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## Case Report

# Ectopic thymoma arising in the pleura: Diagnostic challenges and clinical implications: A case report ☆☆☆

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## ABSTRACT

Thymoma is a rare tumor originating from the thymic epithelium, typically located in the anterior mediastinum. Ectopic thymomas are extremely uncommon and may occur in the neck, middle or posterior mediastinum, lung, or pleura.

We report the case of a 62-year-old woman presenting with cough, weight loss, and asthenia. Chest computed tomography (CT) revealed a right pleural mass. Complete surgical resection was performed, and the postoperative diagnosis confirmed a WHO Type AB thymoma, classified as Masaoka-Koga stage IIa.

Following surgery, she underwent adjuvant radiotherapy, and no recurrence was observed during follow-up.

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## Introduction

Thymomas are epithelial neoplasms of the thymus. They represent less than 1% of all primary malignancies in adults [1], but account for approximately 47% of anterior mediastinal tumors [2], making them the most common primary neoplasm in this region.

Ectopic thymomas comprising about 4% of all thymomas have been well described in the literature, with the most frequent ectopic sites being the neck, the middle and posterior mediastinum, and the lung. The pleural location is extremely rare [3], and diagnosis in such cases can be particularly challenging.

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## Case report

In April 2021, a 62-year-old woman presented with persistent cough, weight loss, and asthenia. Symptoms persisted despite empiric antibiotic therapy; therefore, a chest X-ray in posteroanterior (PA) and lateral projections, along with an abdominal ultrasound, were performed to exclude pathological masses, a primary neoplasm, or metastatic disease. The chest X-ray revealed a mass in the right hemithorax. The patient was hospitalized and, a few days later, underwent a computed tomography (CT) scan of the chest with and without contrast medium administration (Fig. 1) which showed a pleura-based, solid, enhancing lesion located in the lower right thoracic cavity, measuring approximately 11 × 8 cm. The mass exhibited smooth, well-defined margins, internal lobulation and septation, and scattered calcific foci. No evidence of direct endoluminal invasion into the major mediastinal vessels or signs of local infiltration was observed.

Few weeks later, the patient underwent an 18[F]-fluorodeoxyglucose positron emission tomography (FDG-PET) scan (Fig. 2). She received an intravenous injection of 18[F]-FDG (radioactivity: 371 mBq) and rested for 45 minutes before the scan. The lesion demonstrated increased metabolic activity, with a standardized uptake value (SUV) of 3.3.

In May 2021, 1 month after the diagnosis, the patient underwent surgery for mass removal. Surgical access was achieved via a right antero-lateral thoracotomy. Intraoperatively, a well-defined giant mass measuring 11 × 8 cm was identified, exhibiting expansive growth toward adjacent structures without apparent invasion. The tumor was completely resected.

Gross examination revealed an encapsulated mass surrounded by a thin, vascularized membrane. On sectioning, the lesion displayed a lobulated internal architecture, separated by fibrous septa, with a whitish-yellow appearance and soft consistency (Fig. 3). Immunohistochemical analysis revealed that the tumor cells were diffusely positive for CK-19 and p63, and focally positive for CD20, CD21, CD23. Proliferation fraction (ki67+) was low.

Histopathological examination revealed features consistent with a type AB thymoma, according to the World Health Organization (WHO) classification. The tumor was staged as Masaoka–Koga stage IIa. The patient subsequently underwent adjuvant radiotherapy.

Approximately 1 month later, due to the onset of respiratory symptoms, the patient underwent pulmonary function testing, which demonstrated a restrictive ventilatory defect. Serological testing revealed the presence of anti-acetylcholine receptor (AChR) autoantibodies, while anti-muscle-specific kinase (MuSK) antibodies were negative. Despite this serological finding, the patient did not report dysarthria, diplopia, dysphagia, or muscle fatigability. In the absence of clinical signs suggestive of a neuromuscular disorder, no immunosuppressive or disease-specific therapy was initiated at that time.

