HISTOMORPHOLOGICAL ANALYSIS OF MIXED BAG OF MEDIASTINAL LESIONS IN A TERTIARY CARE CENTRE

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ABSTRACT

BACKGROUND

Mediastinum is a Pandora's box consisting of variety of non-neoplastic and neoplastic lesions, which present as masses.

Aims and Objectives- The purpose of this study is to emphasise the role of CT-guided Tru-Cut biopsy in early diagnosis of mediastinal lesions.

MATERIALS AND METHODS

This was a retrospective descriptive study of the histopathological spectrum of the primary mediastinal lesions in a tertiary care hospital between January 2011 and May 2015. Relevant clinical and radiological details were obtained for each case. Histological examination of the true-cut biopsies and resected specimens was carried out followed by immunohistochemistry for confirmation whenever necessary.

RESULTS

Of the 32 cases included in the present study, nineteen cases showed lesions in the anterior, five in the posterior and eight in the middle mediastinum. Most of these patients were in the 2nd decade of life with male preponderance. All these mediastinal lesions were categorised into benign (46.9%), malignant (43.75%) and inflammatory (9.37%), of which the most common malignant lesion was lymphoma (37.5%) followed by thymoma (28.13%) and germ cell tumour (6.25%). Tuberculosis (6.25%) was the commonest inflammatory lesion. The most common lymphoma was nodular sclerosis Hodgkin lymphoma (58.33%) and among the thymomas, it was type AB thymoma (44.44%). Thymic tuberculosis, extragonadal thymic germinoma and mediastinal immature teratoma with vascular proliferation were the rare lesions included in this study. The sensitivity and specificity of this study were 72.72% and 75% respectively.

CONCLUSION

The CT-guided Tru-Cut biopsy is an early diagnostic tool in the evaluation of various mediastinal lesions.

KEYWORDS

Primary Mediastinal Tumours, Thymic Mass, Mediastinal Lymphoma, Thymoma, Thymic Germinoma, Thymic Tuberculosis, Tru-Cut Biopsy of Mediastinal Lesions.

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BACKGROUND

The mediastinum is a Pandora's box which occupies the thoracic cavity between the pleural cavities with the lungs laterally, sternum anteriorly, the vertebral column posteriorly and from the thoracic inlet down to the diaphragm.⁽¹⁾ It has been divided into four compartments, i.e. superior, anterior, middle and posterior. It is a site affected by a wide variety of pathological processes including non-neoplastic and neoplastic lesions, benign and malignant, primary and metastatic, many of which present as mediastinal masses. Anterior mediastinal tumours account for 50% of all mediastinal masses including thymoma, teratoma and lymphoma.⁽²⁾

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Aims and Objectives

1. The purpose of this study was to evaluate our institutional experience of histological spectrum of primary mediastinal lesions.
2. To emphasise the role of CT-guided Tru-Cut biopsy in early diagnosis of mediastinal lesions.

MATERIALS AND METHODS

This was a retrospective descriptive study of 32 patients, who had undergone tru-cut biopsy, resection and both for mediastinal lesions from January 2011 to May 2015 in a tertiary care hospital. Tissue was fixed in 10% buffered formalin and processed by paraffin embedding. The histopathology sections obtained were stained with routine Haematoxylin and Eosin stains. Immunohistochemical (IHC) panel of lymphoma and neuroendocrine tumours were applied for confirmation in some cases. Relevant clinical information that included age and gender of the patients and compartment location of the lesions was recorded for all cases.

RESULTS

A total of 32 cases of mediastinal masses, confirmed by CT imaging included 14 tru-cut biopsies, 7 resected specimens and 11 both tru-cut and resection specimens (Figure 1). The age range affected by the mediastinal tumours were 2 months to 77 years of age (mean age of 36.5 years). The male-to-female ratio was 7:3. Anterior mediastinal lesions were more common (Figure 2). The commonest mediastinal neoplasms were lymphoma (37.5%) followed by thymoma (28.13%) and germ cell tumours (6.25%). Thymic tuberculosis (6.25%) was a common inflammatory lesion. Other cases included in the study are listed in Table 1.

