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(CASE REPORT)

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Pericardial ectopic thymoma: Case report of a rare tumor and a brief review of the literature

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Abstract

Thymoma is an uncommon tumor originating from the thymus. It is often associated with an autoimmune disease such as myasthenia gravis (MG). The majority of thymomas occur in the anterior mediastinum. However, ectopic thymomas tumors, which arise from thymic tissue improperly located because of aberrant embryonic migration, are far rarer. Of these, ectopic thymomas originating in the pericardium are particularly rare and only a few cases were reported. Due to the presence of ectopic pericardial thymoma in an uncommon site, it can be mistaken for various benign and malignant tumors, leading possibly to unnecessarily more aggressive treatment.

A 51-year-old man who had no significant medical history was incidentally detected to have a mediastinal mass on chest X-ray at the preoperative evaluation for an elective orthopedic operation. He had no autoimmune disease or paraneoplastic syndromes. Imaging studies revealed a large mass in the pericardial cavity, anterior to the right atrium, without invading surrounding structures or organs. The CT-guided biopsy led to the diagnosis of a type AB thymoma, confirmed with immunohistochemistry. Video-assisted thoracoscopic surgical resections were carried out. The diagnosis was confirmed on final histology, with a preserved capsule and negative margins. Based on the 2025 AJCC/UICC TNM staging system, the tumor was staged as T1b N0 M0. The patient has been free of recurrence or metastasis for four years.

Keywords: Thymoma; Thymus; Pericardial; Myasthenia gravis; Neoplasm

1. Introduction

Thymomas are neoplasms of the epithelial cells of the thymus that typically present as mediastinal tumors in adults. [1] Thymomas are rare tumors, representing 1.5-1.7 cases per million each year in Europe and the United States. [3] It is rare for thymomas to occur outside the mediastinum due to early thymic tissue that failed to migrate to the mediastinum during embryogenesis. [4] Ectopic localization in the neck, pulmonary hilum, and pericardium has been reported. Pericardial thymoma is very rare and may also cause considerable complications, such as pericardial effusion or cardiac tamponade. [5]

Due to the atypical site for thymus tissue, ectopic thymomas can present a challenging diagnosis. Ectopic thymomas are frequently asymptomatic and are found incidentally in non-thoracic imaging [3] as in the current case, where a chest x-

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ray was performed as part of preoperative evaluation for orthopedic surgery. Symptoms, if present, are typically vague, including chest pain, cough, and dyspnea. [6] Ectopic thymomas are rare, tend to be slow-growing, and can mimic other primary neoplasms of the pericardium and mediastinum, including pericardial cysts, lipomas, germ cell tumors, lymphoma, and secondary tumors. [4]

Most incidentally found masses seen on a chest X-ray require additional investigation with CT or MRI. [7] CT is the best imaging modality for diagnosis of all thymomas. It provides detailed and precise information of the tumor's contact with the surrounding structures, and offers qualitative evaluation on the extent of tumor encasement, calcification, and degree enhancement after contrast medium administration. CT findings are essential for determining severity of the disease for therapeutic decision-making. [7] Additionally, though imaging may be indicative of the diagnosis, subsequent histopathologic evidence is essential. [4] Complete resection of the tumor is usually sought; consequently, preoperative tissue biopsy is frequently not considered. [5]

Surgery is central to the treatment of thymomas, including those that are ectopically located. [8] Adjuvant treatment is commonly used for invasive or recurrent lesions. [4] [9] Prognosis depends on tumor stage and histologic type. Encapsulated, low-grade thymomas, classified as WHO types A or B1, carry an excellent prognosis, with 10-year survival rates exceeding 90%. [8] Ectopic location does not appear to impact overall survival when complete excision is achieved. [10] We describe a case of ectopic pericardial thymoma in a 51-year-old man who was diagnosed early in his disease course and who later underwent surgical resection with a favorable prognosis. We emphasize the importance of including ectopic thymoma in the differential diagnosis of patients presenting with a pericardial mass.

2. Case presentation

A chest radiograph was taken as part of a preoperative work-up for elective orthopedic surgery of a 51-year-old man that demonstrated a mediastinal mass. He was asymptomatic and he did not report cardiopulmonary symptoms, fatigue, weight loss or any other systemic symptoms. He had also no previous autoimmune or paraneoplastic diseases. He was afebrile and hemodynamically stable on exam with no relevant medical or family history.

