Review Article

Mediastinal thymic cysts: a narrative review

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Background and Objective: Mediastinal thymic cysts are a relatively rare pathology. With the expansion of eligible individuals screened with cross-sectional imaging for lung cancer, it is likely that there will be an increase in the number of individuals presenting with these cysts. Understanding this rare pathology will become more important when this incidental pathology is encountered.

Methods: Search of PubMed was undertaken using keywords “mediastinal”, “mediastinum”, “thymic”, “thymus”, “cyst”. Relevant literature was reviewed and selected for this comprehensive narrative review, including case reports, case series, and retrospective reviews.

Key Content and Findings: Thymic cysts in the mediastinum can be classified into two broad categories, congenital and inflammatory. Accurate diagnosis by imaging is challenging and the majority of patients are asymptomatic. Literature suggests that the majority of cysts are benign, however an unknown percentage may harbor neoplastic processes and over time can cause significant compressive symptoms. Definitive treatment and diagnosis is surgical, with overall excellent outcomes. The decision to pursue surgical treatment versus surveillance requires a shared decision making approach with patients.

Conclusions: Given the scarcity of available high quality evidence regarding the management of mediastinal thymic cysts, this review provides practitioners a broad knowledge base to guide patients to make informed decisions.

Keywords: Mediastinum; thymic; cyst

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Introduction

Mediastinal thymic cysts are exceedingly rare and the true incidence is difficult to estimate. In patients undergoing imaging for lung cancer screening, the prevalence of any mediastinal mass was 0.77% and mediastinal thymic cysts were 0.01% (1,2). Other studies have reported that mediastinal thymic cysts represent only 1% to 4% of all mediastinal masses diagnosed (3,4). Because of their relatively scarcity, available evidence regarding thymic cysts within the chest are limited to a few small retrospective observational studies, a number of case series, and a myriad of case reports. Much of the understanding regarding this disease process, including physiology, symptomatology, diagnosis, and treatment has evolved over the decades, and in the context of limited evidence, has been primarily driven by clinical judgment. Despite the low prevalence of this pathology, an increasing number of mediastinal cysts are likely to be incidentally discovered with expansion of lung cancer screening (5). Accordingly, the diagnosis and management of mediastinal thymic cysts will become increasingly important. This chapter will comprehensively discuss mediastinal thymic cysts, including available literature, to give clinicians essential information to best manage this rare pathology. We present the following article in accordance with the Narrative Review reporting

Table 1 Search strategy summary

Items	Specification
Date of search	June 1st 2022
Databases and other sources searched	PubMed
Search terms used	"Mediastinal", "mediastinum", "thymic", "thymus", "cyst"
	Example: (mediastinal) OR (mediastinum)) AND ((thymic) OR (thymus)) AND (cyst)
Timeframe	Date unrestricted to July 2022
Inclusion and exclusion criterion	Inclusion: (I) English language; (II) Case reports, case series, retrospective cohort series; (IIII) Focusing on subtopics of: pathophysiology, histology, diagnosis, symptomatology, and treatment; (IV) Studies of historical relevance
	Exclusion: Studies on cervical located cysts
Selection process	Keaton Cooley-Rieders selected literature, both authors chose those for inclusion
Any additional considerations	References of selected studies were reviewed for inclusion

checklist (available at https://med.amegroups.com/article/view/10.21037/med-22-25/rc).

Methods

With the low incidence of mediastinal thymic cysts in the population, English language, case reports, case series and retrospective studies of patients were selected from PubMed without date restriction up to June 2022. Search keywords including "mediastinal/mediastinum", "thymic/thymus", and "cyst", were used to select representative literature to highlight the pathophysiology, histology, diagnosis, symptomatology, and treatment of this pathology. Published works focusing solely on cervically located cysts were excluded from inclusion in this narrative review. Referenced sources of selected studies, reports, and series were also reviewed and evaluated for inclusion. These referenced sources were included if they contributed comprehensively to outline the sub-topics above, or if they provided historical value. *Table 1* reviews the overall search strategy. *Table 2* includes case reports, case series and *Table 3* outlines retrospective reviews as an example of the broad date ranges and topics used for selection.

Pathophysiology

Mediastinal thymic cysts were first comprehensively described in 1968 by Ronald Seltzer, a radiologist at the University of Cincinnati, and this seminal article has influenced many subsequent writings on the topic (6). Embryologically, the thymus arises from the 3rd pharyngeal pouch during the 6th week of gestation and 2 weeks later descends and fuses at the midline to its proper position in the anterior chest (7,8). This descent has clinical implications, with ectopic thymic tissue possible anywhere from the hyoid to the diaphragm (9). From some of the largest studies, the anterior mediastinum appears to be the most common location for thymic cysts, however middle and posterior locations are also possible (10).

Originally, it was felt that five types of thymic cysts existed: embryological, involutive, neoplastic, degenerative, and mesenchymal (4). However, more recent studies have suggested that broadly these cysts are more simply classified into unilocular, multilocular, congenital, and acquired (3,11). This classification is supported by a prominent theory regarding the formation of inflammatory multilocular thymic cysts secondary to dilation of Hassall's corpuscles in response to antigens (12). Accordingly, congenital cysts tend to be unilocular while inflammatory cysts appear multilocular, although exceptions have been reported in literature (4,13-15).

