

A rare case of necrotic thymoma*

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SUMMARY: A rare case of necrotic thymoma.

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The Authors report the case of a patient who underwent resection of a huge anterior mediastinal mass, revealing to be a necrotic thymoma. The patient had been previously submitted to surgical biopsies of the mass yielding non-diagnostic results due to extensive necrosis. A sternotomy was then performed to resect the mediastinal mass originating from the thymus, en-bloc with the mediastinal fat and the apparently infiltrated lung. Histopathology showed a possible cyst/thymoma in

massive necrosis, not further definable; revision by a specialized experienced pathologist (J. Rosai) confirmed total mass necrosis and no lung infiltration, thus orientating diagnosis towards a necrotic thymoma and excluding a lymphoblastic lymphoma, with similar histopathological features but more frequent in children or characterized by neoplastic infiltration of surrounding lung. Total body computed tomography (CT) scan and fluorodeoxyglucose positron emission tomography (¹⁸F-FDG-PET)/CT, show neither local recurrence, nor distant metastases two years after surgery. In case of anterior mediastinal mass with difficult histopathological diagnosis due to massive necrosis, the hypothesis of a necrotic thymoma should be considered. After radical removal prognosis is generally favourable and no adjuvant treatment is required.

KEY WORDS: Thymoma - Necrosis - Mediastinum - Surgical resection.

Introduction

Thymomas are the most common primary tumors of the anterior mediastinum in the adult (1, 2).

They have a wide pathological differentiation spectrum (WHO classification, proposed in 1999 and updated in 2004) (1, 3-5), being tumors of epithelial origin associated with a variable percentage of non-neoplastic lymphocytes maintaining morphological and functional features of the cells of the thymus. Differential diagnosis with other similar mediastinal lesions includes thymic carcinoma, lymphoproliferative diseases, such as lymphoblastic lymphoma, atypical carcinoids and mesenchymal tumors.

Rarely, thymomas with prominent cystic and hemorrhagic changes and areas of necrosis and infarction have been reported (6). To the best of our knowledge, less than 30 cases of thymoma with extensive or entire necrosis have been described in the Literature (6-8). We report the case of a patient who underwent resection of a huge anterior mediastinal mass, revealing to be a necrotic thymoma.

Case report

A 58-year-old woman was referred to our Institution, because of chest and right arm pain and chest computerized tomography (CT) evidence of a huge antero-superior mediastinal mass with suspected adjacent right lung infiltration and minimal pleural effusion (Figs. 1, 2). She had been previously submitted to left hemi-thyroidectomy for colloid cysts, left hepatectomy for cavernous haemangioma and was affected by another hepatic haemangioma, chronic HCV hepatopathy, right arm and leg hypostenia due to prior subarachnoid haemorrhage and allergic diathesis.

Due to the extension of the mediastinal mass and to differentiate between thymic or lymphoproliferative disease, diagnostic multiple biopsies of the lesion through right mini-thoracotomy were performed; however, they resulted not suitable for pathologic evaluation because of areas of massive coagulation necrosis associated with

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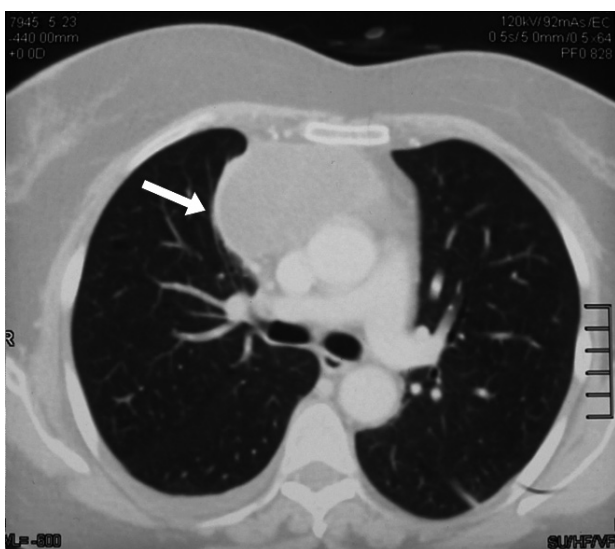


Fig. 1 - Chest CT scan (parenchymal window) showing the huge antero-superior mediastinal mass (indicated by white arrow) with suspected adjacent right lung infiltration and minimal pleural effusion.

