Clinicopathological Profile of Mediastinal Masses: Data from a Tertiary Cancer Centre in Western India

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Summary

The mediastinum is located in the middle of the thoracic cavity and it is home for many vital structures. Mediastinal masses are very rare and require a combined approach for diagnosis and management. In the present study, we aimed to evaluate the clinicopathological characteristics of mediastinal masses along with the utility of immunohistochemistry in diagnosis. This was a retrospective study performed over a period of 6 years (2016-2021). The data of mediastinal masses were collected from the hospital database. A total of 165 cases were enrolled in the study. The majority of cases were located in the prevascular mediastinum (82.2%). The mean age was 37.68 (±19.54) years with male preponderance (68.5%). The most common histology was lymphoma (30.3%) followed by metastatic (22.4%) and thymic (19.4%) lesions. T-Lymphoblastic lymphoma was most common lymphoid lesion while thymoma type B2 was most common thymic lesion encountered. The mediastinum is a pandora's box which contains many vital structures. Detailed Clinicoradiological evaluation along with histomorphology and immunohistochemistry is pivotal for the diagnosis and management of mediastinal masses.

Keywords: Mediastinal mass, Mediastinal lymphoma, Thymoma

Introduction

Primary mediastinal tumors are uncommon and account for only 3% of tumors of the thorax.[1,2] The mediastinum is the visceral compartment located in the middle of the thoracic cavity. It accommodates many vital structures except the lung.[1-3] The mediastinum is divided into three compartments by ITMIG[4] classification, prevascular (anterior), visceral (middle) and paravertebral (posterior) compartments. The majority of tumor involves prevascular mediastinum and the larger part arise from the thymus. Visceral mediastinal lesions include congenital cyst, (pericardial and bronchogenic cyst) while neurogenic tumors form majority of paravertebral mediastinal masses.[1,5,6] Combined approach of radiology, pathological and clinical information is necessary to narrow down the various differentials and for further management.[7,8] Existing literature shows different data regarding the incidence of various lesions arising from the mediastinum. Therefore, the present study aimed to evaluate the clinicopathological characteristics of mediastinal masses in our institution along with the usefulness of various immunohistochemical markers to reach the definite diagnosis.

Material and methods

The present study was retrospective and descriptive, conducted in the department of Oncopathology at The Gujarat Cancer & Research Institute in Western India from the year 2016 to 2021. A total of 165 cases primarily located in the mediastinum were included in the study. Tumors arising from the pleura, pericardium and chest wall structure were excluded. All the relevant clinicopathological parameters were collected from the database. All the specimens were fixed using 10% formalin and then embedded in paraffin. H and E staining and immunohistochemical (IHC) staining were done. Various antibody panels according to clinical and pathological differentials were used. All the obtained data was arranged in a tabulated form and analysed using SPSS software.

Results

A total of 165 cases were included in the study. Detailed clinicopathological characteristics are discussed in Table 1. The mean age was 37.68 (±19.54) years with a range of 1-78 years. Male preponderance with M: F ratio 2.2: 1. Lymphoma was the most common lesion followed by metastatic and thymic lesions. Out of 165 cases, 49 were resection specimen. Of these 49 cases, preresection biopsy was done in 30 cases. There is no major discordance occur between biopsy and resection specimen as prior immunohistochemistry confirmation was done in all difficult cases.

Lymphoid lesion

Of a total of 50 cases, 48 were located in prevascular compartment. The mean age was 23.28 (±13.72) years with a range of 2 to 62 years. The large population was under 20 years of age (65.31%). Slight male preponderance with M:F ratio 1.4:3.

Table 1: Clinicopathological characteristics of mediastinal tumors

Parameter	Number (n=165)	Percentage (%)
Age (Mean±SD)	**37.68 ± 19.54**	**-**
Sex		
Female	52	31.50
Male	113	68.50
Location (n=165)		
Prevascular	136	5.00
Visceral	24	82.20
Paravertebral	3.1	14.70
Histodiagnosis (n=165)		
GCT	17	10.30
Lymphoid lesion	50	30.30
Neurogenic tumors	13	7.88
Mesenchymal lesion	8 37	4.84 22.40
Metastatic lesion	32	19.40
Thymic lesion	8	4.84
GCT (n=17)		
Mature teratoma	6	35.29
Seminoma	4	23.53
Choriocarcinoma	4	23.53
Mixed GCT	3	17.65
Lymphoid lesion (n=50)		
CHL	8	16
T-LBL	27	54
Peripheral T- cell lymphoma	1	2
DLBCL	8	16
PMBCL	3	6
SLL	2	4
BCL-Unclassified	1	2
Thymic lesion (n=32)		
Thymoma Type A	2	6.25
Thymoma Type B1	5	15.63
Thymoma Type B2	8	25.00
Thymoma Type B3	2	6.25
Thymoma Type AB	7	21.89
Thymoma mixed type	6 1	18.74 3.12
Thymic carcinoma Micronodular	1	3.12

(GCT- germ cell tumor, CHL- classic Hodgkin's lymphoma, T-LBL- T-lymphoblastic lymphoma, DLBCL-diffuse large B cell lymphoma, PMBCL- Primary mediastinal B cell lymphoma, SLL- small cell lymphocytic lymphoma, BCL- B cell lymphoma)

Histomorphologically, 16% of cases were of CHL and 84% were of Non-Hodgkin's Lymphoma (NHL).