Patients of any age can be impacted by this rare pathology from 4 weeks (16) to 79 years old (17) with no preference towards biological sex (10).

A variety of inflammatory processes have been associated with development of these cysts, including: lupus (13), Sjogrens (18), Human immunodeficiency virus or HIV (19-21), surgery (22), immunoglobulin-G4 disease (23), and bacterial infection (24). Additionally, neoplastic processes associated with development of multilocular

Table 2 Summary of cited case series (less than 4 patients) and reports

Year	Author	Age/sex	Symptoms	Size/type	Location	Surgical approach	Complications	Associated condition
1961	Schillhammer	14 y/M	Cough	15 cm, unknown	Right, anterior	Thoracotomy	None	None
		29 y/M	Asymptomatic	13×5 cm, unknown	Anterior	Thoracotomy	None	None
		44 y/F	Cough	Unknown, unilocular	Right, anterior	Thoracotomy	Ileus	None
1976	Cuasay	44 y/M	Dyspnea, heart failure	9×6×5 cm, multilocular	Right, anterior	Thoracotomy	None	Mitral valve replacement
1979	Moskowitz	12 y/M	Chest pain	2 cm, multilocular	Anterior	Mediastinoscopy	Death	Aplastic anemia, E. coli bacteremia
		6 y/F	Anemia	8×8×8 cm, multilocular	Left, anterior	Mediastinoscopy	Stridor, death	Aplastic anemia
1983	Dunne	27 y/F	Anemia	3×5 cm, unknown	Right, anterior	Thoracotomy	None	Aplastic anemia
1984	Woolley	55 y/M	Hoarseness, dysphagia	Unknown, unilocular	Anterior	Unknown	None	Vocal cord palsy
1985	Lindfors	20 y/F	Adenopathy	10×7 cm, multilocular	Left	Thoracotomy	None	Hodgkins
		19 y/M	Tracheal compression	9 cm, multilocular	Right, anterior	Thoracotomy	None	Hodgkins
		39 y/M	Chest pain, hoarseness	12 cm, multilocular	Left, anterior	Thoracotomy	None	Hodgkins
1988	Davis	14 y/F	Dyspnea	4×6 cm, multilocular	Anterior	Sternotomy	None	None
1992	Fraile	64 y/M	Asymptomatic	12 cm, unknown	Anterior	Cervical	None	Horner syndrome
1994	Borgna-Pignatti	9 y/ unknown	Weight loss, anorexia, shoulder pain	7.5×5×2.5 cm, multilocular	Anterior, left	Thoracotomy	Recurrence	Non-Hodgkin's lymphoma
1995	Leonidas	11 y/M	Pneumonia	14×10×5 cm, multilocular	Left, anterior	Thoracotomy	None	HIV
		5 y/M	Pneumonia	5×5×4 cm multilocular	Anterior	Not resected	None	HIV
		44 y/M	Pneumonia/sepsis	Unknown, multilocular	Anterior	Thoracotomy	None	HIV
1995	Sirivella	54 y/F	Cough, dyspnea, weight loss	6×5 cm, multilocular	Anterior	Sternotomy	None	None
		34 y/F	Cough, dyspnea, weight loss	6×7 cm, multilocular	Anterior	Mediastinoscopy biopsy, unknown	Infection after biopsy	Compression of pulmonary artery
		31 y/M	Cough, dyspnea, weight loss	7×7 cm, multilocular	Anterior	Sternotomy	Pneumonia	Tracheal shift
1996	Yamashita	60 y/F	Cough, chest pain	14×7 cm, multilocular	Right, anterior	Unknown	Recurrence of SCC	Thymic carcinoma

Table 2 (*continued*)

Table 2 (*continued*)

Year	Author	Age/sex	Symptoms	Size/type	Location	Surgical approach	Complications	Associated condition
1999	Silverman	16 y/M	Fever, weight loss, chest pain	8×5×3 cm, multilocular	Right, anterior	VATS	None	Seminoma
2000	Wakely	58 y/M	Chest pain, right arm numbness	10×7 cm, multilocular	Anterior	Sternotomy	Renal failure, death	Confused as aortic aneurysm, Langerhans histiocytosis
2001	Tollefsen	8 y/F	Neck swelling	5×10.5 cm, unknown	Right, anterior	Cervical incision	None	None
2004	Becit	56 y/M	Chest pain	34×25×16 cm, unknown	Anterior	Sternotomy	Post-op respiratory failure	Cardiac, lung compression
2004	Rakheja	12 y/F	Chest pain, dyspnea	7.5×5.5×3.5 cm, multilocular	Anterior	Unknown	None	Teratoma
		11 y/M	Chest pain, fatigue, flushing	9×6×3 cm, multilocular	Left, anterior	Unknown	None	Teratoma
2005	Lachanas	61 y/F	Chest pain, dyspnea	25 cm, multilocular	Right, anterior	VATS and thoracotomy	None	Lung compression
2006	Stas	68 y/M	Dyspnea, cough	18.5 cm, multilocular	Right, anterior	VATS and thoracotomy	None	SVC, right atrial compression
2007	Constantacos	16 y/F	Chest pain	22×11×2.5 cm, multilocular	Left, anterior	Left VATS	Small Pneumothorax	None
2007	Eifinger	5 w/M	Dyspnea	5×3.5×3.2 cm, multilocular	Anterior	Sternotomy	Hemorrhage into right chest	Thymic hyperplasia
2007	Iyer	40 y/M	Chest pain, facial swelling	3.5×4.9 cm, unknown	Right, paratracheal	Mediastinoscopy	None	SVC compression
2008	Amanatidou	5 y/M	Neck swelling	17×8×6 cm	Left, anterior, cervical	Sternotomy and cervical incision	None	None
2008	Fujiwara	52 y/M	Chest pain	12×8×6 cm, multilocular	Anterior	Unknown	Hemorrhage into cyst	Thymoma
2008	Tiveron	79 y/F	Chest pain, dyspnea	11.5×6.8× 9 cm, unilocular	Anterior	Sternotomy	None	Pericardial effusion
2009	Efthymiou	72 y/M	Dizziness	11×9×3 cm, unilocular	Left, anterior	VATS	None	Tachy-brady syndrome
2009	Morikawa	68 y/F	Asymptomatic	4 cm, multilocular	Right, anterior	VATS	None	Papillary adenocarcinoma, thymoma

