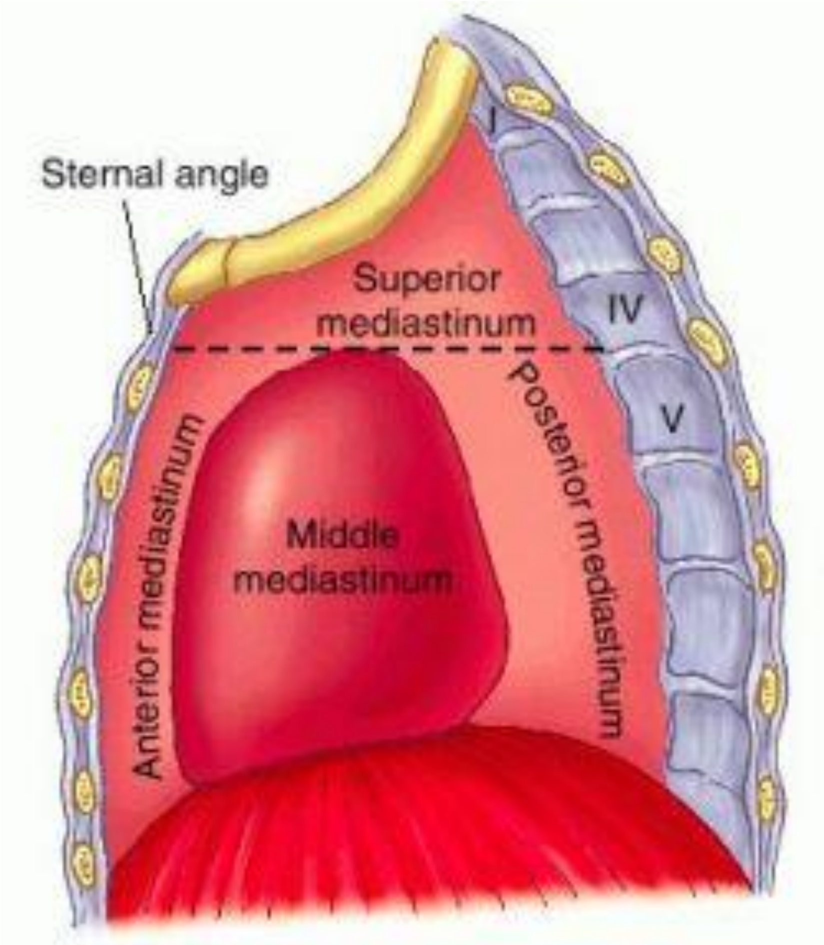
Mediastinal Pathology
A Diagnostic Primer

Dr A Rice
Royal Brompton Hospital
London

What is the mediastinum?

- Superior
  - LN, thyroid, parathyroid
- Anterior
  - Thymus, LN
- Middle
  - Trachea & main bronchi, LN
- Posterior
  - Sympathetic ganglia, paraganglia, LN, oesophagus



Essential information

- **Clinical history**
  - Age, sex
  - Symptoms
  - Past medical history
- **Radiology**
  - SITE (50% mediastinal lesions in anterior compartment)
  - Solid/cystic
  - Solitary/diffuse
- **Organs**
  - Thymus
  - Lymph nodes
  - Ectopic tissues
    - Germ cells
    - Thyroid
    - Parathyroid
  - Soft tissues
  - Oesophagus

Mediastinal lesions – by type

- **Non-neoplastic**
  - Developmental
    - Cysts
    - Tissue in an abnormal location
  - Inflammatory/fibrosing conditions
  - Hyperplasia
    - Thymus
    - Lymph node
- **Neoplastic**
  - Thymic tumours
  - Lymphomas
  - Germ cell tumours
  - Soft tissue tumours (including neural tumours)
  - Oesophageal tumours
  - Metastatic tumours (carcinoma etc)

Mediastinal lesions - by Site

Superior	**Anterior**	**Middle**	**Posterior**
Lymphoid	Thymic	Bronchogenic cyst	Neurogenic tumours
Thymic	Germ cell	Pericardial cyst	Lymphoid
Thyroid	Lymphoid	Lymphoid	Oesophageal
Parathyroid	Thyr/parath		Vascular

Mediastinal lesions - by Pattern

- **Cystic**
  - Primary cystic lesions
  - Cystic reaction to tumours
  - Cystic tumours
- **Inflammatory**
  - Infectious
  - Autoimmune
  - Inflammatory reaction to tumour
- **Sclerotic**
  - Fibroinflammatory lesion
  - Sclerotic reaction to tumour
- **Neoplastic**
  - Epithelioid
  - Sarcomatoid
  - “Small round blue cell”
  - Haematological
  - Germ cell elements
  - Mixed patterns

BEWARE OCCULT MALIGNANCY

Cysts

Cystic lesions

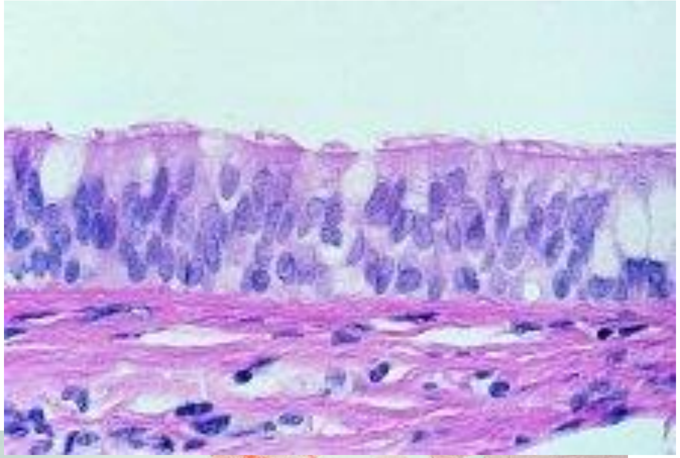
- 10-15% of radiologically detected masses

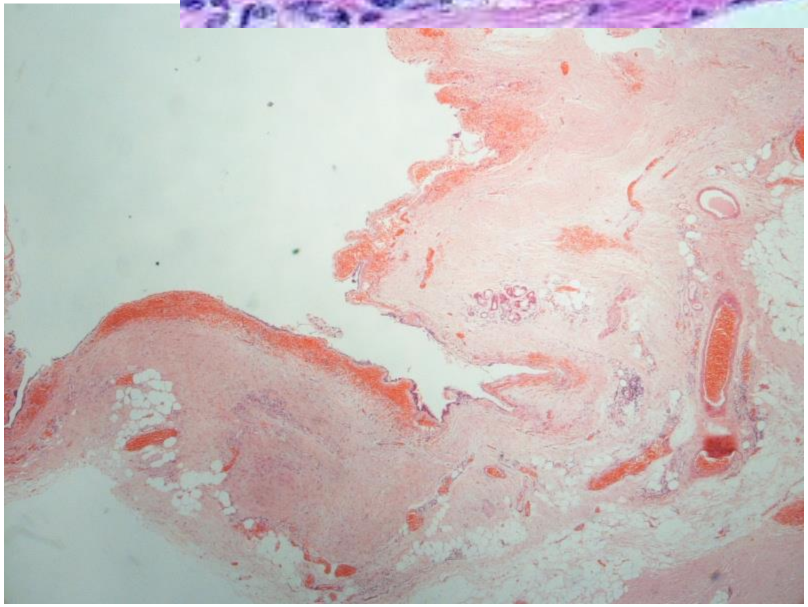
- Bronchogenic
- Thymic
- Pericardial
- Enteric
- Thyroid/Parathyroid
- Vascular

- **DON'T FORGET – SOME NEOPLASMS CAN BE CYSTIC**
  - TERATOMA
  - THYMOMA
  - SEMINOMA
  - VASCULAR

- **SOME BENIGN CYSTS ASSOCIATED WITH NEARBY NEOPLASIA**
  - E.g. HODGKINS LYMPHOMA

Bronchogenic Cyst

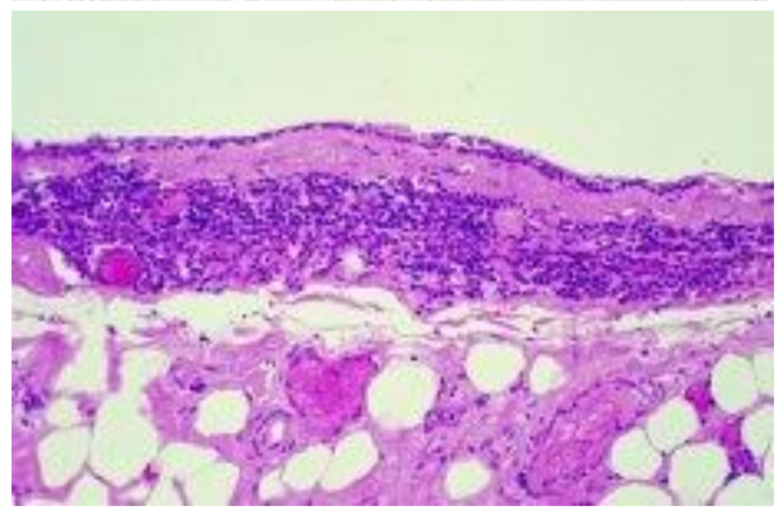




- Wide age range
- Usually posterior to carina but can be intra-pulmonary (the latter often communicating with airways)
- Uni/multilocular, comprising
  - Respiratory epithelium
  - Mature cartilage
  - Smooth muscle
  - May have independent vascular supply
- Tissue is <u>organised</u> compared to teratoma where elements are disorganised and other elements present

Thymic Cysts

- 20-50 yrs
- **<u>Congenital</u>**
  - Unilocular
  - Bland thin squamous epithelium 1-2 cells thick.
- **<u>Post inflammatory</u>**
  - Multilocular
  - Cuboidal, columnar, squamous epithelium which can be hyperplastic or papillary, cholesterol granulomas
- See residual thymus in tissue around cyst.



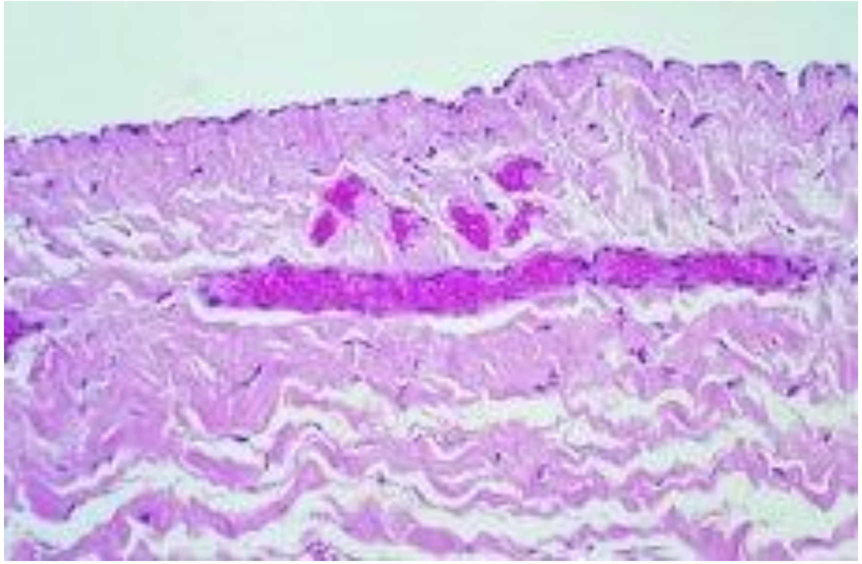
Thymic cysts - pitfalls

- "Proliferating" subtype
  - Squamous proliferation with mitoses, but non-malignant cytology
  - form of PEH, care not to diagnose as malignant transformation (which is Very rare)

- Is there adjacent pathology?
  - Hodgkin's lymphoma
  - Seminoma
  - Cystic thymoma

Pericardial Cyst

- Wide age range and often an incidental finding
- Found at right cardiophrenic angle
- Lined by bland layer of mesothelium which occasional undergoes papillary hyperplasia



Enteric Cysts

- Posterior mediastinum
- Children and adolescents
- Can have co-existant vertebral anomalies (hemivertebra and spina bifida)
- Can be multilocular
  - Double layer smooth muscle
  - Enteric type epithelium (squamous, columnar, mixed)
  - Usually contain at least some specialised gastric glands.
  - NO cartilage

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Other cystic lesions

- **Lymphangiomas/haemangiomas**
- **Thyroid/parathyroid cysts**
- **Mesothelial cysts**
- **Cystic meningocoeles**
  - Posterior mediastinum
  - Paraspinal thin walled cyst which communicates with meninges, ususally through vertebral body defect
  - Lined by arachnoidal cells with variable neural tissue

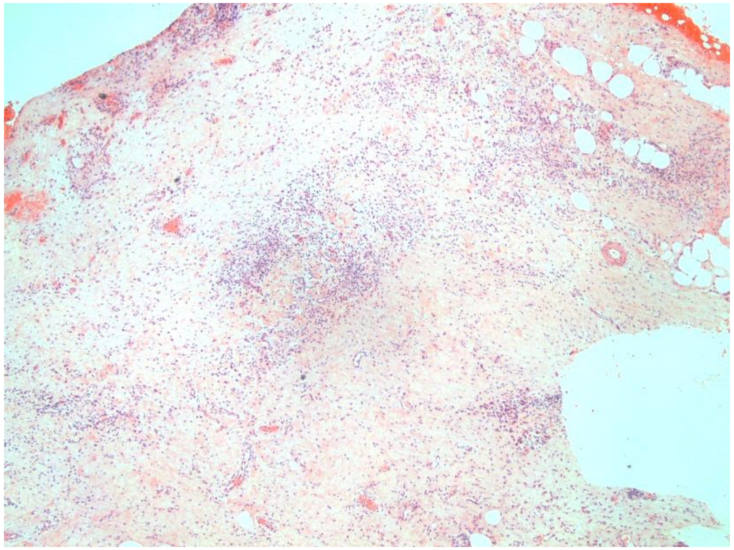
Cysts – Diagnostic pitfalls

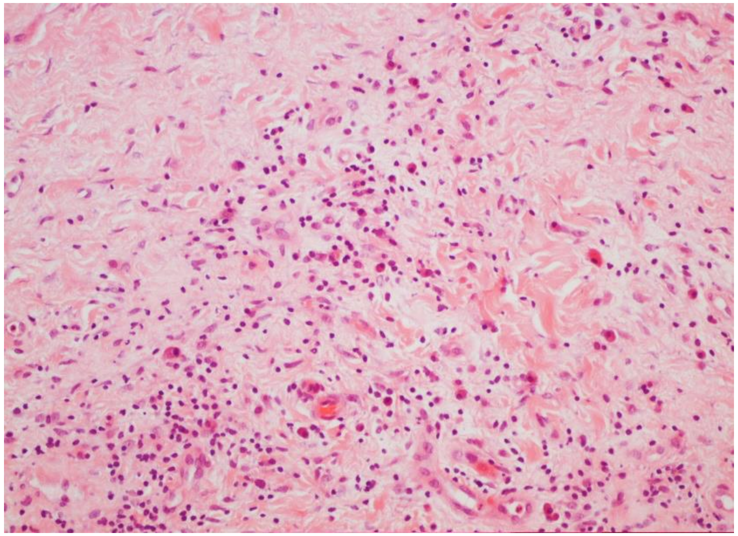
- **Cystic seminoma**
  - Seminoma cells present in cyst wall, but may be infrequent
  - Inflammatory and granulomatous background may obscure cells
- **Cystic teratoma**
  - Mature, immature, somatic malignancy
  - Mistake for bronchogenic or enteric cyst
- **Cystic thymoma**
  - Bland proliferation thymic epithelium in cyst wall

Fibroinflammatory lesions

Fibro-inflammatory lesions

- With any fibro-inflammatory proliferation in mediastinum must consider:
  - Infection
  - Sarcoid
  - Drugs
  - Lymphoma
  - Desmoid type fibromatosis
  - Desmoplastic meso, metastatic ca
  - Idiopathic sclerosing mediastinitis





Clues to differential diagnosis

- Infectious agents
  - Granulomas/histiocytes/necrosis
  - Always do special stains - Histoplasma and other fungi, Nocardia, syphilis, actinomyces
- Sarcoid
  - Sarcoidal granulomas
- Drugs
  - History of methysergide use
- Lymphoma
  - Lymphocyte atypia, RS cells, IHC, molecular studies
- Desmoid type fibromatosis or IMT
  - Morphology
  - beta-catenin
  - Alk-1
- Mesothelioma or carcinoma
  - Cytokeratin stain

Idiopathic sclerosing mediastinitis

Wide age range

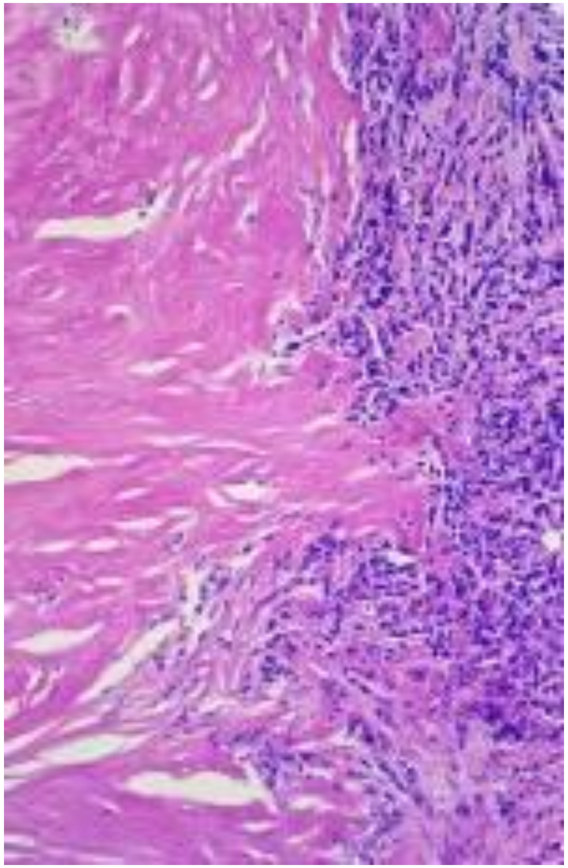
Anterior superior mediastinum

Avascular paucicellular fibrohyaline tissue, lymphocytes (granulomas)

Diagnosis of exclusion

- *Mod Pathol 1999;12:257*

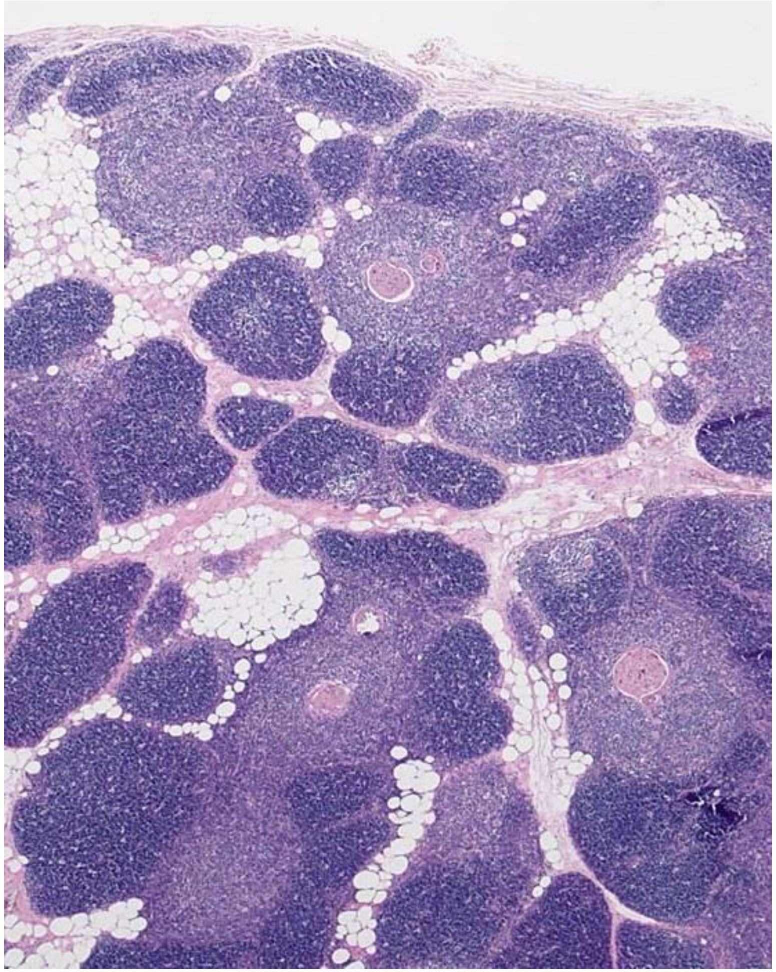
- [IgG4 sclerosing disorders]
  - Autoimmune condition
  - Increased numbers of IgG4 positive plasma cells in tissue and raised serum IgG4 immunoglobulin
  - *World J Gastroenterol* 2008 July 7; 14(25): 3948-3955



