Thymus
&
Other Mediastinal Tumors

→ mediastinum Anatomy ITMIG classification
(International Thymic malignancy Interest Group)

Compartment	Boundaries	Major Contents	Tumors
Prevascular Anterior mediastinum	Superior: thoracic inlet Inferior: diaphragm Anterior: sternum Lateral: parietal mediastinal pleura Posterior: anterior aspect of the pericardium as it wraps around the heart in a curvilinear fashion	Thymus Fat Lymph nodes Left brachiocephalic vein	· Thymic lesions · Germ cell tumors · Lymphoma · metastasis · Intrathoracic goiter · Parathyroid adenoma.
Visceral middle mediastinum	Superior: thoracic inlet Inferior: diaphragm Anterior: posterior boundaries of the prevascular compartment Posterior: vertical line connecting a point on each thoracic vertebral body 1 cm posterior to its anterior margin	Nonvascular: trachea, carina, esophagus, lymph nodes Vascular: heart, ascending thoracic aorta, aortic arch, descending thoracic aorta, superior vena cava, intrapericardial pulmonary arteries, thoracic duct	· Lymphoma · mets · Duplication cyst · Tracheal · esophageal · vascular lesions.
Paravertebral Posterior mediastinum	Superior: thoracic inlet Inferior: diaphragm Anterior: posterior boundaries of the visceral compartment Posterolateral: vertical line against the posterior margin of the chest wall at the lateral margin of the transverse process of the thoracic spine	Thoracic spine Paravertebral soft tissues	· Neurogenic tumors from dorsal root ganglia. · Infections, TB · Traumatic lesions (Hematoma) · Extramedullary hematopoiesis

→ Thymic lesions DD:

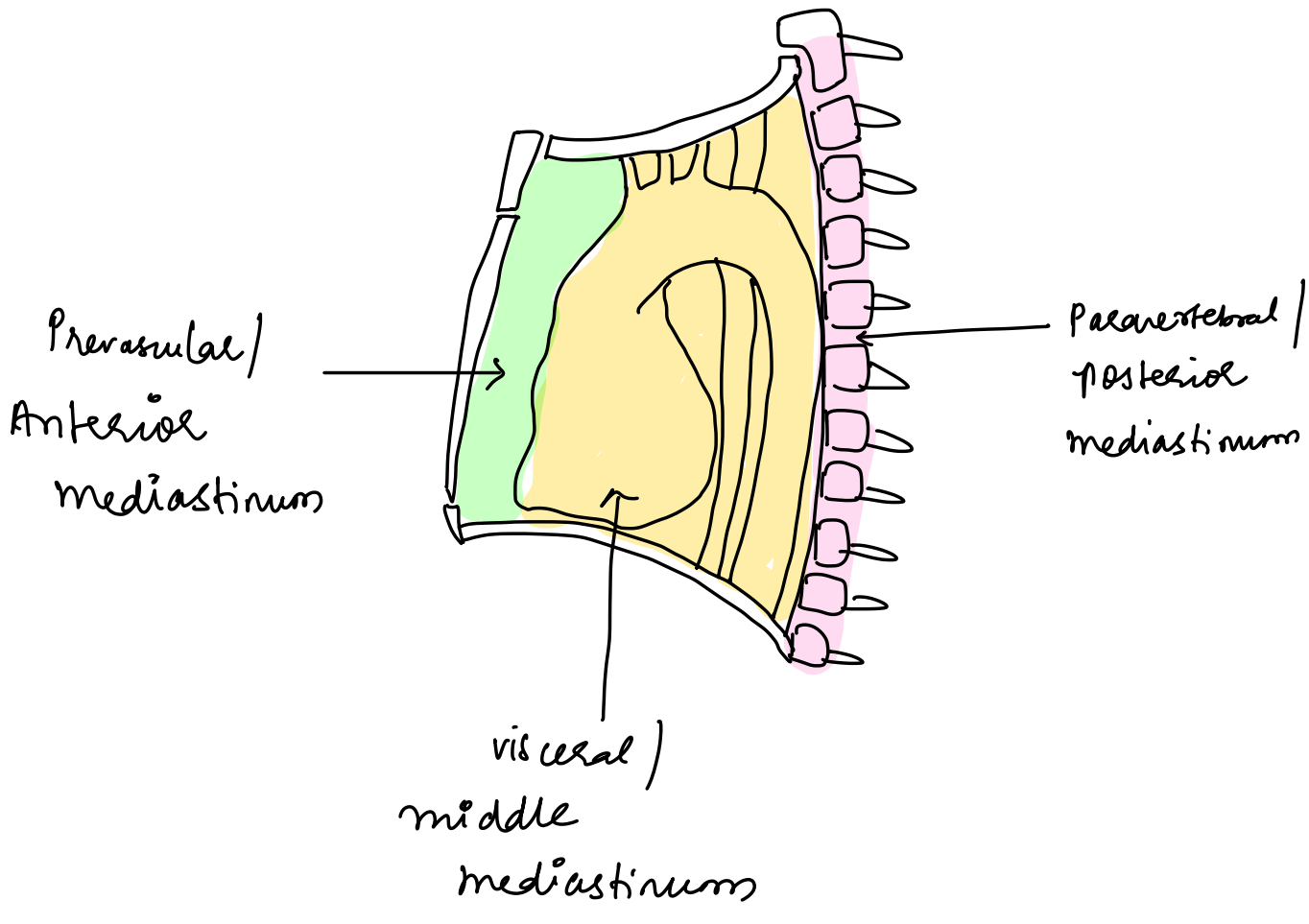
- Thymic cyst
- Hyperplasia
- Thymoma
- Thymic carcinoma
- NET

