

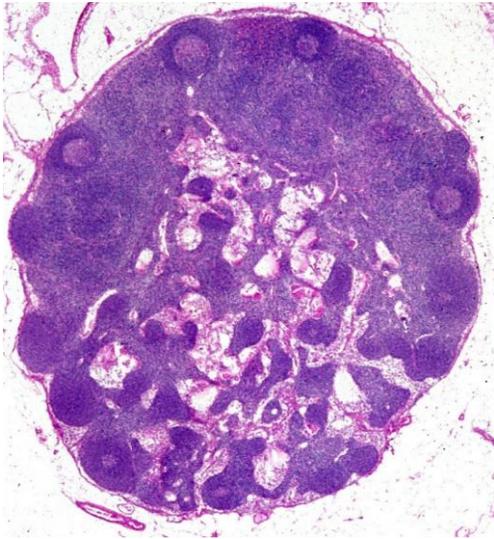
Lymph Nodes, Non-Lymphoma

Follicular Pattern

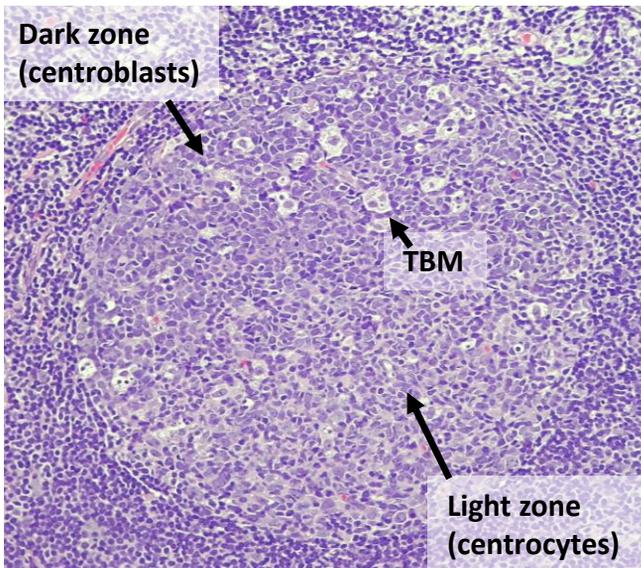
Note: Many of these patterns can be seen in other lymphoid tissues, like tonsil, etc..

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.



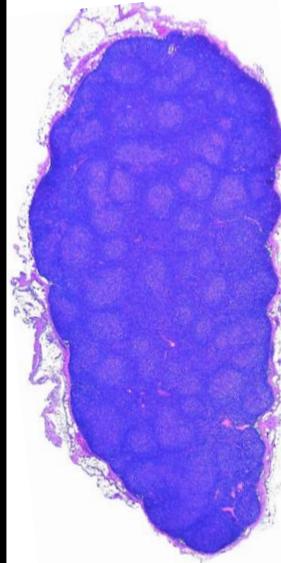
Intact (Normal) Architecture:
 Variably sized follicles in cortex
 Visible mantle zone
 "Open" sinuses



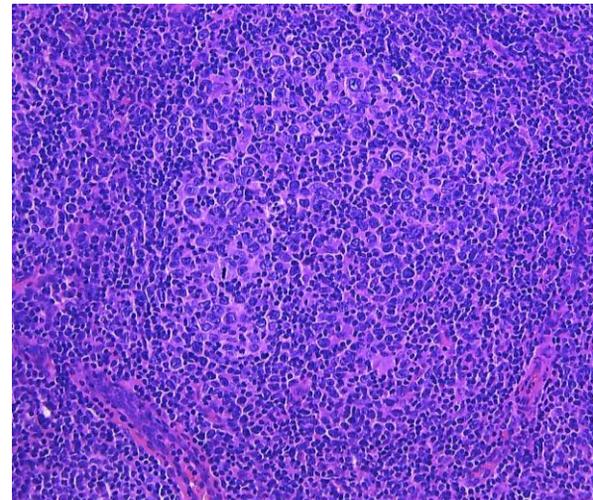
Polarized germinal center with **Polymorphous cells**,
 Lots of tingible body macrophages (TBMs) and apoptoses.
 "Light" (centrocytes) and "Dark" (centroblasts + TBMs) zones
High mitotic activity
Germinal centers BCL-2 Negative

