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Pediatric Thymic Cysts: A Systematic Review of Case Reports

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ABSTRACT

Background: Thymic cysts are frequently disregarded in the differential diagnosis of children who arrive with painless neck masses since they make up fewer than 1% of cystic cervical masses. Furthermore, a high index of suspicion is necessary for the identification of mediastinal thymic cysts since they might present with a range of clinical symptoms.
Objective: To systematically analyze the cases of pediatric thymic cysts reported in the literature.
Patients and methods: A Medline (via PubMed) search was carried out on "Thymic cyst" case reports that were published before February 2023. Search included only reports in children (age 0-18 years) and reports published in English language, excluding cases with HIV. **Results:** Eighty-four patients from 74 reports (59 males and 25 females) were included in the analysis based on the inclusion criteria. The mean age at diagnosis was 7.06 years. The most commonly reported location was the cervical, followed by cervicomediastinal, mediastinal and subglottic, with a tendency for the left side. Neck swelling was the most frequent presentation. Other manifestations such as chest pain, stridor, and respiratory distress were also reported. Cysts varied in size from 3 cm to 20 cm at their largest dimensions. The vast majority of reported cysts were multilocular. Cysts were often related to the carotid sheath, and contained various types of fluids, with hemorrhagic fluid being the most common. **Conclusion:** Thymic cysts in children can manifest in a variety of ways. It should be taken into account while making a differential diagnosis for children and babies who have respiratory distress, stridor, chest discomfort, and cystic cervical swellings. Before a child's neck cyst is surgically removed, the existence of a mediastinal component must be verified.
Keywords: Thymic cyst, Pediatric, Cervical cyst, Mediastinal cyst.

INTRODUCTION

An important organ for the development of the immune system is the thymus, which is located in the upper mediastinum behind the sternum [(1)].

In the sixth week of pregnancy, it begins bilaterally in the third branchial pouch and descends during the following two weeks to the level of the aortic arch. There may be thymic tissue along the descending path. Along the carotid sheath, this path begins in the paratonsillar fossa and travels into the chest. Thymic cysts are uncommon, mostly benign structures that are caused by cystic degeneration of the thymus gland's Hassall corpuscles or by the remains of a prolonged thymopharyngeal duct [(2)].

They are often asymptomatic, but large cysts could constrict neighbors or become complicated by infection or hemorrhage and cause symptoms. In recent years, the number of reports of thymic cyst cases have increased, one possible cause being the heightened awareness of thymic cysts among pathologists [(3)].

The aim of this work was to systemically review cases of pediatric thymic cysts reported in the literature.

PATIENTS AND METHODS

In the present study, a Medline (via PubMed) search was carried out on researches that were published before February 2023. The keywords for search were "Thymic cyst" in the article "Title". Search filters included (1) Article type filter "Case reports", (2) Age filter "Child: birth-18 years", (3) Species filter "Human", (4) Language filter "English". Reports of thymic cysts in patients with HIV infection, reports published in other languages, inadequately reported data and case series with statistical analysis of the results were excluded from the analysis.

Of the total 91 hits, 74 reports were included based on the inclusion criteria; 66 reports of a single patient, 1 report included 4 patients[(4)], and 7 reports included 2 patients each[(5-11)], giving 84 cases for analysis.

To determine their eligibility, two researchers separately looked over each record's abstract and title. Discussion was used to reach an agreement where discrepancies arose.

Data from each case report were tabulated as patient's age, patient's sex, clinical details, location of the lesion (neck, mediastinum, cervicomediastinal, or subglottic), side of the lesion (right, left, bilateral or midline), size of the lesion, clinical diagnosis, investigations, histopathological findings, treatment offered, findings at surgery, and outcomes. A separate table was used to organize the clinical details retrieved from the reports including whether the presentation was a neck swelling or another manifestation, whether the presentation was sudden/acute or chronic, the characteristics of the swelling when present, whether it was painful/tender or painless, whether it was enlarging/progressively growing or stable, and whether there was a history of upper respiratory tract infection in relation to the presentation.

The location, size, type, cyst fluid and wall characteristics of the lesion were retrieved from the clinical description, and the imaging, pathological or operative reports.