— Thymic epithelial tumors

- Thymolipoma — Thymic mesenchymal tumors

mesenchymal tumors can occur in all 3 compartments

- lipoma / liposarcoma
- fibroma / Fibrosarcoma



→ Thymic epithelial Tumors (TET)

→ clinical presentation & diagnosis :

- mc asymptomatic - incidental findings
- symptomatic → d/t mass effect
  - cough, stridor
  - Hoarseness of voice
  - SVC syndrome
  - dysphagia
  - Horner's syndrome
  - Cardiac tamponade
  - d/t systemic effects
    - B symptoms of lymphoma
    - Paraneoplastic syndromes

- Paraneoplastic syndromes associated c TET :

★ Autoimmune conditions :

- myasthenia Gravis – mc 50%.
  - Better prognosis w/2 of early detection
  - Remission rate after thymectomy is 7-63%.
  - Anti AchR Antibody
- Hashimoto's
- SLE
- Sjogren's
- Scleroderma
- Ulcerative colitis
- polymyositis
- Rheumatoid arthritis.

★ Hormonal

- Hyperthyroidism
- Hyperparathyroidism
- Hypopituitarism
- Addison disease.

★ Blood disorders :

- Red cell aplasia
- Panytopenia
- Hypogammaglobulinemia
- pernicious Anemia.

★ Neuromuscular disorders

- myositis
- Eaton - Lambert syndrome
- myotonic dystrophy.

→ Imaging investigations :

- CECT chest / CT angiography chest – IOC
- FDG WB PET-CT – Assess the activity of the mass, Rule out systemic mets
- Cardiac gated MRI – Compression vs invasion of pericardium/cardiac chambers
- Spine MRI – Rule out intraspinal tumor extension in PMT
- Ga-68 DOTATATE PET/CT scan – Thymic NET
- Technetium scan – Suspicion about ectopic thyroid
- Scrotal ultrasound – mediastinal Germ cell tumor.

TABLE 32.3

Systemic Manifestations of Hormone Production by Mediastinal Neoplasms

Symptoms	Hormone	Tumor
Hypertension	Catecholamines	Pheochromocytoma, chemodectoma, neuroblastoma, ganglioneuroma
Hypercalcemia	Parathyroid hormone	Parathyroid adenoma
Thyrotoxicosis	Thyroxine	Thyroid
Cushing syndrome	ACTH	Carcinoid tumor
Gynecomastia	hCG	Germ cell tumor
Hypoglycemia	IGF-II	Mesenchymal tumors
Diarrhea	VIP	Ganglioneuroma, neuroblastoma, neurofibroma

ACTH, adrenocorticotropic hormone; hCG, human chorionic gonadotropin; VIP, vasoactive intestinal polypeptide; IGF-II, insulin-like growth factor type II.

→ Role of tissue diagnosis in mediastinal tumors:

- Anterior mediastinal mass + clinically symptomatic myasthenia gravis → thymoma unless proven otherwise → no need for prep biopsy.

