

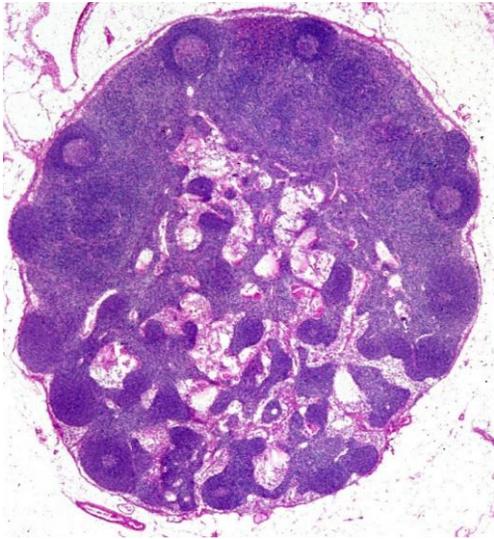
# Lymph Nodes, Non-Lymphoma

## Follicular Pattern

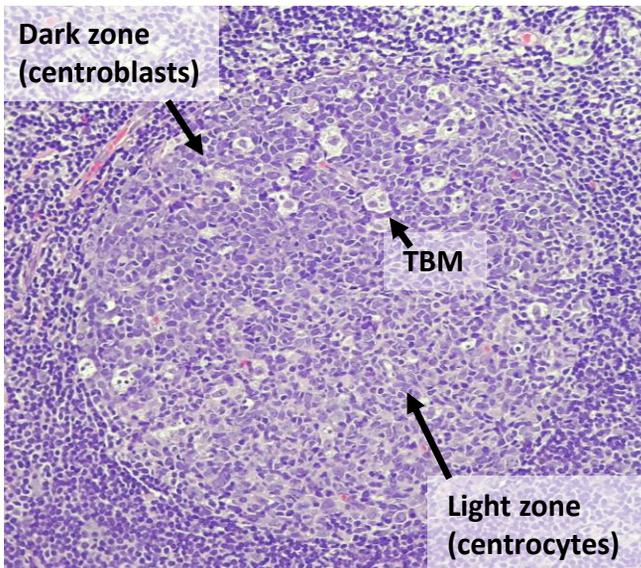
Note: Many of these patterns can be seen in other lymphoid tissues, like tonsil, etc..

### Reactive Follicular Hyperplasia

Increase in secondary (reactive) follicles (germinal centers).  
Very common, particularly in kids.  
Often in **response to an antigen**, illness (e.g., virus), or inflammatory state.  
Usually localized, painful, rapid-onset.



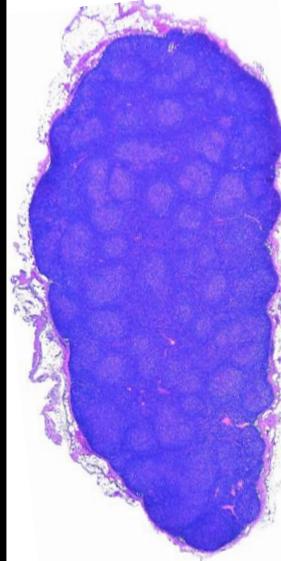
**Intact (Normal) Architecture:**  
Variably sized follicles in cortex  
Visible mantle zone  
"Open" sinuses



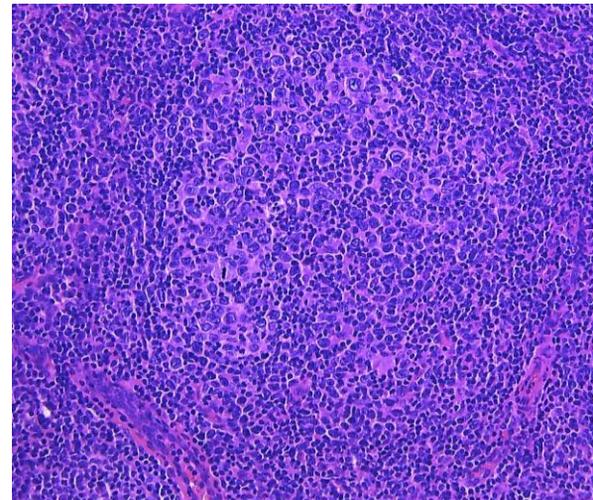
**Polarized germinal center** with **Polymorphous cells**,  
Lots of tingible body macrophages (TBMs) and apoptoses.  
"Light" (centrocytes) and "Dark" (centroblasts + TBMs) zones  
**High mitotic activity**  
**Germinal centers BCL-2 Negative**

### Follicular Lymphoma

**Clonal neoplasm** of germinal center B cells with **retained follicular architecture**  
Usually adults, often systemic, non-painful, slow-onset.



