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[1]Department of General Surgery, King Fahd Hospital of the University, College of Medicine, Imam Abdulrahman bin Faisal University, Dammam, Saudi Arabia

[2]Department of Obstetrics and Gynecology, King Fahd Hospital of the University, College of Medicine, Imam Abdulrahman Bin Faisal University, Dammam, Saudi Arabia

[3]Cardiothiracic Surgery, College of Medicine, Menofia University, Egypt

Corresponding author: Dhuha N. Boumarah. MD. Department of General Surgery, King Fahd Hospital of the University, College of Medicine, Imam Abdulrahman bin Faisal University, Dammam, Saudi Arabia. E-mail: dohanahar@gmail. com.ORCID ID: http// www.orcid.org/:0000-0002-4828-9312.

Clinicopathological Analysis of Mediastinal Masses: a Single-Institute Experience

Zeead M. Alghamdi[1], Sharifah A. Othman[2], Dhuha N. Boumarah[1], Mohammed Sabry Abdelmotaleb[3], Farouk Alrashaid[1], Yasser Aljehani[1], Hatem Y. Elbawab[1]

ABSTRACT

Background: The centrally located portion of the thoracic cavity is called the mediastinum and consists of several essential organs. In the presence of various outcomes and prognostic indicators of mediastinal masses, meticulous diagnosis of these masses is considered crucial. **Objective:** In this study, we analyzed all mediastinal masses observed clinically and pathologically at one institution over a period of ten years. **Methods:** This is a retrospective, single-institution review of 94 patients with mediastinal masses, drawing on existing data recorded by the hospital. The study was carried out at the King Fahd University Hospital, Khobar, Saudi Arabia. Data was collected from 2009 to 2019. Participants were all patients with malignant or benign mediastinal masses admitted to the hospital, or diagnosed incidentally to have mediastinal masses during investigations for other reasons. **Results:** The mean age for developing a mediastinal mass was 33.89 ± 18.91 years of age. Most of the patients (69.1%) were symptomatic at presentation. Overall, (49.23%) of patients who were symptomatic at diagnosis had a malignant mass. Concerning pathologic diagnosis and presentation of the patient (symptomatic versus asymptomatic), there was a significant positive relationship between pathologic diagnosis and symptoms with a P value of 0.020. In our study, only 5.15% of cases experienced recurrence. **Conclusion:** This study provides a great understanding of mediastinal tumor biology and the role of both radiotherapy and chemotherapy in increasing the survival rates of patients suffering from similar malignant conditions.

Keywords: Benign chest tumor, Malignant chest tumor, Mediastinal masses, Thoracic cavity, Thoracic surgery, Thymic lesions, Thymoma.

1. BACKGROUND

Studies indicate that mediastinal tumors account for approximately 3% of all tumors seen within the chest, with prevalent histological types including lymphomas, thymomas and germ cell tumors. Due to the narrow anatomical space involved, mediastinal masses pose a challenge to many thoracic surgeons, both in diagnosis and management. They present as uncommon lesions that are either congenital or acquired, primary or secondary. Even though they are not a common entity, mediastinal masses comprise a wide range of conditions within the heterogeneous category of malignant and benign tumors.

The composition and location of a mass are essential factors in forming a differential diagnosis, thus they are assessed from both pathological and anatomical perspectives. The mediastinum is divided into four compartments (anterior, middle, superior and posterior) in order to facilitate diagnosis of mediastinal pathology, determine extension of the tumor and select an appropriate surgical approach. A new classification system has been proposed by the Japanese Association of Research of the Thymus (JART) based on computed tomography (CT) scan findings included the superior part of the mediastinum, anterior mediastinum (pre-vascular zone), middle mediastinum (peri-tracheoesophageal zone), and posterior mediastinum (para-vertebral zone) (1). Furthermore, anterior mediastinal tumors make up the majority of all mediastinal masses including thymomas, teratomas, lymphomas, and those caused by thyroid diseases. Given their proximity to major cardiovascular and airway structures, there is a likelihood of cardiorespiratory collapse resulting from anterior mediastinal masses, and several case reports describe

near-fatal or fatal complications related to anesthesia with tumors of this type (1).

2. OBJECTIVE

In this study, we analyzed all mediastinal masses observed clinically and pathologically at our institution over a period of 10 years.