Table 2 (*continued*)

Table 2 (*continued*)

Year	Author	Age/sex	Symptoms	Size/type	Location	Surgical approach	Complications	Associated condition
2010	Bruno	37 y/M	Chest pain, dyspnea, lower extremity edema	12 cm, unilocular	Right	Thoracotomy	None	Lung compression
2010	Saito	55 y/M	Chest pain	5×4.5 cm, multilocular	Right, Anterior	Sternotomy	Hemorrhage into right chest	None
2011	Tamango	15 y/F	Dyspnea, chest pain, facial swelling	13×10×17 cm, multilocular	Anterior	Clamshell	None	HIV
2011	Schweigert	41 y/M	Chest pain, cough, dyspnea	20 cm, unilocular	Anterior	Sternotomy	None	Thymoma
2012	Luk	64 y/F	Syncope	5.3 cm, unknown	Posterior	VATS and thoracotomy	None	None
2012	Shi	47 y/F	Cough, chest pain, facial swelling	7.1×2.7×8.8 cm, multilocular	Anterior	Unknown	None	HIV
2012	Stienmuller	19 y/M	Chest pain, dyspnea	17.6 x 7.1 x 6.8cm, multilocular	Right, anterior	Sternotomy	None	Hodgkins
2015	Jennings	76 y/F	Asymptomatic	20.5×16.2×10 cm, unilocular	Anterior	Sternotomy	Atrial fibrillation	None
2016	Kanakis	15 y/F	Asymptomatic	16×8 cm, multilocular	Right, Anterior	Sternotomy	None	Pulmonary valve stenosis
2016	Lee	55 y/M	Asymptomatic	10.8×4 cm, multilocular	Anterior	VATS	Hemorrhage into cyst	None
2018	Gorospe	43 y/F	Asymptomatic	Unknown, multilocular	Anterior	VATS	None	Sjogrens
2019	Oda	44 y/M	Asymptomatic	Unknown, multilocular	Anterior	Subxiphoid, VATS	None	IgG4 disease
2019	Yano	42 y/F	Myasthenia	11 cm, multilocular	Anterior	Subxiphoid, VATS	None	Thymoma
2021	Alzahran	22 m/F	Dyspnea	Unknown, unilocular	Right, anterior	Thoracotomy	Post-op respiratory failure	Spontaneous infection
2021	Feng	67 y/M	Chest pain	11×9.7 cm, unilocular	Right	Thoracotomy	Hemorrhage into cyst	None
2021	Liu	28 y/M	Asymptomatic	7.1×8.1 cm	Anterior, right	EBUS aspiration	Sepsis, mediastinitis, pleural effusion	None

M, male; F, female; w, weeks; m, months; y, years; VATS, video-assisted thoracoscopic surgery; SVC, superior vena cava; HIV, human immunodeficiency virus; SCC, squamous cell carcinoma; EBUS, endobronchial ultrasound.

