

# Cytology of mediastinal lesions

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# Introduction

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The mediastinum can be affected by a heterogeneous group of disease that can cause significant diagnostic difficulties.

Lesions of the mediastinum can be explored by fine-needle aspiration biopsy (FNAB) obtained under radiographic guidance, either through a transthoracic, esophageal or bronchoscopic approach

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Aspiration biopsy of the mediastinum is rare

Imaging and clinical parameters are often diagnostic

Accuracy is approximately 85% for all mediastinal lesions

Aspiration biopsy of **metastatic mediastinal tumors** are more common

# Sensitivity and specificity

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## **Varies with location within the mediastinum**

- Anterior/pre-vascular = 80%/98%
- Posterior= 33%/95%
- Medial/vascular=100%

## **Varies for different classes of diseases**

- Thymoma = 87%/94%
- Germ cell tumor= 100%/99%
- Cyst= 25%/100%



# pattern recognition approach

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- 6 identifiable patterns:
- Spindle shaped cells (Thymoma Type A)
- Lymphocyte-rich (Thymoma B1)
- Epithelioid-rich (Thymoma B2 and B3)
- Small blue cells
- Inflammatory
- Cystic
- Each pattern carries a set of differential diagnosis.

# Spindle shaped cells

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## Differential Diagnosis

Spindle-cell thymoma (W.H.O. type A)

Spindle-cell carcinoid tumor

Schwannoma (posterior mediastinum)

Sarcoma or soft tissue tumor

Mesenchymal component of teratoma

# Case 1

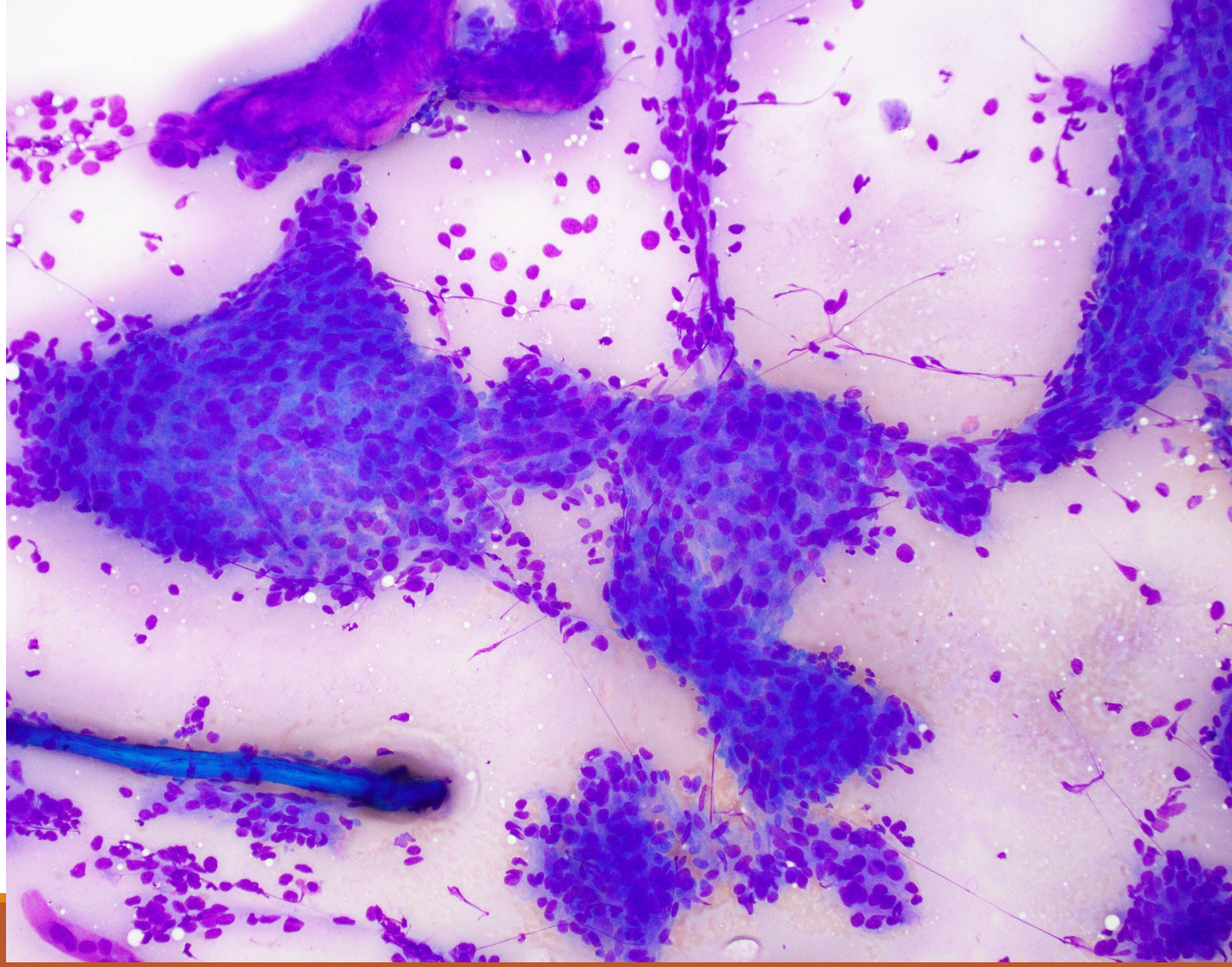
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44 year old man, former smoker with a 34 packs/year.

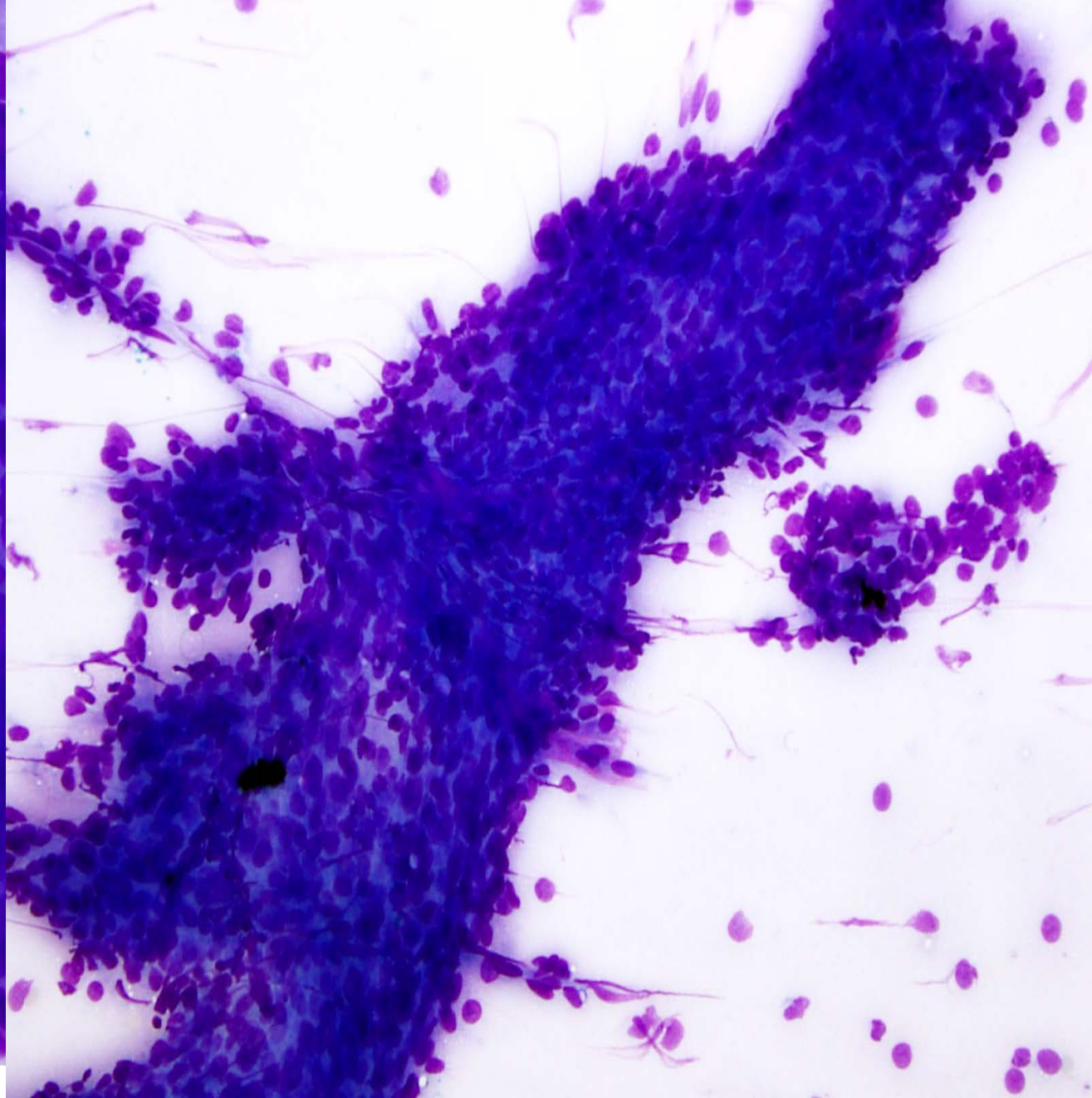
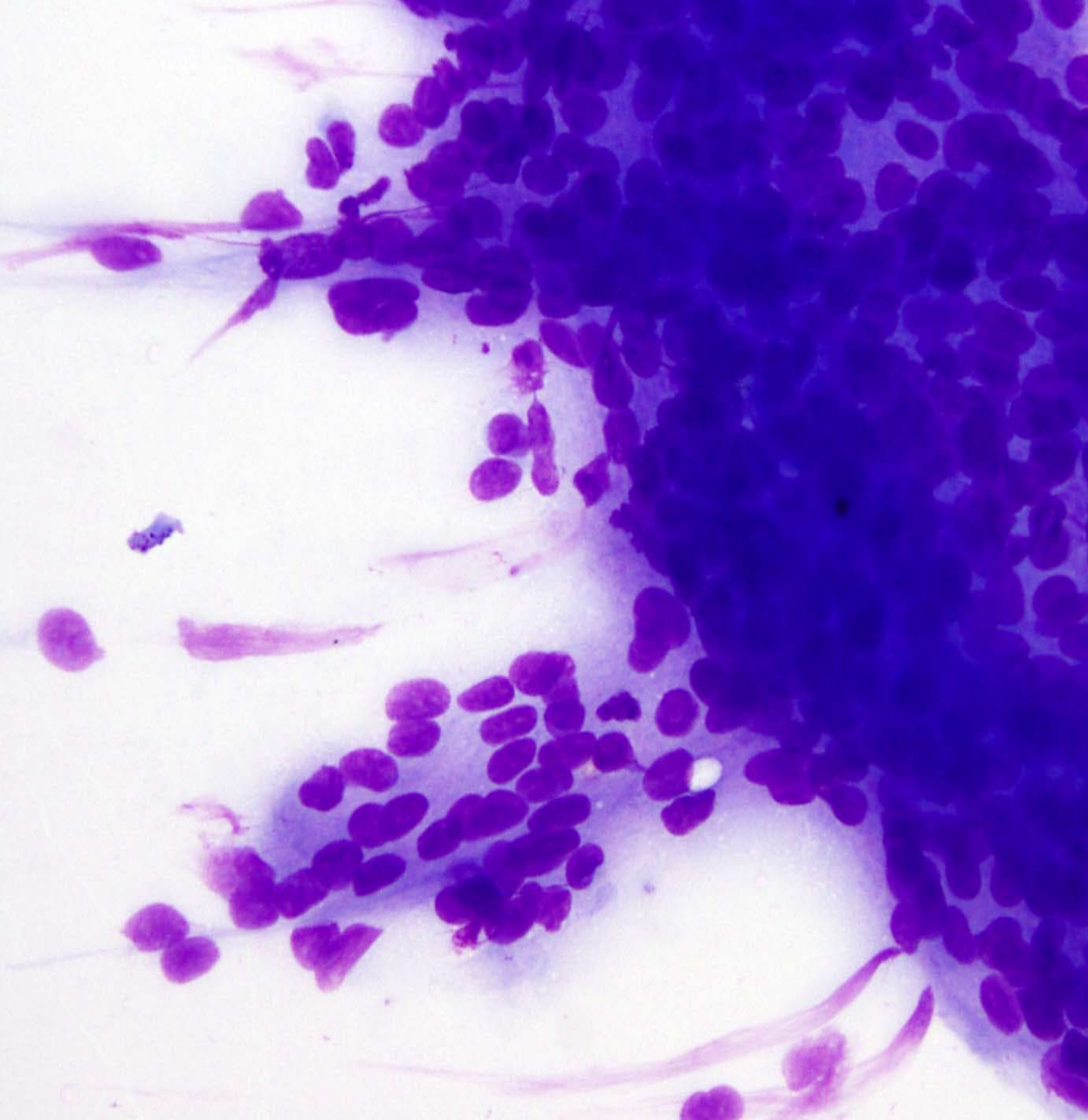
Presents with an anterior mediastinal mass, multiple pleural nodules and pleural effusion.

Aspiration biopsy of a pleural nodule was performed.





