**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
checklist (available at https://med.americanjournals.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                      |
|      | Dunne             | 27 y/F  | Anemia                          | 3×5 cm, unknown | Right, anterior | Thoracotomy       | None                  | Aplastic anemia                      |
|      | 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   | 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)
| 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 | Tollefson| 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                                      |
| 2004 |          | 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 | 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            |
| 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                  |
| 2018 | Oda      | 70 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  | Dypsnea                                           | 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.
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 (8,28). 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.

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).

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
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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