

Lipofibroadenoma of the Thymus: A Case Report With Literature Review and Differential Diagnostic Considerations

Review began 10/07/2026

Review ended 10/17/2026

Published 10/20/2026

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DOI: 10.7759/cureus.118219

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Abstract

Thymic lipofibroadenoma is a rare lesion composed of mature adipose tissue, fibrous stroma, and thymic epithelial elements. We describe a 51-year-old woman with recurrent syncope and a large anterior mediastinal mass compressing adjacent cardiac structures. Complete excision yielded an encapsulated, multilobulated mass measuring 14 × 4 × 2 cm. Histology showed bland epithelial strands and cords within dense hyalinized stroma admixed with mature fat and Hassall corpuscles. Epithelial cells expressed cytokeratins AE1/AE3 and 19, supporting the diagnosis of lipofibroadenoma. At six months, the patient was asymptomatic without imaging evidence of recurrence. A narrative review of 18 previously published cases addresses the clinicopathologic spectrum and differential diagnosis, particularly the overlap with thymolipoma and thymofibroliipoma. Reported outcomes generally favor benign behavior, although limited and uneven follow-up prevents firm conclusions about long-term recurrence risk.

Categories: Radiology, Pathology, Anatomy

Keywords: differential diagnosis, lipofibroadenoma, mediastinal neoplasms, rare thymic neoplasm, thymus

Introduction

Thymic lipofibroadenoma is an uncommon anterior mediastinal lesion characterized by an admixture of mature fat, fibrous stroma, and thymic epithelial strands, often resembling mammary fibroadenoma. The 2021 World Health Organization Classification of Thoracic Tumours places it among thymic epithelial tumors [1]. Its initial description involved a lesion associated with type B1 thymoma and pure red cell aplasia [2]. The relationship between its epithelial and mesenchymal components remains uncertain.

We describe a thymic lipofibroadenoma in a 51-year-old woman with recurrent syncope and radiologic compression of adjacent cardiac structures. We also review 18 previously published cases and discuss diagnostic distinctions and areas of overlap with other fibroadipose thymic lesions.

Case Presentation

A 51-year-old woman was referred to the cardiology outpatient clinic after recurrent syncopal episodes over four months. She had no known relevant medical history. Transthoracic echocardiography demonstrated an extracardiac mass compressing the cardiac chambers.

Contrast-enhanced computed tomography (CT), positron emission tomography-CT (PET-CT), and magnetic resonance imaging (MRI) demonstrated a large, well-circumscribed anterior mediastinal mass extending into the right hemithorax (Figure 1).

How to cite this article

Ntalakos N, Arnaouti M, Chlapoutakis S, et al. (October 20, 2026) Lipofibroadenoma of the Thymus: A Case Report With Literature Review and Differential Diagnostic Considerations. Cureus 18(10): e118219. DOI 10.7759/cureus.118219

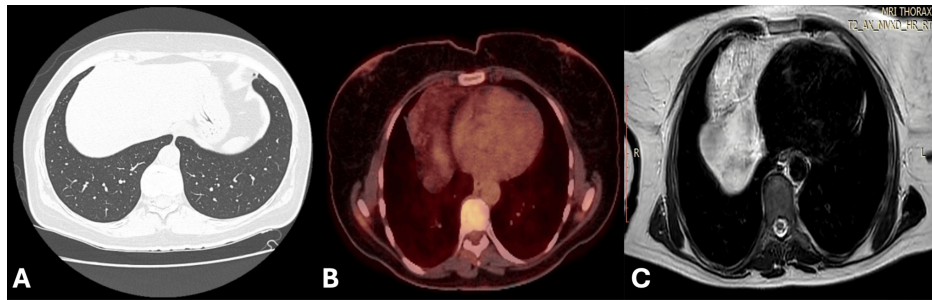


FIGURE 1: Preoperative imaging of the anterior mediastinal mass

(A) Axial contrast-enhanced computed tomography (CT) image of the chest demonstrates a well-circumscribed anterior mediastinal lesion containing fatty and soft-tissue components and extending into the right hemithorax. (B) Axial fused positron emission tomography-CT (PET-CT) image of the chest shows low metabolic activity within the lesion. (C) Axial magnetic resonance imaging (MRI) image of the chest demonstrates the lesion and its relationship to adjacent cardiac structures.

The lesion contained fatty and soft-tissue components and displaced and compressed adjacent cardiac structures without radiologic evidence of invasion. PET-CT showed low metabolic activity. MRI demonstrated a predominantly fatty lesion with internal fibrous septations. Complete surgical excision was performed because of the symptoms and lesion size.

