Case Report

Induction chemotherapy with carboplatin and paclitaxel for thymoma in acute respiratory distress due to myasthenia gravis: a case report

Giovanni Maria Comacchio[1], Beatrice Benetti[2], Elisabetta Di Liso[2], Alice Menichetti[2], Valentina Guarneri[2,3], Federico Rea[1], Giulia Pasello[2,3]

[1]Thoracic Surgery Division, Department of Cardiac, Thoracic, Vascular Sciences, and Public Health, Padova University Hospital, Padova, Italy; [2]Medical Oncology 2, Veneto Institute of Oncology IOV IRCCS, Padova, Italy; [3]Department of Surgery, Oncology and Gastroenterology, University of Padova, Padova, Italy

Correspondence to: Giulia Pasello. Department of Surgery, Oncology and Gastroenterology, University of Padova, 35128 Padova, Italy; Medical Oncology 2, Veneto Institute of Oncology IOV IRCCS, 35128 Padova, Italy. Email: giulia.pasello@unipd.it; giulia.pasello@iov.veneto.it.

Background: Myasthenia gravis (MG) is presented in 30–50% of thymoma cases, particularly in AB, B1 and B2 thymomas, and often associated with antibodies against acetylcholine receptor (AChR). Symptoms include muscle weakness and fatigue, and the severity depends on the muscles involved. Surgery is recommended in resectable thymomas, and after induction chemotherapy in locally advanced cases. The occurrence of acute respiratory insufficiency is a rare but potentially life-threatening event and may preclude the possibility to perform an adequate induction systemic treatment in resectable patients.

Case Presentation: We herein describe a case of a patient who underwent induction chemotherapy with carboplatin and paclitaxel for stage IVa thymoma while on ventilator support for respiratory insufficiency due to MG; the remarkable radiological response and the marked improvement in neurological symptoms made it possible to discontinue ventilatory support and carry out surgery with subsequent complete tumor resection. Unfortunately, due to an infection of the surgical wound, it was not possible to complete the therapeutic process with adjuvant radiotherapy.

Conclusions: Initiation of chemotherapy induction treatment in a patient on mechanical ventilation because of acute MG is a challenge, but this should not hold back from starting a treatment, if it is considered potentially curative. The recommended induction chemotherapy regimen is the combination of doxorubicin, cisplatin, and cyclophosphamide, but in selected cases non-anthracyline regimens may be chosen. Whenever feasible, a multimodal approach including chemotherapy surgery and radiotherapy should be preferred.

Keywords: Thymic epithelial tumors (TETs); myasthenia gravis (MG); respiratory distress; induction chemotherapy; case report.

Submitted Feb 12, 2022. Accepted for publication Jun 27, 2022.
doi: 10.21037/apm-22-199
View this article at: https://dx.doi.org/10.21037/apm-22-199

Introduction

Thymic epithelial tumors (TETs) are rare, with an annual incidence of 1.5/1 million person-year (1) and often have associated autoimmune disease, including myasthenia gravis (MG) in 30–50% of cases. One third of cases present with locally advanced disease or with distant metastases, needing a multimodal approach involving primary chemotherapy, surgery and postoperative radiotherapy (2). Presence and severity of MG may influence the therapeutic pathway of thymoma, precluding the possibility to perform an adequate treatment. So far, a single case undergoing a myasthenic crisis during chemotherapy which was successfully continued, is reported (3); however, the initial decision-making process when an acute respiratory insufficiency

