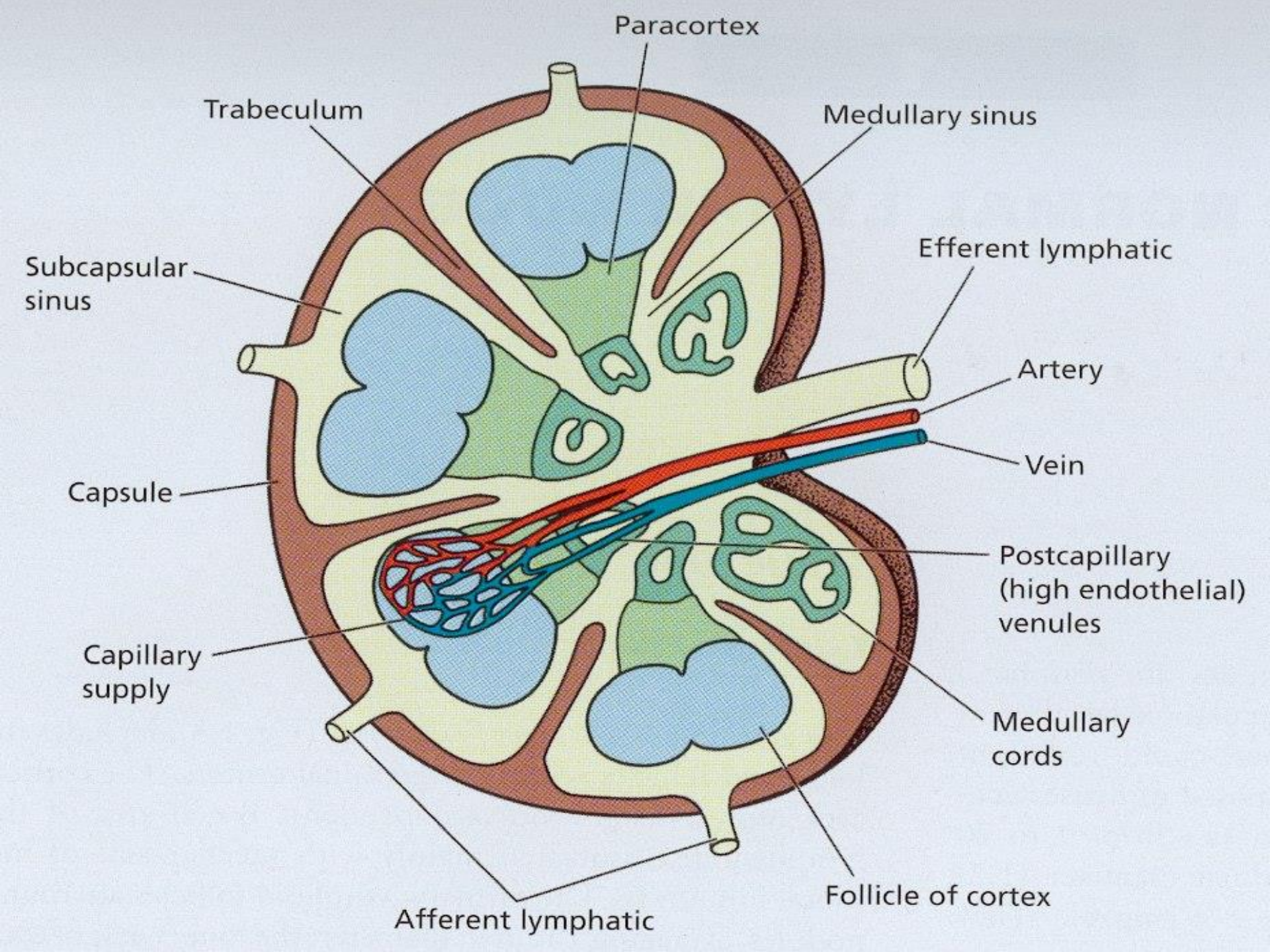
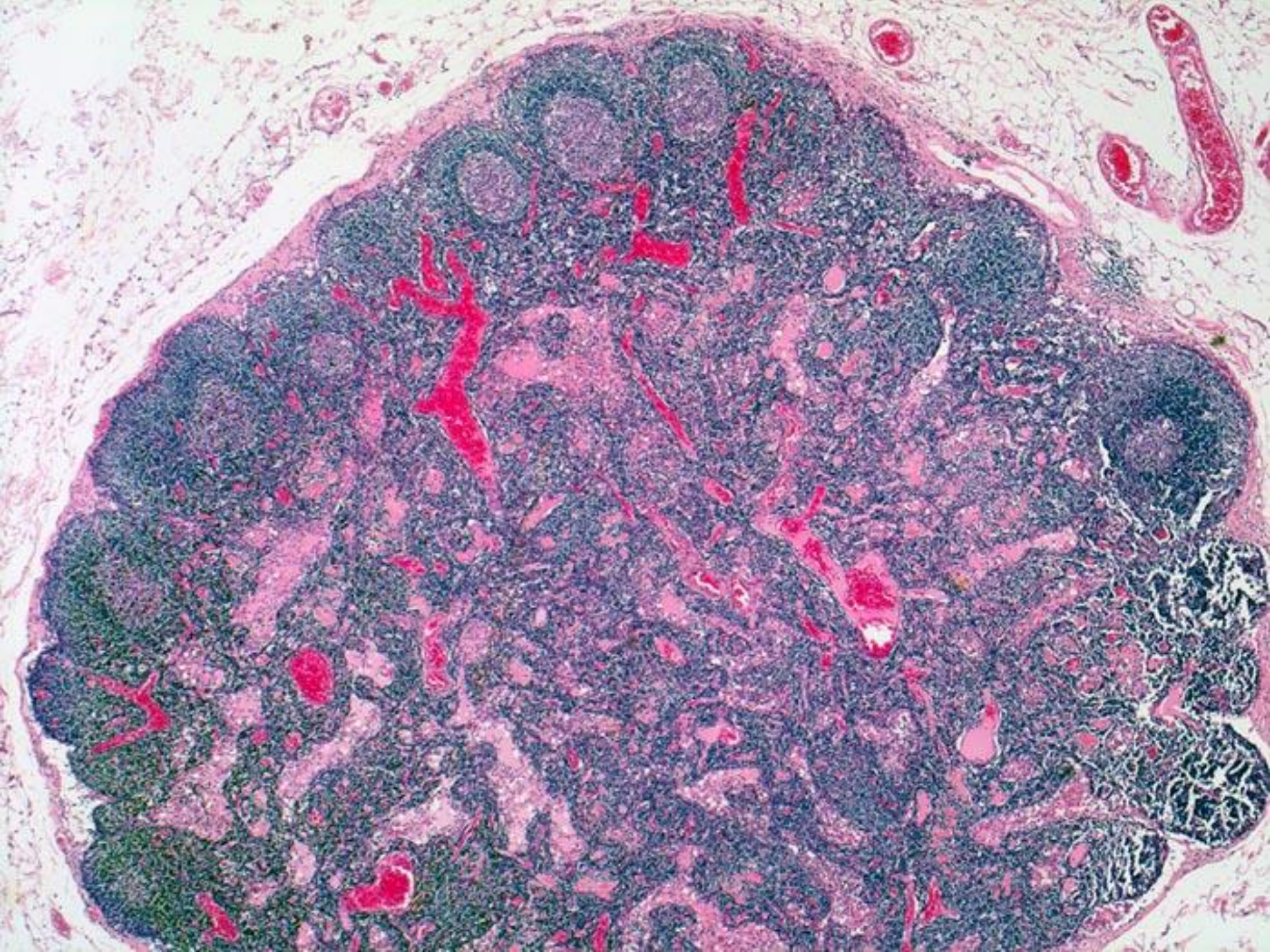
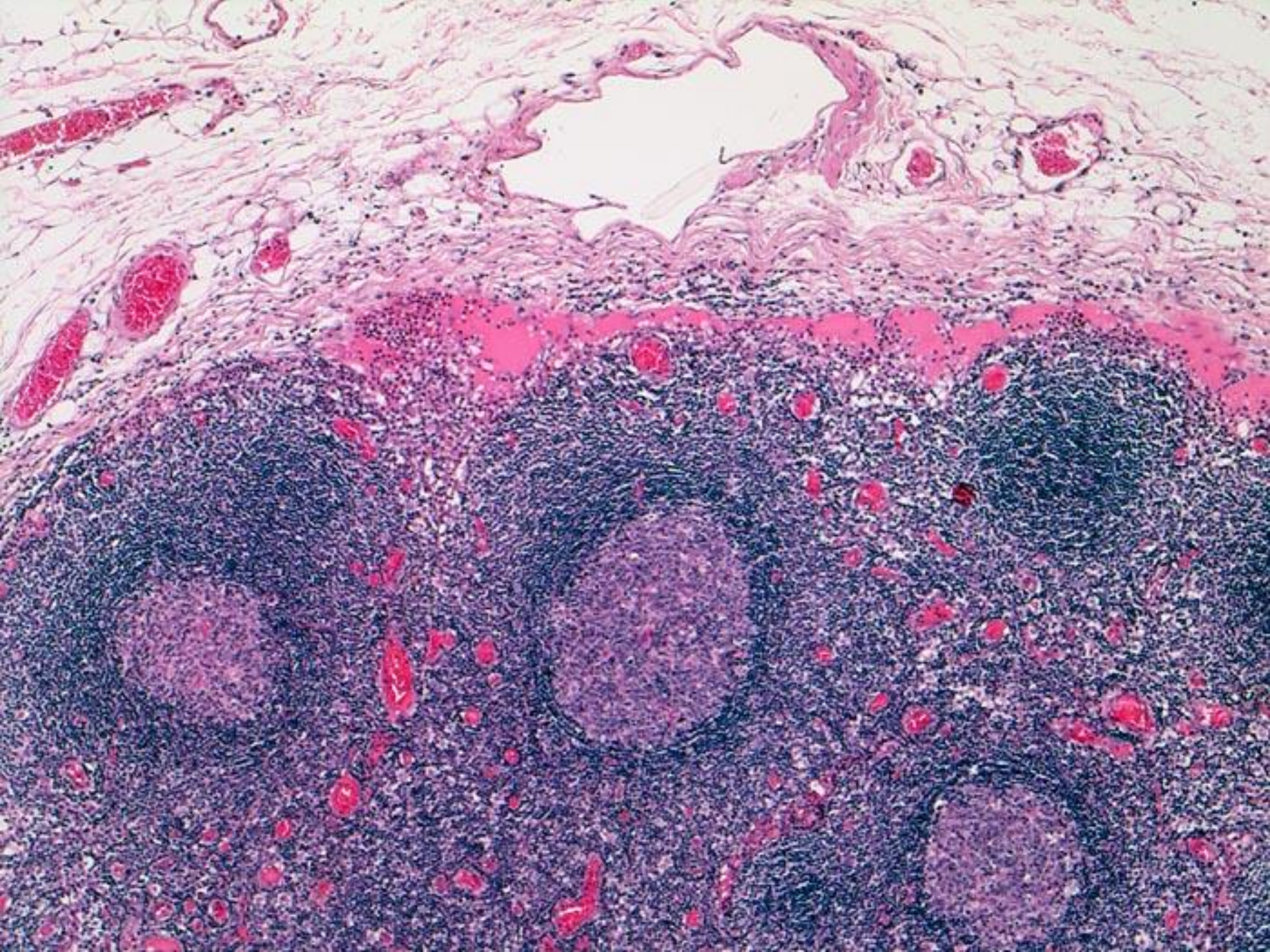
Nonmalignant Lymphadenopathy

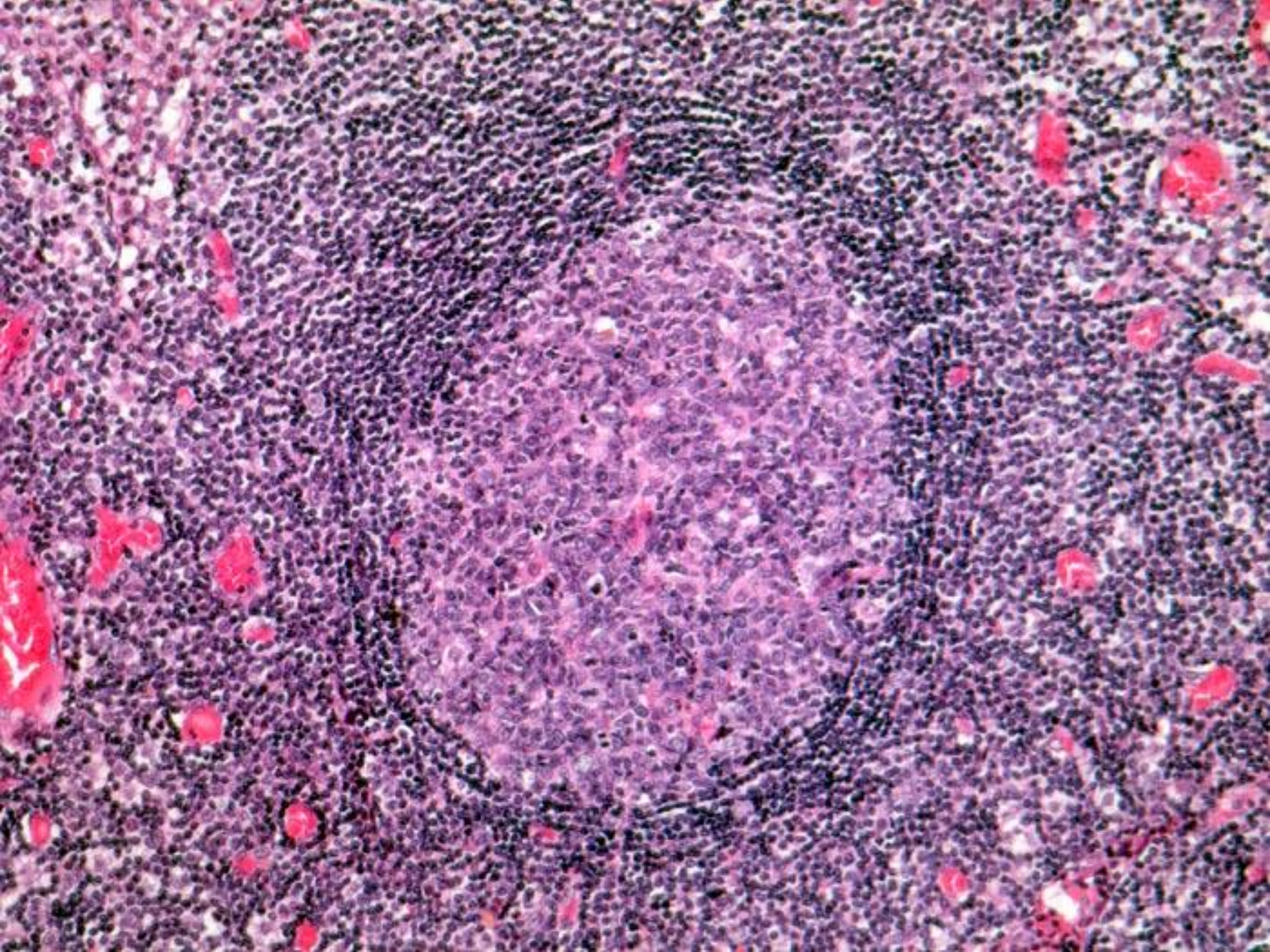
5/14/2018

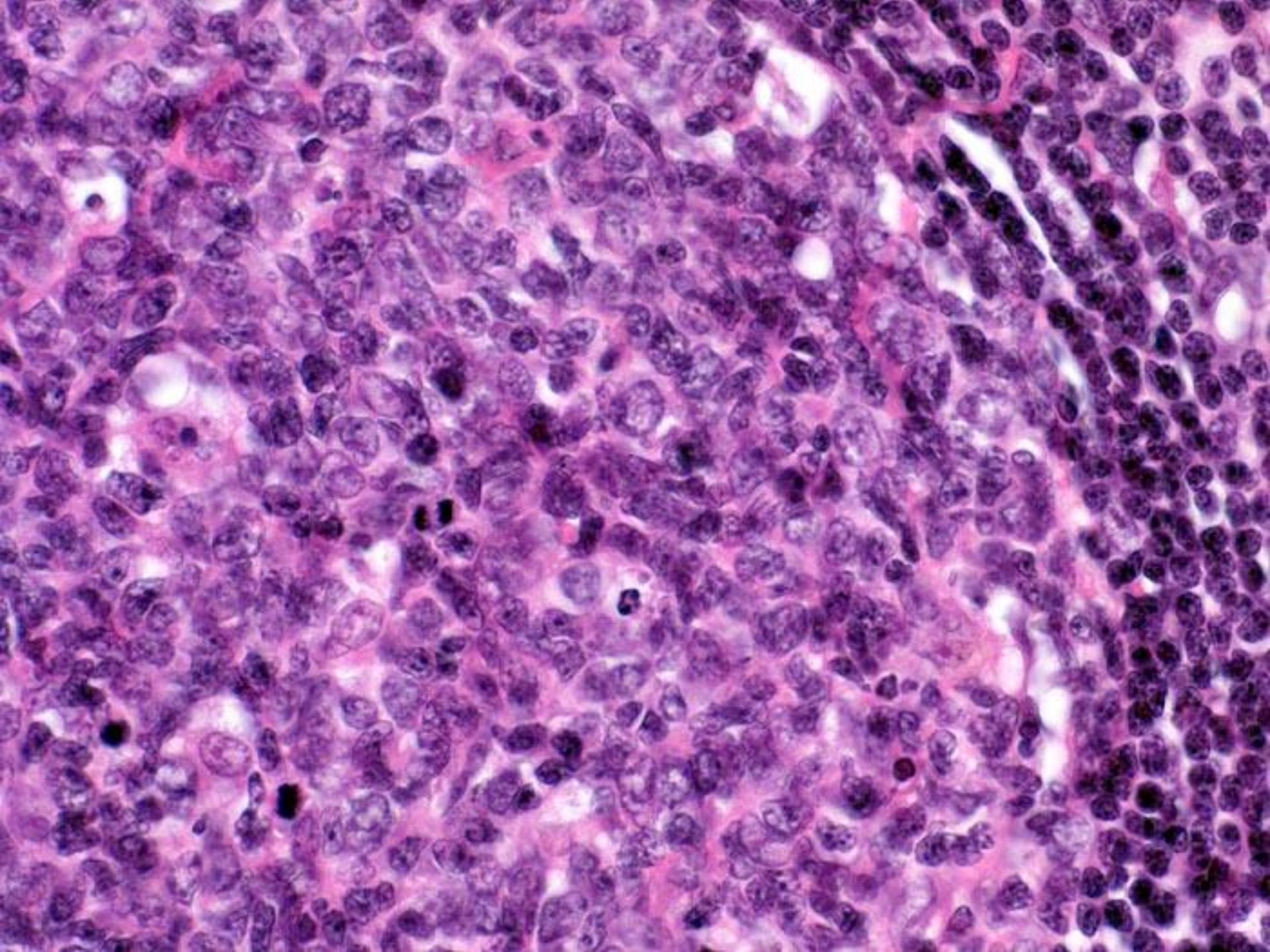
Normal lymph node

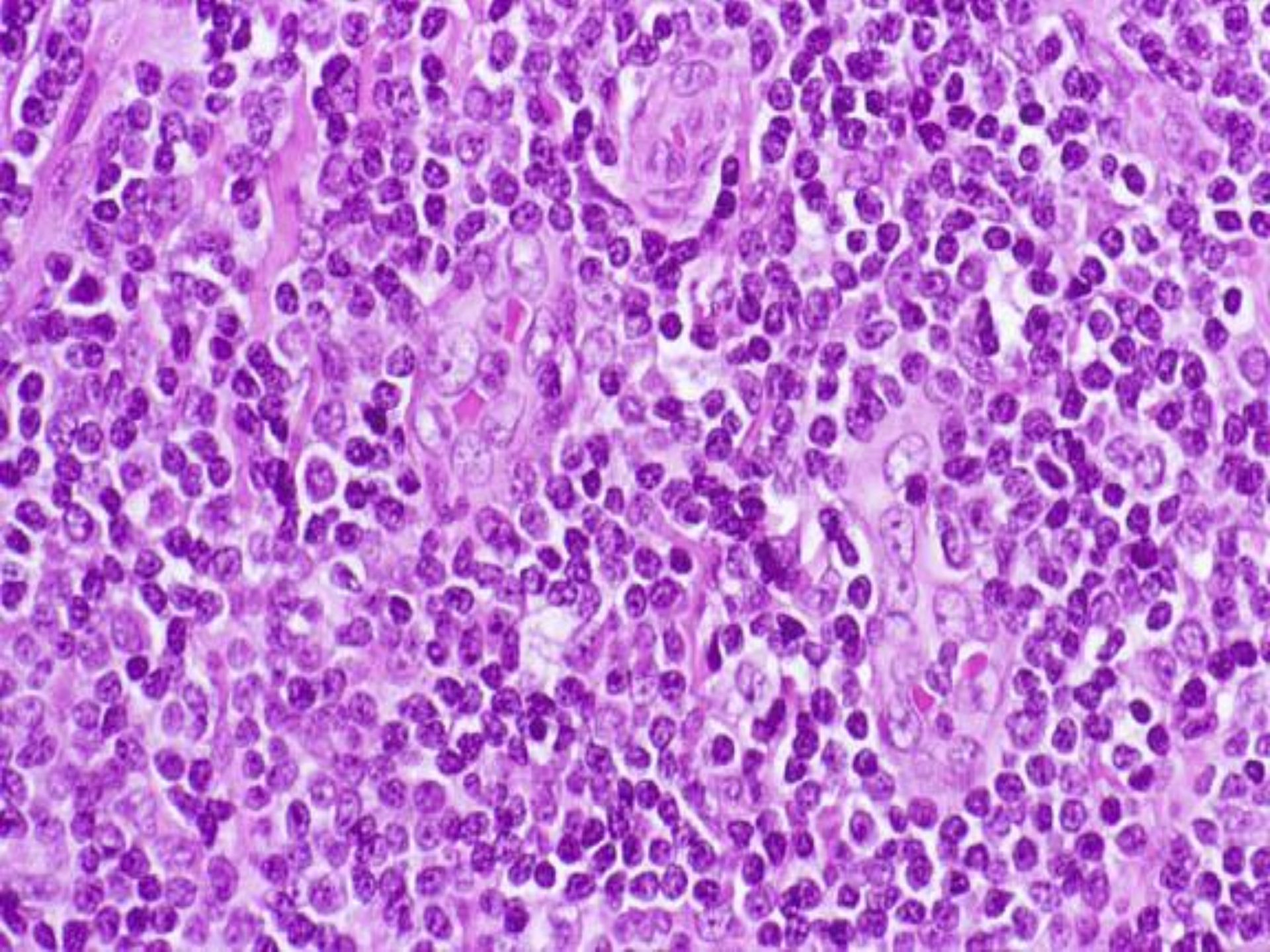

Paracortex
Trabeculum
Medullary sinus
Subcapsular sinus
Efferent lymphatic
Artery
Vein
Capsule
Postcapillary (high endothelial) venules
Capillary supply
Medullary cords
Follicle of cortex
Afferent lymphatic

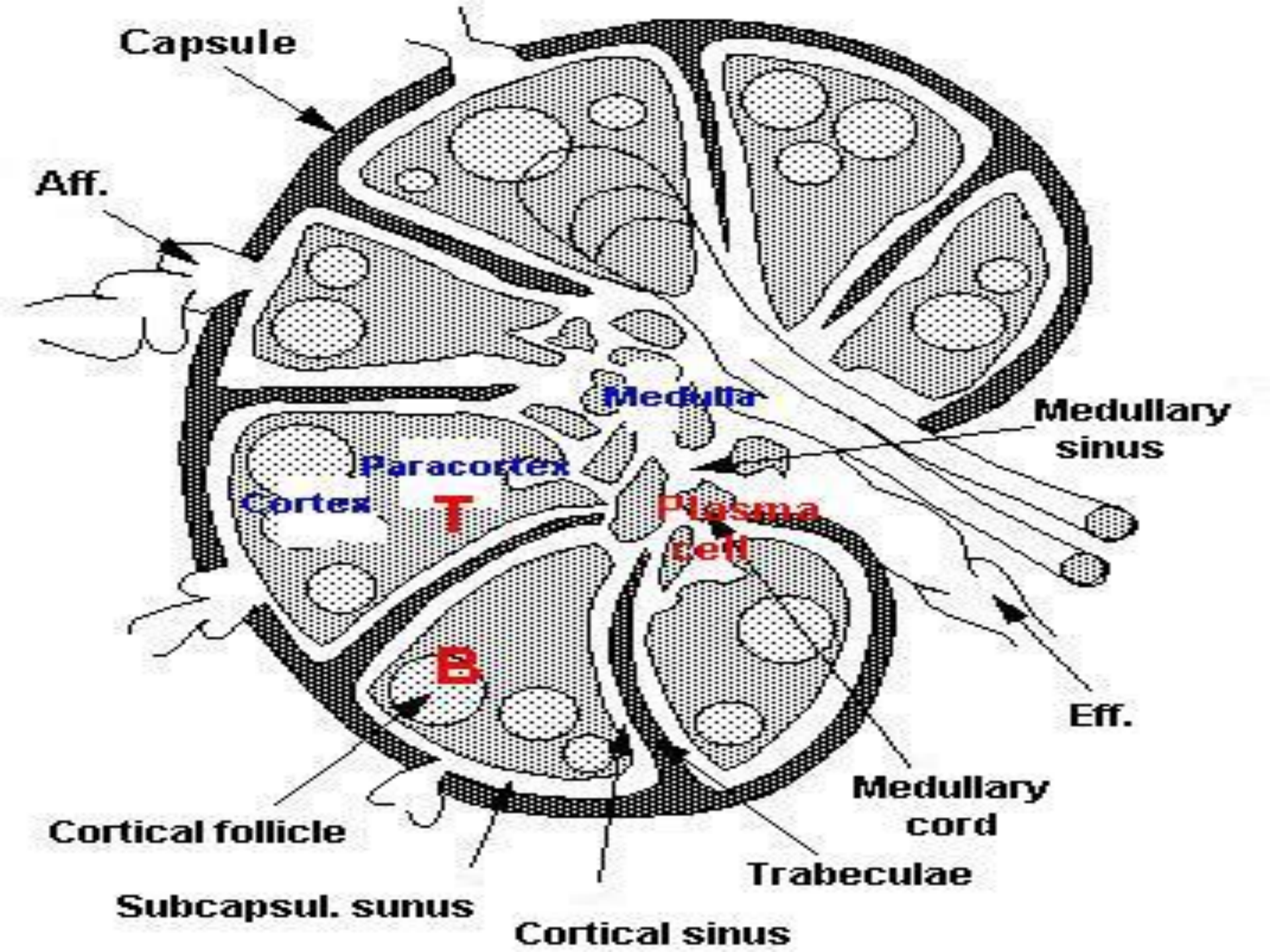


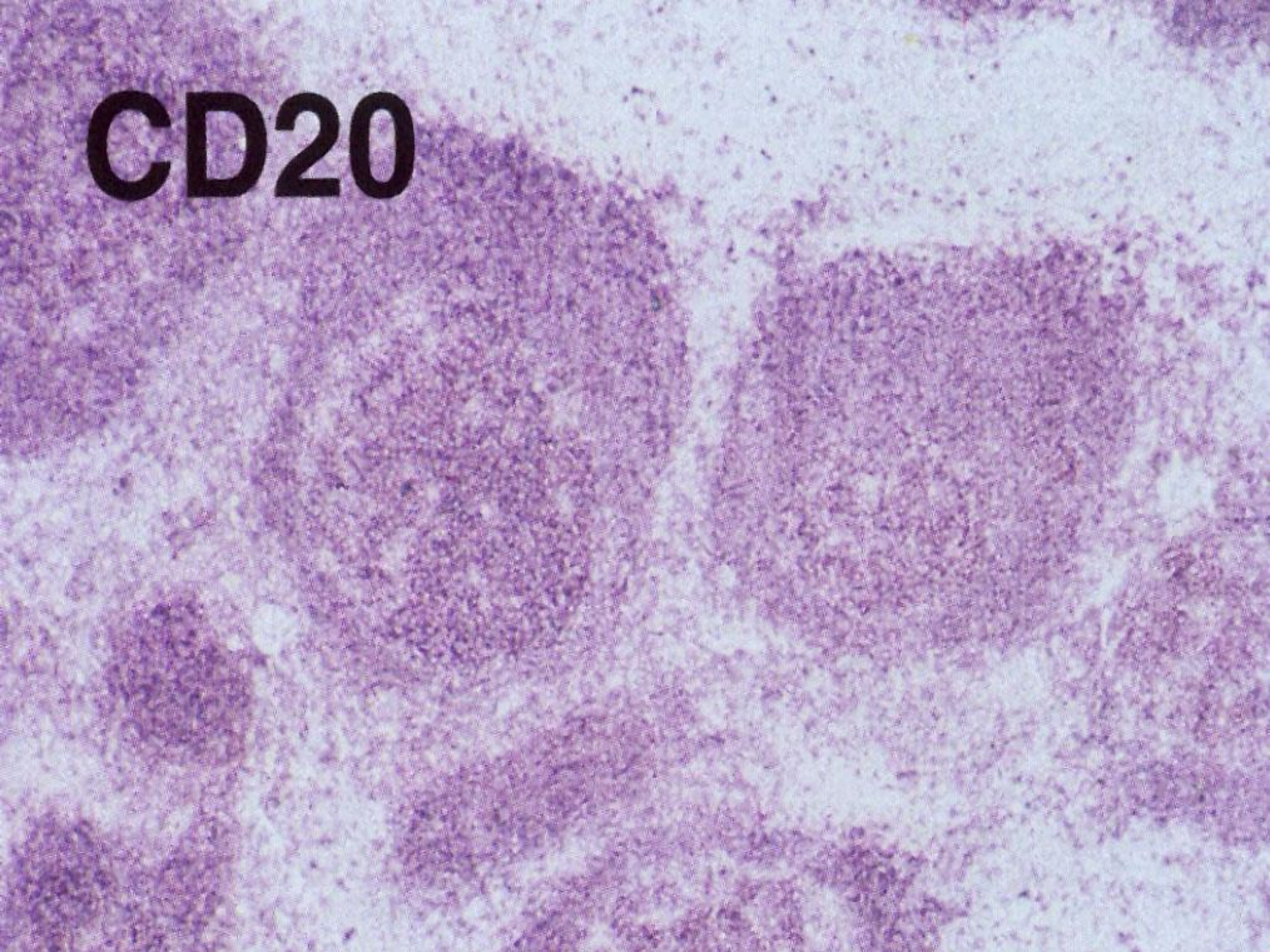


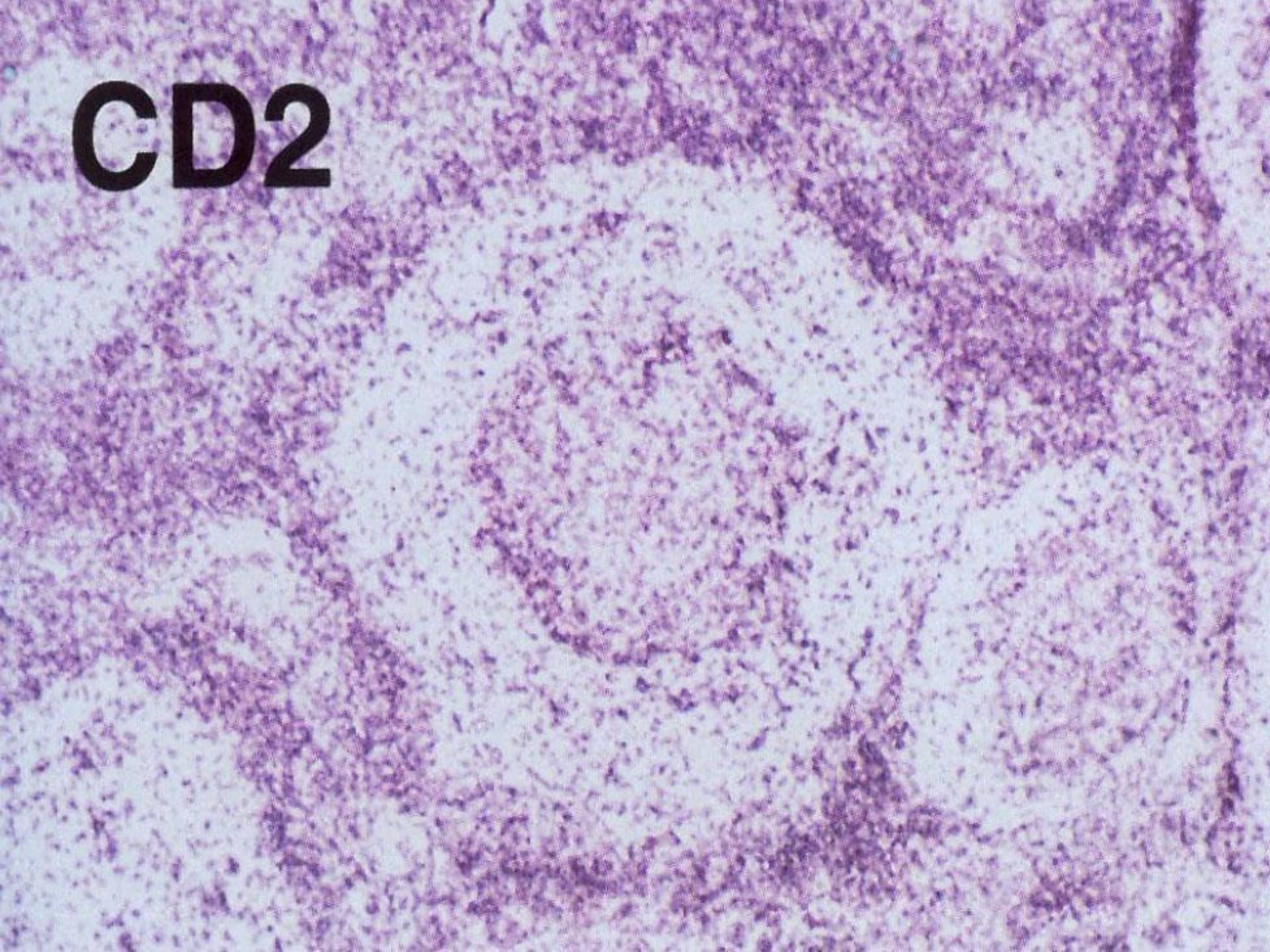







Capsule
Aff.
Medulla
Medullary sinus
Paracortex
Cortex
T
Plasma cell
B
Eff.
Medullary cord
Cortical follicle
Trabeculae
Subcapsul. sunus
Cortical sinus