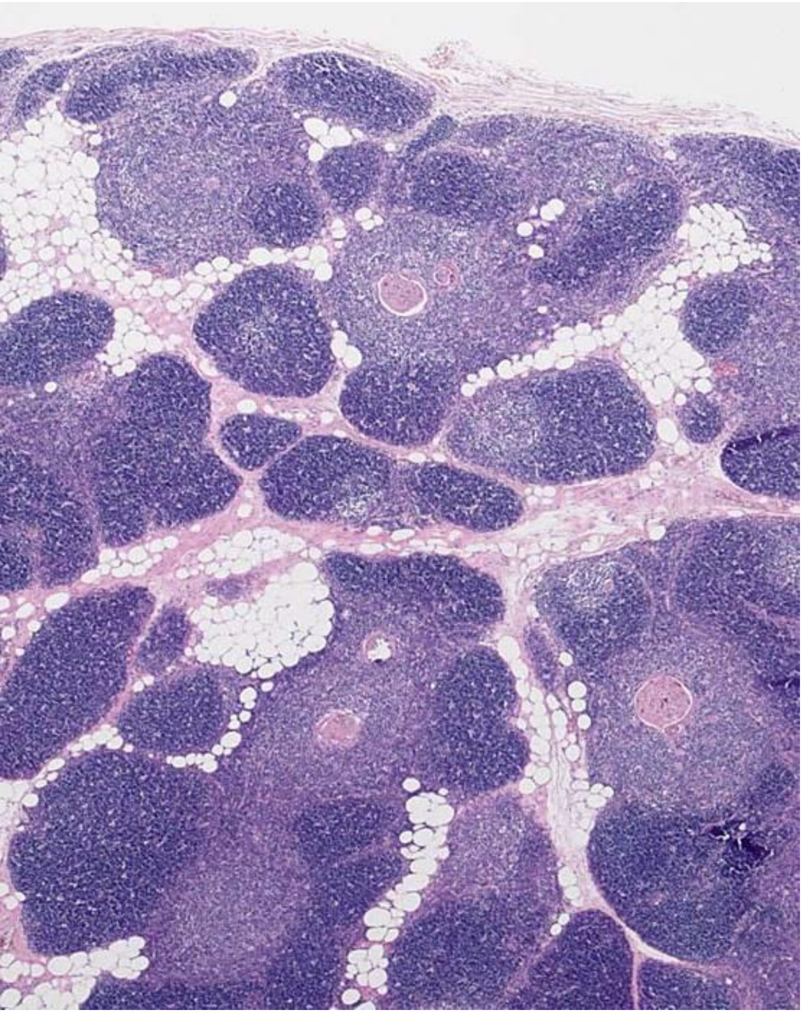
Thymic lesions

Thymus

- Originates from 3rd pharyngeal pouch. Grows until puberty and then involutes
- Responsible for T-cell differentiation
  - Thymic T cells are CD1a and TdT positive
- Located in anterior mediastinum, but thymic tissue can be ectopic (lung, neck, heart)
- Lobulated fat, lymphoid tissue and admixed thymic epithelium (derived from endoderm), organised into cortical and medullary areas
- Ectopic tissue within thymus includes thyroid, parathyroid and germ cells



15gm birth
30-40gm puberty
10-15gm at 60 yrs



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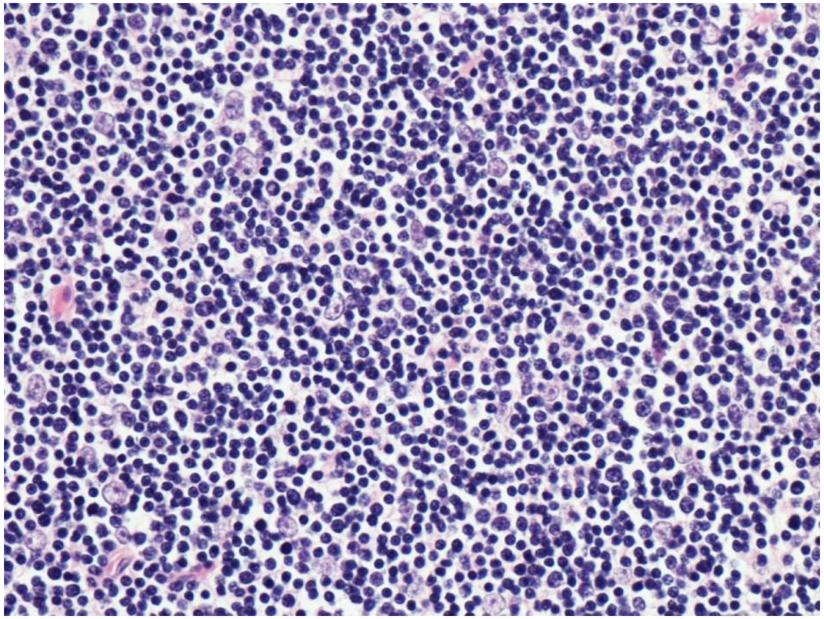
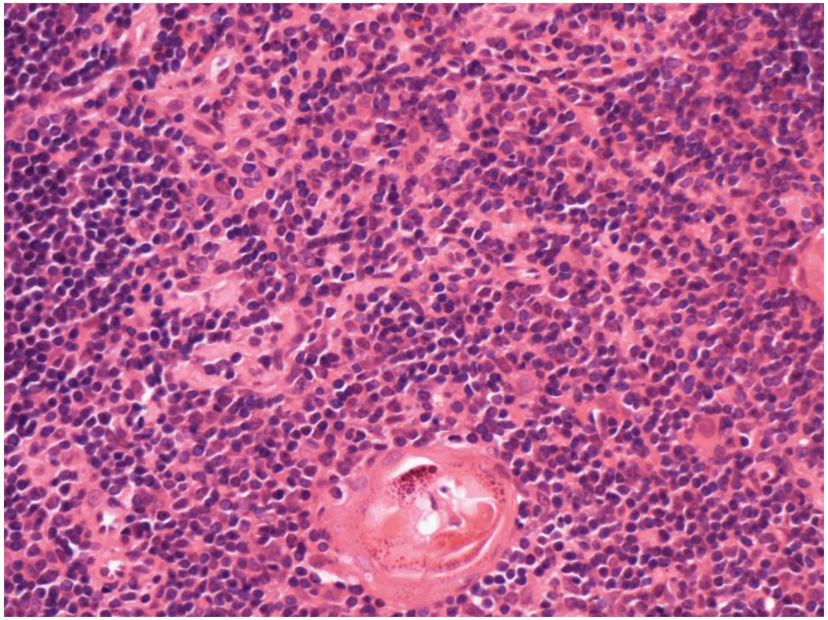




Thymic Lesions

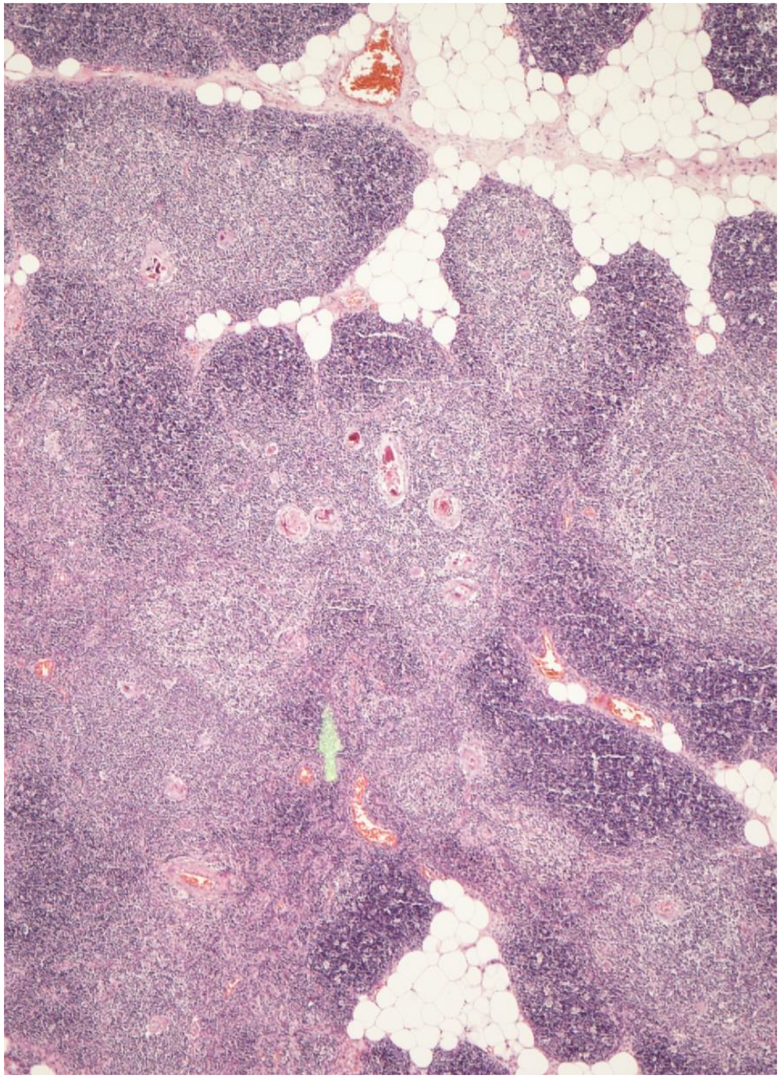
- **Non-neoplastic**
  - Cysts
  - Hyperplasia (inc rebound)
    - True
    - Follicular
  - Acute involution and dysplasia – rarely biopsied

- **Neoplastic**
  - EPITHELIAL: Thymoma, Thymic and neuroendocrine carcinoma
  - GERM CELL
  - HAEMATOLYMPHOID
  - MESENCHYMAL

Thymic Hyperplasia

- **True**
  - Weight increased
  - Infants and post chemotherapy in adults (“rebound” thymic hyperplasia – PET +)
  - Normal histology

- **Lymphoid**
  - Retention normal architecture
  - Marked increase in germinal centres (normal thymus contains occasional germinal centres)
  - Associations with various AI disease, especially MG



Thymomas

- **Rare**: <1% of adult neoplasms
  - 1-5/million population
- **Adults** with wide age range
  - peak 55-65
  - Rare in children/adolescents
- Presentation
  - Asymptomatic : mass on imaging
  - Symptomatic : cough, pain, mass effect, or paraneoplastic syndrome
    - MG most common, but other AI conditions seem
    - Associated with thymoma>>thymic ca
- Neoplasm of thymic epithelium, exhibiting organotypic features
  - Lobular architecture, fibrous septa, perivascular spaces, immature T cells in varying number

Paraneoplastic syndromes associated with thymomas

- Myasthenia gravis most common (AB, B2, B3 types)

- Hypogamaglobulinaemia 12% (type A)
- Red cell aplasia 5% (type A)

- Rarely - Myositis, myocarditis, neuropathies, SLE, myeloma

Handling thymic specimens ITMIG Guidelines

Issues for Surgeons and Pathologists

What is the status of the margins?

– Have they been examined appropriately?

– What really constitutes a surgical margin?

– How do we report out microscopic findings?

If there is a problem, where is it?

– Where on the specimen?

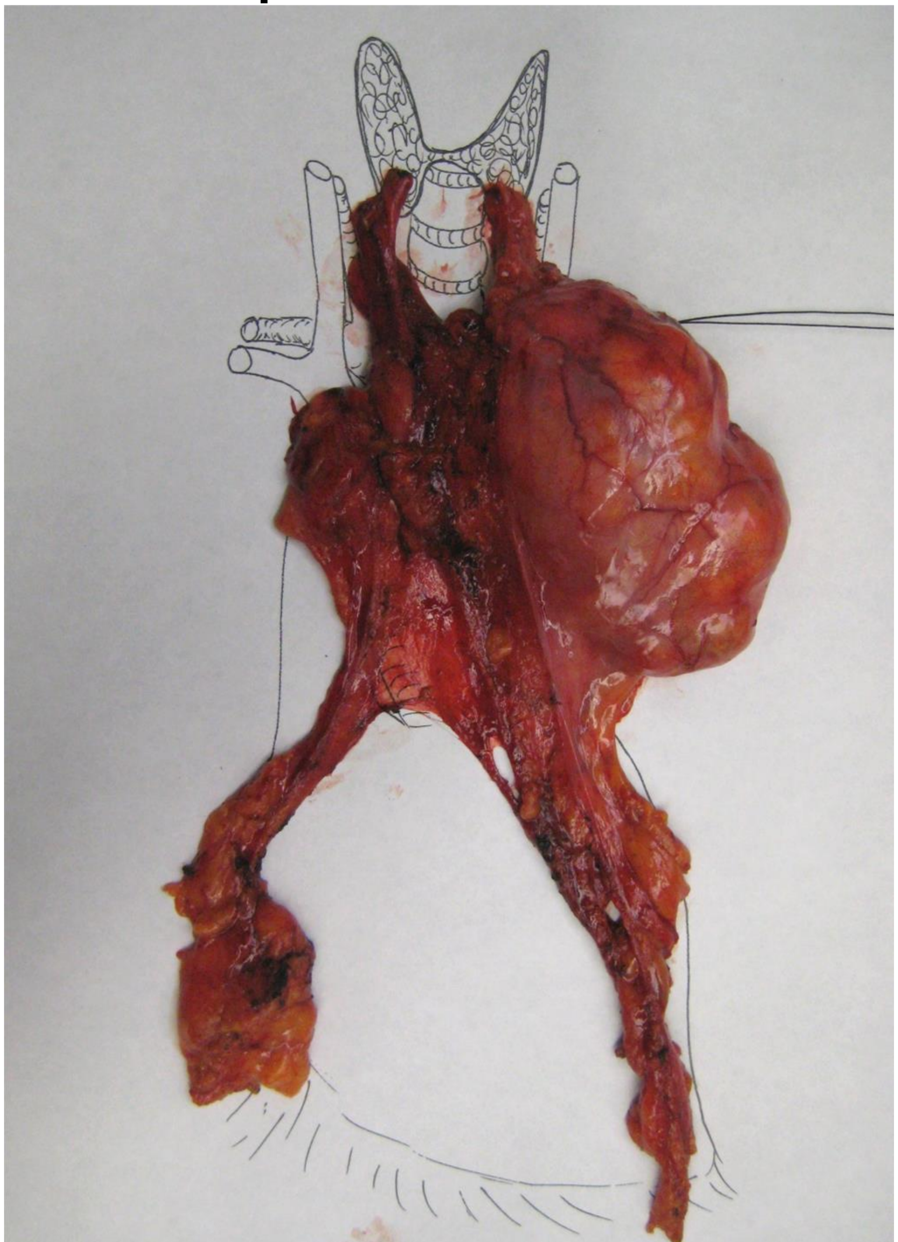
– Where in the patient?

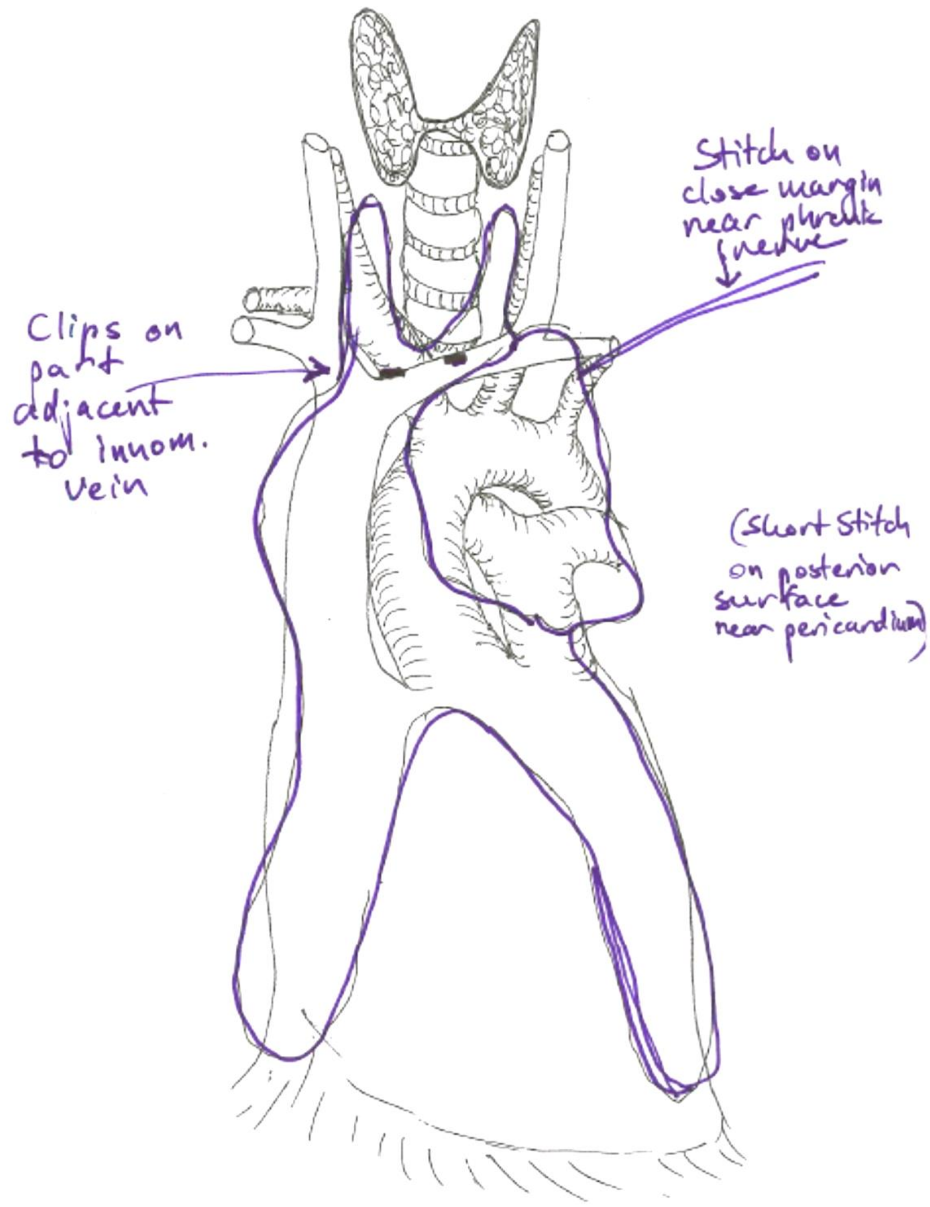
Frozen Section

- A frozen section for diagnosis should be interpreted cautiously, and should be **limited to cases with unexpected features or suspected to not be a thymic malignancy (e.g. lymphoma, germ cell tumor)**. The clinical diagnosis of thymoma is generally at least as reliable as a frozen section diagnosis.

- Frozen section determination of adequacy of margins is difficult (high false negative and false positive rates); the clinical impression should be carefully considered as well as the microscopic impression

Specimen oriented on Mediastinal Board





Specimen Handling

- **Record components**: Weight and total size specimen, tumour size, other tissues present, separate nodules – site, size, etc

- Identify areas of concern prior to sectioning, and areas of tissue disruption occurring during handling

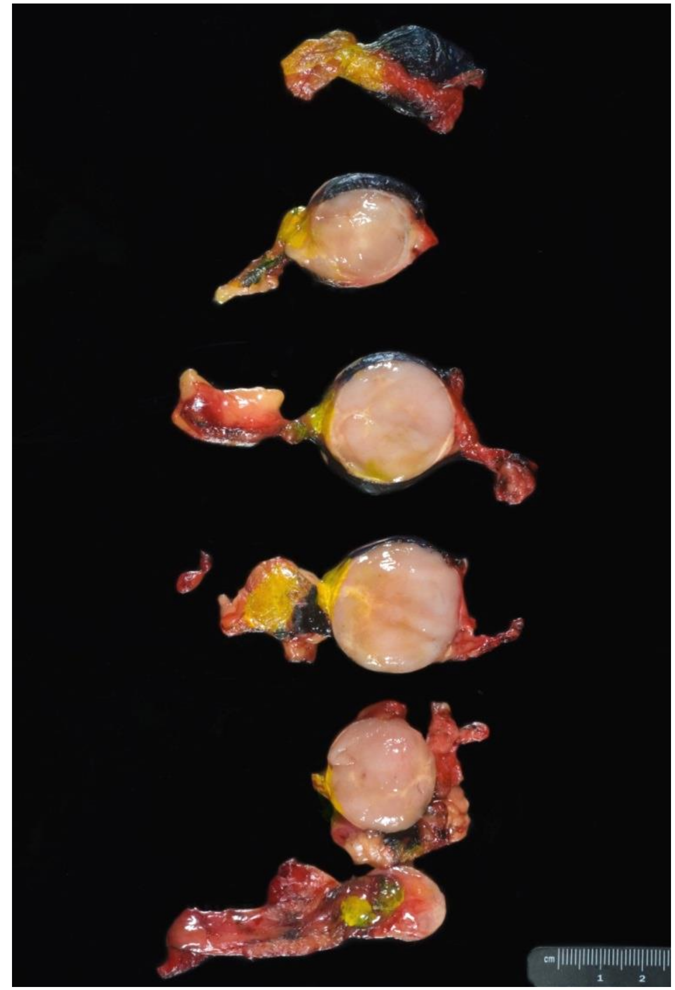
- **Orientation**: Anterior, posterior, right and left surfaces should be clearly distinguished (e.g. inked with different colors or with a detailed block key)

- **Slicing**: Tumor bread-loafed from superior to inferior, and sections serially ordered and submitted

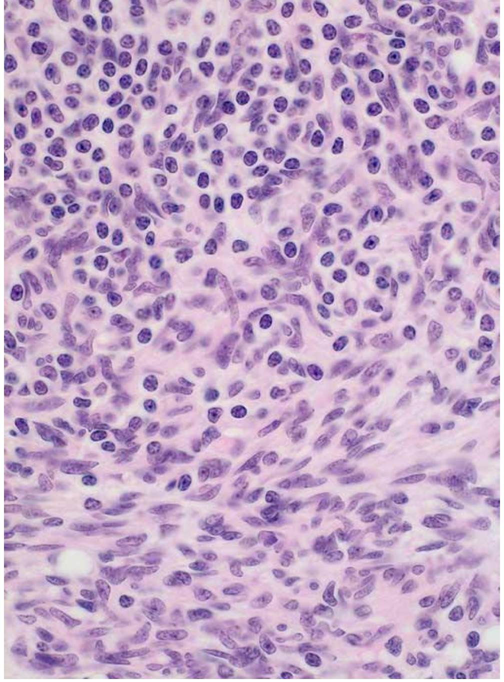
- **Description**: Tumour size, distance to margins, extension into adjacent fat/tissues, additional nodules etc.