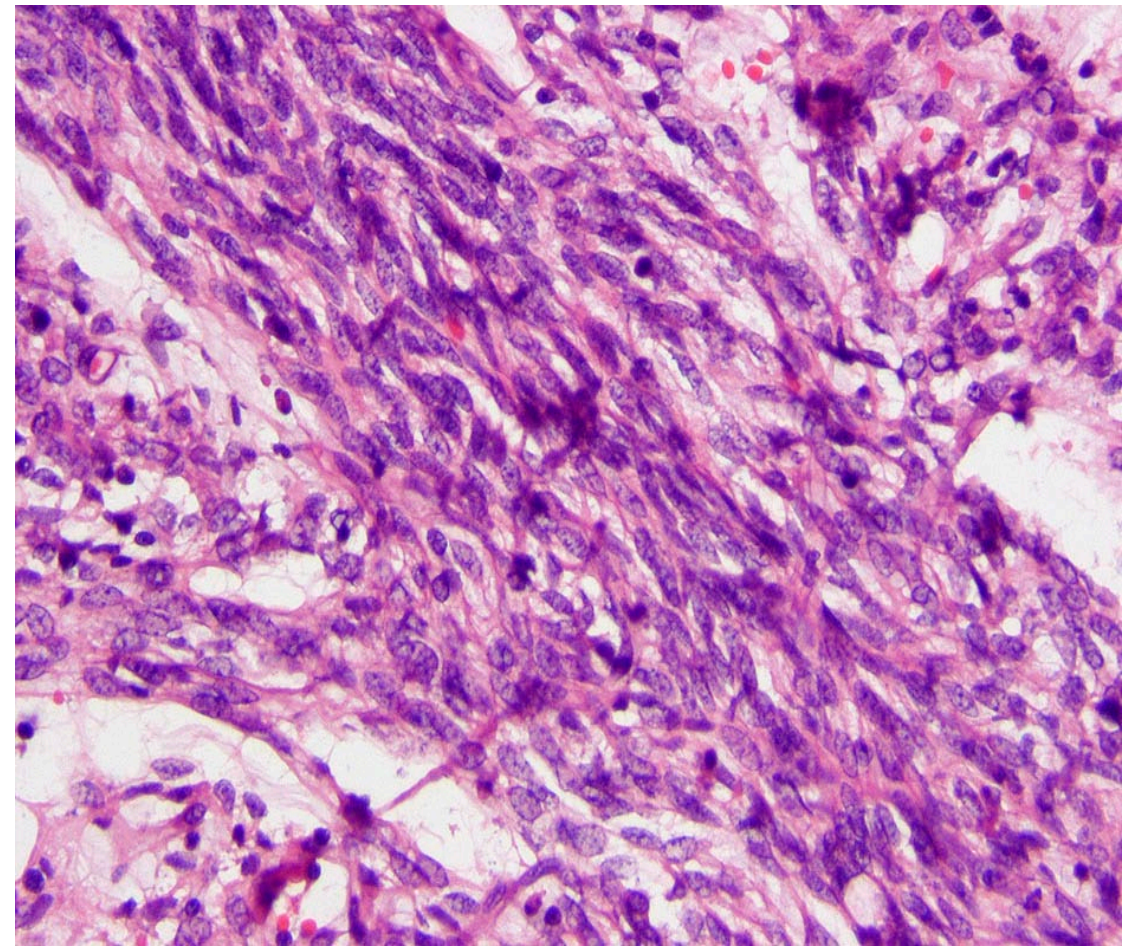
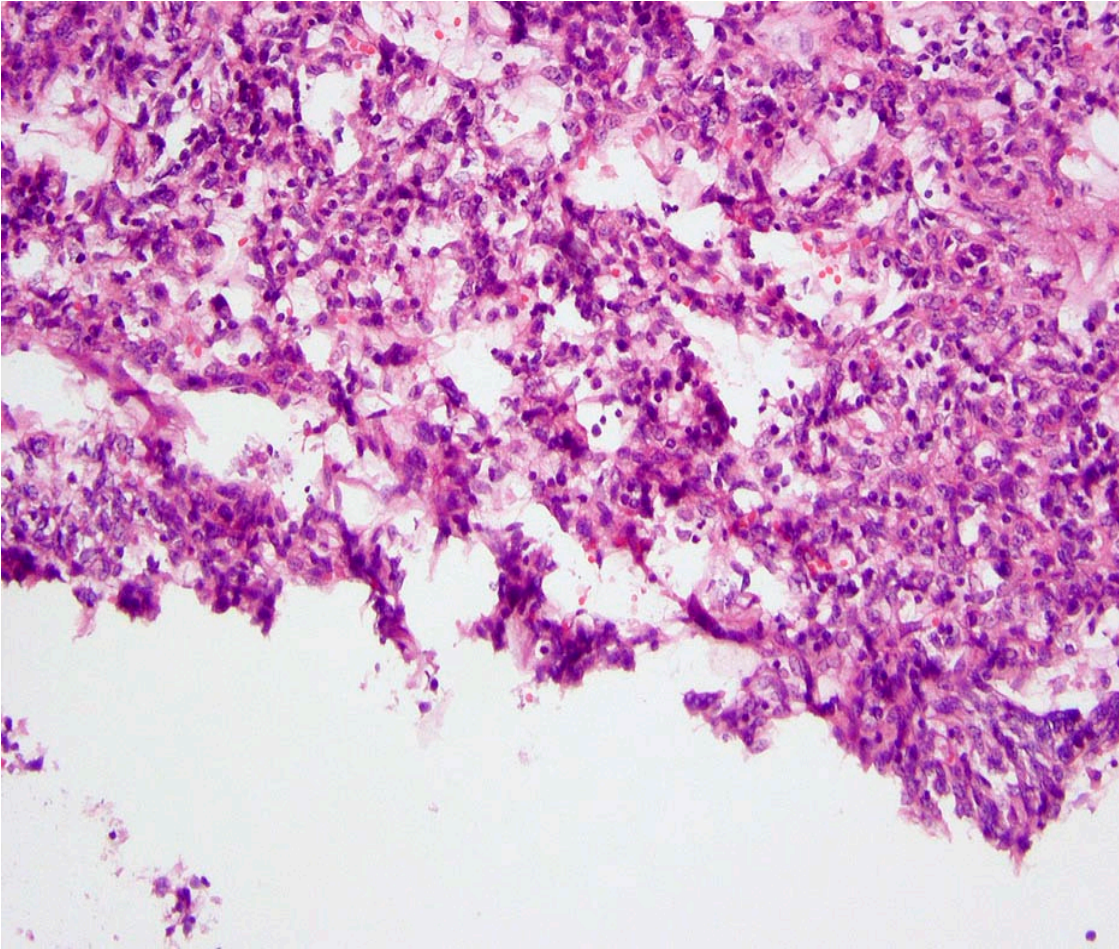






# Cell block material

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# IHC

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Positive for pan-cytokeratin and p63

Negative for WT-1, Calretinin, TTF-1, cytokeratin 7, neuroendocrine markers, CD34, STAT6, and other organ specific markers.

# Thymoma type A

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Cohesive tissue fragments.

Elongated cells embedded in a metachromatic matrix (Diff-Quick)

Presence of lymphocytes in the background

Absence of lymphocytes do not exclude the diagnosis



# Thymoma type A

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Tumor cells are positive for pan-cytokeratin

Can be positive for CD56 (but negative for other NE markers)

If present, lymphocytes are immature thymic lymphocytes (CD5, CD99, TdT positive)

# Lymphocyte-rich tumors

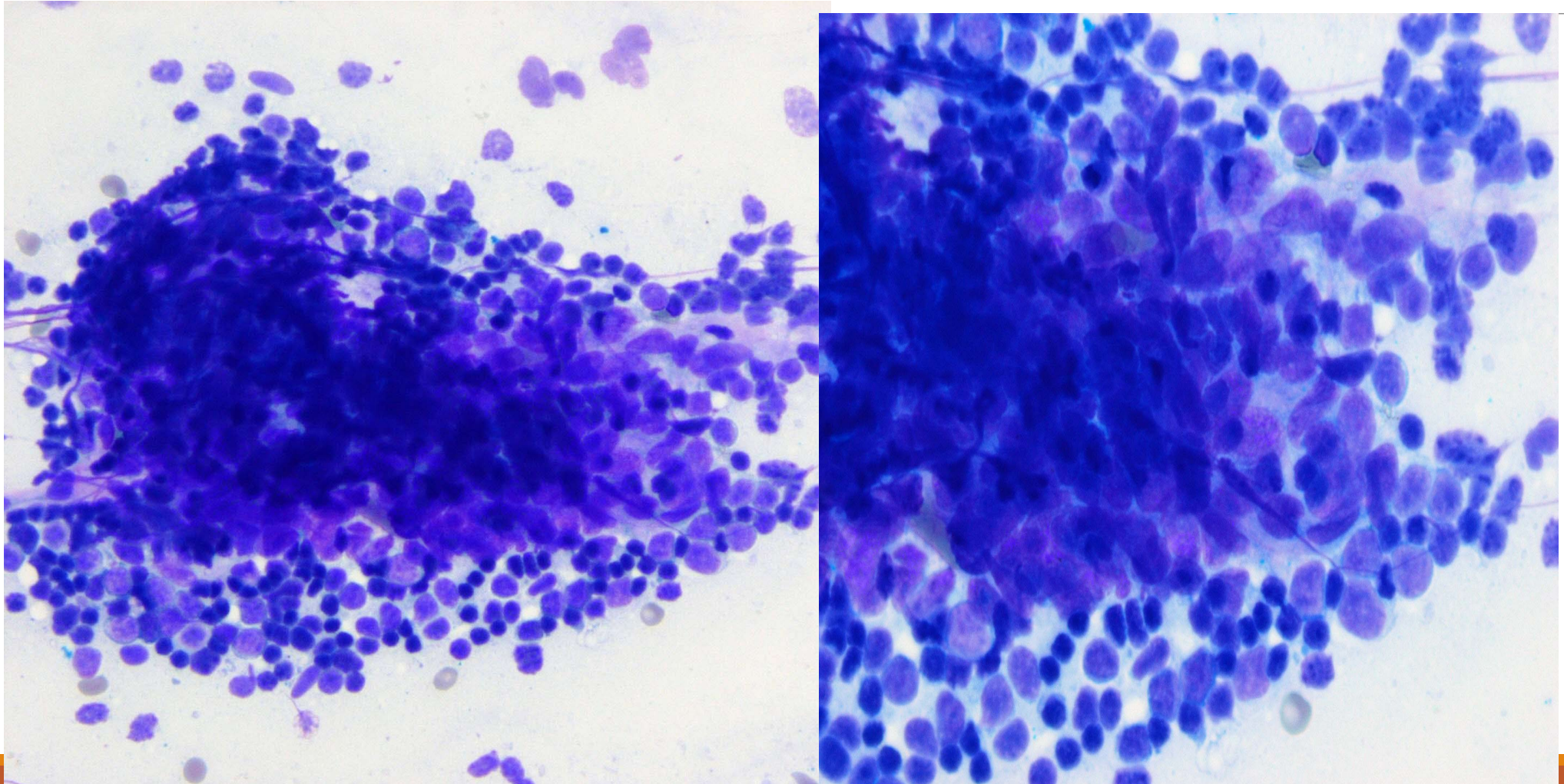
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Lymphoma

Thymoma (W.H.O. type B1)