Table 3 Summary of retrospective series

Year	Author	Number of patients	Study objectives	Major findings
1968	Seltzer	12 patients (all thymic cysts)	Describe mediastinal thymic cysts	58% symptomatic (cough and chest pain), all anterior, all multiloculated, 58% right sided, 25% left sided, 17% bilateral
2001	Choi	8 (all multilocular thymic cysts)	CT *vs.* histologic findings	50% of unilocular appearing cysts on imaging actually multilocular, 83% of solid appear lesions non-neoplastic
2003	Takeda	105 patients (30 thymic cysts)	Characterize congenital cysts	Second most common cyst type (28.6%), 97% thymic cysts anterior, average age 43.9, predominantly symptoms: none (60%), chest pain (20%), hoarseness (13%), dyspnea (10%)
2006	Henschke	9,263 patients (1 thymic cyst)	Describe incidentally found mediastinal masses from lung cancer CT screening	0.77% incidence of mediastinal masses, 0.43% anterior located, 0.01% thymic cyst, all asymptomatic
2011	Weissferdt	7 (all thymic cysts with associated thymic carcinoma)	Characterize thymic cysts associated with thymic carcinoma	All multilocular, all alive at follow-up (43% with disease), emphasis on importance of surgical resection for diagnosis and treatment of anterior cystic mediastinal masses
2018	Hwang	18 (3 thymic cysts)	MRI characterization of anterior mediastinal solid lesions versus cysts	T2 bright and relative enhancement ratio <26.1% associated with increased rate of correct diagnosis of cyst
2018	Shen	18 patients (all thymic cysts with thymic carcinoma or thymoma)	Characterize thymic cysts associated with thymic carcinoma and thymoma	All multilocular, all with solid component, 56% patients without cysts on CT, all alive at follow-up (11% with disease), major symptoms: none (39%), chest pain (39%), cough (22%)
2020	Wang	282 patients (120 thymic cysts)	Outcomes of VATS resection of cysts	Most common cyst (43%), 98% thymic cysts anterior. 50.7% of all cysts correctly diagnosed with CT. Only 1 thymic cyst with associated thymoma. Low rate of complications (5.7%), low rate of conversion to thoracotomy (1%), no recurrence
2018	Yoon	56,358 patients (14 thymic cysts)	Describe incidentally found anterior mediastinal masses from asymptomatic CT scans	0.73% incidence, 0.03% thymic cysts

CT, computed tomography; MRI, magnetic resonance imaging; VATS, video-assisted thoracoscopic surgery.

cysts are broad, and have included: Thymic carcinoma (12,15,25), Hodgkin's lymphoma (26,27), Non-Hodgkin's lymphoma (28), Langerhans histiocytosis (29), thymoma (15,30,31), papillary adenocarcinoma (32), seminoma (33) and, mature teratomas (34).

Although original and newer large studies suggest mediastinal thymic cysts to be a benign pathology (2,10,35) the tremendous number of case reports and case series suggest otherwise, with a clear association between neoplastic processes and inflammatory cysts.

Histology

Histologically, thymic cysts are most readily identified by the inclusion of Hassall's corpuscles in the cyst wall (22,36-40). These swirl-shaped keratinized structures surrounded by epithelial cells are unique to the thymus (40). Cyst walls are also prominent for fibrous stratified squamous epithelium (8,28). Aspiration of cyst contents usually is non-diagnostic and only lymphocytes are seen (41).

Multilocular cysts microscopically contain numerous cystic spaces lined with squamous epithelium (12,26). Additionally, these spaces are prominent for their inflammatory changes which can include necrosis, cholesterol granulomas, fibrosis, germinal centers, calcifications, and hemorrhage (7,13,16,42-45).

Based on underlying inflammatory process driving cyst formation, additional histologic findings can be

observed, such as Reed Sternberg cells in Hodgkin's lymphoma (26,27), cuboidal or columnar cells in papillary adenocarcinoma (32), dense oval cells with central nuclei in seminoma or thymoma (15,30,33), myofibroblasts in teratoma (34), follicular hyperplasia in HIV (21), and nests of spindle, basaloid, papillary, and squamous cells in thymic carcinoma (12,25).

Diagnosis

CT (computed tomography) imaging, preferably with contrast, is frequently obtained in the evaluation of mediastinal masses. Based on the largest series analyzing the CT characteristics of thymic cysts, these masses appear to be most commonly well defined, round/oval, and laterally positioned in the anterior mediastinum (35). Specific to thymic cysts, contiguous involvement with the thymus is usually present (13). Right, left and bilateral laterality are possible with sizes as large as 34 cm in diameter (46). Case series have suggested that cyst margins tend to be uniformly enhancing. Relative to surrounding structures, margins may be poorly apparent or well delineated on imaging. Gross appearance can also be variable, being smooth or lobular and unilocular or multilocular based on type. Internal components vary and frequently contain solid components (13). Cyst fluid when simple varies from 0 and 62 Hounsfield units (9,13,17,35). Although routinely non-calcified (13) focal (47) and grossly calcified (44,48) mediastinal thymic cysts have been reported.

Serum markers including alpha fetoprotein and human chorionic gonadotropin are routinely obtained in the preoperative assessment and customarily are negative (7,20,41,47)

Definitive diagnosis based on imaging is challenging and ultimately diagnosis is based upon histological evaluation of surgical specimens. Large series demonstrate that the diagnostic sensitivity of CT in making an accurate diagnosis was less than 55% (35). Incorrect diagnosis was especially common with masses less than 3 cm and Hounsfield units greater than 20 on imaging (35). Tissue sampling before surgical excision should not be undertaken, as biopsy of cysts results are often unrevealing (39,49) and risk bacterial seeding, subsequent sepsis and death (41,42,50). Given preoperative diagnostic uncertainty, and overall rarity of this pathology, workup requires a broad differential.

Underscoring the diagnostic uncertainty associated with mediastinal thymic cysts, are case reports where the misdiagnosis of aortic intramural hematomas and Type A dissections have been made (17,29). If a question of diagnosis exists, additional imaging should be obtained with echocardiography which can provide more dynamic information with doppler flow to help exclude vascular or cardiac chamber involvement (7,51,52).