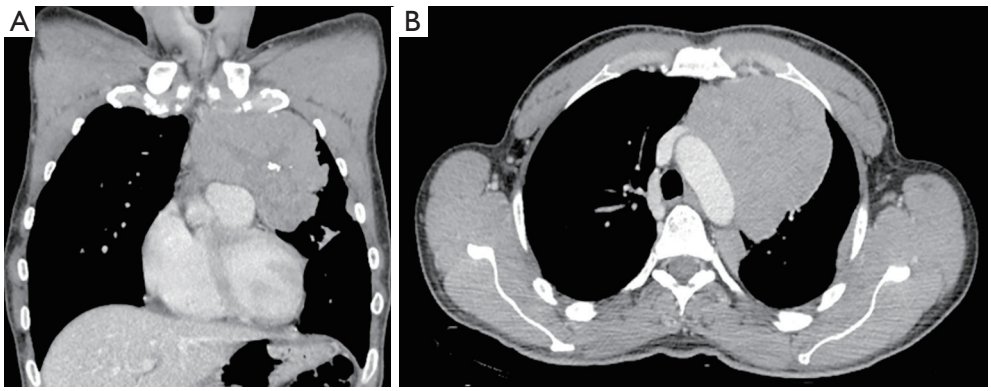

Figure 1 Coronal CT (A) and axial CT (B) images show mediastinal mass and a pleural lesion at diagnosis. CT, computed-tomography.

occurs at the baseline is still challenging. We present the following case in accordance with the CARE reporting checklist (available at https://apm.amegroups.com/article/view/10.21037/apm-22-199/rc).

Case presentation

The patient is a 42-year-old Caucasian male with previous unremarkable medical history. He was admitted to the neurological department of another hospital in April 2020 because of an acute appearance of diplopia with associated deficit of the III, IV and VI cranial nerves and muscular weakness of the lower limbs. Electromyography was compatible with a postsynaptic disorder and blood tests showed high titer of anti-acetylcholine receptor (AChR) antibodies (>20 nmol/L), thus MG was diagnosed. Because of a progressive worsening of the symptoms, a cycle of intravenous immunoglobulins (IVIg) 0.4 g/kg/die in combination with methylprednisolone 80 mg was started. Diagnostic work-up was completed with a contrast-enhanced chest computed-tomography (CT) scan that revealed a 12.5 cm mediastinal mass with complete encasement of the left subclavian vein and multiple solid lesions in the left pleural cavity. The day after the CT-scan the patient experienced sudden onset of acute dyspnea with severe respiratory failure refractory to oxygen therapy, thus requiring tracheal intubation and mechanical ventilation in the intensive care unit (ICU). According to the Myasthenia Gravis Foundation of America (MGFA) clinical classification, the clinical picture was classified as the most severe (MGFA V) (4). The cycle of IVIg was completed with no clinical benefits, therefore plasma exchange therapy was performed and prednisone was administered, still without clinical benefits. A second cycle of IVIg was started. Meanwhile a biopsy of the lesion and a surgical tracheostomy were performed, with diagnosis of B2 thymoma, Masaoka clinical stage IVa. The patient was transferred to the ICU of our institution in June 2020. The patient was evaluated by the neurologist and by the multidisciplinary thoracic oncology team. The lesion was deemed surgically resectable after induction chemotherapy, therefore weekly chemotherapy with carboplatin at area under the curve of 2 and paclitaxel 50 mg/m^2 was started with the patient still in the ICU. A slight improvement in the neurological symptoms occurred into few days and the patient was moved to the respiratory ward where he began a rehabilitation process and was disconnected for progressively longer times from the ventilator support, up to a complete weaning. The patient was then moved to the oncology ward to complete chemotherapy. The chest CT was performed after eight doses of chemotherapy showing a 40% reduction in mediastinal mass and other pleural lesions (*Figures 1*,*2*).

Neurological evaluation based on MGFA score showed a marked improvement in the myasthenic symptoms (*Figure 3*).

In August 2020 the patient underwent surgical operation. Through a left sternothoracotomic approach the thymoma was removed *en-bloc* with the pericardium, the left brachiocephalic vein then replaced with a prosthetic graft, the left phrenic nerve, a portion of the right upper lobe and the left parietal pleura. Histological examination confirmed the diagnosis of a B2 thymoma, Masaoka IVb because of a single lymph node metastasis in the anterior mediastinum (ypT4N1M1a). The subsequent hospital stay was uneventful; the tracheostomy was closed, and neurological evaluation showed a marked improvement in the myasthenic symptoms (MGFA I) and suggested a progressive reduction of steroid therapy and the introduction of acetylcholinesterase inhibitors. The level