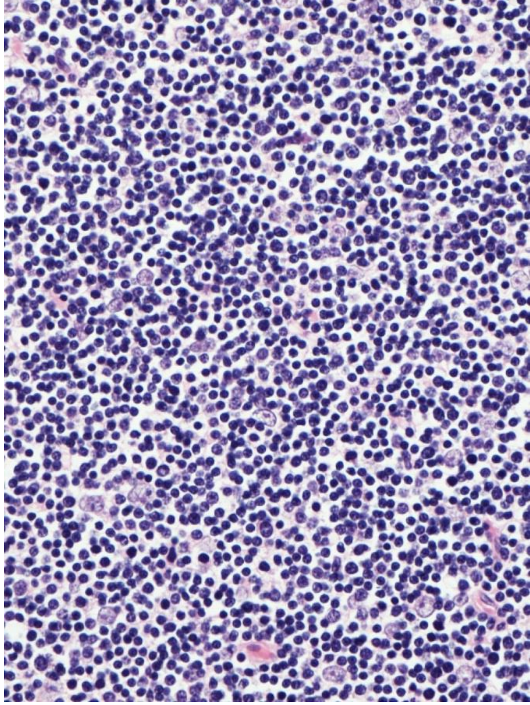
- **Blocking**: <2cm all submitted, >2cm 1 block/cm of tumor, margins, capsule, surrounding tissue/cysts etc

Inked Specimen



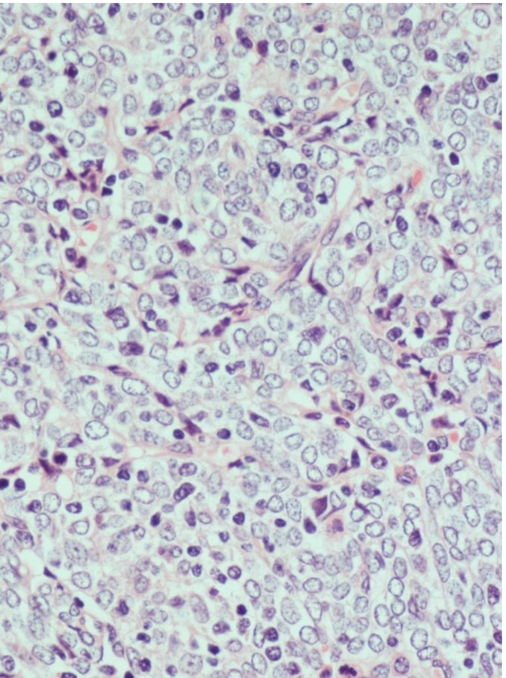
Histopathology of Thymoma

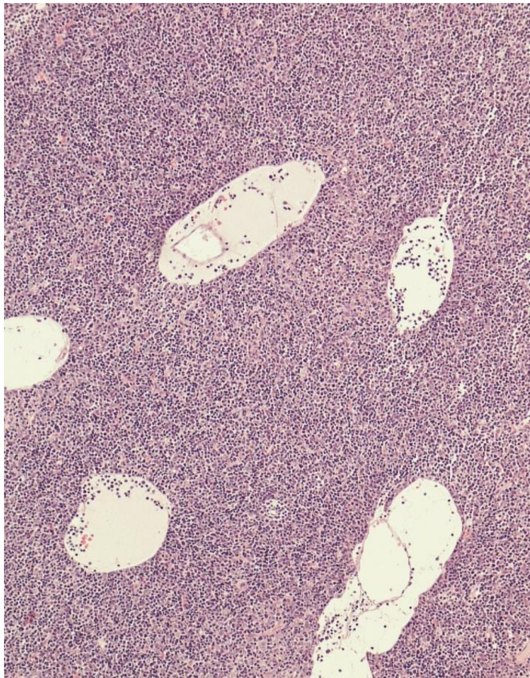




Diagnostic Pitfalls

- Heterogenous appearances and confused classification
- Lymphocytes may obscure epithelial element
- Can be found in ectopic sites (pleural, intrapulmonary, neck)
- Thymic carcinoma looks like Ca from elsewhere





Classification of thymoma

- An adequate classification system must:
  - Be reproducible amongst pathologists
  - Provide prognostic data
  - Ideally have some histogenic correlate

- Previously
  - Muller-Hermlink attempt at histogenic classification
  - Suster Moran

Suster and Moran A J Clin Pathol 2006;125:542

- Currently
  - WHO/ITMIG

WHO Classification

- Recognises previous attempts at histogenic classification at same time as tries to provide prognostic information

- Better differentiated tumours appear to recapitulate normal organ structure
  - Immature T cells, lobular, perivascular spaces, septa
  - Cytology:
    - Spindle cells (Type A), like medullary epithelial cells
    - Epithelioid cells (Type B), like cortical epithelial cells

- Poorer differentiation recognised by
  - Increase in epithelial component
  - Increasing epithelial atypia

WHO 2004

Qu

1. Recognisably thymic in nature?

- Organotypic features

Qu: Cell type?

- Bland spindle cells -> **Type A**
- Dendritic or epithelioid cells -> **Type B**

Qu: B1 B2 B3

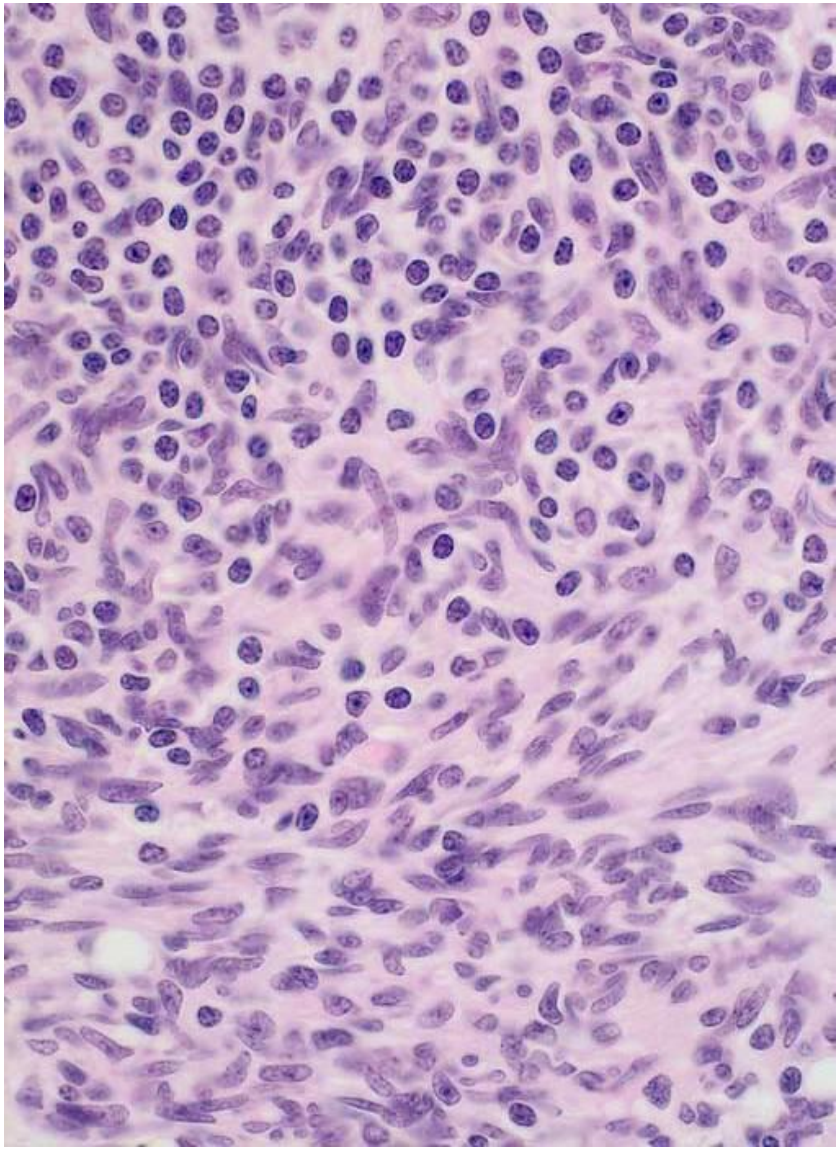
Increasing epithelial component and fewer lymphocytes, and increasing epithelial atypia

2. Overtly malignant? -> Thymic carcinoma (Type C avoided)

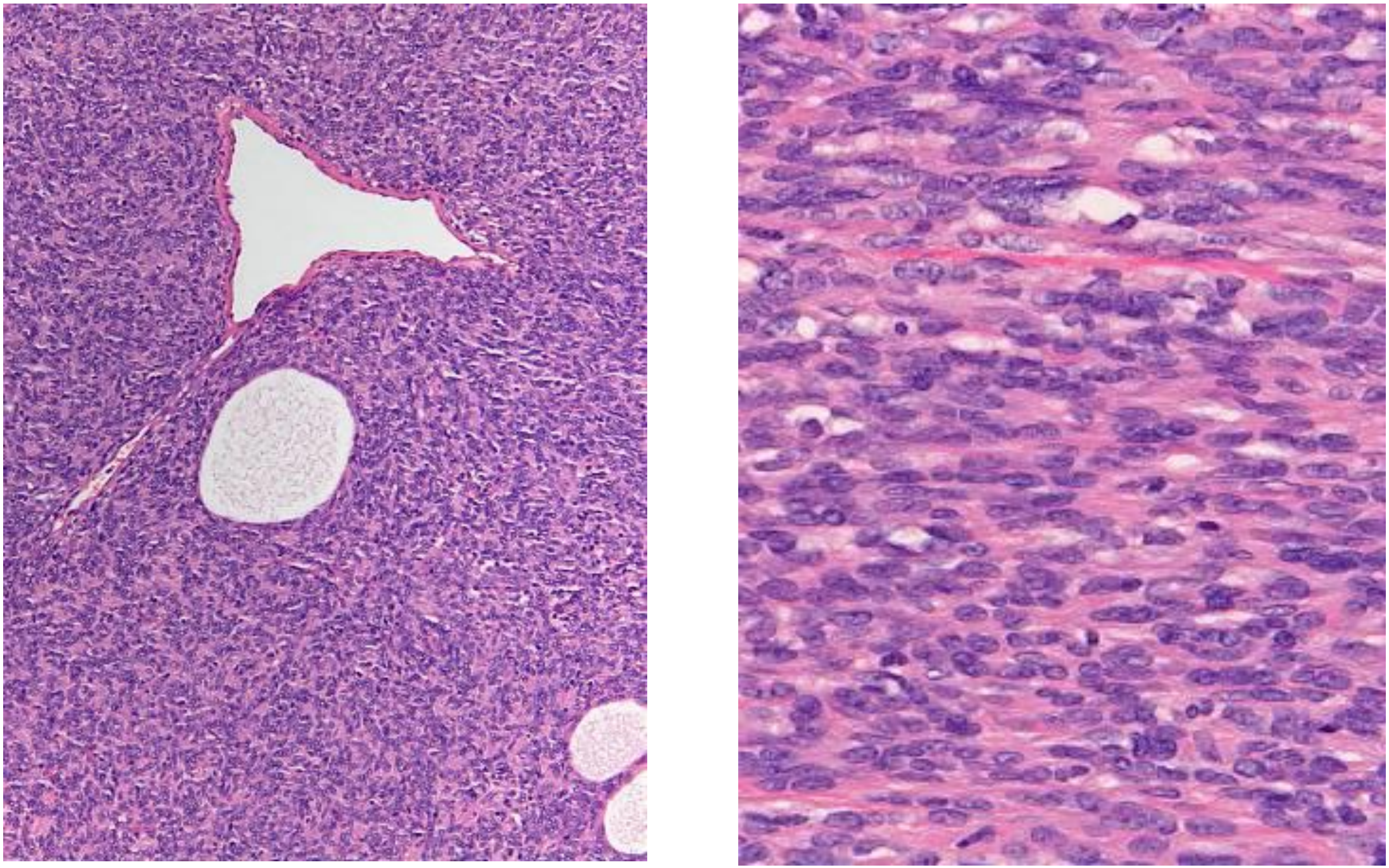
Organotypic features
Bland spindle cells

Thymoma – WHO type A

- Spindle/ovoid cells with little atypia and a few admixed lymphocytes
- Can have glandular, glomeruloid, rosettes and meningioma like architecture
- Reticulin around single cells not reliable
- CK +, CD20 f+, EMA variable, CD5-, bcl2-



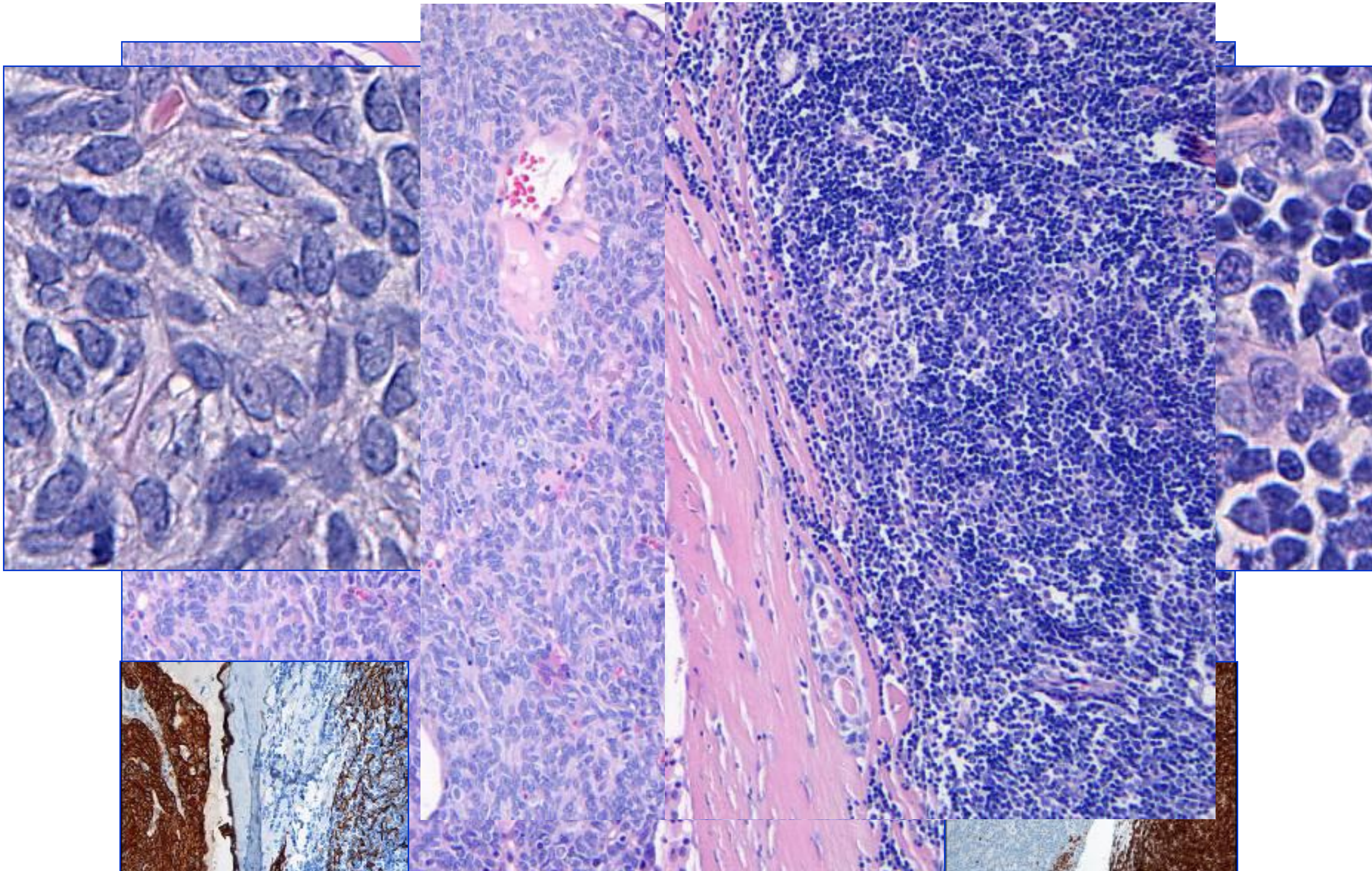
A



Thymoma – Type AB

- Confused descriptions in WHO
- Has lymphocyte rich areas, but cytology remains that of type A
- Essentially is a lymphocyte rich variant of type A thymoma

AB



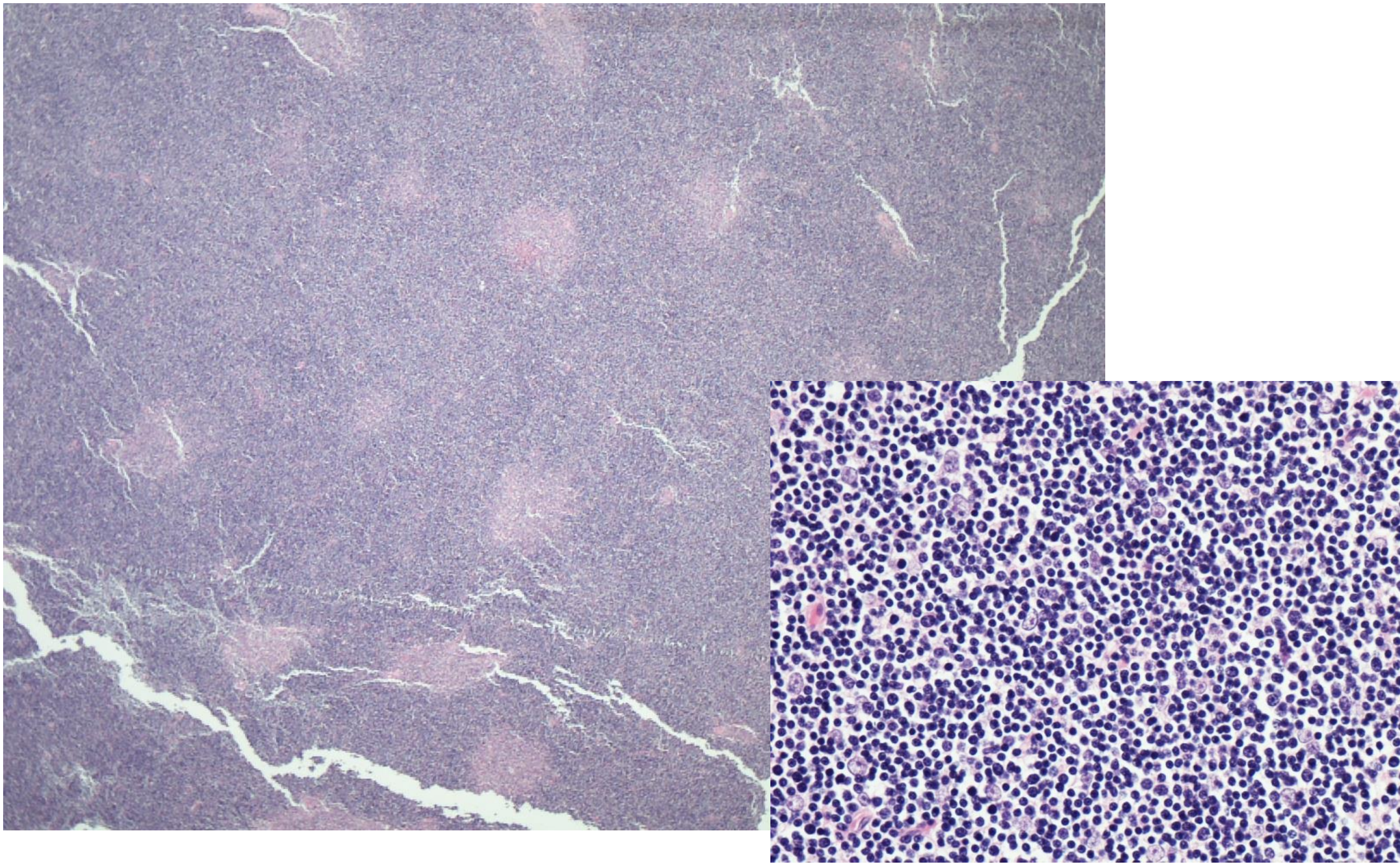
Organotypic features
Epithelioid cells

Assess -Lymphoid:Epithelioid cell ratio

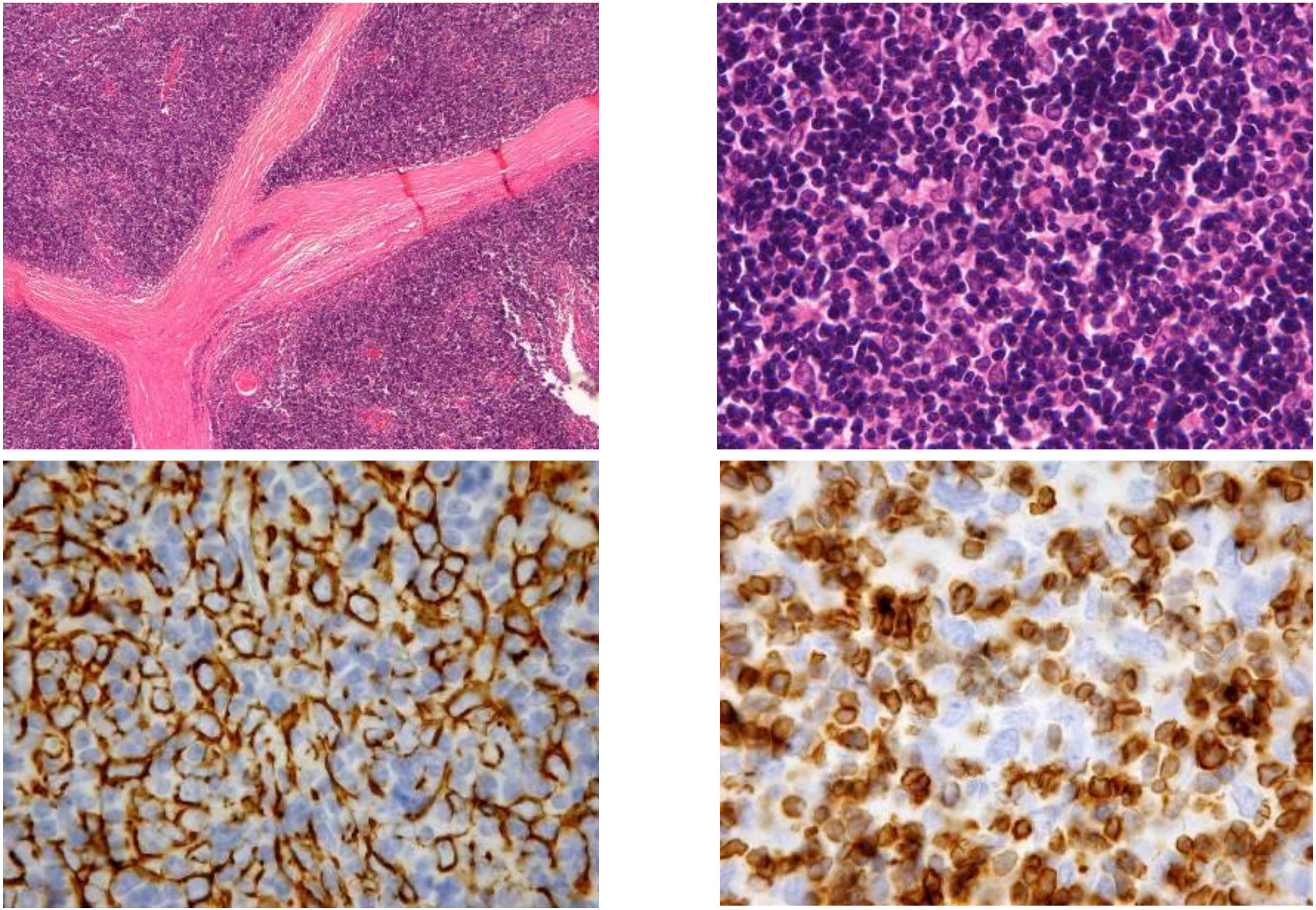
WHO B1

- Resembles normal thymus
  - Lobulation with fibrous capsule and septae
  - High L:E ratio. Large expanses look like cortex : lymphocyte rich with sparse epithelioid cells (oval with small nucleoli) – cytokeratin useful to highlight epithelial network.
  - Pale medullary-like areas
  - Perivascular spaces rare