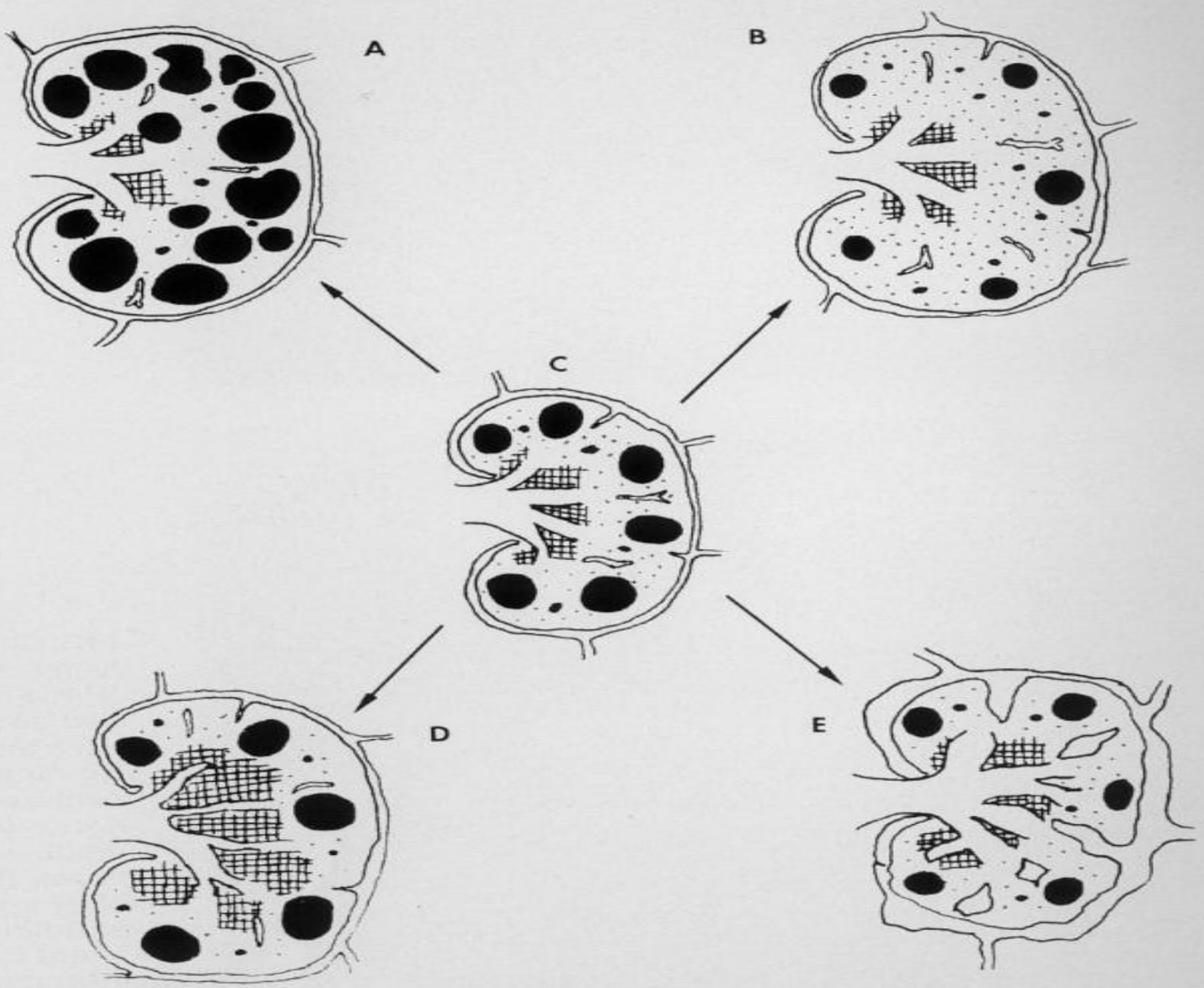

CD20


CD2

Lymph Node Pathology

**covered here

- Lymphadenitides **
- Lymphadenopathies **
- Lymphomas
- Granulocytic, Histiocytic, and Dendritic Cell Neoplasms
- Other primary neoplasms
- Metastatic neoplasms


A
B
C
D
E

Lymph Node Pathology Diagnostic Methods

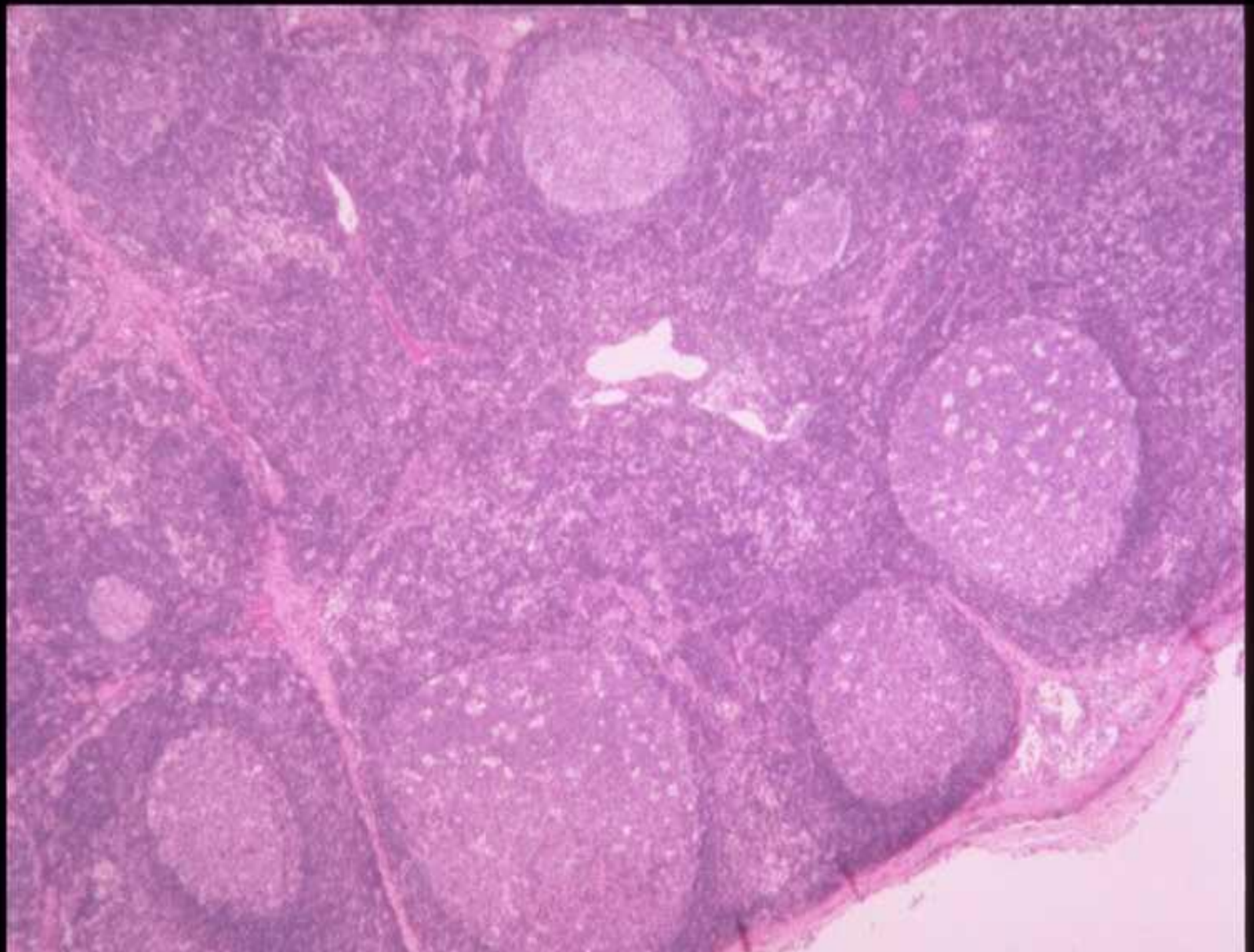
- Fixed tissue:
  - Routine histomorphology
  - Immunohistochemistry
  - PCR
- Touch preparations
  - Wright (Diff-Quick) stain
- Cell suspension from biopsy:
  - Flow cytometry
  - Cytogenetics
  - Molecular diagnostics (gene rearrangement)

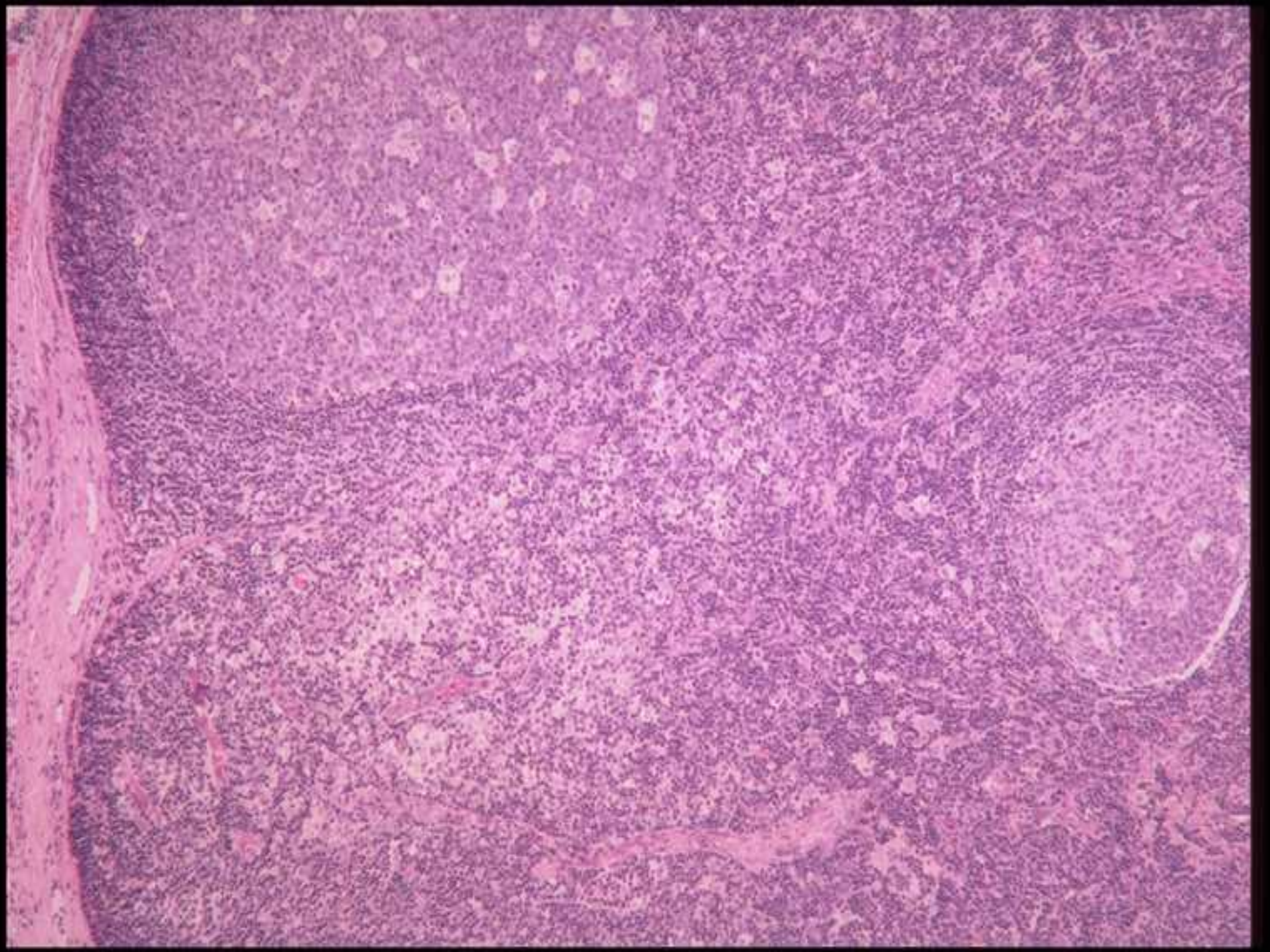
Hyperlasia:

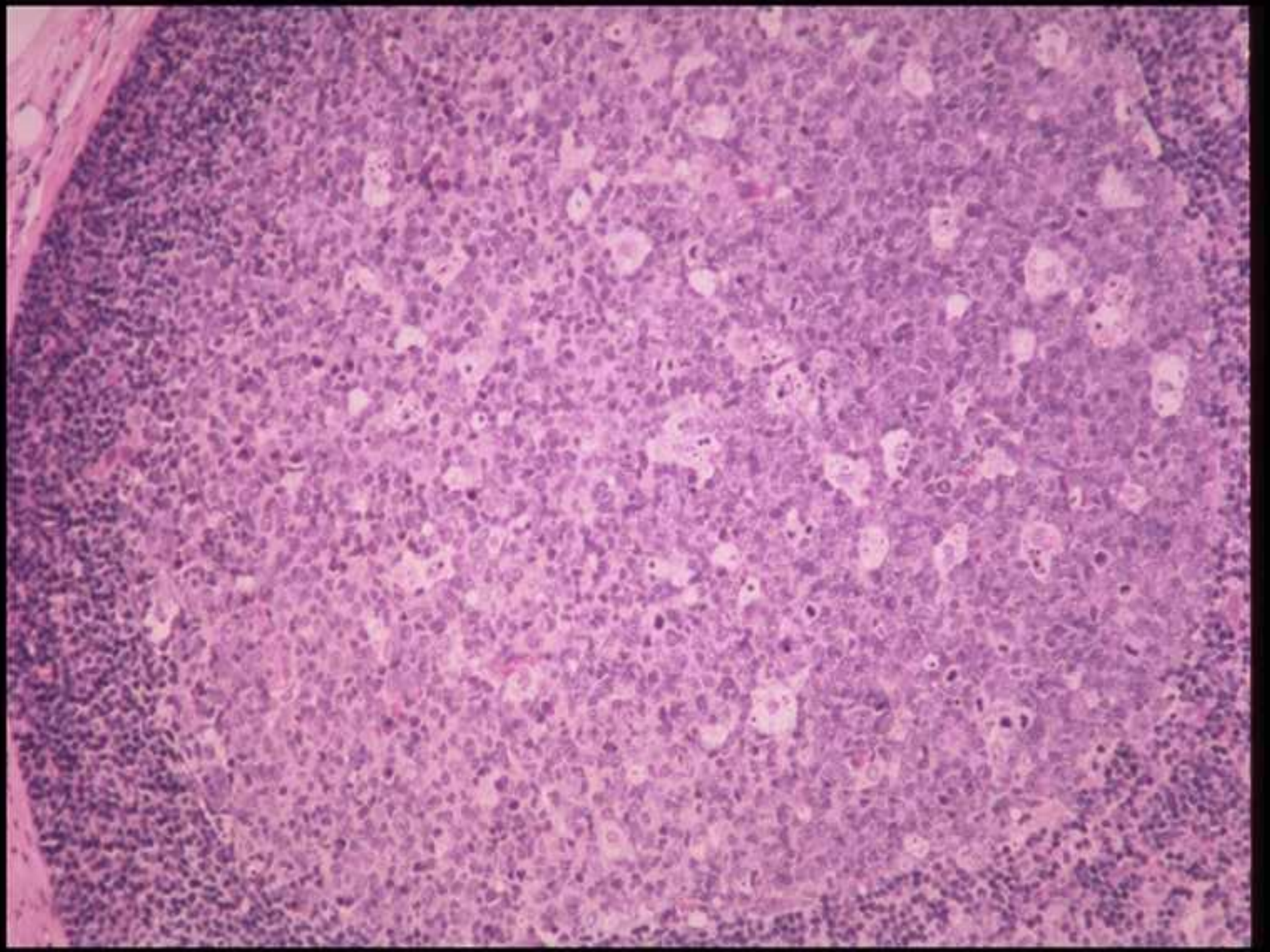
-Follicular
-Sinus
-Follicular and sinus

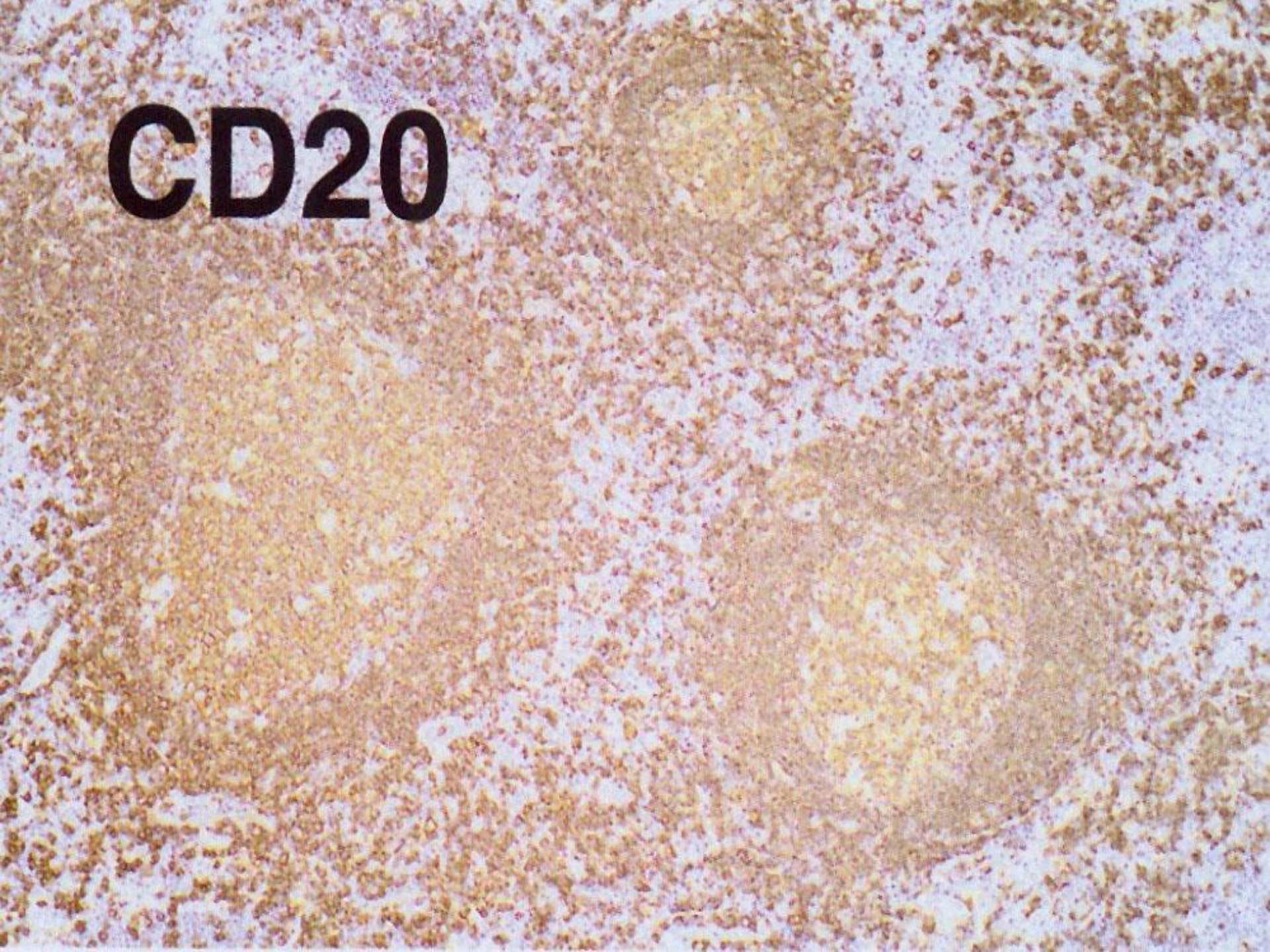
Reactive Lymphoid Hyperplasia Follicular Pattern

- Numerous enlarged, oddly shaped follicles
- Prominent germinal centers
- Tingible body macrophages
- Nonhomogenous lymphoid population
- Frequent mitoses
- Polyclonal surface immunoglobulins
- Germinal centers negative for bcl-2





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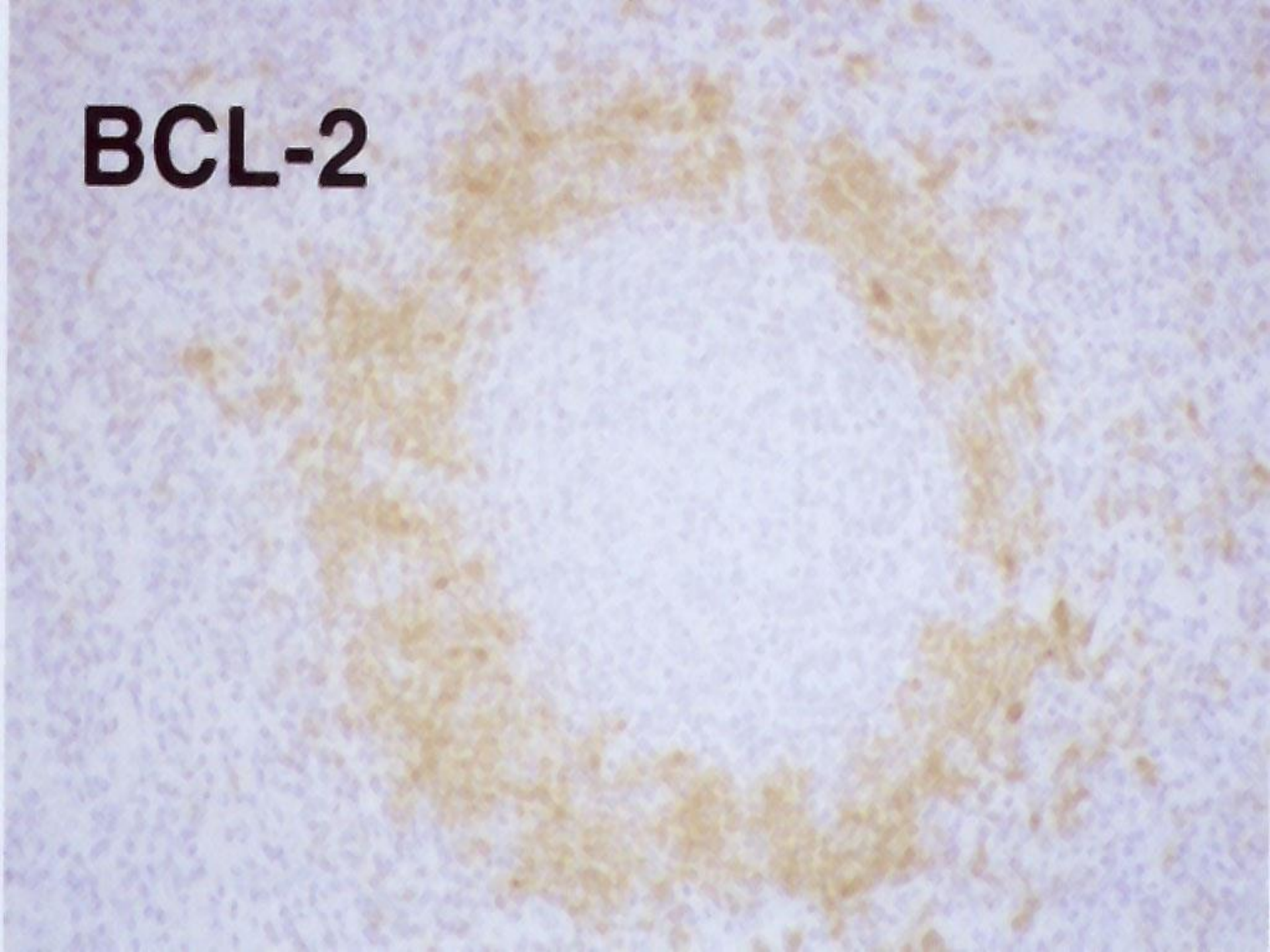
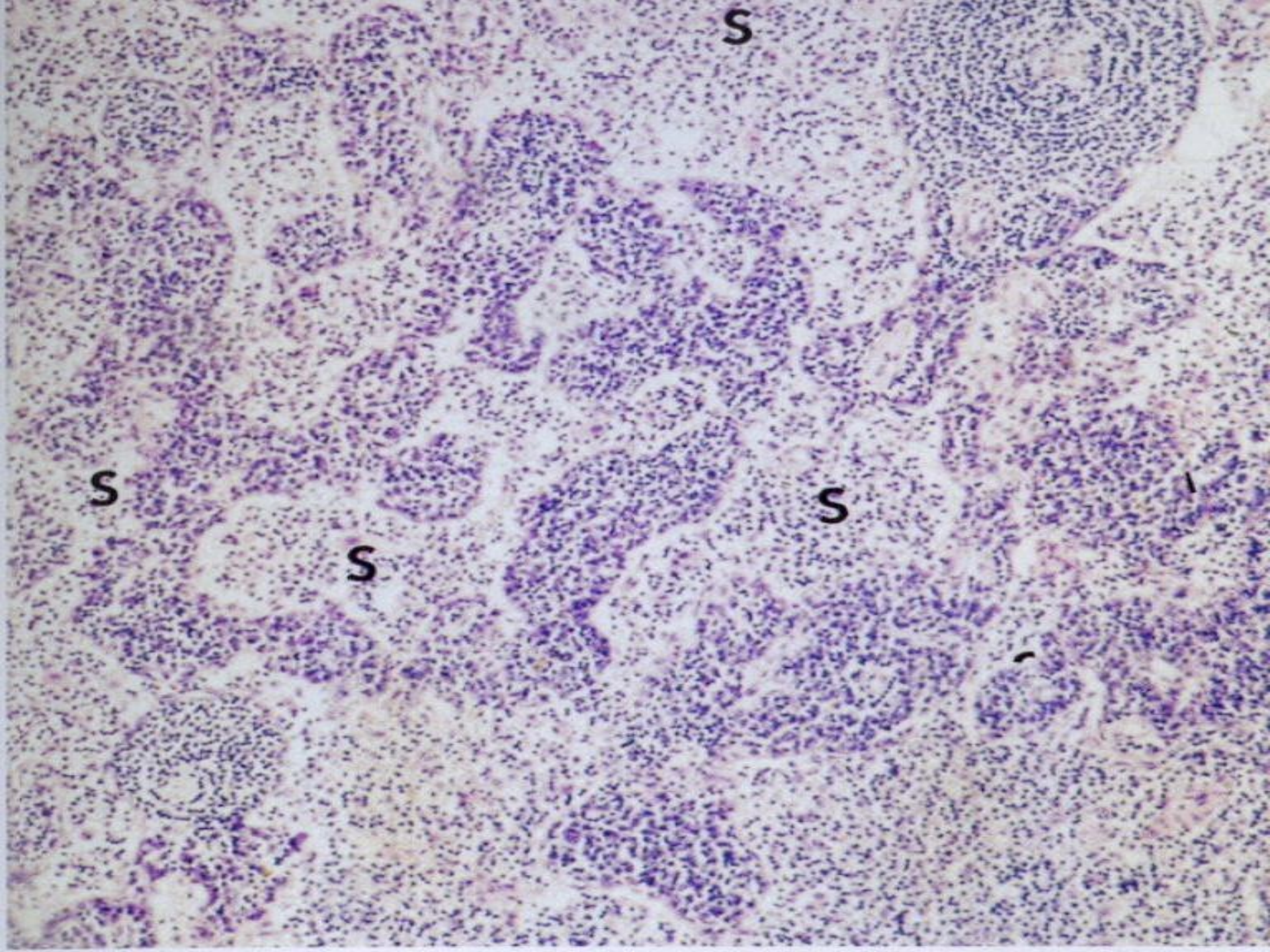