Three years later, the patient presented with unintentional weight loss, mild fatigability of the lower limbs, the sensation of an esophageal bolus, and difficulty maintaining head posture, particularly in the upright position. A repeat computed tomography (CT) scan ruled out thymoma recurrence (Fig. 4). Based on the clinical presentation and the presence of acetylcholine receptor (AChR) antibodies, a diagnosis of AChR-positive myasthenia gravis was established, corresponding to Myasthenia Gravis Foundation of America (MGFA) classification 2A. Treatment with pyridostigmine and corticosteroids was initiated, leading to a marked improvement in symptoms.

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## Discussion

Thymoma is the most common tumor of the thymus and the most frequent primary neoplasm of the anterior mediastinum. It can occur at any age, with a broad peak incidence between 35 and 70 years.

The gender distribution is approximately equal, although thymoma is slightly more frequent in older women [2]. Embryologically, the thymus originates from the third and fourth branchial pouches and migrates caudally to the anterior mediastinum by the fifth or sixth week of gestation. Aberrant migration can occur anywhere along this path, leading to ectopic foci of thymic epithelial cells. Ectopic thymomas are thought to arise from these ectopic remnants [4,5]. Thymomas may be asymptomatic and incidentally detected on chest CT scans performed for unrelated reasons. Some patients present with local symptoms due to compression of adjacent structures such as chest pain, cough, dyspnea, superior vena cava syndrome, dysphagia, or hoarseness while others may exhibit neuromuscular manifestations of myasthenia gravis. A smaller proportion of patients present with systemic paraneoplastic syndromes, including pure red cell aplasia, dermatomyositis, systemic lupus erythematosus, Cushing syndrome, or syndrome of inappropriate antidiuretic hormone secretion.

A minority of patients report constitutional symptoms such as fever and night sweats, which can make it difficult to differentiate thymoma from lymphoma [2].

Radiological features of pleural thymomas on chest X-ray are usually nonspecific. On CT scans, pleural thymomas typically appear as one or more unilateral, well-demarcated, round or oval pleural nodules, with smooth or occasionally lobulated margins and homogeneous density [6]. Various patterns of calcification may be present. After intravenous iodinated contrast, thymomas show homogeneous enhancement, although larger lesions may appear heterogeneous due to necrosis, hemorrhage, or cystic components.



**Fig. 1 – Preoperative patient assessment. (A) CT scanogram shows a right thoracic mass. (B, C) Coronal views of the thoracic CT scan demonstrate a large, heterogeneous right-sided lesion with possible internal necrotic foci, encapsulated and in close contact with the mediastinal visceral pleura. (D, E) Axial views of the CT scan show the thoracic mass.**

**Table 1 – World Health Organization classification of thymic epithelial tumors [6].**

Type	Histological findings
A	Medullary thymoma
AB	Mixed thymoma
B1	Predominantly cortical thymoma
B2	Cortical thymoma
B3	Epithelial thymoma
C	Thymic carcinoma

The main differential diagnoses include pleural tumors (such as mesothelioma, pleural metastases, and solitary fibrous tumors of the pleura) and chest wall sarcomas [4]. Differentiation by CT imaging can be challenging due to similar morphologic appearances [6].

Definitive diagnosis requires histological confirmation. The World Health Organization (WHO) histological classification (Table 1) is the most widely used system, based on microscopic appearance and correlating with the likelihood of invasiveness. Types A and AB are typically encapsulated and clinically indolent, while type B tumors are more prone to invasion. Type C (thymic carcinoma) is almost always aggressive and invasive.