Despite the known limitations of imaging, recent advances in technology such as "radiomics" have proven to be valuable to assist in the accurate diagnosis of cysts by using computer analysis of acquired images (53). Magnetic resonance imaging (MRI), has often been described as an additional adjunctive imaging modality with cysts to aid in diagnosis (19,43). T2 sequences appearing very bright, is a specific, but not sensitive quality that can help aid in identifying thymic cysts from other pathologies (54). T1 MRI sequences also appear to be of value, with signal intensity ratios of 1 to 1.5 being useful in identifying thymic cysts.

Positron emission tomography (PET) is another adjunctive imaging modality to differentiate cysts, with low maximum standardized uptake value, suggesting benign features (55).

Endoscopic ultrasound is a newer technology that can potentially aid in diagnosis of thymic cysts (56-58). As previously discussed, caution should be taken with endoscopic aspiration of cyst contents when diagnosis of thymic or mediastinal cyst is suspected, as analysis of fine needle aspiration is usually non-diagnostic 73% of the time, with risk of infection, sepsis, and death (41,42,50,58).

However, for thymic cysts with significant solid components, which are commonly seen in thymoma or thymic carcinoma, percutaneous needle biopsy is an option for diagnosis with appropriate patient counseling on risks (15).

Prior to cross sectional computed tomography imaging, chest radiographs were the primary diagnostic modality to assess mediastinal masses (8). Because of the varied appearance and locations thymic cysts can occur, heterogeneous radiographs, with obscurement of cardiac borders, sometimes containing calcifications, were described. Historically, lateral chest radiographs were suggested in routine workup, as an anterior location of mass was suggested to be a common feature of thymic cysts (6). Although better imaging technologies exist today, plain chest radiographs could still be useful in resource limited environments.

Symptoms

The majority of patients with thymic cysts are asymptomatic (3,35). In symptomatic patients, chest pain, hoarseness, dyspnea, cough (3,35), and compressive symptoms appear to be most common. Compressive symptoms are variable

and unique based on cyst location. Right atrial (59) or right cardiac chamber compression can mimic symptoms of right heart failure, with elevated jugular venous pressures, hepatic congestion, and peripheral edema (7,46). Facial congestion in the setting of superior vena cava (SVC), extrinsic obstruction by cysts is possible (37). Atrial fibrillation and reversible heart failure has been described in the setting of cysts in proximity of the SVC and right atrium (22). Syncope is possible in the setting of left atrial compression (44). Left sided cysts have also been associated with tachy-brady syndrome (60).

Mass effect on pulmonary structures and resulting atelectasis secondary to cysts has explained dyspnea in otherwise healthy individuals (47). Reversible impairments in formal pulmonary function testing have been demonstrated (38) as well as airway compression related pneumonias (49).

Spontaneous cyst rupture has been reported in literature, mimicking pleural effusions with associated pleuritic chest pain (36).

Neurological symptoms, as prominent as Horner syndrome with anhidrosis, miosis and ptosis have been caused by extrinsic compression of sympathetic structures (61). Temporary unilateral vocal cord paralysis has also been described from probable recurrent laryngeal nerve impingement (62).

Bleeding seems to occur with thymic cysts in patients with thrombocytopenia (11,42) or on platelet inhibitors (39). Cases of spontaneous bleeding in the absence of an identifiable source with associated anemia, rapid cyst enlargement, pleural effusions and mediastinal widening have been described requiring urgent surgical treatment (10,43,45,48).

Treatment

Definitive treatment of mediastinal thymic cysts is surgical. The decision to offer surgical treatment however requires clinical judgment. In the setting of symptomatic cysts, given excellent surgical outcomes and complication rates of 1.1% to 6.5% (10,35) surgical resection should be offered to patients.

The treatment of asymptomatic cysts is less straightforward. The best available literature suggests that the majority of thymic cysts are benign (10) however this contradicts the numerous case reports describing occult neoplastic processes, spontaneous hemorrhages, and substantial insidious subclinical compressive symptoms (38). This conflicting evidence likely stems from the overall rarity of this pathology and an inherent bias of case reports reporting unique patients with mediastinal thymic cysts (1).

Determining a method to stratify asymptomatic cysts based on risk of neoplastic potential poses further challenges. While nearly all neoplastic cysts are multilocular, only approximately half have this appearance on CT imaging (13,15,35). Solid components seem to be common features of neoplasia (12,15), however these do not always appear to be apparent on cross-sectional imaging, and previous research has shown that solid components among multilocular thymic cysts can represent various non-neoplastic tissue such as thymic hyperplasia, normal thymic remnants, hemorrhagic cysts, or numerous small cysts septated by thick inflammatory thymic tissue (13).

Because no reliable risk stratification can be made based on the presence or absence of imaging features, a shared decision making approach with patients is appropriate regarding management. Risk of malignancy is likely less than 1% (63) and the rate operative of complications is 1% to 5% (10,35). With surgical resection being the only way to establish a concrete diagnosis (13,64), observation with serial imaging, pursuing additional imaging such as MRI, or surgical resection are all reasonable management options and should be driven by patient preference. *Figure 1* outlines an approach to treatment of mediastinal thymic cysts.