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



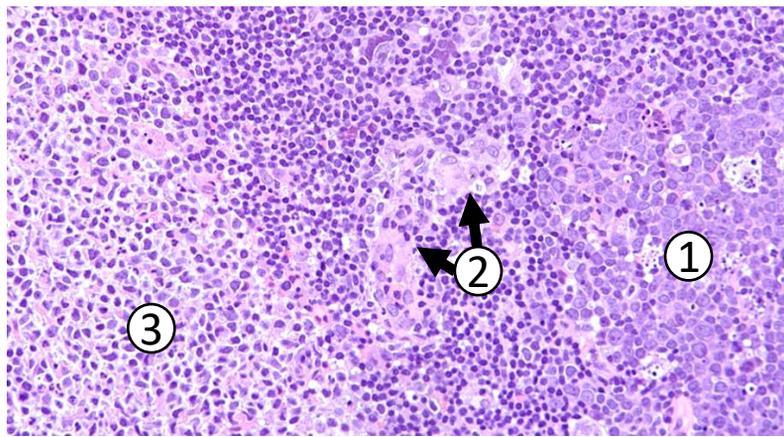
No polarization.
Monotonous, dysplastic cytology
 Few tingible body macrophages
 Mitotic figures scarce
Germinal centers usually BCL-2 Positive
 Frequent t(14;18), IGH-BCL2 translocation

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)**

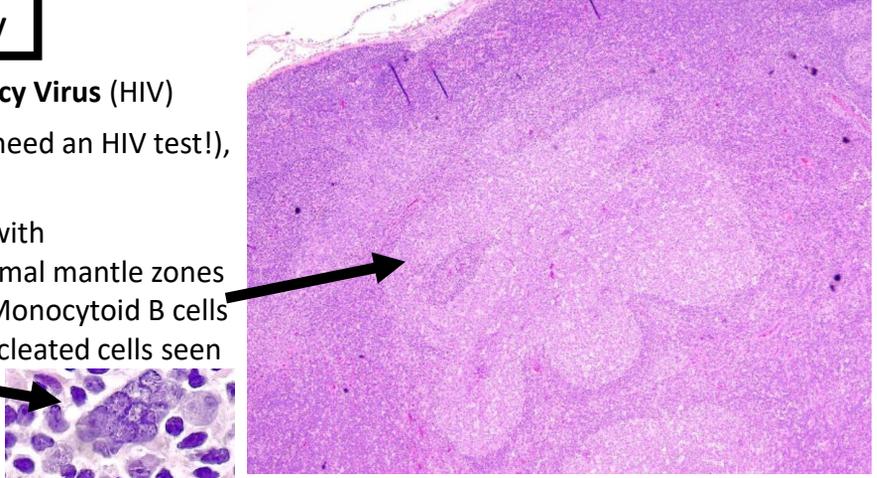
Generally *nonspecific findings* (still need an HIV test!), but somewhat distinctive.

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.

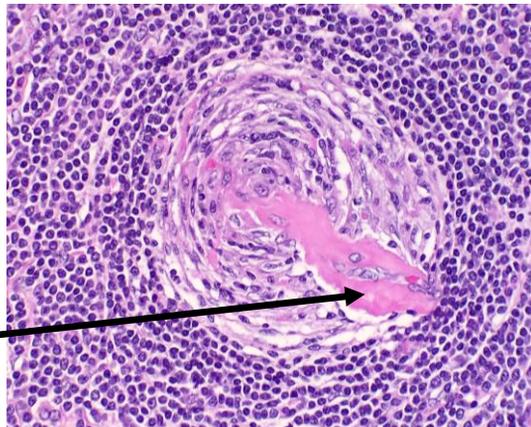
Likely a benign neoplasm of follicular dendritic cells.