Cardiopulmonary exam was normal with no murmurs and clear lungs bilaterally. The physical exam was unremarkable for peripheral edema, lymphadenopathy, or significant neurological and muscular findings. On chest X-ray, a well-circumscribed, lower mediastinal lesion was identified. An enhanced CT of the chest revealed a lobulated well-defined soft tissue mass (6.0 × 4.8 cm) in the pericardial space anterior to the right atrium. The mass was well contained with no extension into adjacent cardiac, lung, or pericardial fatty tissues. Mediastinal or hilar lymphadenopathy, pericardial or pleural effusions were not detected. The MRI set forth the existence of a non-infiltrative nodule with well-defined borders in line with the pericardial planes. Positron emission tomography-computed tomography (PET-CT) revealed that metabolic activity was only slightly high to moderate in the tumor area, and indicated no distant spread. The differential diagnosis of this pericardial mass was very broad.–Lymphoma was entertained but usually manifests with systemic B symptoms and demonstrates marked FDG avidity on PET-CT. Although relatively common, pericardial cysts are fluid-containing masses that are non-enhancing and generally benign. Infiltrating masses with effusion may be present in pericardial mesotheliomas, but these were not present in this case. The clinical presentation was not suggestive of metastasis. Solitary fibrous tumors (SFTs), if present, typically have a staghorn vascular pattern and are positive for CD34 and STAT6 but negative for cytokeratin, unlike thymomas.

Following the recommendation of a multidisciplinary tumor board, the patient was treated with complete resection of the mass through video-assisted thoracoscopy (VATS). On gross examination, the tumor was lobulated and well-circumscribed. Intraoperative frozen section consultation confirmed the thymic nature of the mass with deferring subtyping to permanent tumor examination. Microscopic examination of the excised tumor confirmed the diagnosis of type AB ectopic pericardial thymoma. The tumor appeared as a lobulated mass infiltrating the pericardium without involvement of pericardial fat or surrounding soft tissue. The tumor had an intermediate-grade morphology, composed of bland spindle and polygonal epithelial cells with granular chromatin and inconspicuous nucleoli, haphazardly intermingled with, and surrounded by abundant lymphocytes. Mitotic figures were lacking or rare, and no necrosis was present**.** **(**Figure 1 A, B, C, D**)** No invasion of neighboring organs was observed. Complete surgical resection was achieved; the capsule was intact, and the surgical margins were negative. All identified five mediastinal lymph nodes were negative for tumor.

The tumor was a T1b N0 M0, according to the American Joint Committee on Cancer/ Union for International Cancer Control Tumor, Node, and Metastasis (AJCC/UICC TNM) 9th edition (2025) TNM classification of thymic epithelial tumors that describes T1b as any microscopic invasion of the pericardium through one of the three methods, direct

extension, invasion of pericardial fibrous layer, or invasion of the serosa. [1] [6] Histomorphology and IHC studies were adequate for the diagnosis achieved in this case, and no molecular studies were performed.

Postoperative follow-up included enhanced chest CT every 6-12 months and physical examination every year. There has been no recurrence or metastasis, and the patient remained disease-free at the 4-year follow-up.