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Ethical approval:
This study has been approved by the Sohag Faculty of Medicine's Ethics Committee [Soh-Med-25-5-15PD]. Following receipt of all information, signed consent was provided by each participant. The study adhered to the Helsinki Declaration throughout its execution.

Statistical analysis: The process of managing information and analysis of statistics was conducted using SPSS version 24.0. Quantitative data were presented as mean ± standard deviation, median, and range. Qualitative data were presented as frequency and percentage.

RESULTS

The analysis included 84 patients: 59 males (70.24%), 25 females (29.76%). The mean age at diagnosis was 7.06 ± 4.74 years and the median age was 7 years (1-day to 16-years).

The lesion was mainly cervical in 32 (38.10%) patients and cervicomediastinal in 28 (33.33%) patients (Table 1). Among the 84 lesions, 52 (61.90%) were left sided, 21 (25.00%) were right sided, and 11 (13.10%) were not specified.

Table (1): Location of the thymic cysts

Location	Number (%)
Cervical	32 (38.10)
Cervicomediastinal	28 (33.33)
Mediastinal	22 (26.19)
Subglottic	2 (2.38)

The most common complaint was a neck swelling, which was reported in 60 patients (71.43%). The swelling was reported to be present since birth in 14 patients (16.67%) and was described as progressively growing in 25 patients (29.76%), and as painful or tender in 2 patients (2.38%). Other manifestations are reported in table (2).

Table (2): Clinical presentations of thymic cysts

Presentation	Number (%)
Neck swelling	60 (71.43)
Other manifestations	44 (52.38)
Swelling progressively growing	25 (29.76)
Sudden or acute presentation	22 (26.19)
Swelling present since birth	14 (16.67)
History of upper respiratory tract infections	13 (15.48)
Swelling is painful or tender	2 (2.38)

Apart from neck swelling, other manifestations were reported in 44 patients (52.38%). The most common of these were chest pain and stridor which were reported in 7 patients (8.33%) each, followed by dyspnea in 5 patients (4.95%) and respiratory distress in 4 patients (4.76%). Apneic attacks and feeding difficulty were reported in 3 patients (3.57%) each. Hoarseness and upper abdominal pain were reported in 2 patients (2.38%) each. Other manifestations and their rate of occurrence are listed in table (3).

Table (3): Other clinical manifestations of thymic cysts

Manifestation	Number (%)	Cyst location
Chest pain	7 (8.33)	Cervicomediastinal, Mediastinal
Stridor	7 (8.33)	Cervical, Cervicomediastinal, Subglottic
Dyspnea	5 (5.95)	Mediastinal
Respiratory distress	4 (4.76)	Cervicomediastinal, Mediastinal
Feeding difficulty	3 (3.57)	Cervical
Apneic attacks	3 (3.57)	Cervicomediastinal
Hoarseness	2 (2.38)	Cervical
Upper abdominal pain	2 (2.38)	Mediastinal
Cyanotic episode	1 (1.19)	Cervicomediastinal
Diminished breath sounds	1 (1.19)	Mediastinal
Dysphagia to solid foods	1 (1.19)	Cervical
Epistaxis, easy bruising and anemia	1 (1.19)	Mediastinal
Frequent insomnia	1 (1.19)	Cervicomediastinal
Grand mal seizures	1 (1.19)	Cervical
Increasing lethargy, pallor and tachypnea	1 (1.19)	Mediastinal
Intercostal protrusions during cough	1 (1.19)	Mediastinal
Kyphosis	1 (1.19)	Mediastinal
Neck abscess	1 (1.19)	Cervical
Snoring	1 (1.19)	Cervicomediastinal

The size of the lesion was reported for 70 cases. The largest reported size was 20.00 cm x 8.00 cm, and the smallest reported size was 3.00 cm x 0.9 cm. The

average size was 7.24±3.71 cm at the largest dimension (range: 3.00 to 20.00 cm) the cyst was reported as multilocular in 54 (64.28%) patients, and unilocular in 7 (8.33%), and no mention of the cyst type was given in the remaining 23 cases. Reported cyst relations during surgery are given in table (4).