Numerous follicles with burnt out germinal centers,

onion skinning lymphocytes

Hyalinized vessels often leading into germinal centers

→ look like a "Lollipop"



Plasma cell variant

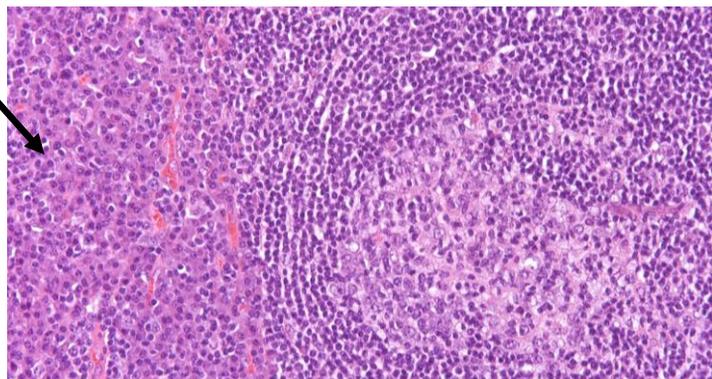
Often multicentric with systemic type B symptoms. Lab abnormalities.

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.

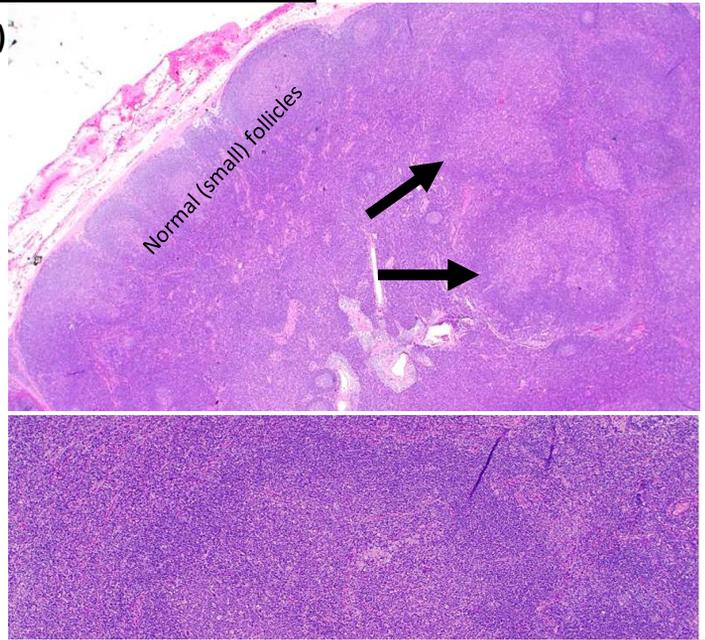
Usually self-limited and involves a small subset of follicles.

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

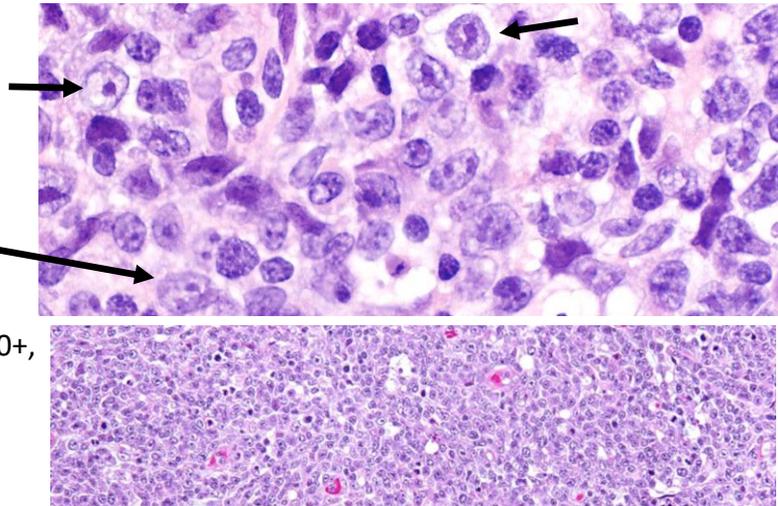
Numerous immunoblasts

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]