Gross examination showed a multilobulated, completely encapsulated mass measuring $14 \times 4 \times 2$ cm. The cut surface was predominantly yellow-tan and firm, without necrosis or hemorrhage (Figure 2).

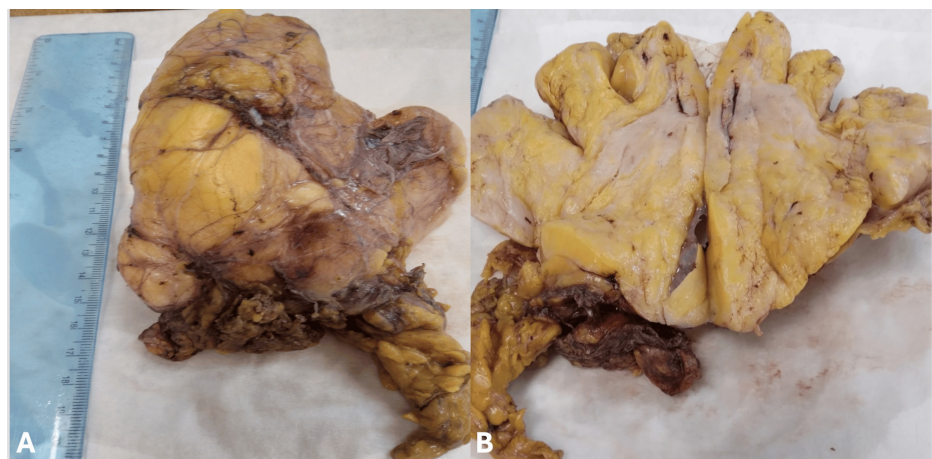


FIGURE 2: Gross appearance of the resected mass

(A) The external surface is encapsulated and multilobulated. (B) The cut surface is predominantly yellow-tan and firm, with interspersed fibrous areas.

Microscopically, dense fibrous and hyalinized stroma contained narrow cords and strands of cytologically bland epithelial cells, mature adipose tissue, and sparse lymphocytic infiltrates. Structures consistent with Hassall corpuscles were identified (Figure 3).

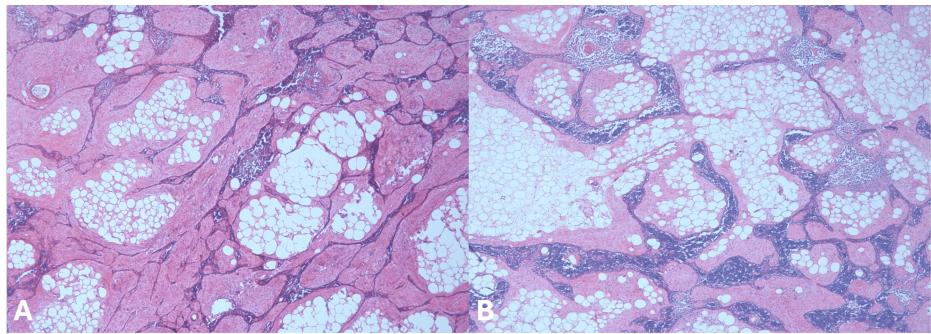


FIGURE 3: Histologic features of thymic lipofibroadenoma

(A, B) Hematoxylin and eosin–stained sections show dense fibrous and hyalinized stroma admixed with mature adipose tissue and bland epithelial strands (×20 in both panels).

The epithelial cells showed diffuse cytoplasmic staining for cytokeratin AE1/AE3 (CKAE1/AE3) and cytokeratin 19 (CK19) (Figure 4).

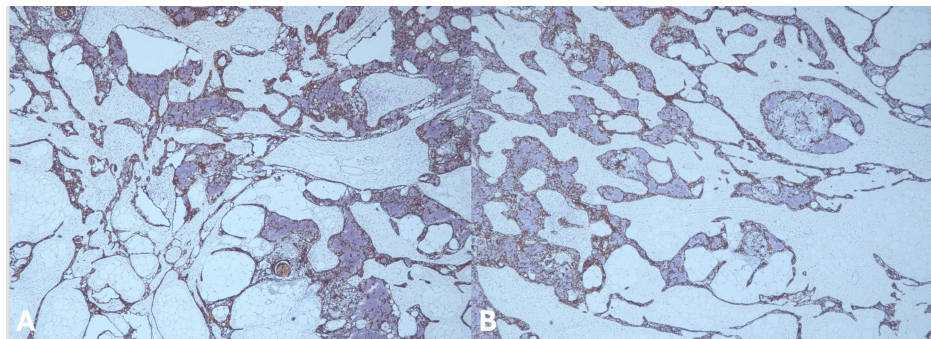


FIGURE 4: Immunohistochemical demonstration of the epithelial component

(A) Cytokeratin AE1/AE3 and (B) cytokeratin 19 (CK19) highlight the epithelial strands and cords (×20 in both panels).