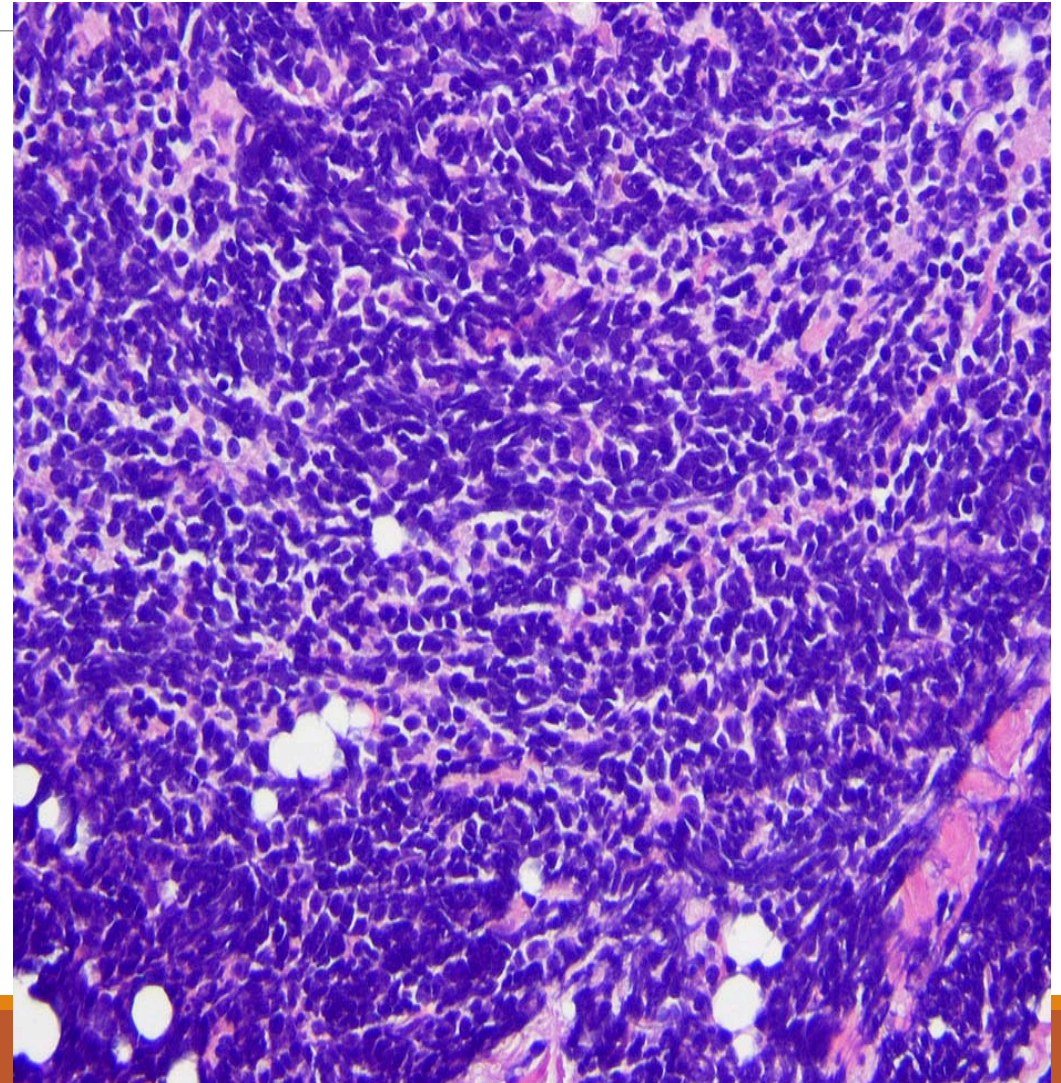
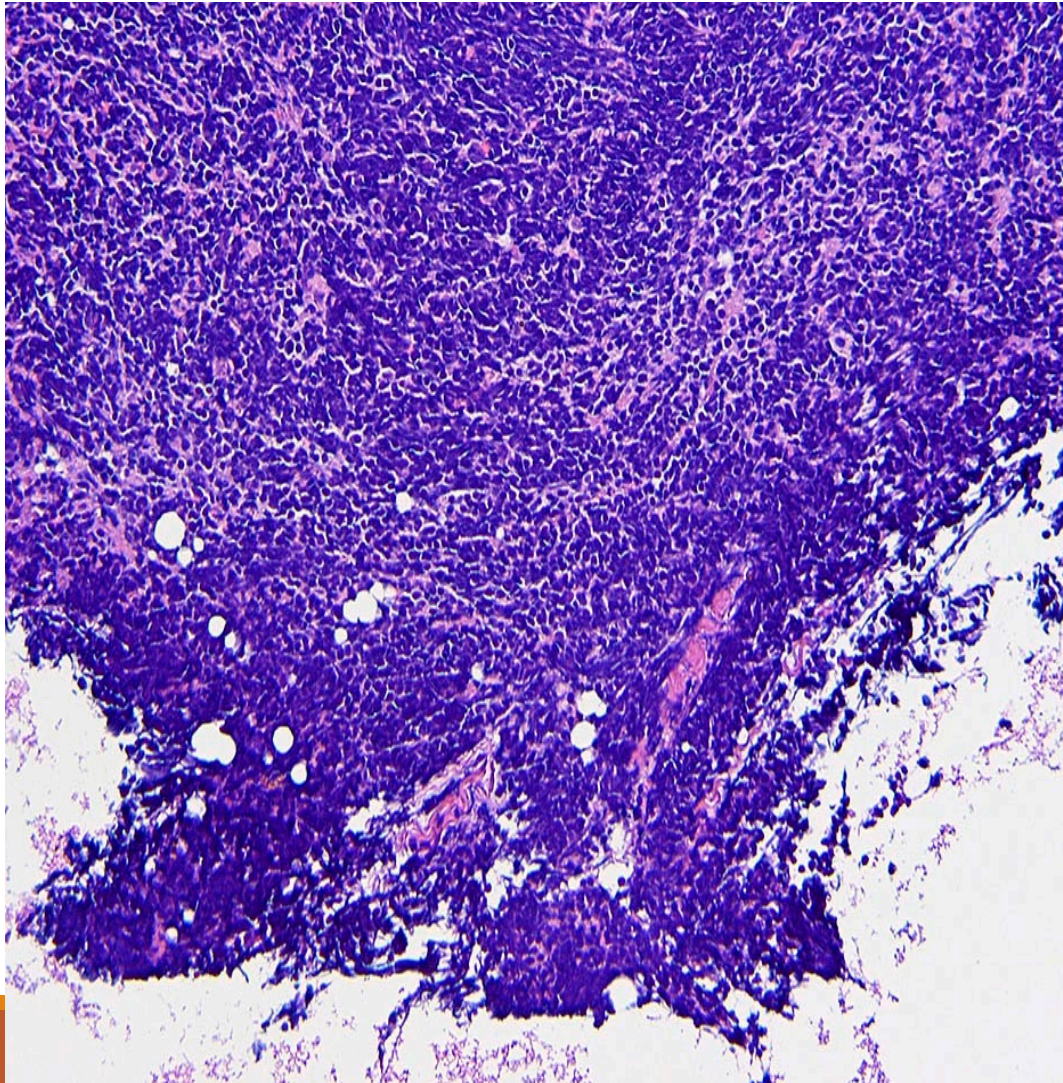
Thymic hyperplasia

# Case 2 FNA of a mediastinal mass on a 78 year old man



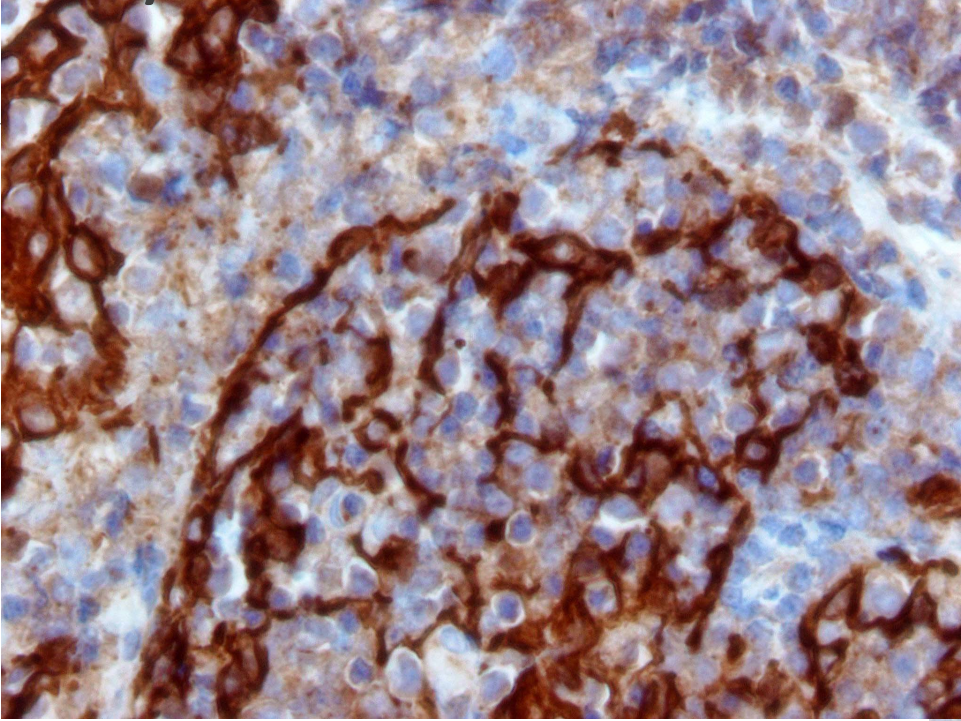


# Excision



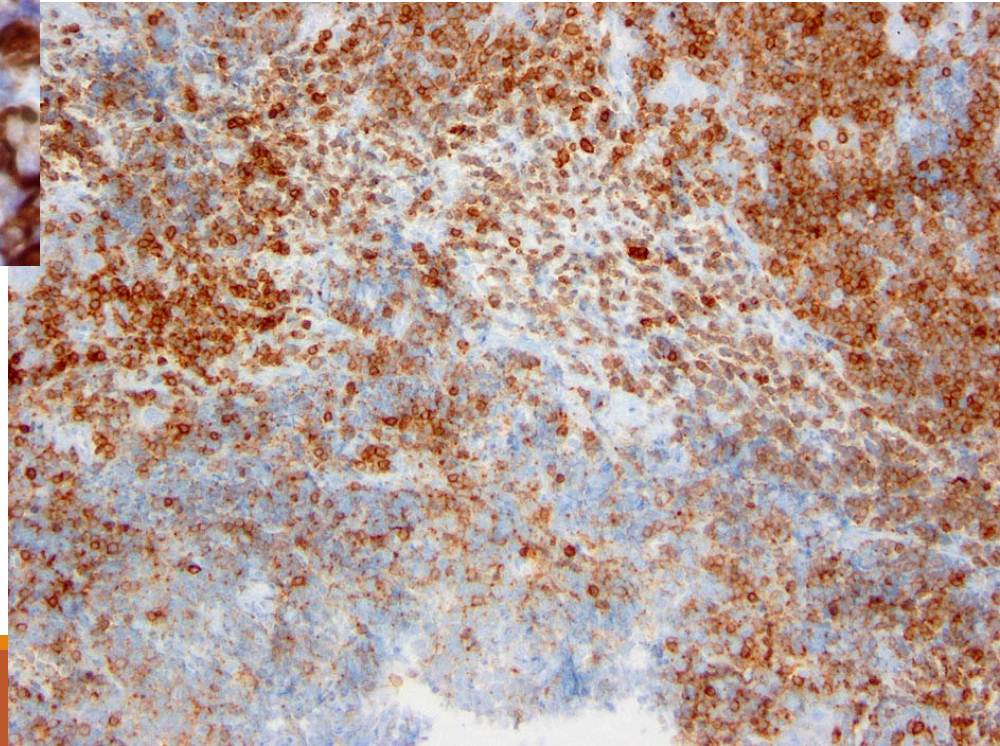


# B1 Thymoma



Cytokeratin AE1/AE3

CD5



# B1 thymoma

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Predominance of heterogeneous lymphocytes

Small discrete clusters that resembles “lymphoid tangles” containing cells with open chromatin, nucleoli can be prominent or not

Flow cytometry shows a predominance of T lymphocytes

Immunohistochemical stains for keratin show a network of keratin positive cells, lymphocytes are immature T cells (CD3, CD5, CD4, CD8, TdT, CD99, CD1a positive)

# Thymic Hyperplasia

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Follicular hyperplasia is most common

Often associated with autoimmune disorder or history of chemotherapy

Can be very difficult to differentiate in an aspiration biopsy from a B1 Thymoma

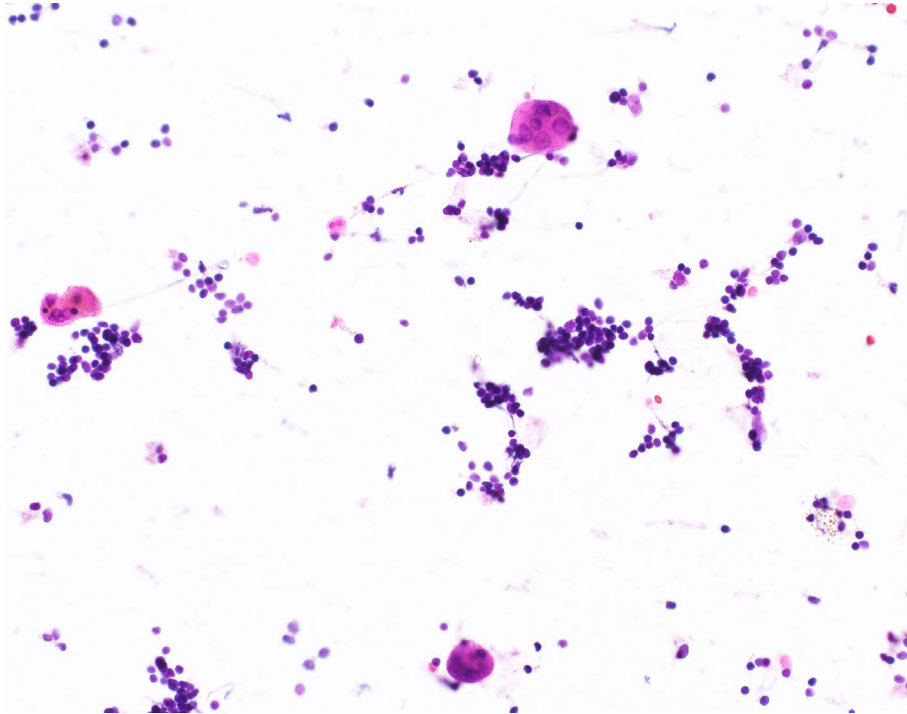
MRI is the best pre-surgical test for the diagnosis

Often scant cellular smears, Hassall's corpuscles are easier to find, but are not specific