**Abnormal Architecture:**  
Effacement of normal architecture  
"Back to back" similarly-sized follicles throughout  
Attenuated/absent mantle zones



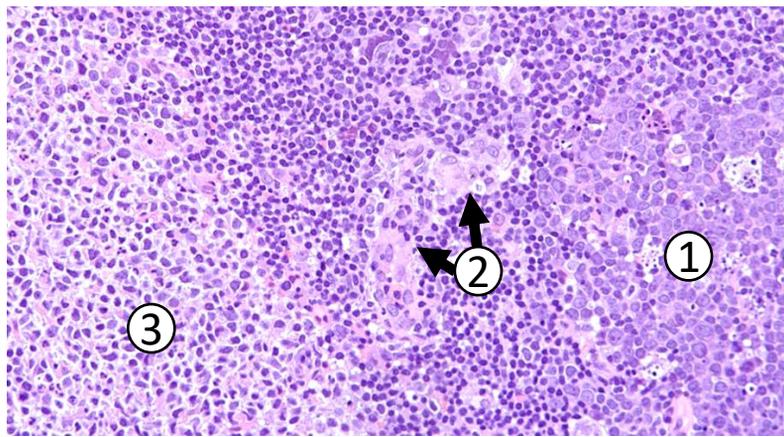
**No** polarization.  
**Monotonous**, dysplastic cytology  
Few tingible body macrophages  
Mitotic figures scarce  
**Germinal centers usually BCL-2 Positive**  
Frequent t(14;18), IGH-BCL2 translocation

# Toxoplasma Lymphadenitis

*Toxoplasma gondii* acquired from **feces of cats**. Presents with acute lymphadenitis +/- fever; can disseminate in immunocompromised

## Key findings:

- 1) **Reactive follicles**
- 2) **Epithelioid histiocytes** in loose clusters and encroaching on follicles
- 3) **Monocytoid B cells** in sinuses



# HIV Lymphadenopathy

Caused by **Human Immunodeficiency Virus (HIV)**

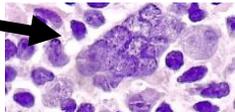
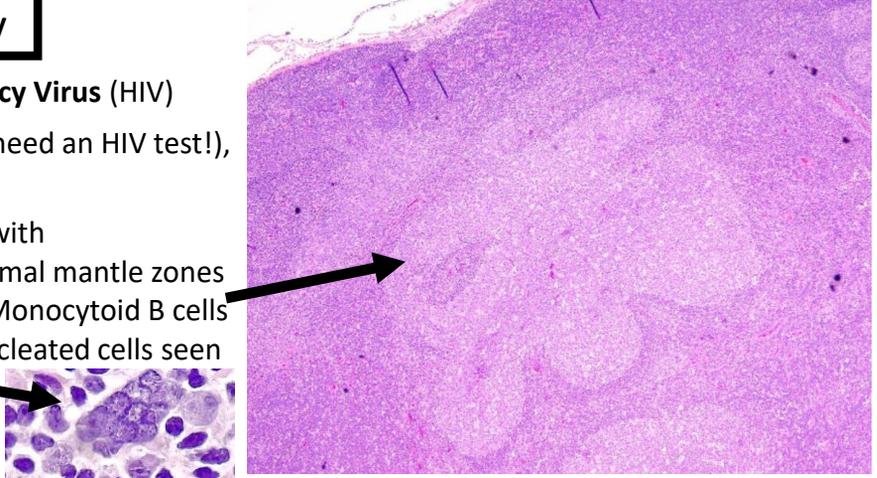
Generally *nonspecific findings* (still need an HIV test!), but somewhat distinctive.

**Early:** **Florid follicular hyperplasia** with Irregularly-shaped follicles and minimal mantle zones  
Follicle lysis (highlight with CD21); Monocytoid B cells and Warthin-Finkeldy cells (multinucleated cells seen in HIV and measles)

**Late:** **Atrophic "burnt out" follicles**

Diffuse Vascular proliferation

Can mimic Castleman's



# Castleman's disease

**Hyaline Vascular type** (*Most common type*)

Usually unicentric and asymptomatic.

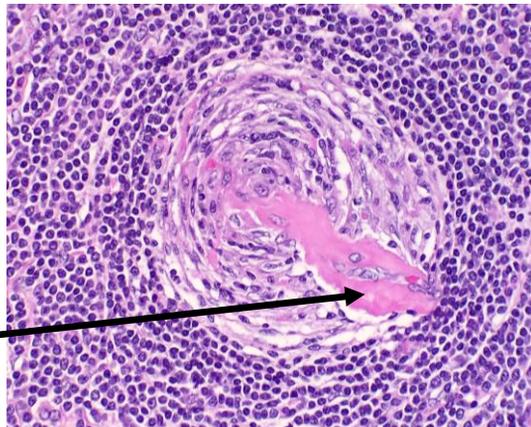
Likely a benign neoplasm of follicular dendritic cells.