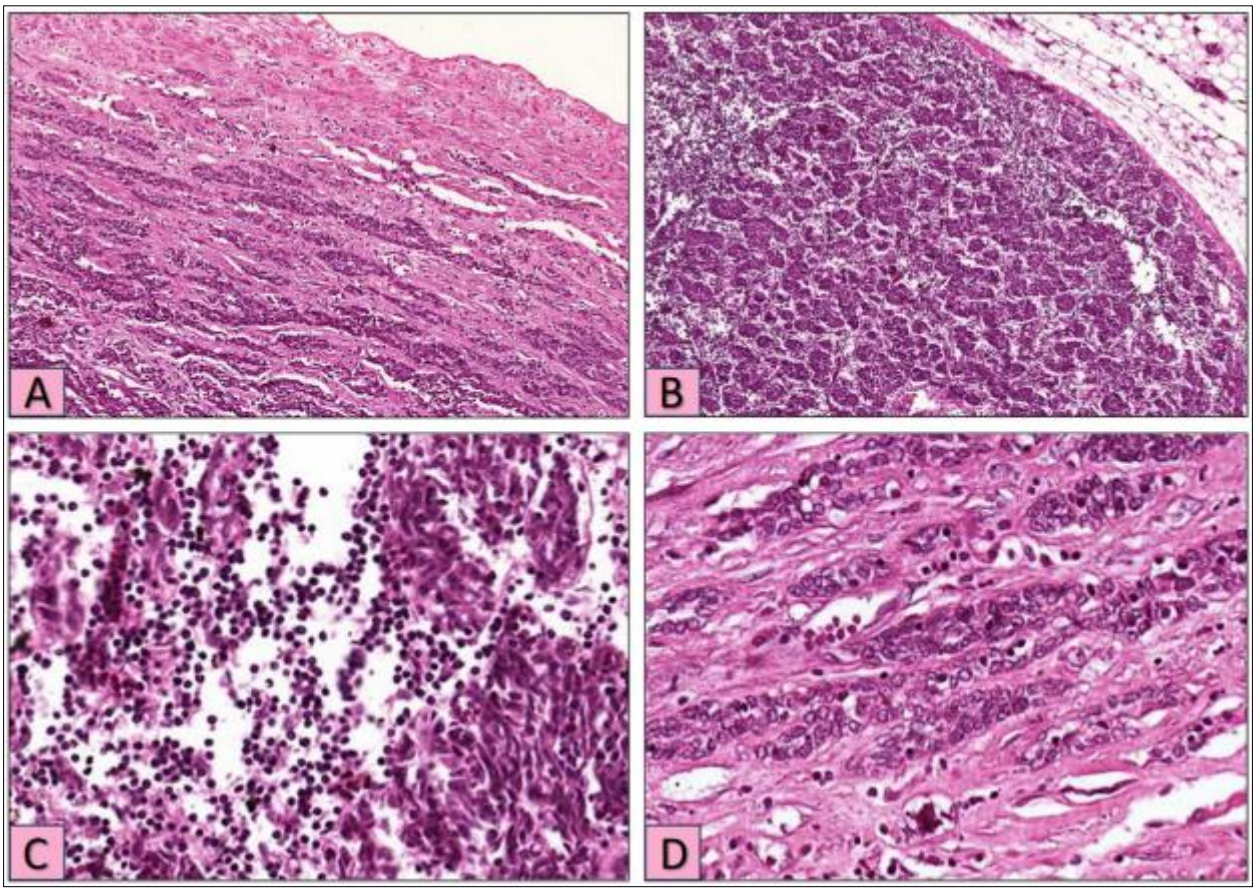

Figure 1 Histomorphologic features of the excised thymoma

- **1A** Low power view showing lobulated mass infiltrating the pericardial tissue (H&E stain X20)
- **1B:** Low power view showing thymoma without extension into the pericardial fat or adjacent tissue (H&E stain X20)
- **1C:** Intermediate power view showing the tumor bland spindle and polygonal epithelial cells among and intermixed with abundant lymphocytes (H&E stain X40)
- **1D**: High power view showing the tumor cells with dispersed chromatin and inconspicuous nucleoli. Mitotic is absent or rare, and necrosis is not found (H&E stain X60)

3. Discussion

- **History and Epidemiology:** Tumors of the thymus are uncommon. However, they are the most frequent masses of the anterior mediastinum. The prevalence has been estimated to be 0.13 to 0.32 per 100,000 population per year. Thymomas also account for only 0.2-1.5% of all cancers. [6] In addition, sex does not significantly influence the development of disease. [8] Research on thymomas began in the early 20th century. Bell et al. noted an association between thymomas and epithelial tissue, as well as Myasthenia gravis (MG). [6] [8] In 1985, Marino et al. proposed that thymomas can be classified as originating from a neoplastic proliferation of cortical, medullary, or mixed thymic origin. [11] In 1978, Levine and Rosai proposed that thymomas contained within the thymic capsule are benign [12] [13]. These thymomas represent the A and AB subtypes. However, more recent evidence suggests that they are not benign. [12]

Dr. Juan Rosai introduced the modern nomenclature for major thymoma types, and they became part of the 1999 WHO guidelines [4]. The 1999 WHO guidelines classified thymomas into six subtypes: A, AB, B1, B2, B3, and C, based on histological findings. In 2004, WHO modified these guidelines and changed subtype C to the term 'thymic carcinoma. [12] The current WHO guidelines, from 2021, are based on the fifth edition of the classification of thymic epithelial tumors. [4] While few changes have occurred between the fourth and fifth editions of the WHO classifications, several scientific achievements warrant discussion. The new edition has emphasized molecular profiles of tumors thanks to The Cancer Genome Atlas (TCGA). [10] Molecular profiles of thymoma subtypes have also strengthened the evidence for the 1999 WHO classifications. [4] Despite a few changes to the new classifications, some modifications have been made. Microscopic thymomas have been renamed to nodular epithelial hyperplasia