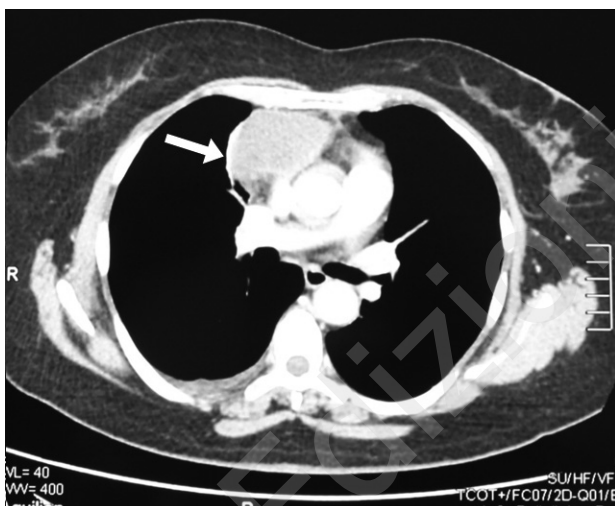


Fig. 2 - Chest CT scan (mediastinal window) showing the huge antero-superior mediastinal mass (indicated by white arrow) with minimal pleural effusion in the right hemithorax.

lympho-mononuclear flogistic cells; immunohistochemistry for CKpool, CD3, CD20, CD15 and CD30 could not be evaluated due to extensive necrosis. Cytological examination of pleural fluid was negative.

As surgical biopsies of the mass yielded non-diagnostic results, a sternotomy was performed to resect the mediastinal mass, originating from the thymus, en-bloc with the mediastinal fat and the apparently infiltrated lung of the upper and medium lobes and right phrenic nerve.

Histopathological examination of the capsulate mass, adherent to but not infiltrating the lung parenchyma, characterized by total and massive necrosis peripherally surrounded by histiocytes, macrophages, lymphocytes, calcinosis and granulomatous tissue, reported a possible cyst/thymoma in massive necrosis, not further definable.

Revision by a specialized pathologist (Prof. Juan Rosai) confirmed a total, massive, ischemic necrosis of the mass, with no vital cel-



Fig. 3 - Hematoxylin-eosin: necrotic thymoma with tumoral coagulation necrosis (indicated by black arrow); at the bottom, fibro-sclerotic tissue with inflammatory cells (capsule).

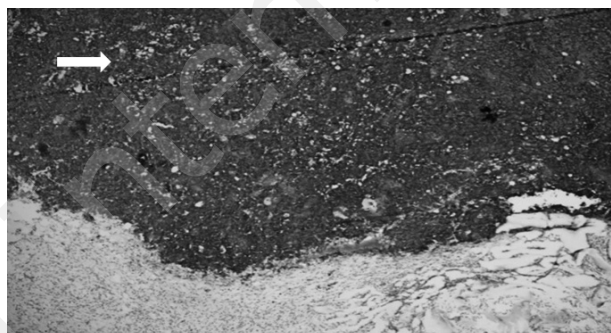


Fig. 4 - Immunohistochemistry: necrotic component of the thymoma (indicated by white arrow) staining intensely positive for cytokeratin 19 (CK19).

ls, surrounded by a thick capsule rich in inflammatory cells (lymphocytes, histiocytes and plasma cells) and with residual islands of non-neoplastic thymic tissue, and no lung infiltration (Fig. 3); thrombosis of blood vessels of the mass was present; at immunohistochemistry, necrotic cells within the mass stained positive for cytokeratins (Fig. 4), typical of thymic epithelial cells, thus orientating diagnosis towards a totally necrotic thymoma and excluding a lymphoblastic lymphoma, which has similar histopathological features but is usually non-encapsulated and characterized by neoplastic infiltration of the adjacent lung and more frequent in children.

After oncology consult, no adjuvant therapy was administered.

Follow-up was performed at 6-months intervals with total body CT scan and fluorodeoxyglucose positron emission tomography (¹⁸F-FDG-PET)/CT, which show neither local recurrence, nor distant metastases two years after surgery.

Discussion

Thymic tumors are the most common neoplastic lesions of the anterior mediastinum in the adult (20% of mediastinal tumors and 50% of all anterior mediastinal tumors) (1, 2).

Thymomas are tumors originating from the epithelial cells of the thymus (1). They generally affect adults between the fourth and fifth decade of age (as our patient), with no sex predilection (1).

Patients can be asymptomatic and thymomas accidentally detected (30-50% of cases) or present with symptoms related to paraneoplastic syndromes (up to 50% of cases), predominantly myasthenia gravis, or due to compression or infiltration (30-40% of cases) of adjacent structures (chest pain, cough, dyspnoea, dysphagia, dysphonia), as in our case; in some cases (20-30%) only generalised systemic symptoms (weight loss, tiredness, fever) may be present (1, 9, 10).

Imaging diagnosis is often made by chest x-ray or chest CT, showing a mediastinal mass in the anterior compartment. Total body CT scan allows to evaluate the extension of the disease, its margins and the relationship with surrounding mediastinal structures, lymph node involvement and local or distant metastases (1). Magnetic resonance imaging (MRI) is extremely useful to study the margins of the thymus and thymic tumors, especially as concerns adjacent big vessels (aorta, pulmonary artery, superior vena cava) (1). (¹⁸F-FDG-PET)/CT can be useful in differentiating subgroups of thymic epithelial tumors (thymomas, thymic carcinomas, thymic carcinoid tumor) and for the staging of the disease (11).