Table (4): Reported thymic cyst relations

Observation	Number (%)
Cyst related to carotid sheath	29 (34.52)
Cyst related to thyroid lobe	22 (26.19)
Cyst related to phrenic nerve	2 (2.38)
Cysts related to hypoglossal Nerve	2 (2.38)
Cyst related to cervical spine	2 (2.38)
Cyst related to thoracic spine	1 (1.19)
Cyst related to esophagus	1 (1.19)
Absent thyroid lobe or parathyroid glands	5 (5.95)

The nature of the cyst fluid was reported in 71 patients (84.52%). The most commonly reported cyst fluid was described as hemorrhagic (27 patients; 32.14%) and purulent (9; 10.71%). Other descriptions included straw-colored, foul smelling and necrotic (7; 8.33% each). A list of cyst fluid types is presented in table (5).

Table (5): Reported cyst fluid types

Finding	Number (%)
Hemorrhagic fluid	27 (32.14)
Purulent fluid	9 (10.71)
Straw-colored fluid	7 (8.33)
Foul-smelling fluid	7 (8.33)
Necrotic material	7 (8.33)
Thick brown material	6 (7.14)
Green gelatinous material	5 (5.95)
Clear yellow fluid	3 (3.57)

In 10 patients (11.90%) the cyst was reported as thick walled and in 8 patients (9.52%) it was reported as thin walled, but the wall thickness was not described in the remaining 66 patients. A variety of tissues and cells were reported in the cyst wall. The most commonly reported tissue (in 72 patients; 85.71%) was thymic tissue with Hassall's corpuscles. Cholesterol clefts/crystals and cholesterol granulomas were reported in 34 patients (40.48%). The most commonly reported epithelial type was squamous epithelium (26 patients; 30.95%), followed by cuboidal epithelium (18 patients; 21.43%). Pathological findings of the cyst wall are given in table (6).

Table (6): Histopathological findings of the cyst wall

Finding	Number (%)
Thymic tissue with Hassall's corpuscles	72 (85.71)
Cholesterol clefts/crystals and granulomas	34 (40.48)
Squamous epithelium	26 (30.95)
Lymphocytes infiltration, lymphoid aggregates or follicles	22 (26.19)
Cuboidal epithelium	18 (21.43)
Foreign body giant cell and granulomas	12 (14.29)
Macrophages; foamy, lipid-laden, starry sky	10 (11.90)
Ectopic parathyroid tissue	8 (9.52)
Other inflammatory cells	8 (9.52)
Flattened epithelium	7 (8.33)
Ciliated columnar epithelium - respiratory type	6 (7.14)
Calcifications	6 (7.14)
Various other epithelia	5 (5.95)
Ectopic thyroid tissue	5 (5.95)
Hemosiderin deposits	3 (3.57)
Histocytes, foamy histiocytes	3 (3.57)
Benign cystic teratoma or mature teratoma	2 (2.38)
Hodgkin's disease tissue or lymphoblastic lymphoma	2 (2.38)
Mucinous-type epithelium	1 (1.19)
Serous-type epithelium	1 (1.19)
Germinal centers	1 (1.19)
Granulation tissue	1 (1.19)
Polypoid formations	1 (1.19)
Rhabdomyomatous elements	1 (1.19)
Xanthoma cells	1 (1.19)

DISCUSSION

Thymic cysts are uncommon, benign, fluid-filled lesions that can develop in the mediastinum and cervical area. They are frequently misdiagnosed because of their rarity and similarity to other illnesses. Because it affects therapy and results, an accurate diagnosis is crucial [(12)].

Thymic cysts can develop anywhere from the anterior mediastinum to the mandibular angle. The thymus's embryological genesis is most likely the cause

of its broad anatomical distribution. In the sixth week of development, the thymus develops bilaterally from the third branchial pouch. The thymus elongates, the buds fuse, and the thymus takes on its shape and place in the mediastinum between weeks seven and eight. Along the descending path, thymic tissue may be seen [5]. On rare occasions, a thymic cyst may attach itself to adjacent nerves such as the recurrent laryngeal, vagus, phrenic, or hypoglossal nerves [12,13].

There are several theories as to why thymic cysts occur, however the cause is not entirely clear. They might be sequestration products from thymic involution or degeneration of Hassall's corpuscles, or they could be embryonic remains of branchial clefts, thymic tubules, or thymopharyngeal clefts [8].

Thyroglossal duct cysts, branchial cleft cysts, cystic hygromas, cystic teratoma, dermoid cysts, epidermoid cysts, thymic cysts, bronchogenic cysts (visceral cysts), and laryngoceles are examples of differential diagnostic possibilities [14–15].

