CASE REPORT

Multidisciplinary Approach to Advanced Thymoma with Pleural Dissemination: A Case of Complete Resection through Pleurectomy Decortication

Abordagem Multidisciplinar de Timoma com Disseminação Pleural: Um Caso de Ressecção Cirúrgica Completa por Pleurectomia Descorticação

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ABSTRACT

Advanced-stage thymoma may present, in rare cases, with extensive pleural disease at the time of diagnosis (Masaoka IVA). Accounting for the low incidence and the variety of therapeutic strategies available in the literature, no consensual treatment has been established. A multimodal treatment plan including surgery, radiotherapy and chemotherapy should be preferred, allowing for a more favorable prognosis. Complete resection constitutes the basis of treatment for thymomas. Herein, we present a case of an advanced thymoma with extended pleural dissemination for which complete resection was achieved through pleurectomy decortication, through a multidisciplinary approach.,

Keywords:
Pleural Neoplasms/secondary; Pleural Neoplasms/surgery; Thoracic Surgical Procedures; Thymoma/surgery

RESUMO

Timomas em estadio avançado podem exibir doença pleural extensa aquando do diagnóstico (Masaoka IVA). Considerando a baixa incidência da patologia e da variedade de estratégias terapêuticas disponíveis e apresentadas na literatura científica, não foi ainda possível estabelecer um tratamento consensual. Um plano terapêutico multimodal, englobando cirurgia, radioterapia e quimioterapia, destaca-se ao permitir um prognóstico mais favorável. Ademais, a resseção completa é a base do tratamento do timoma. Deste modo, apresentamos um caso de um timoma em estadio avançado com disseminação pleural extensa, cuja ressecção completa foi conseguida através da cirurgia de pleurectomia decorticação, inserida numa abordagem terapêutica multidisciplinar.

Palavras-chave:
Neoplasias da Pleura/cirurgia; Neoplasias da Pleura/secundárias; Procedimentos Cirúrgicos Torácicos; Timoma/cirurgia

INTRODUCTION

Thymoma constitutes an indolent malignancy of the anterior mediastinum. In rare incidences, accounting for approximately 6.8% of thymoma cases, it may present as a locally advanced disease.[1] Stage IVA thymomas are defined by confirmed pleural or pericardial nodules, with no evidence of distant metastasis. The management of advanced-stage thymomas is based on multidisciplinary collaboration.[2,3]

Surgical resection is the mainstay of treatment for thymomas and complete excision prevails as the most important prognostic factor.[3,4] However, the ideal procedure for pleural involvement remains a topic of debate from local pleurectomy, and extended pleurectomy decortication to extra pleural pneumonectomy.[5] Systemic treatment may be employed as the initial approach to achieve disease control and allow for resectability.[2] Radiation therapy portrays an important adjuvant treatment, reflecting superior survival outcomes, especially in those with incomplete resections.[4,6]

Given the uncertainty regarding optimal treatment, we present an advanced-stage thymoma and the therapeutic approach performed in our center.

CASE REPORT

A 28-year-old woman was referred for further investigation due to persistent chest pain. She was healthy without any relevant past medical history and showed no signs of myasthenia gravis. On account of religious belief, she rejected the possibility of blood transfusions.

Evaluation with computed tomography (CT) scan exhibited an anterior mediastinal mass with extension to the aortopulmonary window as well as broad vascular contact without apparent infiltration of the supra-aortic and pulmonary vessels. Multiple

nodules in the ipsilateral pleural cavity, depicting widespread pleural compromise were present. A fluorodeoxyglucose positron emission tomography (FDG-PET) scan demonstrated intense uptake in the mediastinal tumor and left pleural implants (SUVmax of 15) (Fig. 1). Whole-body CT scan and brain magnetic resonance imaging (MRI) disclosed no nodal or distant metastasis. Percutaneous CT-guided biopsy was performed and established the diagnosis of type B1 thymoma. Cardiac evaluation showed no impairment. Pulmonary function tests indicated mild dysfunction [forced vital capacity (FVC) 2.33 L and 63%; forced expiratory volume in 1 second (FEV1) 1.87 L and 58%; lung diffusion capacity (DLCO) of 51%].