Approach to resection should be tailored based on cyst location and urgency of symptoms. A video assisted thoracoscopic (VATS) technique (3,10,32,35,36,39,47) with conversion to anterior thoracotomy (59) as required should be sufficient in the majority of cases, although median sternotomy in instances of very large cysts or clinical instability is appropriate (14,16,17,30,38,43,46). Posterolateral thoracotomy may also be utilized in the setting of a rare posterior mediastinal cyst (44). Robotic resection, although rare, has been utilized (65). Subxiphoid and transcervical approaches seem to be effective in selected patients with anterior midline location cysts with sufficient operator familiarity (9,23,31,66). Clamshell approaches have also been utilized (20) however are morbid and should be cautiously undertaken. Reports of mediastinoscopy for resection have also been described (37,64) however should only be undertaken if complete resection is possible. Incomplete resection from this approach has resulted in deaths from sepsis (42).

Conclusions

Over the many decades since the first comprehensive case series of mediastinal thymic cysts were published, much has

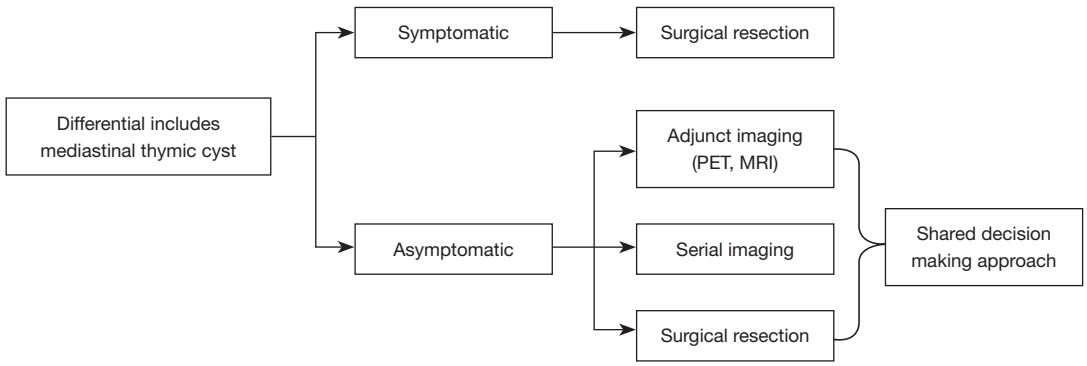

Figure 1 Treatment algorithm. PET, positron emission tomography; MRI, magnetic resonance imaging.

changed with regards to understanding pathophysiology, presentation, diagnosis, and treatment of this rare pathology. Inflammatory processes appear to be a dominant driver of cyst formation. While the majority of patients appear to be asymptomatic, mass effect and compressive symptoms can occur. Tissue sampling in this pathology should be avoided for its low diagnostic yield. Finally, surgical resection should be pursued with a shared decision making approach when thymic cysts are on the differential because of the strong association with neoplastic etiologies reported in literature, and excellent short and long term surgical results.

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References

1. Henschke CI, Lee IJ, Wu N, et al. CT screening for lung cancer: prevalence and incidence of mediastinal masses. Radiology 2006;239:586-90.
2. Yoon SH, Choi SH, Kang CH, et al. Incidental Anterior Mediastinal Nodular Lesions on Chest CT in Asymptomatic Subjects. J Thorac Oncol 2018;13:359-66.
3. Takeda S, Miyoshi S, Minami M, et al. Clinical spectrum of mediastinal cysts. Chest 2003;124:125-32.
4. Dyer NH. Cystic thymomas and thymic cysts. A review. Thorax 1967;22:408-21.
5. US Preventive Services Task Force; Krist AH, Davidson KW, et al. Screening for Lung Cancer: US Preventive

