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Unilocular and multilocular thymic cysts: A study on the possible histomorphological and/or clinical differences

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ABSTRACT

Objective: Thymic cysts are rare mediastinal cystic pathologies and have two subtypes namely unilocular and multilocular. This study aims to investigate the clinicopathological characteristics of thymic cysts and to compare the clinical and histopathologic features of multilocular thymic cysts (MTCs) and unilocular thymic cysts (UTCs).

Patients and Methods: Twenty-three patients with the diagnosis of thymic cyst between 2012 and 2020 were included. We compared the clinicopathological characteristics of unilocular and multilocular thymic cysts.

Results: The mean age of patients was 43 years, ranging from 6 to 80 years. Fourteen cases were UTCs and 9 cases were MTCs. MTCs were found to be statistically more common in younger patients, and have much more histomorphological changes pointing to the complicated cysts ($p<0.05$). Moreover, we noted that patients with MTCs were found to be more symptomatic before diagnosis. Furthermore, in our study when we compared MTCs and UTCs, UTCs were slightly (64.2%) more frequent in female patients.

Conclusion: According to our results, thymic cysts may also be seen at younger ages. MTC and UTC can have different histomorphological characteristics, such as foreign body reaction and hemorrhage. Moreover, there can be different clinical features, such as age, gender, and symptoms, between these two subtypes.

Keywords: Thymus, Cyst, Multilocular, Unilocular, Pathology, Histomorphology

1. INTRODUCTION

Thymus is a specialized lymphoid organ located in the anterior mediastinum. Thymic cysts (TCs) are uncommon benign lesions arising in the anterior mediastinum or cervical region. Either congenital or acquired in origin they comprise 1-3% of all mass lesions in the anterior mediastinum. However, they should be kept in mind in the differential diagnosis of mediastinal lesions. The two subtypes of TC are multilocular thymic cysts (MTCs) and unilocular thymic cysts (UTCs). According to the reports, UTCs are congenital lesions with thin walls that do not exhibit inflammatory changes, whereas, MTCs are acquired lesions that develop as a result of inflammatory conditions. These inflammatory conditions have thick fibrous walls [1, 2]. Neoplastic and other pathologies originating from the thymus or non-thymic tissues may be linked to TCs, particularly to MTC [4-8]. Therefore, it is crucial to examine these lesions in detail and make a precise diagnosis.

The purpose of this study is to describe the clinicopathological characteristics of thymic cysts and to compare the clinical and histomorphological characteristics of MTCs and UTCs, as well as to investigate possible pathologies that could coexist or be related to thymic cysts.

2. PATIENTS and METHODS

The demographic and clinical features of 23 cases with thymic cysts admitted to Marmara University Hospital, Istanbul between 2012 and 2020, were obtained from the data of our hospital management system. All patients underwent resection by video-assisted thoracic surgery, and the diagnoses were confirmed by histopathological examination. All hematoxylin and eosin (H&E) stained slides were evaluated by the researcher. Histomorphological findings including the diameter of cysts,

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unilocular or multilocular structure of lesions, the epithelial lining of cysts, and the structure/contents of the cyst wall and lumen were examined in detail.

The present study was approved by the Marmara University, School of Medicine, Clinical Research Ethics Committee (dated, Jan 2017; Approval No. 09.2017.69).

Statistical Analysis

One sample t-test and chi-square test were used for statistical analysis. A p value of < 0.05 was considered statistically significant. Data were analyzed with *Jamovi* (The jamovi project 2021-Version 1.6) [3].

3. RESULTS

The main demographic and clinical features of the patients with TCs are listed in Table I. Of the 23 patients, 10 (43.4%) were male and 13 (56.5%) were female. The mean age of the patients was 43 years (ranging from 6 to 80 years).