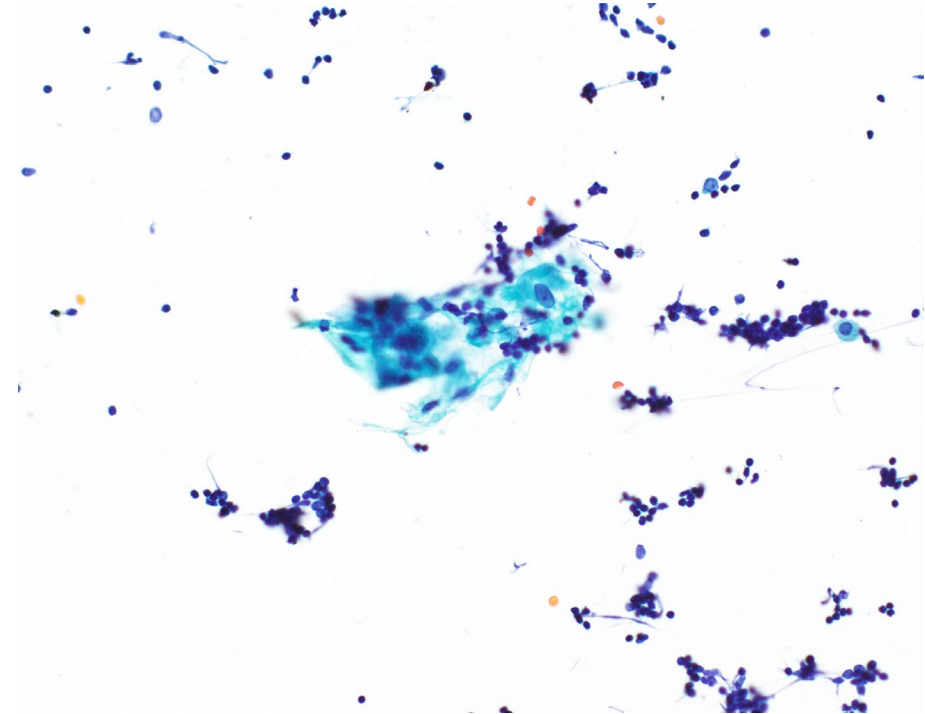
# Thymic hyperplasia

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HASSALL'S CORPUSCLES H&E



HASSALL'S CORPUSCLES PAP

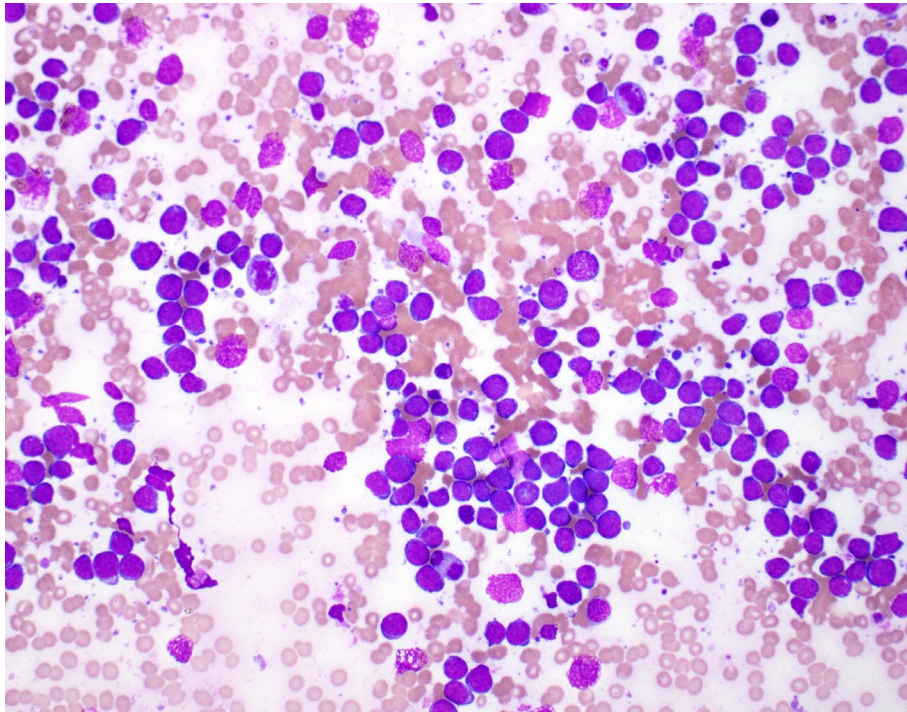




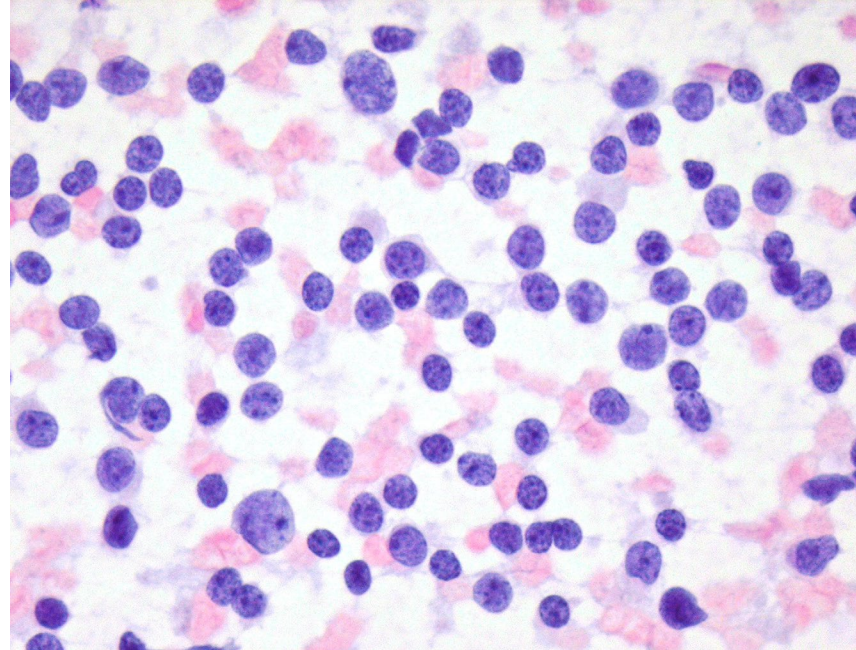
# Lymphoma

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LARGE B-CELL LYMPHOMA



ACUTE LYMPHOBLASTIC LYMPHOMA



# Epithelioid-rich pattern

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Metastatic carcinoma

Thymoma, type B2-B3

Thymic carcinoma

Carcinoid tumor

Germ cell tumor

# Case 3

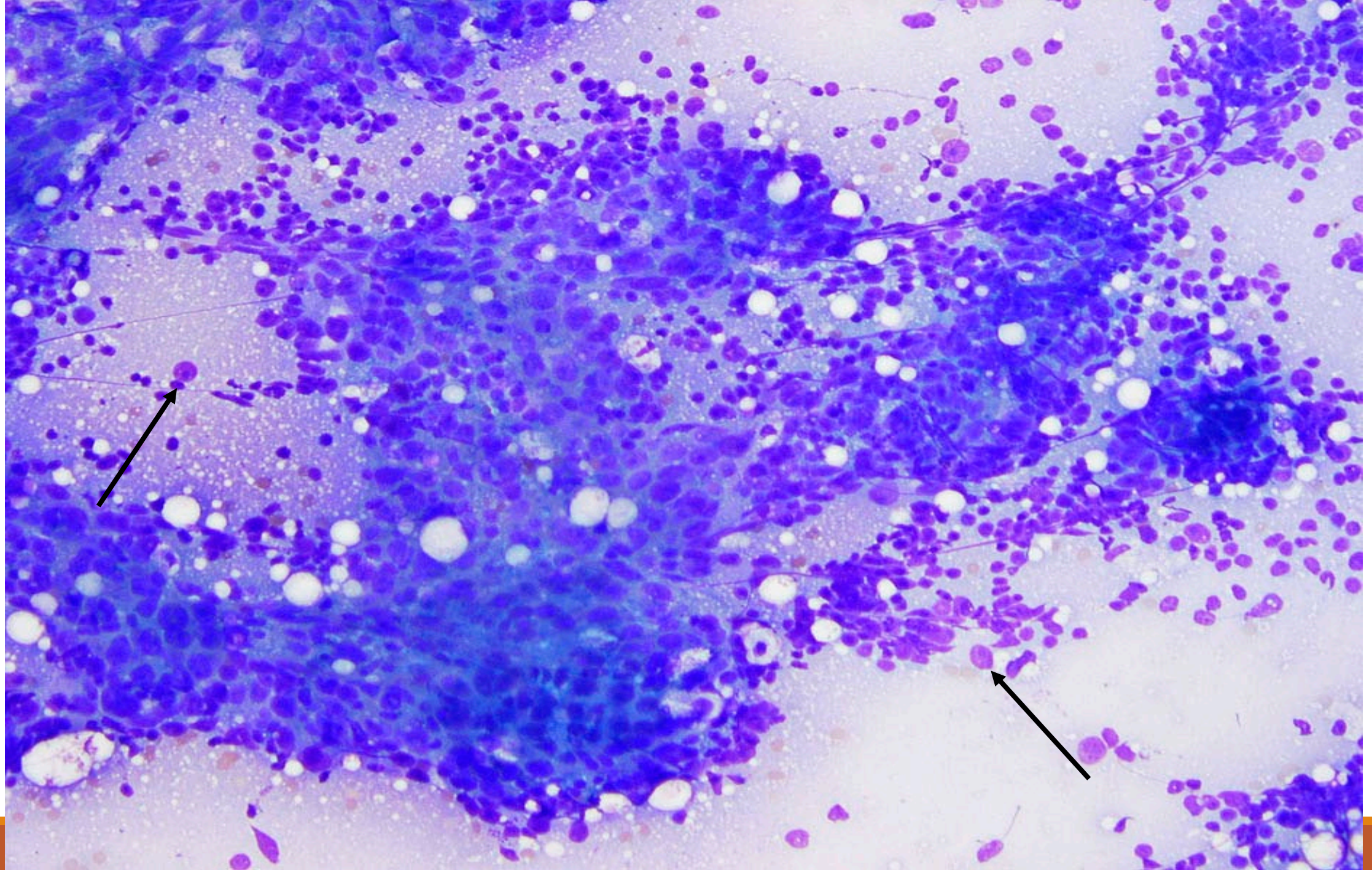
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57 year old woman, presented with chronic cough.

A CT-Scan showed a large mediastinal mass with pericardial effusion

An aspiration biopsy of the mediastinal mass was performed





# IHC work up

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**Thymoma-** keratin and p40+, immature lymphocytes TdT +

**Thymic carcinoma-** keratin, p40, CD5, CD117+

**Metastatic carcinoma and germ cell tumor-** Clinical history and target IHC

**Metastatic squamous cell carcinoma**



# FNA – Thymoma Type B2-B3

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Moderate to highly cellular smears

Duo population of epithelial and lymphoid cells  
**(classical cytologic features)**

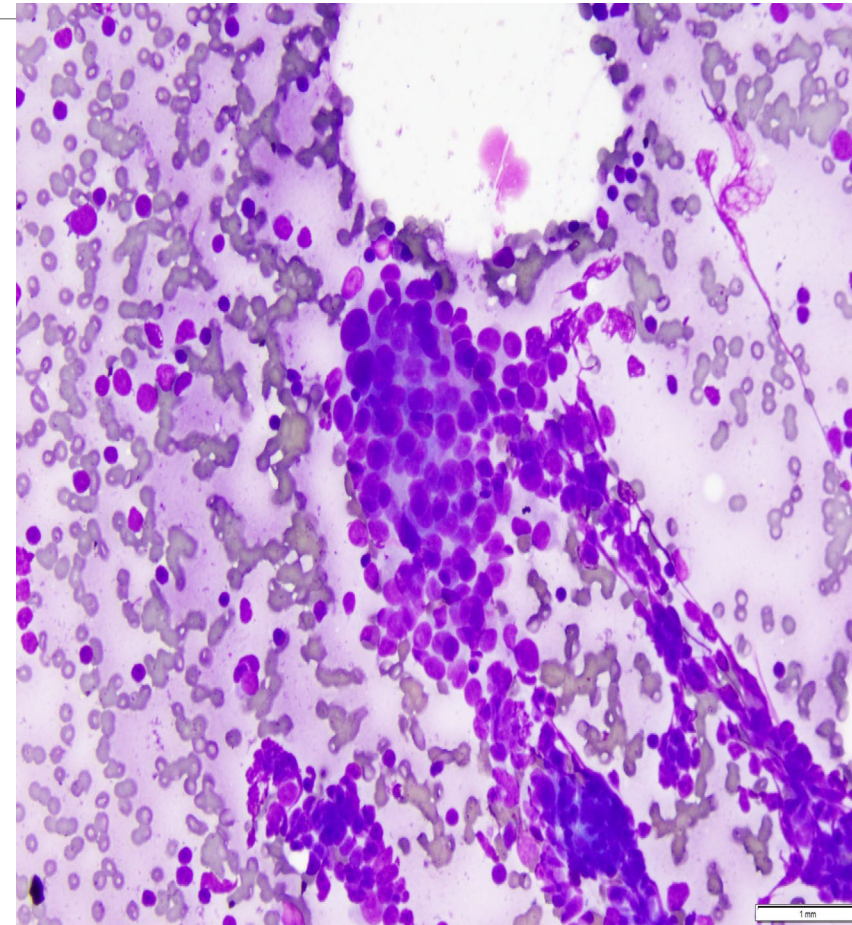
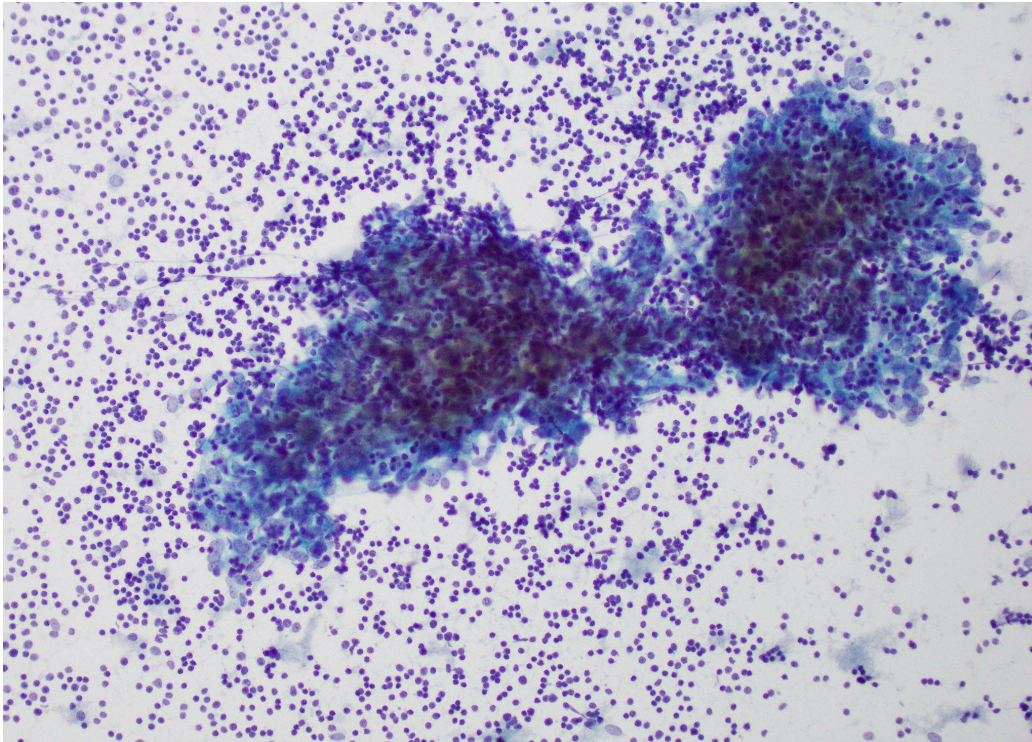
Epithelial arranged in cohesive tri-dimensional clusters

Open chromatin with delicate or prominent nucleoli

Can be confused with carcinoma!