Numerous follicles with burnt out germinal centers,

onion skinning lymphocytes

Hyalinized vessels often leading into germinal centers

→ look like a "Lollipop"



**Plasma cell variant**

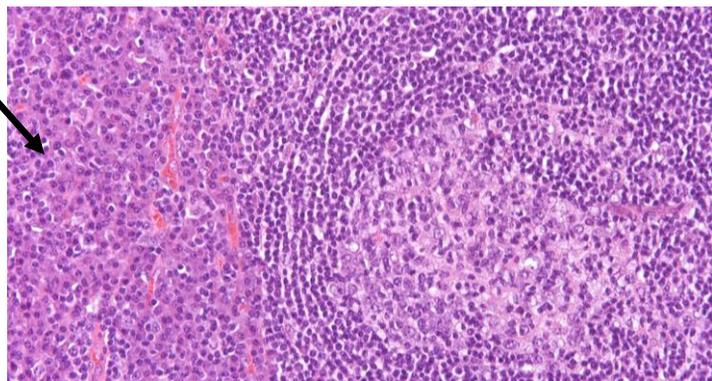
Often multicentric with systemic type B symptoms. Lab abnormalities.

Similar follicular features as above, but with

numerous plasma cells in interfollicular region

Associated with HHV8, HIV, and POEMS syndrome.

Often lambda-monotypic plasma cells.



# Progressive Transformation of Germinal Centers

“PTGCs”

**Markedly enlarged germinal centers (3-5x normal); Ill-defined; infiltrated by small lymphocytes from mantle zone.**

Disordered follicular dendritic cell network.

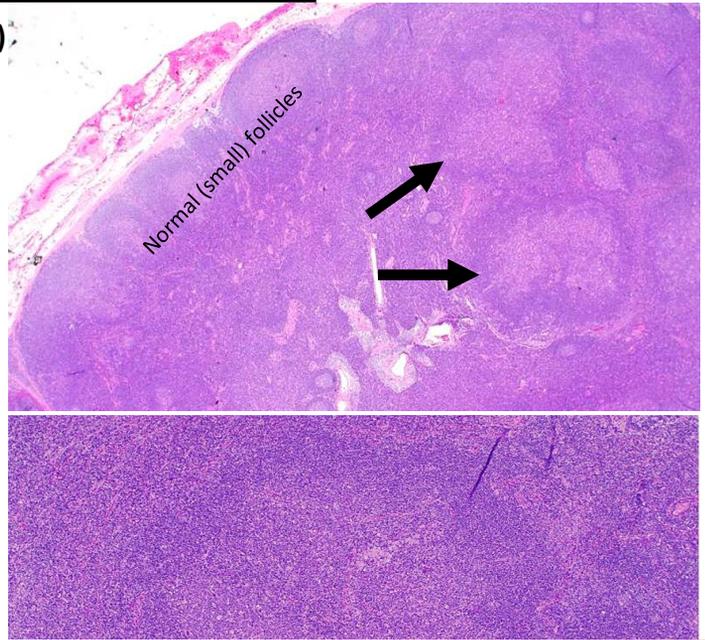
Usually self-limited and involves a small subset of follicles.

**Often young, asymptomatic** with massive LN.

BCL-2 and IgM highlight invasion of mantle zone B cells into germinal centers.

Some association with NLPHL, but not significant risk factor.

*If see: LP “popcorn” cells and nodal effacement → consider lymphoma (NLPHL)!*



## Paracortical Pattern

Expansion of paracortex area between follicles

## EBV Lymphadenitis

Usu. Young adult. Fever & pharyngitis.

**Expanded paracortex.** Follicular hyperplasia.

**“Moth eaten” appearance** with TBMs

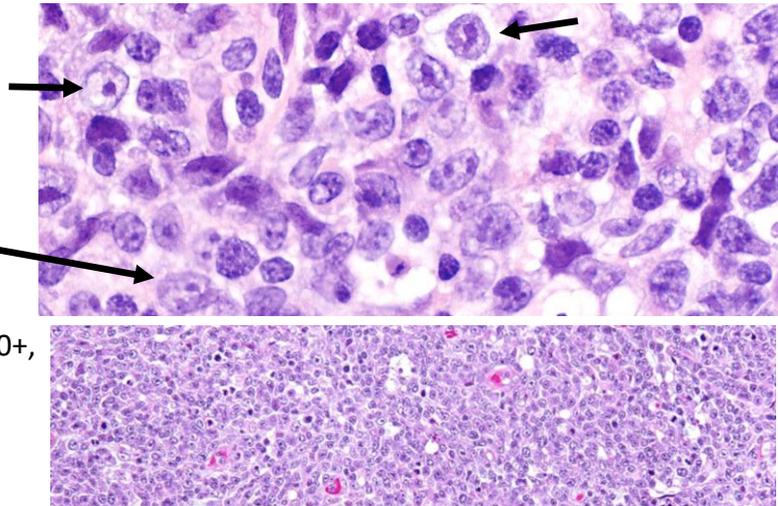
**Numerous immunoblasts**

Can see necrosis

Lots of T cells: CD8+>CD4+

EBV-infected immunoblast B cells: CD20+, CD30+, Polytypic kappa/lambda, EBER+

(EBV-positive cells are small and large, unlike lymphoma where they are all the same size)