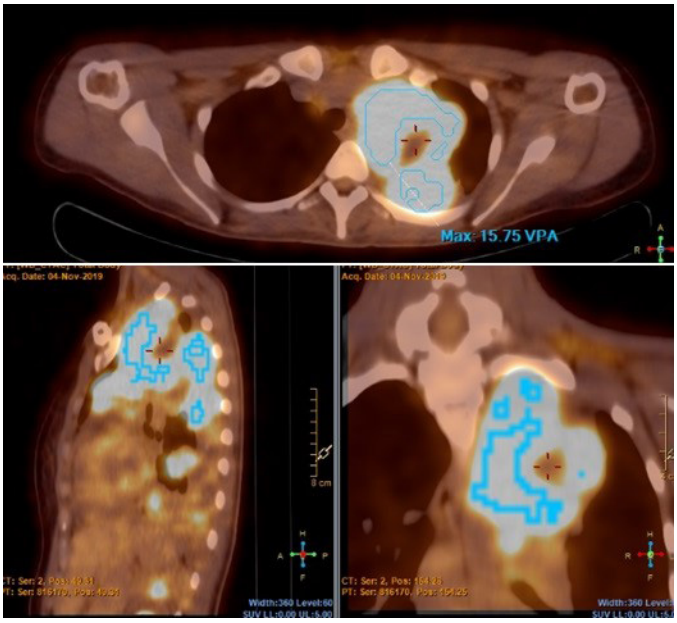

Figure 1 PET scan at the time of diagnosis, revealing metabolic uptake in the mediastinal mass and left pleura nodules

The patient was discussed by the multidisciplinary team (MDT) to delineate the best multi-modality treatment. She underwent four cycles of neoadjuvant chemotherapy (composed of cisplatin, doxorubicin and cyclophosphamide). Subsequent imaging reassessment exhibited a volume tumor reduction of around 25% (Fig. 2). The clinical case was reevaluated, with surgery now being deemed feasible and validated in MDT setting.

Through a posterolateral thoracotomy, we proceeded with extra pleural dissection of the left parietal pleura leading to pleurectomy decortication, thymectomy and wedge resection of the left lower lobe, accomplishing en bloc complete macroscopic resection. Due to dense fibrosis and possible malignant infiltration, resection of the ipsilateral vagus, recurrent laryngeal and phrenic nerves and additional removal of the aortic adventitia layer were necessary. Three thoracic drains were positioned to evacuate the left pleural cavity and anterior mediastinum. Adequate pulmonary expansion was accomplished at the end of the procedure.

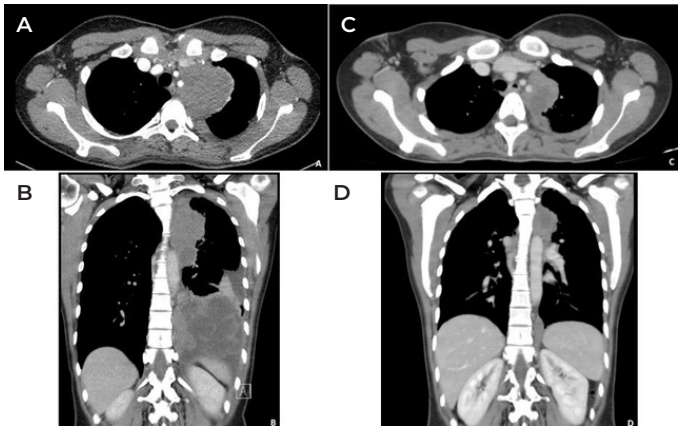

Figure 2 **A** and **B)** Presentation CT scan; **C** and **D)** Post-chemotherapy CT scan, showing a volume tumor reduction of 25%.

The postoperative course was uneventful, with drainage removal on the third postoperative day and ensuing hospital discharge (Fig. 3). Pathologic examination confirmed involvement of the parietal pleural but no evidence of lung or nodal disease and, determined free surgical margins (R0 resection). The final thymoma classifications were Masaoka stage IVA and pT1bN0M1a, respectively.