BCL-2

Reactive Lymphoid Hyperplasia Sinus Pattern

- Prominent sinuses
- Histiocyte hyperplasia
- Proliferation of plasma cells
- Polyclonal surface immunoglobulins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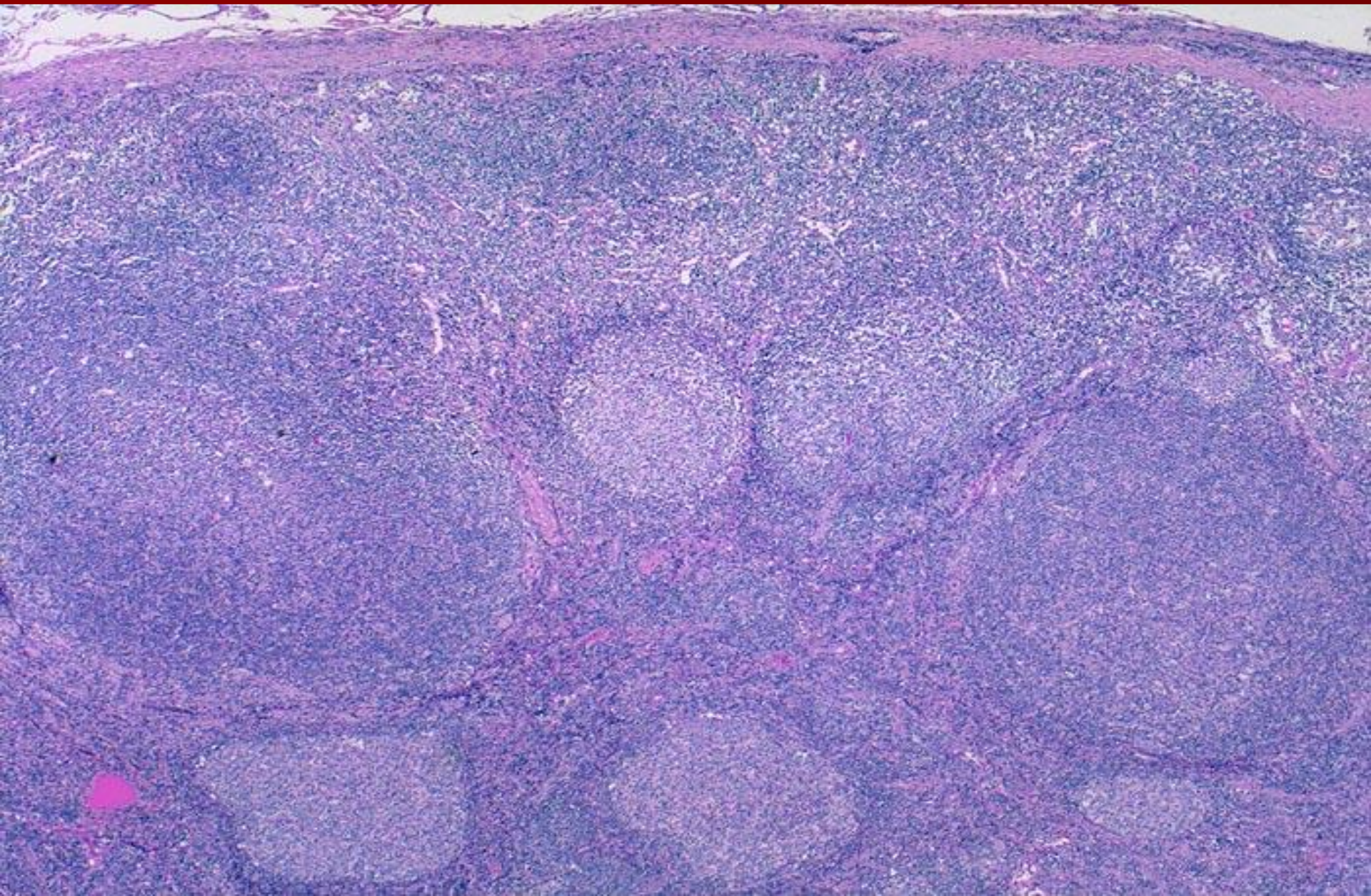
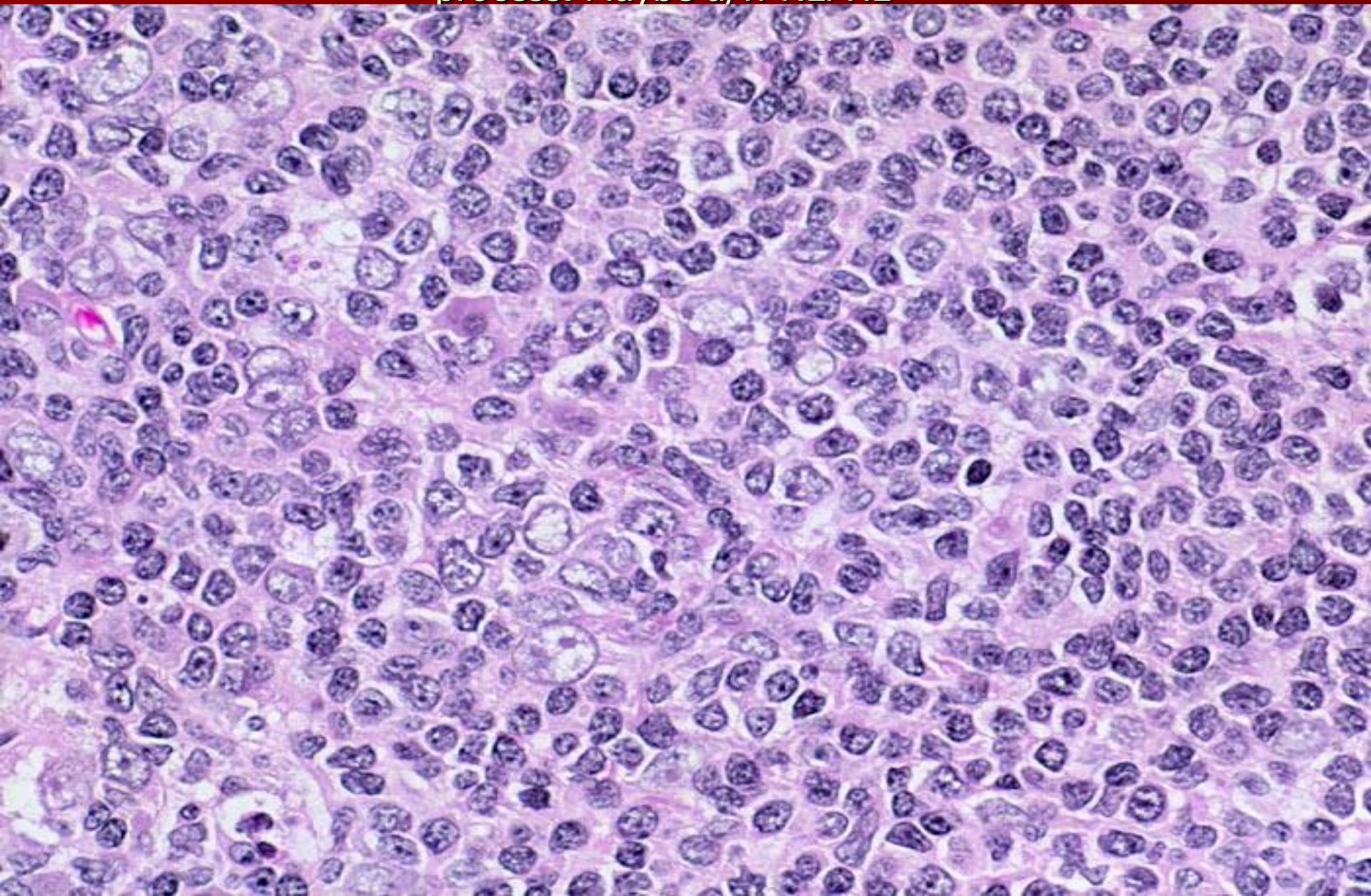
Progressive Transformation of Germinal Center



Progressive Transformation of Germinal Center:

expanded follicular center infiltrated by mantle cells. A benign process. Maybe a/w NLPHL



Lymph Node Pathology: Lymphadenitides

- Viral
- Bacterial
- Mycobacterial
- Fungal
- Protozoal

Viral Lymphadenitides

- Infectious Mononucleosis
- Cytomegalovirus
- Herpes Simplex Virus
- Varicella-Zoster Virus
- Measles
- HIV

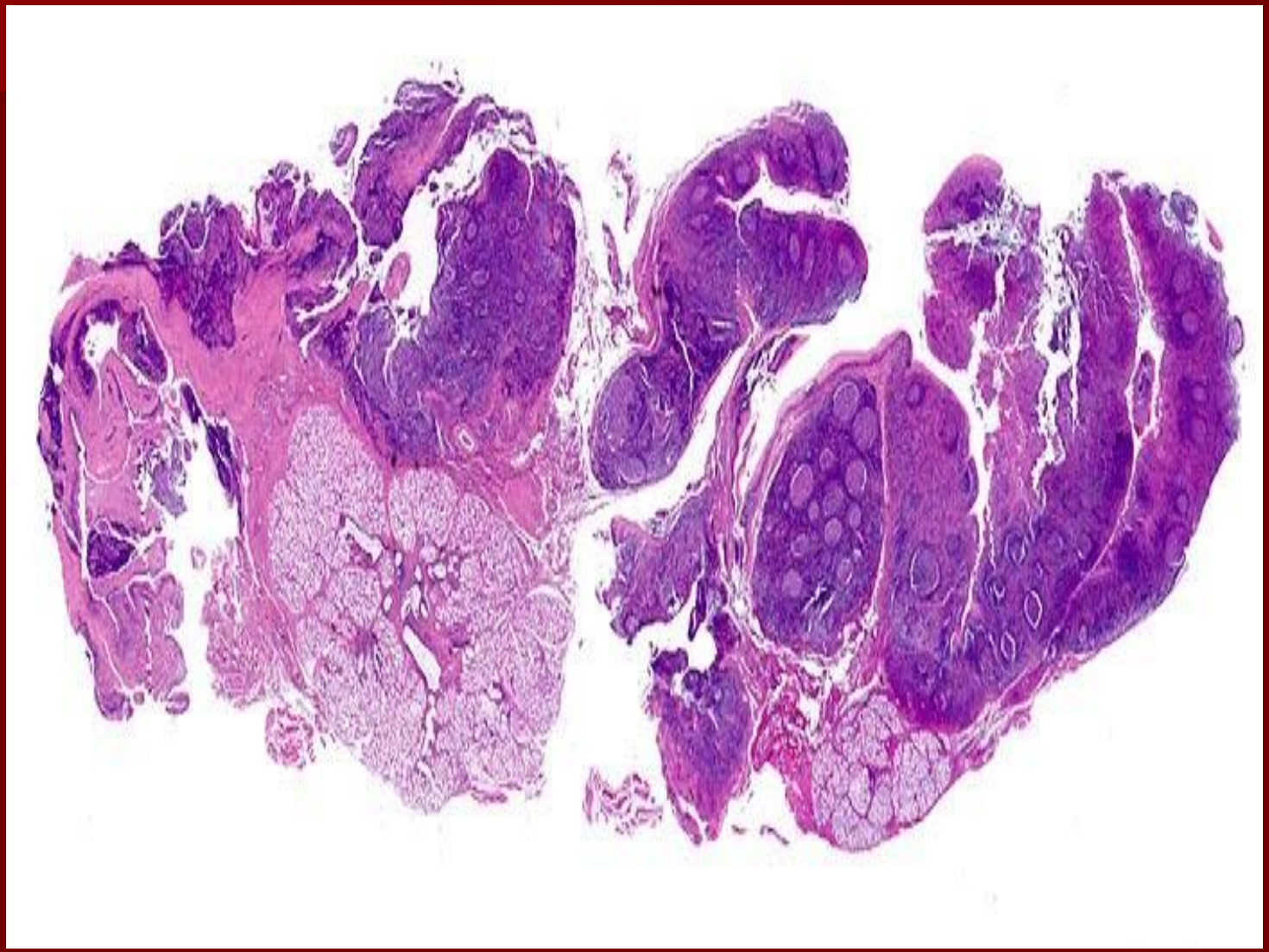
Viral Lymphadenitis

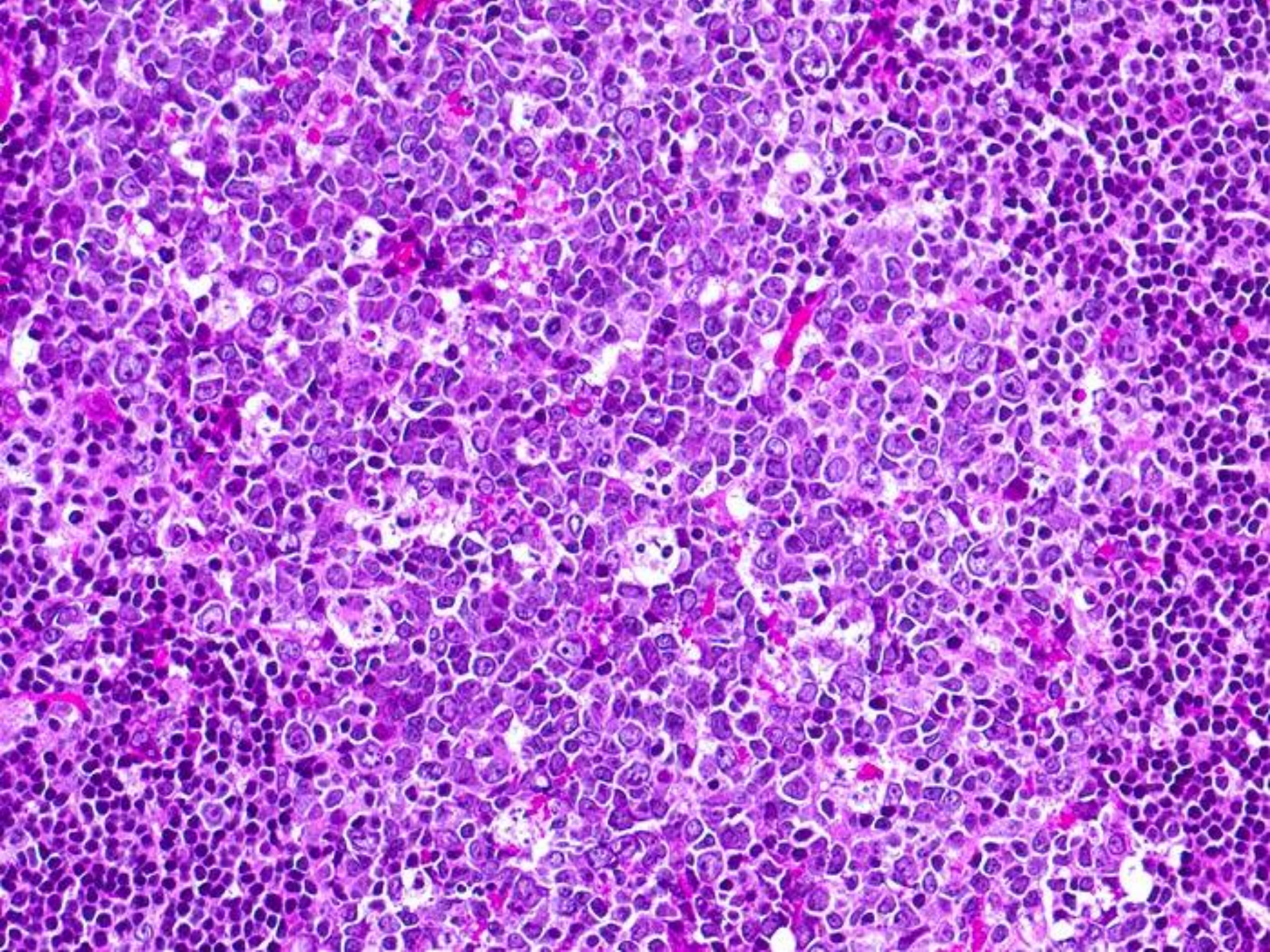
- Clinical findings/serologies
- Peripheral blood lymphocytosis (sometimes)
- Atypical lymphocytes
- Expanded paracortex (T-cell zone)
- Mottled pattern
- Immunoblasts & R-S like cells
- Virus-specific findings (sometimes) such as large cells with eosinophilic intranuclear inclusion in CMV

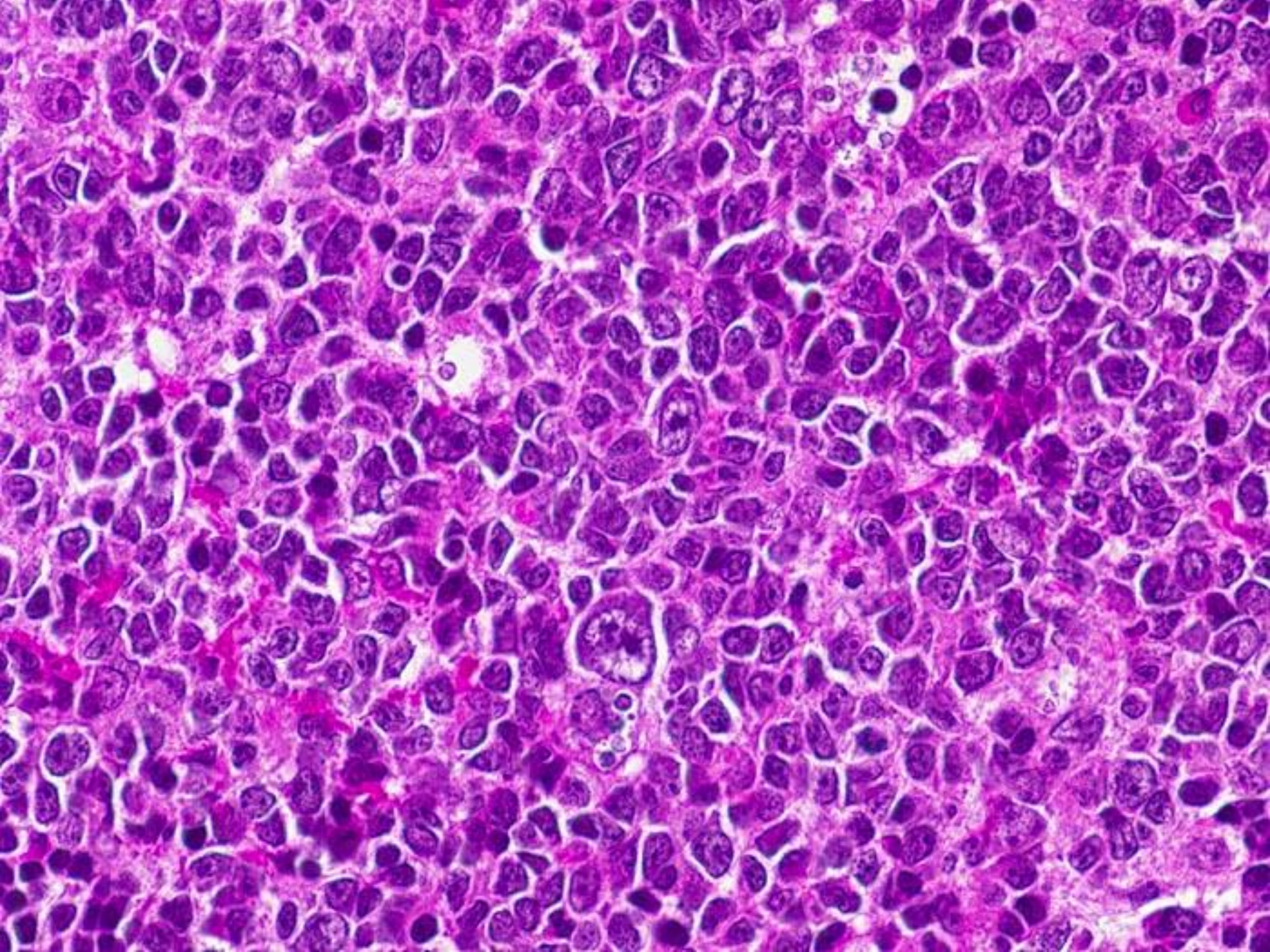
Infectious Mononucleosis

- EBV virus
- Clinical information: febrile, exudative pharyngitis, cervical lymphadenopathy, splenomegaly, abnormal LFTs, common in adolescence/young adulthood, rare after 40 y/o
- Peripheral blood lymphocytosis with atypical lymphocytes
- Expanded paracortex (T-cell zone) by many immunoblasts & R-S like cells
- Mottled pattern, foci of necrosis
- Different from NHL: polymorphous background of transformed lymphocytes, persistent of reactive follicles, architecture preservation. Immuno for R-S like cells: (+) for CD30 and CD20; (-) for CD15. Also many large CD8-pos cells

Case Illustration





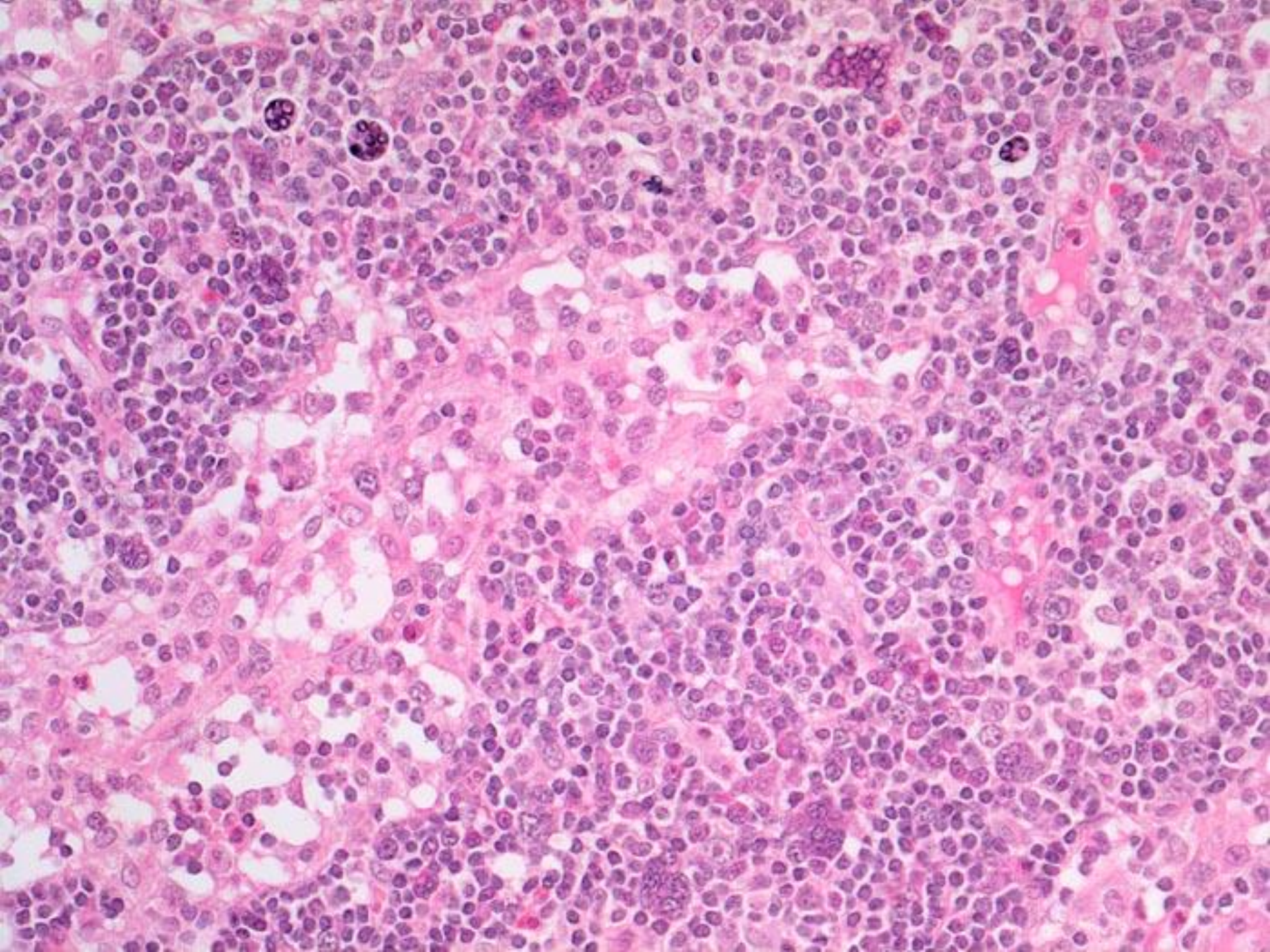


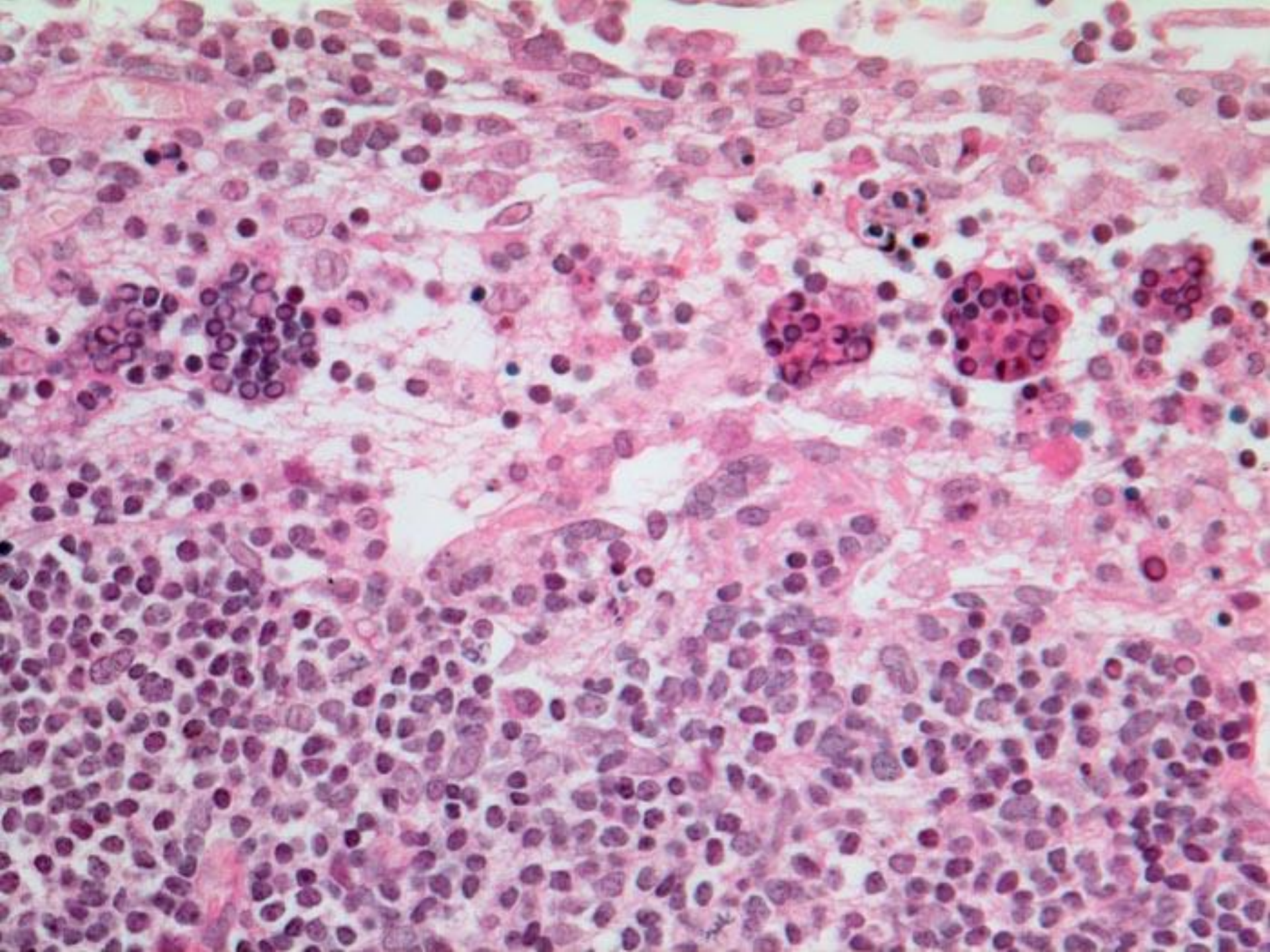
Measles Lymphadenitis

- Measles (rubeola) or history of recent vaccination
- Axillary, cervical, inguinal lymph nodes
- Mottled histologic pattern
- Follicular hyperplasia
- Proliferation of immunoblasts
- Warthin-Finkeldey giant cells (syncytia of lymphocytes)

Case Illustration

- 4-year-old boy with pharyngitis, conjunctivitis
- Axillary and cervical tender, lymphadenopathy