## Dermatopathic Lymphadenitis

Seen in lymph nodes **draining an area with a rash/irritated skin**

*[THINK: itching → knocks pigment out of skin (incontinence) → brought to lymph node by histiocytes along with Langerhans cells]*

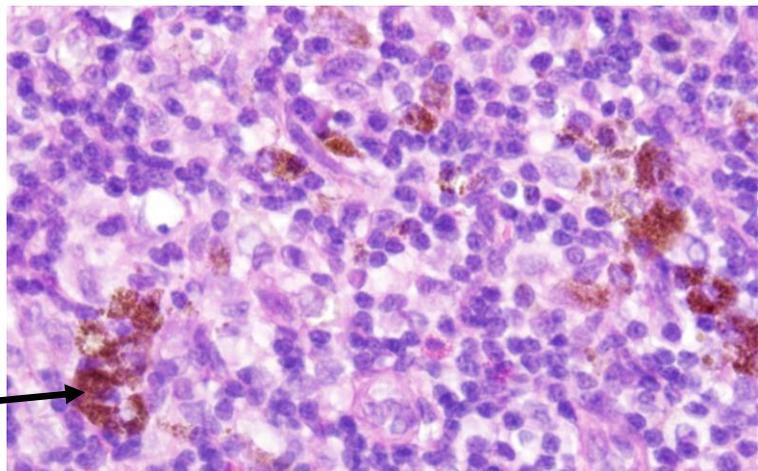
**Expanded paracortex**

**“Moth eaten” appearance**

**Histiocytes “raining down” from capsule**

**Melanin pigment**

**Langerhans cells** (folded nuclei with open chromatin, S100&CD1a+, MelanA-)



# Sinus Expansion

## Langerhans Cell Histiocytosis

Usually **children**. Can be localized or multifocal.  
Commonly involves **bone**.  
(If in LN, usually systemic)

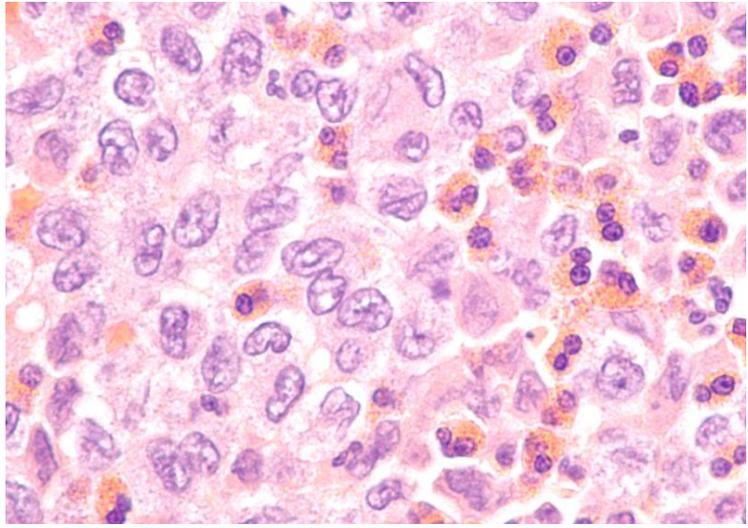
### Langerhans cell proliferation

Folded "coffee bean" nuclei  
Open chromatin

**Eosinophils often also present**

**IHC: (+)S100, CD1a, Langerin; (+/-) CD68**

MAPK pathway mutations, usually BRAF V600E



## Rosai-Dorfman Disease

*Official name: Sinus histiocytosis with massive lymphadenopathy*

Histiocytic proliferation of unclear etiology.