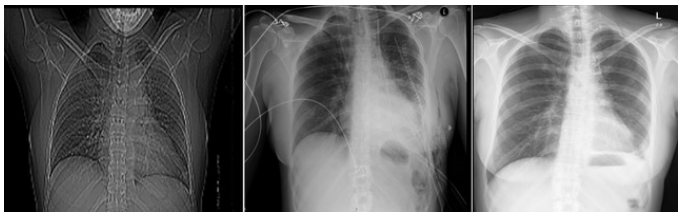

Figure 3 Evolution of chest X-ray (on the left, preoperative X-ray; in the center, initial postoperative and on the right, the final X-ray, at the time of hospital discharge)

Two months after surgery, the patient was proposed for left hemipleural radiation therapy with 13 Gy in 13 fractions (fr), with an additional boost over the thymic tumor bed of 39.6 Gy in 22 fr (total dose of 52.6 Gy in 35 fr, volumetric modulated arc therapy (VMAT) with daily image-guided radiation therapy (IGRT), as shown in Figs. 4 and 5).

Following the surgical procedure, she displayed left Horner's syndrome and dysphonia, benefiting from physical therapy, with gradual symptomatic improvement. Four years after multimodal treatment, the patient is stable and free of disease.

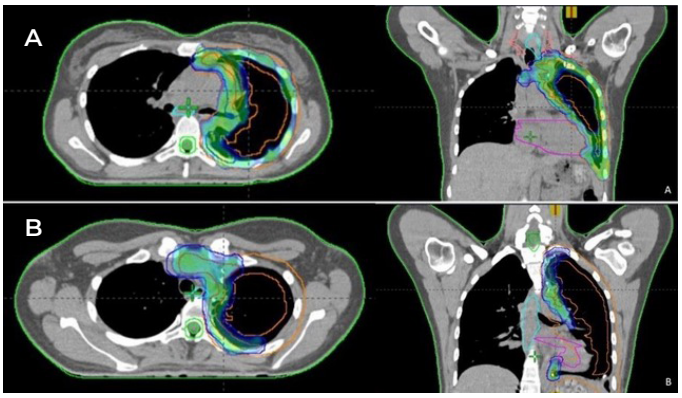

Figure 4 **A)** First phase of radiotherapy - left hemipleural radiation therapy with 13 Gy; **B)** Second phase of radiotherapy - boost of radiation therapy completing a total dose of 52,6 Gy, over the mediastinal tumor bed

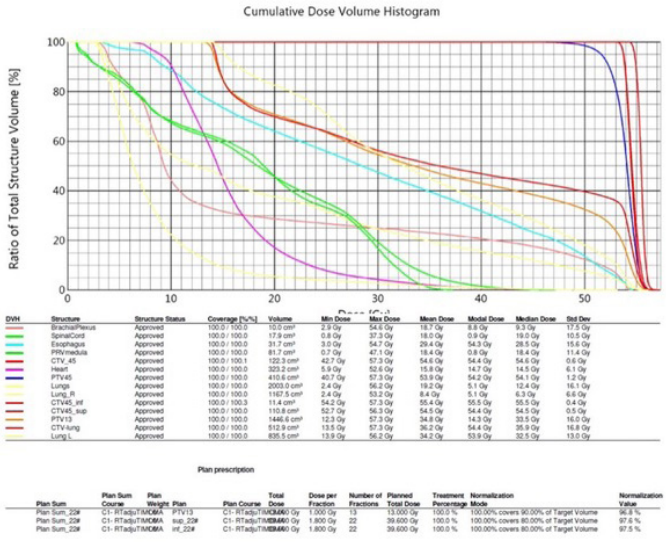

Figure 5 Dose-volume histogram of radiotherapy

DISCUSSION

Advanced stage thymomas with pleural dissemination are rare mediastinal tumors, representing a specific oncologic entity[7,8] for which no treatment strategy has been clearly defined.[2]