Among the mediastinal lymphomas, Hodgkin Lymphoma (HL) exclusively including Nodular Sclerosis HL (NSHL) constituted about 58.33% cases, whereas Non-Hodgkin Lymphoma (NHL) accounted to only about 44.67% cases (Table 2) including Precursor T-cell Lymphoblastic lymphoma (pre-T LBL) and diffuse large B-cell lymphoma (DLBCL). NSHL showed male preponderance. Age group ranged from 15 - 29 years with a mean age of 22 years. Histopathology sections of these lymph nodes showed lacunar cells and diagnostic Reed Sternberg (RS) cells with extensive area of sclerosis. IHC performed in 5 cases showed Golgi and membranous positivity for CD15 and CD30, which confirmed the diagnosis (Figure 3).

One of the cases of pre-T LBL was observed in a 17-year-old male where the lymph node architecture was completely replaced by large neoplastic cells with high N: C ratio, convoluted nuclei with membrane folding, delicate chromatin, small nucleoli and scant cytoplasm with the starry sky pattern, diffuse and single file pattern of perinodal infiltration along with high mitotic rate. IHC markers such as CD3, CD99 and TDT positivity confirmed the diagnosis of pre-T LBL. Another case of Pre-LBL was morphologically confused with B1 thymoma, but was finally confirmed by negativity of cytokeratin.

Among the older age group DLBCL was more common (16.67%) and showed diffuse sheets lymphoma cells had large non-cleaved with round-to-oval vesicular to hyperchromatic nuclei, small nucleoli and scant cytoplasm. IHC markers done for the confirmation of non-germinal centre DLBCL were positive for CD20, MUM-1, BCL-6 and negative for CD10.

According to WHO classification of thymomas, 2 cases of type A, 4 cases of type AB, 2 cases of type B1 and one case of type B2-B3 thymoma were noted. One out of these cases showed transcapsular invasion and other with mediastinal fat and pericardium (Figure 4).

A 72 years female with an anterior mediastinal mass morphologically displayed organoid clusters, ribbons, festoons and sheets of polygonal tumour cells having pleomorphic oval nuclei, fine chromatin indistinct nucleoli and eosinophilic granular cytoplasm. The differential diagnosis of thymic paraganglioma and metastatic carcinoma from the lung were ruled out by the positivity for CK7 and negativity for TTF-1 respectively. Hence, diagnosis of thymic atypical carcinoid was considered with the positivity for synaptophysin and chromogranin along with CK7 positivity (Figure 5).

Two cases (6.45%) constituted germ cell tumours, which included one case of primary thymic germinoma and immature teratoma each respectively. The extragonadal

thymic germinoma was noted in the middle mediastinum of a 23-year-old female without any ovarian pathology and normal levels of serum AFP, B-hCG. It had microscopic picture of seminoma and was confirmed by the positivity of epithelial marker CD117 and negativity for CK7. Another case was of immature cystic teratoma in a 5-year-old baby, which showed vascular proliferation with endothelial cells within the glial tissue (Figure 6).

There was a case of 14-year-old female who presented with cough, right-sided neck swelling and matted cervical lymph nodes. The FNAC of the enlarged lymph node confirmed the diagnosis of tuberculosis and was treated with antitubercular drugs. But after 5 months when she presented with breathlessness, a chest x-ray showed a mediastinal mass. This lesion was excised and microscopic examination revealed the thymic tissue with Hassall's corpuscles and large foci of tuberculosis with dispersed foci of dystrophic calcification, haemorrhage surrounded by reactive lymphoid tissue (Figure 7).