WHO type B1
“looks blue”

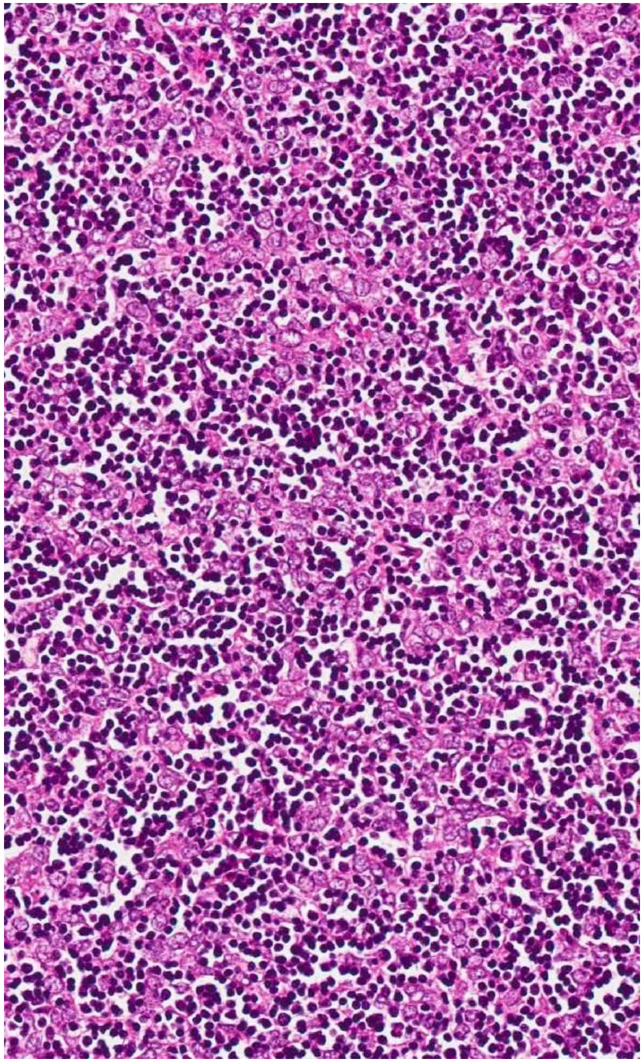


B1



WHO Type B2

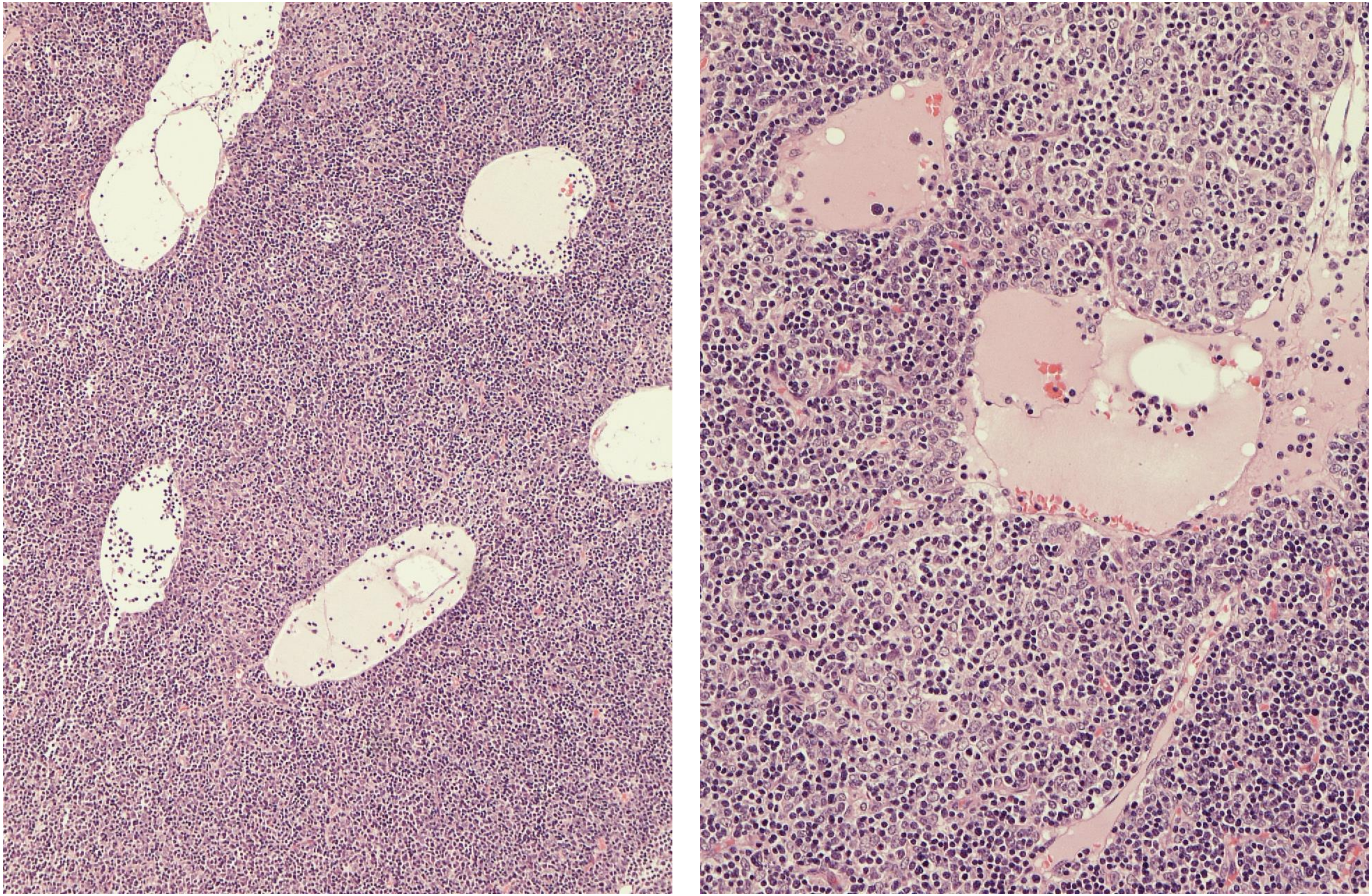
"less blue"



- Epithelial cells larger and somewhat more prominent - <u>clusters three or more epithelial cells</u>

- Perivascular spaces and perivascular epithelial palisading are common

B2 : Perivascular spaces



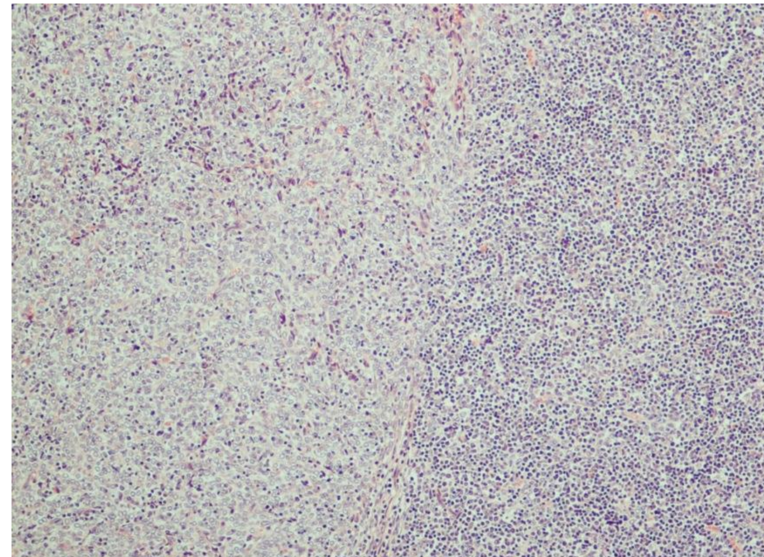
WHO Type B3

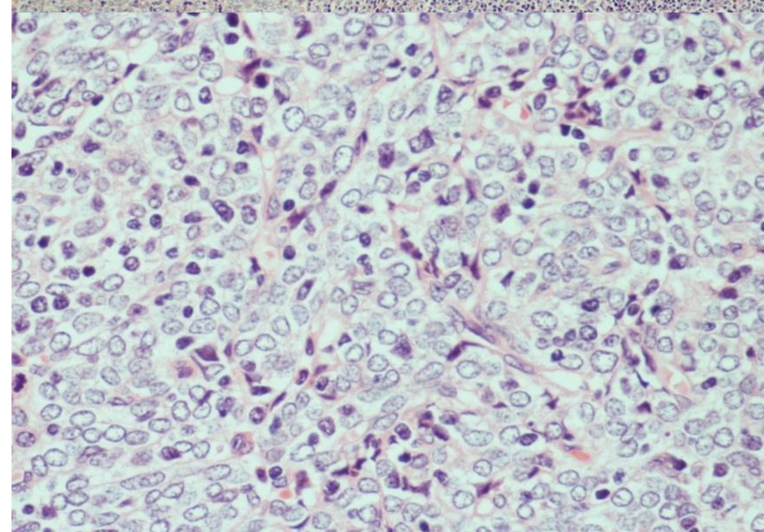
- Mainly epithelial but still admixed immature T cells, perivascular spaces, lobulation etc

- Cytological atypia, but can be mild

- EMA +, CD5-

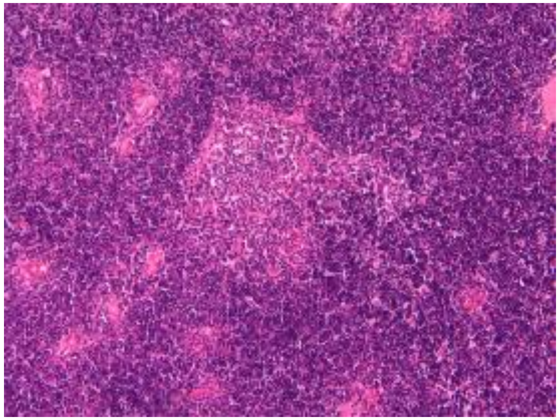
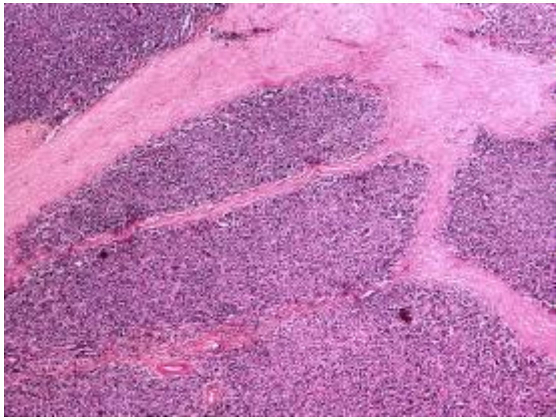
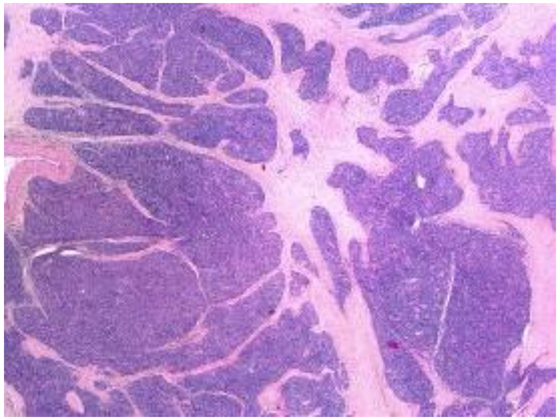
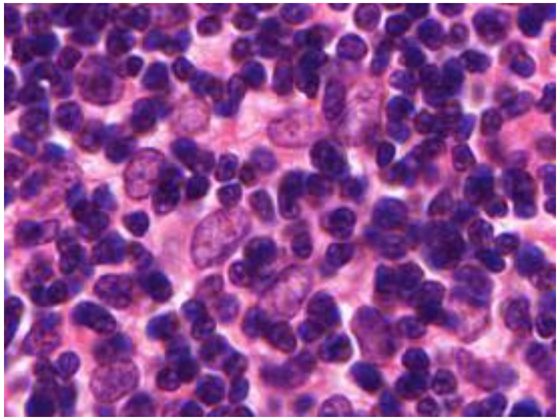
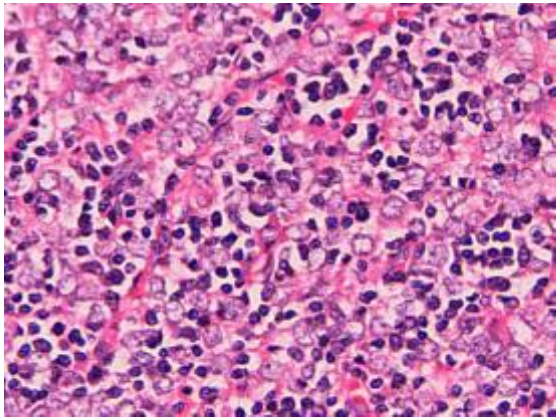
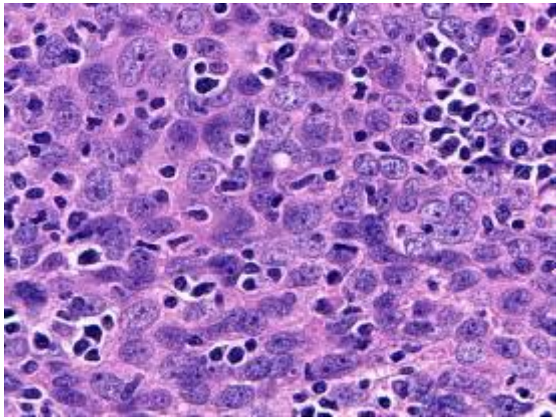
"pale"





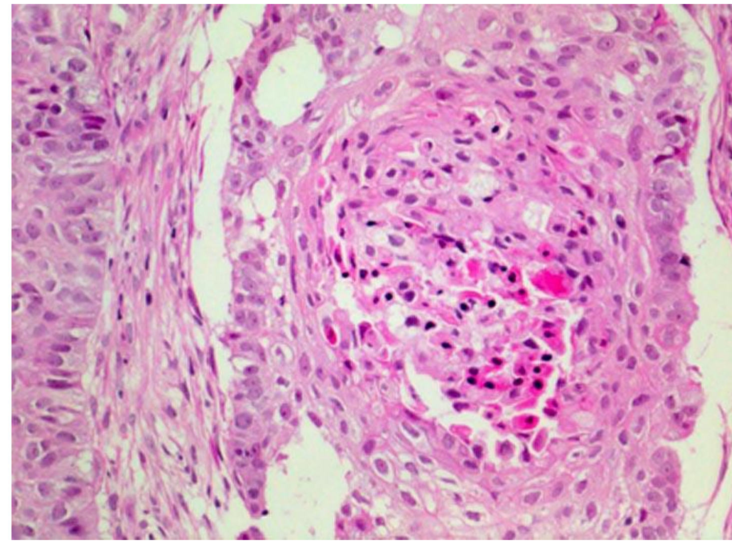
Type B thymomas: Summary

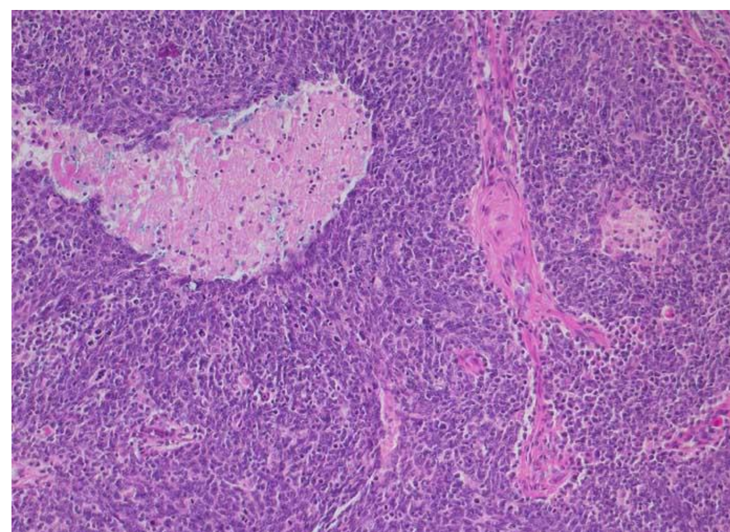
B1 B2 B3

Thymic carcinoma

- Formerly WHO Type C
- Clear cut malignant features
- +/- Thymic features
- Subtypes
  - Keratinising, non-keratinising, clear cell, sarcomatoid, anaplastic, basaloid etc)
  - Includes NUT carcinoma
- Can co-exist with thymoma
- Poor prognosis
- CD5, CD70 and CD117 positive, foxn1 CD205
- Some other tumours CD5 & 117+





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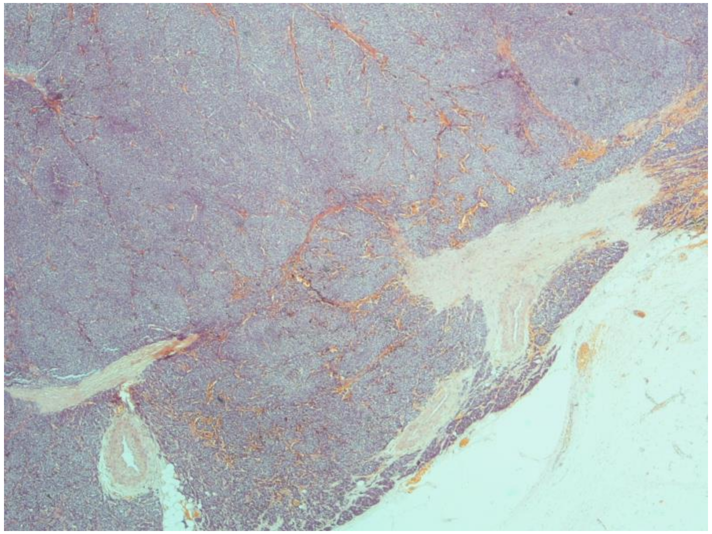
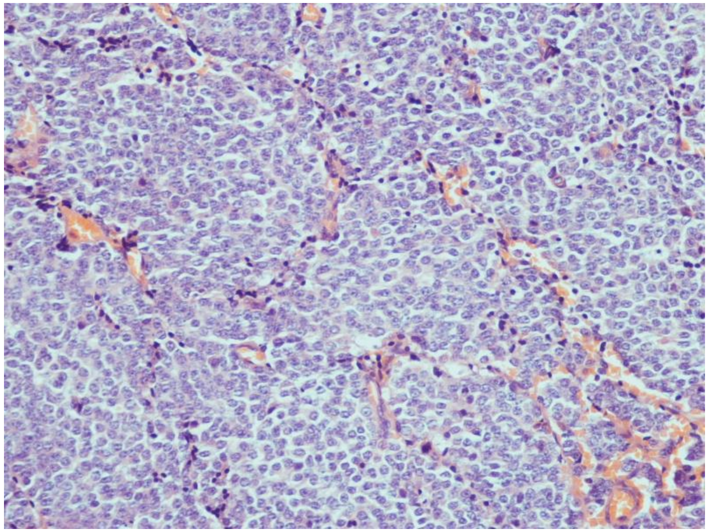
Thymic Neuroendocrine tumours

- Thymic carcinoid
- Associated with carcinoid tumours at other sites and MEN I and IIa
- Majority are atypical if classified by pulmonary criteria
- TTF-1 negative
- 30% associated with cushing syndrome
- Prognosis:
  - Similar to lung when classified carefully





Lymph Nodes

Thymoma: Incidence of + nodes 2% (19/1064)

- 0.4% for Stage I, 6% for stage III
- But how often were they even sampled?
- 90% in ant mediastinum, 25% middle mediastinum

Thymic Carcinoma: Incidence 27%

- 70% anterior, 35% middle, 30% extrathoracic

Thymic Carcinoid: Incidence 28%

- 90% anterior, 60% middle, 30% extrathoracic

Kondo Ann Thor Surg. 2003;76(6):1859-64

Reporting Microscopic Findings

Histological sub-type

- If mix subtype present give % each type in 10% increments

Capsular Integrity and Invasion

- Thymoma, non-invasive (encapsulated, although capsule may be partially absent)
- Thymoma, minimally invasive (penetration through capsule but only minimally into adjacent fat, i.e. $\leq$3 mm)
- Thymoma, invasive (with infiltration of surrounding structures including mediastinal fat)

Distance to closest margin

- Distance in mm reported whenever $\leq$3 mm
- If $\leq$ 1 mm (or $\leq$ 1 hpf) at least 3 additional levels should be examined