Services Task Force Recommendation Statement. JAMA 2021;325:962-70.
6. Sltzer RA, Mills DS, Baddock SS, et al. Mediastinal thymic cyst. Dis Chest 1968;53:186-96.
7. Bruno VD, Mariscalco G, Franzi F, et al. Ectopic congenital thymic cyst in the right pleural cavity. Asian Cardiovasc Thorac Ann 2010;18:486-8.
8. SCHILLHAMMER WR Jr, TYSON MD. Mediastinal thymic cysts. Report of three cases and review of the literature. Arch Surg 1962;85:410-7.
9. Tollefsen I, Yoo M, Bland JD, et al. Thymic cyst: is a correct preoperative diagnosis possible? Report of a case and review of the literature. Eur J Pediatr 2001;160:620-2.
10. Wang X, Li Y, Chen K, et al. Clinical characteristics and management of primary mediastinal cysts: A single-center experience. Thorac Cancer 2020;11:2449-56.
11. Davis JW, Florendo FT. Symptomatic mediastinal thymic cysts. Ann Thorac Surg 1988;46:693-4.
12. Weissferdt A, Moran CA. Thymic carcinoma associated with multilocular thymic cyst: a clinicopathologic study of 7 cases. Am J Surg Pathol 2011;35:1074-9.
13. Choi YW, McAdams HP, Jeon SC, et al. Idiopathic multilocular thymic cyst: CT features with clinical and histopathologic correlation. AJR Am J Roentgenol 2001;177:881-5.
14. Kanakis MA, Danias PG, Chatzis AC. Thymic Cyst Popping Up in a Patient With Congenital Heart Disease. World J Pediatr Congenit Heart Surg 2016;7:372-4.
15. Shen X, Jin Y, Shen L, et al. Thymoma and thymic carcinoma associated with multilocular thymic cyst: a clinicopathologic analysis of 18 cases. Diagn Pathol 2018;13:41.
16. Eifinger F, Ernestus K, Benz-Bohm G, et al. True thymic hyperplasia associated with severe thymic cyst bleeding in a newborn: case report and review of the literature. Ann Diagn Pathol 2007;11:358-62.
17. Tiveron MG, Dias RR, Benvenuti LA, et al. Thymic cyst as a differential diagnosis of acute thoracic aortic disease. Rev Bras Cir Cardiovasc 2008;23:575-7.
18. Gorospe L, García-Villanueva MJ, García-Cosío-Piqueras M, et al. Multilocular thymic cyst in a patient with Sjögren syndrome. Rheumatology (Oxford) 2019;58:369.
19. Leonidas JC, Berdon WE, Valderrama E, et al. Human immunodeficiency virus infection and multilocular thymic cysts. Radiology 1996;198:377-9.
20. Tamagno M, Bibas BJ, Bernardi F, et al. Giant multilocular thymic cyst in an HIV-infected adolescent. J Pediatr Surg 2011;46:1842-5.
21. Shi X, Nasseri F, Berger DM, et al. Large Multilocular Thymic Cyst: A Rare Finding in an HIV Positive Adult Female. J Clin Imaging Sci 2012;2:55.
22. Cuasay RS, Fernandez J, Spagna P, et al. Mediastinal thymic cyst after open heart surgery. Chest 1976;70:296-8.
23. Oda R, Okuda K, Murase T, et al. Thymic inflammatory pseudotumor with multilocular thymic cyst caused by immunoglobulin G4-related disease. Thorac Cancer 2019;10:116-9.
24. Alzahran A, Shebli B, Dabbas S, et al. Rare mediastinal thymic cyst infection without predisposing disease: a case report. JRSM Open 2021;12:2054270421991801.
25. Yamashita S, Yamazaki H, Kato T, et al. Thymic carcinoma which developed in a thymic cyst. Intern Med 1996;35:215-8.
26. Lindfors KK, Meyer JE, Dedrick CG, et al. Thymic cysts in mediastinal Hodgkin disease. Radiology 1985;156:37-41.
27. Steinmüller F, Traeger T, Kühn JP, et al. Rare case of a large mediastinal cyst involved in Hodgkin's lymphoma. Pathol Res Pract 2012;208:306-9.
28. Borgna-Pignatti C, Andreis IB, Rugolotto S, et al. Thymic cyst appearing after treatment of mediastinal non-Hodgkin lymphoma. Med Pediatr Oncol 1994;22:70-2.
29. Wakely P Jr, Suster S. Langerhans' cell histiocytosis of the thymus associated with multilocular thymic cyst. Hum Pathol 2000;31:1532-5.
30. Schweigert M, Kaiser J, Fuchs T, et al. Thymoma within a giant congenital thymic cyst. Interact Cardiovasc Thorac Surg 2011;13:442-3.
31. Yano M, Numanami H, Akiyama T, et al. Thoracoscopic Thymectomy for Large Thymic Cyst: Myasthenia Gravis With Thymoma Concealed by Thymic Cyst. Surg Laparosc Endosc Percutan Tech 2019;29:e34-6.
32. Morikawa H, Tanaka T, Hamaji M, et al. Papillary adenocarcinoma developed in a thymic cyst. Gen Thorac Cardiovasc Surg 2010;58:295-7.
33. Silverman JF, Olson PR, Dabbs DJ, et al. Fine-needle aspiration cytology of a mediastinal seminoma associated with multilocular thymic cyst. Diagn Cytopathol 1999;20:224-8.
34. Rakheja D, Weinberg AG. Multilocular thymic cyst associated with mature mediastinal teratoma: a report of 2 cases. Arch Pathol Lab Med 2004;128:227-8.
35. Wang X, Chen K, Li X, et al. Clinical features, diagnosis and thoracoscopic surgical treatment of thymic cysts. J Thorac Dis 2017;9:5203-11.