The accompanying lymphocytes included CD3–positive T cells and CD20–positive B cells. The Ki-67 proliferation index was <3%. The morphology and immunophenotype supported a diagnosis of thymic lipofibroadenoma.

At six months after surgery, the patient remained asymptomatic, with resolution of the syncopal episodes and no imaging evidence of recurrence.

Discussion

Literature review

This narrative review focuses on 18 previously published cases of thymic lipofibroadenoma [2–17]. The case compilation is selective and does not represent an exhaustive count of all reported cases.

Table 1 summarizes the clinical presentation, coexisting thymic lesions and systemic conditions, treatment, and follow-up of these 18 patients together with the present patient (19 patients in total).

Source	Age (y)/sex	Presentation	Coexisting thymic lesions and systemic conditions	Treatment	Outcome / follow-up
Kuo and Shih, 2001 [2]	62 M	Dyspnea, dizziness	B1 thymoma; PRCA	Excision	NED; duration NR
Onuki et al., 2009 [3]	32 M	Incidental	NR	Excision	NR
Wang et al., 2009 [4]	56 M	Cough, expectoration	B1 thymoma	Excision	NED; duration NR
Aydin et al., 2012 [5]	23 F	Chest pain, dyspnea	B1 thymoma	Excision	NED; duration NR
Qu et al., 2013 [6]	21 M	Incidental	NR	Excision	NED at 46 mo
Makdisi et al., 2015 [7]	20 M	Fever, cough	NR	Excision	NED; duration NR
Hui et al., 2018 [8]	29 M	Cough, expectoration	B1 thymoma	Excision	NR
Kojima et al., 2018 [9]	29 M	Asymptomatic	NR	Excision	NR
Hakiri et al., 2021 [10]	28 M	Incidental	NR	Excision	NED at 6 mo
Kurebayashi et al., 2021 [11]	55 F	Incidental	Thymic hyperplasia	Excision	NED; duration NR
Matyjek et al., 2021 [12]	35 F	Fatigue, cough	ANCA-associated vasculitis with renal involvement	Excision	NED; duration NR
Bolca et al., 2021 [13]	64 F	Progressive dyspnea	NR	Excision	NED; duration NR
Fu et al., 2022 [14]	21 M	Fever	NR	Excision	NED at 12 mo
den Bakker et al., 2023 [15]	17 M	Incidental	NR	Excision	NED; follow-up 9 mo in case text, 13 mo in abstract
Yang et al., 2023, case 1 [16]	59 F	Chest tightness	NR	Excision	NED at 19 mo
Yang et al., 2023, case 2 [16]	33 F	Incidental	Thymic hyperplasia	Excision	NED at 7 mo
Yang et al., 2023, case 3 [16]	37 M	Dyspnea	NR	Excision	NED at 30 mo
Kazemi et al., 2024 [17]	30 F	Incidental	No related comorbidity reported	Excision	NED; duration not stated
Present case	51 F	Recurrent syncope	No relevant history reported	Complete excision	Asymptomatic; NED at 6 mo

TABLE 1: Previously reported thymic lipofibroadenoma cases and the present case

The column "Coexisting thymic lesions and systemic conditions" records additional thymic lesions and systemic conditions reported in each case; coexistence does not establish causation. NR does not mean that a finding was absent. References correspond to the main manuscript.

F, female; M, male; y, years; mo, months; NED, no evidence of disease; NR, not available in the source material reviewed; PRCA, pure red cell aplasia; ANCA, antineutrophil cytoplasmic antibody.

The 18 previously reported patients range in age from 17 to 64 years and include both sexes. Presentations include incidental discovery and symptoms associated with mediastinal mass effect. Coexisting type B1 thymoma, thymic hyperplasia, pure red cell aplasia, and antineutrophil cytoplasmic antibody-associated

vasculitis have been described; coexistence does not establish causation. Published reports generally describe favorable postoperative courses, but follow-up is inconsistently documented, and an absence of reported recurrence does not establish a precise recurrence rate.

Diagnostic interpretation and differential diagnosis

The present lesion shows the characteristic combination of bland epithelial cords, hyalinized stroma, and mature fat. Keratin staining highlights the epithelial component but does not, by itself, establish that this component is neoplastic. The relative contributions of the epithelial and stromal components to the lesion's development remain uncertain.