Margin Status

Negative

- intact normal tissue overlying the tumor, *or*
- invasion of structures bounded by a space (i.e. pleura or pericardium) *or*
- inked outer surface of specimen consisting of intact capsule, *or*
- tumor extending up to inked margin in an area of tissue disruption that was identified as not grossly concerning intraoperatively

Positive

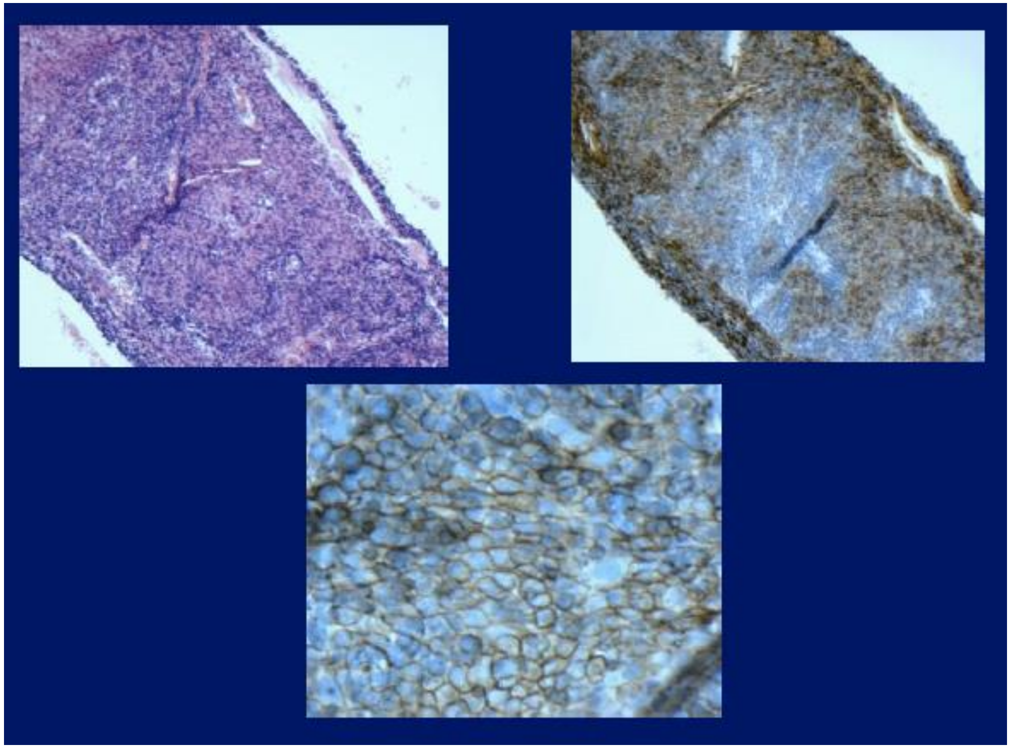
- tumor extending to an inked cut margin

Therapy

- Surgery: Mainstay therapy
- Radiotherapy (post operative):
  - Thymomas are moderate-highly sensitive to radiotherapy. Post op DXT only in cases with high risk recurrence (completely resected stage ¾ or any incompletely resected tumour – site of +ve margin imp).
  - All thymic ca
- Chemotherapy:
  - Thymoma is chemosensitive
  - Thymic carcinoma, modest response to chemo depending on histological type
  - Pre-op Induction chemo for high stage tumours
- Small molecule TKI and Immune checkpoint inhibitors

Immunotherapy in thymic epithelial tumours

- Increased epithelial PDL1 expression with higher stage and more aggressive histology
- 23% of thymoma and 70% thymic carcinoma are positive for PD-L1 (Katsuya et al)
- ? Response to pembrolizumab (case reports)
- Trials in progress



Pre-operative Treatment related effects

- Steroids
  - Reduced number of lymphocytes
- Chemo/radiotherapy
  - Necrosis, foamy macrophages

Prognosis Thymic Tumours

AJSP 2002;26:1605 & 2001;25:1086

- Completeness of excision
- Stage
  - Capsular invasion (macro or micro)
    - Macroscopic invasion is significant
    - Microscopic of uncertain significance
- Mets
  - LN mets are rare
  - Distant mets to liver, lung, bone reported
- Histological type
- Size
  - Significant cut off 11 & 15cm reported

Malignant Potential according to Type - WHO

Histology	**Tumour Stage**	**Malignant potential**
A,AB,B1	I & II III	None Low
B2, B3	I II & III	Low Moderate
Thymic ca Low grade squamous, basaloid, MEC better prog	I & II III	Moderate High
Thymic ca Other types	Any	High

Staging: Thymoma

Masaoka-Koga Staging System

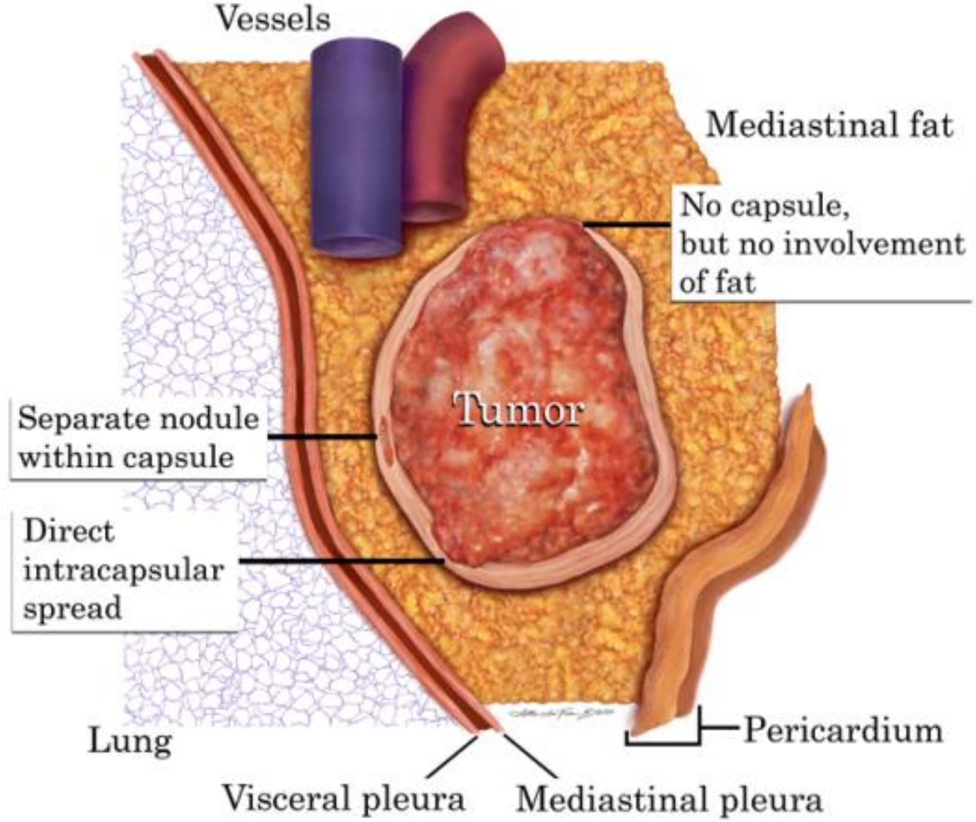
I		Grossly and microscopically completely encapsulated tumor
II	a	Microscopic transcapsular invasion
	b	Macroscopic invasion into thymic or surrounding fatty tissue, or grossly adherent to but not breaking through the mediastinal pleura or pericardium
III		Macroscopic invasion into neighboring organs (i.e. pericardium, great vessel or lung)
IVa		Pleural or pericardial metastases
	b	Lymphogenous or hematogenous metastasis

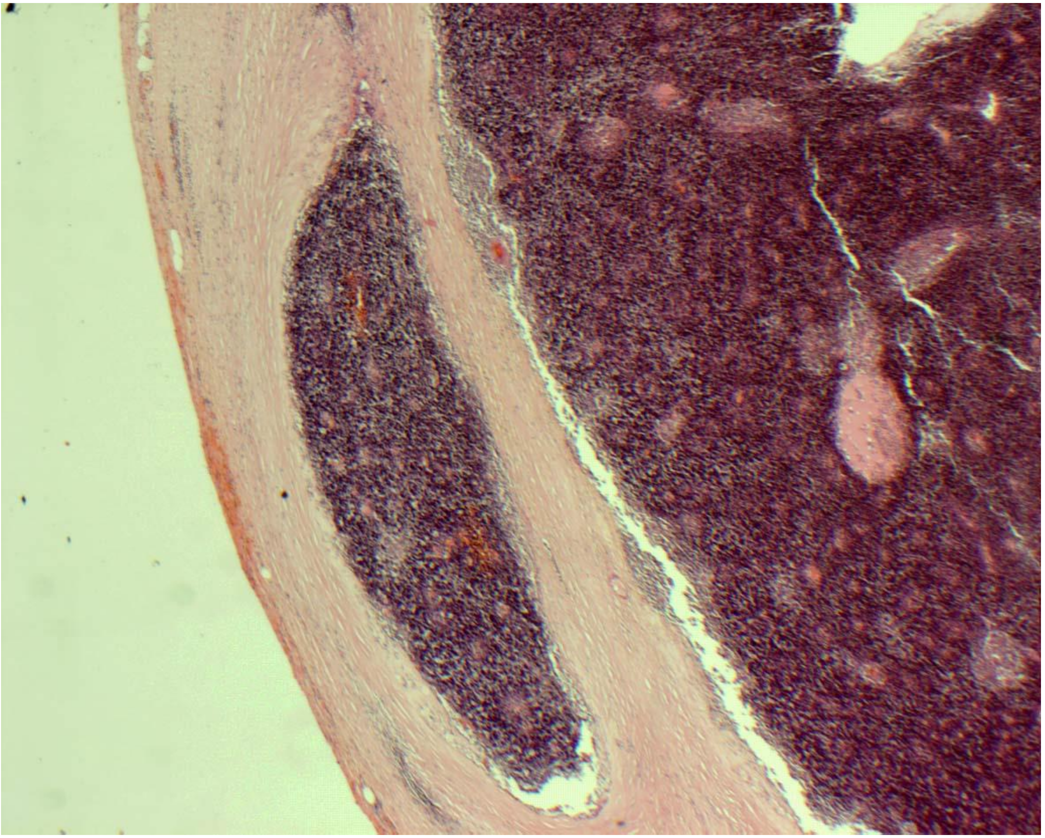
Masaoka-Koga Staging System

I Grossly and microscopically completely encapsulated

Stage I

Figure 1





In the capsule but not through

Stage I

Masaoka-Koga Staging System

II	a	Microscopic transcapsular invasion
	b	Macroscopic invasion into thymic or surrounding fatty tissue, or grossly adherent to but not breaking through the mediastinal pleura or pericardium

Stage IIa

Stage IIb

Figure 2

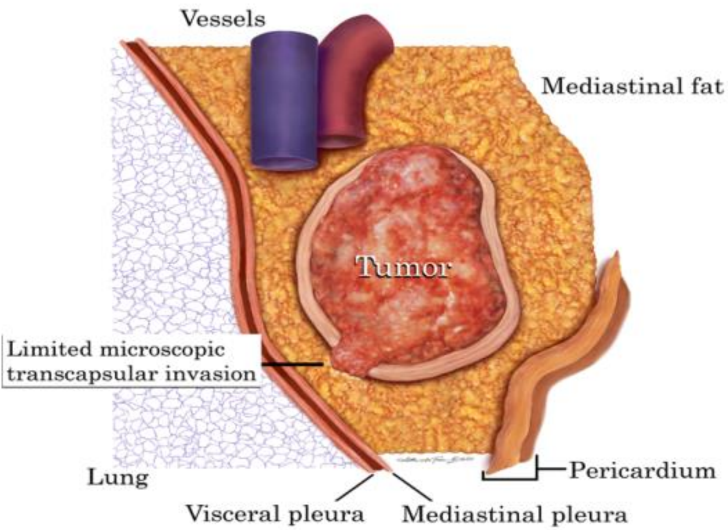


Figure 3a

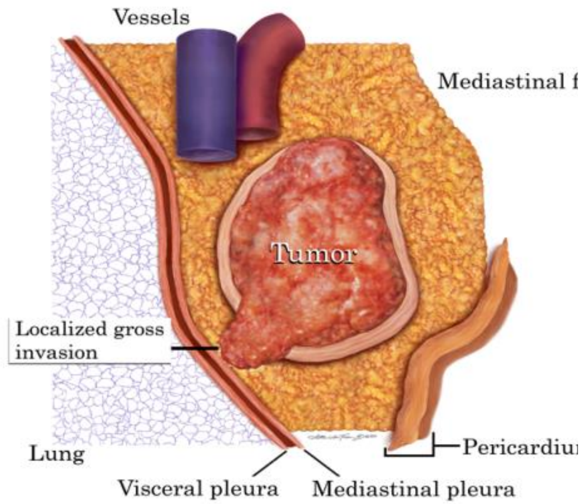
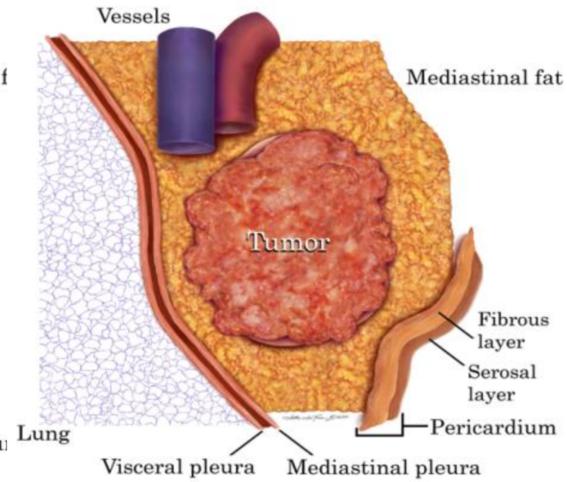
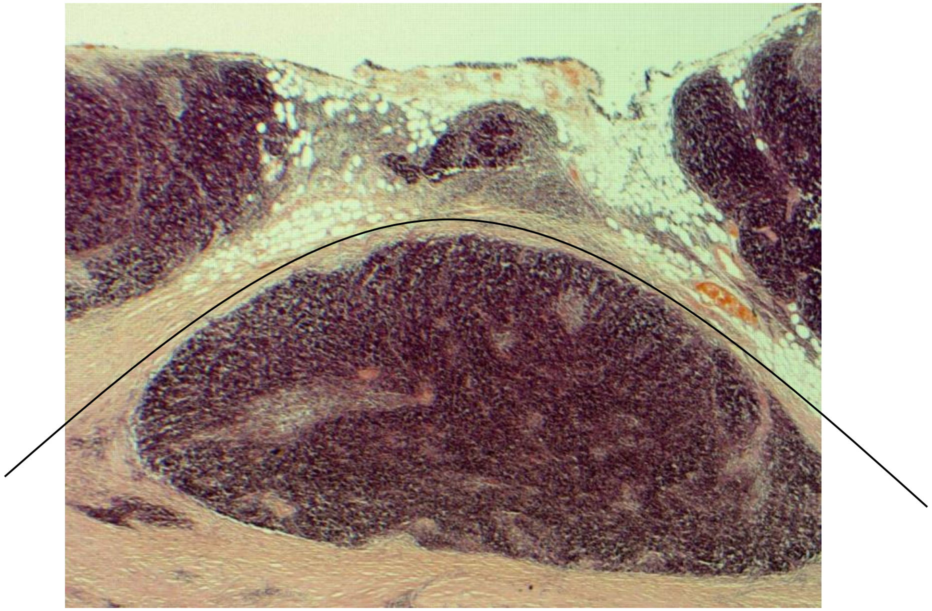


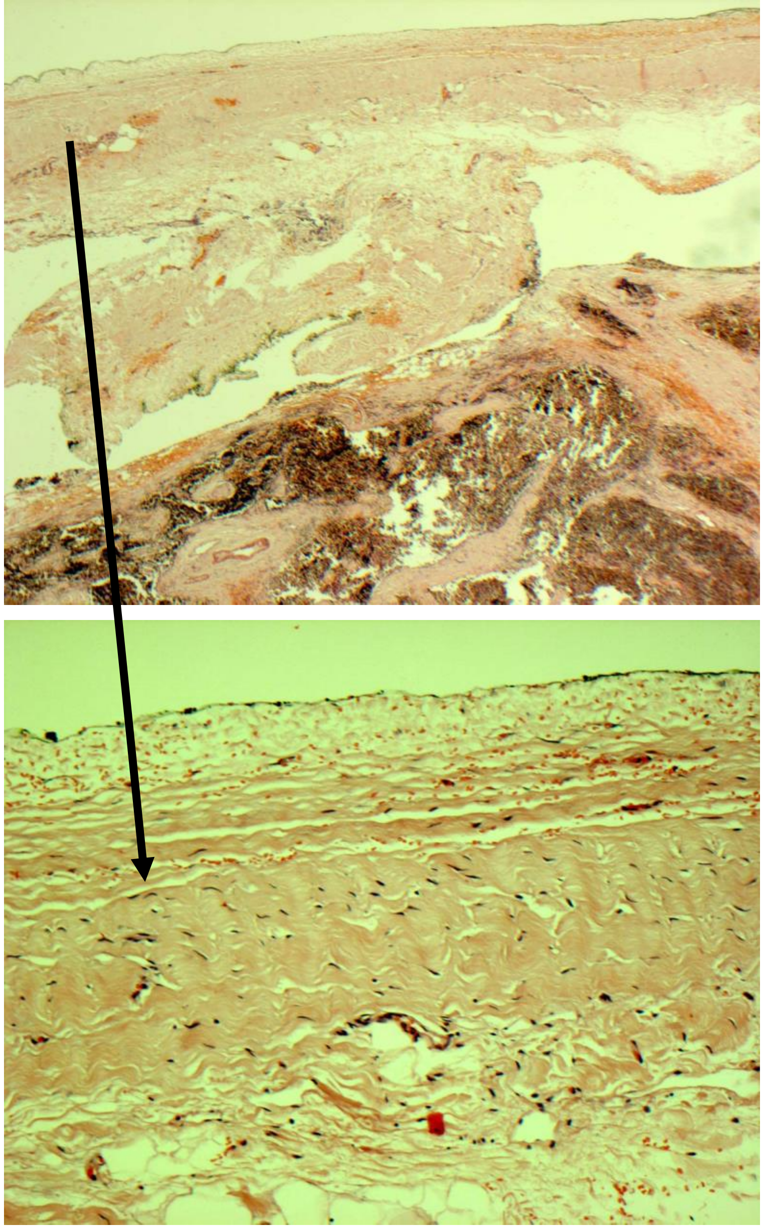
Figure 3b



Through the capsule for < 3mm (2mm)



Microscopic through the capsule but > 3mm (5mm)



Tumour comes up to but not into the fibrous compartment of the pericardium

Stage IIB

Histology of pericardium

Masaoka-Koga Staging System

III Macroscopic invasion into neighboring organs (i.e. pericardium, great vessel or lung)

Stage III

Figure 4a

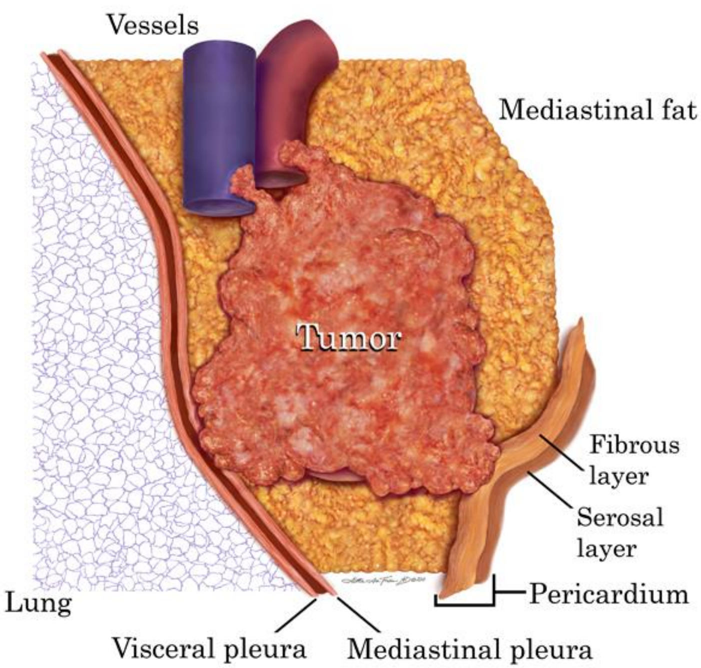
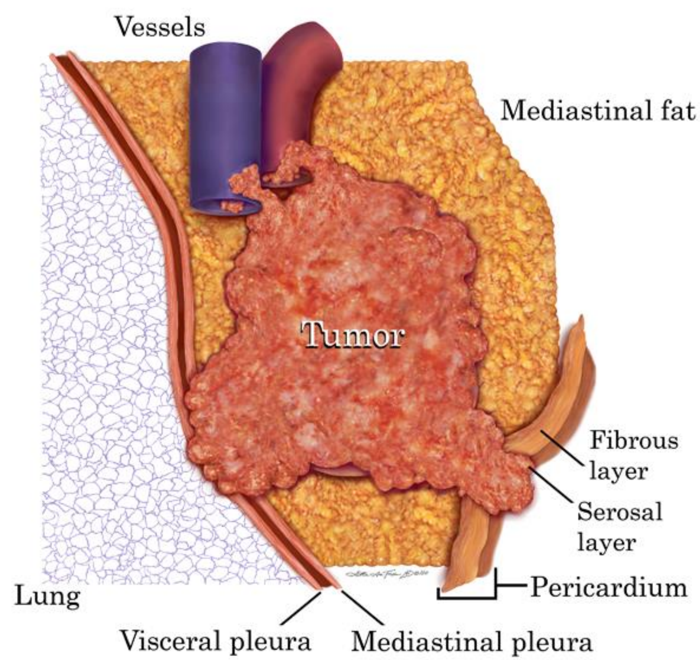
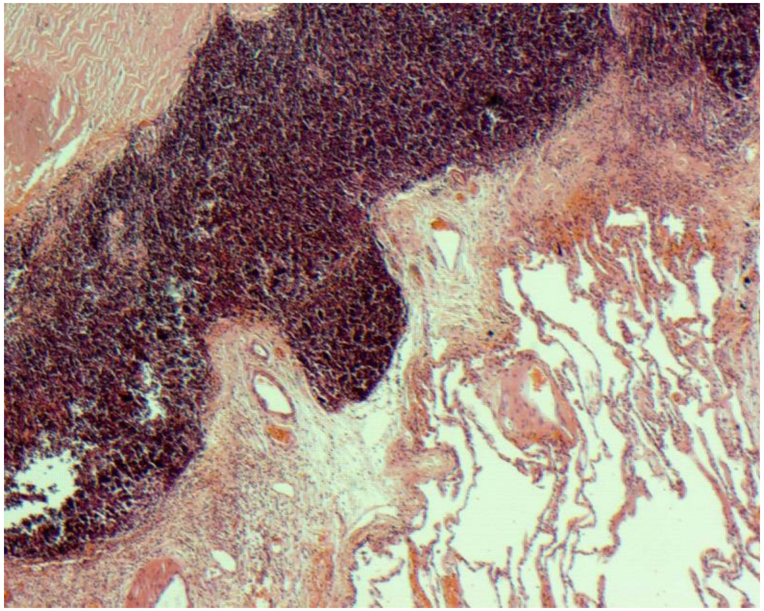
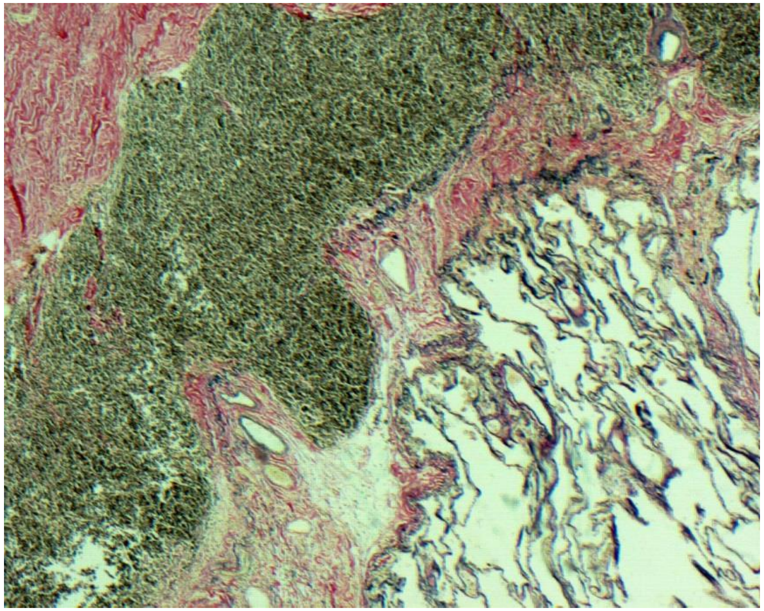