### Atypical Histiocytes:

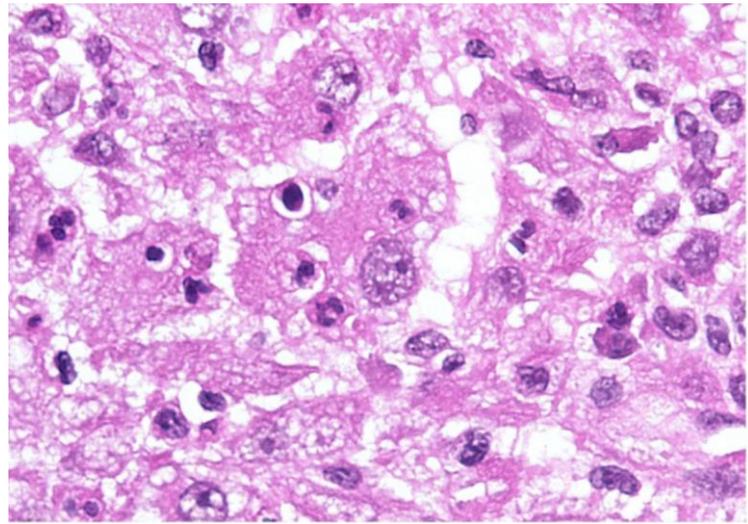
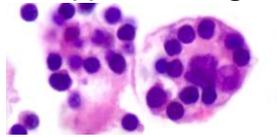
**Round nuclei with prominent nucleoli**

**Emperipolesis** (Engulfing live lymphocytes)

Associated reactive plasma cells (polytypic)

**IHC: (+)S100, CD163, CD68; (-)CD1a, Langerin**

Usually indolent  
Observed clinically

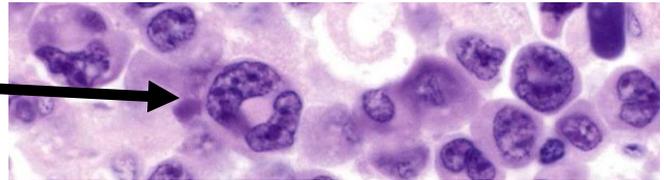


## **Malignant** things that can expand the sinuses to look out for:

### Anaplastic large cell lymphoma

Cytologically malignant hallmark cells

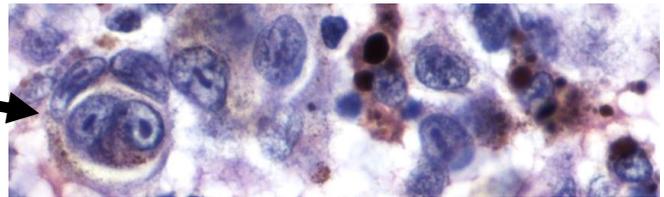
IHC: (+)CD30, (+/-)ALK, (-)S100



### Metastatic melanoma

Cytologically malignant cells, epithelioid to spindled. Pigment. Prominent nucleoli or intranuclear pseudoinclusions

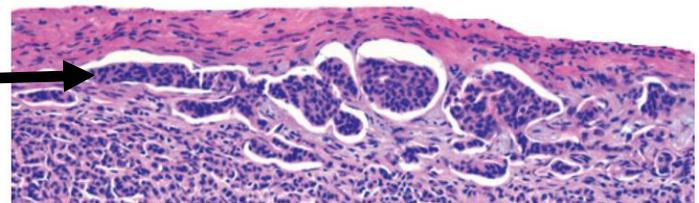
IHC: (+)S100, HMB45, MelanA



### Metastatic carcinoma

Cytologically malignant; often cohesive

IHC: (+)Cytokeratin



# Necrosis

## Kikuchi Lymphadenitis

Head/Neck of young Asian Women  
Unilateral, Cervical LN enlargement

Pale-appearing areas of necrosis

**Absent** neutrophils; Nuclear debris/apoptoses

Crescent shaped histiocytes

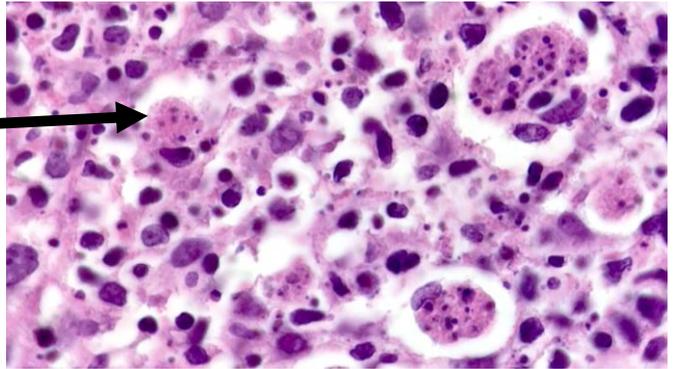
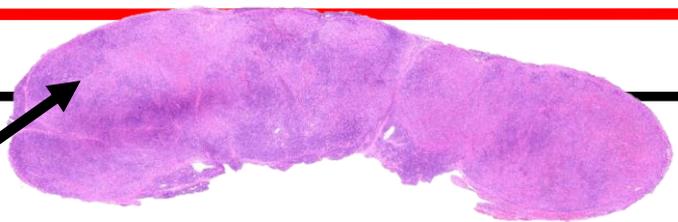
(IHC: (+)CD163, MPO, CD68)

Plasmacytoid dendritic cells

Systemic symptoms, self-resolves.