A comprehensive medical history and physical examination are part of the first evaluation. For preoperative assessment, MRI, CT scan, ultrasonography, and neck and chest X-rays are utilized. However, there isn't a common imaging diagnostic to diagnose thymic cysts before surgery [16]. The thymic parenchyma's connective-tissue septa and blood arteries provide a distinctive echo pattern on ultrasonography [14]. These cysts have good margination and attenuation on CT scans that is comparable to that of water. On the other hand, T2-weighted lesions have intermediate to high signal intensity on MRI, whereas T1-weighted lesions have low signal intensity [17, 18]. The presence of Hassall's corpuscles and the histological identification of thymic tissue remains corroborate the definite diagnosis of a thymic cyst. Cholesterol crystals and granulomas are frequently seen but are not specific [6].

Seldom are fetal mediastinal cystic lesions documented. **de Miguel Campos *et al.*** [19] revealed the discovery of an intrathoracic cyst during pregnancy. A potential thymic origin was shown by postnatal MRI. **Luthra *et al.*** [20]**,** reported MRI detected cyst draping the left side of the fetal heart at 32 weeks of gestation. Fetal echo suggested a pericardial cyst, and postnatal MRI suggested cystic lymphangioma. Surgical excision and histological analysis of the lesion established the diagnosis of thymic cyst.

A few cases of familial thymic cysts were reported. **Joshua *et al.*** [6] described two brothers with cervicomediastinal thymic cysts. The first was an 8-year-old boy with swelling of the anterior neck, which became accentuated during speech. The second was a 5-year-old male, presented with asymptomatic suprasternal neck mass that was proven to extend into the mediastinum.

The vast majority of thymic cysts are asymptomatic [21], cervical thymic cyst can lead to compression of neighboring structures and cause dyspnea, dysphagia, pain, or hoarseness. Mediastinal thymic cysts can cause respiratory symptoms by compression of the trachea or by major intrathoracic extension[22]. Irritation of the pleura by mediastinal cysts can lead to chest pain[2].

Acute complications of thymic cysts namely hemorrhage, rupture, and infection were reported by many investigators. **Moskowitz *et al.*** [9] reported two children with acute respiratory symptoms in association with chest pain and sudden widening of the mediastinal shadow on chest radiographs. Evidences of hemorrhage into thymic cysts were established in both patients. **Davis and Florendo** [23] reported a hemorrhagic thymopharyngeal duct cyst causing airway obstruction in a 2-month-old female infant. **Woolley *et al.*** [24] had previously described 2 neonates with hemorrhagic thymus but without hyperplasia, and **Koopman *et al.*** [25] reported a 4-week-old boy with acute respiratory distress, due to massive hemorrhages in multiple thymic cysts.

Although hemorrhage is not uncommon, rupture of a thymic cyst is unusual. **Leibman *et al.*** [26] reported spontaneous rupture of a mediastinal thymic cyst in a 13-year-old boy who presented with acute onset of increasing pleuritic chest pain and dyspnea. A chest tube yielded hemorrhagic fluid, and a ruptured thymic cyst was revealed at surgery.

Occasionally thymic cysts are connected to the pyriform fossa by an internal sinus allowing access of bacteria to the cyst. **Youngson *et al.*** [27] reported a 15-month-old boy who presented with cyanotic attacks and positional stridor. A pus-filled thymic cyst was revealed on mediastinal exploration. In addition, **Hsu *et al.*** [28] reported a 3-day-old patient with feeding difficulties, lethargy, and apnea. Imaging revealed a cystic lesion causing laryngotracheal deviation, and again, a pus-filled cyst was found in the left pyriform sinus during surgery. Culture showed oral flora, suggesting the mass possibly enlarged due to food introduction through a connection to the oral cavity.

Frequently, masses in the cervical region or mediastinum present with airway compromise, particularly in younger patients. **Wagner *et al.*** [8] reported three patients with thymic cysts causing tracheal compression. In the three of them, apneic attacks were the presenting symptom. Similarly, **Komura *et al.*** [29] reported a 20-month-old girl that suddenly developed apnea after crying, and a cervicomediastinal cyst severely compressing the trachea was confirmed by CT. Thymic origin was confirmed on histopathology after surgical resection.