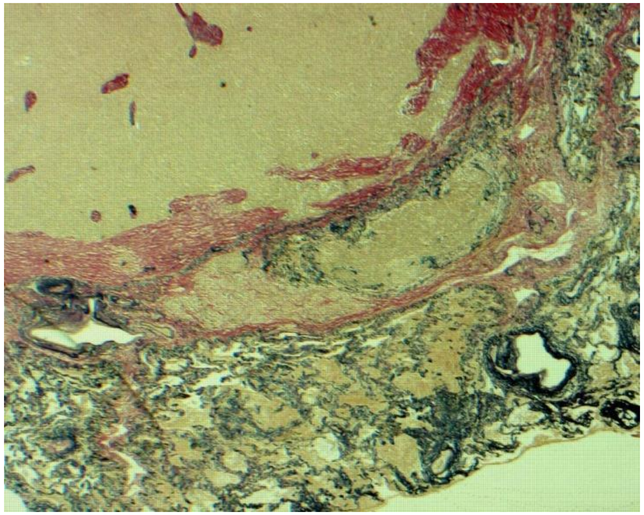
Figure 4b





- Into but not through the visceral pleura
- Stage III (but not yet in lung)



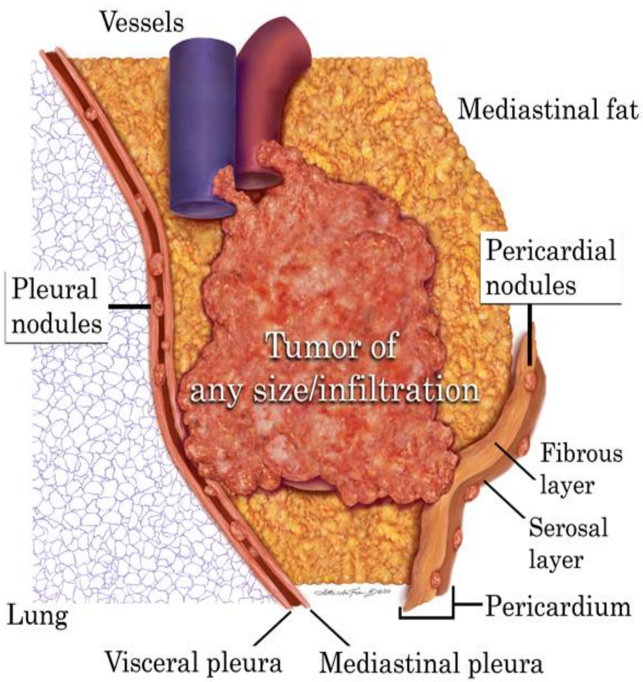


Masaoka-Koga Staging System

IV a Pleural or pericardial metastases
b Lymphogenous or hematogenous metastasis

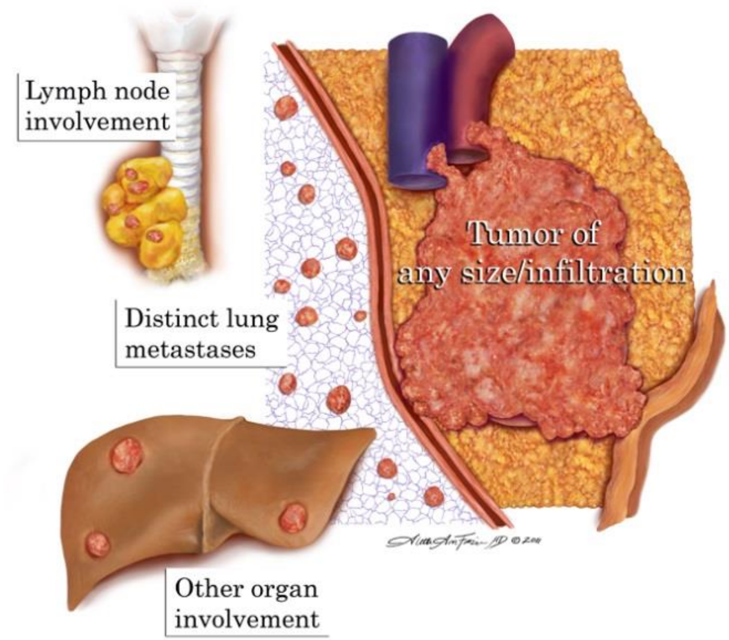
Stage IVa

Figure 5a



Stage IVb

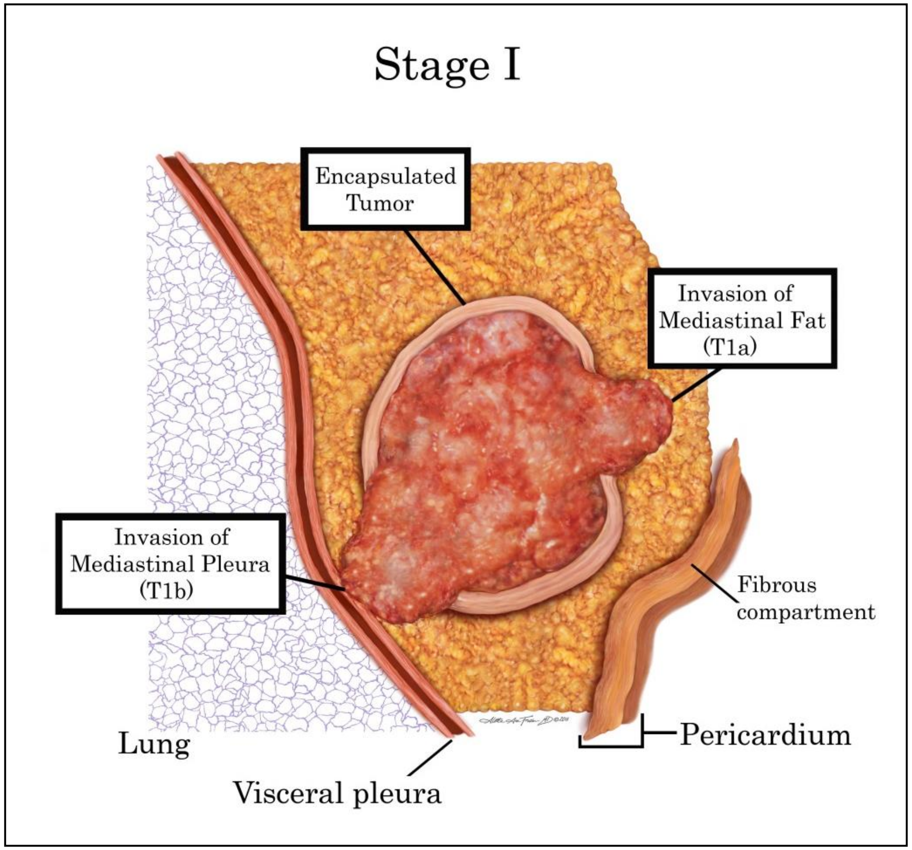
Figure 5b



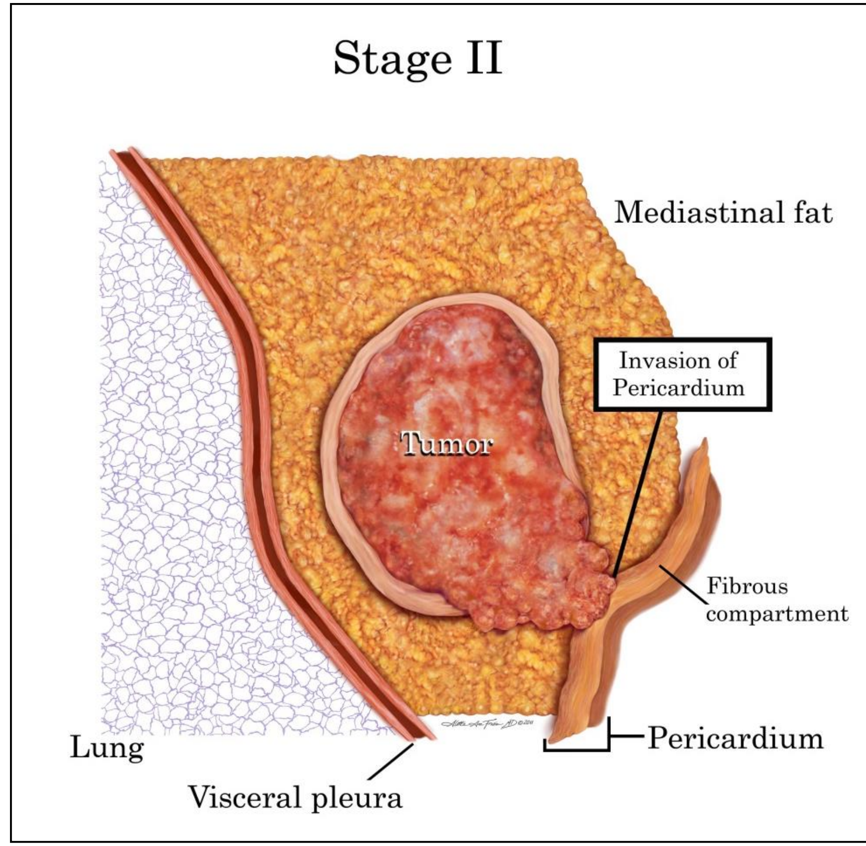
TNM 8th Edn

Stage group I: a tumor that is either "encapsulated" or extending into the anterior mediastinal fat (T1a) or with direct involvement of the mediastinal pleura (T1b); Stage group II: tumor invading the pericardium (either partial or full thickness).

A



B

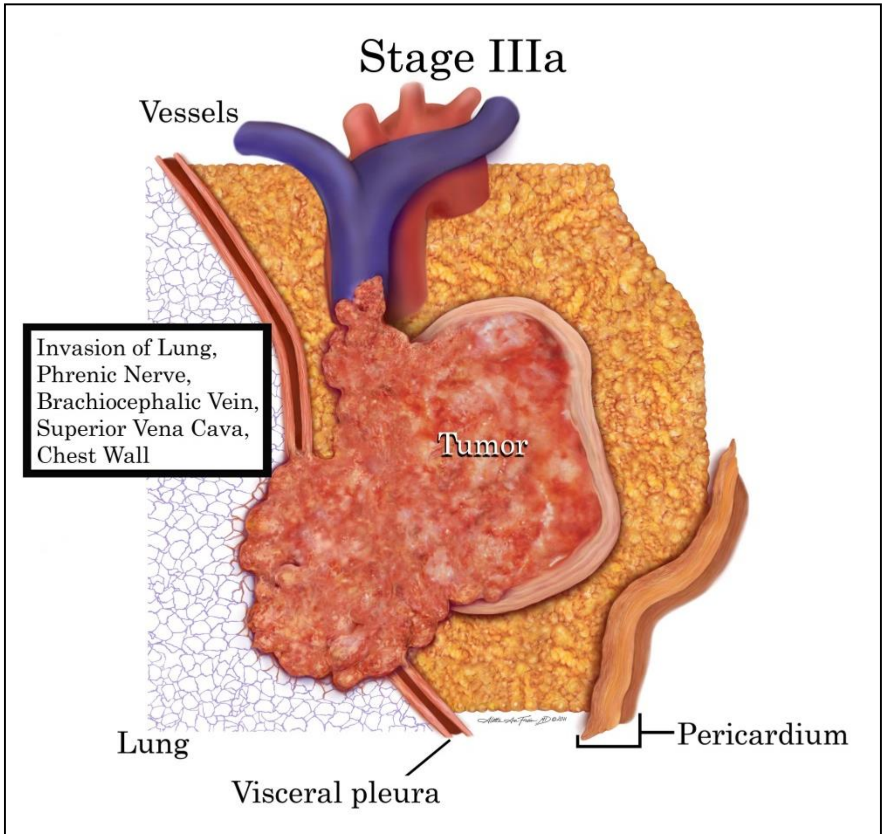


TNM 8th Edn

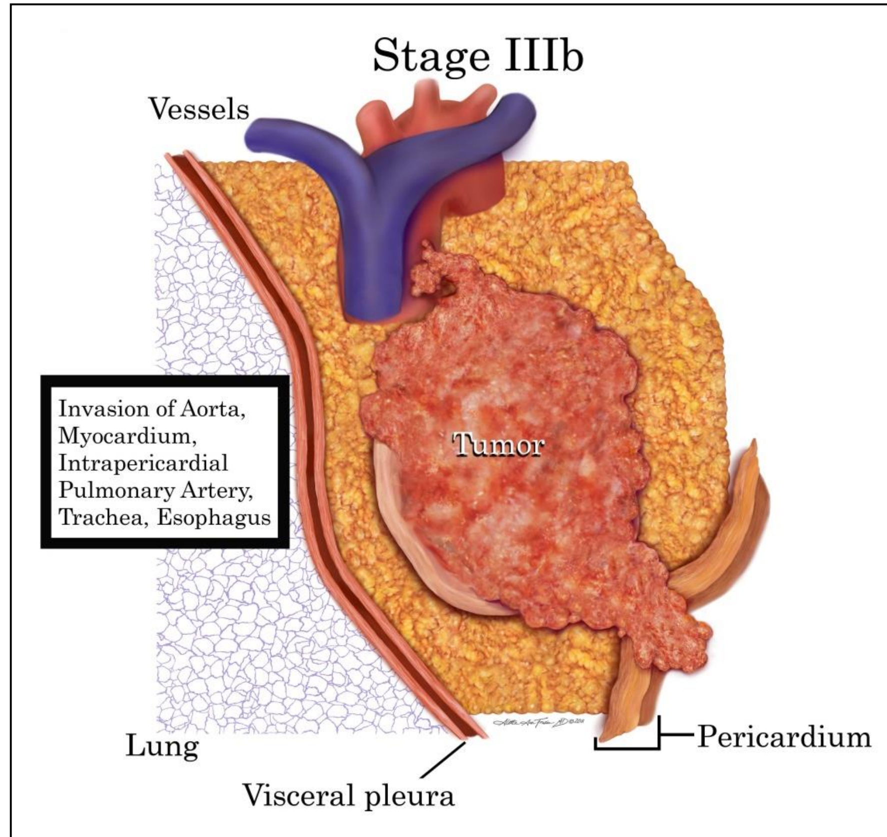
Stage group IIIa: Tumor invading the lung, phrenic nerve, brachiocephalic vein, superior vena cava, chest wall;

Stage group IIIb: Tumor invading the aorta, intrapericardial pulmonary artery, myocardium, trachea, esophagus.

A



B

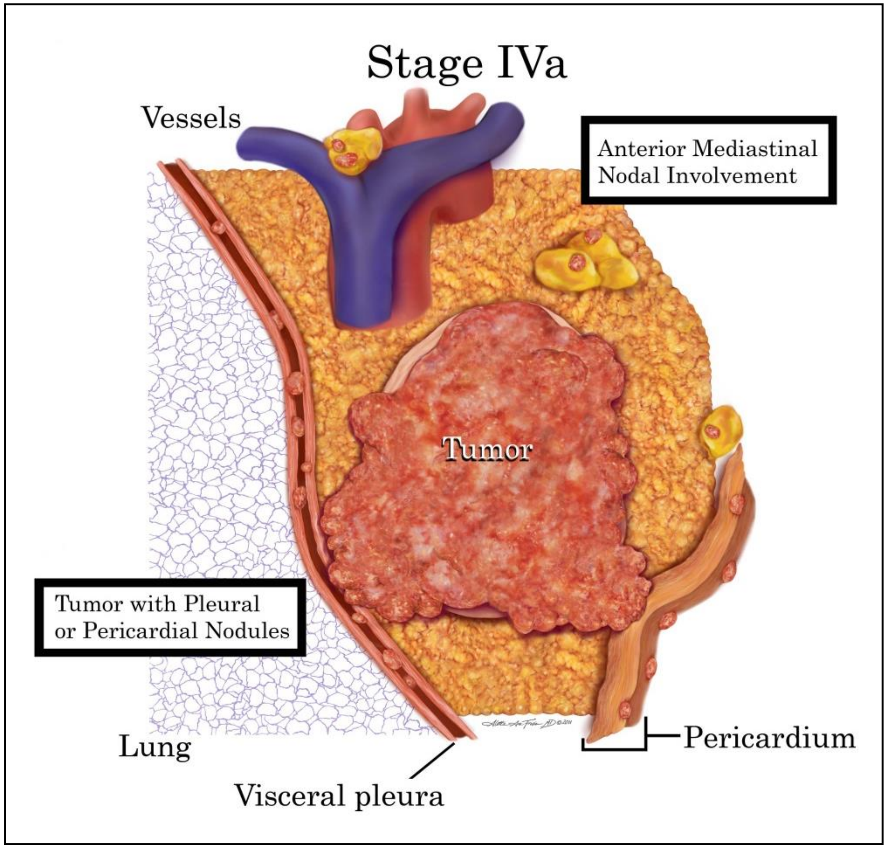


TNM 8th Edn

Stage group IVa: Tumor with separate pleural or pericardial nodules (M1a) or anterior region node involvement (N1);

Stage group IVb: Tumor with deep region node involvement (N2) or distant metastases including intraparenchymal pulmonary nodules (M1b).