3. MATERIAL AND METHODS

Study design

A retrospective, single-site review of 94 patients with mediastinal masses, drawing on existing data recorded by the hospital.

Setting

The study was carried out at the King Fahd University Hospital, located in Khobar, Saudi Arabia, based on data collected from 2009 to 2019.

Participants Inclusion criteria consisted of patients with malignant or benign mediastinal masses admitted to the King Fahd University Hospital from 2009-2019, who presented with chest pain, shortness of breath, or a chronic cough. We also included all patients with mediastinal masses found incidentally during investigations for other issues. Excluded from the study were patients with mediastinal metastatic disease or lesions involving the pleura, pericardium or the chest wall and associated structures.

Data Extraction

Records of patients with primary mediastinal tumors who had undergone treatment at the hospital were reviewed under a protocol approved by the Institutional Review Board (IRB) at Imam Abdulrahman bin Faisal University. Complying with all ethical requirements, the study extracted historical data from medical records and reviewed postoperative morbidity and mortality, histologic diagnosis, surgeon-determined tumor invasion, location, operative procedure, diagnostic investigations, demographic data and follow-up. Clinical data consisted of magnetic resonance imaging (MRI), chest CT scans, chest X-rays, history and physical examinations.

Data Analysis

The data were entered in Microsoft Excel, and analyzed using the statistical package for social sciences (SPSS); expressed in text and tables. Variables were described in frequencies and percentages, and continuous variables were summarized with mean and standard deviation. Fisher's exact test and the Mann-Whitney U-test were applied where appropriate. Statistical significance was set at ($P<0.05$).

4. RESULTS

The mean age for developing a mediastinal mass was 33.89 ± 18.91 years. There were 11 (11.7%) pediatric patients (aged 14 years and more) and 83 adult patients. Out of the 94 patients, 49 (52.1%) were male and 45 (47.9%) were female, with a male-to-female ratio of 1.08:1. Most of the patients (69.1%) were symptomatic at presentation, with cough (14.9%), chest pain (14.9%), and shortness of breath (25.5%) cited as the predominant complaints. Sixteen percent experienced a superior vena cava obstruction (SVCO). Twenty-two patients had myasthenia gravis (MG), and 15 (16%) demonstrated a worsening of their MG symptoms at the time of diagnosis.

Overall, 49.23% of patients who were symptomatic at diagnosis had a malignant mass, with an absence of symptoms correlating more closely with thymic lesions and either endocrine or neurogenic tumors. concerning pathologic diagnosis and clinical manifestations (whether symptomatic or asymptomatic), P value was 0.020 (sta-

Variables		Values
Patient characteristics:		
Age (years)	Mean ± SD (range)	33.89±18.92 (.084-85)
Gender	Male (%) Female (%)	49 (52.1%) 45 (47.9%)
Clinical Presentation:	Symptomatic (%) Asymptomatic (%)	65 (69.1%) 29 (30.9%)
Anatomical location:	Anterior Mediastinal (%) Posterior Mediastinal (%) Superior Mediastinal (%) Middle Mediastinal (%)	70 (74.5%) 8 (8.5%) 5 (5.3%) 3 (3.2%)
Diagnostic/treatment approach: Tumor Resection	Thoracotomy Resection (%) VATS Resection (%) Thymectomy (%) Resection with unknown approach (%)	
Biopsy	CT-guided biopsy (%) Excisional biopsy (%) VATS biopsy (%) Thoracotomy biopsy (%)	
Pathological findings:		
	Thymic Lesion (%)	39 (41.5%)
	Lymphoma (%)	13 (13.8%)
	Germ Cell Tumors (%)	9 (9.6%)
	Neurogenic tumors (%)	7 (7.4%)
	Carcinoma (%)	5 (5.3%)
	Mesenchymal Lesion (%) Cysts (%) Endocrine Tumors (%) Others (%)	3 (3.2%) 3 (3.2%) 2 (2.1%) 13 (13.8%)
Length of hospital Stay (Days)	Mean ± SD (range)	15.57±15.60 (1-103)
Recurrence:		
	Yes (%)	9 (9.6%)
	No (%) Missing Data (%)	69 (73.4%) 16 (17%)

SD: standard deviation; CT: computed tomography.