Table I. *Demographic and clinical features of patients with thymic cyst.*

Case number	Age	Gender	Symptoms	Initial clinical/ radiological diagnosis related to thymic cysts
1	72	F	Not known	AMM
2	48	F	Screening for MG	MG/AMM
3	40	F	Dyspnea	Cervical mass
4	39	F	Screening for MG	MG/AMM
5	7	M	Mass lesion protruding below sternum with cough	Thymic hyperplasia
6	21	F	Screening for MG	MG/AMM
7	37	F	Dry cough	Pericardial mass
8	53	F	Dyspnea	AMM/Cyst
9	9	M	Servical swelling	Thymic cyst
10	66	M	Dry cough	AMM/Cyst-Thymic cyst
11	32	M	Incidental	AMM/Cyst
12	6	F	Chest pain	Mediastinal cyst
13	11	M	Servical swelling	Cervical mass
14	70	F	Incidental	Pericardial cyst
15	53	F	Incidental	AMM
16	62	M	Incidental	Pericardial cyst
17	55	F	Incidental	Thymoma
18	39	M	Screening for MG	MG/Thymoma
19	48	F	Dorsalgia	AMM/Cyst
20	57	M	Screening for MG	MG/AMM
21	49	M	Dyspnea	AMM
22	80	M	Chest pain	AMM/Cyst
23	36	F	Incidental	AMM/Cyst

M: Male, F: Female, AMM: Anterior mediastinal mass, MG: Myasthenia gravis.

Patients presented to the clinic with a wide range of symptoms; 3 (13%) with dyspnea, 2 (8.6%) with dry cough, 1 (4.3%) with cough and protruding mass lesion below the sternum, 2 (8.6%) with chest pain, 2 (8.6%) with cervical swelling and 1 (4.3%) with dorsalgia. TCs were noticed incidentally on radiological imaging in six (26%) patients and five (21.7%) of 23 were detected during the screening of thymus by virtue of Myasthenia gravis. No clinical data were obtained for one patient and patients with known clinical history had no previous trauma or thoracic surgery. Median follow-up was 4.7 years for TCs.

Ten (43.4%) of 23 patients had cystic lesions initially diagnosed by radiological evaluation. Only one patient had a diagnosis of a thymic cyst according to his radiological report. Two of ten (20%) were described as having a pericardial cystic lesion. Other than cystic lesions, 13 (56.5%) anterior mediastinal masses, 2 (8.6%) cervical masses, 1 (4.3%) pericardial mass, 2 (8.6%) thymomas and 1 (4.3%) thymic hyperplasia were detected on radiological imaging.

Histomorphologically, two of 23 (8.6%) were diagnosed as cervical TCs. The rest of the cases had mediastinal TCs.

The mean diameter of thymus and the largest cystic lesion were 5.8 cm (min:0.5, max:14 cm) and 2.7 cm (min:0.5, max:8 cm), respectively (Table II). In 7 (30.4%) cases, the cyst walls were single-layered and two-layered epithelioid cells, and in 9 (39.1%) cases, the cyst walls were lined with ciliated pseudostratified epithelium (Figure 1). Cholesterol cleft, histiocyte, hemorrhage, and foreign body reaction pointing to the complicated cysts were found in the cyst wall and lumen in 6 (26%) and 9 (39.1%) cases, respectively, (Figure 1). Fifteen (65.2%) residual thymus tissue, 1 (4.3%) thymic hyperplasia, 4 (17.2%) thymic tissue with reactive follicular hyperplasia, and 3 (13%) thymomas were detected in the thymic tissue adjacent to the thymic cysts.

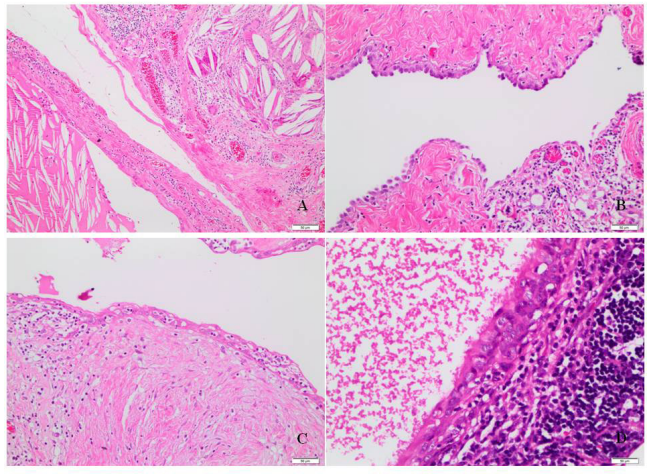

Figure 1. A: Foreign body type reaction with cholesterol clefts, H&E-4x. **B:** One-layered epithelium of cyst wall, H&E-10x. **C:** Two-layered epithelium of cyst wall, H&E-10x. **D:** Pseudostratified epithelium of cyst wall, H&E-20x.