Thymolipoma typically consists predominantly of mature adipose tissue containing thymic parenchyma, including epithelial elements and Hassall corpuscles [1,18]. The prominence and organization of the fibrous component help in assessing the differential diagnosis, but the presence of thymic epithelium alone does not distinguish thymolipoma from lipofibroadenoma.

Thymofibrolipoma also contains mature fat, collagenous stroma, and thymic tissue [19,20]. These components overlap with those of lipofibroadenoma, making their relative proportions and arrangement important in the morphologic assessment. The fibroadenoma-like architecture should therefore be interpreted in the context of the entire lesion.

Thymoangiolipoma and thymohemangiolipoma feature conspicuous vascular components admixed with mature fat and thymic tissue [21,22]. Sclerosing thymoma shows extensive collagenization with residual thymomatous epithelial foci; adequate sampling is important to identify these foci [23,24]. Table 2 summarizes the main morphologic considerations.

Entity	Key morphology	Diagnostic consideration
Lipofibroadenoma [1,2]	Mature fat, dense fibrous/hyalinized stroma, and bland epithelial strands or cords	Fibroadenoma-like architecture; interpret the epithelial component in its stromal context.
Thymolipoma [1,18]	Predominantly mature adipose tissue with thymic parenchyma and Hassall corpuscles	Fibrosis is usually less prominent. Thymic epithelial elements occur in both lesions.
Thymofibrolipoma [19,20]	Mature fat, prominent collagenous tissue, and residual thymic islands or strands	Morphologic overlap with lipofibroadenoma; assess the proportions and arrangement of fat, collagen, and thymic tissue.
Thymoangiolipoma/thymohemangiolipoma [21,22]	Mature fat and thymic elements with a prominent vascular component	Conspicuous vascular channels distinguish the dominant pattern.
Sclerosing thymoma [23,24]	Extensive collagenization with residual thymomatous epithelial foci	Search adequately sampled tissue for conventional thymoma; interpret fat in the overall architecture.
Lipoma [1]	Predominantly mature adipocytes without the characteristic epithelial–fibrous architecture	Distinguish a true lesional epithelial component from adjacent or entrapped thymus.
Well-differentiated liposarcoma [1]	Atypical adipocytic/stromal cells, often in fibrous septa; lipoblasts may be inconspicuous	Stromal atypia and appropriate ancillary findings are more useful than the absence of thymic epithelium.
Solitary fibrous tumor [1]	Spindle-cell proliferation, collagen, and characteristic branching vessels; fat may be present	The spindle-cell and vascular architecture, supported by appropriate immunohistochemistry, is central.
Desmoid fibromatosis [1]	Infiltrative fibroblastic/myofibroblastic proliferation in collagenous stroma	Infiltrative architecture and the lesional spindle-cell phenotype; interpret nuclear β-catenin in context.

TABLE 2: Morphologic differential diagnosis of thymic lipofibroadenoma

Original table created by the authors as a synthesis of the cited literature [1,2,18-24]. The table has not been reproduced or adapted from a previously published table. These are diagnostic considerations rather than absolute exclusion criteria; architecture, sampling, cytology, and appropriate ancillary findings should be assessed together.

For other mesenchymal tumors, diagnosis depends on the architecture and cytology of the lesional component and, where appropriate, ancillary studies. The presence or absence of entrapped thymic tissue should not be used as the sole exclusion criterion.

Conclusions

A distinctive clinical feature of the present case is the association of recurrent syncope with compression of adjacent cardiac structures. Resolution after excision supports a possible contribution from the mass, although the available observations do not prove the mechanism of syncope. The six-month follow-up is reassuring but provides limited evidence about long-term behavior.

The available literature supports a generally indolent course after surgical excision, while recognizing the limited number of patients and uneven follow-up. Coexisting thymoma or systemic disease should be assessed on its own clinical merits. Recognition of the fibroadipose architecture and thymic epithelial component helps establish the diagnosis, while the overlap with related thymic lesions and the uncertain histogenesis should be acknowledged.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Concept and design: Nektarios Ntalakos, Maria Arnaouti, Evdokia Arkoumani, Serafeim Chlapoutakis

Acquisition, analysis, or interpretation of data: Nektarios Ntalakos

Drafting of the manuscript: Nektarios Ntalakos, Maria Arnaouti

Critical review of the manuscript for important intellectual content: Nektarios Ntalakos, Maria Arnaouti, Evdokia Arkoumani, Serafeim Chlapoutakis

Supervision: Nektarios Ntalakos, Maria Arnaouti, Evdokia Arkoumani, Serafeim Chlapoutakis

Disclosures

Human subjects: Informed consent for treatment and open access publication was obtained or waived by all participants in this study. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received 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 have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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