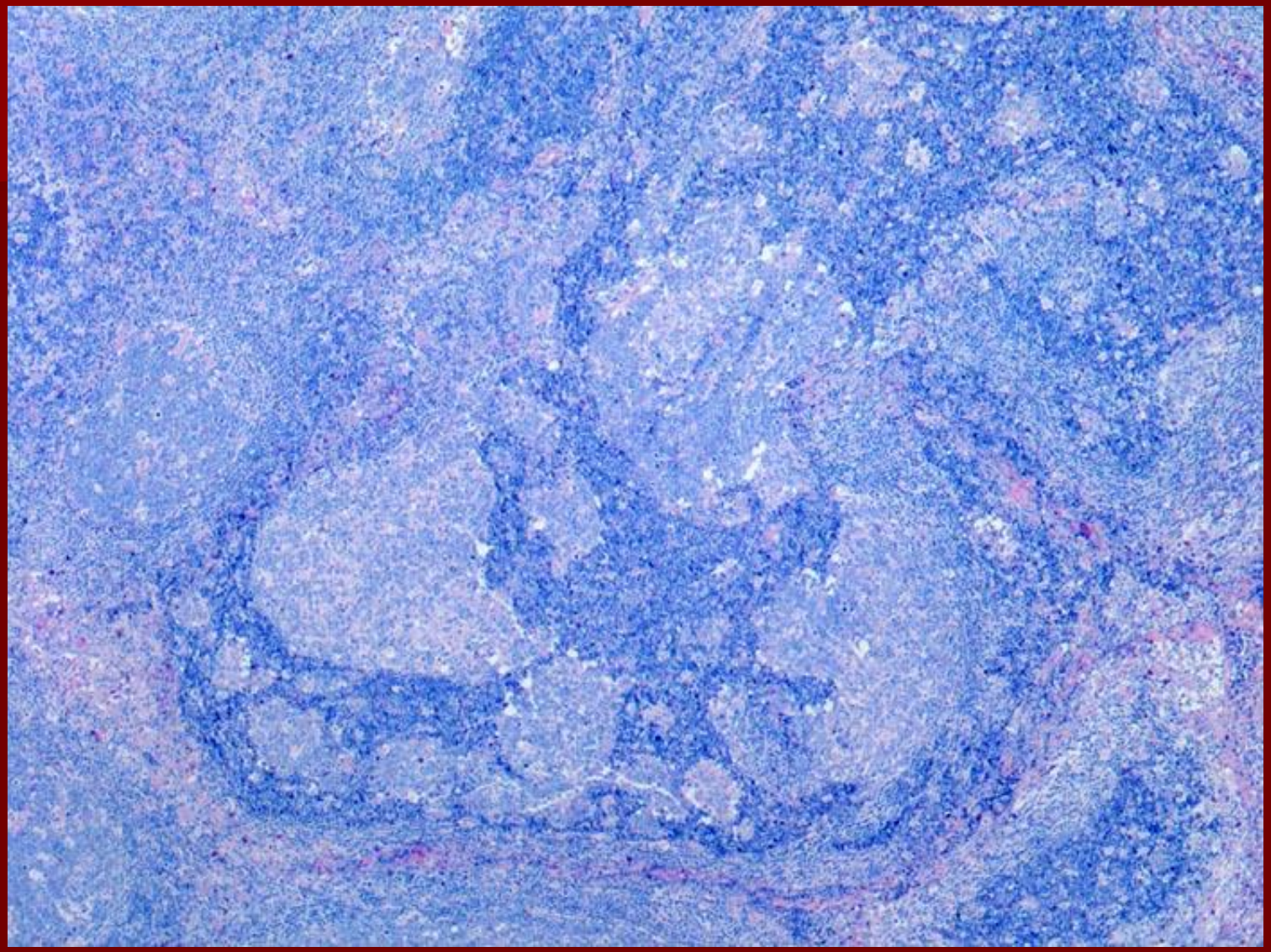
HIV Lymphadenitis (persistent generalized lymphadenopathy)

- Pattern A (Acute): Enlarged lymph node with hyperplastic follicles and reactive germinal centers, naked follicular centers, folliculolysis by mantle-zone cells, monocytoid B cells in sinus, Warthin-Finkeldey giant cells
- Pattern B (Chronic): Involution of germinal centers, depletion of lymphocytes, increased plasma cells, vascular hyperplasia
- Pattern C (Burnout): Small or absent follicles with hyalinized germinal centers and collagen-ensheathed arterioles ("lollipop"), plasma cells, more severe lymphocyte depletion-> naked stroma

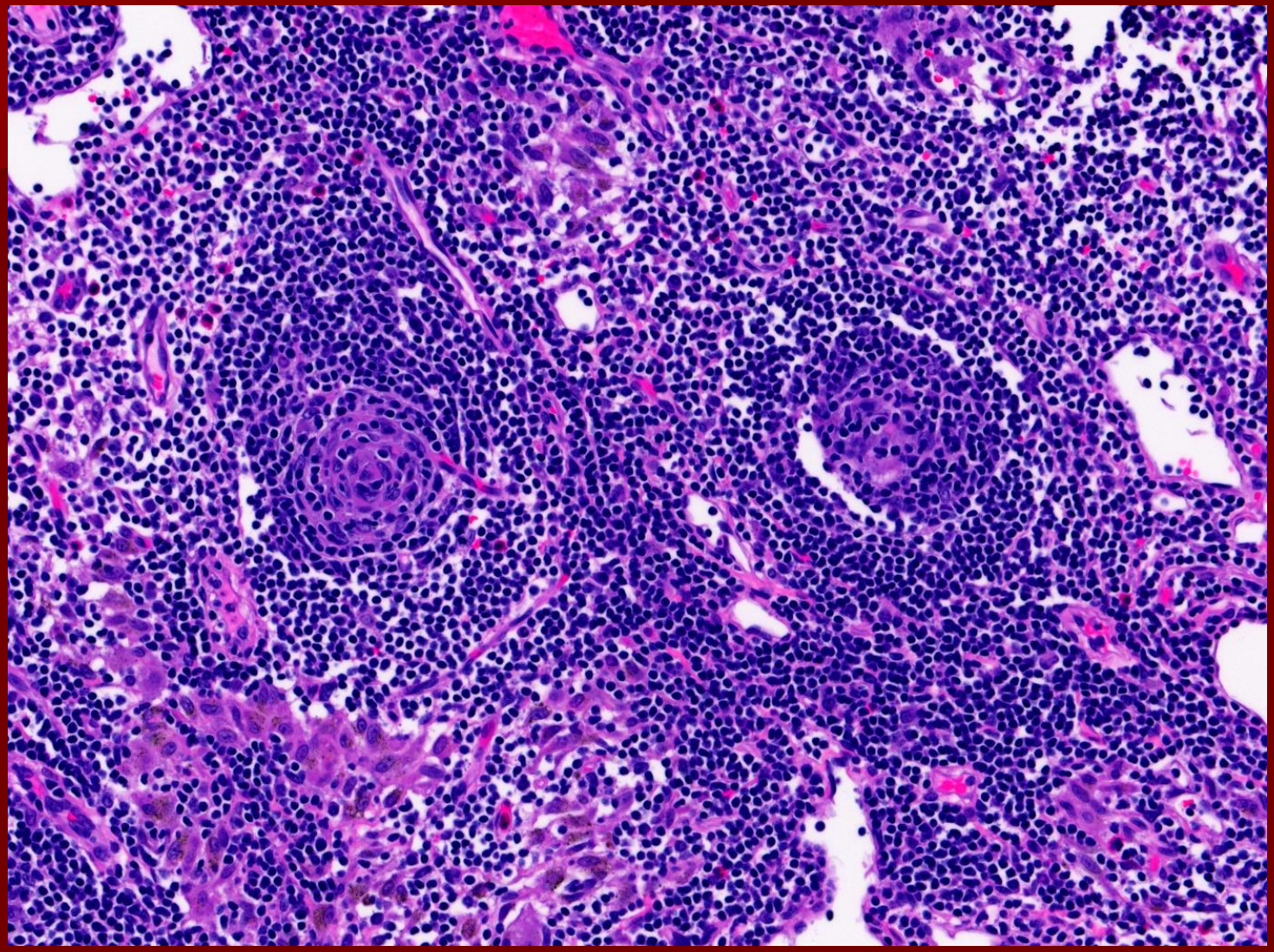
Case Illustration

- 32-year-old man with fatigue, weight loss, diffuse lymph node enlargement

Pattern A (Acute)



Pattern B (Chronic)



Bacterial Lymphadenitis

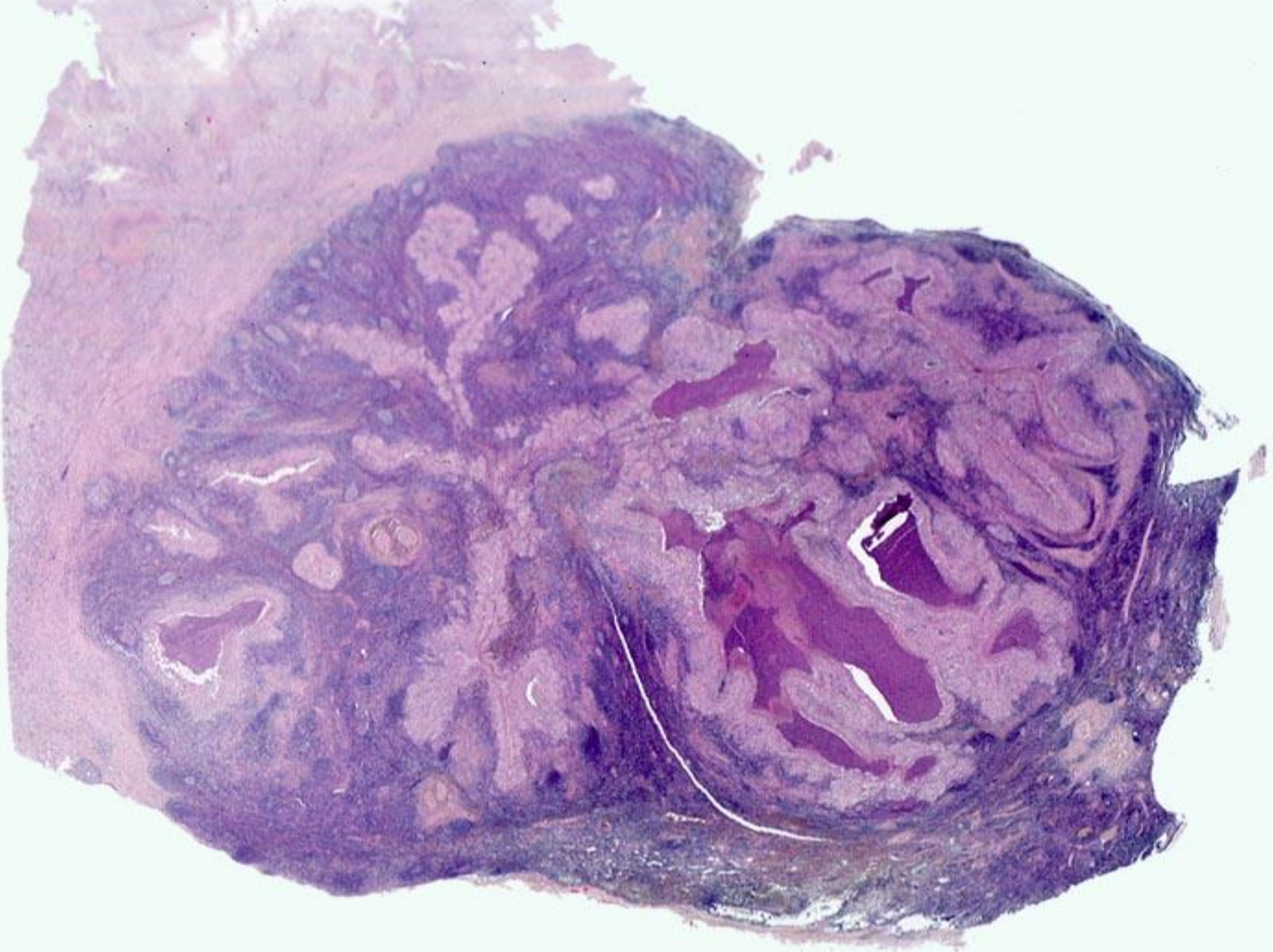
- Ordinary Bacterial
- Cat-Scratch
- Bacillary Angiomatosis
- Lymphogranuloma Venereum
- Syphilitic
- Whipple's

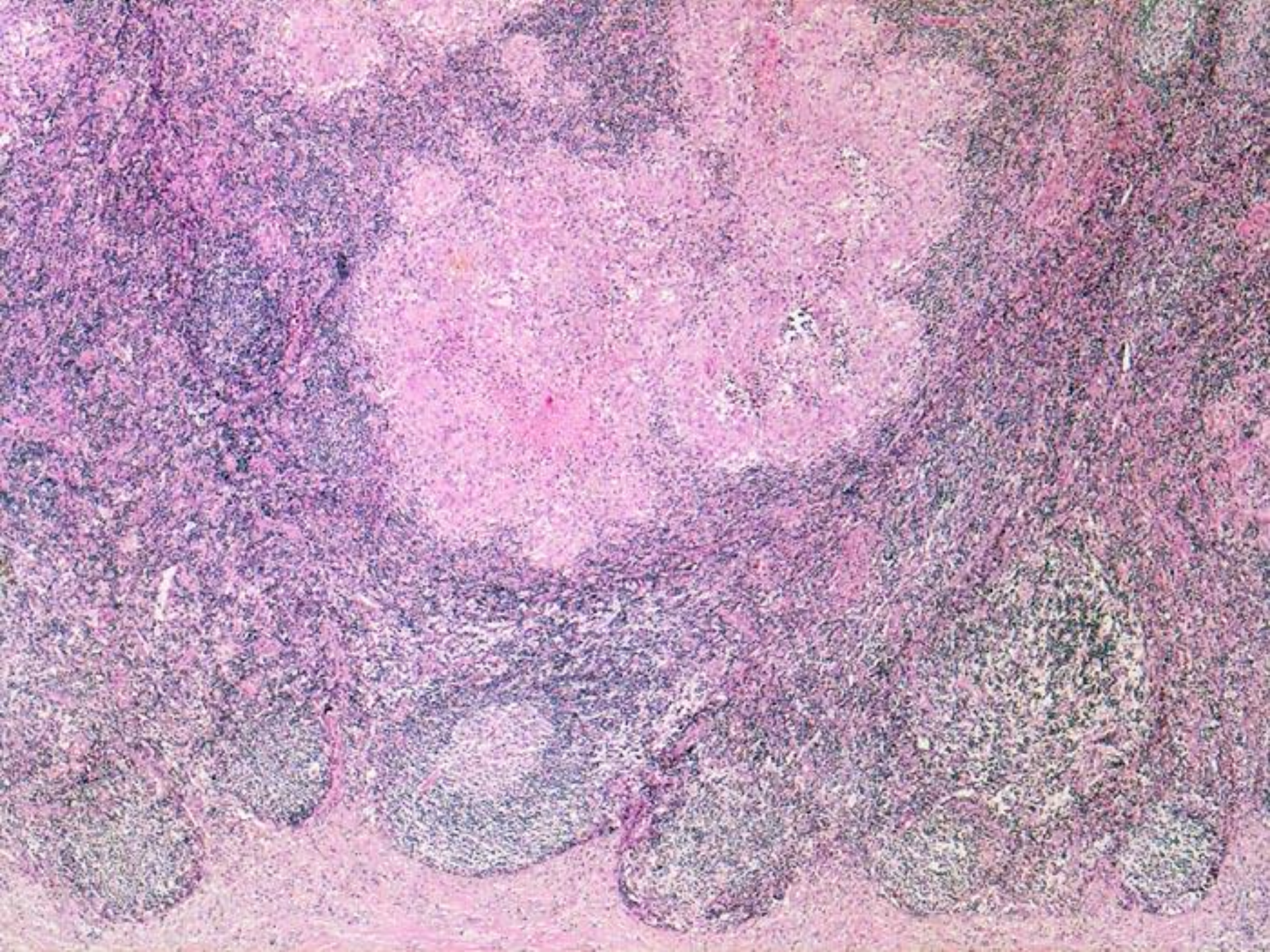
Cat Scratch Lymphadenitis

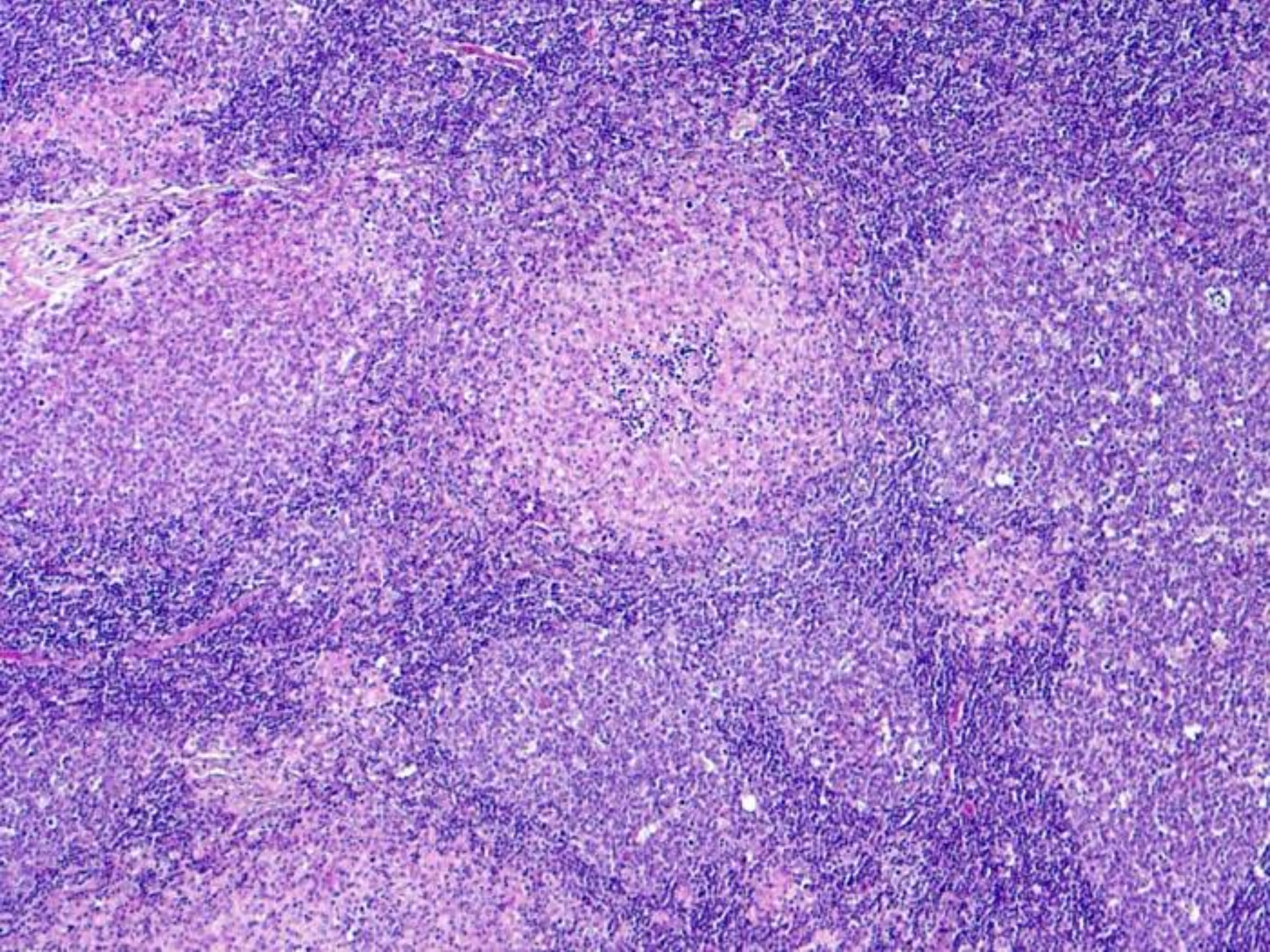
- Contact with cats
- *Bartenella henselae*, gram-negative bacillus/Warthin-Starry stain
- Unilateral, matted lymph nodes
- Necrotizing granulomas; central microabscesses with neutrophils, surrounded by histiocytes
- Disseminated disease in AIDS

Casse Illustration

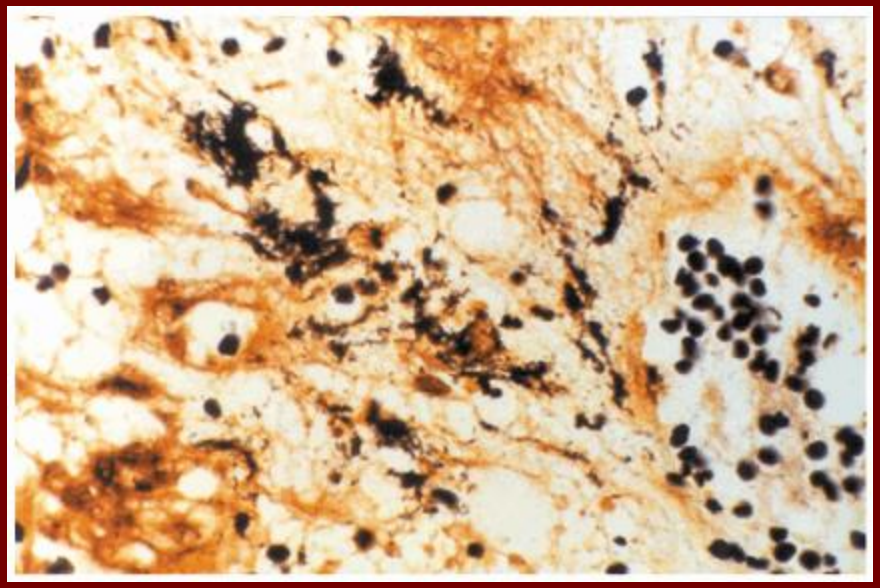
- 10-year-old girl with enlarged, tender axillary lymph nodes







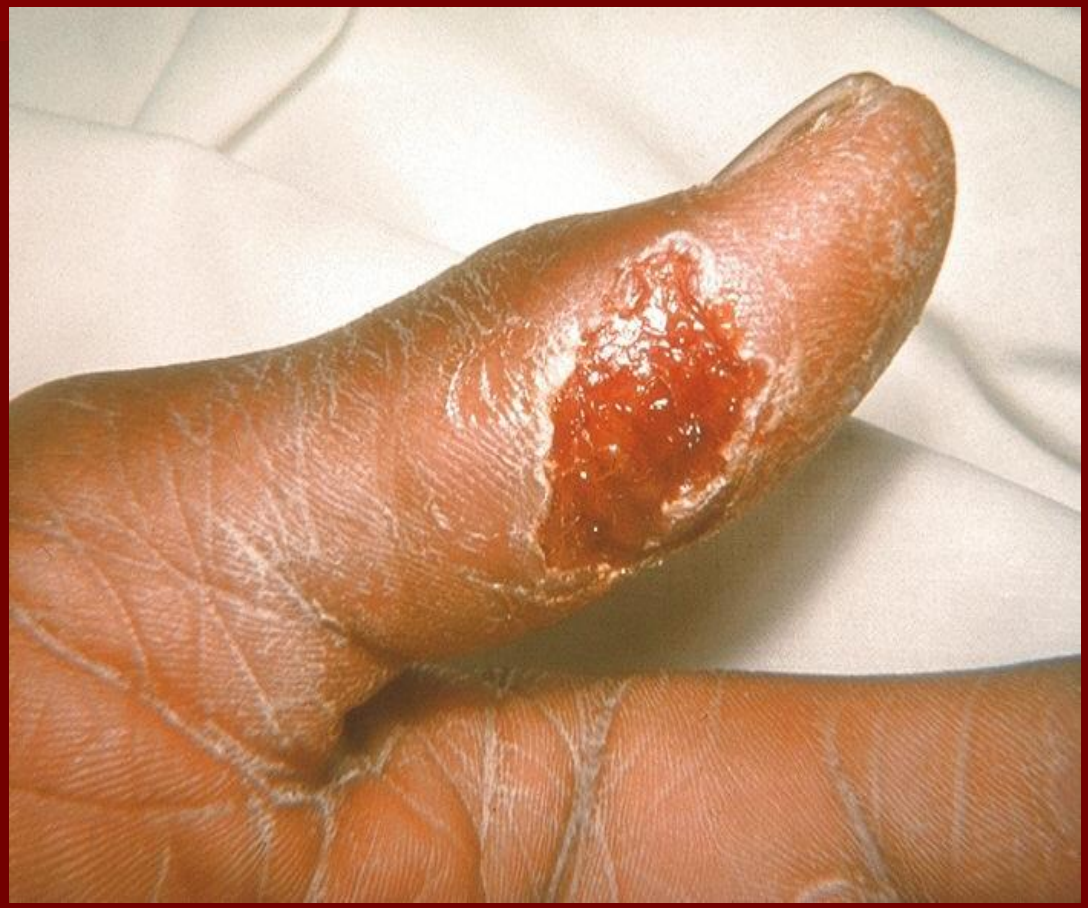
Warthin-Starry stain

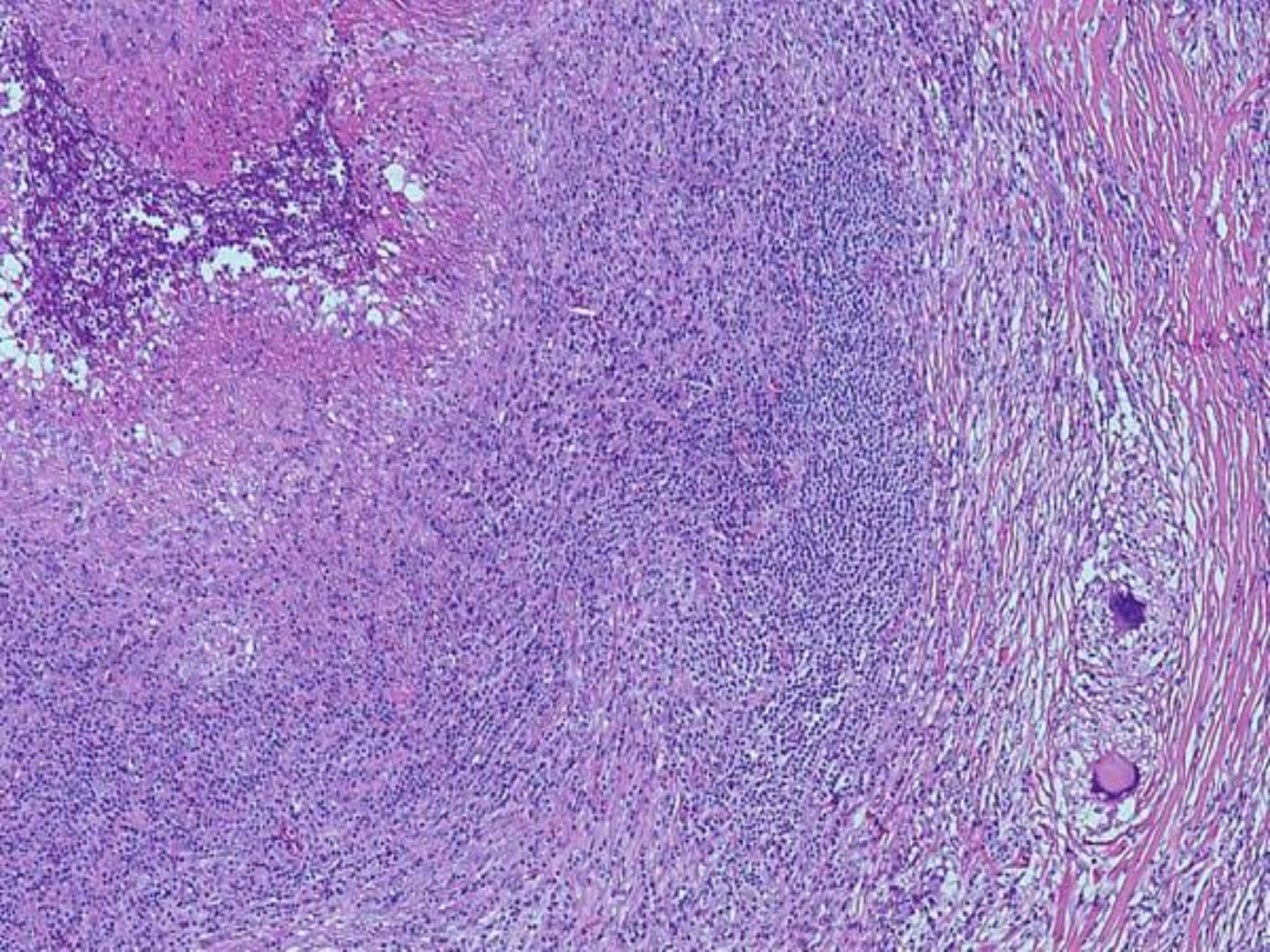


Cat Scratch Lymphadenitis Differential Diagnosis

- Suppurative lymphadenitis by a variety of bacteria
- Lymphogranuloma venereum (Chlamydia trachomatis): idential histology as cat scratch
- Tularemia (Franciscella tularensis, from rabbits)
- Brucellosis (Brucella abortus, from cattle)
- Plaque (Yersinia pestis, from rodents via fleas)
- Possibly mycobacterial or fungal
- Gram stain, AFB, GMS and Warthin-Starry stains helpful

