.

Results

To date, only a limited number of studies have investigated the effect of steroids on tumour size, particularly in the context of thymoma, which is relatively rare. Our case, described below, may contribute valuable insights to this field, as it demonstrates a notable reduction in tumor size following steroid therapy, accompanied by significant improvement in MG symptoms.

Our experience

We present the case of a 53-year-old male patient admitted to our ICU in June 2023 due to weakness in the lower limbs and dysphagia, associated with respiratory failure necessitating endotracheal intubation and artificial ventilation. A clinical suspicion of Myasthenia Gravis (MG) was raised. The assay for antibodies against the Acetylcholine Receptor (AChR) yielded positive results, and electromyographic examination confirmed the diagnostic hypothesis of MG.

A whole-body CT scan was performed, revealing a solid tissue with heterogeneous density in the anterior mediastinum, measuring approximately 53x41x70 mm, extending to the anonymous vein without an evident cleavage plane (Figure 1).

Subsequently, the patient underwent standard therapy, receiving intravenous immunoglobulins, pyridostigmine 60 mg four times daily, and prednisone 50 mg a day, resulting in partial clinical improvement.

Despite initial improvement, while undergoing a rehabilitation program, the patient experienced worsening in strength in the upper limbs, along with the onset of dysphagia and rhinolalia. In response, therapy was intensified, with prednisone increased to 75 mg/day and pyridostigmine to 60 mg five times daily, but no clinical benefit was observed. With the emergence of bulbar symptoms, a cycle of plasmapheresis (and a cycle of intravenous immunoglobulins (120 g) were initiated, resulting in modest clinical benefit. Due to persistent symptoms, the patient commenced treatment with 2 infusions of Rituximab (1000 mg per infusion), which yielded clear partial symptomatic relief.

To monitor for potential neoplastic growth during the ongoing therapy, the patient underwent a follow-up CT and PET CT scan in October 2023. The scans revealed a reduction in the size of the solid tissue, with no further contact with the anonymous vein (measuring 34.5x16x70 mm compared to the previous 53x41x70 mm) (Figure 3). Additionally, a low-grade increase in metabolic activity was noted in the tissue located in the anterior mediastinum (Figure 2).

In November 2023, due to inadequate symptomatic control of MG, treatment with Ravulizumab was started, leading to clinical benefit.

Considering the stabilization of the myasthenic condition, the patient underwent re-evaluation for surgical intervention. Following a multidisciplinary assessment, the patient was deemed suitable for thymectomy. In January 2024, robot-assisted radical thymectomy via a left approach was performed The procedure involved radical thymectomy with resection of the thymoma, thymus gland, and perithymic fat tissue while preserving the left phrenic nerve, which was found to be encased by the thymoma (Figure 4b) at the beginning of the surgical procedure. Moreover, dissection of the Anonymous Vein was carried out successfully, with no evidence of invasion by the thymic neoplasm.

In the immediate post-operative period, the patient underwent multiparametric monitoring in ICU. On the first post-operative day, he was transferred back to the ward without complications. On the second post-operative day, the chest tube was removed, and the patient was discharged home.

The definitive histological examination showed a thymoma, classified as B2 type according to WHO, with a stage of pT1a Nx (AJCC, 8th edition, stage IIb according to Masaoka-Koga) (Figure 5).

Conclusion

Our review serves as an interesting report highlighting the effect of corticosteroid on dimension of thymic epithelial tumour. However, to further solidify and expand our understanding of this phenomenon, studies involving larger cohorts would be invaluable. Such research endeavors would contribute to a more comprehensive consolidation of knowledge regarding the therapeutic role of corticosteroids in managing thymic epithelial tumors.

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