# Thymoma B2 and B3

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# Thymic carcinoma

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Positivity for CD5 and CD117 in epithelial cells (40-60% of thymic carcinomas).

## **Lymphocytes are not immature T-cells**

Diverse differentiation that resembles carcinomas arising anywhere else

**Examples:** squamous cell carcinoma, basaloid carcinoma, clear cell carcinoma, mucoepidermoid-carcinoma, adenocarcinomas, sarcomatoid, and NUT carcinoma



# metastatic squamous cell carcinoma

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Almost impossible to differentiate a Thymic carcinoma (SQCC) from a SQCC from another site (lung)

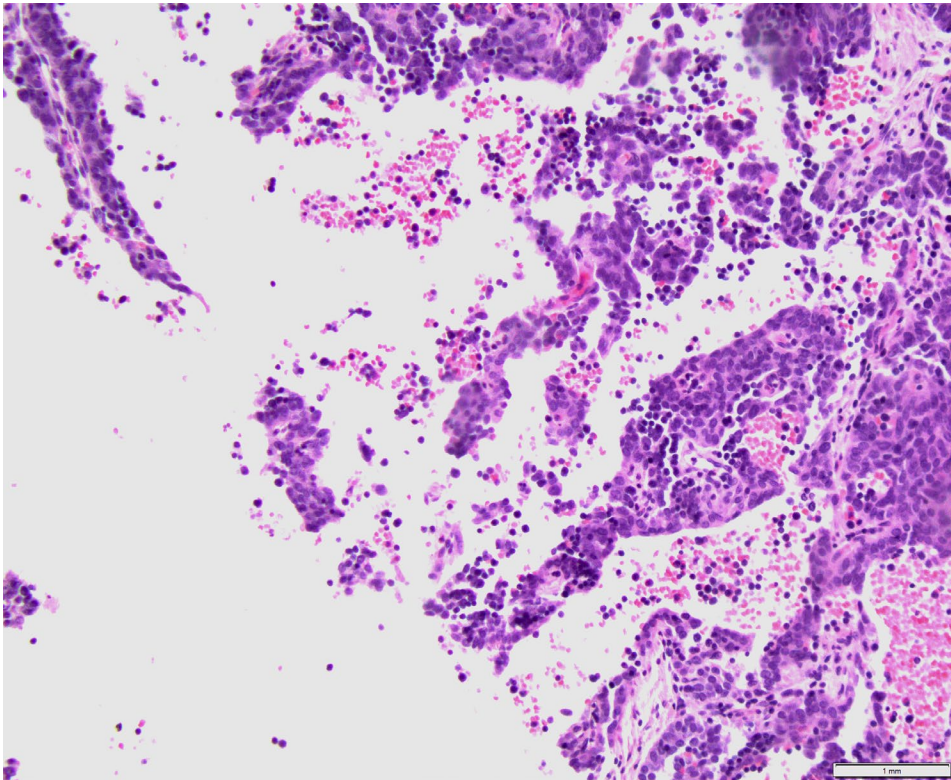
CD5 and CD117+ is seen in about 60% of TC, but CD117 can be seen focally in other SQCC

Correlate with history and Imaging studies

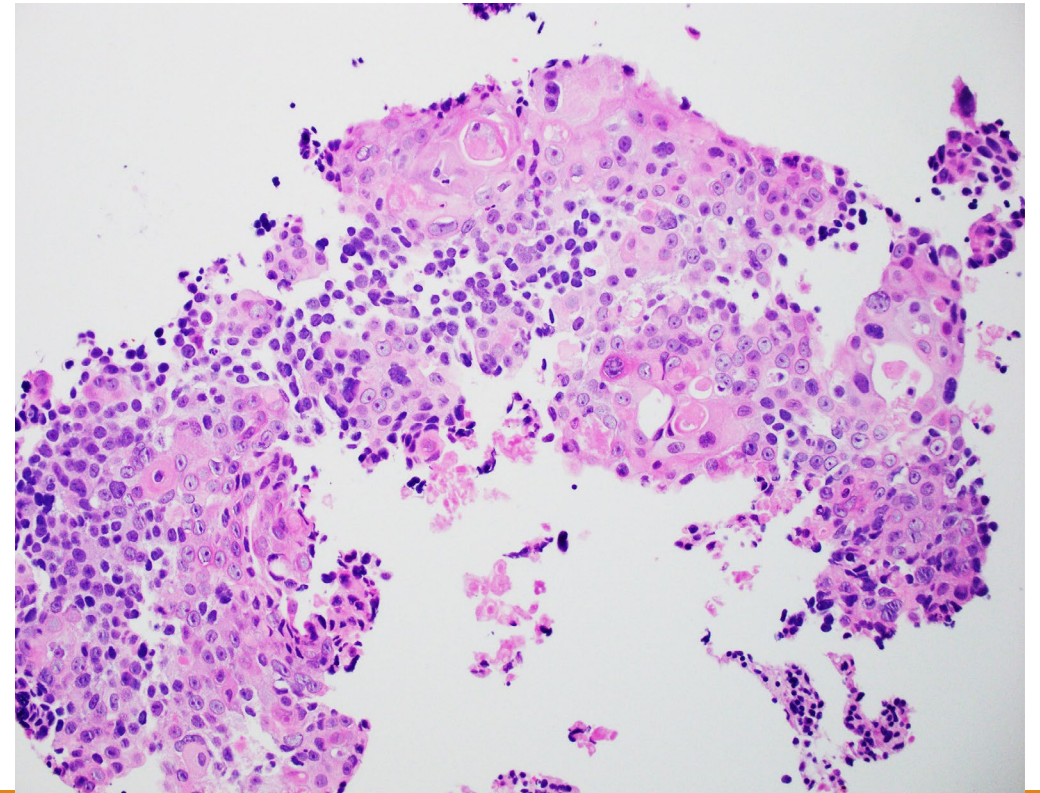
# Pitfalls

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THYMOMA



THYMIC CARCINOMA



# Take home message

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- Thymomas often metastasizes to the pleura
- Thymoma should always enter into the differential diagnosis when an anterior mediastinal mass is present.
- Thymic tumors are positive for p63, p40, and cytokeratins.
- Always look for thymic lymphocytes (TdT, CD99, CD1a positive)

# Take home messages for thymoma

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Thymomas can have different cytologic patterns, which is similar to histologic classification

**There is no need to classify thymomas into subtypes in cytology**

Correct diagnosis and disease stage are enough for clinical management

# Case 4

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22 year old man, non-smoker

Presented with fever, cough, and malaise

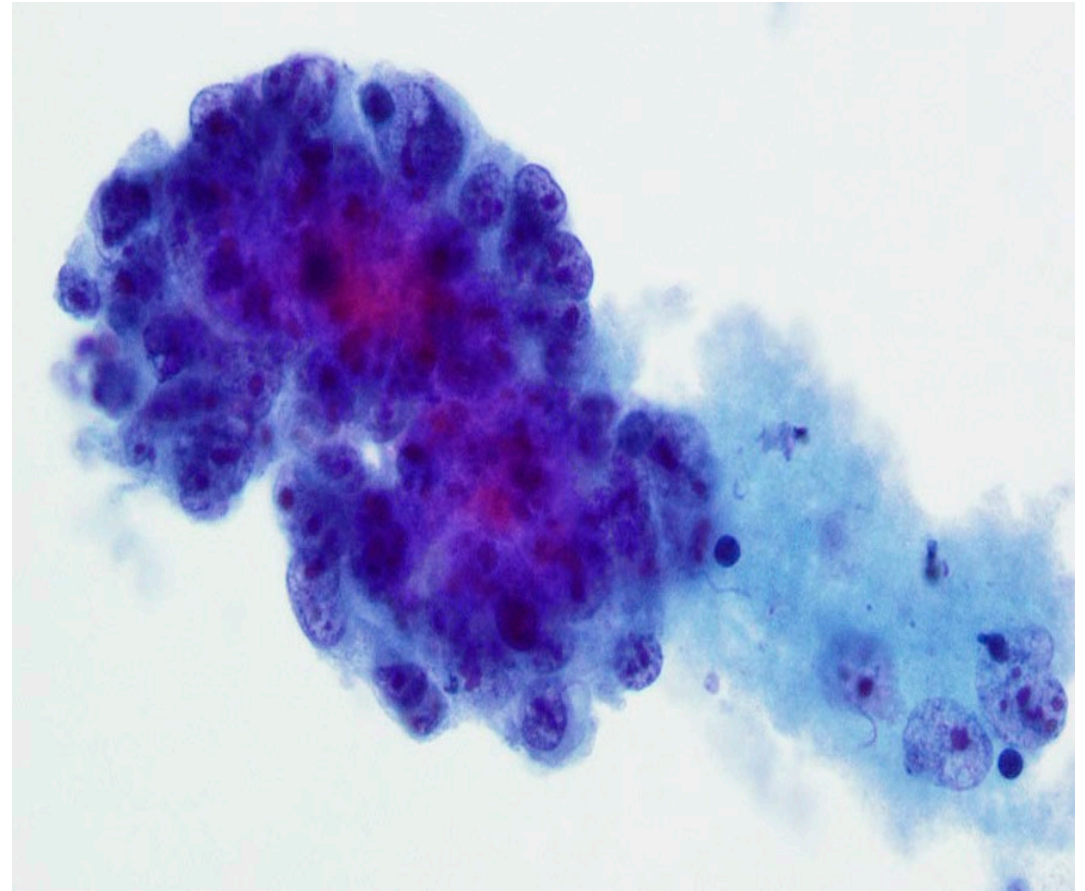
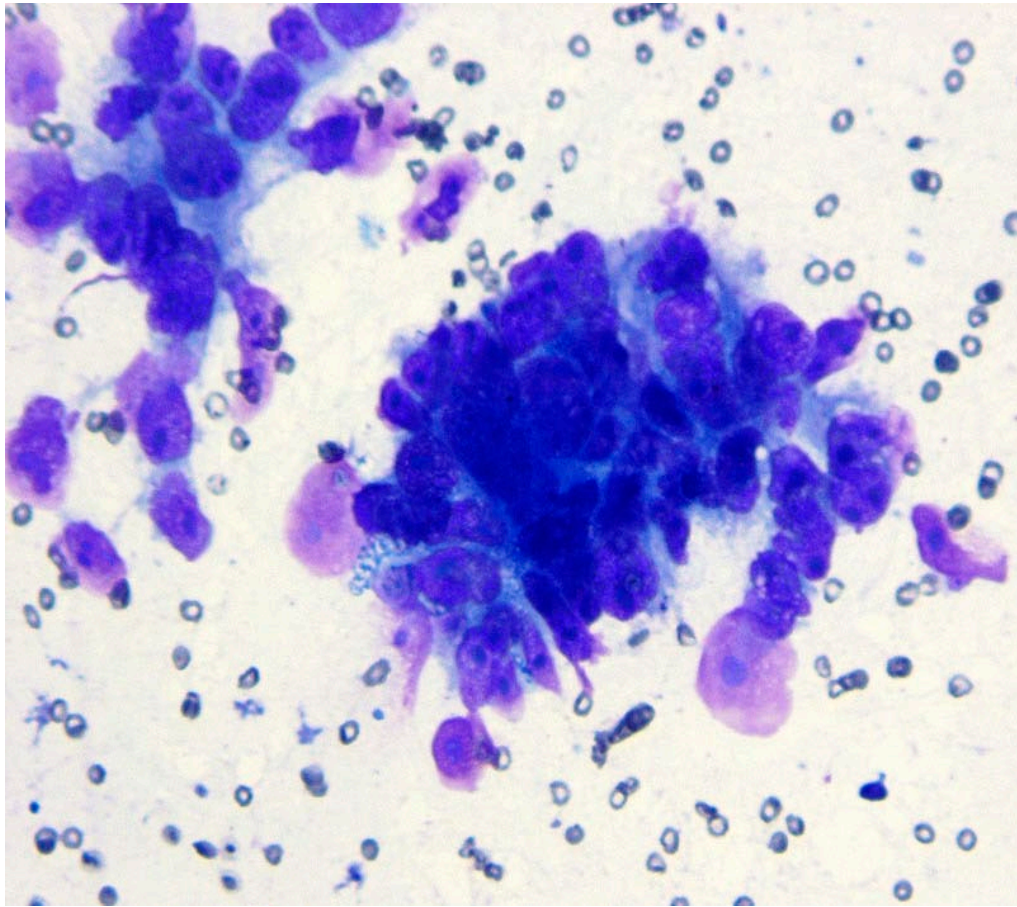
A Chest X-Ray was performed to rule out pneumonia