Morphologically similar to syphilis.

Can mimic T cell lymphoma.



## Cat Scratch Disease

Caused by *Bartonella henselae* from contact with cats. Unilateral.

**Early:**

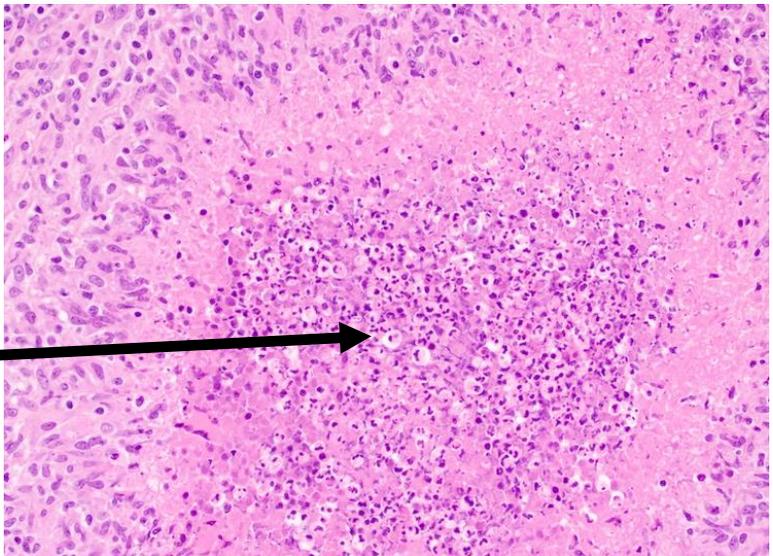
Follicular hyperplasia, Monocytoid B cells

**Late:**

**Suppurative granulomas**—stellate abscesses with central necrosis surrounded by palisading histiocytes

Organisms stain with **Warthin-Starry**

Morphologically similar to Lymphogranuloma venereum and Tularemia.



## Granulomas

Well-formed collections of histiocytes and multinucleated cells.

May have central “caseating” necrosis.

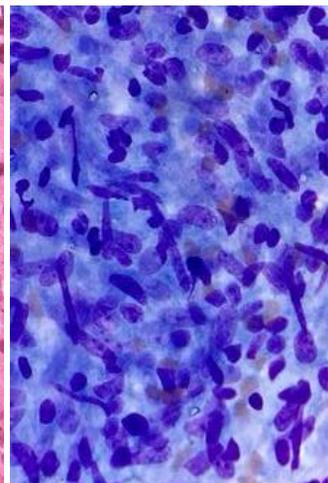
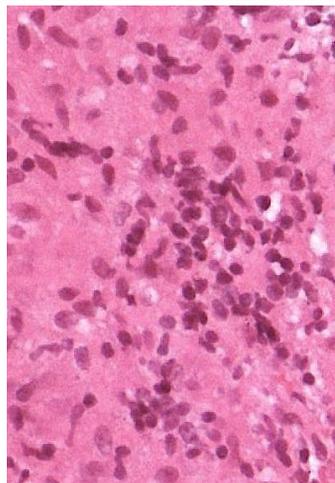
**Main DDX:**

**Mycobacterium tuberculosis** (usually necrotizing)

**Fungal infections** (rare)

**Sarcoidosis** (usually non-necrotizing, Dx of exclusion)

**Get Bug Stains!**



**Other causes of necrosis:**

**Herpes Simplex Virus (HSV) lymphadenitis:** Usually inguinal, localized. Also has follicular and paracortical patterns. Punched out areas of necrosis with classic viral inclusions and neutrophils.

**Malignancy** → Always consider and rule out!

## Benign Inclusions/Changes

(Usually incidental findings)

### Endosalpingiosis/ Müllerianosis

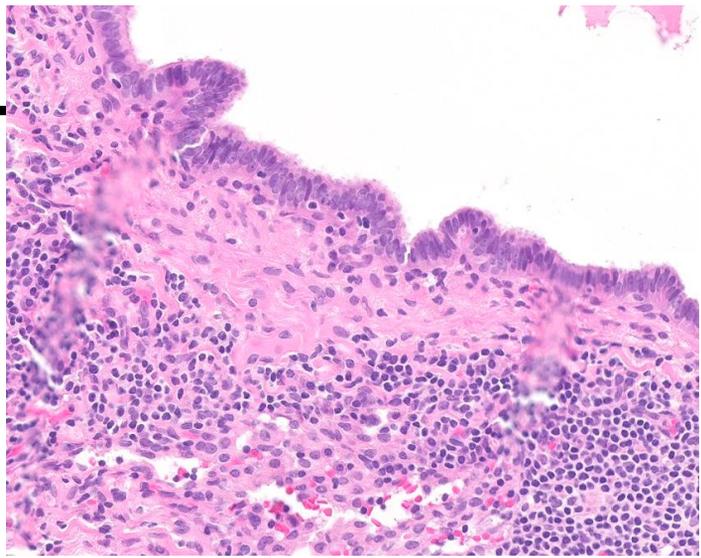
**Benign fallopian tube inclusions in lymph nodes of women.**

Most common in pelvic, but can see other places

**Ciliated epithelium**, can have peg cells.

No atypia, mitoses.