36. Lachanas E, Konofaos P, Birba G, et al. A rupture of a huge thymic cyst into the pleural cavity: A case report. Respir Med 2006;100:1858-60.
37. Iyer AP, Sadasivan D, Yadav S, et al. Thymic cyst causing superior venacava syndrome relieved by mediastinoscopy--a rare presentation. Heart Lung Circ 2008;17:510-2.
38. Jennings S, Stuklis RG, Chan J, et al. Successful Giant Thymic Cyst Removal: Case Report and Review of the Literature. Heart Lung Circ 2015;24:e89-92.
39. Lee JH, Kim EC, Lim YS, et al. Spontaneous thymic cyst hemorrhage manifesting as a mediastinal mass. Korean J Med 2016;91:62-5.
40. Suster S, Rosai J. Histology of the normal thymus. Am J Surg Pathol 1990;14:284-303.
41. Liu W, Wang Y, Zhang W, et al. Pneumonia, pleurisy, mediastinitis, and mediastinal cyst infection secondary to endobronchial ultrasound-guided transbronchial needle aspiration: A case report. Medicine (Baltimore) 2021;100:e25973.
42. Moskowitz PS, Noon MA, McAlister WH, et al. Thymic cyst hemorrhage: a cause of acute, symptomatic mediastinal widening in children with aplastic anemia. AJR Am J Roentgenol 1980;134:832-6.
43. Saito Y, Murai K, Kawai Y, et al. Spontaneous hemorrhage of a thymic cyst in an adult: report of a case. Surg Today 2010;40:958-62.
44. Luk L, Maldjian PD, Kumar A, et al. Thymic cyst arising in the middle mediastinum posterior to the left atrium--a peculiar location. Clin Imaging 2012;36:837-9.
45. Fujiwara T, Mizobuchi T, Noro M, et al. Rapid enlargement of a mediastinal mass: thymoma hemorrhage into a thymic cyst. Gen Thorac Cardiovasc Surg 2008;56:472-5.
46. Becit N, Koçak H, Koçoğullari CU. Giant thymic cyst presenting as cardiac compression. Heart 2005;91:104.
47. Constantacos C, Lawson NM, Votanopoulos KI, et al. Giant thymic cyst in left lower hemithorax of a healthy teenaged athlete. J Thorac Cardiovasc Surg 2007;134:1373-4.
48. Feng Q, He X. Huge Simple Mediastinal Cyst With Hemorrhage and Calcification. Ann Thorac Surg 2021;112:e475.
49. Sirivella S, Gielchinsky I, Parsonnet V. Mediastinal thymic cysts: a report of three cases. J Thorac Cardiovasc Surg 1995;110:1771-2.
50. Mohamed S, Patel AJ, Mehdi R, et al. Infected mediastinal cysts following endobronchial ultrasound guided biopsy-a case series. J Surg Case Rep 2022;2022:rjac158.
51. Dunne MG, Weksberg AP. Thymic cyst: computed tomography and ultrasound correlation. J Comput Tomogr 1983;7:351-5.
52. Liu J, Lv Q, Wang J, et al. Diagnostic value of echocardiography in paracardiac cystic lesions: 43 cases from one single medical center. Int J Cardiovasc Imaging 2021;37:1961-6.
53. Zhang C, Yang Q, Lin F, et al. CT-Based Radiomics Nomogram for Differentiation of Anterior Mediastinal Thymic Cyst From Thymic Epithelial Tumor. Front Oncol 2021;11:744021.
54. Hwang EJ, Paek M, Yoon SH, et al. Quantitative Thoracic Magnetic Resonance Criteria for the Differentiation of Cysts from Solid Masses in the Anterior Mediastinum. Korean J Radiol 2019;20:854-61.
55. Sugawara H, Ito K, Watanabe H, et al. Clinical usefulness of PET/MRI in differentiating anterior mediastinal masses. Nucl Med Commun 2022;43:92-9.
56. Zhao Y, Wang R, Wang Y, et al. Application of endoscopic ultrasound-guided-fine needle aspiration combined with cyst fluid analysis for the diagnosis of mediastinal cystic lesions. Thorac Cancer 2019;10:156-62.
57. Yang H, Zhao H, Garfield DH, et al. Endobronchial ultrasound-guided transbronchial needle aspiration in the diagnosis of non-lymph node thoracic lesions. Ann Thorac Med 2013;8:14-21.
58. Aravena C, Patel J, Goyal A, et al. Role of Endobronchial Ultrasound-guided Transbronchial Needle Aspiration in the Diagnosis and Management of Mediastinal Cyst. J Bronchology Interv Pulmonol 2020;27:142-6.
59. Stas P, Declercq I, Van Raemdonck D, et al. Cardiac compression by a thymic cyst. Int J Cardiol 2007;114:e91-2.
60. Efthymiou CA, Thorpe JA. Thymic cyst presenting as tachy-brady syndrome. Eur J Cardiothorac Surg 2009;35:1108-10.
61. Fraile G, Rodriguez-Garcia JL, Monroy C, et al. Thymic cyst presenting as Horner's syndrome. Chest 1992;101:1170-1.
62. Woolley SL, Espeso A, Smith DR. Complete recovery of an isolated left vocal fold palsy associated with a benign mediastinal thymic cyst. J Laryngol Otol 2008;122:e4.
63. Kirmani B, Kirmani B, Sogliani F. Should asymptomatic bronchogenic cysts in adults be treated conservatively or with surgery? Interact Cardiovasc Thorac Surg 2010;11:649-59.
64. Burjonrappa SC, Taddeucci R, Arcidi J. Mediastinoscopy in the treatment of mediastinal cysts. JSLS 2005;9:142-8.

65. Peer M, Azzam S, Gofman V, et al. Robotic Mediastinal Surgery in Patients with Suspected Thymic Neoplasms: First Israeli Experience. Isr Med Assoc J 2018;20:637-41.

66. Amanatidou V, Mavrokosta M, Kourtesis A, et al. Cervicomediastinal thymic cyst--report of a case. Thorac Cardiovasc Surg 2008;56:177-8.

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