A large mediastinal mass was found incidentally

An aspiration biopsy of the mass was performed



# FNA of a mediastinal mass

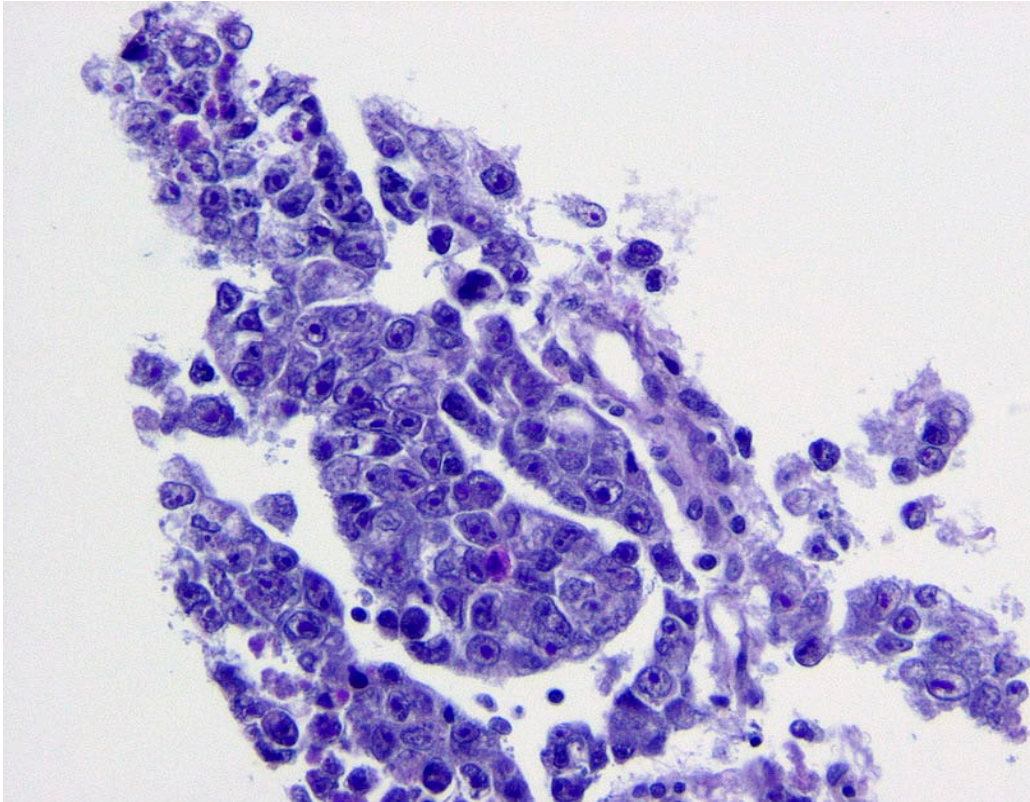




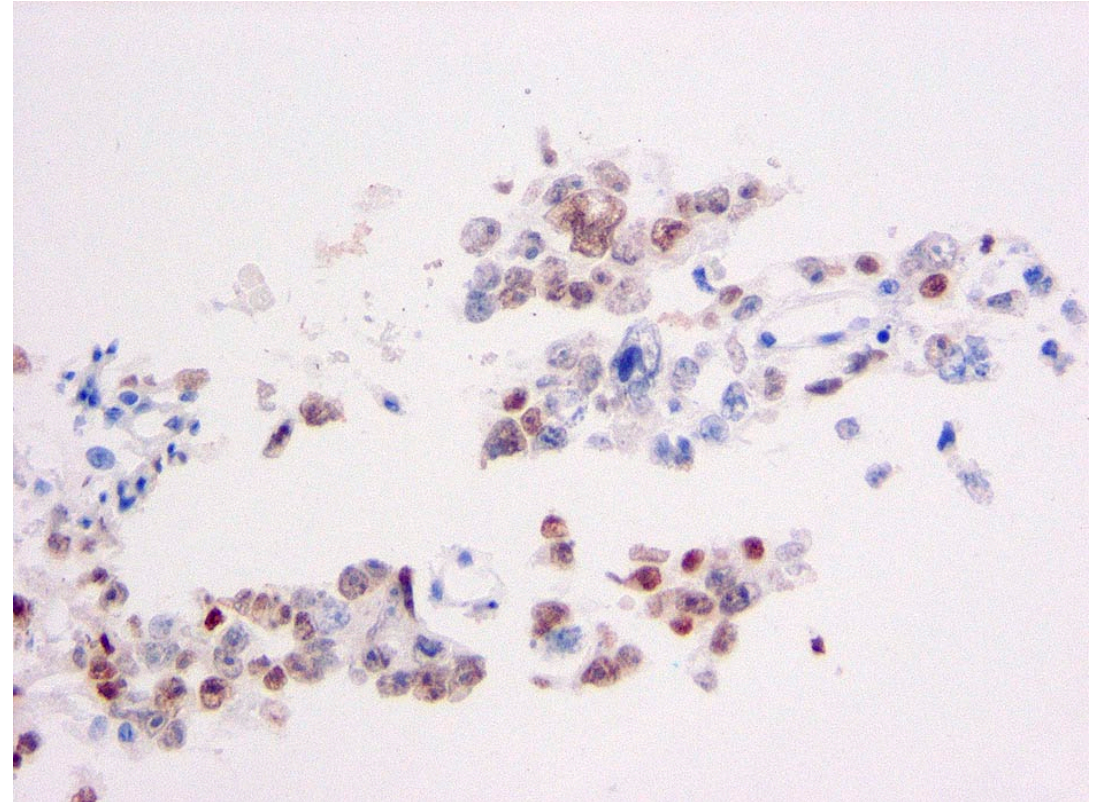
# Embryonal carcinoma

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CELL BLOCK



POSITIVE FOR OCT 4



# Germ Cell Tumors

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Rare

Mediastinal germ cell tumors account for less than 5% of all germ cell tumors

The components of a germ cell tumor is important for the management of the patient

Not all components of a GCT may be sampled in an aspiration biopsy.

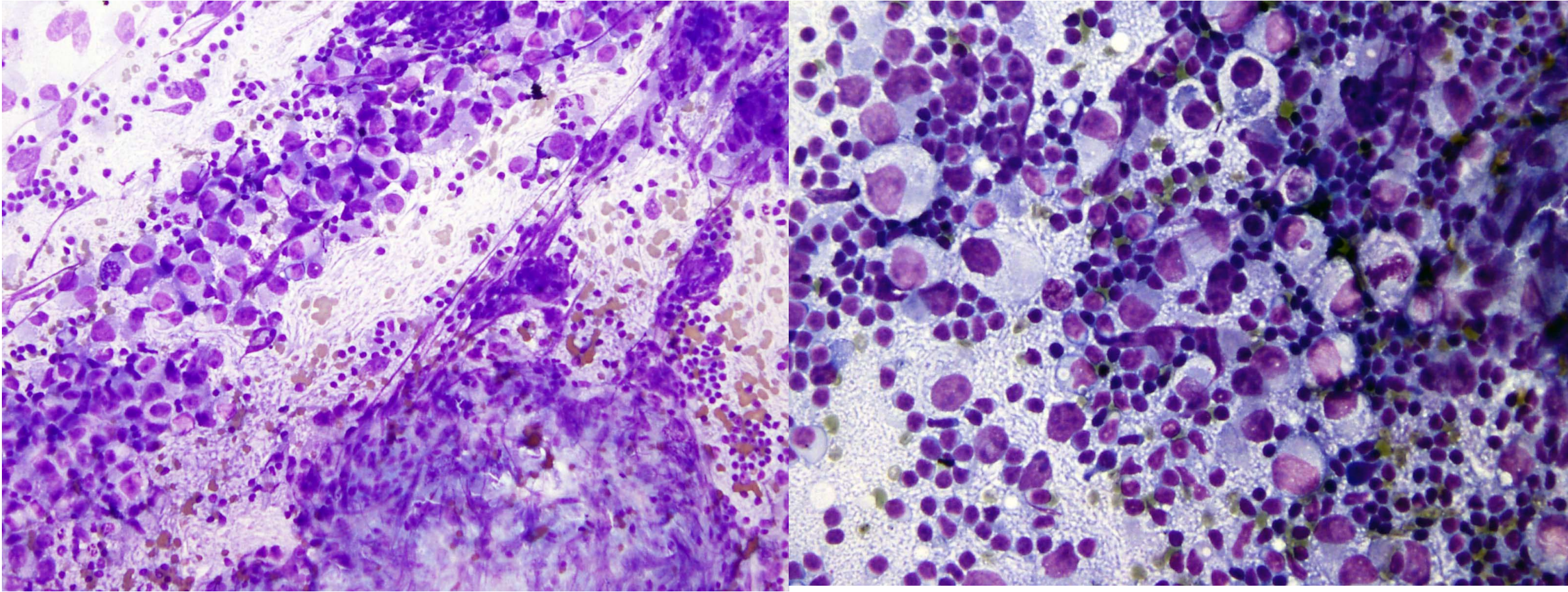
There is good correlation with serum markers.



Germ cell tumor type	Cytokeratin	OCT4 (OCT3/4)	SALL4	CD117	CD30	AFP	b HCG	Glypican3
Seminoma	Neg*	+	+	+	Neg	Neg	Neg	Neg
Embryonal carcinoma	+	+	+	-/+	+	+/-	Neg	Neg
Yolk sac tumor	+	Neg	+	+/-	Neg	+	Neg	+
Choriocarcinoma	+	Neg	+ (mononuclear trophoblast)	Neg	Neg	Neg	+	+ (syncytiotrophoblast)
Teratoma	+ (epithelial component)	Neg	-/+ (focal staining in enteric glands; and primitive neuroepithelium and blastema-like stroma of immature teratoma)	-/+	Neg	-/+ ***	Neg	+/-

# FNA mediastinal mass in 20 year old man

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# IHC

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Tumor cells are positive for:

SALL 4

D2-40

CD117



# Seminoma, mediastinal

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Pure seminoma is rare

Often part of a mixed germ cell tumor

Post-pubertal occurrence

40% metastasize to lymph nodes and lung

Histologic diagnosis	Therapeutic option
Seminoma	Chemotherapy
Yolk sac tumor	Chemotherapy, followed by resection of remaining tumor mass
Embryonal carcinoma	Chemotherapy, followed by resection of remaining tumor mass
Choriocarcinoma	Chemotherapy, followed by resection of remaining tumor mass
Mixed germ cell tumor	Chemotherapy, followed by resection of remaining tumor mass
Mature teratoma	Surgical resection
Immature teratoma	Surgical resection

# Pitfalls for the diagnosis of germ cell tumors

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Mix germ cell tumors are more common

Always correlate with serum markers that may indicate another component

Embryonal carcinoma and Yolk Sac tumors mimic high grade carcinomas.

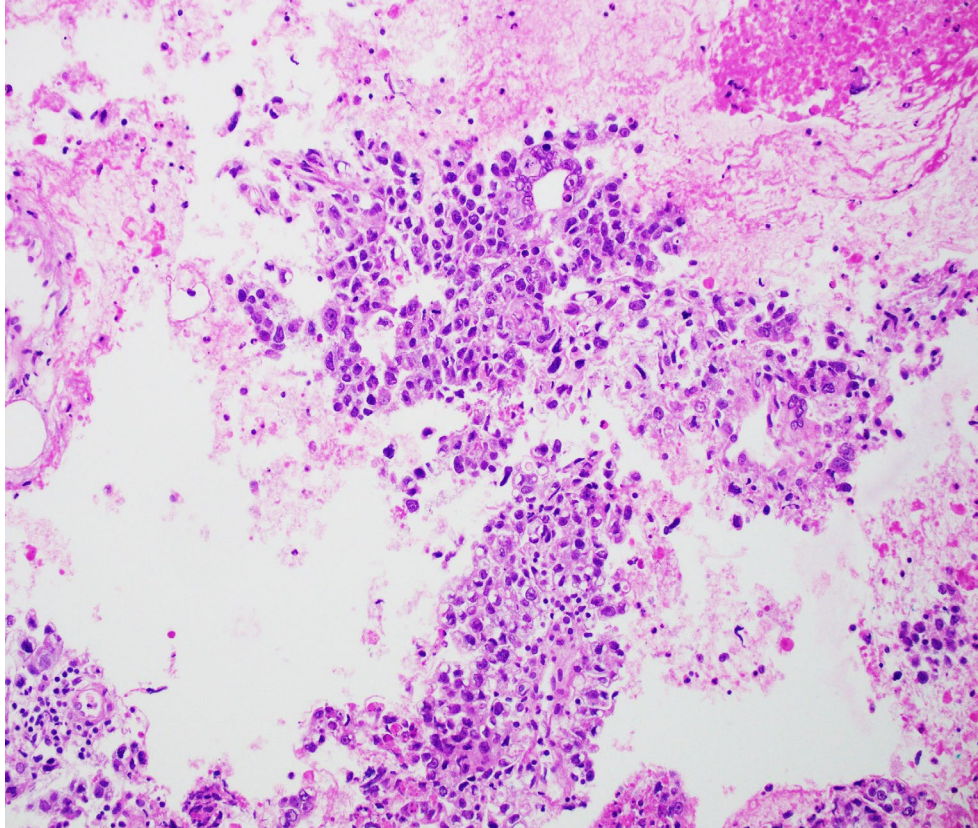
Clinical correlation is very helpful!