Table 1. General characteristics of the patients and mediastinal tumors with pathological features

		Location of Mediastinal Mass			
		Anterior Mediastinal	Middle Mediastinal	Posterior Mediastinal	Superior Mediastinal
Pathological Diagnosis	Thymic Lesions	39			
	Carcinoma Tumors	2	1		
	Cysts	1			1
	Endocrine Tumors		1		
	Germ cell tumor	6	1		2
	Lymphoma	12			
	Mesenchymal Lesions			1	
	Neurogenic Tumors			6	1
	Others	10		1	1
Total		70	3	8	5

Table 2. Incidence of histological diagnosis of primary mediastinal tumors in various anatomical locations

went video-assisted thoracoscopic surgery (VATS) for biopsy, and one required a thoracotomy to obtain a biopsy, which revealed necrotizing granulomatous inflammation. Our study indicates a significant positive relationship between pathologic diagnosis and method of diagnosis, with a P value of 0.001.

The most predominant pathological diagnoses were thymic lesions [39 (41.5%)] consisting of benign and malignant thymomas, thymolipomas, thymic cysts, and thymic hyperplasias. Lymphomas were the second most frequent lesion, presenting in 13 patients (13.8%). Of all patients, 76.9% had Hodgkin's lymphomas. Non-Hodgkin's lymphomas occurred in 23.07% of all patients diagnosed with lymphoma. Germ cell tumors consisting of germinomas and teratomas, accounted

Characteristics	Thymic lesions	Lymphoma	Neurogenic	Carcinoma	Mesenchymal	Endocrine	GCT*	Cysts
N	39	13	7	5	3	2	9	3
Mean age (years)	35.2±18.0	29.0±7.4	14.9±12.2	64.8±13.7	16.3±14.2	69.0±9.8	27.3±14.0	26.0±22.8
Male: Female	1:1.44	0.86:1	2.5:1	4:1	1:2	Males	2:1	1:2
SVCO**	2	4		2			2	3
Treatment modality:								
Chemotherapy, radiotherapy, or both	5	9	2	2		1	2	
Surgery	29	2	6		1		6	2
Surgery+adjuvant therapy								

Table 3. Characteristics of the patients and outcome of different pathological diagnoses of primary malignant mediastinal tumors. *GCT: germ cell tumors Superior vena cava obstruction syndrome**

tistically significant), indicating that there is a significant positive relationship between pathologic diagnosis and presentation. Most of the patients underwent a CT scan; revealing mediastinal masses with features indicating the varying pathology of each one. Table 1 illustrates the general characteristics of included patients and mediastinal tumors with pathological features.

Based on the subdivision of the mediastinum, the majority of masses [70 (74.5%)] had an anterior mediastinal presentation. Posterior mediastinal masses were seen in eight (8.5%) of the patients. Five (5.3%) had a superior mediastinal mass and three (3.2%) had middle mediastinal masses. The relative incidence of histological diagnosis of primary mediastinal tumors distributed throughout anatomical subdivisions is presented in Table 2. Thymic lesions, lymphomas, germ cell tumors, and carcinomas were typically located in the anterior mediastinum. In contrast, neurogenic tumors and mesenchymal tumors were usually located in the posterior mediastinum. Our study revealed a significant positive relationship between pathologic diagnosis and location of mediastinum mass with a P value of 0.000.

Pathological diagnosis achieved through complete resection was performed on 37 (39.36%) patients, or biopsy in 26 (28.80%) patients in establishing a diagnosis prior to formulating a treatment plan, fifteen (15.46%) were diagnosed by CT-guided biopsy and seven (7.2%) with an excisional biopsy. Four patients (4.12%) underfor 9.6%. Neuroblastoma and schwannoma neurogenic tumors totaled 7.4%. Carcinomas (5.3%), and other lesions included sclerosing inflammation, chronic granulomatous inflammation, necrotizing granulomatous inflammation, and Castleman's disease. Benign lesions were found in 54 (57.4%) patients, while 40 (42.5%) had a malignant mediastinal mass. Table 3 shows characteristics of the patients and outcomes of different pathological diagnoses of primary malignant mediastinal tumors whereas Table 4 illustrates pathological distribution of the primary mediastinal tumors and cysts.