- Rest all lesions mandate preop tissue diagnosis.

- Bx preferred one FNA (60%) (77%)

- core biopsy method
  - CT/USG guided - mc
  - EBUS - in para tracheal lesions
  - Endoscopic / EUS
  - Surgical Bx
    - Anterior mediastinotomy - chamberlain procedure
    - cervical mediastinoscopy
    - VATS.

→ WHO classification of thymic tumors:

TABLE 32.1

World Health Organization Classification System for Thymic Epithelial Tumors

Thymoma Subtype	Obligatory Criteria (Thymoma)	Optional Criteria (Thymoma)
Type A	Occurrence of bland, spindle-shaped epithelial cells (at least focally); paucity[a] or absence of immature (TdT^+) T cells throughout the tumor	Polygonal epithelial cells $CD20^+$ epithelial cells
Atypical type A variant	Criteria of type A thymoma; in addition: comedo-type tumor necrosis, increased mitotic count (>4/2 mm^2), nuclear crowding	Polygonal epithelial cells $CD20^+$ epithelial cells
Type AB	Occurrence of bland, spindle-shaped epithelial cells (at least focally); abundance[a] of immature (TdT^+) T cells focally or throughout tumor	Polygonal epithelial cells $CD20^+$ epithelial cells
Type B1	Thymus-like architecture and cytology: abundance of immature T cells, areas of medullary differentiation (medullary islands); paucity of polygonal or dendritic epithelia cells without clustering (i.e., fewer than three contiguous epithelial cells)	Hassall corpuscles; perivascular spaces
Type B2	Increased numbers of single or clustered polygonal or dendritic epithelial cells intermingled with abundant immature T cells	Medullary islands; Hassall corpuscles; perivascular spaces
Type B3	Sheets of polygonal slightly to moderately atypical epithelial cells; absent or rare intercellular bridges; paucity or absence of intermingled TdT^+ T cells	Hassall corpuscles; perivascular spaces
Rare others[b]		
Thymic carcinomas	Squamous cell carcinoma; basaloid carcinoma; mucoepidermoid carcinoma; lymphoepithelioma-like carcinoma; clear cell carcinoma; sarcomatoid carcinoma; adenocarcinomas (several); NUT carcinoma; undifferentiated carcinomas; rare others	

→ Staging of thymic tumors:
- Both systems are used.

1. Masaoka-Koga stage system
- 1994.

TABLE 32.4

Thymoma Staging System According to Masaoka-Koga

Masaoka-Koga Stage	Pathologic Criteria	Five-/Ten-year Survival (%)
I	Macroscopically and microscopically completely encapsulated tumor	94/83
IIa	Microscopic transcapsular invasion up to 3 mm into surrounding tissue	93/86
IIb	Macroscopic invasion into thymic or mediastinal fat or grossly adherent to (but not breaking through) mediastinal pleura	
III	Macroscopic invasion into neighboring organs (e.g., pericardium, lung, great vessels)	87/74
IVA	Pleural or pericardial metastasis	63/47
IVB	Lymphogenous or hematogenous metastasis	58/44

2. AJCC 8th edition

TABLE 32.5

Tumor-Node-Metastasis (TNM) Staging System

T Stage	Descriptor
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
T1	Tumor encapsulated or extending into the mediastinal fat or pleura
T1a	Tumor without mediastinal pleural involvement
T1b	Tumor with direct invasion into mediastinal pleura
T2	Tumor with direct invasion into the pericardium (partial or full thickness)
T3	Tumor with direct invasion into lung, brachiocephalic vein, superior vena cava, phrenic nerve, chest wall, and/or extrapericardial pulmonary artery or vein
T4	Tumor with direct invasion into aorta, arch vessels, intrapericardial pulmonary artery, myocardium, trachea, and/or esophagus
N Stage	
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastases
N1	Metastases in perithymic (anterior mediastinal) lymph nodes
N2	Metastases in cervical or deep intrathoracic lymph nodes
M Stage	
M0	No pleural, pericardial, or distant metastases
M1	Pleural, pericardial, and/or distant metastases are present
M1a	Metastatic pleural or pericardial nodule(s)
M1b	Metastatic nodules in pulmonary parenchyma or distant organs
Stage Groupings	
Stage I	T1a-b,N0,M0
Stage II	T2,N0,M0
Stage IIIA	T3,N0,M0
Stage IIIB	T4,N0,M0
Stage IVA	T1-4,N1,M0 or T1-4,N0-1,M1a
Stage IVB	T1-4,N2,M0-1a or T1-4,N0-2,M1b

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THYMOMA

→ Management - Masaoka Koga stage wise :

- Non invasive thymoma (Stage I)
  Invasive but Resectable thymoma (Stage II A)
  → R0 resection.
  Post operative RT in R1/R2 resection.
  No role for adjuvant chemo.