Thymic lesion

Thirty-two cases were of thymic origin and all were located in the prevascular compartment. The mean age was 53.5± (14.49) years with a range of 24 to 79 years. It shows male preponderance with M: F ratio 2.2:1. Maximum population (78.13%) was >40 years of age. Masaoka- Kaga staging was used. Total 40.63% cases were in stage I followed by stage IIa (37.5%). Stage IIb, IVa and IVb had two cases each while stage III had a single case.

Germ cell tumor

A total of 17 cases were of GCT, all were male and located in prevascular mediastinum. The mean age was 26 (±14.97) years with range of 1 to 65 years. A total of 52.94% of cases were between 20-30 years of age group. Mixed GCT includes immature teratoma with yolk sac tumor and seminoma with teratoma two cases each.

Neurogenic tumor

Out of 13, 7 were male and 6 females. All were located in paravertebral mediastinum. The majority cases (53.85%) were below 35 years of age. Out of 5 Ganglioneuroblastoma/neuroblastoma (GNB/NB) cases, 4 were < 20 years of age. Histomorpholigically, GNB/NB (5/13) was most common followed by malignant peripheral nerve sheath tumor (MPNST) (3/13) cases. Neurofibroma and schwannoma had 2 cases each and one case had ganglioneuroma.

Mesenchymal lesions

Of the total 8 cases, 6 were male and 2 females. Total 62.5% of cases were more than 30 years of age. Most cases (87.5%) were located in paravertebral locations while 12.5% were in prevascular compartment. Histomorphological monophasic synovial sarcoma (SS) (3/8) and Ewing's sarcoma/PNET (3/8) were the most common followed by epithelioid sarcoma (1/8) and Solitary fibrous tumor (SFT) (1/8).

Metastatic lesion

Metastatic tumor was the second most (22.42%) frequently seen lesion in mediastinum. It affects the most commonly prevascular compartment (91.89%) followed by visceral (5.41%) and paravertebral (2.70%). The mean age was 54.46 (±55) years with range of 17-75 years, of these, 91.89% of cases had ≥40 years of age. Adenocarcinoma (19/37) was the most common morphology followed by small cell carcinoma (SMCC) (12/37). Other include two cases of squamous cell carcinoma (SCC) and single case of choriocarcinoma, non-small cell lung carcinoma, NOS and poorly differentiated tumor. Lung (26/37) was the most common site of origin followed by breast (4/37). Another site includes colon, esophagous, gastrointestinal tract, ovary, pancreas, prostate, and testis. IHC panel used were AE1/AE3, CK7, CK20, p63 (SCC), Napsin A and TTF1 (lung), PAX8 and WT1 (Ovary), CDX2 (colon), GATA3 (Breast), PSA (prostate), B-hCG (choriocarcinoma).