The mean length of hospital stay (LOS) was 15.75 ± 15.60 days (range: 1-103 days) prolonged hospital stay was due to MG deterioration. Most of the patients showed no complications post-operatively. However, of the two patients who experienced a postoperative complication, one had a diaphragmatic elevation due to phrenic nerve injury post-thymectomy, and the other presented with a pneumothorax on the third day postoperatively.

Approximately 2 percent experienced some amount of blood loss, with the largest volume being 350 cc. One death occurred among the reviewed patients, who received a diagnosis of carcinoma on a CT-guided biopsy, without surgical intervention. Only 5.15% of cases experienced recurrence. One recurrence occurred in a patient with lymphoma, germ cell tumors (teratoma) and cysts, while 2 patients experienced a recurrence with a thymus lesion. Table 5 summarizes the relation

Type	Number of patients	%
Thymic	39	41.5
Thymus hyperplasia	16	
Thymolipoma	8	
Thymoma	14	
Thymic cyst	1	
Lymphoma	13	13.8
Hodgkin's lymphoma	10	
Non-hodgkin's lymphoma	3	
Neurogenic	7	7.4
Neuroblastoma	5	
Schwannoma	2	
Carcinoma	5	5.3
Undifferentiated carcinoma	2	
Basaloid carcinoma	1	
Squamous cell carcinoma	1	
Small cell carcinoma	1	
Mesenchyma	3	3.2
Sarcoma	3	
Endocrine	2	2.1
Neuroendocrine	2	
Germ Cell Tumor	9	9.6
Germinoma	4	
Teratoma	5	
Cysts	3	3.2
Benign cystic lesion	1	
Cystic lymphangioma	1	
Dermoid cyst	1	
Others	13	13.8

Table 4. Pathological distribution of the primary mediastinal tumors and cysts

(2) Alternatively, patients with mediastinal masses may be asymptomatic.

Those with tracheobronchial obstructions may cite complaints of chest discomfort, nonspecific cough, noisy breathing, and dyspnea. Signs can include reduced breath sounds, rhonchi, stridor, and tachypnea (3). However, in many cases, a physical examination is unremarkable. As a result of venous drainage obstruction in the upper part of the thorax, superior vena cava syndrome may present as edema of the arms, neck, and face; dilated collateral veins in the body's upper section, visual disturbances, dyspnea, and CNS symptoms such as headaches. Pulmonary vascular and right heart compression may present as a cardiac murmur, arrhythmia, syncope during the process of a forced Valsalva maneuver, or dyspnea (4).

In our study, the mean age for developing a mediastinal mass was 15.75 years. This is consistent with earlier studies, which indicate that the prevalence of mediastinal masses is relatively rare in children and adolescents. Other studies indicate that mediastinal masses typically occur in patients aged 30-50 years; which is still within the scope of our report. Concerning neurogenic tumors, the pediatric age group has more predominance compared to adults (5). The pediatric group in our study accounts for 11.34% and neuroblastoma was 26.45% among this group. Five patients with thymus lesion, two with teratoma and one with cystic lymphangioma.

Our analysis indicated that mediastinal masses occur slightly more frequently in males when compared to females. Clinicians and radiologists may encounter various forms of lesions while investigating mediastinal

		Location of mediastinum mass	presentation	Hospital stay	Diagnosed by	Recurrence
Pathologic diagnosis	Correlation coefficient	0.430**	0.239**	0.021	0.333**	-0.070
	Sig. (2-tailed)	0.000	0.020	0.850	0.001	0.502
	N	85	94	87	91	94

** Correlation is significant at the 0.01 level (2-tailed)

Table 5. Relation between pathological diagnosis and location, presentation, diagnostic approach, LOS, and recurrence

between pathological diagnosis and location, presentation, diagnostic approach, LOS, and recurrence.