Tularemia



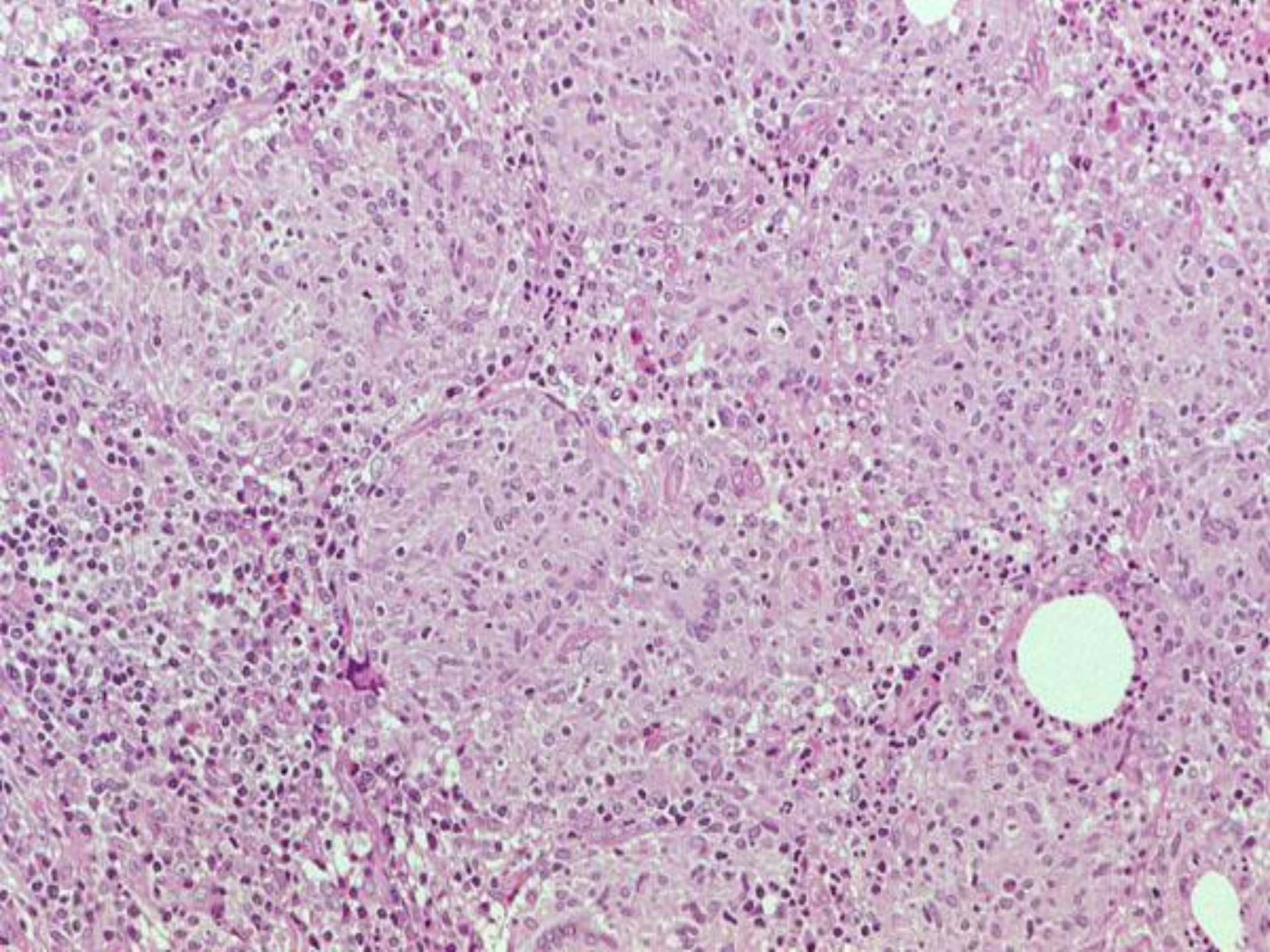


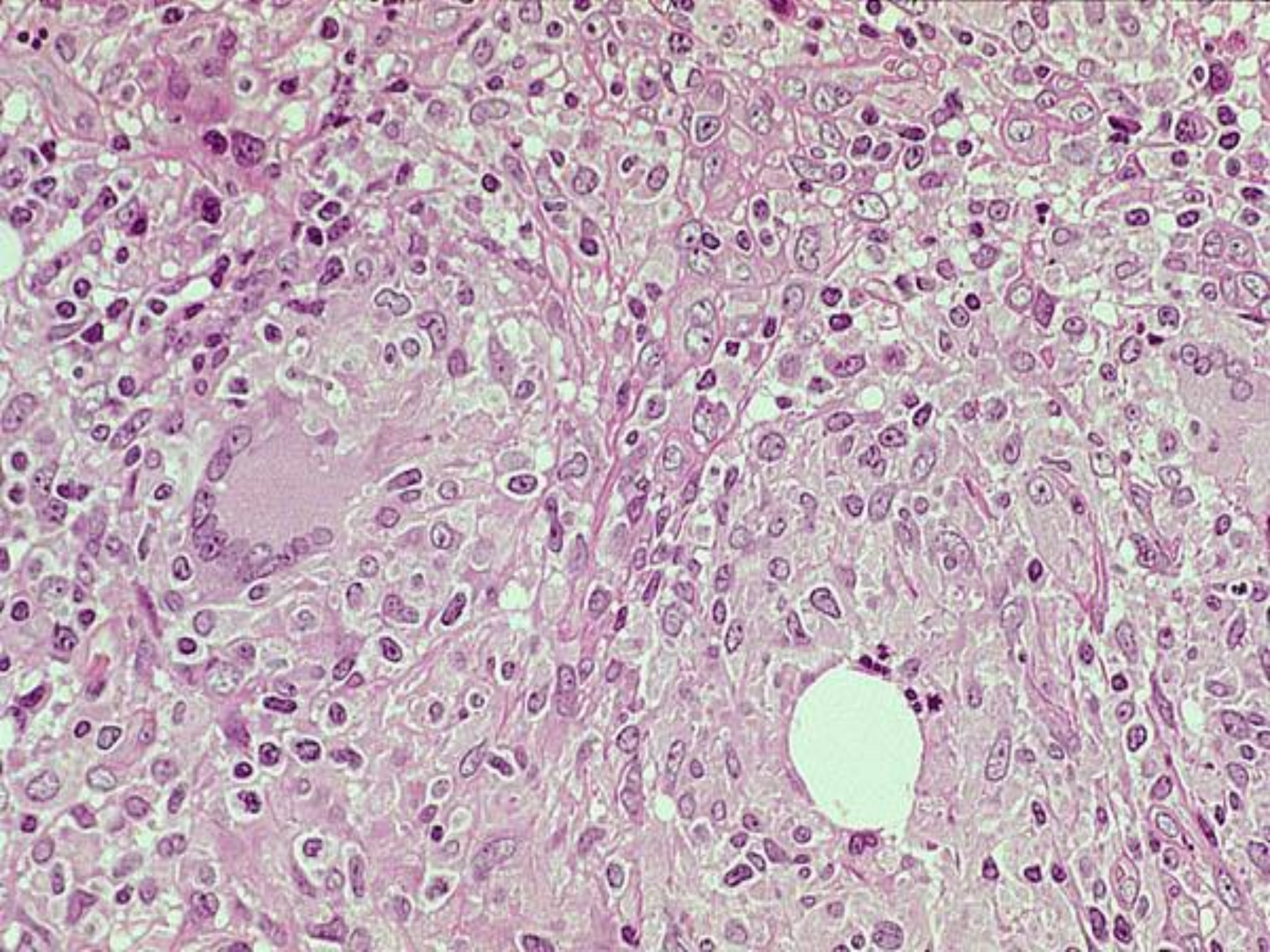
Syphilitic Lymphadenitis (Treponema pallidum)

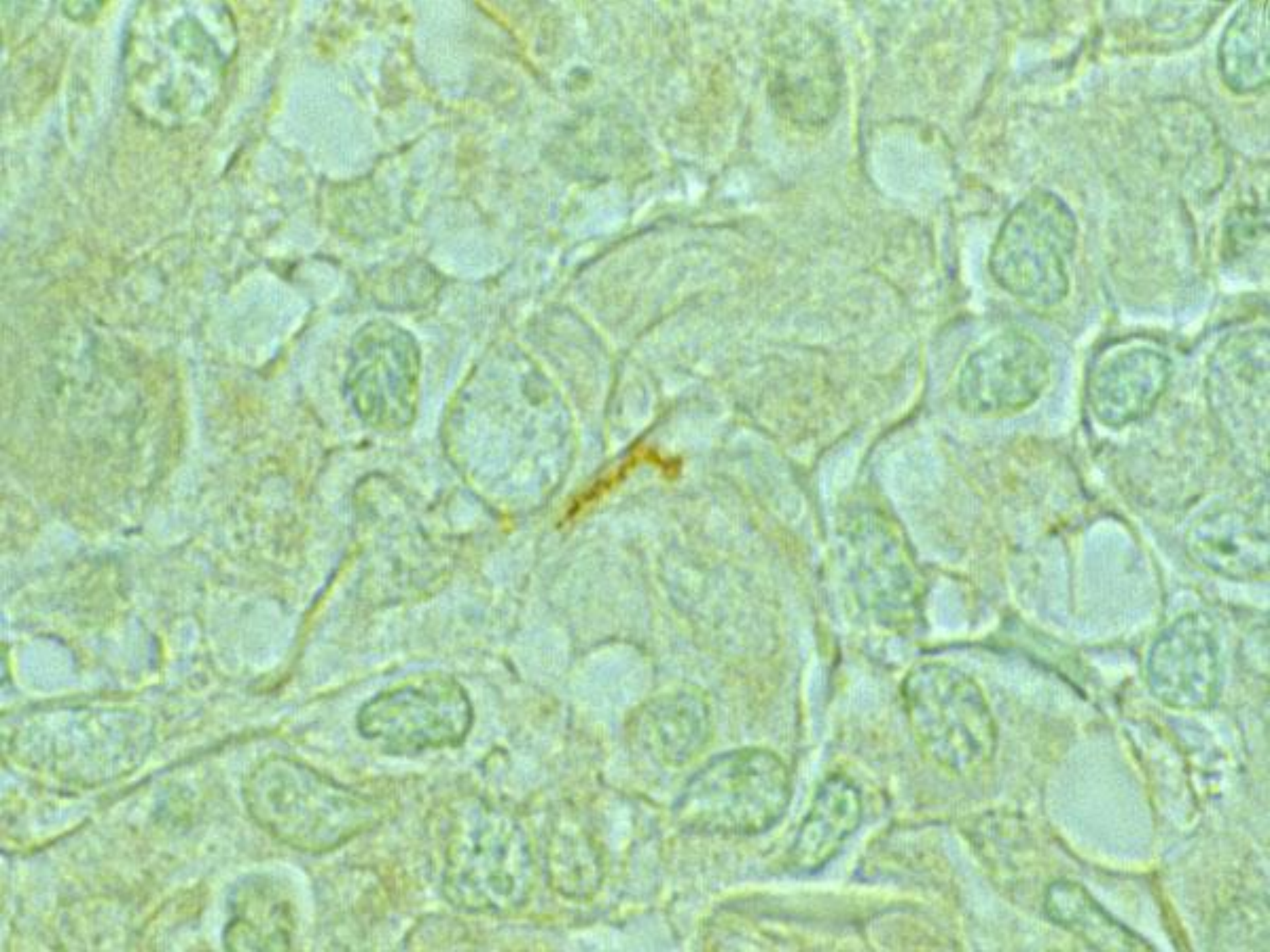
- Inguinal lymphadenopathy more common
- Follicular hyperplasia
- Perivascular lymphoplasmacytic infiltrate (endarteritis)
- Plasma cells in clusters or sheets (interfollicular)
- Epithelioid granulomas; isolated multinucleated giant cells
- Capsular fibrosis with infiltrating plasma cells
- Serology and Warthin-Starry or immunofluorescence

Case Illustration

- 65-year-old man with inguinal lymphadenopathy, mental status changes





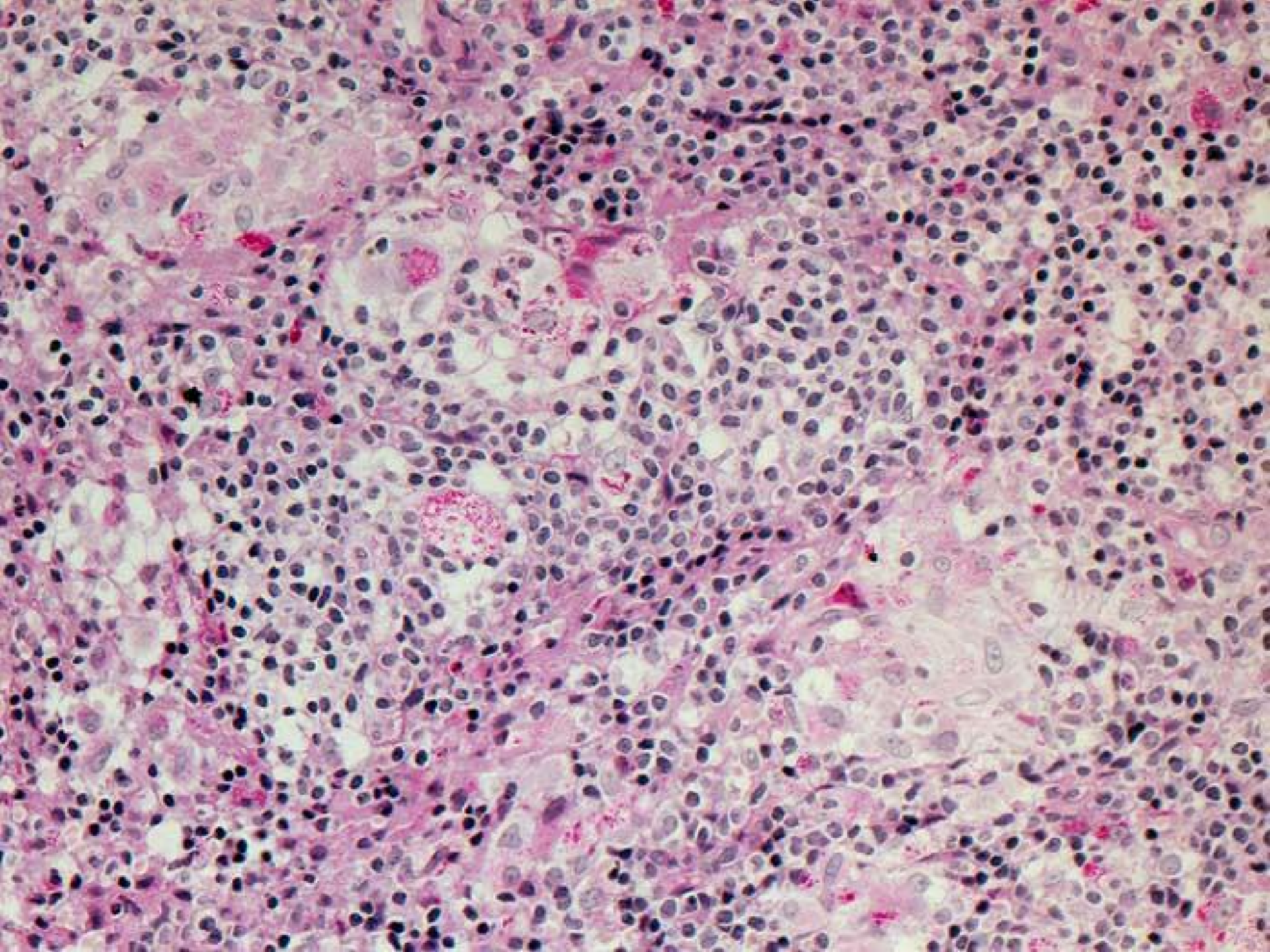


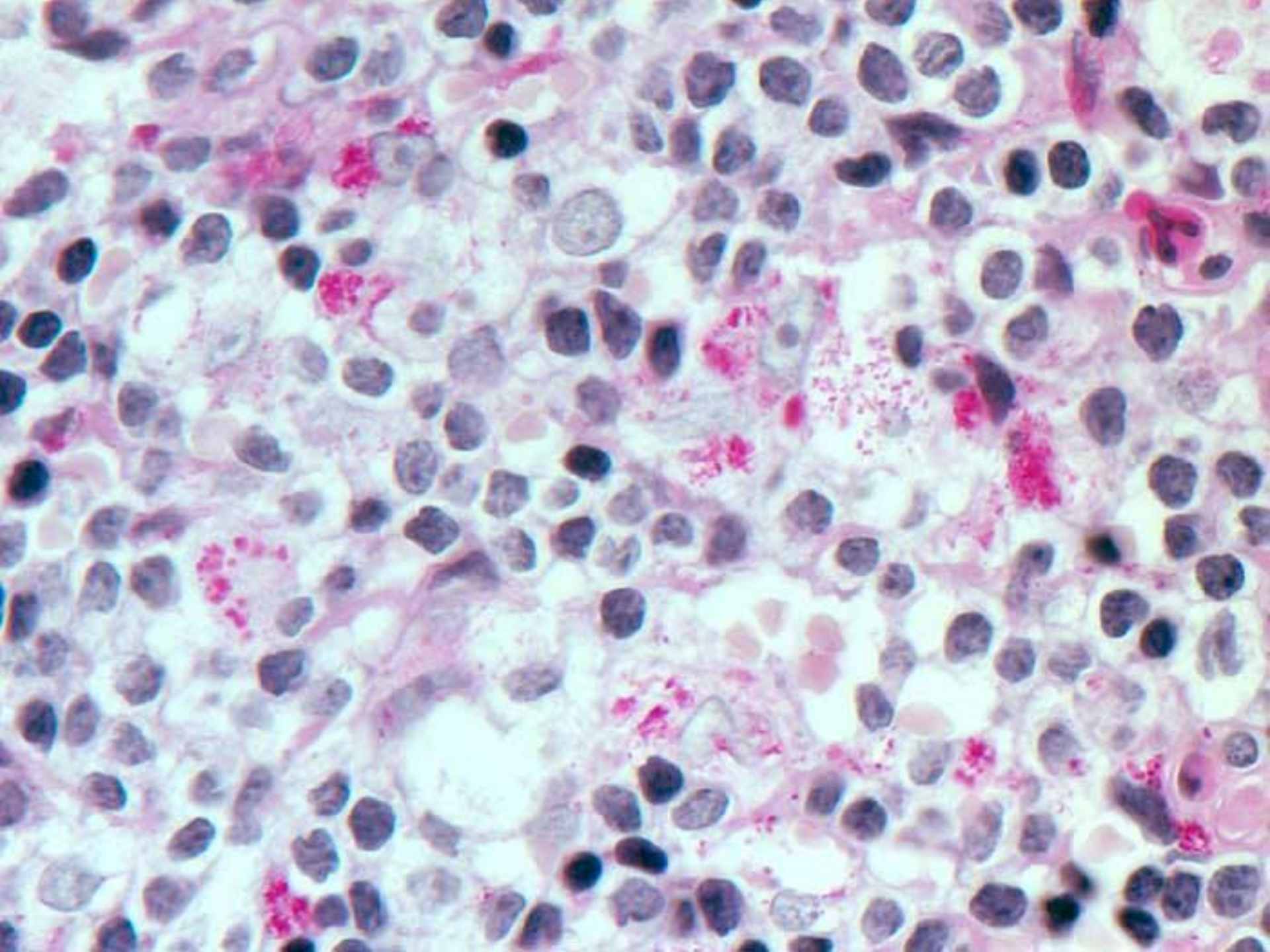
Lymphadenitis of Whipple's Disease

- Diarrhea, wasting illness
- Multiple enlarged lymph nodes (may also see in small intestine and disseminated)
- Foamy histiocytes
- Intracellular and extracellular PAS+ deposits of degenerated bacteria
- Rod-shaped bacilli with trilaminar walls (EM)
- Organism: *Tropheryma whippelii*

Case Illustration

- 54-year-old man with fever, diarrhea, weight loss, arthralgia, and headache
- Hepatomegaly
- Mediastinal and abdominal lymphadenopathy

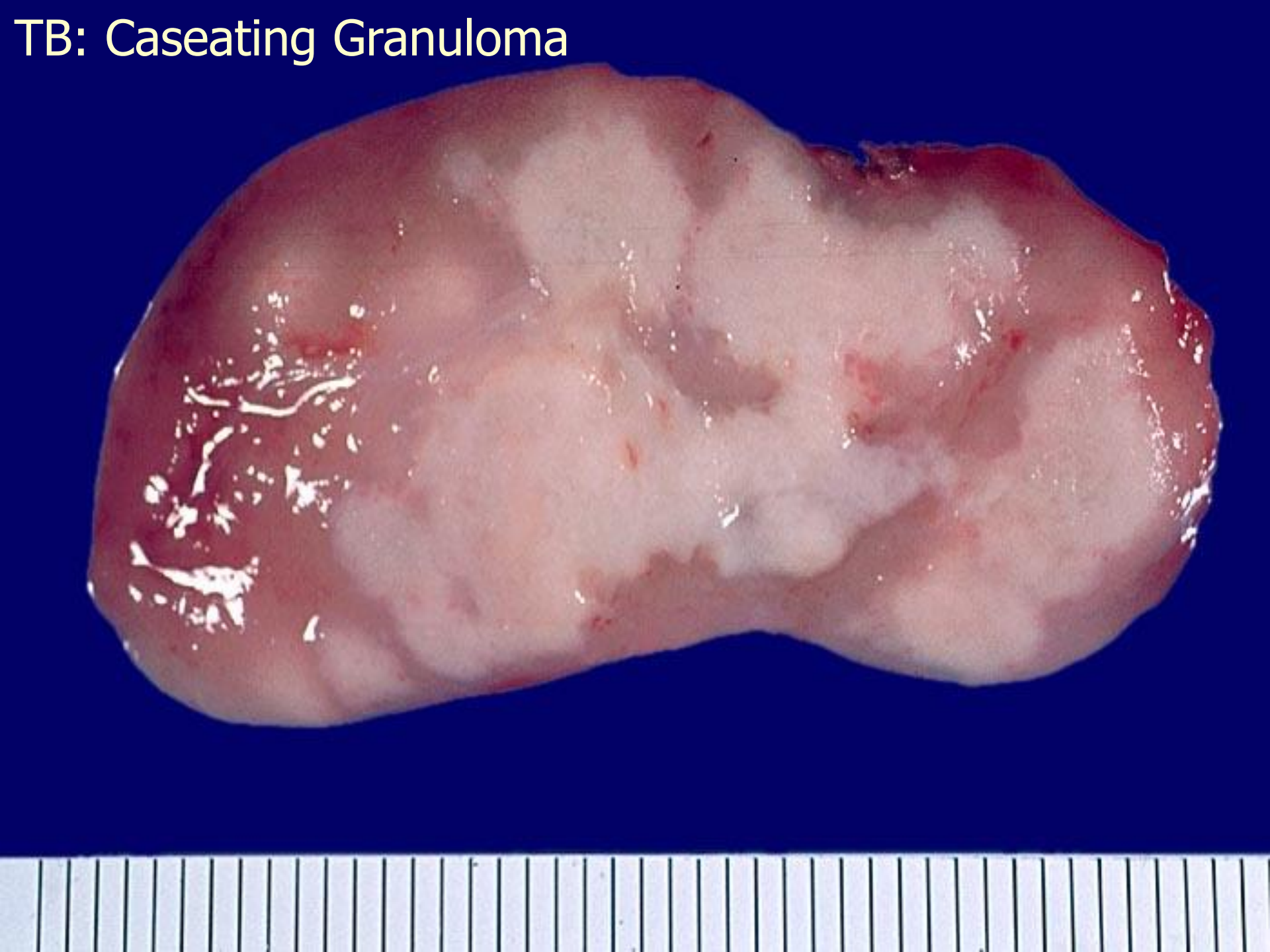




Mycobacterial Lymphadenitides

- *Mycobacteria tuberculosis*
- Nontuberculous Mycobacteria
- *Mycobacterium leprae*

TB: Caseating Granuloma



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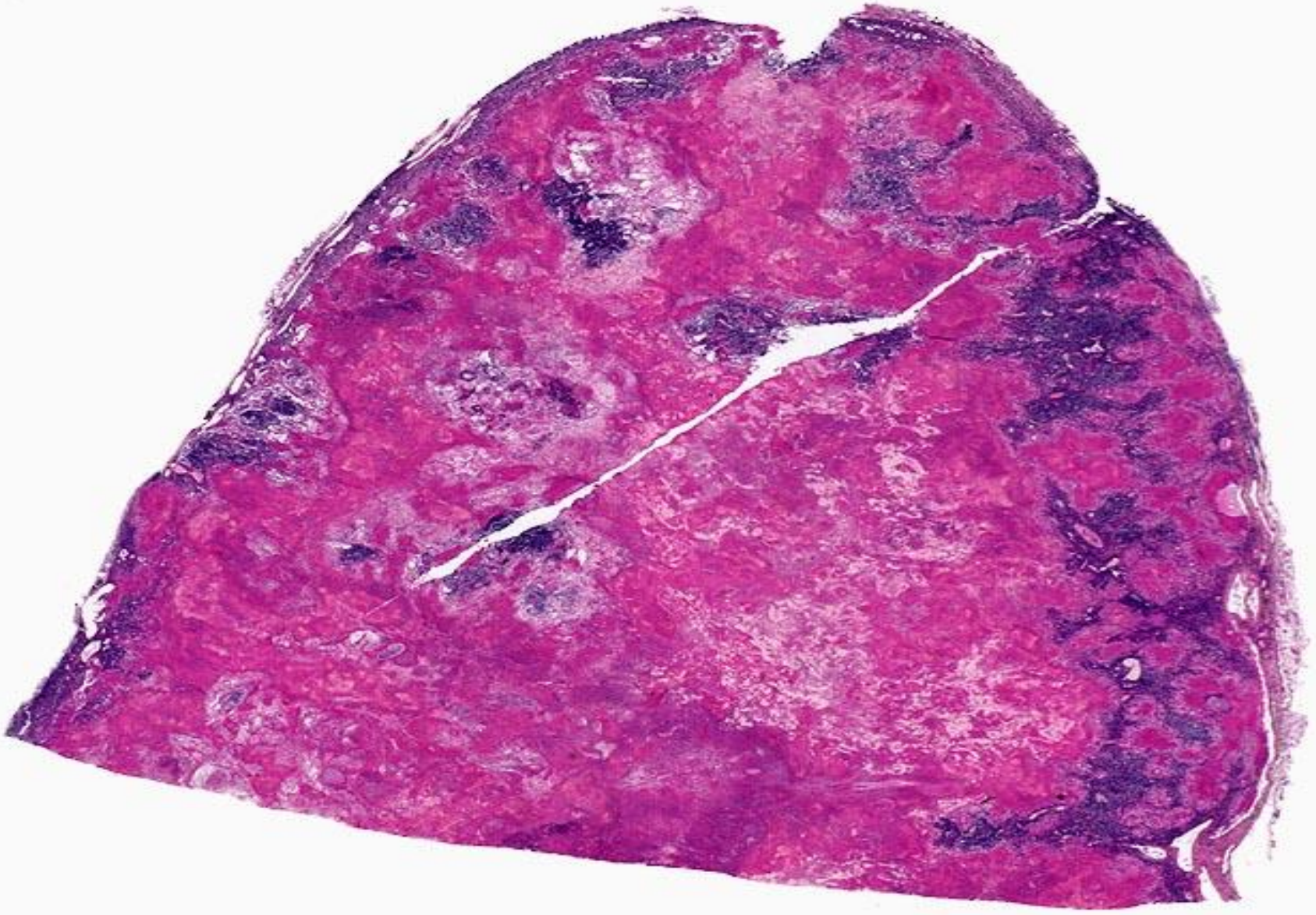

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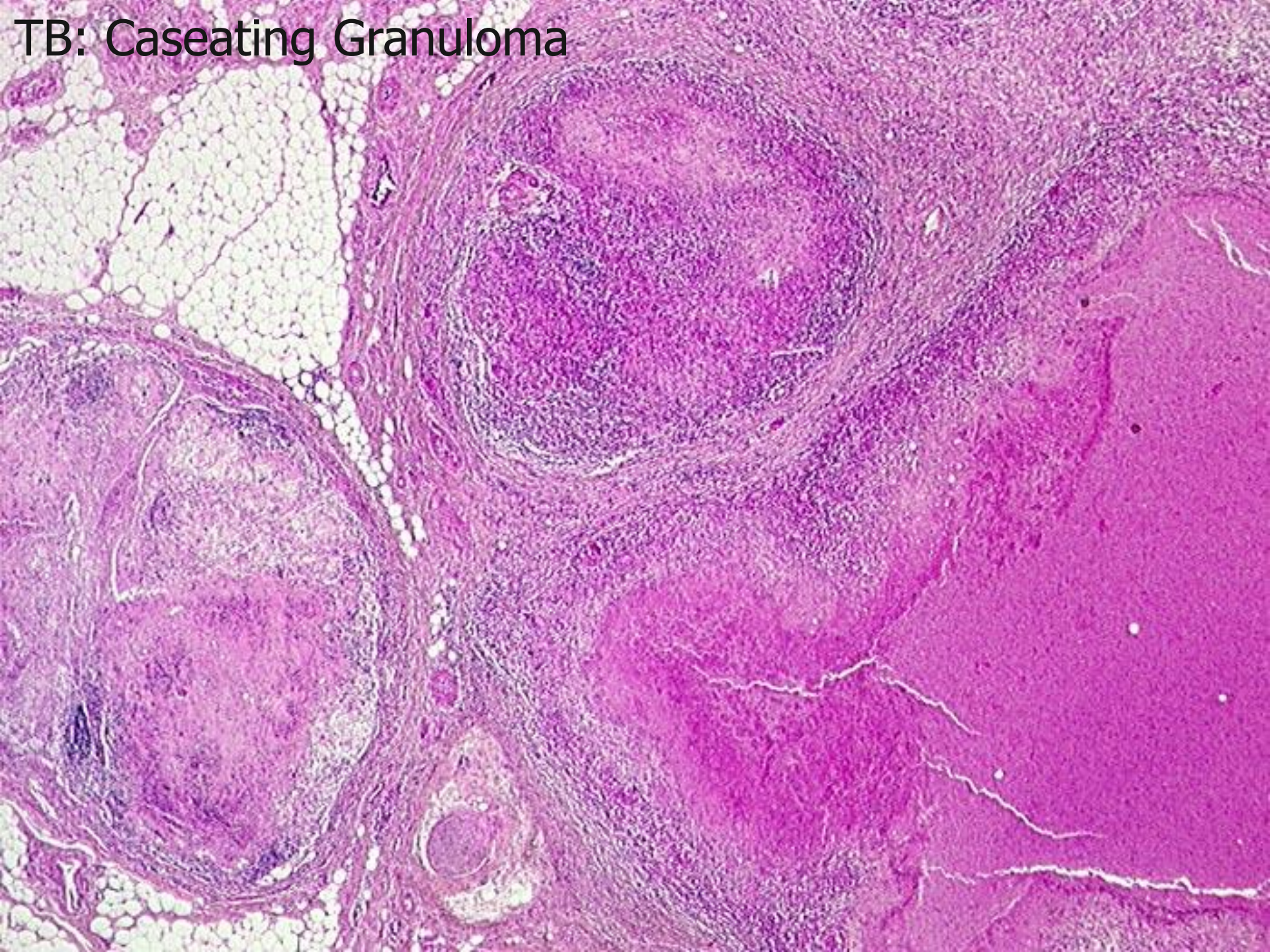

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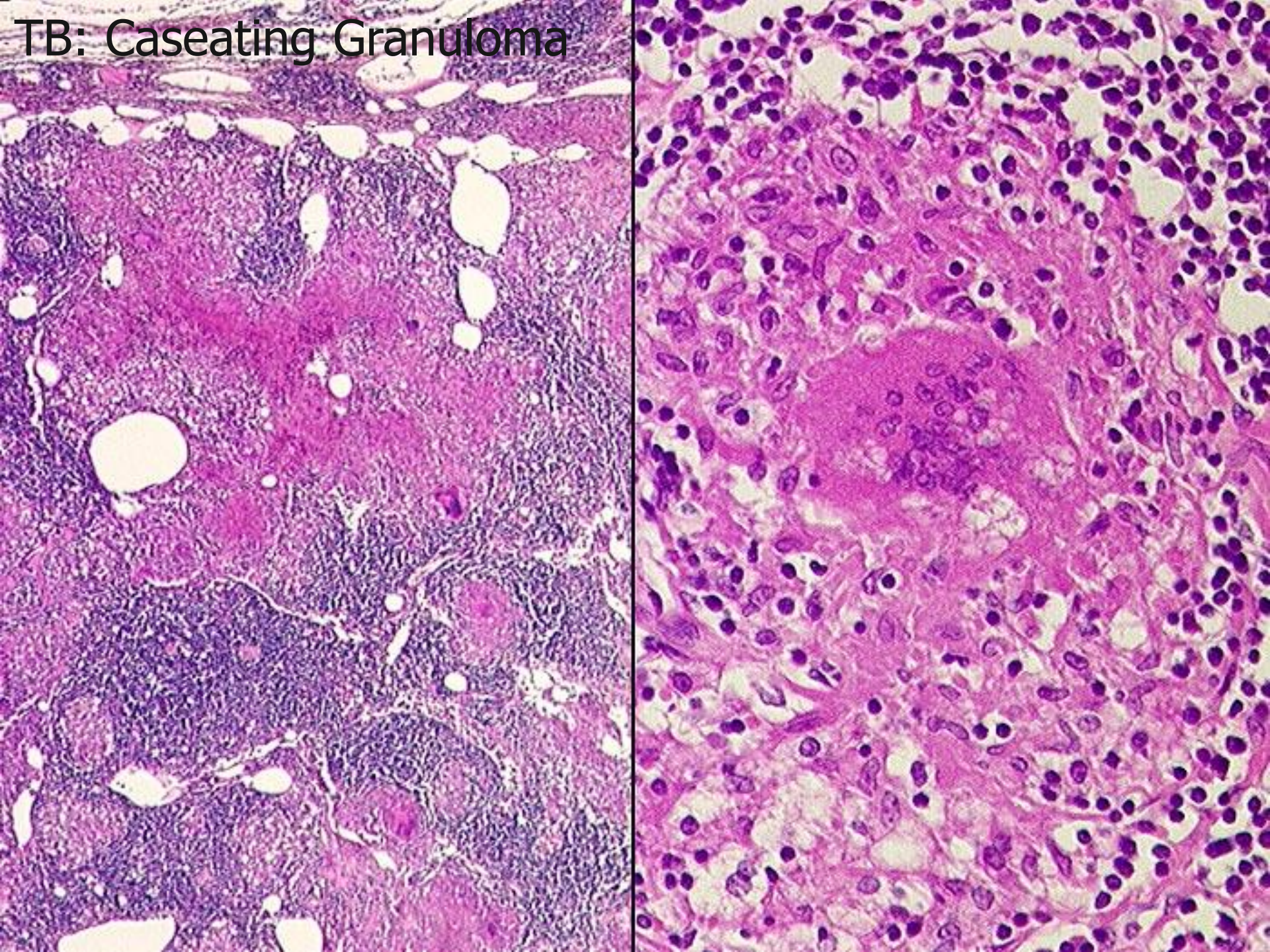