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Table II. *Histomorphological findings of thymic cysts of patients.*

Case number	Size of total lesion [cm]	Diameter of largest cystic lesion [cm]	M/U	LE of cyst	Fibrous wall of cyst	Complication on wall of cyst	Complication in lumen of cyst	Accompanying thymic tissue
1	1.5	1.5	U	OE	Present	Absent	Absent	RT
2	6	3	U	CP	Absent	Absent	Absent	RFH
3	4.6	1.5	M	CP	Present, focal	Absent	Absent	Thymic hyperplasia
4	10	1	M	CP	Present	Absent	Absent	Thymoma, B1
5	5.5	1	M	TE	Present	FBR, CC	FBR, CC	RT
6	5	2	U	OE	Absent	Absent	Absent	RFH
7	3	3	U	OE	Present	Absent	Absent	RT
8	4.5	4.5	U	TE	Present	Absent	Absent	RT
9	4	1.5	M	TE	Present	FBR, CC	FBR, CC	RT
10	6.5	6.5	U	TE	Absent	Absent	Absent	RT
11	5	5	U	CP	Present	LK , H, HI	LK, H, HI	RT
12	6.5	2	M	TE	Present, focal	FBR, CC	FBR, CC	RT
13	6	2.5	M	OE	Present	FBR, CC	FBR, CC, H	RT
14	8	8	U	OE	Present, focal	Absent	Absent	RT
15	4.5	4.5	U	CP	Present, focal	Absent	Absent	RT
16	0.5	0.5	U	CP	Present	Absent	Absent	RT
17	3.5	3.5	U	CP	Present	Absent	Absent	RT
18	7	0.8	U	TE	Present, focal	Absent	Absent	Thymoma, B2
19	2	2	U	CP	Present	Absent	Absent	RT
20	6	1.5/0.8	M	OE	Present	Absent	Histiocytes	Thymoma, B2
21	16	7/3.5	M	OE	Absent	Absent	Focal FBR, CC	RFH
22	4	4	U	TE	Absent	Absent	Absent	RT
23	14	8/1.5	M	CP	Absent	Absent	CC, H	RFH

Multiloculation: M, Uniloculation: U, LE: Lining epithelium, OE: One-layered epitheloid, CP: Ciliated pseudostratified, TE: Two-layered epitheloid, FBR: Foreign body type reaction, CC: Cholesterol clefts, LK: Lamellar keratin, H: Hemorrhage, HI: Histiocytes, RT: Residual thymus, RFH: Reactive follicular hyperplasia.

When we grouped the cases as MTC and UTC, the number of cases was 9 and 14, the mean age was 28.2 years (ranging from 6 to 49 years) and 52.6 years (ranging from 21 to 80 years), and the ratio between the male and female was 4/5 and 9/5, respectively (Table II). In terms of mean age, MTC cases were found to be statistically more common in younger patients ($p<0.05$). Moreover, UTC cases were more frequent in female patients. The total lesion diameters of MTC and UTC cases (6 and 5.4 cm, respectively) were identical. Morphologically, the ciliated pseudostratified epithelium was slightly more frequently seen in UTCs. In MTC cases, histomorphological features pointing to the complicated cysts, such as foreign body type reaction, cholesterol clefts, lamellar keratin, hemorrhage, and histiocytes, in the cyst wall and lumen were seen more frequently ($p<0.05$) (Table II). It was discovered that cases with the diagnosis of MTC were more symptomatic ($p=0.193$). Regarding the presence of Myasthenia gravis disease and other accompanying thymus pathologies, there was no statistically significant difference between the MTC and UTC groups.

4. DISCUSSION

In our study, the mean age of cases with TC was 43 years, and the most common symptom of in these cases was dyspnea. Clinical or radiological cystic lesions at initial diagnosis were defined in almost half (43.4%) of TCs. When we compared features of MTCs and UTCs of our cases, MTCs were detected in younger age groups, were more symptomatic, and represented more histomorphological features pointing to the complicated cysts than UTCs.

Thymic cysts are rare lesions arising from embryonic remnants along the course of thymic migration or acquired lesions in the neck or the anterior mediastinum. Cervical TCs represent 1% of all cervical cystic masses. Cervical TC is a rare lesion, mostly described in pediatric patients, and much more rarely seen in adults [4-8]. We discovered that cervical TCs were not that infrequent since two (8.6%) of our 23 cases were cervical TC. In addition, the ratio of adult cervical TC of our TCs was 4.3% (a patient at 40 years) which may represent adult patients with cervical TC are more common than known. But the last inference is uncertain because of the limited number of our cases.