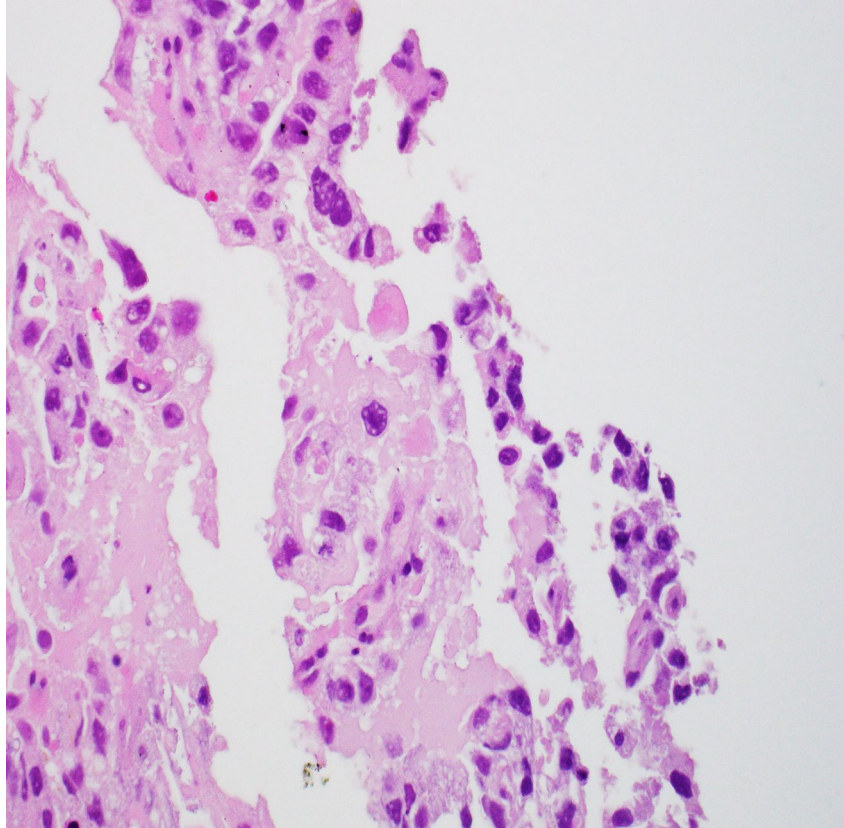
# Germ cell tumor

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YOLK SAC TUMOR



EMBRYONAL CARCINOMA



# Inflammatory pattern

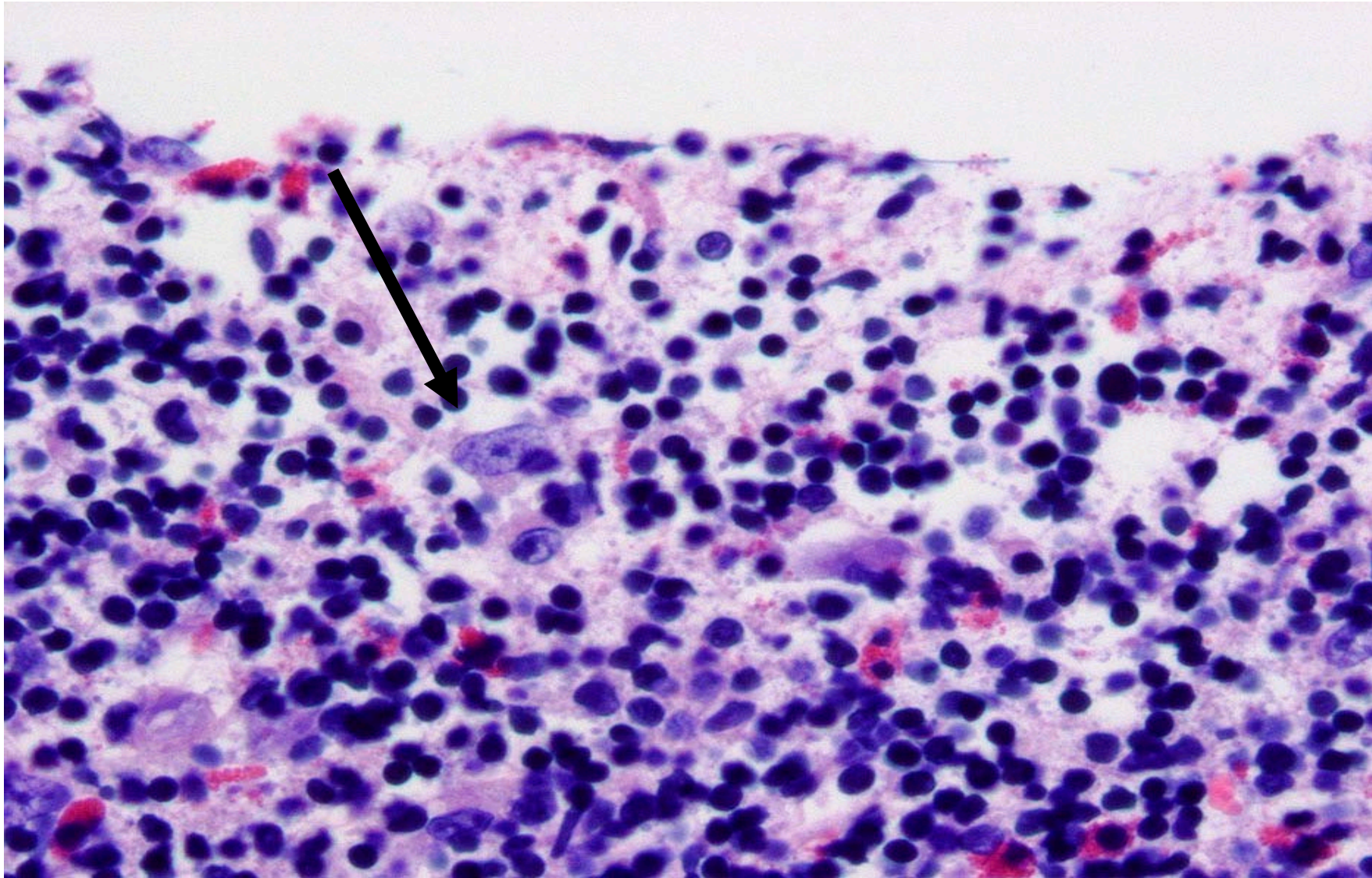
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Hodgkin lymphoma

Sarcoidosis

Other granulomatous inflammation







# Hodgkin's lymphoma of the mediastinum

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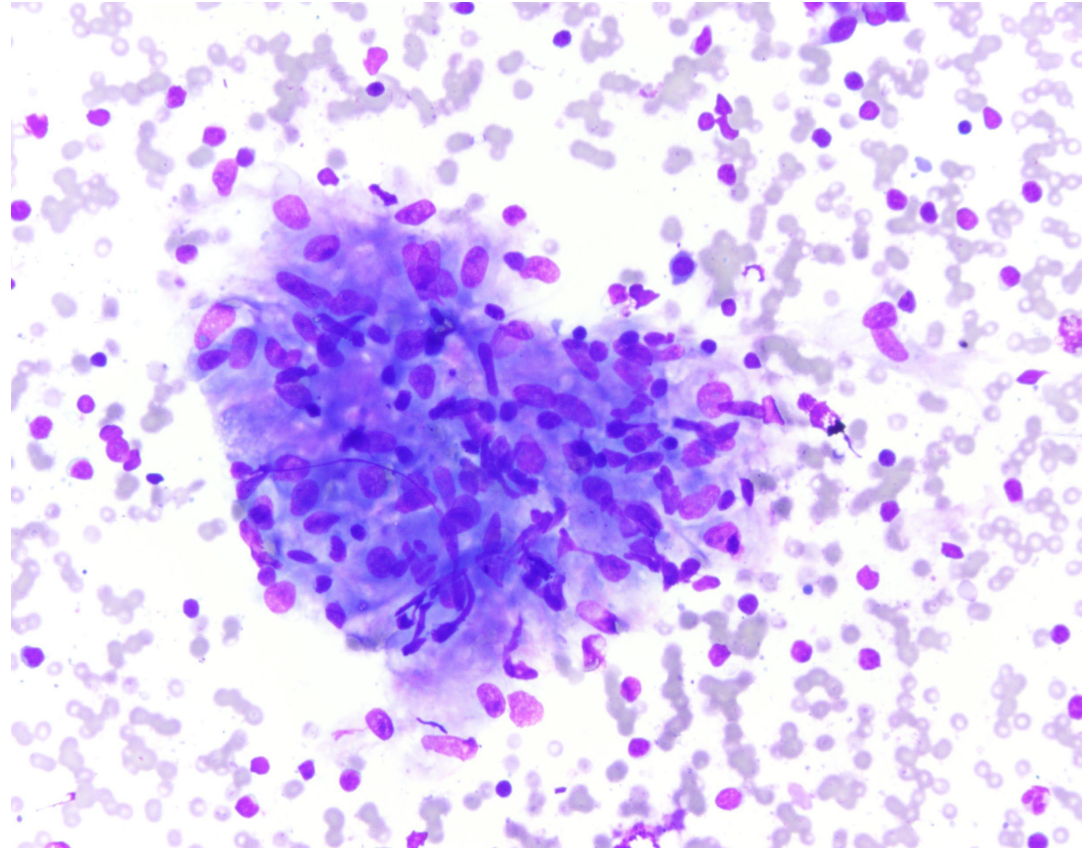
Classical Hodgkin's lymphoma is the most common type in the mediastinum

It can arise from the thymus or in mediastinal lymph nodes

The tumor can be associated with cystic changes or thymic hyperplasia

# Granulomatous inflammation

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# granuloma

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Infectious

Sarcoidosis

Component of lymphoma (Hodgkin)

Component of germ cell tumor (seminoma)