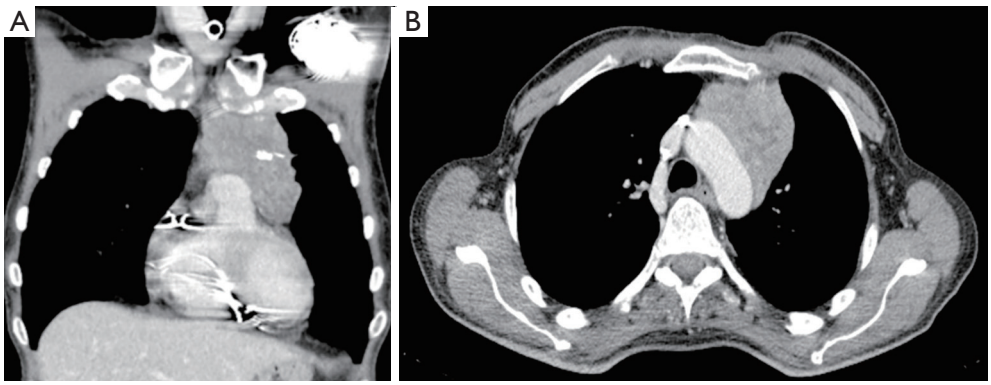

Figure 2 Coronal CT (A) and axial CT (B) images show marked reduction of the main lesion and pleural lesion after induction chemotherapy. CT, computed-tomography.

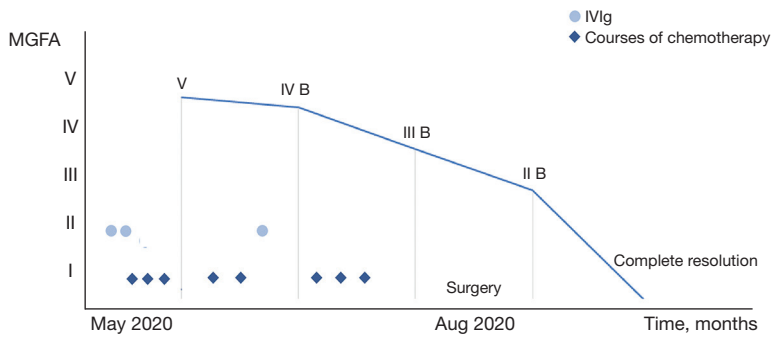

Figure 3 Graphical representation of the clinical improvement in the myasthenic-dependent clinical picture, with particular reference to symptoms according to MGFA score in relationship to chemotherapy and IVIg administration. MGFA, Myasthenia Gravis Foundation of America; IVIg, intravenous immunoglobulin.

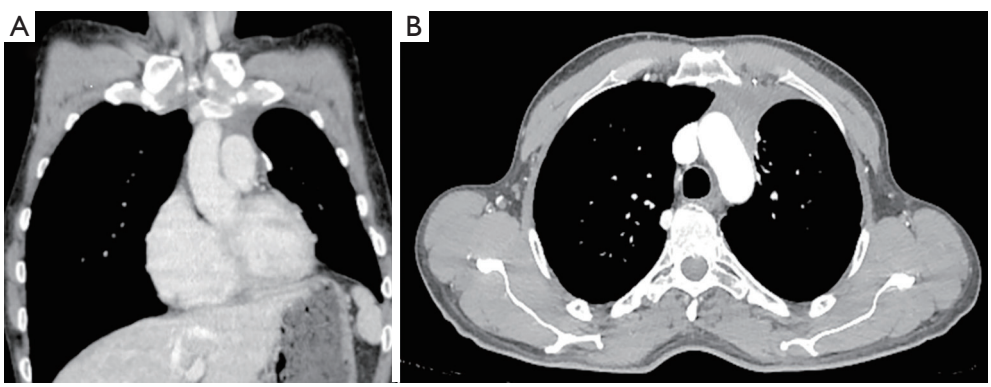

Figure 4 Coronal CT (A) and axial CT (B) images show the absence of disease relapse during follow-up. CT, computed-tomography.

of antibodies against AChR has markedly decreased (from 20 nmol/L in the preoperative period to 3.5 nmol/L in January 2022). Adjuvant radiotherapy was not performed because nearly two months after the operation he developed a wound infection with a mediastinal abscess surgically treated. The patient is currently in good clinical conditions and with no clinical or radiological signs of thymoma recurrence at 17 months from the surgical procedure (*Figure 4*).