In some patients, respiratory manifestations precede the observation of neck cyst. Progressive neonatal airway obstruction secondary to cervical thymic cyst was reported in a 1-month-old newborn suffering increasing tachypnea and inspiratory stridor. The initial diagnosis was laryngomalacia. Two weeks later a soft mass was identified in the left cervical area, which later proved to be a thymic cyst [30]. **Hsu *et al.*** [28] reported respiratory distress from airway compression by an acutely infected thymic cyst in a 3-day old newborn.

Stridor secondary to airway narrowing was reported in relation to cervical, mediastinal and subglottic thymic cysts. Moreover, **Youngson *et al.*** [27] reported a 15-month-old boy with a mediastinal thymic cyst who presented with positional inspiratory stridor and ultimately cyanosis. Similarly, **Davis and Florendo** [23] reported a 2-month-old female infant with cervical thymic cyst who presented with stridor and new onset of a neck mass. Ectopic subglottic thymic cyst as a rare cause of congenital stridor was reported by **Sahhar *et al.*** [31] in a 10-day-old boy.

Chest pain is among the commonly reported manifestations of mediastinal thymic cysts. Explanations include irritation of the pleurae or inflammation or hemorrhage of the cyst itself. The first reports in the literature of chest pain secondary to thymic cyst hemorrhage were in two cases by **Moskowitz *et al.*** [9]. Moreover, **Rakheja and Weinberg** [10] reported two patients; a 12-year-old girl with a 2-week history of chest pain and dyspnea, and a hemorrhagic mediastinal thymic cyst detected at surgery, and an 11-year-old boy with a 1-month history of chest pain and flushing with physical activity, and again, thymic cyst hemorrhage was established as the cause. Likewise, **Constantacos *et al.*** [2] reported a healthy 16-year-old girl, who presented with intermittent, sharp, lateral chest pain with Valsalva maneuver, aggravated by deep inspiration. CT scan revealed a multiloculated, cystic mass seated on the left hemidiaphragm. Operative findings were significant for a cystic lesion attached to the left lobe of the thymus.

Reports of several other manifestations were found including feeding difficulty, epistaxis, easy bruising and anemia, increasing lethargy and pallor, frequent insomnia, grand mal seizures, kyphosis, and abdominal pain [32].

Thymic cysts can be categorized as unilocular or multilocular. Unilocular cysts are typically congenital, characterized by thin walls and filled with clear, acellular fluid. In contrast, multilocular cysts are mostly acquired, often due to hemorrhage, infection, or degeneration of the thymus gland, and often have thicker walls and contain dark-brown fluid[9]. Most of the cases reported in the present study were of the multilocular variety.

Thymic cysts are true cysts with an epithelial lining. Squamous epithelium in the lining of the thymic cyst was the most commonly reported type, followed by cuboidal epithelium, flattened epithelium, ciliated columnar epithelium of respiratory type, mucinous-type and serous-type epithelium and various other epithelia[33].

Branchial anomalies involving the third pouch may present as ectopic glands. Ectopic parathyroid tissue in a thymic cyst wall was present in nearly 10% of the reported cases, and ectopic thyroid tissue was reported in 6% [34].

Tumorous tissue in thymic cyst wall is an uncommon finding. This includes lymphoma (Hodgkin and non-Hodgkin lymphoma), mature cystic teratoma and rhabdomyoma[35].

CONCLUSIONS

Thymic cysts are rare, benign, fluid-filled lesions that can occur in the neck or mediastinum. They can be congenital or acquired, with congenital cysts typically are unilocular, have thin walls and contain clear fluid, while acquired cysts are typically multilocular, have thick-wall, often resulting from hemorrhage, infection, or degeneration, and contain dark-brown fluid. The most common presentation of thymic cysts is neck swelling. Other symptoms, such as chest pain stridor, or other respiratory symptoms have been reported as the presenting symptoms. Thymic cysts are often misdiagnosed due to their rarity and similarity to other conditions. Diagnosis is challenging and requires high index of suspicion, but can be suggested on imaging studies. However, definite diagnosis is confirmed only after histological analysis. Surgical excision is typically required for treatment. Given the frequent occurrence of cervicomediastinal thymic cysts, it is essential to confirm the presence of a mediastinal component before proceeding with the surgical resection of neck cysts in children.

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