- macroscopic invasive, but Resectable (II B)

↓

R0 resection

↓ WHO typing

A, AB, B1	B2, B3
↓	↓
No adjuvant therapy	PORT

- Stage III - Any WHO type - Sx Hb PORT.

* Role of adjuvant chemo
  - All thymic carcinoma irrespective of stage & resection status.
  - All R2 thymoma.

Thymic carcinoma

- Adjuvant chemo in all stages & resection status
- Adjuvant RT in R1 resection & R0 + stage II a,b, III

Role of Adjuvant RT
- All thymic carcinoma irrespective of stage & resection status.
- R1/R2 stage I, II A
- R0 stage II B type B2 B3
- All Stage III thymoma.

→ Role of neoadjuvant chemotherapy in unresectable tumors @ presentation

↓

Biopsy

↓

Induction chemotherapy - Cisplatin + Doxorubicin + Ifosfamide

- Unresectable → Definitive CT/RT irrespective of histology.
- Resectable → Thymic Carcinoma → Sx Hb CT/RT
- Resectable → Thymoma → R0/R1 → PORT; R2 → CT/RT.

→ Role of lymphadenectomy in thymic tumors

- All suspicious nodes on imaging to be removed irrespective of type
- Anterior nodes to be removed in all tumors
- Deep regional node sampling to be done in thymic carcinoma & NET.

* Rate of LN spread [in thymoma ≤ 2%
  in TC / NET - 20%

→ Extent of Surgery :

Thymectomy vs Thymomectomy
(En bloc resection of adherent structures also)

→ Points against it are
1. development of postop MG in remnant.
2. Local recurrence
3. Non anatomical resection is against oncological principles.
4. Presence of microcapsular invasion.

→ Surgical approach :

Open - Transsternal
Transcervical

MIS - BIL VATS
- unilateral thoracoscopic
- Robotic transthoracic
- Robotic subxiphoid approach.

Thymus is midline structure, can be approached from both sides.

(R) VATS vs (L) VATS

- more space
- easier port placement.
- Better dissection in aorto caval groove.

- Better dissection in AP window
- more pericardial fat.

may be combined with a cervicotomy incision.

→ Germ cell tumors of mediastinum:

- 50-70% of all extragonadal GCT
- mc in men 20-30 years

↓

βHCG, AFP, LDH as gonadal tumors

Teratoma

- mature - benign
- immature - malignant
- mixed.

↓

- Sx for mature teratoma. No role of RT/CT
- Immature teratoma are potentially malignant ∴ varying Prognosis.

Germ cell tumor

Seminoma

↓

- Highly Radiosensitive. But usually large bulky tumors which need large RT fields

↓

Induction chemotherapy PEb ± Supradiaphragmatic RT

↓

Salvage surgical resection only for residual tumors ∴ activity on PET/CT. Otherwise NO role of Sx.

Non Seminoma

- choriocarcinoma
- Embryonal
- Yolk sac tumor

↓

- Poor prognosis
- mostly metastatic @ Presentation.
- cisplatin based chemotherapy.

→ Posterior mediastinal tumors :

- mostly benign
- mostly neurogenic.

Origin	Benign	Malignant
Nerve sheath	Neurilemmoma (Benign Schwannoma)	Neurofibrosarcoma
	Neurofibroma	Malignant Neurofibroma
	Granular Cell tumour	Malignant Schwannoma
Autonomic Ganglia	Ganglioneuroma	Ganglioneuroblastoma
	Chemodactoma	Neuroblastoma
	Pheochromocytoma	

- Indication of MRI
  - when CT shows [tumor close to neural foramen
    widening of neural foramen
    vertebral destruction.
  - CT misses intraspinal extension.
  - Thoracic Dumbell tumor — intrathoracic + intraspinal component
    VATS / thoracotomy + Laminectomy spinal approach.