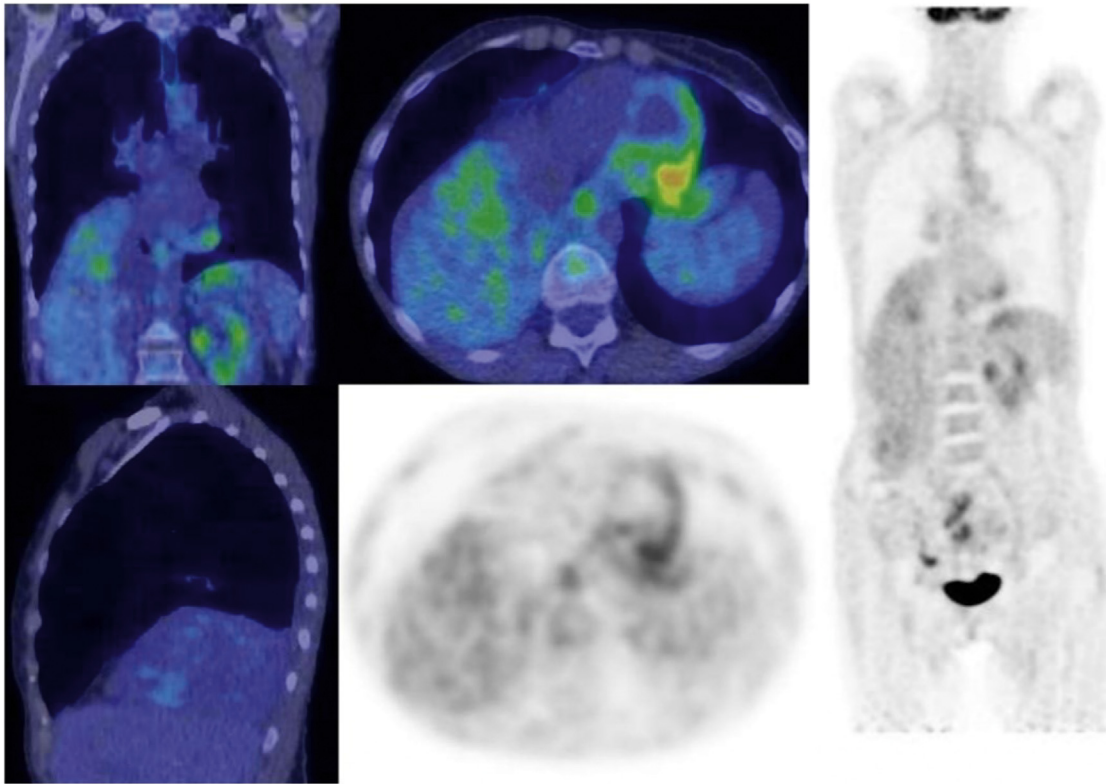
Despite being slow-growing tumors, thymomas can infiltrate adjacent structures (e.g., local vasculature, pericardium)

and metastasize. The Masaoka-Koga staging system (Table 2) is commonly used to stage thymic epithelial tumors and guide treatment decisions. Although this classification can only be fully assessed postoperatively, contrast-enhanced CT (CECT) serves as the primary preoperative tool to evaluate tumor extent and metastatic spread. Preservation of fat planes between the thymoma and adjacent structures suggests a noninvasive tumor, whereas their absence may indicate local invasion.