# Small blue cell pattern

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Small cell carcinoma

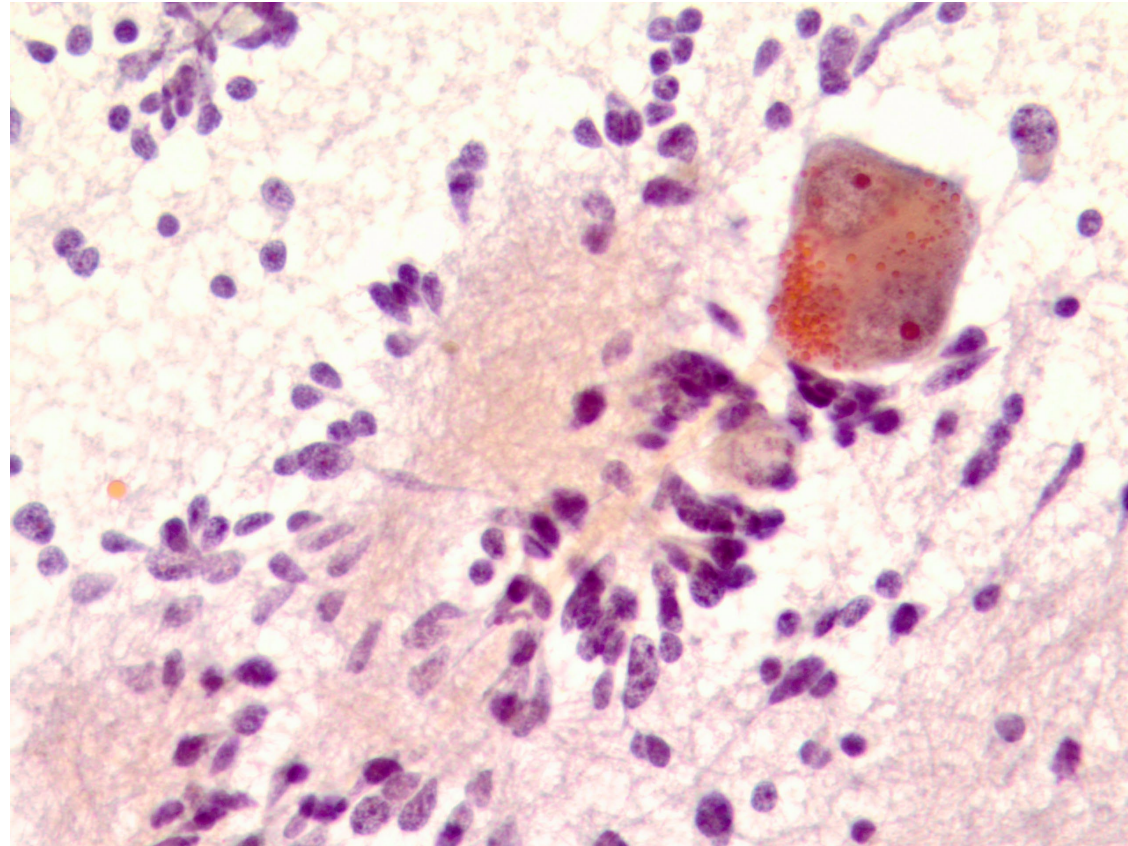
Ewing sarcoma

Neuroblastoma

Immature neuroepithelium of teratoma

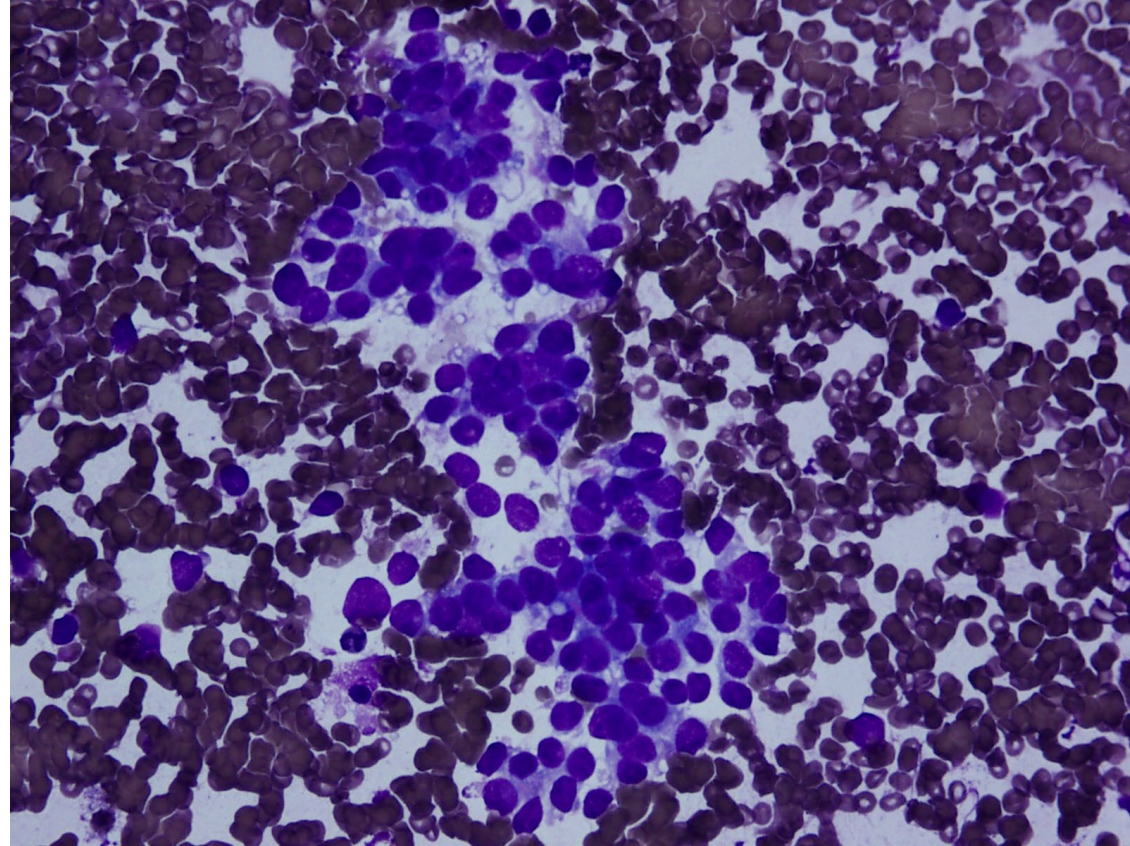
# ganglioneuroblastoma

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# Ewing sarcoma

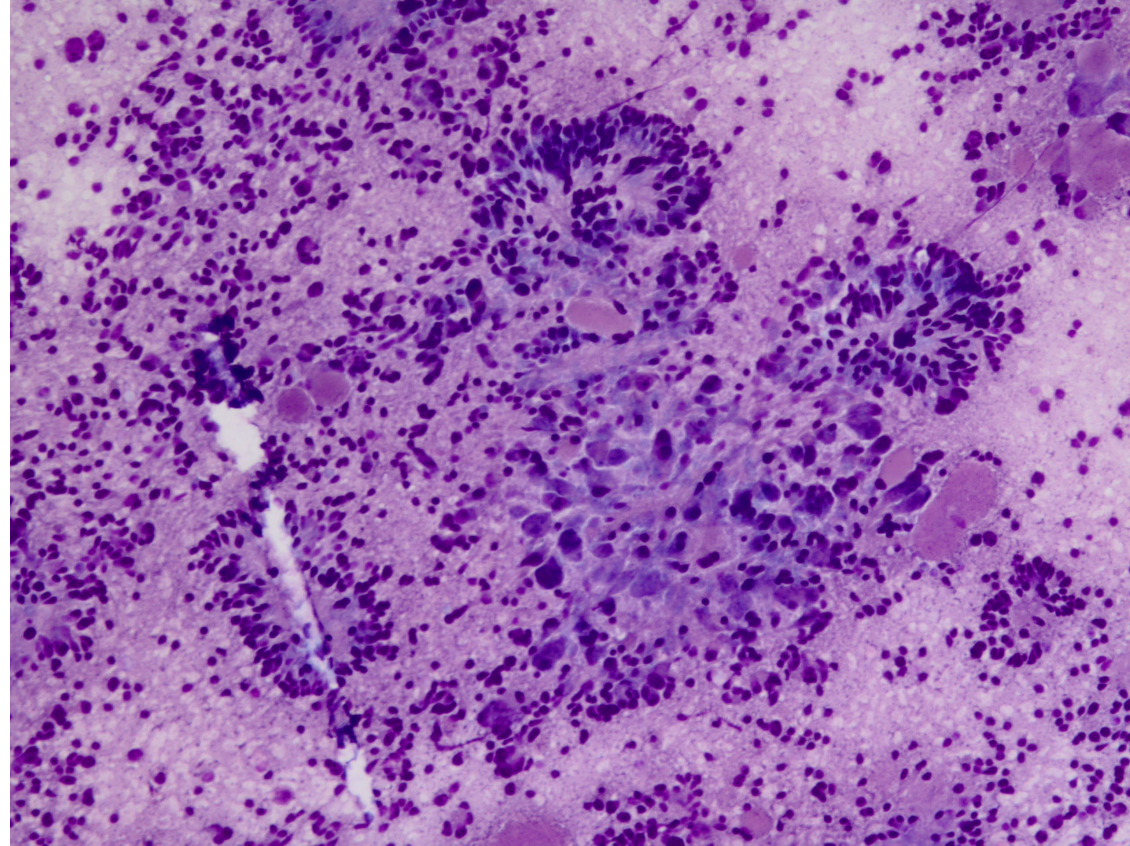
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# neuroblastoma

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# Cystic pattern

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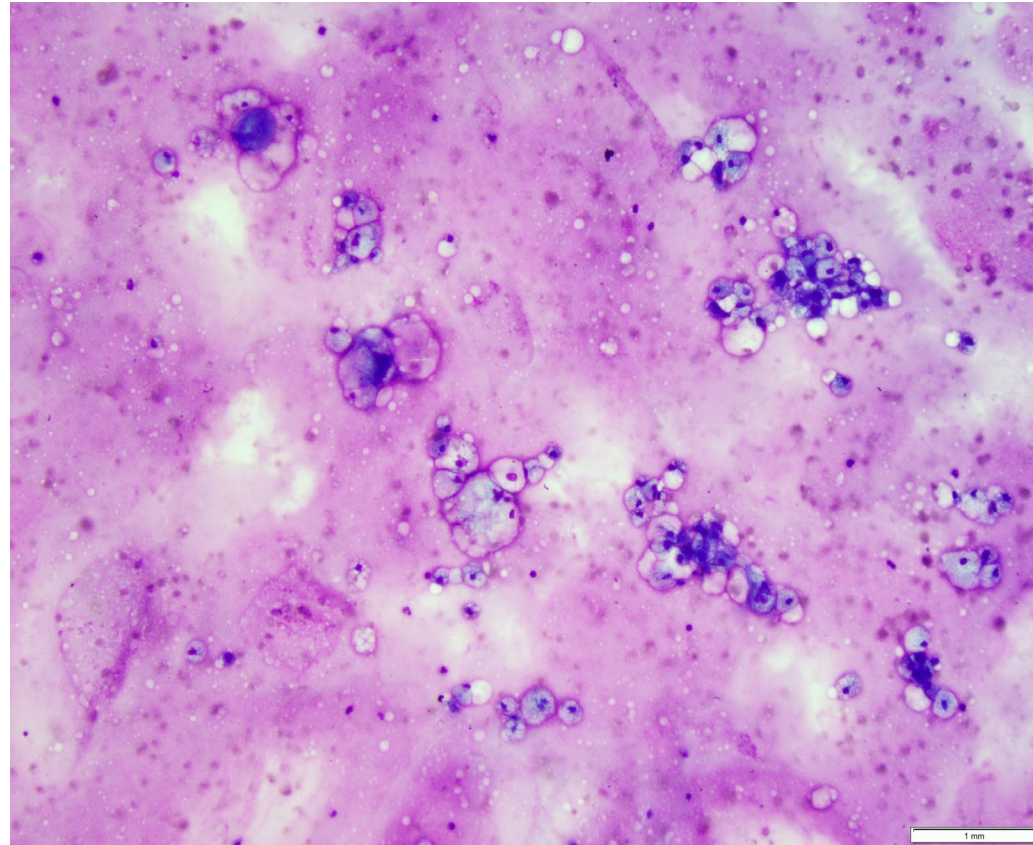
Difficult to diagnosis before surgery!

Cystic lesions- thymic cyst, mesothelial cysts, bronchogenic cysts

More likely diagnosed as unsatisfactory or non-diagnostic

# Cyst content

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# Thymic cyst

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Benign process thought to be acquired or reactive.

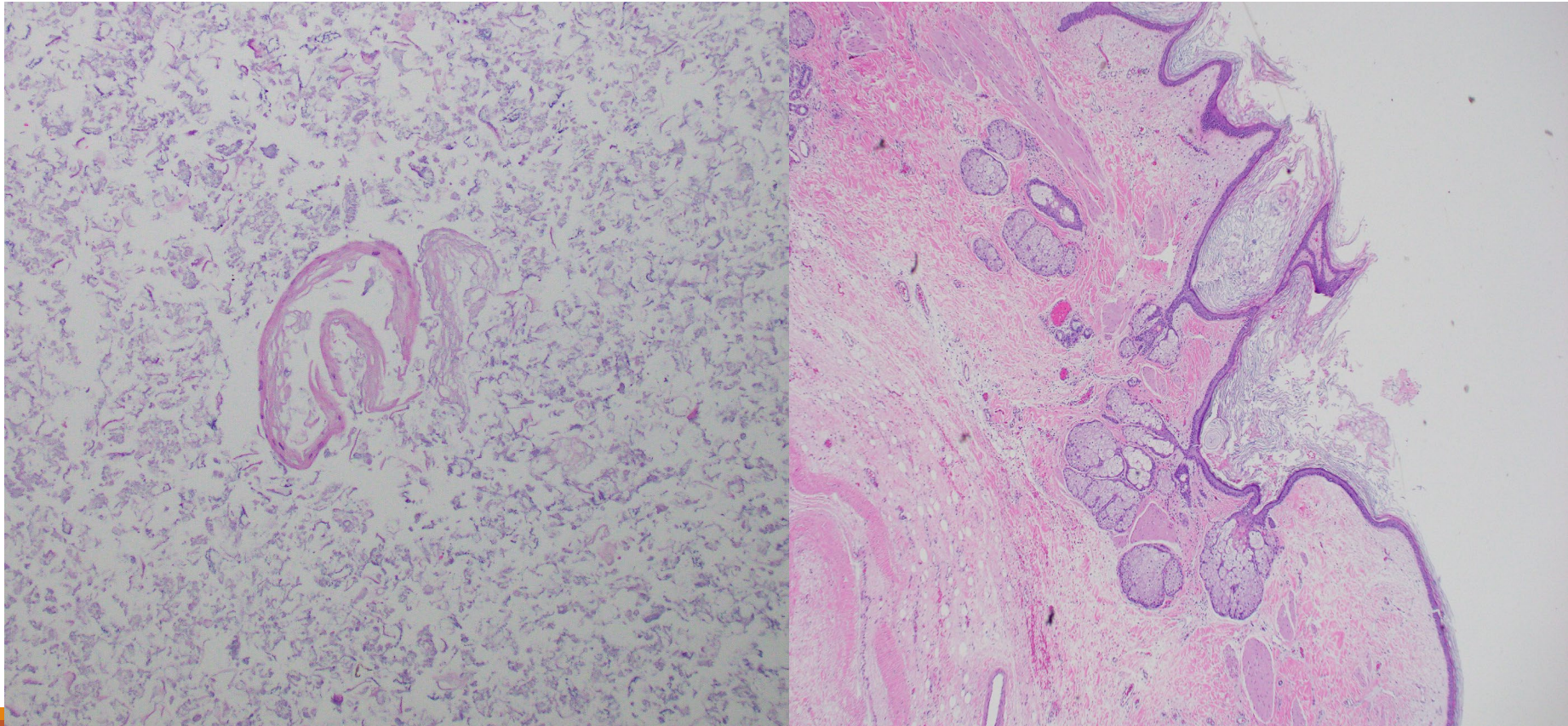
Can be lined by cuboidal, flat, squamous or ciliated epithelium

Biopsy is generally not diagnostic, needs radiographic correlation

Often associated with neoplastic process, that are NOT necessarily located within the thymus

# teratoma

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# Thank you!

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