IHC: (+) PAX8, CK7, WT-1, ER



### Other epithelial inclusions

Can see: **Salivary gland** (upper neck), **thyroid** (lower neck), **breast (axilla)**, mesothelial cells (thorax)

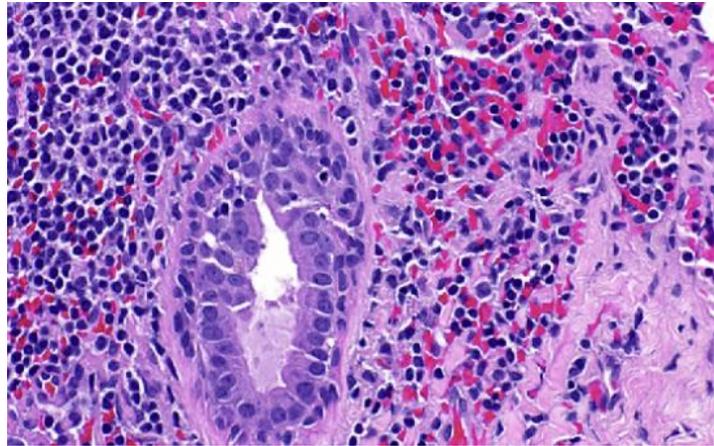
***Must consider metastasis!***

Look for: **Bland cytology**

Myoepithelial cells in axilla/breast

No mitoses or invasion

Usually capsular/subcapsular



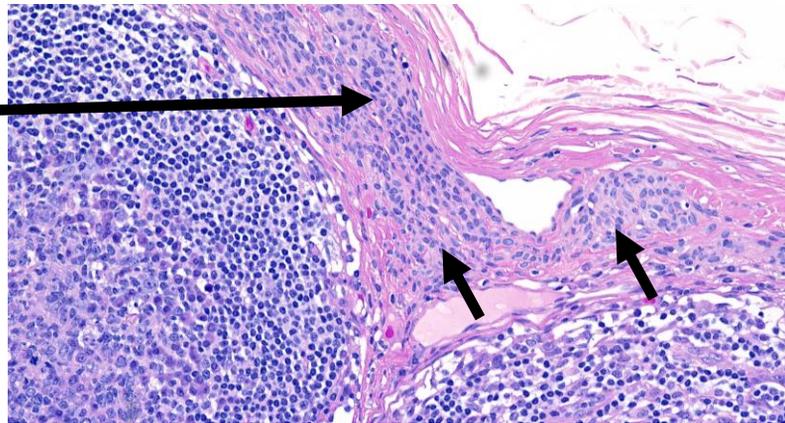
### Capsular Nevi

**Linear arrangement of bland melanocytes** *within* collagen of **capsule** or fibrous septa.

Can be multifocal.

No atypia, prominent nucleoli, or mitoses.

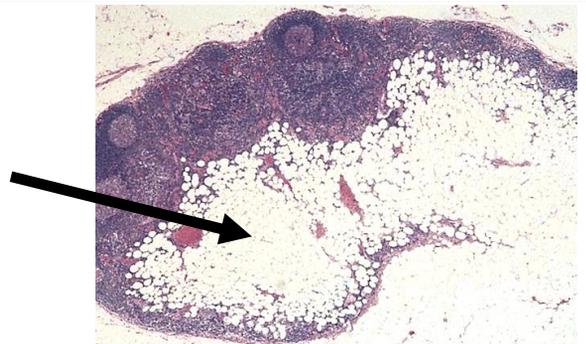
IHC: (+)S100, MelanA; (-)PRAME, HMB-45;  
Ki67<1%



### Lipomatosis

**Non-neoplastic fatty infiltration**

Most common in pelvis, abdomen, and axilla

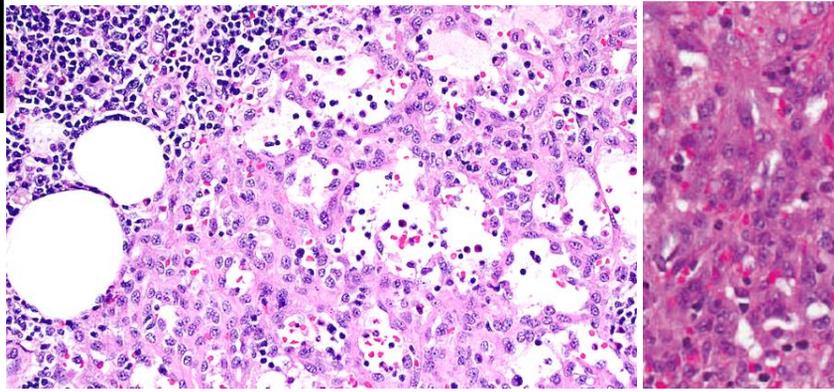


## Vascular transformation of sinuses

**Change of sinuses to anastomosing small vascular channels.**

Usually incidental finding.