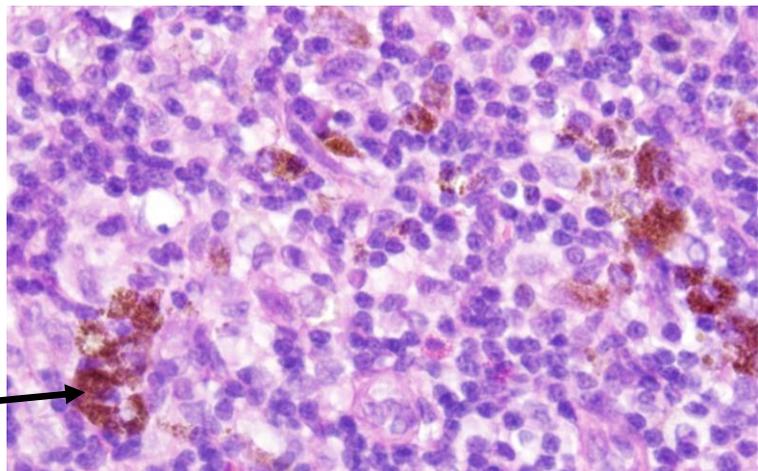
Expanded paracortex

“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)

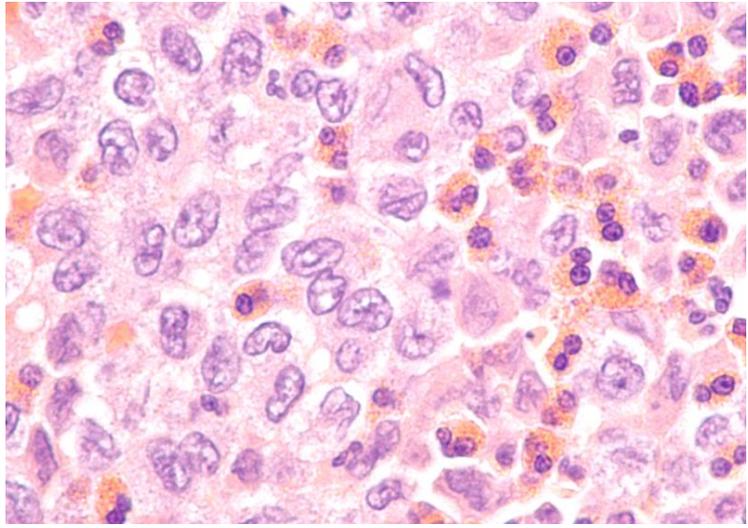
Langerhans cell proliferation

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:

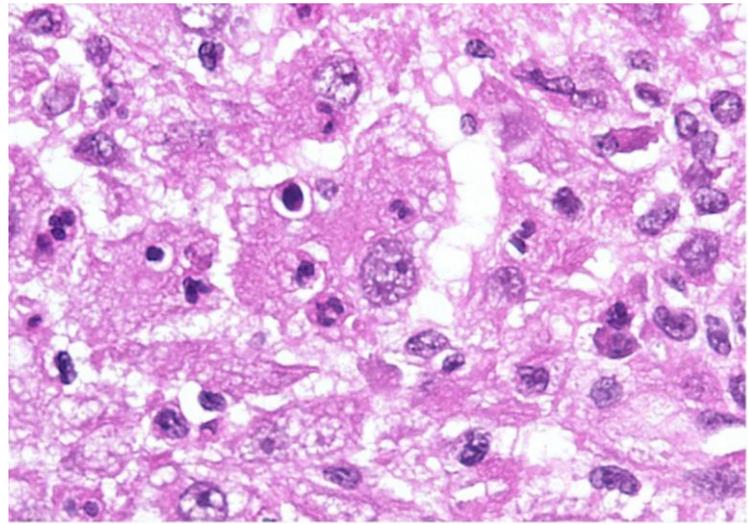
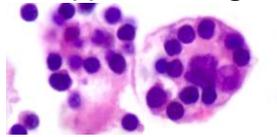
Round nuclei with prominent nucleoli