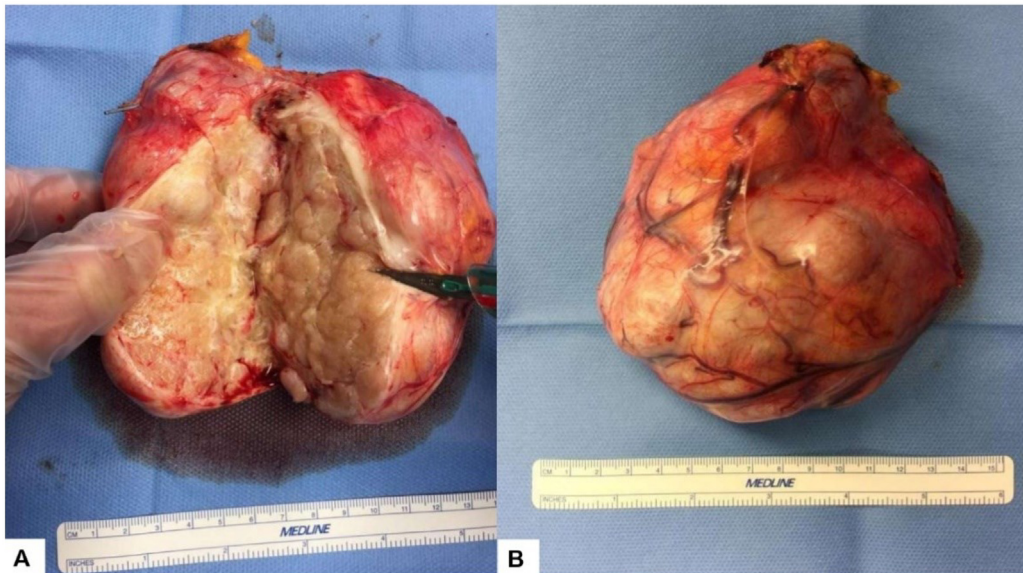
Small to medium-sized tumors without signs of local invasion may be resected without prior biopsy. In contrast, large tumors or those with suspected invasion require tissue sampling to differentiate thymoma from thymic carcinoma [2]. FDG-PET may assist in this differentiation: low-risk thymomas (WHO types A, AB, B1) and benign tumors typically demonstrate low FDG uptake (mean SUVmax <3.2), whereas aggressive neoplasms (WHO types B2, B3, and C) exhibit higher uptake (SUVmax >5) [7].

Surgical resection remains the treatment of choice for stage I and II thymomas and is generally performed without adjuvant radiotherapy, as postoperative radiation though previously common has shown limited benefit following complete resection.

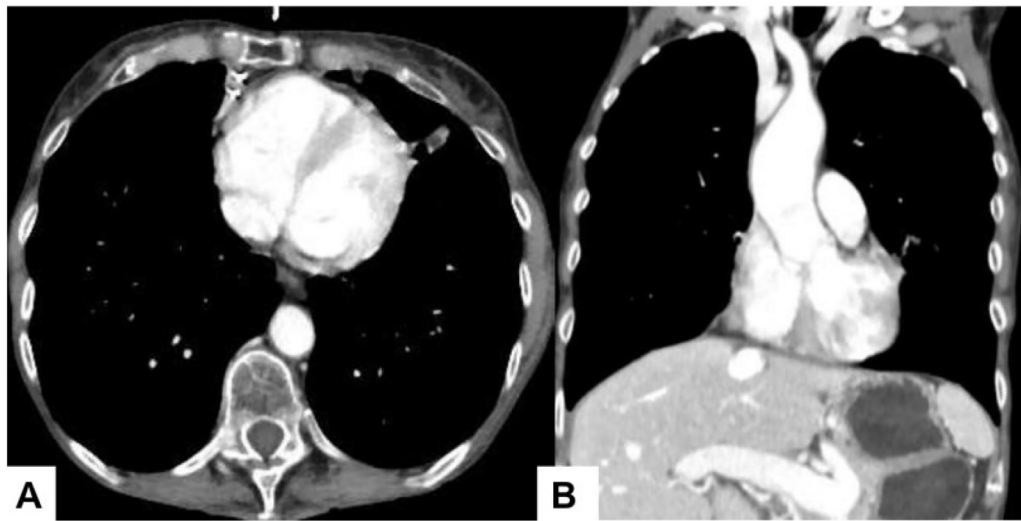
For clinical stage III and IVa tumors, preoperative cisplatin-based chemotherapy is recommended to increase the likelihood of complete (R0) resection. Postoperative radiotherapy may be considered in cases with residual disease. For unre-



**Fig. 2** – Positron emission tomography (PET) images. PET images in multiple spatial planes show a mildly increased uptake of  $^{18}\text{F}$ -fluorodeoxyglucose in the right-sided thoracic lesion, with a standardized uptake value (SUV) of 3.3.