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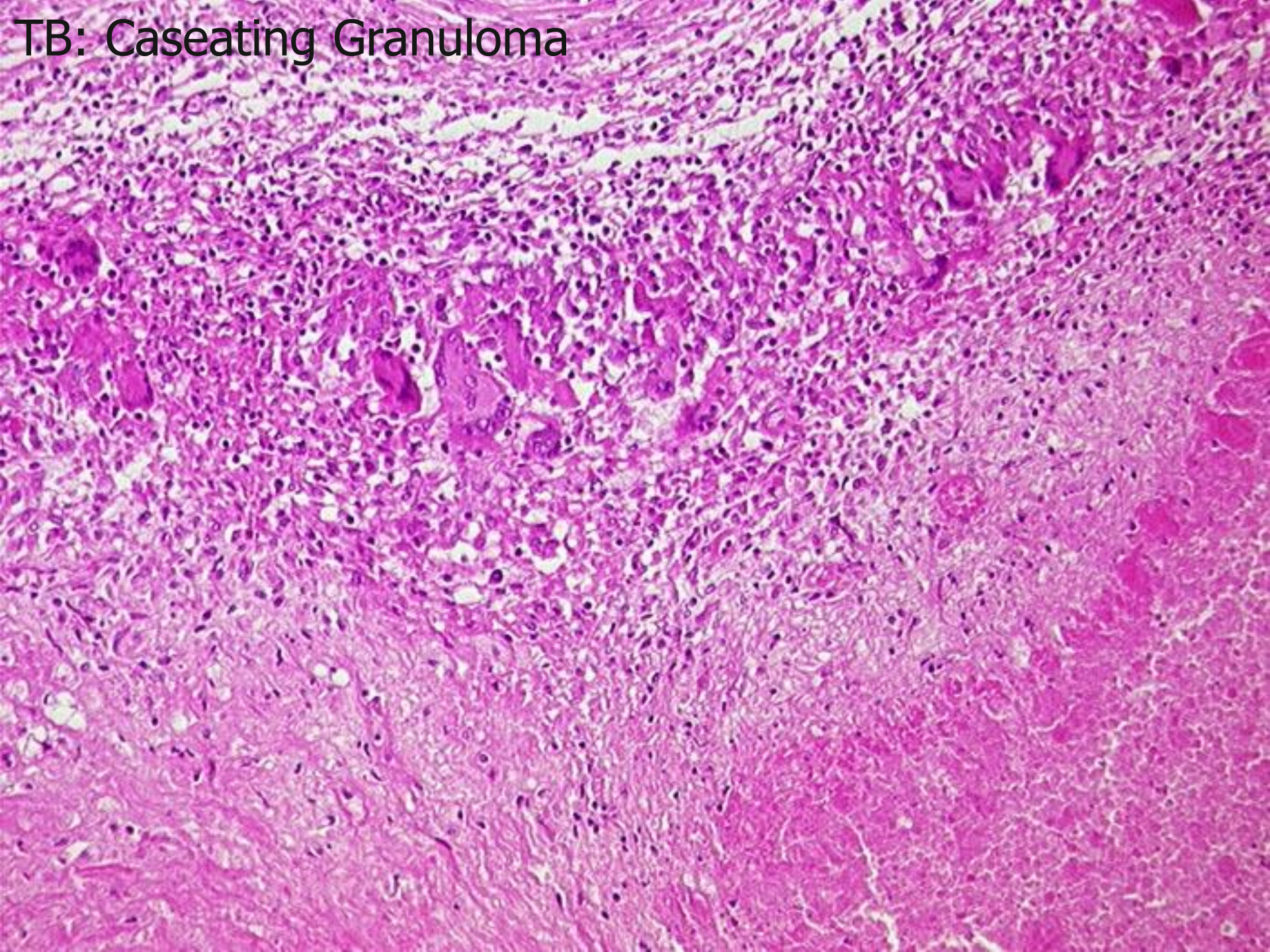

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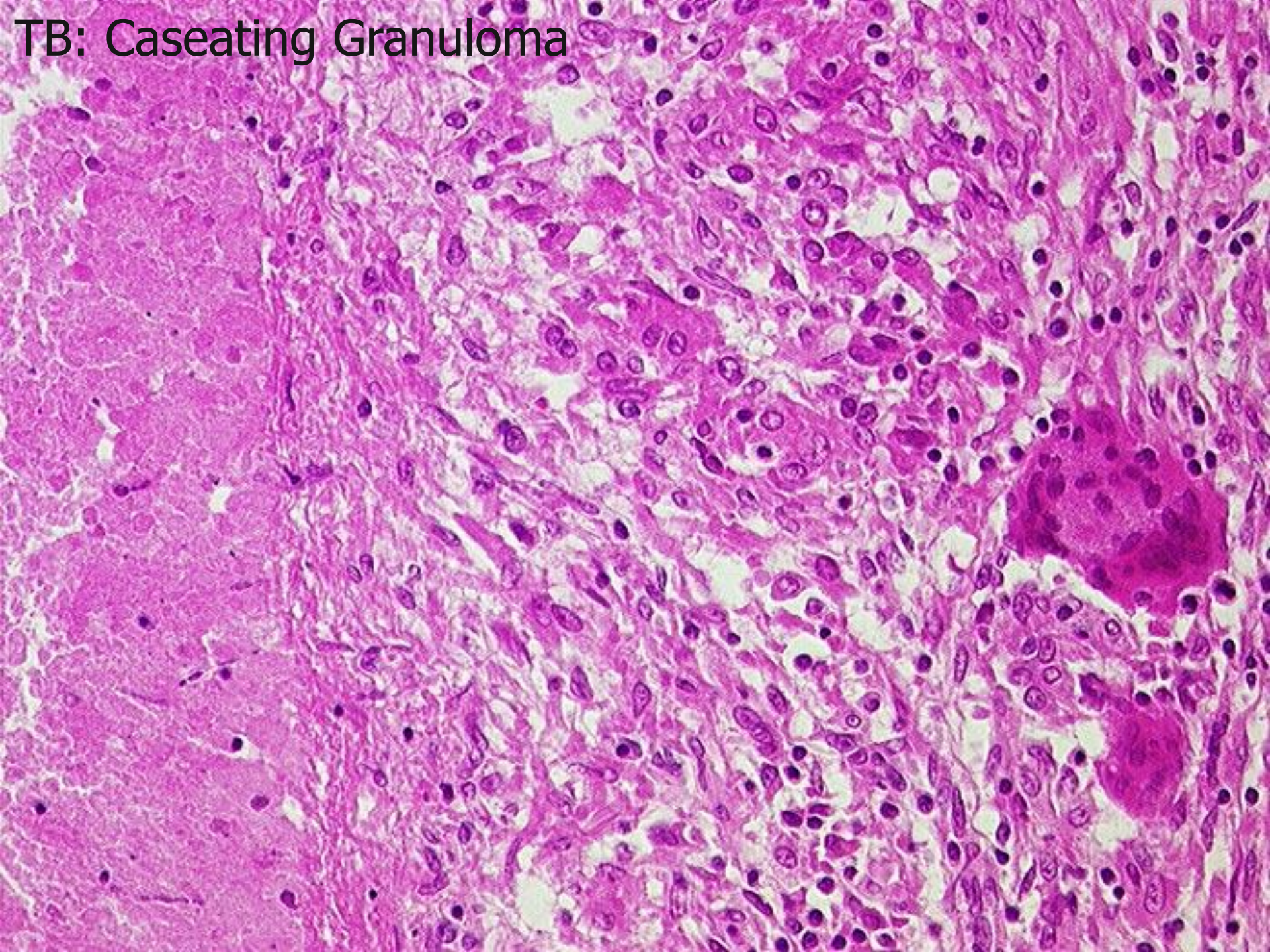
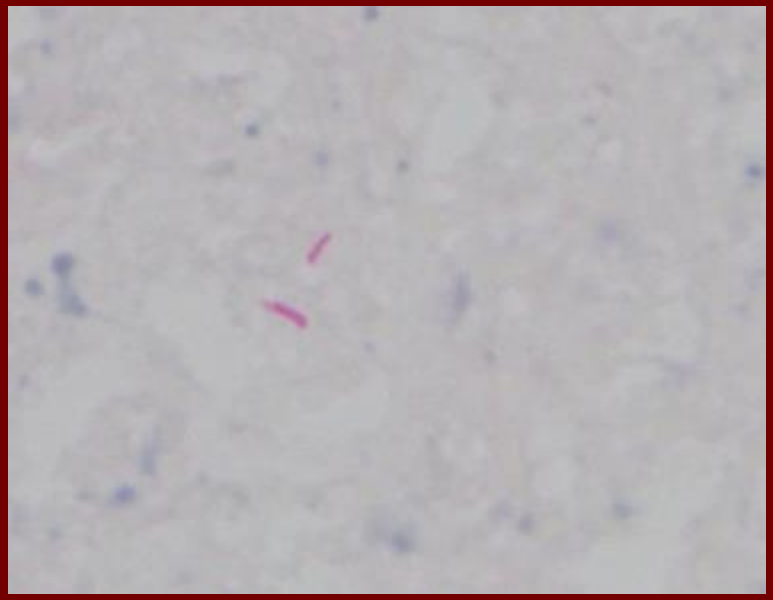


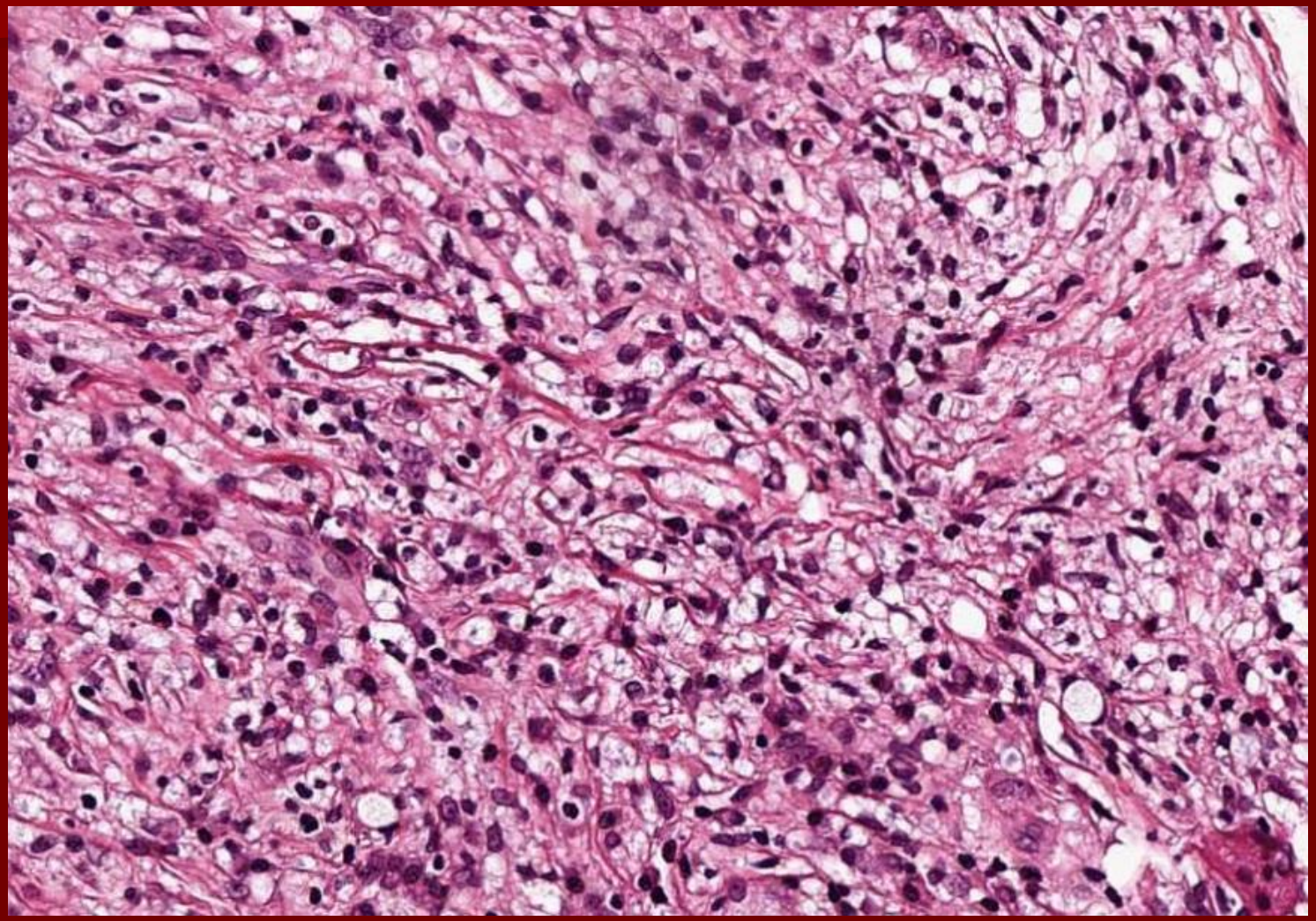
AFB Stain



Lepromatous Leprosy

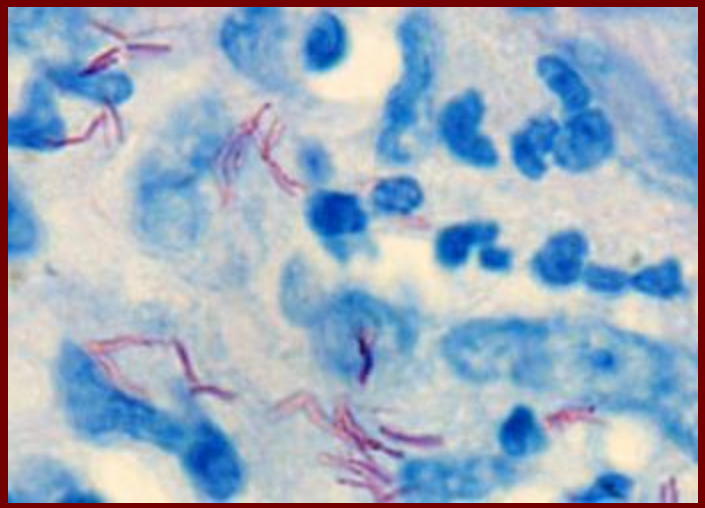
Lepromatous Leprosy

Lepra cells (histiocytes with large cytoplasmic vacuoles containing mycobacteria)



Lepromatous Leprosy

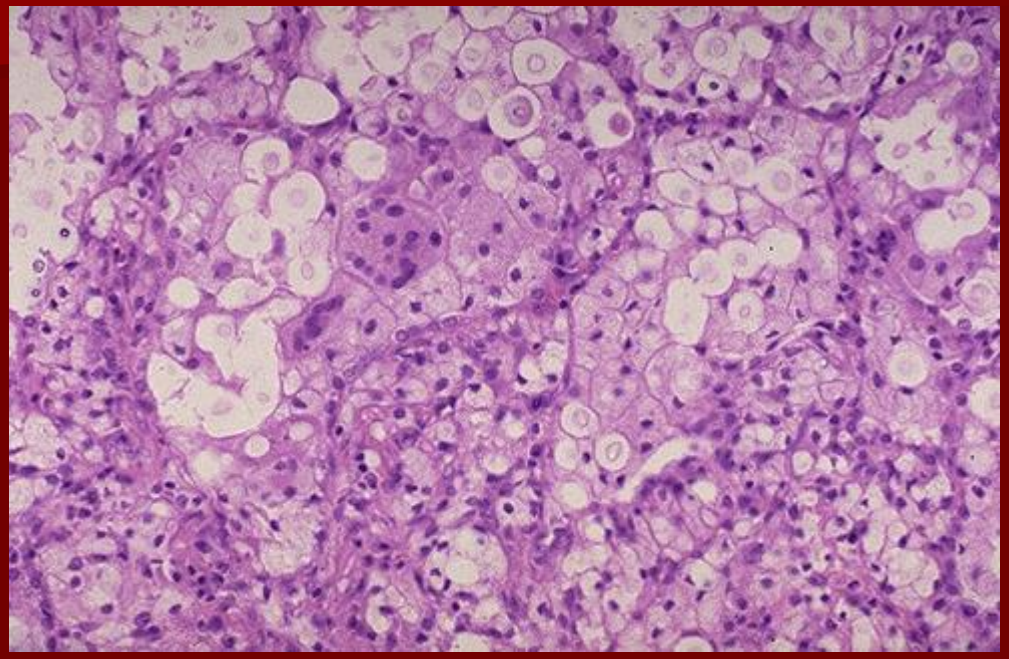
AFB stained with Fite-Faraco stain

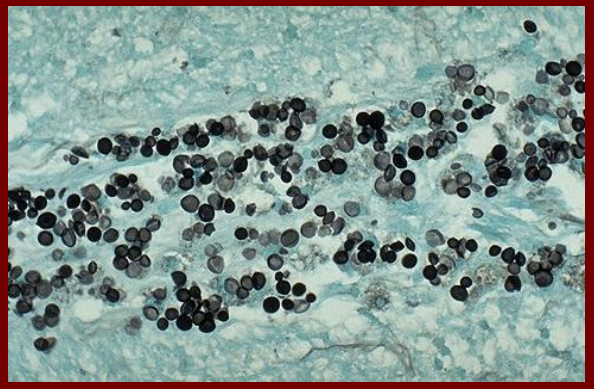


Fungal Lymphadenitides

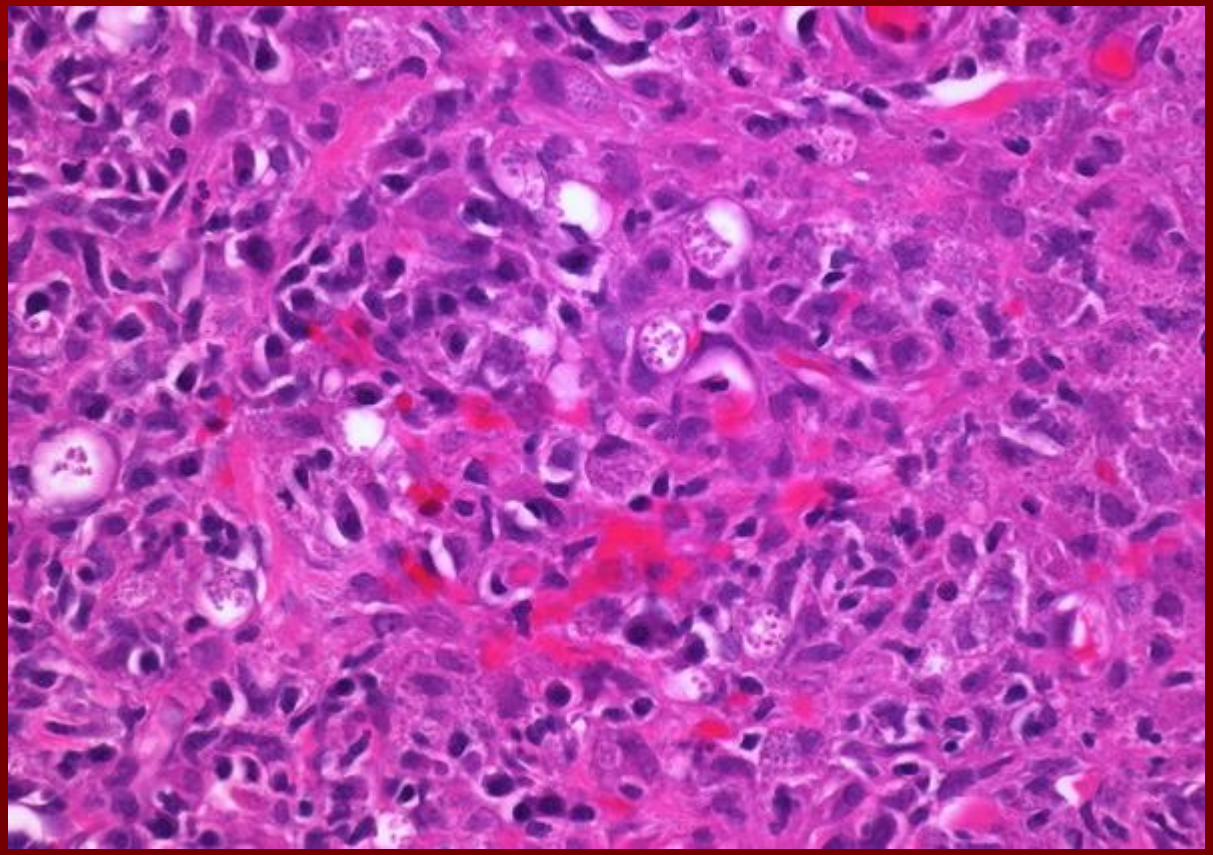
- *Cryptococcus neoformans*
- *Histoplasma capsulatum*
- *Coccidioidomycosis immitis*
- *Pneumocystis (carinii) jiroveci*