Table 2: Detailed immunohistochemical profile and differentials

Tumor	Immunohistochemistry	Differential Diagnosis
Lymphoma		
CHL	PAX 5 Weak+*, CD45-*, CD3+/-, CD20-, CD15+*, CD30+*, MUM1+	Thymoma, PMBL
B-NHL	PAX 5+, CD3- , CD20+, CD15-, CD30-, CD2-, CD79A+, AE1/AE3-	CHL, Thymoma type B1, seminoma, T-LBL
T-NHL	PAX 5+, CD3+, CD20-, CD15, CD30-, CD99+, CD2+, TDT+, desmin-, AE1/AE3-, SYN-	Thymoma type B1, large B cell lymphoma, NB, RMS, PNET, NEC
Thymic lesion		
Thymoma type A	AE1/AE3+, CK19+/-, p63+, CD20-, CD5-	Thymoma type B3, SFT, Thymic spindle cell carcinoma
Thymoma type B1	AE1/AE3-, EMA-, CD99+#, CD3+#, CD5+#, TdT+#	Thymoma type B2, T-LBL
Thymoma type B2	AE1/AE3+, EMA-, CD20-, CD99+#, TdT+#, CD3+#	Thymoma type B1, Thymoma type AB
Thymoma type B3	AE1/AE3+, EMA+/-, CD20-, CD5-, CD3+#, TdT+#, TTF1-	Thymoma type A, Metastatic carcinoma
Thymic carcinoma	Cd5+, CD117+, p63+, PLAP-, EMA-/+	Metastatic carcinoma, GCT,
GCT		
Seminoma	PLAP+, CD117+, OCT3/4+, AFP+/-, LCA-, HMB45-	Metastatic GCT, Metastatic melanoma, DLBCL, CHL
Choriocarcinoma	PLAP+, EMA-/+, AE1/AE3+, B-hCG+	Metastatic carcinoma
Neurogenic lesion		
Ganglioneuroblastoma/ NB	NSE+, SYN+, CgA+, S100+, EMA-, vimentin-, WT-1-, CD99-, CD45-, Desmin-	Lymphoma, SMCC RMS, PNET
Ganglioneuroma	S100+, SYN+, desmin-, CK-, EMA-, WT1-	Neurofibroma, Schwannoma, DSRCT
Schwannoma	S100+, CD34 scattered, SMA-	Leiomyoma, GN
Neurofibroma	S100 weak+, CD34 strong, SOX10+, SMA-	Schwannoma, GN, leiomyoma
MPNST	S100+, EMA-, CD34-, SX10+, SMA-, Desmin-, SMA-	Leiomyosarcoma, RMS, SFT, Schwannoma
PNET	CD99+, SYN-, desmin-, WT1-	RMS, NB, DSRCT
Mesenchymal		
Synovial sarcoma	CK+, TLE1+, FL1-, CK5/6-, myogenin-, Desmin-, S100-SOX10-	Thymoma type A, Spindle cell thymic carcinoma, Cellular schwannoma, SFT, LMS, spindle cell RMS
Solitary fibrous tumor	CD34+, STAT6+, TLE1+/-, S100-, AE1/AE3-, desmin-	Thymoma type A, Spindle cell thymic carcinoma, monophasic SS, Schwannoma

(* in RS cells, # in lymphoid cells, RMS- rhabdomyosarcoma, DSRCT- desmoplastic small round cell tumor, + positive, - negative)

Other rare tumors include paraganglioma, neuroendocrine tumor and benign thyroid lesion two cases each followed by papillary thyroid carcinoma and neuroendocrine carcinoma single case each.

Various differential diagnosis was arising from the clinical and histological approaches. IHC plays the decisive role in confirmation of diagnosis. Detailed IHC and differentials were discussed in table 2.

Discussion

Mediastinal tumors are very rare and an integrated approach is needed to establish the accurate diagnosis. In our study, we found primary mediastinal tumors more frequent than metastatic, which was concordant with other studies.[2,4,9-13] We found 82.2% of cases were arises from prevascular compartment which was similar to the study of Sundaram and Vidhyalakshmi. There was a male predominance in the present study which was comparable with previous studies.[10-13]

In the current study lymphoma was the most common neoplasm with 54% T-LBL which was concordant with other studies.[15-17] PMBCL accounts for 2-3% of all NHL and is the second most common NHL after T cell[18], in our study 6% cases were of PMBL.

All thymic lesion originated from prevascular compartment[3,5,14] which was comparable with our study. Thymic carcinomas are rare malignancies

affecting 30 to 60 years age group with slight male preponderance.[19] In our study single 53 year old case of male thymic carcinoma was noted.

Primary mediastinal GCTs are very rare and account for 10-15% of mediastinal tumors in adults and 19-25% in children.[20,21] GCT most commonly affects the prevascular compartment most common.[22,5] Teratoma was the most common morphology encountered followed by seminoma[20] which was similar to our study.

Primary mediastinal MPNST is rare and the majority arises in the posterior mediastinum[23] all three cases in our study were located in posterior compartment. PNET is uncommon. It most frequently affects children and young adults.[24] we also found similar findings

Primary soft tissue tumor is unusual in mediastinum and comprising of <10% of mediastinal tumor,[25] which support our study. The histopathological spectrum of sarcoma is broad and includes pleomorphic tumors (liposarcoma, leiomyosarcoma and RMS) and monophasic spindle cell pattern (monophasic SS, sarcomatoid/spindle cell carcinoma, sarcomatoid malignant mesothelioma, solitary fibrous tumor, MPNST and fibrosarcoma).[26,27] Broad spectrum of tumors arises from the mediastinum. Definite histological diagnosis on biopsy material has several challenges. IHC overcome this limitation and plays a pivotal role in supplementing histology for clinching the diagnosis.

Conclusion

Large number of tumors arise from the mediastinum and knowledge of it is utmost necessary for diagnosis and management. The present study enumerates the histomorphological spectrum of mediastinal tumors. Definitive diagnosis requires collaborated approach of clinicoradiology, histopathology and immunohistochemistry(IHC) findings.

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