Thymic cysts and conditions characterized by cystic changes in the thymus can cause non-specific symptoms such as chest pain, dyspnea, and cough [9, 10]. Cervical swelling, sternal swelling, and dorsalgia were observed in our patients and the most common symptom of TCs was dyspnea. Statistically, significant difference was not found between UTC and MTC, even though MTC cases were more frequently symptomatic in terms of the symptoms that led patients to apply to the clinic, in our study.

Mediastinal cystic lesions are infrequent but have a variety of histological types, not only thymic but also bronchogenic, pericardial, enteric, Müllerian, lymphatic, and parathyroid types [11, 12]. Several radiological researches study the differential diagnosis of thymic cystic and thymic epithelial tumors, but it has not been well understood yet [13, 14]. The radiological or clinical diagnosis of the cystic mediastinal or thymic lesion could be described for approximately only half of our thymic cysts (43.4%). Histomorphological evaluation of mediastinal/thymic lesions is mandatory for precise diagnosis. Diagnosis for our patients were precise as all of our cases were evaluated histomorphologically.

Although, in some researches, it has been shown that the mean age of patients with TCs was 50 years and older, the mean age of our patients was 43 years [15]. We divided our cases into two groups as UTCs and MTCs. The mean age for UTCs (52.6 years) was statistically older than that of MTCs (28.2 years) . No gender difference was observed in our patients, which is consistent with studies in the literature [14]. On the other hand, in females, UTCs were seen slightly more frequently when compared with males, but there was no statistical difference between the genders.

In one of the earliest studies on MTC cases, Suster et al., defined histomorphological findings in MTCs, such as cholesterol granulomas and hemorrhage accompanying acute and chronic inflammation, and revealed that this inflammation played a role in the development of MTCs [1]. In contrast, UTCs are known to be congenital lesions with thin walls that do not exhibit inflammatory changes [2]. In our study, MTC cases had more frequent morphological findings that indicated complications/inflammation in the cyst wall and lumen, such as foreign body reaction and hemorrhage. However, not all of our MTC cases exhibited the histomorphological changes suggestive of this complication, but also some of UTCs represented these complicated features with inflammation. This might imply that not all MTCs are necessarily caused by acquired inflammation, and vice versa for UTC but to be certain, further clinical follow-up and histomorphological analysis of larger series are required.

Although, they are not very common, concomitant lesions such as thymoma in the thymus tissue, and thymic and reactive follicular hyperplasia have been described in the literature [10, 16-18]. In fact, in one instance, no solid component was seen, and all of the thymoma areas surrounding the thymic cyst had a cystic structure [19]. Furthermore, it is important to keep in mind cystic morphology when making a differential diagnosis of thymic cysts, since, it may play a crucial role in the development of mediastinal seminoma and micronodular thymoma [9, 20]. In addition, it should be noted that malignant neoplastic proliferations originating from the thymus or other origins may especially develop in MTCs [21-23]. In our study, thymoma, or thymic or reactive follicular hyperplasia was found accompanying thymic cysts in 8 (34.8%) cases.

According to the previous studies, it has been revealed that the incidence of Sjögren's syndrome and similar autoimmune diseases was high in MTC [16, 24-26]. However, no myasthenia gravis, Sjögren's syndrome, or a similar autoimmune disease was observed during preoperative or postoperative follow-up in MTCs with reactive follicular hyperplasia in our study. This situation may be related to short mean follow-up time.

Due to its retrospective nature and focus on cases from a single center, our study has some limitations. Additionally, the small number of cases prevented us from producing results from some statistical analyses.

Conclusion

As a result, thymic cysts are rare mediastinal or cervical lesions that can be unilocular or multilocular. They should be kept in mind in the differential diagnoses during the evaluation of any thymic cyst. Detailed and careful sampling is important to make a definite diagnosis. MTCs and UTCs have clinical differences such as age and gender of the patient, being symptomatic, and histomorphological differences such as hemorrhage and foreign body reaction.

The only radical treatment is the complete surgical removal of the cyst, which can suppress symptoms, provide a formal diagnosis, and prevent complications.

Compliance with Ethical Standards

Ethical Approval: This study was approved by Marmara University The School of Medicine Clinical Research Ethics Committee with the approval number 09.2017.69, dated Jan 2017.

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Conflict of Interest: There are no conflicting interests.

Author Contribution: EB: Drafting of the work, data acquisation, critical revision, concept, design of the study and statistical analysis.

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