Emperipolesis (Engulfing live lymphocytes)

Associated reactive plasma cells (polytypic)

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

Usually indolent
Observed clinically

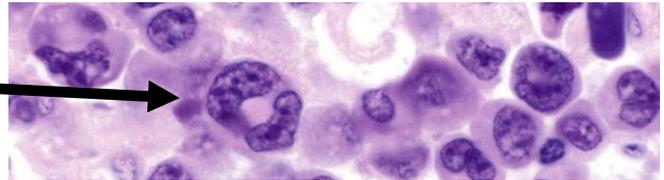


Malignant things that can expand the sinuses to look out for:

Anaplastic large cell lymphoma

Cytologically malignant hallmark cells

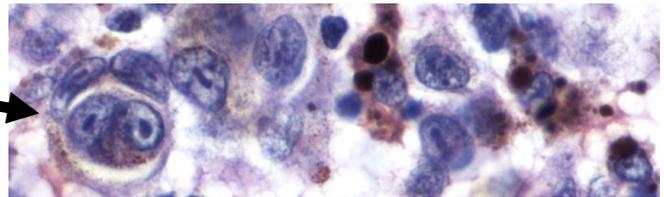
IHC: (+)CD30, (+/-)ALK, (-)S100



Metastatic melanoma

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

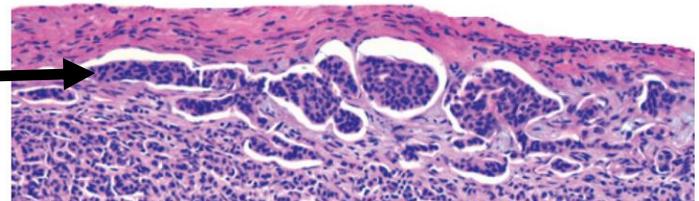
IHC: (+)S100, HMB45, MelanA



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

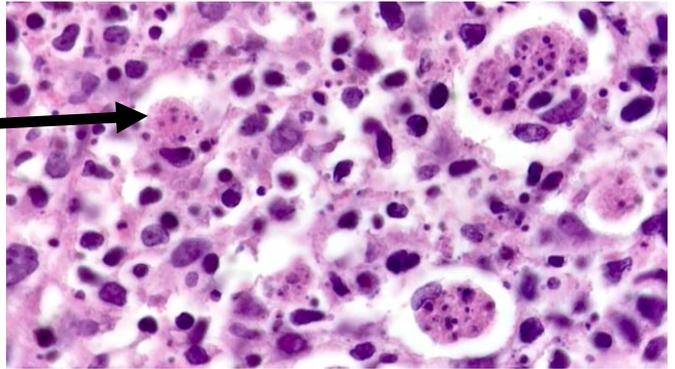
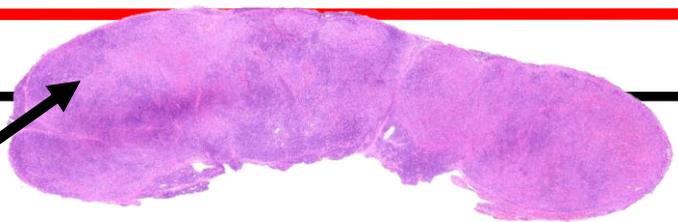
(IHC: (+)CD163, MPO, CD68)

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:

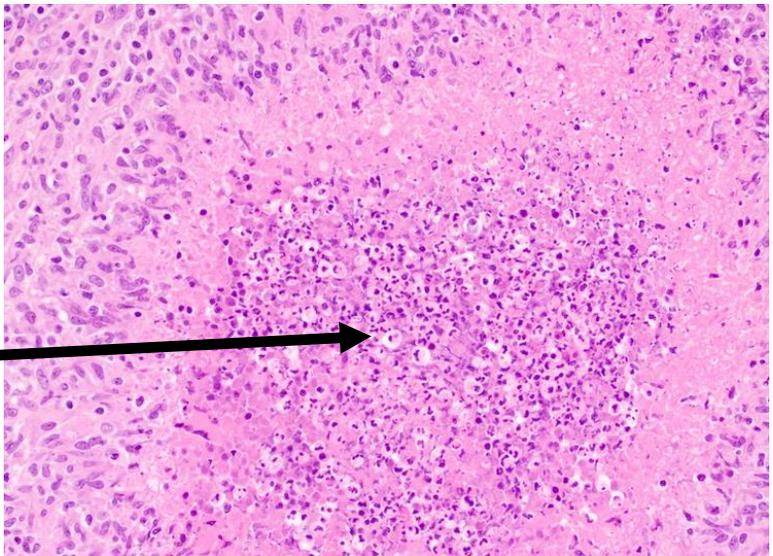
Follicular hyperplasia, Monocytoid B cells

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.

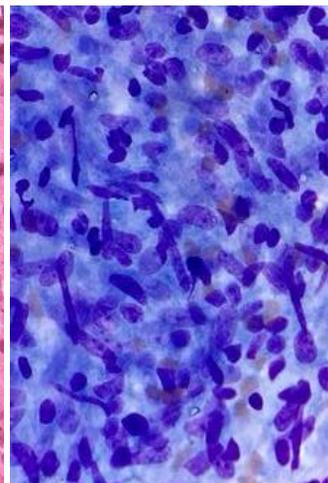
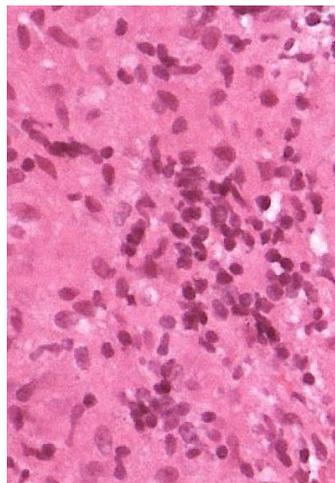
Main DDX:

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

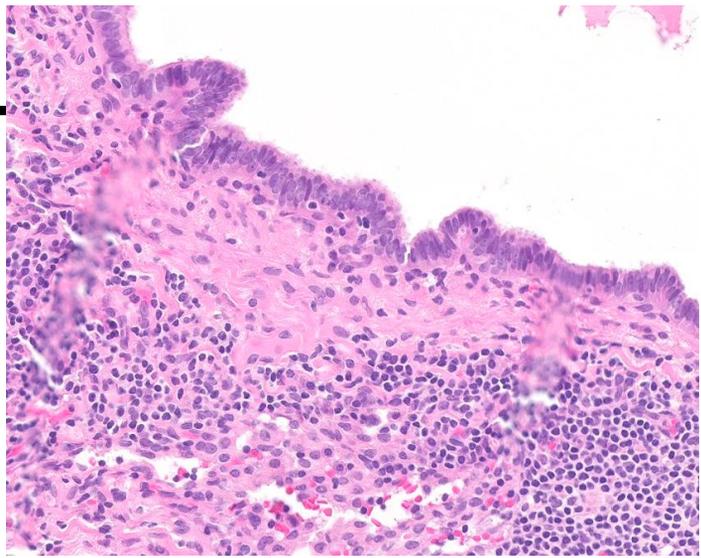
Benign fallopian tube inclusions in lymph nodes of women.