Occlusion → more vascular proliferation



## Lymphangiomyomatosis

aka "LAM"

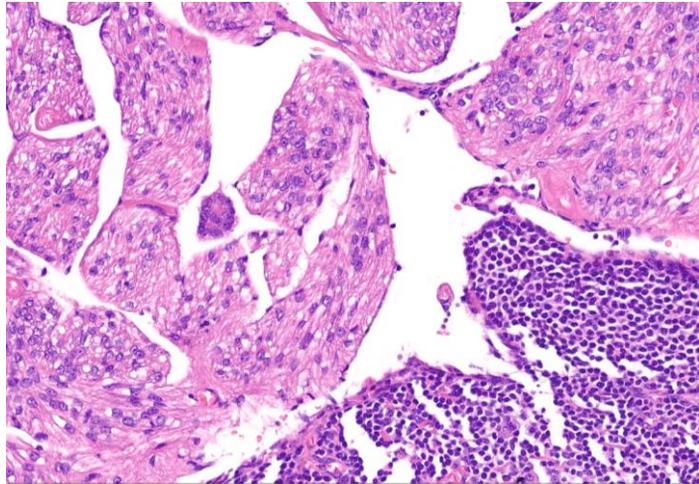
Sometimes also called angiomyolipoma

**Spindle cells exhibiting melanocytic and myoid differentiation.**

Usually pelvic/peritoneal lymph nodes.

Often incidental, not associated with pulmonary LAM or Tuberous sclerosis.

IHC: (+) HMB45, MITF, SMA, Desmin, ER.

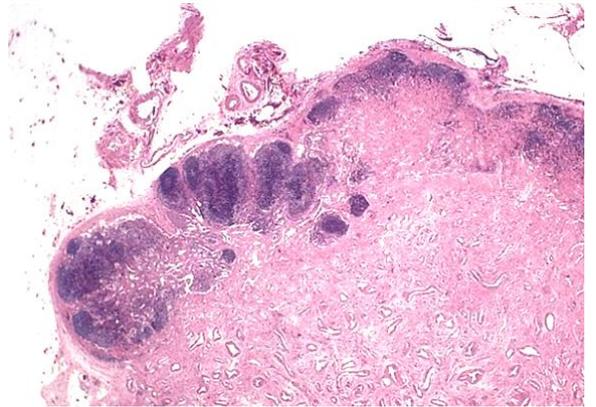


## Angiomyomatous hamartoma

Most common in males, **inguinal lymph nodes**

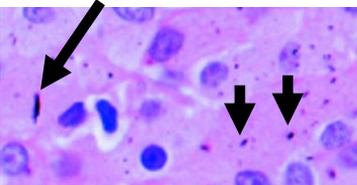
**Extensive replacement with sclerotic fibrous tissue** and thick-walled blood vessels with smooth muscle.

Starts in hilar region.

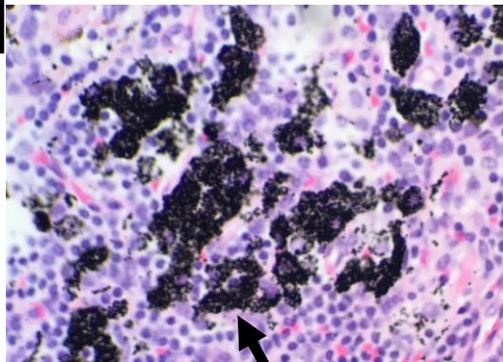


## Foreign Material

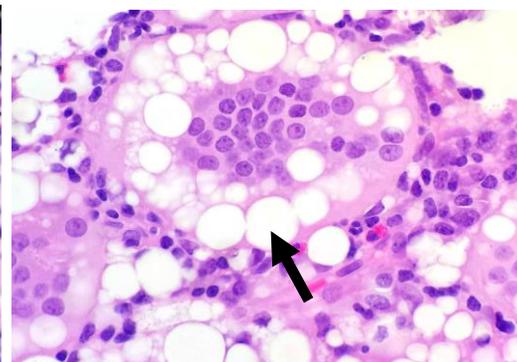
*Lots of foreign material can be seen in histiocytes in draining lymph nodes, including:*



Metal particles after joint replacement



Tattoo pigment



Silicone in axilla after breast implants