5. DISCUSSION

Tumor location in the mediastinum varies according to a pathological diagnosis. Theoretical evidence correlates with our findings that the most common mediastinal tumors are located in the anterior mediastinum. Each type of mediastinal mass typically has a specific location of origin. For example, thymomas and lymphomas usually emanate from the anterior mediastinum, while germ cell tumors most often arise from the middle mediastinum. Neurogenic tumors customarily originate from sympathetic nerve chains or the spinal roots of the posterior mediastinum. Mediastinal masses manifest in a variety of clinical presentations. Some of the most common are observed in systemic syndromes such as thymic disease and myasthenia gravis, pulmonary vascular and right-heart compression, superior vena cava syndrome, and tracheobronchial obstruction pathological entities resulting from mediastinal masses. An important tool in establishing a presumptive diagnosis is through imaging, which provides guidance in confirmatory testing (6). A major objective in mediastinal mass evaluation is to determine the tumor's size, relationship with essential vascular structures, and the tracheobronchial tree, along with the degree and location of any compression (7). This is most effectively established through CT scans and chest radiographs. Thoracic CT scans are particularly efficient in determining an accurate level and degree of cardiovascular/tracheobronchial compression, which plays an integral role in anesthetic plan formulation. While magnetic resonance imaging (MRI) is less routinely employed, it can be used in diagnosing vascular and neurogenic lesions, particularly when there is a contraindication of contrast material usage (8). Notably, the use of transthoracic echocardiography is recommended with suspicion of cardiovascular structure invasion or compression, or

when a considerable pericardial effusion is established through CT scans (3).

In the presence of classic features, clinicians may make presumptive diagnoses with some confidence based on imaging alone. This is less the case when determining the presence of anterior mediastinal lesions. The establishment of an appropriate differential diagnosis for each patient helps in preventing non-essential and at times misleading, additional tests or inaccurate biopsies (8). Due to significant variations and rising controversy in identifying and treating mediastinal masses, it has become increasingly critical to assess the precision and accuracy of presentations, the quality of the diagnostic tools adopted, the validity of histological findings, and the effectiveness of treatment outcomes.

Diagnostic surgical procedures are utilized for biopsy tissue procurement to guide treatment and frame a histological diagnosis. Percutaneous CT-guided biopsy, performed under local anesthesia, is a less costly and relatively safe method to obtain adequate histological diagnostic tissue (9). Also under local anesthesia, the other diagnostic procedures include endobronchial ultrasound-guided, transbronchial needle aspiration (EBUS), anterior mediastinotomy, anterior mediastinoscopy, cervical mediastinoscopy, and biopsy of an extra-thoracic mass (4).

Surgical resection is necessary for the majority of mediastinal masses, particularly when a presumptive clinical diagnosis is made without a confirmatory histopathological diagnosis. Precise operative planning is paramount in cases with invasion of the surrounding structures. Key surgical approaches consist of video-assisted thoracoscopic surgery, thoracotomies, and sternotomies. In a few situations, surgeons face challenges with undiagnosed mediastinal masses intraoperatively (10-11).

Under general anesthesia, patients with mediastinal masses causing considerable cardiovascular or respiratory compression are normally at high risk for cardiopulmonary collapse. These patients may benefit from preoperative treatments of radiotherapy, chemotherapy, or steroids, to first shrink the tumor and alleviate the obstruction. However, the role of pre-treatment faces considerable debate. Even though some studies link preoperative radiation therapy to decreased postoperative complications, the shrinkage of the tumor may in fact, negatively impact histological accuracy, resulting in diagnostic confusion. This does not seem to apply to tissue diagnosis, however, when the biopsies are extracted within 72 hours after the commencement of treatment. As in Heck et al. study, a clear result in nearly 95% of high-risk children was established after receiving steroids prior to diagnosis (3).

Literature indicates that approximately 60% of patients are symptomatic, however, in our study, this was true in 96.1% (3). Other studies have produced varied indices of malignancy. Drawing on a database from Duke University Hospital in North Carolina, USA, a study reported that 85% of patients with malignancies were symptomatic, and only 46% of the patients with benign tumors presented with identifiable complaints (2). Lastly, recurrence of these conditions is rare in the majority of the cases analyzed, which may indicate the efficacy of contemporary treatment processes.

6. CONCLUSION

This study provides a great understanding of mediastinal tumor biology and the role of both radiotherapy and chemotherapy in increasing the survival rates of patients suffering from similar malignant conditions. Interestingly, this study demonstrated that anterior mediastinal masses are highly common throughout the Kingdom of Saudi Arabia, therefore, physicians must be highly vigilant regarding abnormalities detected on chest radiographs.

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