A



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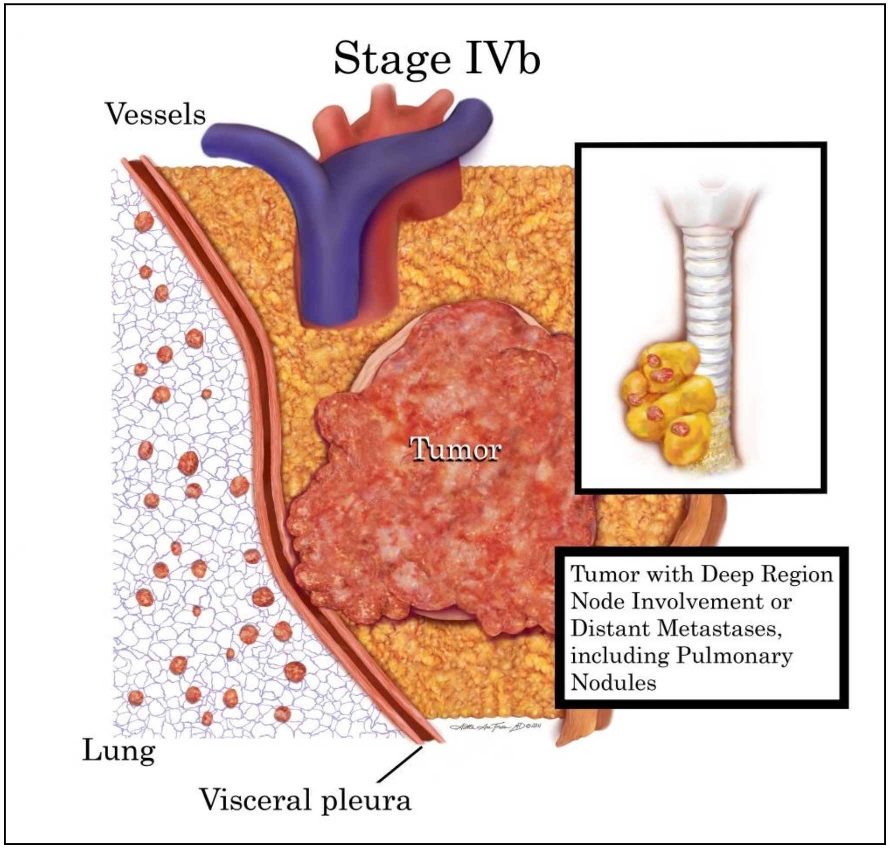
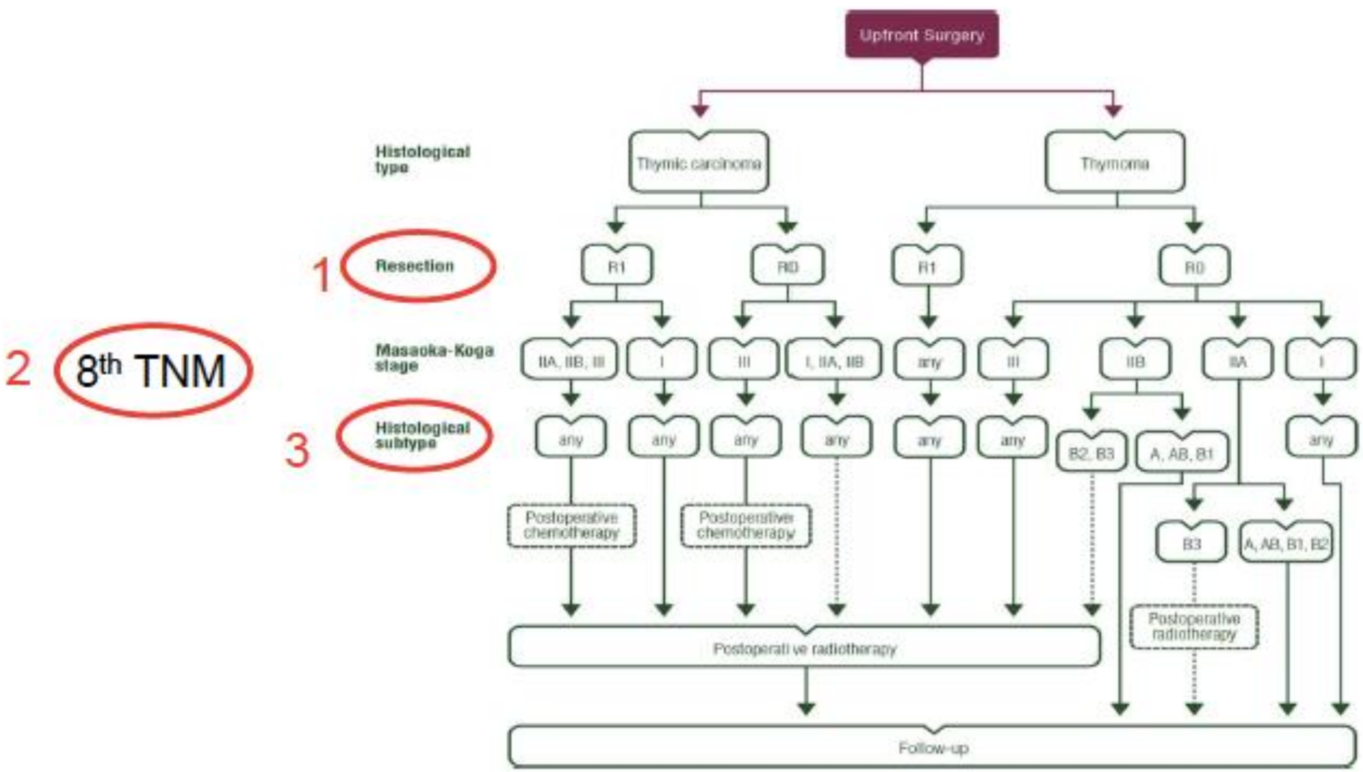


Does it matter?

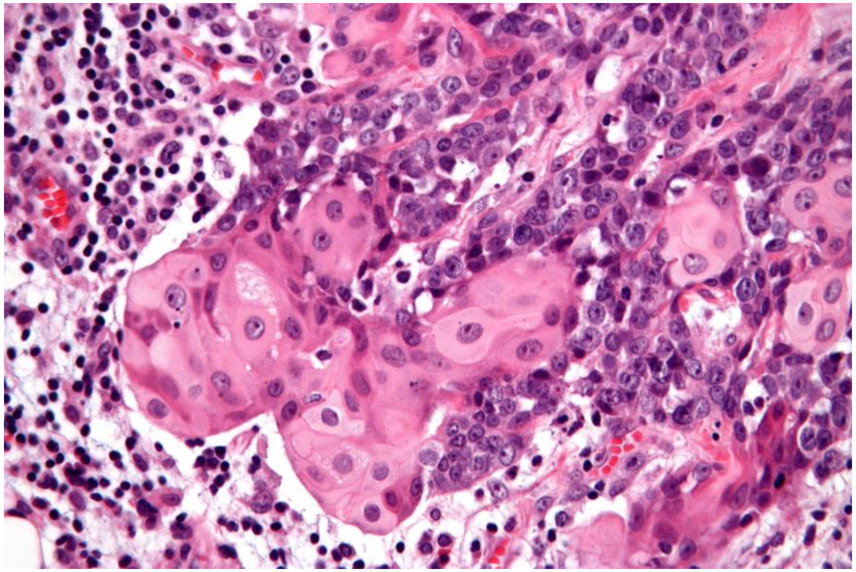


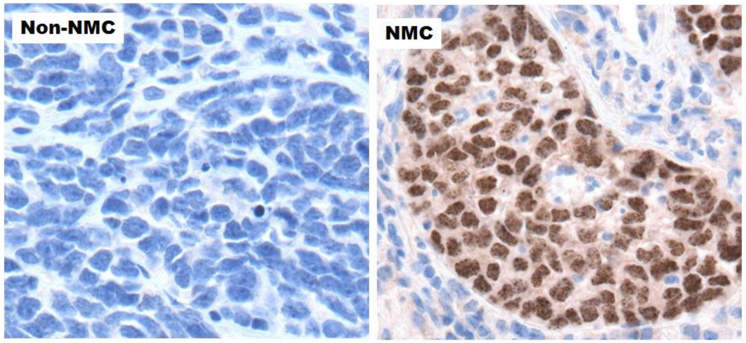
Thymic epithelial tumours: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†

Ann Oncol. 2015;26(suppl_5):v40-v55. doi:10.1093/annonc/mdv277

NUT midline carcinoma

- Poorly differentiated carcinoma with NUT gene rearrangement
- 15;19
- Thoracic NUT 57% cases
- Monomorphic basaloid cells with focal abrupt squamous differentiation
- Nuclear NUT expression
- Aggressive behaviour





	% Sensitivity	% specificity	% PPV	% NPV
C52 IHC	87	100	100	97
FISH	93	100	100	98
FISH + C52 IHC	100	100	100	100

Mediastinal Germ Cell Tumours

Primary mediastinal GCT

- 10% of mediastinal tumours
- Malignant GCT <1% of mediastinal tumours
- Histogenesis remains unclear
  - Germ cell rests
  - Embryonic stem cells
  - Reverse migration from gonads

WHO Classification

As for gonads

<u>One histological type</u>

- Seminoma
- EC
- YST
- CC
- Mature teratoma
- Immature teratoma

<u>More than one histological type</u>

- GCT mixed
- GCT with somatic malignancy
- GCt with haematologic malignancy

Prognosis with age

Age Px	Histology	Sex	Clinical Behaviour
Pre-pubertal	Teratoma* YST	M=F F>M	Benign Malignant (80% SR)
Adolescent & adult	Teratoma - mature Teratoma - immature Malignant GCT (all)	M>=F M>>F M>>F	Benign Guarded Malignant (50% SR)

* Mature and Immature

Germ Cell Tumours

Moran and Suster Cancer 1997;80:681-707

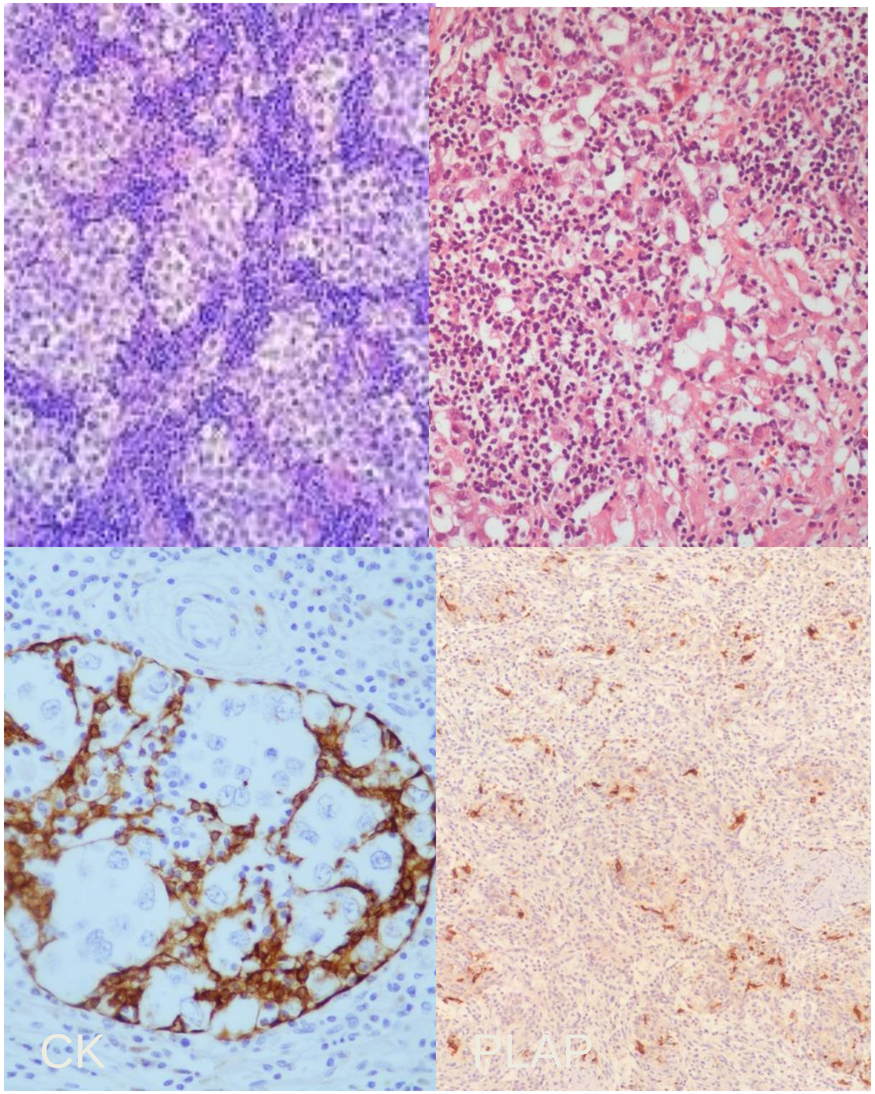
- Present with chest pain, SOB, SVCO, fever, hormone effect
- 6-20cm masses, sometimes cystic
- Histology similar to gonadal counterpart
- **Mediastinal mass man 20-50 presumed to be germ cell tumour till proven otherwise**
- Poorer prognosis: 5YSR seminoma 50-90%, others 20%
- New markers - Oct4, D2-40, i12p

2004 WHO classification
Tumours of one histological type
Seminoma
With syncytiotrophoblastic giant cells
Spermatocytic seminoma
Embryonal carcinoma
Yolk sac tumour
Choriocarcinoma
Other trophoblastic tumours
Monophasic choriocarcinoma
Placental site trophoblastic tumour
Teratoma
Dermoid cyst
Monodermal teratoma
Teratoma with somatic transformation
Tumours of more than one histological type
Embryonal carcinoma/yolk sac and teratoma
Choriocarcinoma and other non-seminoma
Seminoma and non-seminoma

Seminoma

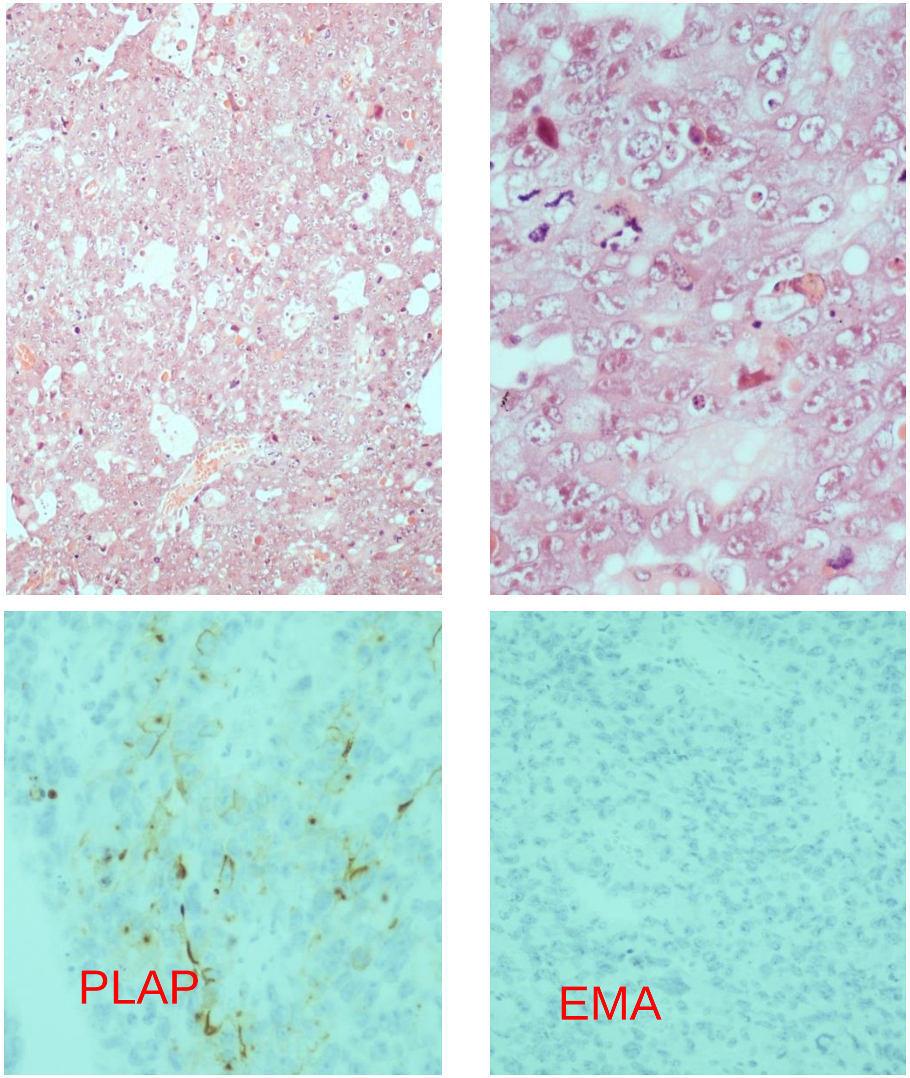
Moran and Suster Cancer 1997;80:681-707

- All male, 14-79 yrs
- Soft tan lobulated tumours
- Microscopy identical to gonadal counterpart
- Diagnostic Pitfalls: cystic change, lymphoid hyperplasia, sclerosis
- **80% PLAP positive, 70% dot like CK positivity**
- Early stage and young good prognostic features.



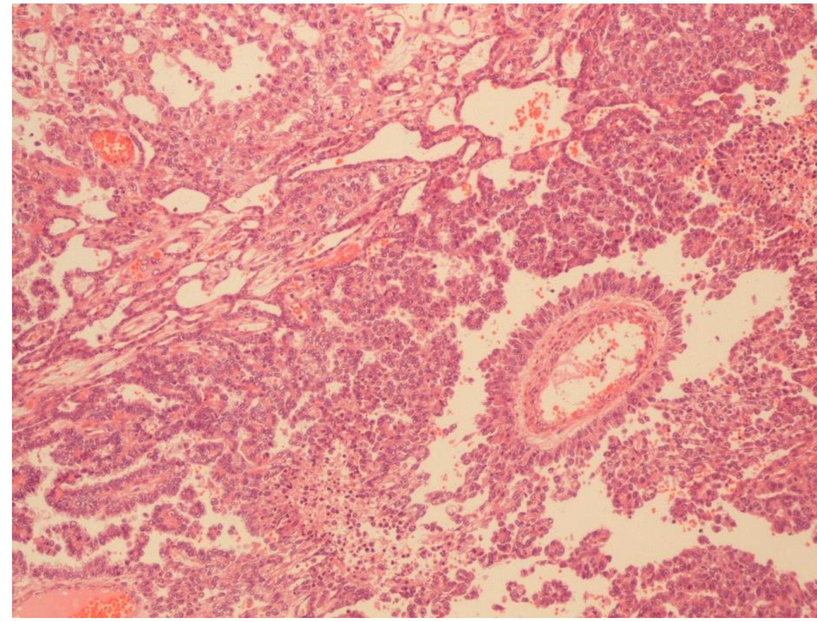
Embryonal carcinoma

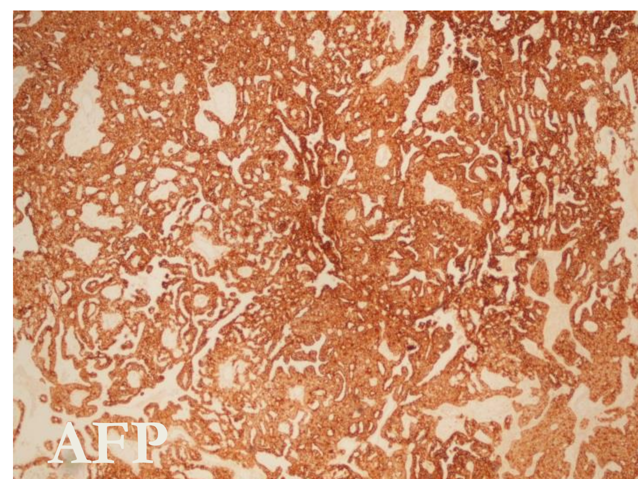
- Males
- Histology as for testis - Invasive, pleomorphic cells with necrosis
- **PLAP +, CK+, CD30+, EMA -**
- **ip12**
- Diagnostic pitfalls
  - Misdiagnose as carcinoma
  - PLAP expression may be seen in other tumours
  - CD30 expression may be lost after chemo



Yolk Sac tumour

- **<u>Bimodal</u>**
  - Infants and young children F>>M
  - Adults M
- Elevated AFP
- Histology as for testis
- AFP(v) and CK +
- Resectability & age -> prognosis