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committees and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

Discussion

TETs represent a rare disease, whose complexity requires a multidisciplinary evaluation from diagnosis to therapy. The primary goal should be radical treatment, even in stage IV. The aim of induction chemotherapy is to make as many cases as possible resectable. Sometimes respiratory muscle involvement from MG requires intensive care and mechanical ventilation, thus affecting the possible treatment strategies in these patients, precluding the possibility to perform an adequate induction treatment. In our case, the patient had an Eastern Cooperative Oncology Group (ECOG) grade 4, thus a possible contraindication for chemotherapy, but we considered the possibility of an improvement of the paraneoplastic symptoms together with the response of the tumor to the therapy. Generally, anthracycline-based regimens with cisplatin, doxorubicin and cyclophosphamide (PAC) are recommended in thymomas but, in order to minimize adverse effects, it is possible to choose non-anthracyline regimens (5,6). In our case, although carboplatin and paclitaxel may be not considered as the first option in fit thymoma patients, we achieved an excellent clinical-radiological response making surgery possible. In addition, the weekly schedule has made the treatment more tolerable. Initiation of chemotherapy induction treatment in a patient on mechanical ventilation because of acute MG presents a challenge, but, as demonstrated by our experience, this should not hold back from starting a treatment, if it is considered potentially curative.

Acknowledgments

Funding: None.

Footnote

Reporting Checklist: The authors have completed the CARE reporting checklist. Available at https://apm.amegroups.com/article/view/10.21037/apm-22-199/rc

Peer Review File: Available at https://apm.amegroups.com/article/view/10.21037/apm-22-199/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://apm.amegroups.com/article/view/10.21037/apm-22-199/coif). VG reports the following conflicts of interest: consulting fees payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events for ELI LILLY, NOVARTIS, GSK; patent pending for REVAEL GENOMICS; participation on a Data Safety Monitoring Board or Advisory Board for ELI LILLY, NOVARTIS, MSD, GILEAD. The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committees and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

References

1. de Jong WK, Blaauwgeers JL, Schaapveld M, et al. Thymic epithelial tumours: a population-based study of the incidence, diagnostic procedures and therapy. Eur J Cancer 2008;44:123-30.
2. Girard N, Ruffini E, Marx A, et al. Thymic epithelial tumours: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2015;26

Suppl 5:v40-55.
3. Patelli G, Bencardino K, Tosi F, et al. Chemotherapy-induced myasthenic crisis in thymoma treated with primary chemotherapy with curative intent on mechanical ventilation: a case report and review of the literature. J Med Case Rep 2021;15:32.
4. Jayam Trouth A, Dabi A, Solieman N, et al. Myasthenia gravis: a review. Autoimmune Dis 2012;2012:874680.
5. Conforti F, Marino M, Vitolo V, et al. Clinical management of patients with thymic epithelial tumors: the recommendations endorsed by the Italian Association of Medical Oncology (AIOM). ESMO Open 2021;6:100188.
6. Lemma GL, Lee JW, Aisner SC, et al. Phase II study of carboplatin and paclitaxel in advanced thymoma and thymic carcinoma. J Clin Oncol 2011;29:2060-5.

Cite this article as: Comacchio GM, Benetti B, Di Liso E, Menichetti A, Guarneri V, Rea F, Pasello G. Induction chemotherapy with carboplatin and paclitaxel for thymoma in acute respiratory distress due to myasthenia gravis: a case report. Ann Palliat Med 2022;11(11):3562-3566. doi: 10.21037/apm-22-199