In our center, the management of these tumors is based on personalized treatment, by way of careful appraisal on a case-to-case basis by the multidisciplinary tumor board. Defining the surgical resectability of an advanced thymic tumor strongly depends on the magnitude of the tumor infiltration and the surgical team's experience. In this particular case, upfront surgery at the time of presentation would require an extensive resection associated with a high risk of significant blood loss and, as such, was not considered a viable option. For patients presenting with a thymic neoplasm and extensive pleural disease, neoadjuvant chemotherapy is recommended to reduce tumor burden, showing a good response rate and allowing for subsequent resectability.[2]

Surgery is the mainstay of treatment of thymomas.[4] Moser *et al*, in a multicenter analysis implemented by the European Society of Thoracic Surgeons (ESTS) thymic working group, emphasized the value of surgery in stage IVA thymomas. This paper established R0 resections as the most significant prognostic factor while viewing no statistically significant differences in survival when comparing the surgical approach (local or total pleurectomy and extra pleural pneumonectomy).[9]

The choice of the surgical procedure is based on the extension of disease, balancing maximal preservation of healthy tissues while aiming to achieve complete malignant resection. The benefit of one surgical technique over the other has not been demonstrated. Extra pleural pneumonectomy is associated with higher morbidity and operative mortality,[3] although frequently employed in more advanced tumor states.[10] This case demonstrated very extensive and confluent pleural disease and extended parietal pleurectomy offered the possibility of achieving a complete resection while preserving lung capacity, allowing for a promising outcome. In the past five years, four additional cases of stage IVA thymoma underwent extensive pleurectomy decortication in our center, with varying periods of time to recurrence but all are still alive today.

Recently, a novel treatment modality has emerged with the development of hyperthermic intrathoracic chemotherapy (HITHOC). It consists in delivering a cisplatin-based chemotherapy regimen directly in the pleural cavity after surgical resection, to eradicate microscopic residual disease and improve disease-free survival. Although the long-term evidence is still scarce, it exhibits promising results, improving overall survival of stage IVA thymomas, to levels ranging between 67% to 89%, according to Ruffini *et al*.[5,11]

Thymomas demonstrate a high sensitivity to radiotherapy, which is often introduced as an adjuvant treatment.[4,11] Recently, in a joint venture of the American College of Surgeons and American Cancer Society, Khorfan *et al* reviewed the cases of stage III and IV thymomas of the US national cancer database (2004-2016) and reported the best survival outcomes in the group of combined surgical resection and radiation therapy.[4] On the other hand, total hemi thoracic irradiation has been advocated by some authors

such as Uematsu *et al* and Soares *et al* as a potential and well-tolerated modality to expand disease-free survival.[12] Wang *et al* in the Shanghai Chest experience also reinforced the benefit of adjuvant entire hemi thoracic radiotherapy in local disease control.[13] New radiation techniques should be preferred (like intensity-modulated radiation therapy/IMRT), because of their ability to conform de dose to the treatment volume, improving the outcome by increasing the dose and reducing the toxicity. A phase II trial study of hemi thoracic intensity-modulated pleural radiation therapy (IMPRINT) for patients with pleural metastases from thymic malignancies is now open and will probably give us some insight about the treatment of these patients.[14]

CONCLUSION

Due to the rarity of advanced-stage thymomas, randomized studies are scarce and no standardized treatment has been accepted. Complete surgical resection exhibits the best outcomes, however the surgical procedure may vary depending on the extent of disease involvement. Systemic chemotherapy and radiotherapy are the cornerstones of the treatment of stage IVA thymomas, contributing to sustained treatment responses in these high-sensitivity tumors. HITHOC is a promising modality, which we hope to implement in our center in the coming years.

Overall, this case highlights the complexity of the surgical approach as well as the importance of a multimodal therapeutic course to achieve prolonged disease control.

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CPM: Performed the manuscript writing.
CT: Collaborated in the manuscript writing and revision.
IV: Contributed in the elaboration of the idea and manuscript revision and supervision.
CC, TA and NA: Contributed in the manuscript revision.
All authors approved the final version to be published.

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CPM: *Efectuou a redação do manuscrito.*
CT: *Colaborou na redação e revisão do manuscrito.*
IV: *Contribuiu na elaboração da ideia e na revisão e supervisão do manuscrito.*
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Todos os autores aprovaram a versão final a ser publicada.

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