Diagnosis	0-9	10-19	20-29	30-39	40-49	50-59	60-69	70-79	Total
Thymoma			1			5	2	1	9
Lymphoma	1	2	5	1		2	1		12
Tuberculosis		1					1		2
Inflammatory myofibroblastic tumour			1						1
Calcifying fibrous pseudotumour				1					1
Germ cell tumour	1		1						2
Infected pericardial cyst	1								1
Lipoma			1						1
Lymphangioma				1					1
Thymic atypical carcinoid								1	1
Schwannoma					1				1
Total	3	3	9	3	2	7	4	1	32

Table 1. Distribution of Various Types of Mediastinal Lesions as per Age

Type of Lymphoma	No. of Cases (%)
Nodular Sclerosis Hodgkin Lymphoma	7 (58.33%)
Precursor T-cell lymphoblastic lymphoma	3 (25.0%)
Diffuse large B-cell lymphoma	2 (16.67%)

Table 2. Incidence of Various Types of Lymphomas in the Mediastinum

Study	Present Study	Karki et al ³	Dubashi et al ⁴	Bhageri et al ⁵
Anterior mediastinum	59	70.3	93.6	69.5
Middle mediastinum	25	3.8	0	10.5
Posterior mediastinum	16	25.9	6.4	20

Table 3. Comparison of Distribution of Mediastinal Lesions in Various Studies according to Location

Study	Present Study	Sharma et al ¹	Karki et al ³	Aroor et al ⁴	Aggarwal et al ⁵
Benign	40.7%	73.33%	66.6%	68.57%	34.5%
Malignant	45.15%	26.67%	26%	31.43%	27.6%

Table 4. Comparison of Distribution of Malignant and Benign Lesions in various Studies

Study	Temes et al ⁶ (1999)	Shrivastava, et al ⁷ (2006)	Dubashi, et al ⁸ (2009)	Present Study (2017)
Lymphoma (%)	55	29	30.6	38.7
HL (%)	18	24	6.5	58.33
NHL (%)	37	5	24.1	41.67

Table 5. Comparison of Distribution of various Types of Lymphomas in the Mediastinum

Study	Present Study	Karki et al ³	Dubashi et al ⁸	Baram et al ⁹	Shamsuddin et al ¹⁰
Thymoma	29.3%	80%	30.76	28.57%	22.7%
Age Group (years)	50-69	40-59	36-64	48-75	22 -65

Table 6. Incidence of Thymoma in various Age Groups

Diagnosis

Figure 1. Type of Specimen

Figure 2. Incidence of Mediastinal Lesion according to i) Location, ii) Age, iii) Gender and iv) Type of Lesion

Figure 3. NSHL- A: Neoplastic RS Cells and Mitotic Figure within Lacunar Cell (H and E x1000). B: Increased Bands of Sclerosis around the Nodules (Masson Trichrome x40). IHC Markers- C, D: CD15 and CD45- Positive in RS Cells

Figure 4. Thymoma (B2, B3)- A: Thymectomy Specimen m/s 8 x 6 x 2.8 cm with Grey-Brown Tumour Separated into Nodules by g/w Fibrous Septae. B: Pericapsular Infiltration of the Tumour into the Mediastinal Fat (Modified Masaoka Stage III) C: Neoplastic Tumour Cells are Polygonal in morphology having Open Nuclear Chromatic and Prominent Nucleoli admixed with few Nuclei having coarse Chromatin and scant Cytoplasm. D: PAS positive Proteinaceous Material in the Perivascular Space and Lymphocytic Infiltrate are Noted

Figure 5. Thymic Atypical Carcinoid. A: Neoplastic Polygonal Tumour Cells with Pleomorphic Nuclei and Eosinophilic Granular Cytoplasm arranged in Organoid Clusters and Sheets. IHC- B, C: Chromogranin and TTF-1-negative in Tumour Cells. D, E: CK7 and Synaptophysin-positive in Tumour Cells

Figure 6. Immature Teratoma m/s 16 x 12 x 6.5 cm weighing 550 gms. A: Cut Surface- variegated with Solid and Cystic Areas. B: Mature Endodermal Elements like Mucinous Glands and Respiratory Epithelium. C: Proliferating Capillaries within the Glial Tissue. D: Immature Neuroectoderm forming Rosettes and Tubules

Figure 7. Thymic Tuberculosis. A. Thymectomy Specimen m/s 9 x 3.5 x 1.5 cm, Cut Surface shows Cystic Spaces Rimmed by Fibrous Capsule and containing Whitish Granular Material. B. Thymic Tissue showing Extensive Fibrosis, Necrosis, Studded with Caseating and Non-Caseating Granulomas (H and E x100) with Langhans' Giant Cell (Inset)