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)

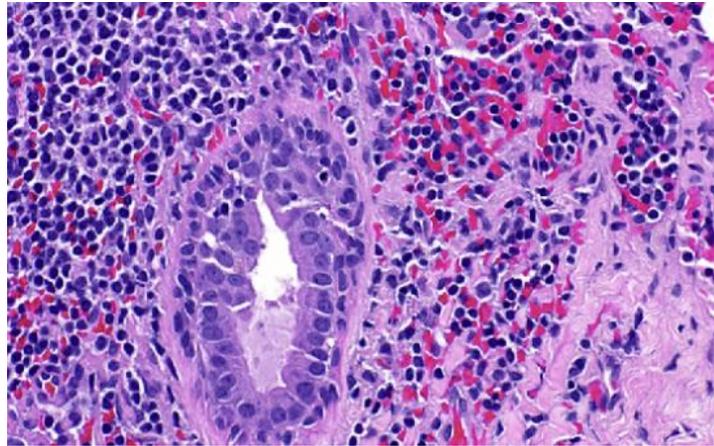
Must consider metastasis!

Look for: **Bland cytology**

Myoepithelial cells in axilla/breast

No mitoses or invasion

Usually capsular/subcapsular



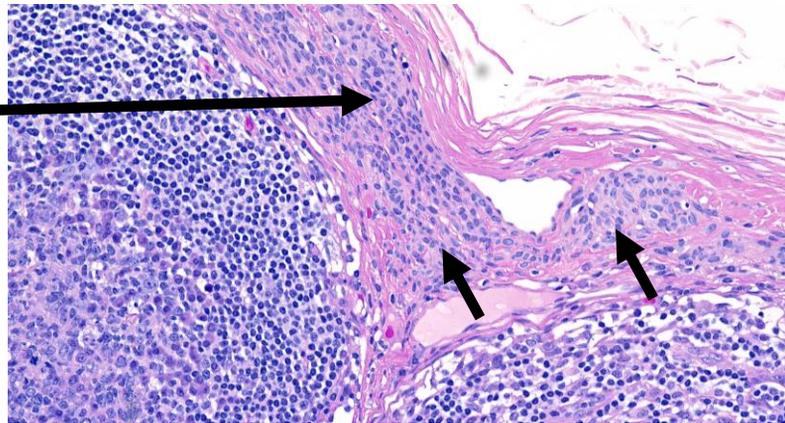
Capsular Nevi

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

Can be multifocal.

No atypia, prominent nucleoli, or mitoses.

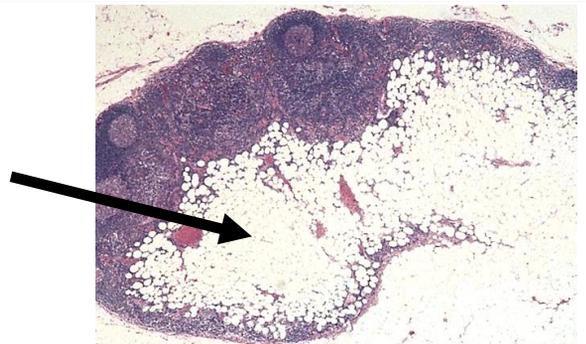
IHC: (+)S100, MelanA; (-)PRAME, HMB-45;
Ki67<1%



Lipomatosis

Non-neoplastic fatty infiltration

Most common in pelvis, abdomen, and axilla

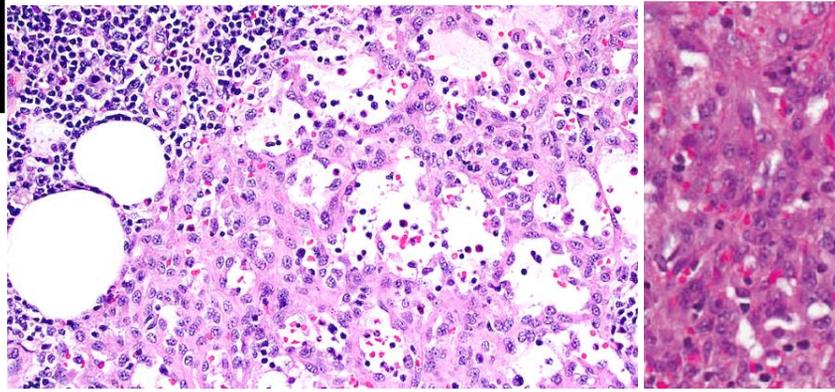


Vascular transformation of sinuses

Change of sinuses to anastomosing small vascular channels.