The most commonly used staging system for thymic tumors is the Masaoka staging system, proposed in 1981 (12), subsequently updated in 1994 as Masaoka-Koga staging system (13) and in 2011 by the International Thymic Malignancy Interest Group (ITMIG) (14); this staging system focuses on the local extension of the tumor, including macro- and microscopic invasion of the capsule and surrounding structures (stages I to IV) (1, 12-14) and has been proven to have a prognostic significance (1, 14).

Macroscopically, thymomas may be small (4-5 cm) or of very huge dimensions (more than 20 cm), are usually encapsulated (thick fibrous capsule) and sometimes invasive, can be smooth or polilobulated, solid or cystic in consistency and containing areas of calcification, haemorrhage, infarction and necrosis (15).

Microscopically, thymomas have a great histological variability and intratumoral heterogeneity (1); the most widely used classification system is the WHO classification, proposed in 1999 and updated in 2004 (1, 3-5) which focuses on the histological evaluation of the morphology of the neoplastic epithelial cells and the non-neoplastic lymphocytic elements (15), distinguishing progressively more aggressive histotypes (A, AB, B1, B2, B3) which strongly correlate with prognosis (1, 16).

Differential diagnosis with thymic carcinoma and lymphoma can be challenging, especially in case of large mediastinal mass with cystic and/or necrotic areas. In these cases surgical biopsies of the mass are necessary to establish the correct treatment strategy. In our patient, unfortunately, surgical biopsies of the mass yielded non-diagnostic results due to extensive necrosis.

Some Authors have reported thymomas with pre-

dominant cystic and hemorrhagic changes and areas of necrosis and infarction (6) but very few cases of thymoma with extensive or total necrosis have been described in the Literature (6-8).

In our patient we decided to perform a complete surgical resection through sternotomy in order to obtain a definitive histological diagnosis. However, the final diagnosis was very difficult because of the total and massive necrosis of the mediastinal mass. A specialized pathologist (Prof. Juan Rosai) was involved for the revision and he confirmed the extensive, ischemic necrosis of the mass, with no vital cells, surrounded by a thick capsule rich in inflammatory cells and residual non-neoplastic thymic tissue, not infiltrating the lung parenchyma; vessels thrombosis was present and as reported by other Authors may be the underlying physiopathological mechanism. In fact Moran and Suster typically described areas of infarction associated with ischemic necrosis due to vaso-occlusive and thrombotic phenomena ("tumour-induced vasculopathy"), together with cystic and hyperplastic changes of adjacent thymic epithelium and signs of acute and chronic inflammation with granulation tissue (6, 17). Moreover, areas of necrosis and hemorrhage in encapsulated non-invasive thymomas associated with inflammatory and cystic changes do not indicate an unfavourable prognosis, especially if coupled with absence of cytological atypia and mitotic activity (6, 17).

Main problems of differential diagnosis with lymphoblastic lymphoma can be solved thanks to immunohistochemistry, because thymic epithelial cells stain positive for cytokeratins, as was in our patient, thus orientating diagnosis towards a totally necrotic thymoma; moreover, lymphoblastic lymphoma usually affects children, is non-encapsulated and characterized by neoplastic infiltration of the adjacent lung parenchyma (15).

Some differential diagnosis problems with mediastinal mesenchymal tumors and thymic atypical carcinoids can arise in case of thymomas predominantly made of spindle cells or rosette-like/trabecular structures, respectively; at immunohistochemistry thymoma tumour cells usually stain positive for cytokeratins and immature T lymphocytes (typically associated to neoplastic epithelial thymic cells) for other markers of differentiation, such as CD1a, CD3, TdT e CD99 (15).

Complete surgical resection, including en-bloc removal of infiltrated adjacent structures, is the gold standard of the treatment of thymomas, as it is the most important prognostic factor. In our patient the entire mass was removed, together with the contiguous mediastinal fat and the apparently involved lung (1).

Adjuvant radiotherapy or chemotherapy is usually reserved to higher stages (1, 17). In our case, the mass was completely removed by surgery and resection margins were free from tumoral invasion, thus, after oncologic consult, we decided not to administer any adjuvant the-

rapy, even because areas of necrosis and hemorrhage in non-invasive thymomas, without mitotic activity, have not demonstrated to correlate with an aggressive behaviour (6, 17).

Follow-up after resection of thymomas is usually made with total body CT scan and (¹⁸F-FDG-PET)/CT (1), as in our patient, who shows neither local recurrence, nor distant metastases two years after surgical resection.

Conclusions

In conclusion, in case of anterior mediastinal mass with difficult histopathological diagnosis due to

massive necrosis, the hypothesis of a necrotic thymoma should be considered. Differential diagnosis problems may be overcome by an experienced pathologist and immunohistochemistry. Complete surgical resection, en-bloc with suspected involved structures, is the mainstay of treatment. After radical removal prognosis is generally favourable and no adjuvant treatment is required.

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