- **Pathogenesis**: The rarity of pericardial ectopic thymoma precludes a comprehensive understanding of its pathophysiology. However, the underlying biological processes likely stem from the effects of misplaced thymic tissue in inappropriate sites, with the potential for neoplastic conversion and mechanical cardiac complications. [8]
- **Staging, Masaoka staging vs TNM staging:** In 1978, Bergh et al. proposed a three-tiered staging system to classify the extent of thymomas: stage I represented a tumor within the capsule, stage II was assigned if a tumor extended into mediastinal fat, and stage III was assigned if there was intrathoracic metastasis or invasion of surrounding organs. In 1981, the four-tiered Masaoka staging system was proposed. In 1994, this was further modified by Koga et al. In 1991, a tumor, node, metastasis (TNM) classification was proposed by Yamakawa et al., which utilized the Masaoka system. [14**]**
- **Association with myasthenia gravis (MG):** The association between thymomas and MG was first reported last century. The prevalence of thymomas in MG patients is 10–15%, and approximately 50% of thymomas are associated with MG. Thymomas associated with MG are usually of the cortical subtype (WHO type B). [15] Another study looked at a different cell type. Neuromuscular medullary thymic epithelial cells (nmTECs) are cells that have an intermediate profile between cortex and medullary thymic epithelial cells. Bulk RNA-seq data from TCGA reveal that thymomas associated with MG have an increased frequency of these intermediate cells. [16] Acetylcholine receptors (AChRs), Titin, and ryanodine receptor autoantibodies have been associated with thymoma and MG. In MG patients younger than 60 years, the presence of Titin and ryanodine receptor antibodies is associated with a strong correlation with thymoma. Similarly, the absence of these antibodies can strongly rule out the presence of thymoma. [15] In addition to autoantibodies, seropositive thymomas exhibited an increase in MG thymoma-specific genes, including NEFM, KRT6A, and KRT15. [16]
- **Imaging and differential diagnosis:** Ectopic thymomas are extremely rare and have only been reported in a few cases. Their atypical locations often result in being incidentally found on cross-sectional imaging. Most patients, as in our case, are asymptomatic at the time of diagnosis. When symptomatic, they usually present with mass effects (e.g., chest pain, shortness of breath, cough). However, they can be associated with paraneoplastic syndromes, such as MG. [17] Most radiological characteristics vary according to tumor size and location. Non-specific findings, such as mediastinal widening or "apparent cardiomegaly," may be visible on chest X-rays. CT with contrast typically reveals circumscribed, lobulated soft tissue masses without invasion. [16] MRI provides a clear depiction of tissue planes and their relationship with surrounding anatomy, and PET-CT is the most reliable due to its ability to detect metabolic changes and identify negative metastases. According to the pathology report of our case, the lesion exhibited low to intermediate radiotracer fluorodeoxyglucose (FDG uptake), a characteristic feature of WHO-type AB thymomas. [18]
- **Immunohistochemistry (IHC) markers in identifying thymomas**: Thymomas and thymic carcinomas are often positive for FOXN1, polyclonal PAX8, and CD205, which may aid in identifying the origin of the tumor. CD5 and CD115 (cKIT) are often positive in thymic carcinoma but not in thymomas. [19] [20] To distinguish thymic carcinomas compared to metastasis from other sites, a few markers can be used in conjunction with IHC markers. For example, to differentiate between primary lung neoplasm and one of thymic origin, the coexpression of two or three markers CD5, PAX8, and CD117, can improve the sensitivity of the results. [19]
- **Genomics of thymoma**: Next-generation sequencing has revealed the prevalence of three genes in thymomas: GTF2I (58%), TP53 (36%), and HRAS (2%). An increased frequency of mutations in the GTF2I gene has been documented in type A and AB thymomas. [22] [23] More specifically, one study observed that 100% of samples obtained mutations in type A thymomas, and 70% of samples obtained mutations in type AB thymomas. [23] Thymomas associated with the GTF2I gene contained a mutation at a single codon, L424H. Furthermore, data from 10,000 other cancer samples obtained from the Cancer Genome Atlas (TCGA) did not include this single codon mutation. [23] In type A and AB thymomas, HRAS is the second most common mutated gene. [24]

Other characteristics of type A and AB thymomas include a large microRNA cluster on chromosome 19 that showed overexpression. This cluster has been associated with PI3K/AKT activation. [23] TP53 mutations in thymomas are associated with a loss of function in p53, and they are more commonly found in type B thymomas and thymic carcinomas. [4] In addition, increased gene copy number has been most notable in B3 thymomas and thymic carcinomas. [20] The PD-1 (immune checkpoint Programmed Death-1) works as an immunosuppressor, expressed when T-cells are activated. The Food and Drug Administration (DFA) now endorses medications that target PD-1 for treating various cancers, including Nivolumab, Pembrolizumab, and cemiplimab. Likewise, agents that focus on programmed death ligand 1 (PD-L1), such as Avelumab, Durvalumab, and Atezolizumab, have also received FDA approval. [4] [25] [26] It is of value to consider the known frequent expression of PD-L1, which could present a potential target study. [25]