Usually incidental finding.

Occlusion → more vascular proliferation



Lymphangiomyomatosis

aka "LAM"

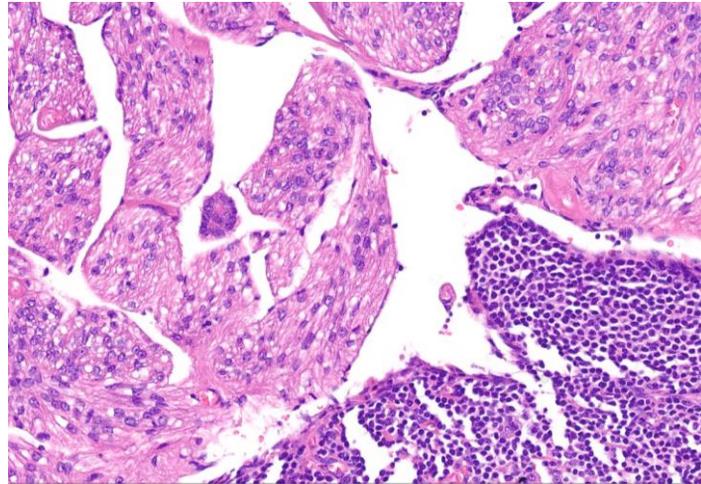
Sometimes also called angiomyolipoma

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.

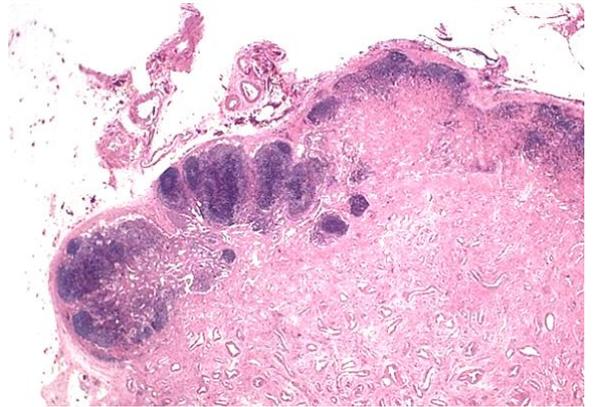


Angiomyomatous hamartoma

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

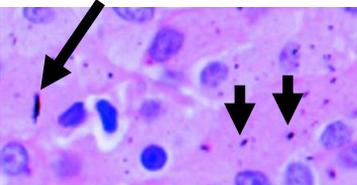
Extensive replacement with sclerotic fibrous tissue and thick-walled blood vessels with smooth muscle.

Starts in hilar region.

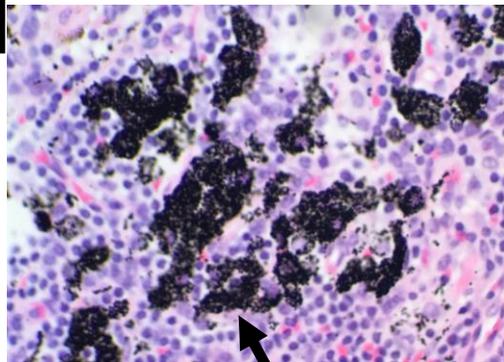


Foreign Material

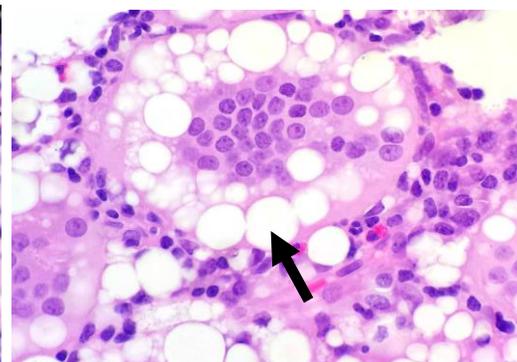
Lots of foreign material can be seen in histiocytes in draining lymph nodes, including:



Metal particles after joint replacement



Tattoo pigment



Silicone in axilla after breast implants