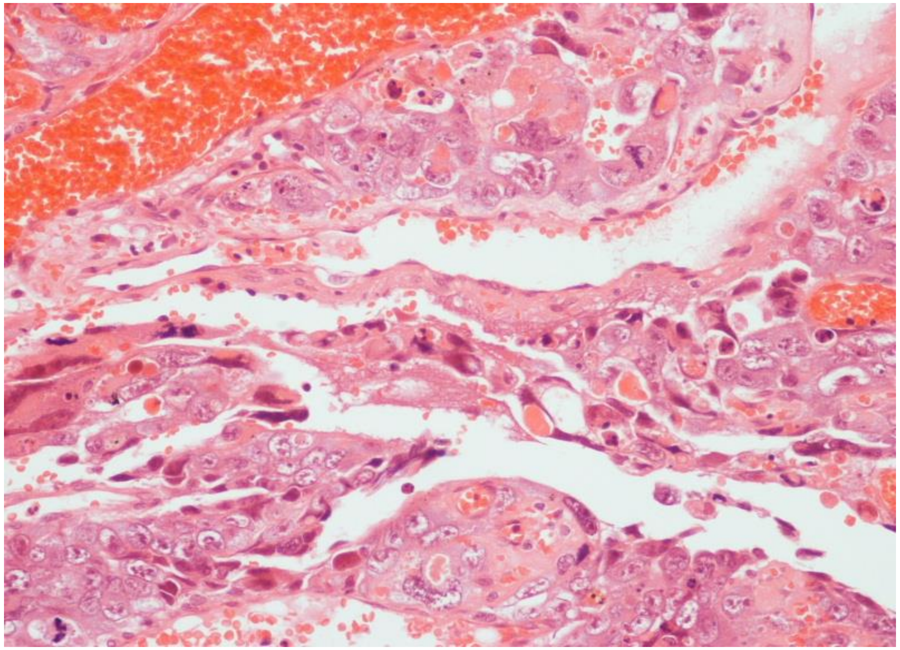


Choriocarcinoma

- Young males
- Elevated hCG
  - Gynaecomastia
  - Impotence

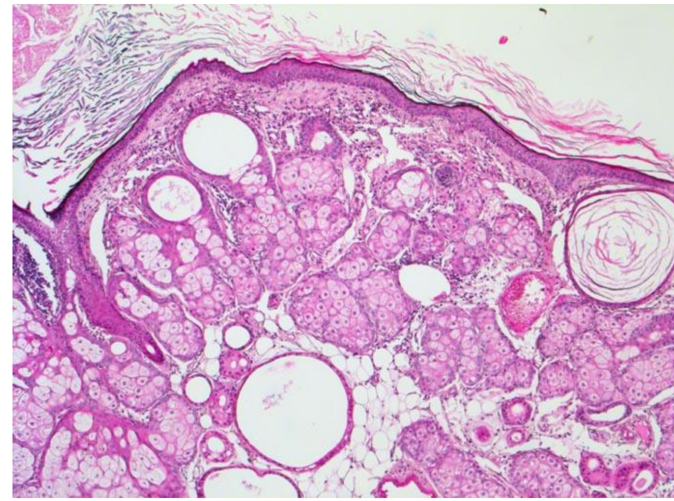
- CK +, EMA +, hCG +

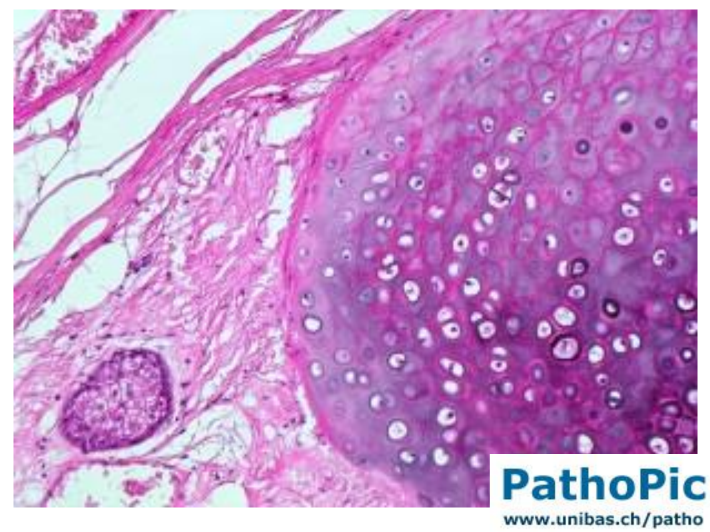
- Dismal prognosis



Mediastinal teratoma

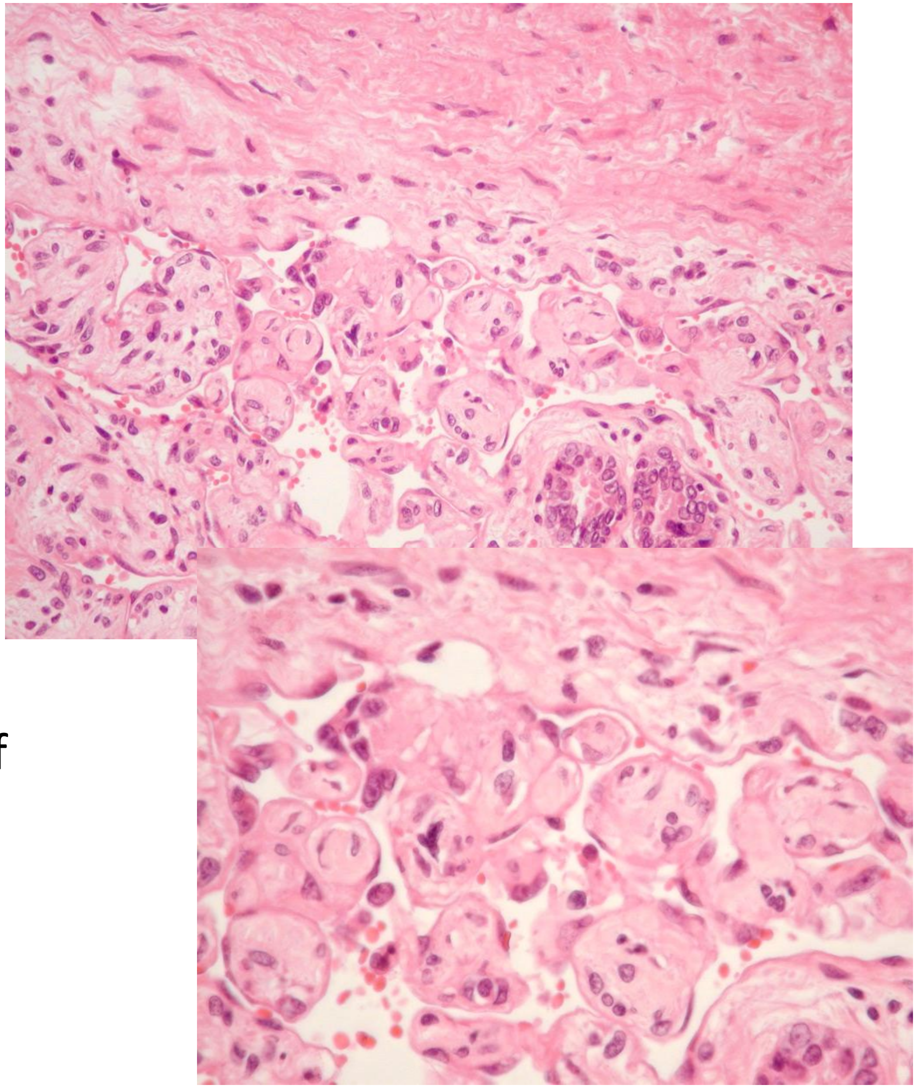
- 1-15% mediastinal tumour in adults, 25% in children
- Solid or cystic
  - Mature
  - Immature
  - With other malignant elements (germ cell or somatic)
- Stage indicative of prognosis





Germ cell tumour with somatic malignancy

- Frequency somatic malignancy varies type of GCT
  - Teratoma 10-20%
  - Non-teratomatous GCT (YST and seminoma) <5%
  - **Mixed GCT >75%**
- Sarcoma more common than carcinoma. RMS most common
- More common post chemo and in late recurrences
- Embryonal RMS, AS, LMS, NB – have i12p, but also specific translocation of sarcoma e.g. 11;22 PNET
- **Dismal** prognosis



Bx: Rare or uncommon tumour in a young man

Think: somatic malignancy in a teratoma

e.g. “Mediastinal squamous cell carcinoma”

Mediastinal lymphomas

Mediastinal Lymphomas

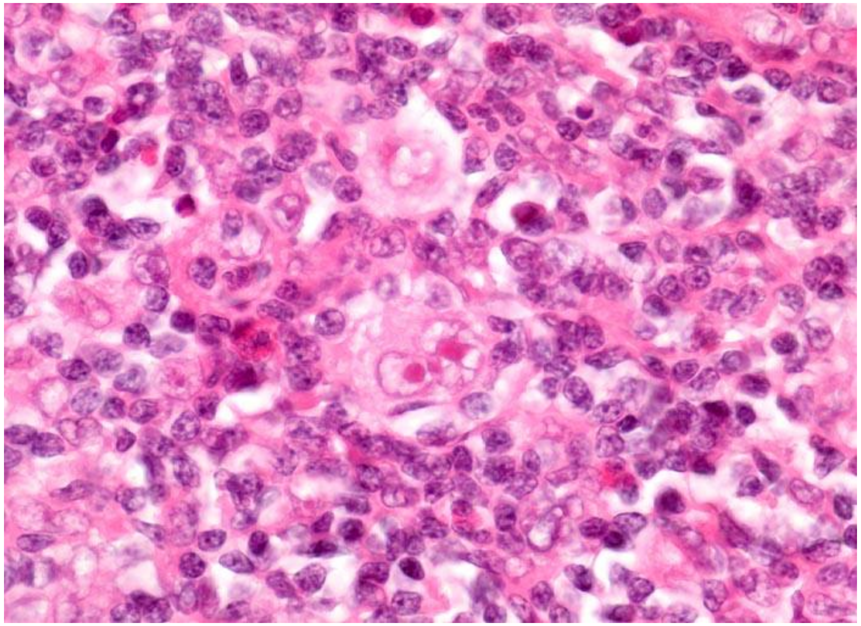
- **Common**
  - **Hodgkins lymphoma**
  - **Primary mediastinal large B-cell lymphoma**
  - **Precursor T lymphoblastic lymphoma/leukaemia**

- Other
  - MALT
  - ALCL
  - Histiocytic tumours
  - Acute Myeloid Leukaemia

Hodgkin lymphoma

- Usually NS type
- Nodal thymic or both

- Diagnostic Pitfalls
  - Cyst formation
  - Excessive fibrosis with sparse Hodgkin/RS cells.

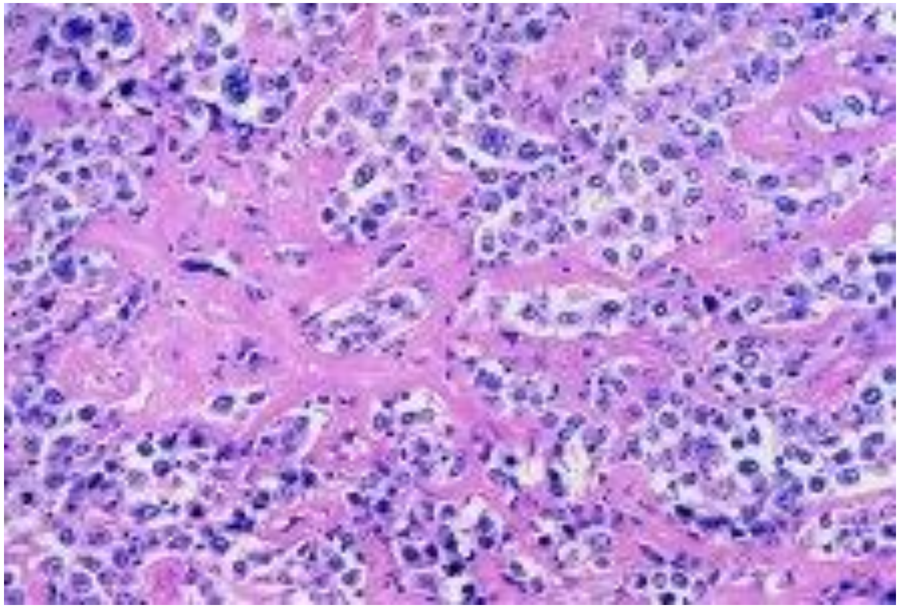


Primary DLBC lymphoma

- Young women
- SVCO, cough, dyspnoea
- <25% distant disease
- Sclerosis with infiltrate large B lymphocytes, often with clear cytoplasm
- May seen entrapped thymic epithelium

- **CD23 may be expressed**
- **MAL**

- DD – syncitial Hodgkins (CD45-), ALCL (CD30+, Alk-1 +), carcinoma (CK+)
- “grey zone” lymphoma – gene array



PathoPic
www.unibas.ch/patho

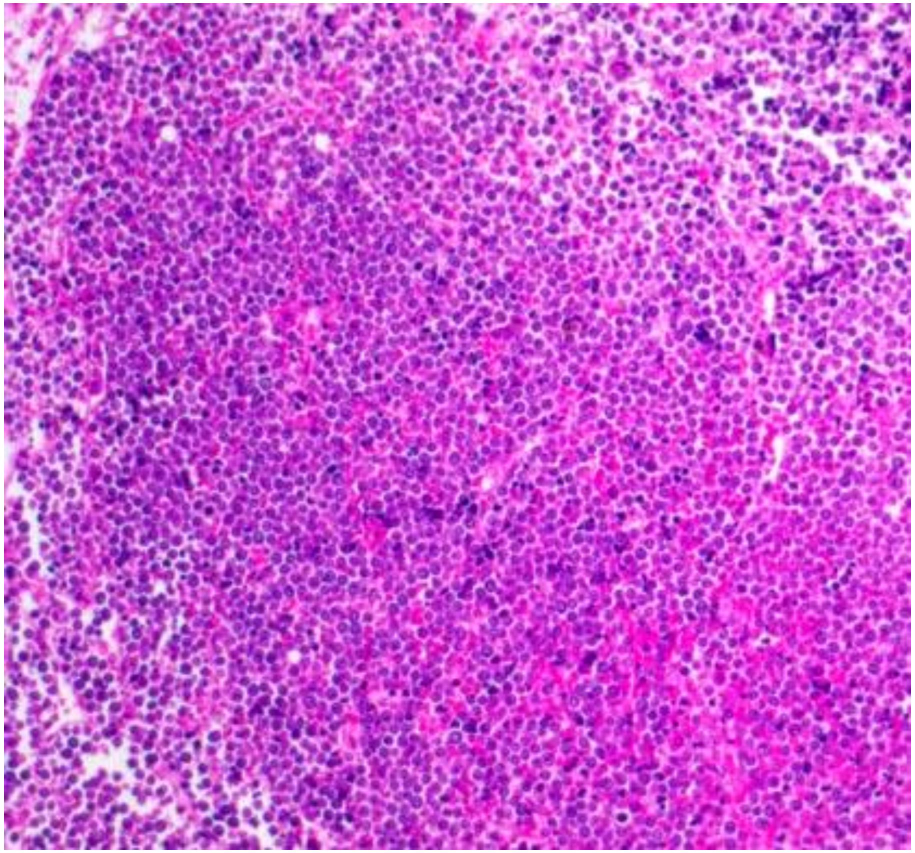
- Diagnostic Pitfalls
  - Mistake for carcinoma

Lymphoblastic lymphoma

- Males>females
- Children
- Immature T lymphocytes
- Immuno Tdt+,CD99+,CD3+

- DD from normal thymic tissue on small biopsy
  - Cytokeratin
  - PCR TCR

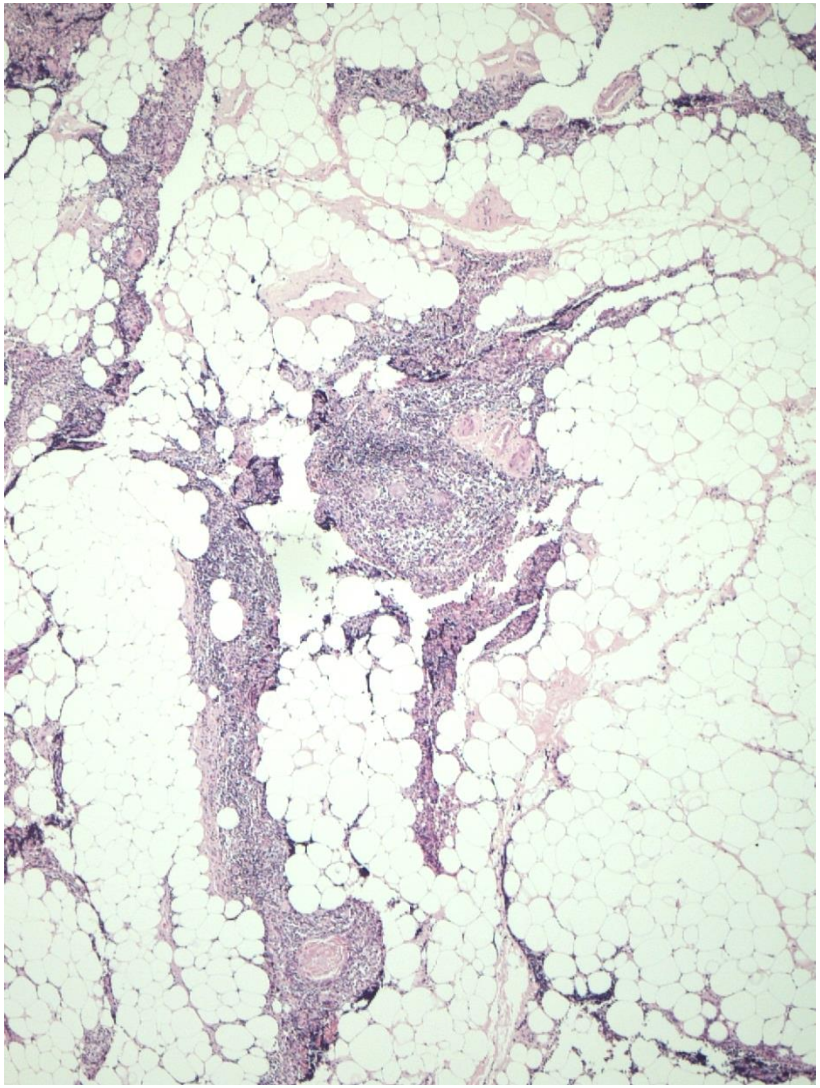
- Diagnostic Pitfalls
  - Mistake for normal thymus/other SRBCT
  - Can see circulating immature T cells with thymomas : misdiagnose as LL



PathoPic
www.unibas.ch/patho

Soft tissue tumours

- **Vascular** – Lymphangioma, haemangioma, angisarcoma
- **Fat** – lipoma, lipoblastoma, thymolipoma, liposarcoma
- **SM** – leiomyoma, leiomyosarcoma
- **Bone** – chondroma, chondrosarcoma
- **Other** – SFT (benign and malignant), mesothelioma

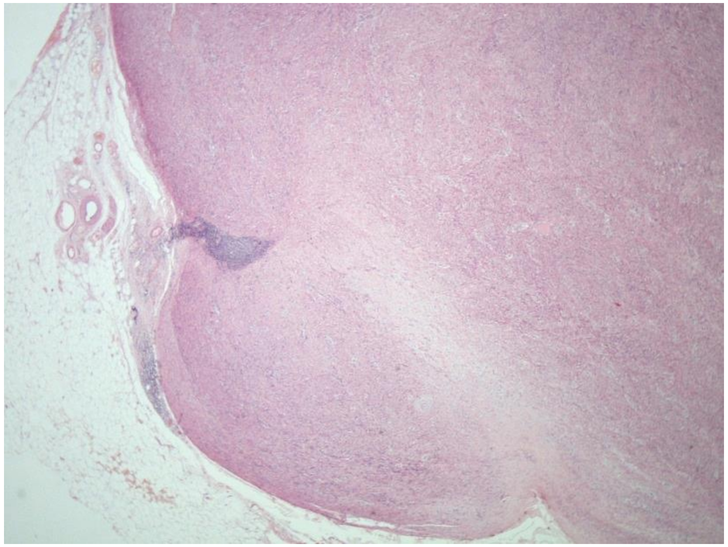


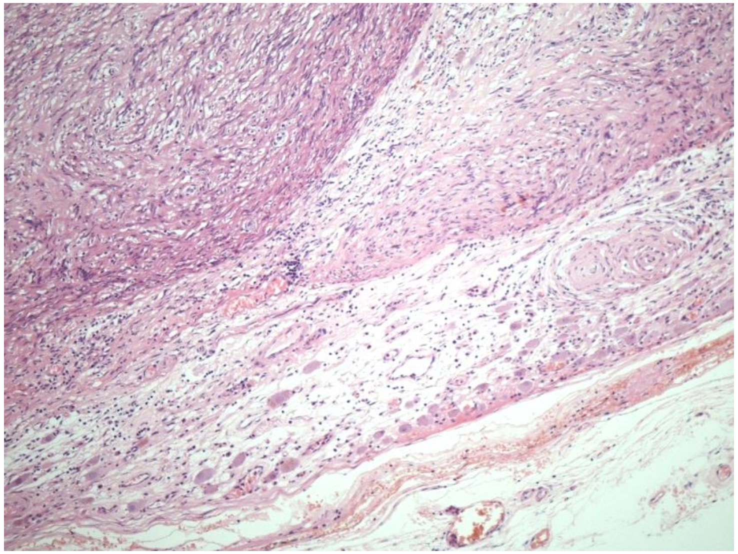
Neurogenic tumours

- Posterior mediastinum related to sympathetic chain and nerve roots

- Sympathetic nervous system
  - Neuroblastoma
  - Ganglioneuroblastoma
  - Ganglioneuroma

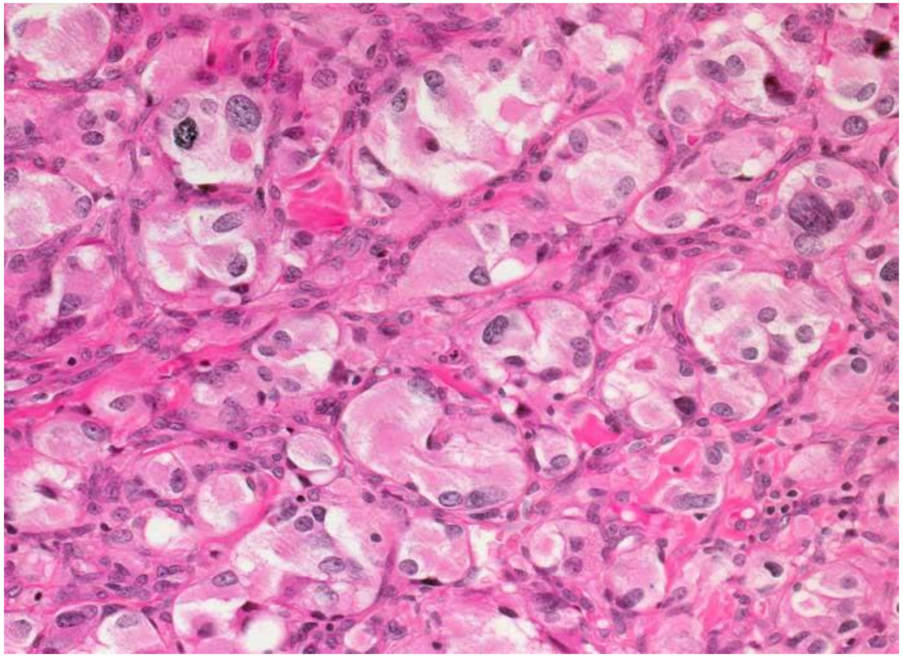
- Peripheral nerve sheath tumours
  - Schwannoma
  - Neurofibroma
  - MPNST – do novo, VonRecklinghausens, post-DXT





Mediastinal Paraganglioma

- Aorto-pulmonary:antero-superior mediastinum
- Aortosympathetic: posterior mediastinum
- Variably non-functioning
- Can be associated with Carney Triad
  - Paraganglioma, pulmonary chondroma, GIST
- Up to 40% behave aggressively
- Diagnostic pitfalls
  - Mistake as carcinoma



PathoPic
www.unibas.ch/patho

Tumours from other tissues

- **Ectopic tissue**
  - Thyroid lesions
  - Parathyroid lesions

- **Metastases**

- **Unusual tumours and tumour like conditions**
  - Meningioma
  - Chordoma
  - Myxoma
  - Granular cell tumour
  - Amyloid
  - Langerhans cell histiocytosis

Diagnostic Dilemmas

- Thymic hyperplasia vs thymoma
  - LP Architecture
- WHO subtyping of thymoma
  - Organotypic, cytology, ratio
- Thymoma vs thymic carcinoma
  - Overtly malignant
- Thymoma vs thymic neuroendocrine neoplasms
  - Immuno
- Thymoma vs lymphoma
  - Cytokeratin, TCR PCR
- Thymic epithelial tumors vs metastases and/or other primary tumors of the mediastinum
  - Clinical history/ radiology
  - Immuno: CD5, CD117

Recap

- Wide spectrum mediastinal lesions
- Often limited biopsy material
- Beware of diagnostic pitfalls
- Guidelines published for reporting of thymic tumours
- Further reading:
  - Histopathology Jan 2009 Review issue
  - Diagnostic Histopathology 2009 16;3
  - Journal Thoracic Oncology 2011 - ITIMG Guidelines
  - Journal Thoracic Oncology May 2014 ITMIG consensus statement Histology Thymomas
  - Journal Thoracic Oncology Sept 2014 IASLC/ITMIG proposals staging thymomas
  - TNM 8th Edn

END