- **Treatment and prognosis**: The cornerstone of treatment for pericardial ectopic thymoma, particularly WHO type AB, is complete surgical resection. When feasible, this approach is associated with excellent outcomes and long-term disease control. Surgical excision not only offers curative potential but also prevents life-threatening complications such as cardiac tamponade, constrictive pericarditis, or progression to heart failure due to local invasion or mass effect. [5] [17] In our case, a complete surgical resection was performed through a video-assisted thoracoscopic procedure with negative margins and capsule preservation. Based on the 2023 AJCC UICC TNM staging system, the stage of the tumor was T1b N0 M0, indicating pericardial invasion without involvement of adjacent structures. A favorable prognosis was expected with this stage of the tumor, especially with total resection of the mass. [2] In cases where a residual tumor is present due to incomplete surgical resection, adjuvant therapies are utilized. These may involve radiotherapy, which is commonly used for local control. For unresectable or advanced diseases, platinum-based chemotherapy is given. [1] As an example, in a report by Jiang et al. [9], a 16.8 × 7.8 cm large thymoma with right atrial invasion underwent induction chemotherapy (CAP: cyclophosphamide, doxorubicin, cisplatin) and radiotherapy prior to complete resection. The survival rate of the disease has been improved by multimodal therapy, including neoadjuvant chemotherapy, surgical resection, and adjuvant external radiotherapy, particularly for advanced-stage disease and elderly patients in whom surgical resection alone is insufficient or palliative [7]

The prognosis of thymomas, irrespective of the location (ectopic), is primarily determined by the stage of disease, histologic type, and the appropriateness of surgical excision. Type AB thymomas are usually indolent but not consistently benign. The 10-year overall survival after complete surgical resection for stage I is 80%, and for stage IV, it is around 42%. [3] The disease rarely recurs in those with early disease adequately resected, with our patient being disease-free at 4 years follow-up. Long-term monitoring, including periodic imaging, is necessary, as late recurrences have been described.

Although thymomas are often considered benign, studies suggest that they may exhibit malignant clinical characteristics. [27] In multiple instances, including ours, they are found accidentally, such as during standard preoperative assessments for unrelated surgeries, like orthopedic operations. A case described by Arai et al. [5] involved a patient with cardiac tamponade caused by a pericardial thymoma, emphasizing a more rapid and symptomatic emergence. In contrast to our patient, who showed no symptoms, this instance highlights the risk of abrupt hemodynamic instability when the tumor extensively infiltrates the pericardial area. The tumor, in that case, was also surgically resected with favorable outcomes.

- **What we learned from this case:** Ectopic thymomas are rare and must be considered in the differential diagnosis of any mass in the anterior or middle mediastinum and the pericardium. The thymic tissue present in the pericardium is quite uncommon and can result in misdiagnosis. Radiological investigations are indispensable for the initial workup, and the definitive diagnosis is always histopathological. Radical excision is usually curative for the majority of early thymomas. Knowledge of this rare condition can aid in earlier diagnosis and treatment.

4. Conclusion

We report a rare case of an ectopic pericardial thymoma incidentally discovered in a 51-year-old man. The diagnosis, although rare in this location, was both clinically and radiologically accurate and was also confirmed by histopathology and IHC. Complete surgical resection by VATS resulted in a favorable outcome, and no recurrences were observed for up to 4 years. This patient case also highlights the need for other medical practitioners to consider an ectopic thymoma in their differential diagnosis for pericardial masses, along with the fact that early identification and complete removal can lead to a favorable prognosis, even when the ectopic thymoma involves rare sites.

Compliance with ethical standards

Disclosure of conflict of interest

All authors declare the following.

- *Payment/services information*

All authors have declared that they received no financial support from any organization for the submitted work.

- *Financial relationships*

All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might be interested in the submitted work.

- *Other relationships*

All authors have declared that no other relationships or activities could appear to have influenced the submitted work.

Data access statement

All relevant data are included in the paper.

Author contributions

All authors contributed equally to producing this manuscript.

Statement of ethical approval

Ethical review and approval were not required for the study on human participants. The paper has been sufficiently anonymized to maintain the patient's confidentiality.

Statement of informed consent

The patient was lost to follow-up, and all attempts to reach the family members were unsuccessful. Therefore, the paper has been sufficiently anonymized to maintain patient confidentiality.

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