DISCUSSION

Primary mediastinal tumours are uncommon and represent about 3% of the tumours within the chest wall. Most of the tumours were anterior mediastinal masses as in the present study and other studies (Table 3).^{3,8,11} According to Aroor et al and Aggarwal et al, these lesions were mainly noted in the third decade.^{4,5} Whereas most of the cases were in the sixth decade in the present study. Male preponderance was noted in all the cases including the present study. Benign lesions were higher in number in all the studies (Table 4).^{1,3,4,5}

In the present series, lymphomas formed the predominant group constituting 37.5% of mediastinal lesions followed by thymoma (28.13%), which was comparable with the other studies (Table 5) (Table 6).

Zubair et al described an incidence of 32% mediastinal involvement by NSHL.¹² In the present study the incidence of NSHL was 58.33% (Table 2), which was confirmed by IHC. Mediastinal involvement was noted in 3 cases of pre-LBL, which was in concordance with the study by Nathwani et al¹³ and positivity for IHC markers like CD99 and TDT confirmed

the diagnosis in the present study as well as the study by Maitra et al.¹⁴

According to Dasgupta et al, thymoma was more common between the age group of 30 to 56 years.¹⁵ The present study showed a wide range of age of its incidence between 25 to 75 years. The most common variant of thymoma was AB subtype followed by B1 subtype in the present series and study by Sharma et al.¹ The lymphocyte rich thymoma (B1 subtype) could be misdiagnosed as lymphoma.¹⁶ Similarly, in the present study we encountered diagnostic dilemma in the diagnosis of one of the cases of B1 subtype, because of lymphoid rich background. Later, it was confirmed by subsequent biopsy. Thymomas though indolent their behaviour cannot be predicted based on its histology, because it may invade locally and give rise to implants or metastasise.^{17,18} Masaoka system of staging has been widely used as it takes into account the local extension of the tumour.² In the present study one case of type A and type B2-B3 each presented with stage IIa and stage III respectively.

Germ cell tumours constituted 6.25% of cases in the present study which was discordant when compared with the observations of Aroor et al and Dasgupta et al.^{1,15} Mature glial tissue with bordered proliferating capillaries is a feature of malignant glial tumour in the brain, but it can be seen in the mature teratoma in the mediastinum.¹⁹ In the present study, a 4-year-old male child presenting with an immature mediastinal teratoma had the combination of mature glial tissue rimmed by proliferating vascular proliferation with adjacent foci of an immature neuroepithelial component.

In the literature, primary mediastinal seminoma was first described by Woolner et al.²⁰ Chan et al had first reported a primary thymic seminoma in a 32-year-old female.²¹ According to Iczkowski et al, CD117 (C-kit) was equivalently superior to PLAP in the diagnosis of extragonadal germ cell tumour (especially seminoma).²² Thus, in the present study with the normal levels of serum AFP and B-hCG, the CD117 positive extragonadal germinoma was proved to be of thymic origin because of the negativity for CK.²¹

In the literature, only few case reports have been mentioned about the thymic tuberculosis.²³⁻³⁷ In the present study, we had thymic tuberculosis in a 10-year-old seronegative female child.

Pericardial cysts are the congenital cysts formed due to the failure of one of multiple disconnected lacunae to merge with others. These are more common in third or fourth decade of life.³⁸ In the present study, we had an infected pericardial cyst in a 10-month-old male baby.

The present study has 75% specificity and 72.7% sensitivity, which is comparable with the study by Aggarwal et al.

CONCLUSION

Mediastinum is a complex anatomic area playing host to a wide range of neoplastic and non-neoplastic lesions. The most common malignant tumour was lymphoma and benign tumour was thymoma with Tru-Cut biopsy being diagnostic in most of the cases. This study emphasises the role of CT-guided Tru-Cut biopsy in early exact diagnosis of mediastinal lesions with adequate sampling and least risk surgical complications. It is also a strong determinant for the treatment options ranging from medication and surgery to irradiation and chemotherapy.

The availability of small amount of data regarding the mediastinal lesions, the present study highlights the rarity yet diversity in morphology of these lesions.

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