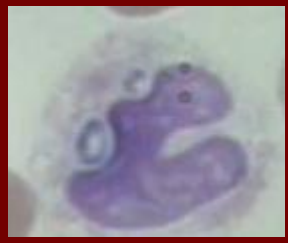
Cryptococcus neoformans



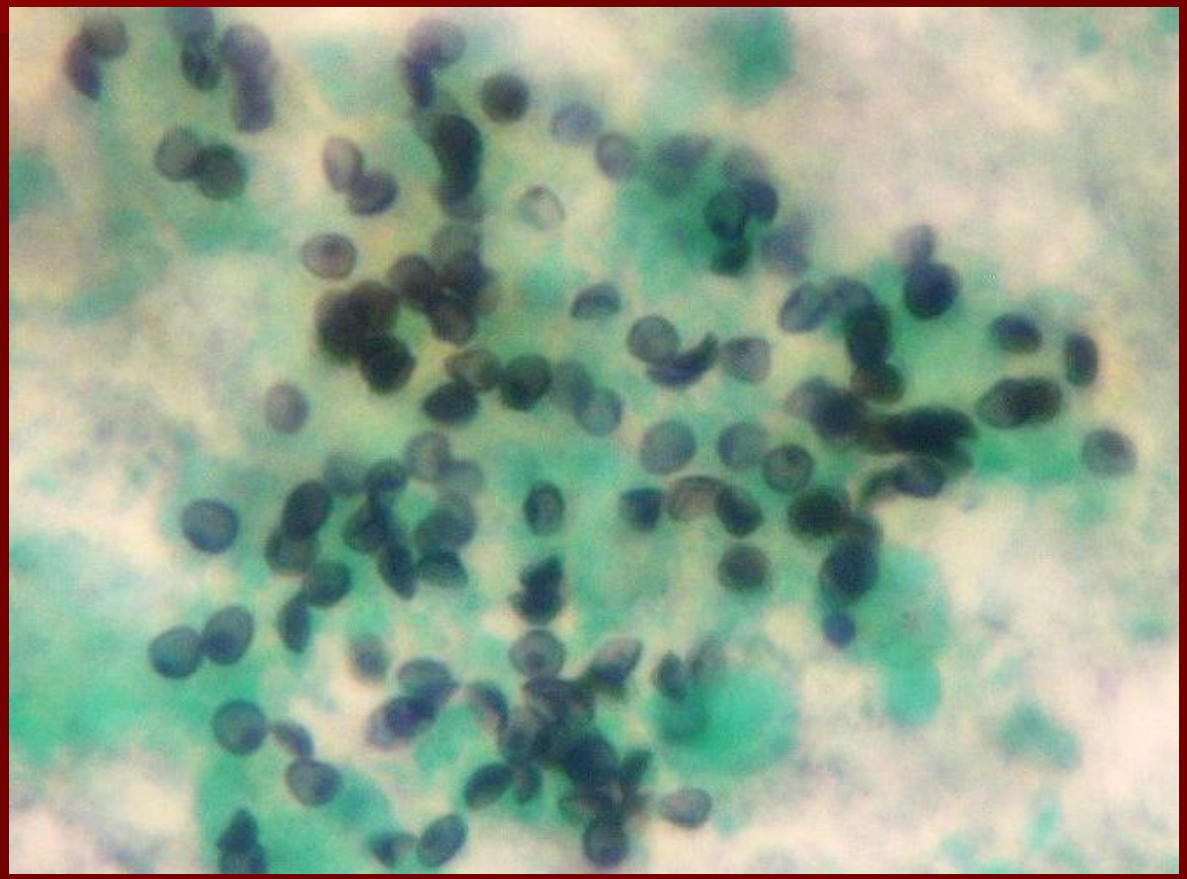


Histoplasma Capulatum





Pneumocystis (carinii) jiroveci

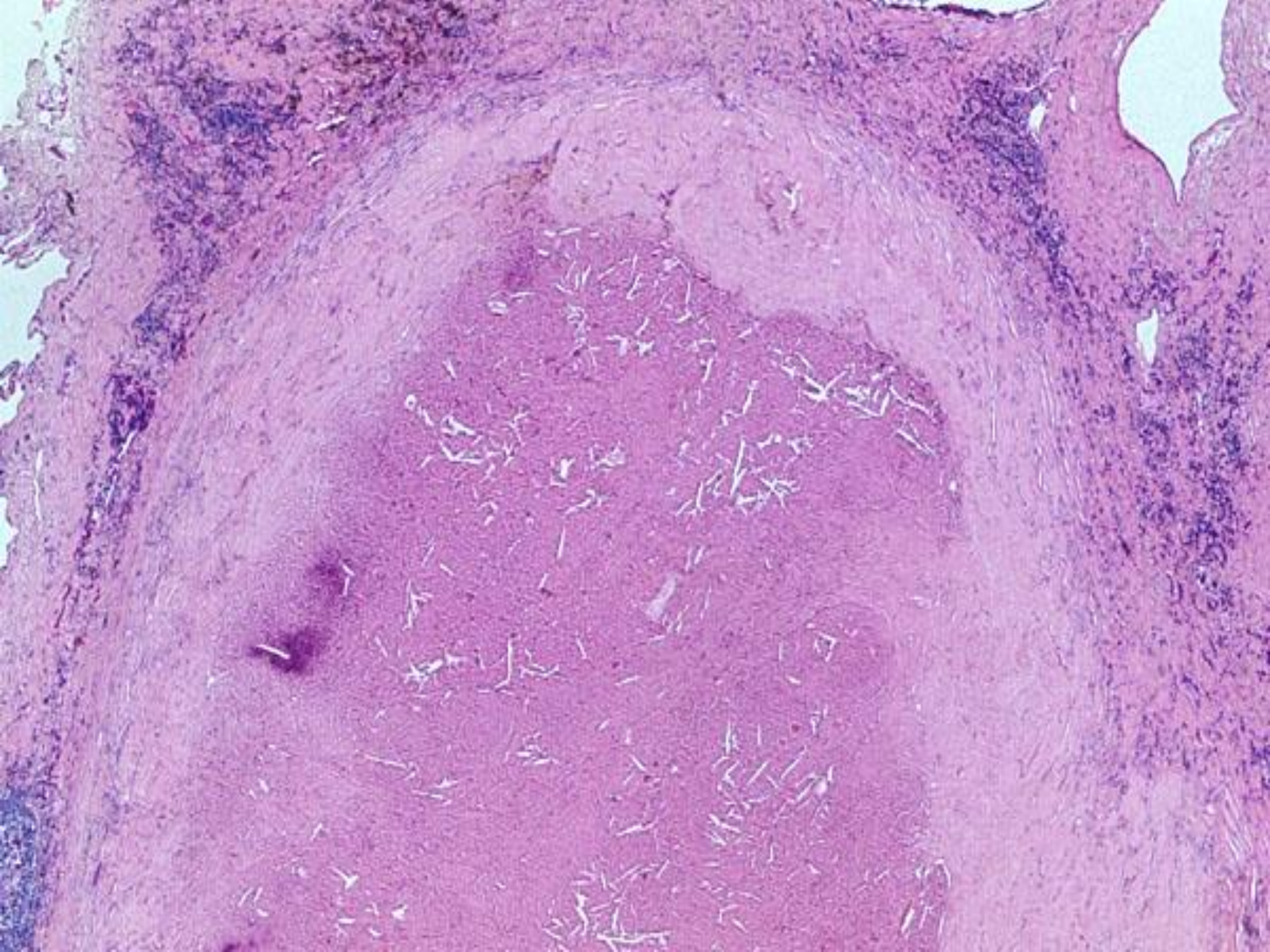


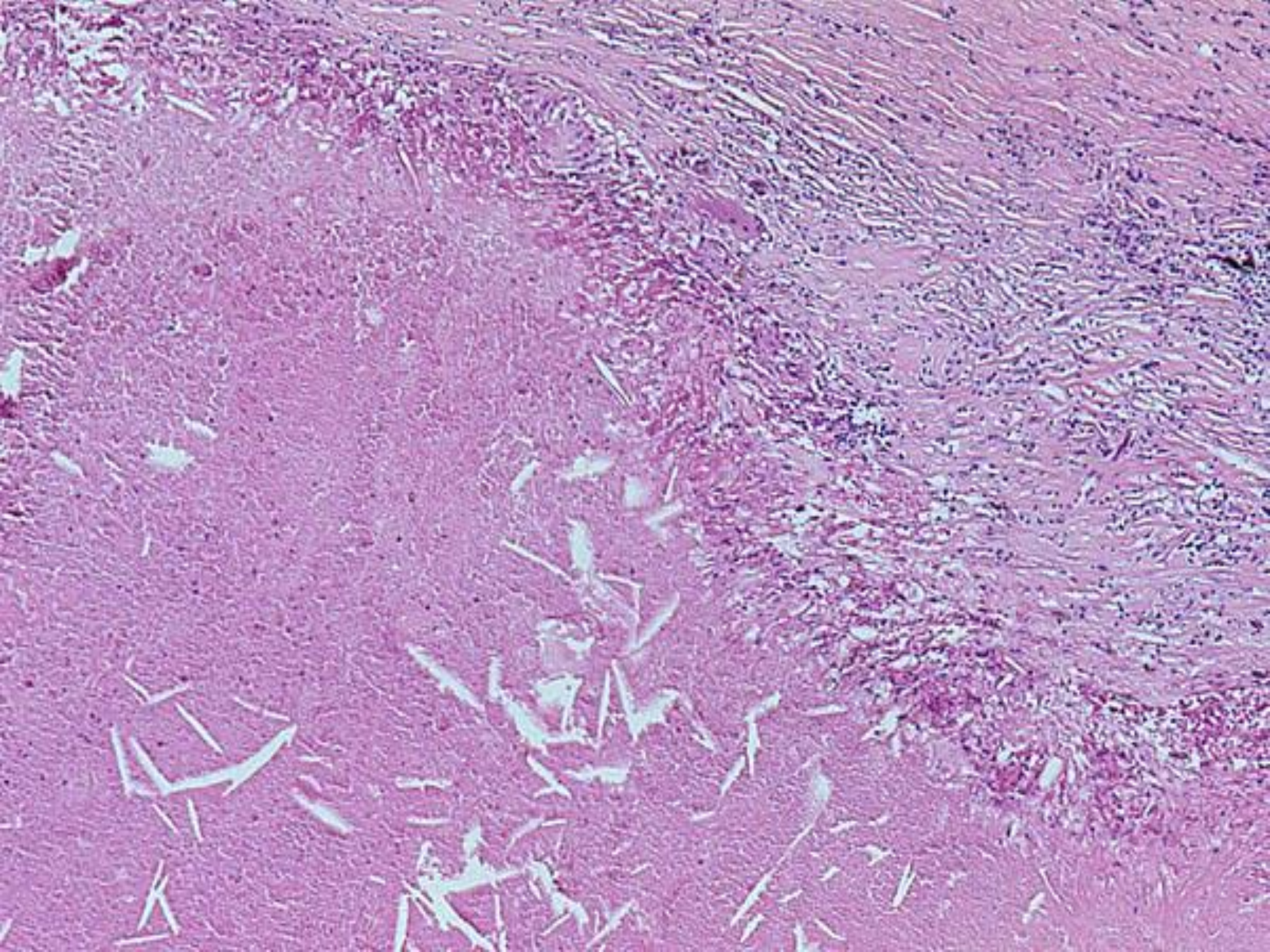
Coccidiodomycosis Lymphadenitis

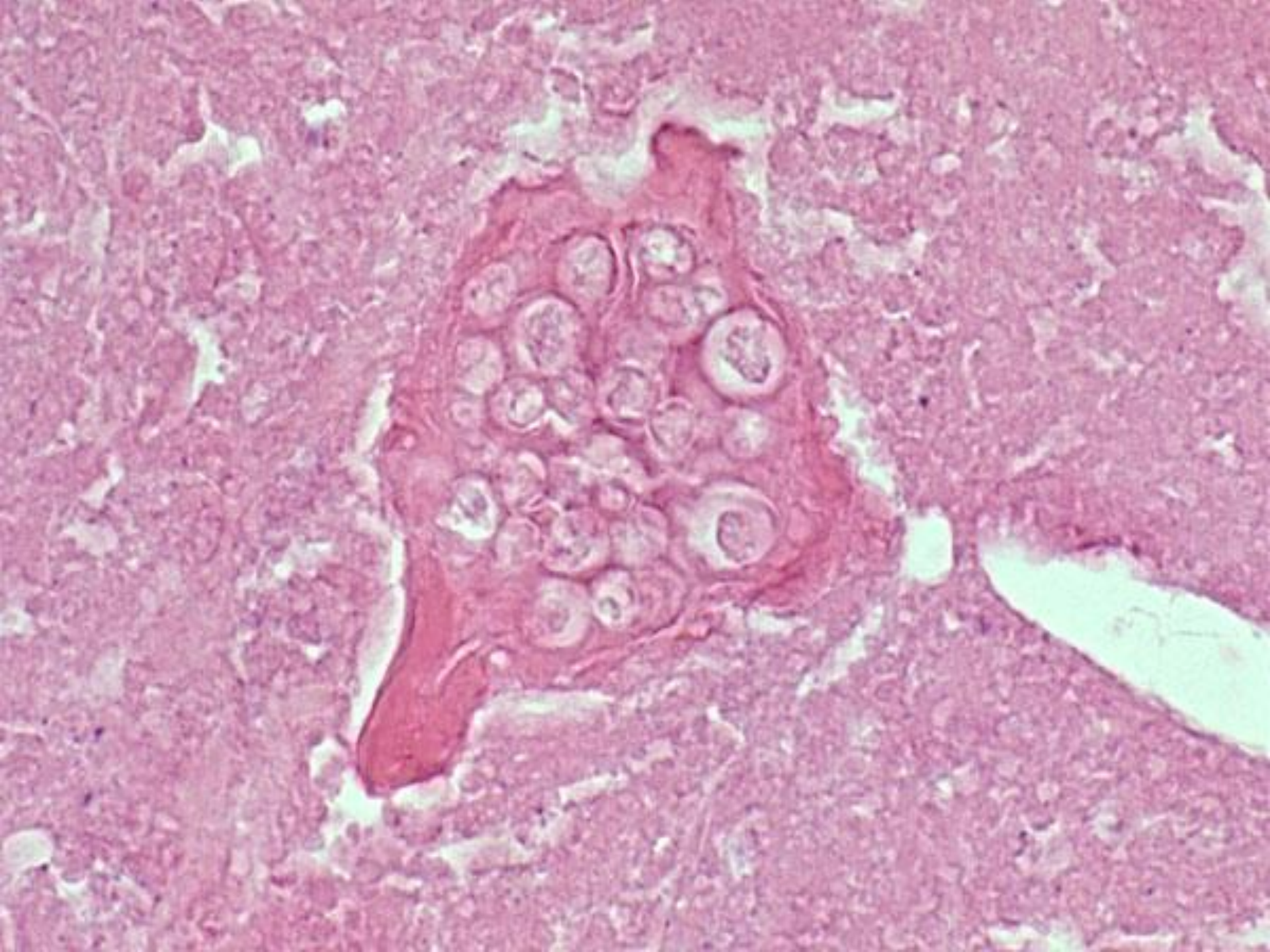
- Persons from endemic areas
- Dimorphic fungus with yeast and hyphae
- Sporangium with multiple endospores and thick, double capsule
- Cysts and spores that stain with PAS and GMS
- Necrotizing granulomas
- Giant cells containing sporangia
- Often immunodeficient patients

Case Illustration

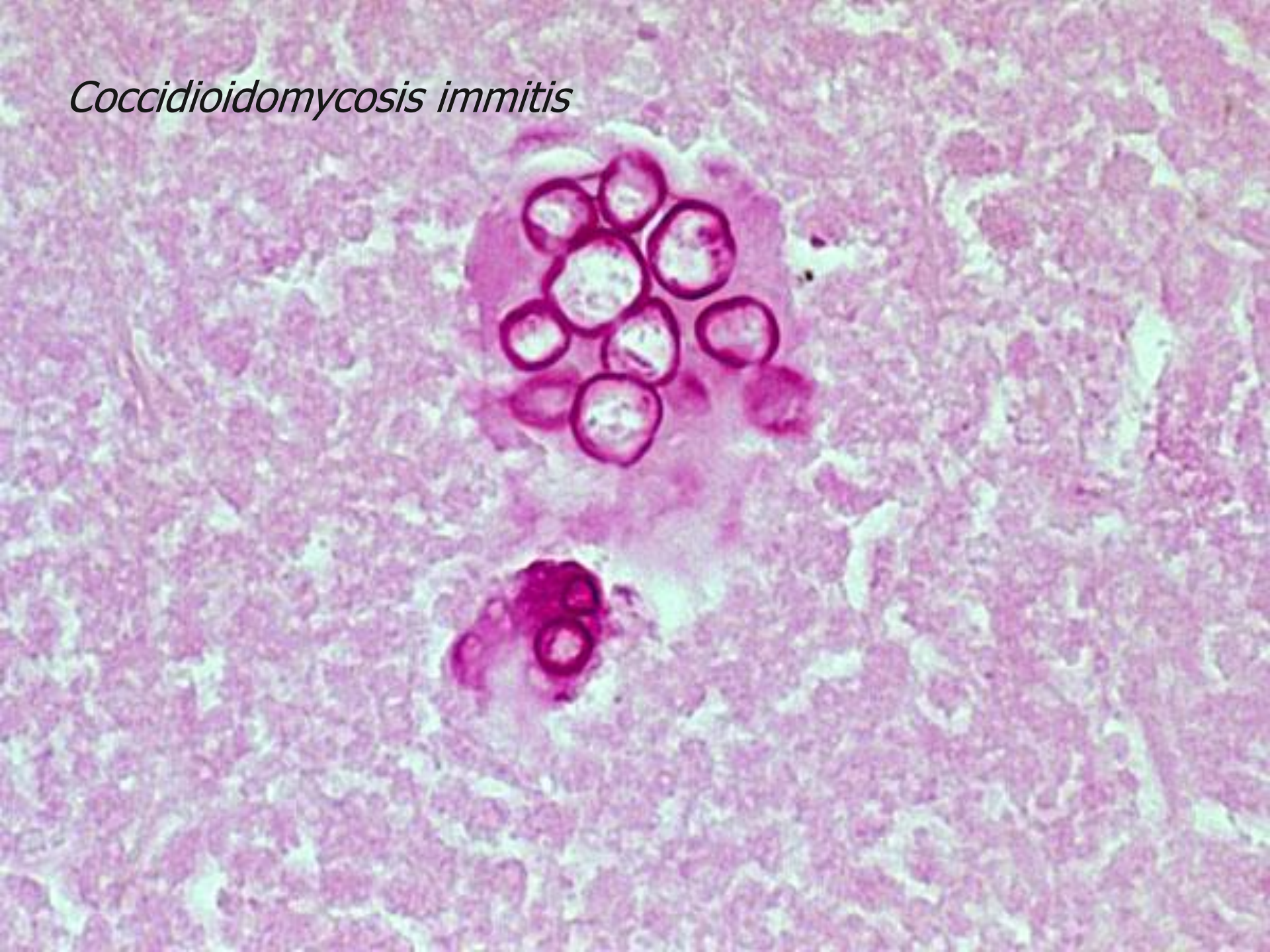
- 42-year-old HIV+ man from west Texas with flu-like illness and lymphadenopathy

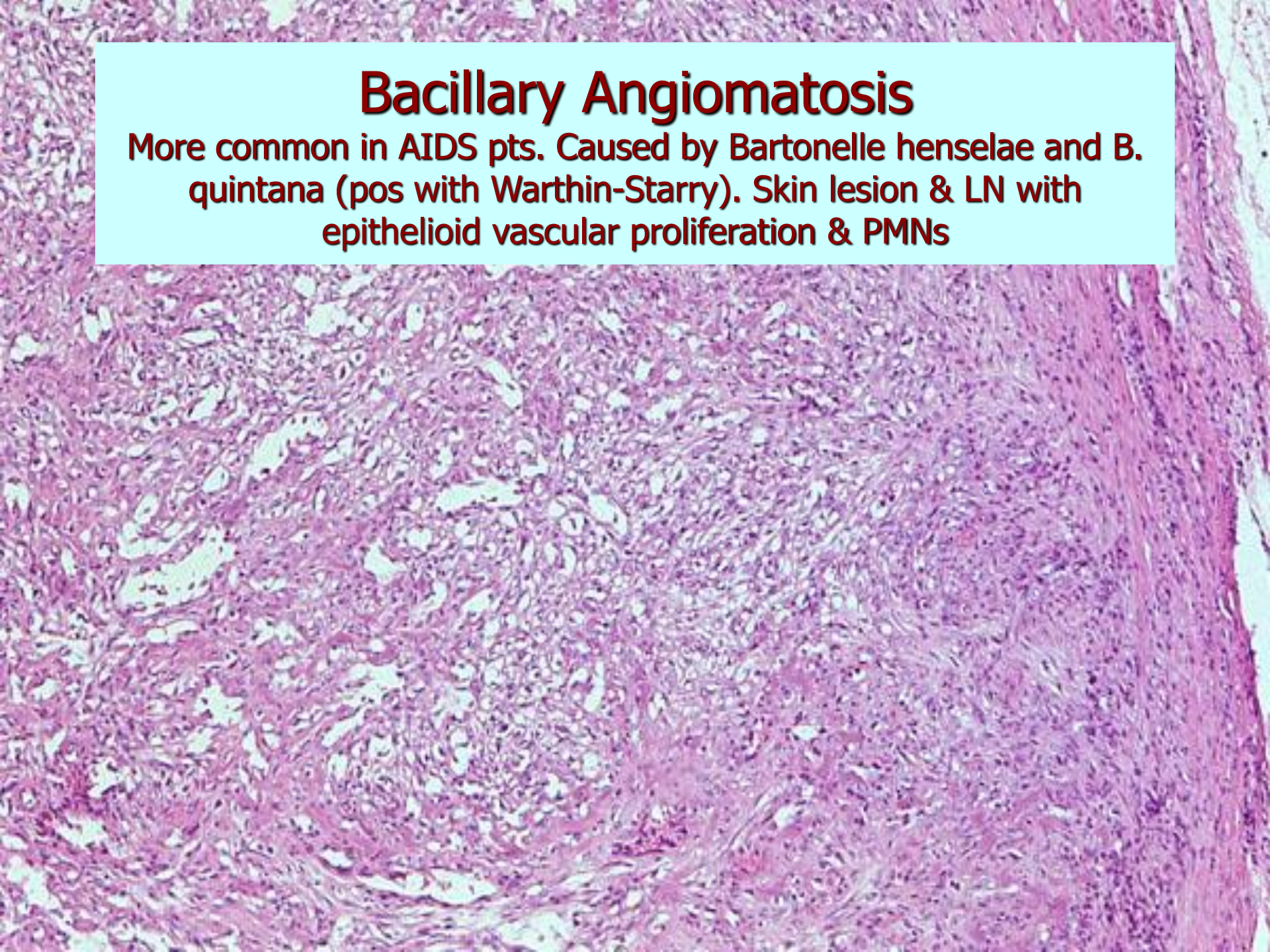






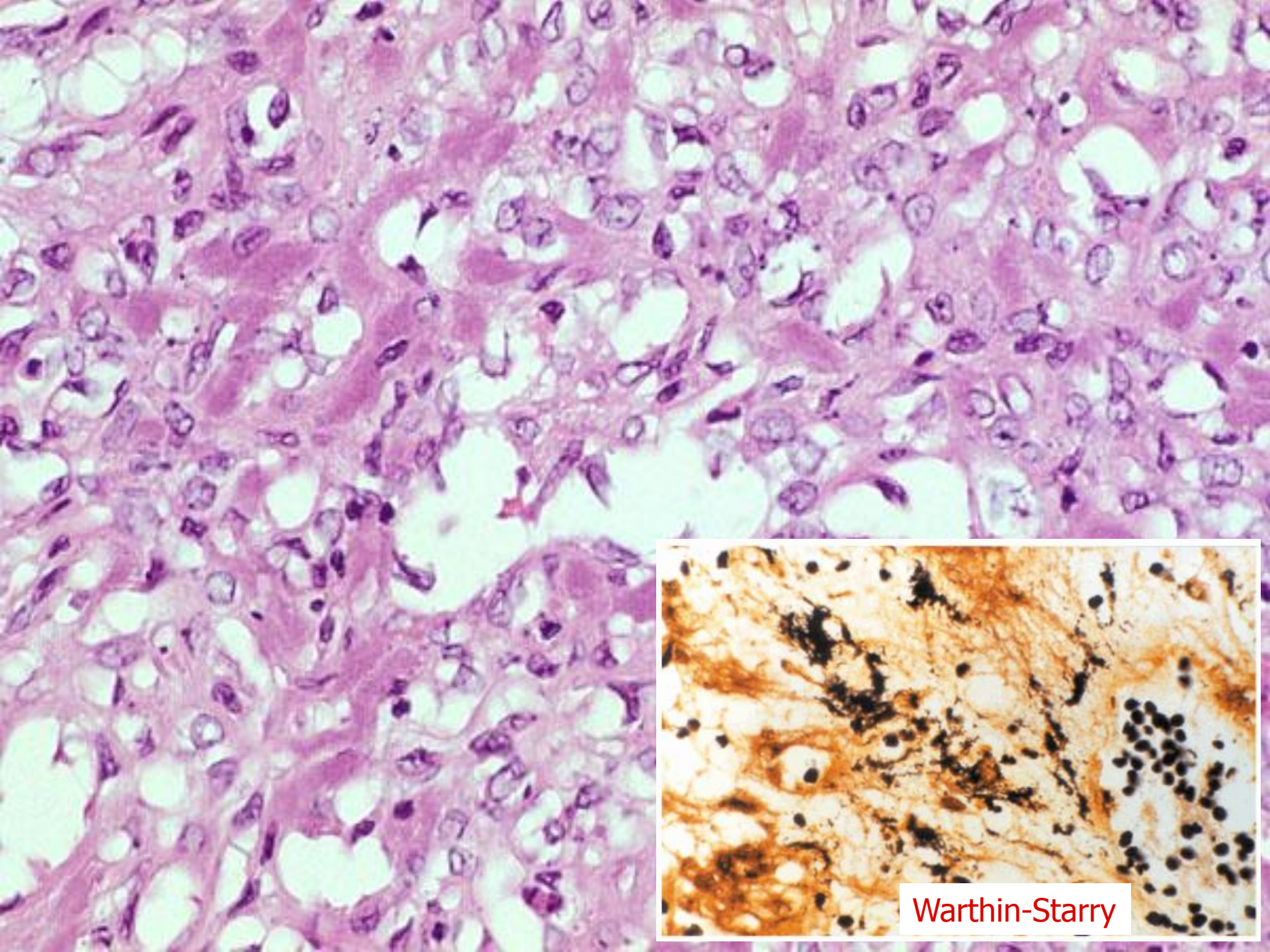
Coccidioidomycosis immitis





Bacillary Angiomatosis

More common in AIDS pts. Caused by Bartonelle henselae and B. quintana (pos with Warthin-Starry). Skin lesion & LN with epithelioid vascular proliferation & PMNs


Warthin-Starry

Protozoal Lymphadenitides

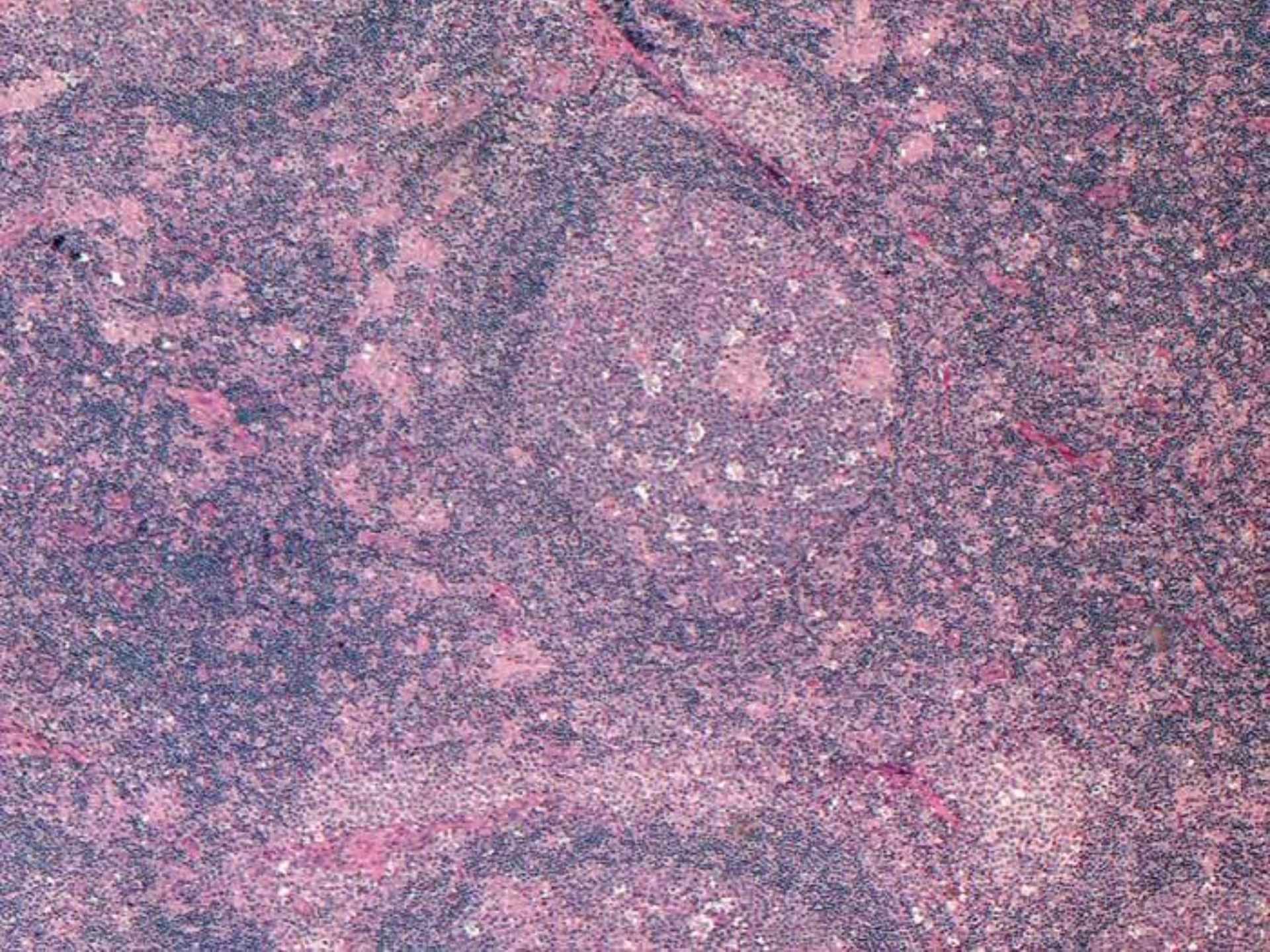
- Toxoplasma
- Leishmania
- Filaria (Wucheria bancrofti, Brugia malayi)

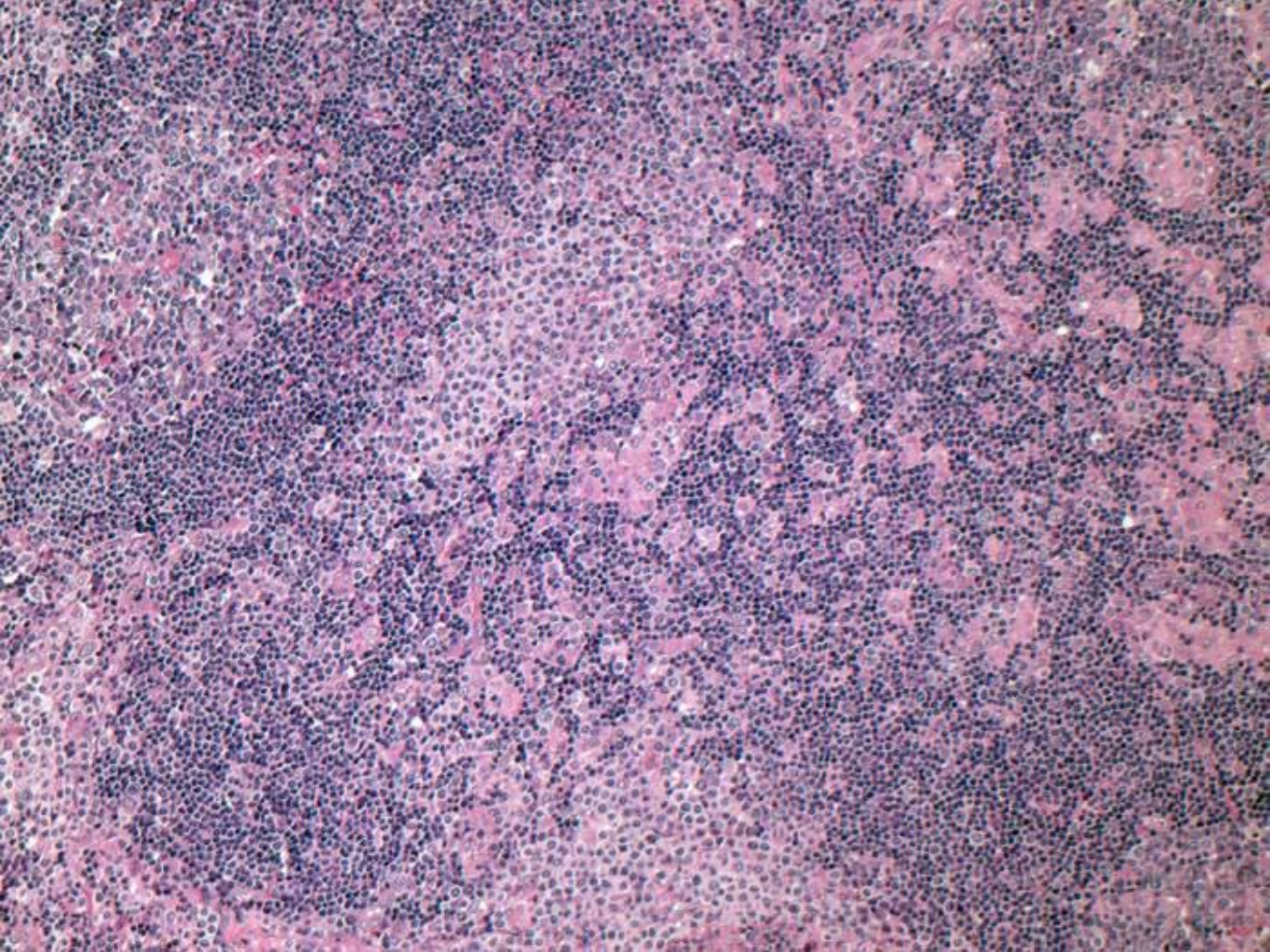
Toxoplasma Lymphadenitis

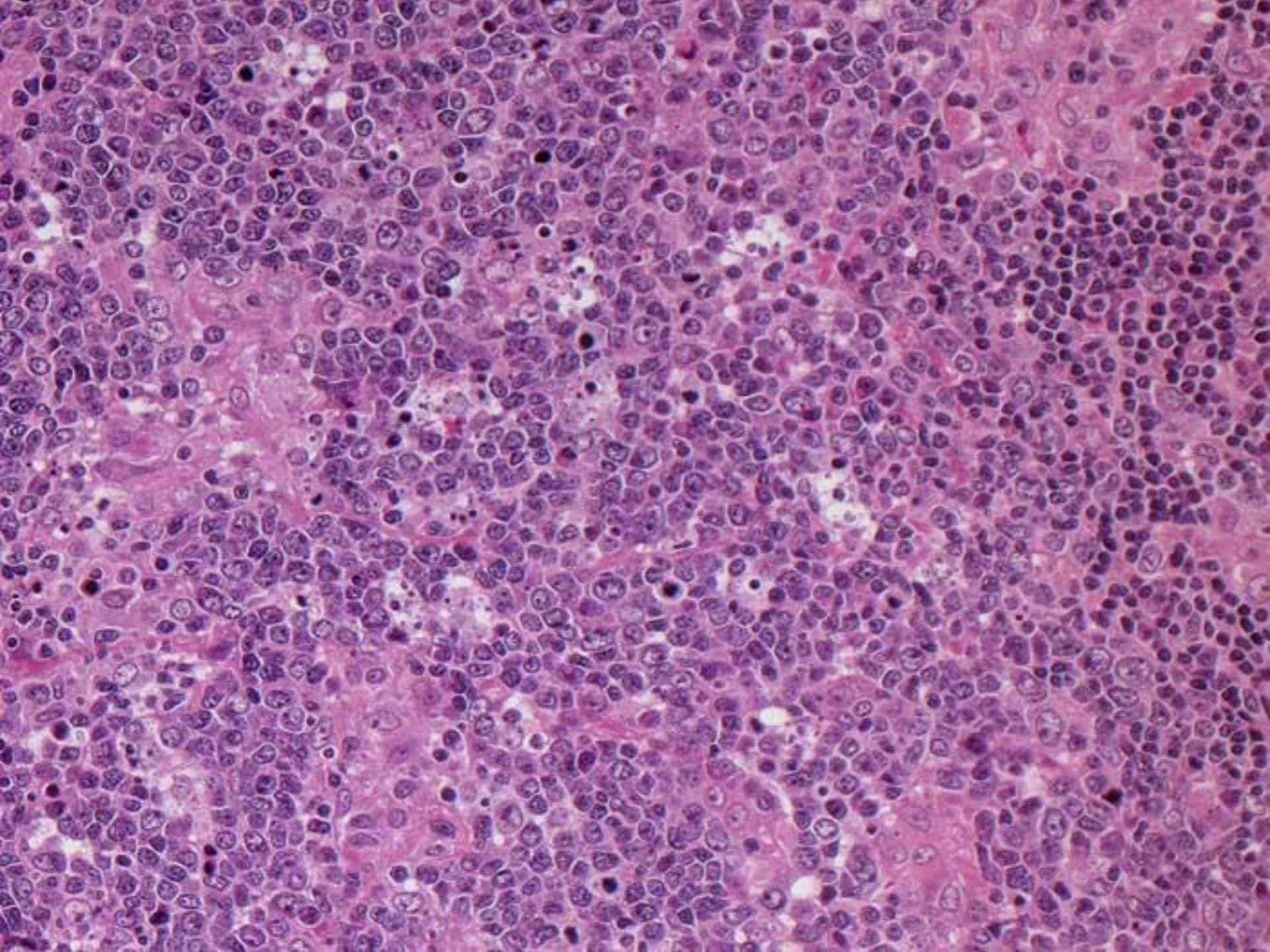
- Most common parasitic infection in US
- Cat definitive host; Toxoplasma gondii
- Posterior cervical LN most often affected
- Triad: Reactive germinal centers; perifollicular and intrafollicular clusters of epithelioid histiocytes; patches of monocytoid cells in sinus
- Serologic tests for confirmation