**Fig. 3** – Intraoperative view of the large necrotic tumor. (A) sectioned lesion showing a lobulated internal architecture, separated by fibrous septa, with a whitish-yellow appearance and soft consistency; (B) the encapsulated mass surrounded by a thin, vascularized membrane.



**Fig. 4 – Follow- up at 3 years after surgery. CT scan shows no evidence of residual or recurrent disease in the axial view (A) and coronal view (B).**

**Table 2 – The Masaoka-Koga staging system [6].**

Stage	Definition
I	Grossly and microscopically completely encapsulated tumor <ul style="list-style-type: none"> <li>• This includes tumors with invasion into but not through the capsule, or tumors in which the capsule is missing but without invasion into surrounding tissues.</li> </ul>
IIa	Microscopic trans-capsular invasion <ul style="list-style-type: none"> <li>• Microscopic trans-capsular invasion (not grossly appreciated).</li> </ul>
IIb	Macroscopic invasion into thymic or surrounding fatty tissue, or grossly adherent to but not breaking through mediastinal pleura or pericardium <ul style="list-style-type: none"> <li>• Gross visual tumor extension into normal thymus or perithymic fat surrounding the thymoma (microscopically confirmed), or</li> <li>• Adherence to pleura or pericardium making removal of these structures necessary during resection, with microscopic confirmation of perithymic invasion, or</li> <li>• (but without microscopic extension into or through the mediastinal pleura or into the fibrous layer of the pericardium).</li> </ul>
III	Macroscopic invasion into neighboring organ (i.e. pericardium, great vessel or lung) This includes extension of the primary tumor to any of the following tissues: <ul style="list-style-type: none"> <li>• Microscopic involvement of mediastinal pleura (either partial or penetrating the elastin layer); or</li> <li>• Microscopic involvement of the pericardium (either partial in the fibrous layer or penetrating through to the serosal layer); or</li> <li>• Microscopically confirmed direct penetration into the outer elastin layer of the visceral pleura or into the lung parenchyma; or</li> <li>• Invasion into the phrenic or vagus nerves (microscopically confirmed, adherence alone is not sufficient); or</li> <li>• Invasion into or penetration through major vascular structures (microscopically confirmed); or</li> <li>• Adherence (i.e. fibrous attachment) of lung or adjacent organs only if there is mediastinal pleural or pericardial invasion (microscopically confirmed).</li> </ul>
IVa	Pleural or pericardial metastases <ul style="list-style-type: none"> <li>• Microscopically confirmed nodules, separate from the primary tumor, involving the visceral or parietal pleural surfaces, or the pericardial or epicardial surfaces.</li> </ul>
IVb	Lymphogenous or hematogenous metastasis <ul style="list-style-type: none"> <li>• Any nodal involvement (e.g. anterior mediastinal, intrathoracic, low/anterior cervical nodes, any other extrathoracic nodes).</li> <li>• Distant metastases (i.e. extrathoracic and outside the cervical perithymic region) or pulmonary parenchymal nodules (not a pleural implant).</li> </ul>

sectable tumors, radiation therapy alone or in combination with chemotherapy represents the standard treatment approach [2].

CT is also the recommended modality for follow-up, with thoracic scans every 6 months for the first 2 years, and annually thereafter [1].

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## Conclusions

This case highlights the importance of considering ectopic thymoma in the differential diagnosis of pleural masses, despite its rarity. Early recognition through imaging and prompt histological confirmation are essential for appropriate management. Complete surgical resection remains the cornerstone of treatment, with an excellent prognosis in cases of noninvasive disease.

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## Author contributions

All authors participated in conception, analysis, interpretation, drafting, and critical revision of the manuscript.

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## Patient consent

Informed written consent was obtained from the patient for publication of the case report and all imaging studies.

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