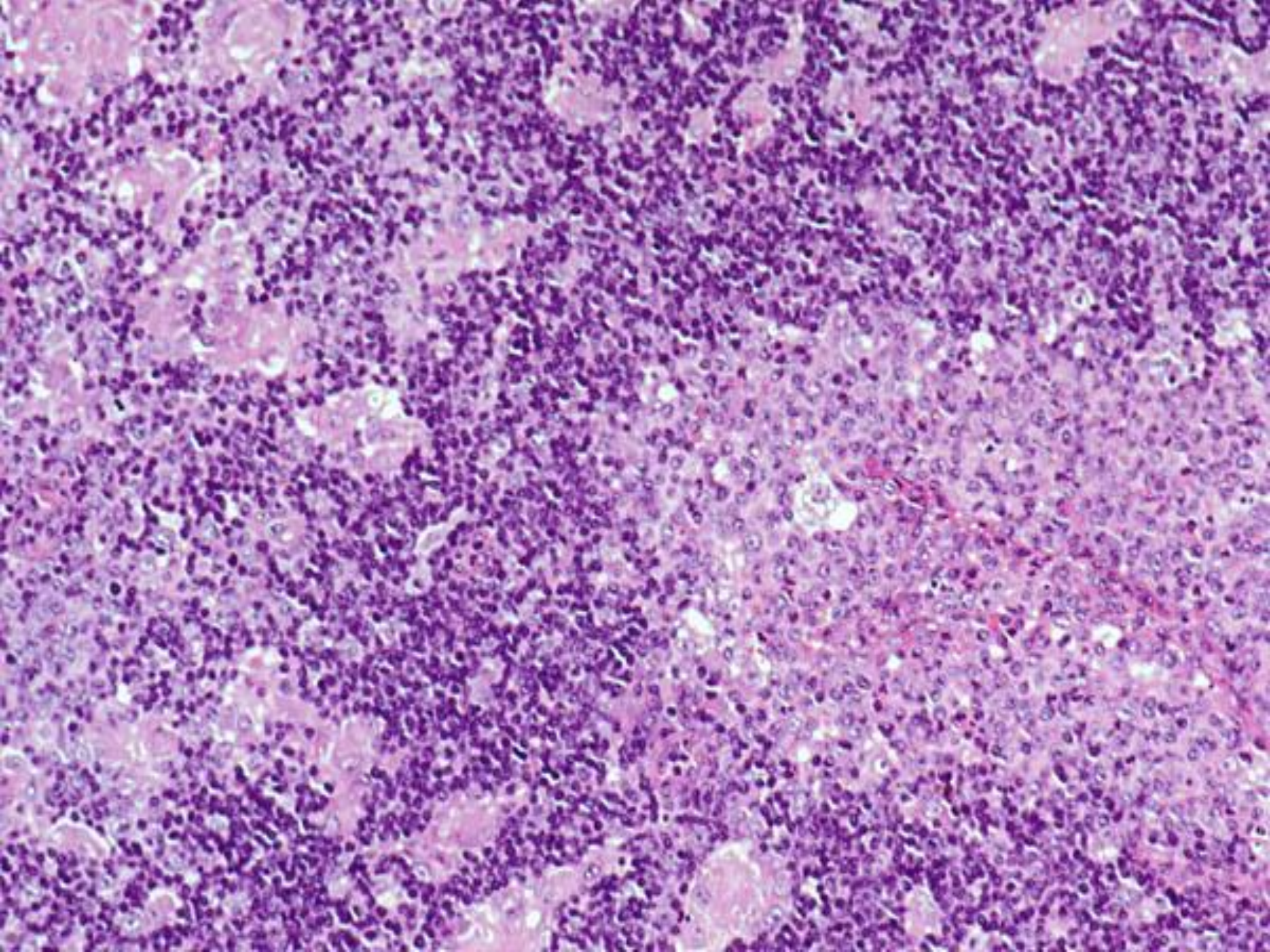
Case Illustration

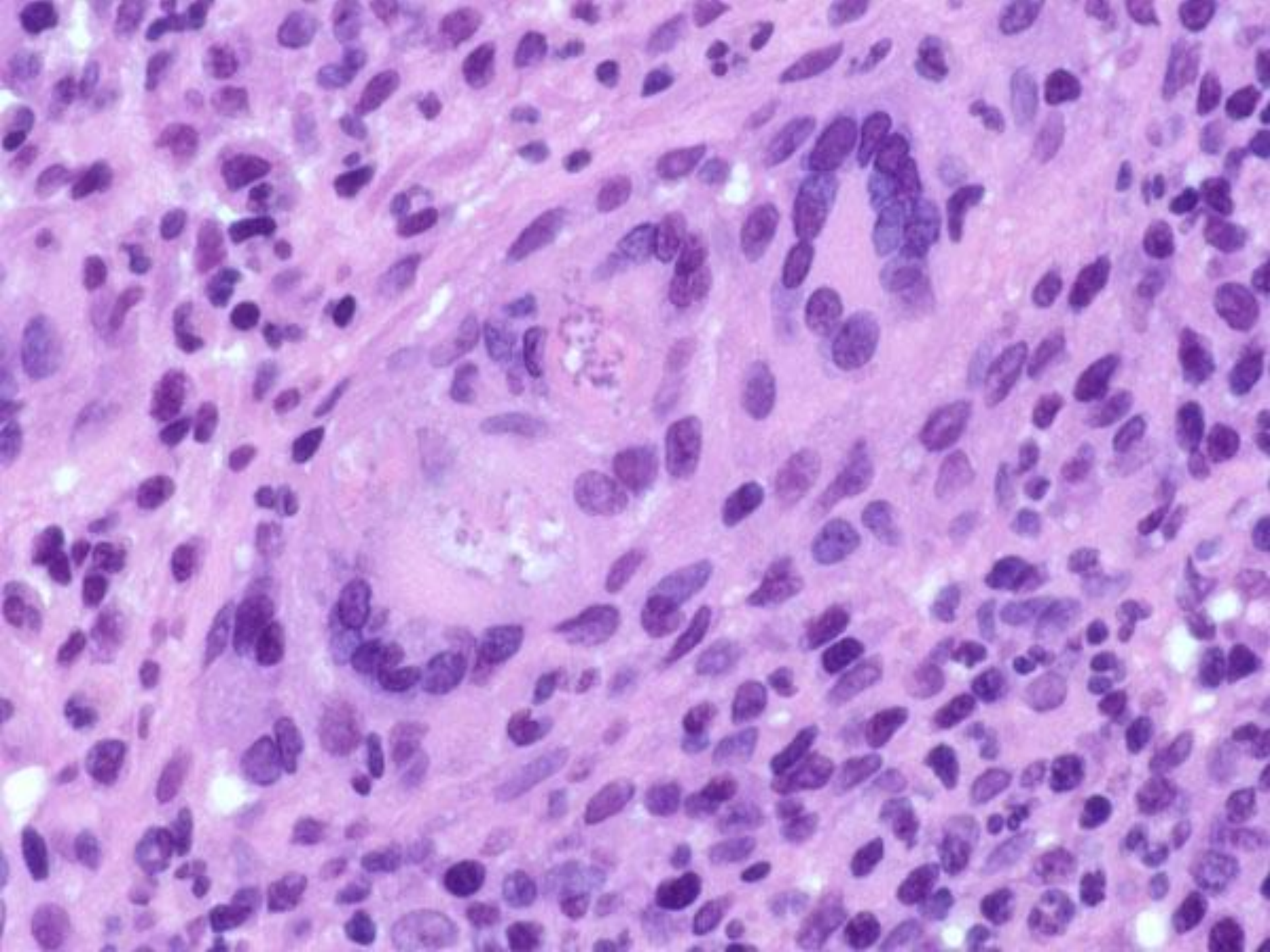
- 5-year-old girl with cervical and axillary lymphadenopathy







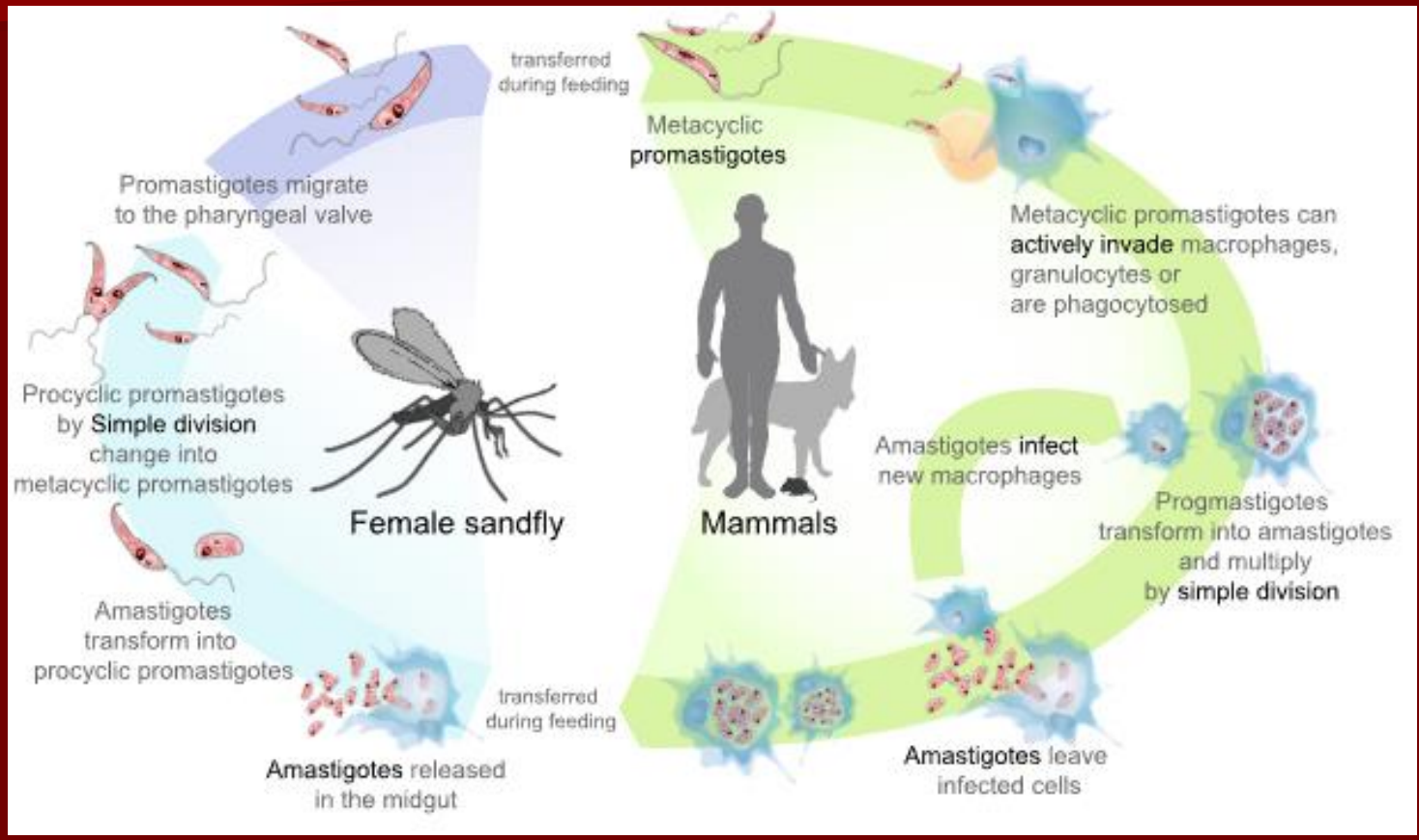


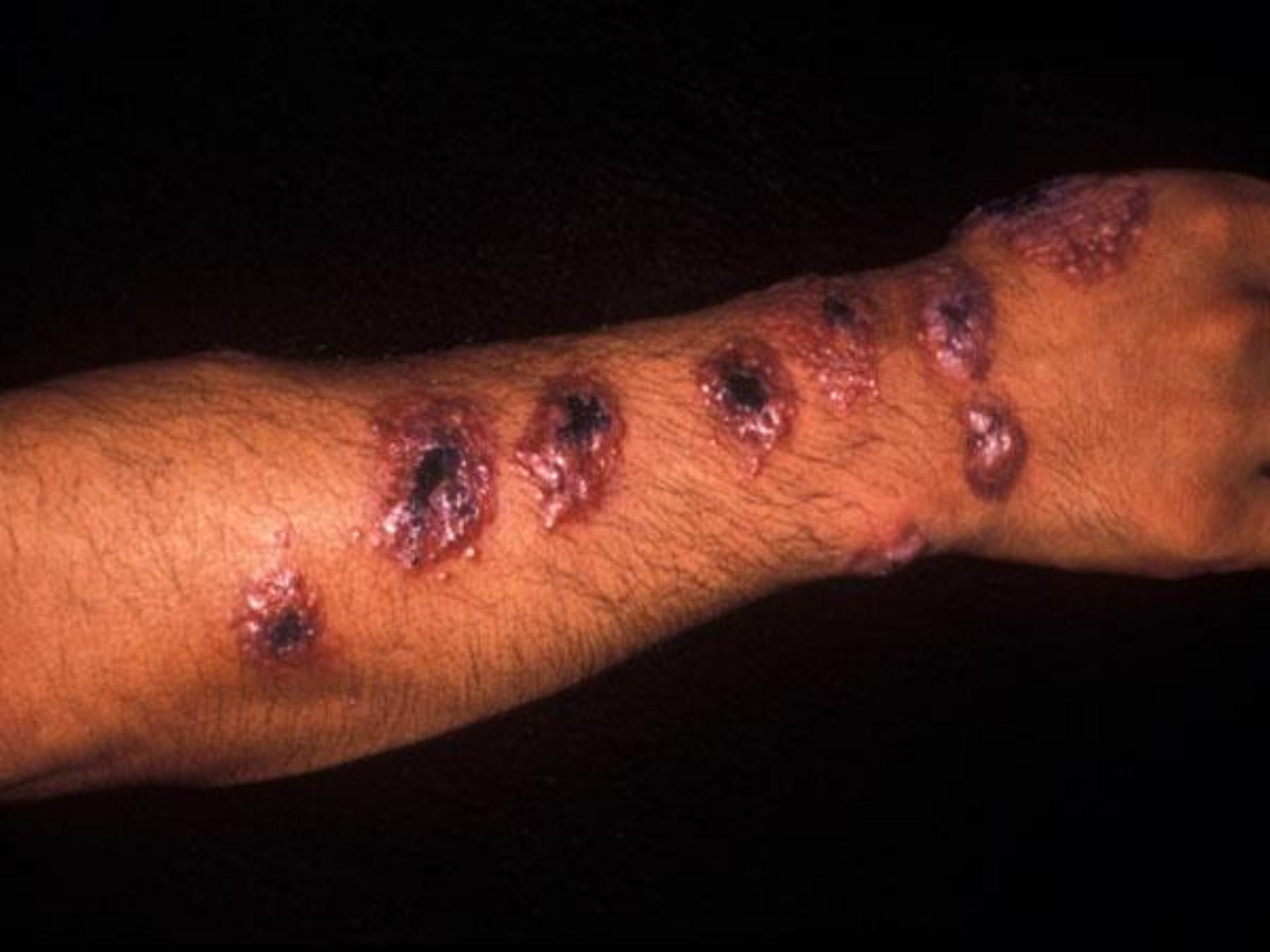


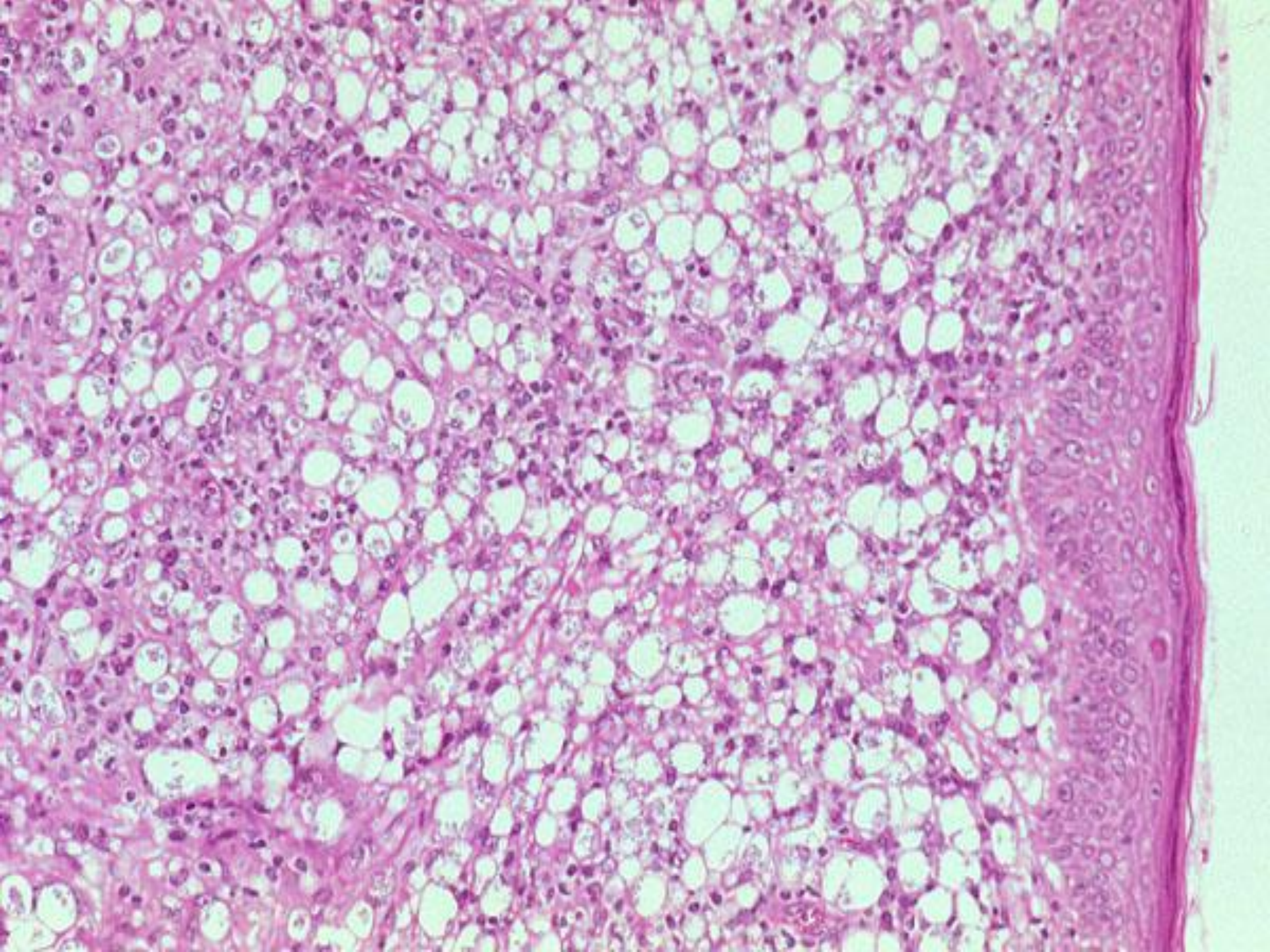
Leishmania Lymphadenitis

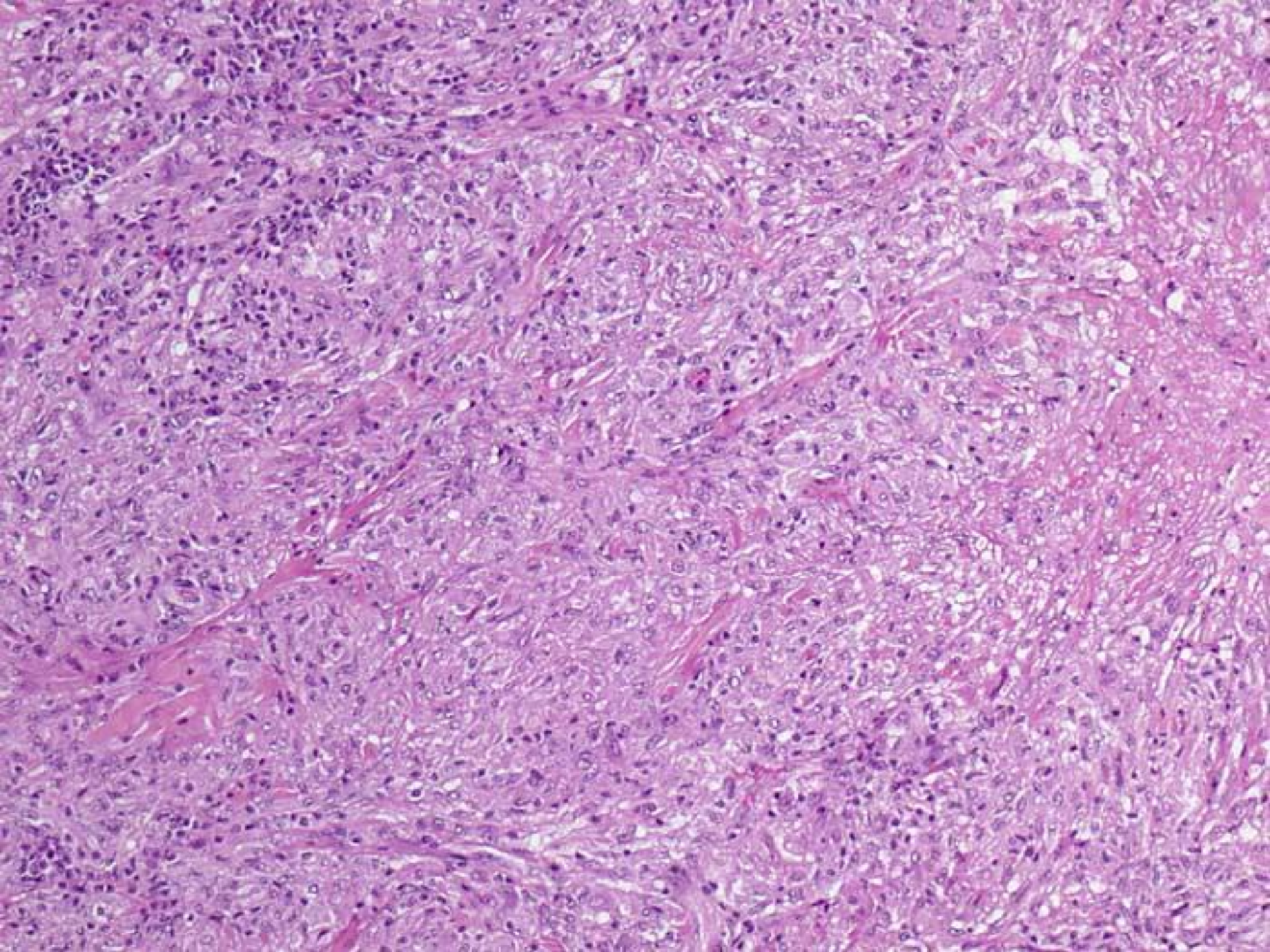
- Microscopic protozoa transmitted by sandflies
- Cutaneous, localized, and visceral forms
- Granulomas forming starry sky pattern
- Necrosis more common in immunodeficient
- Histiocytes and giant cells with intracellular amastigotes

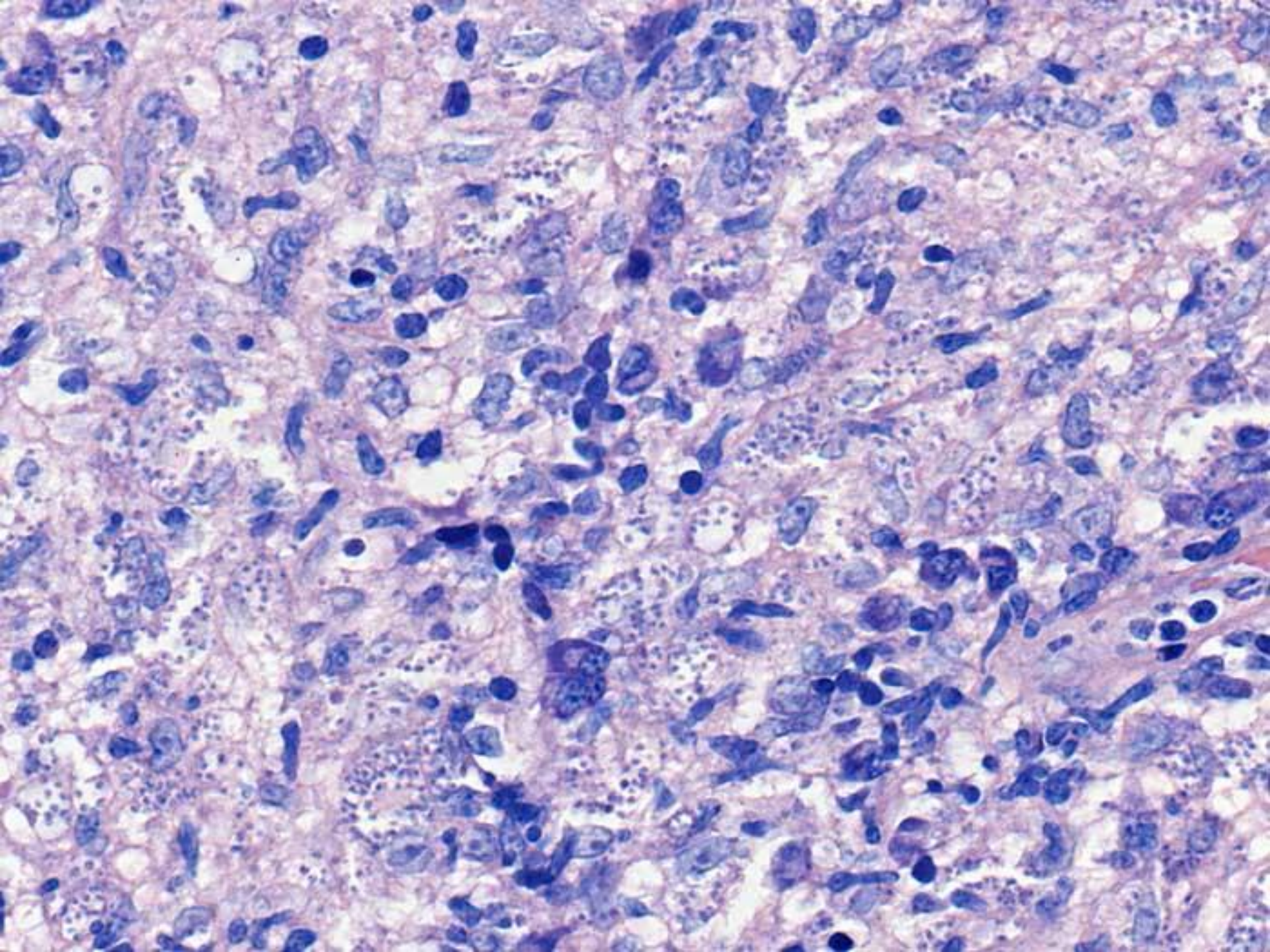
Leishmania Lymphadenitis

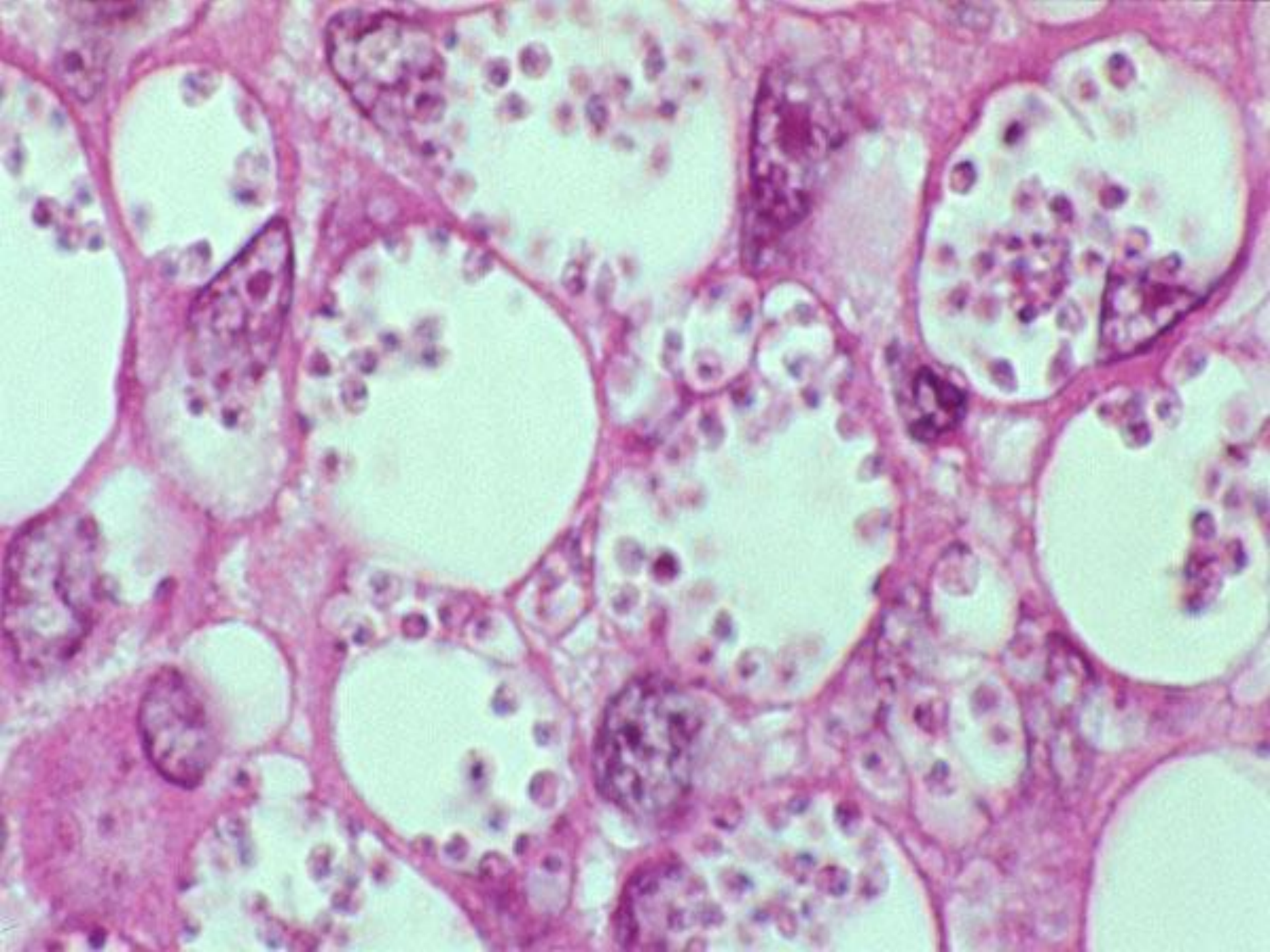


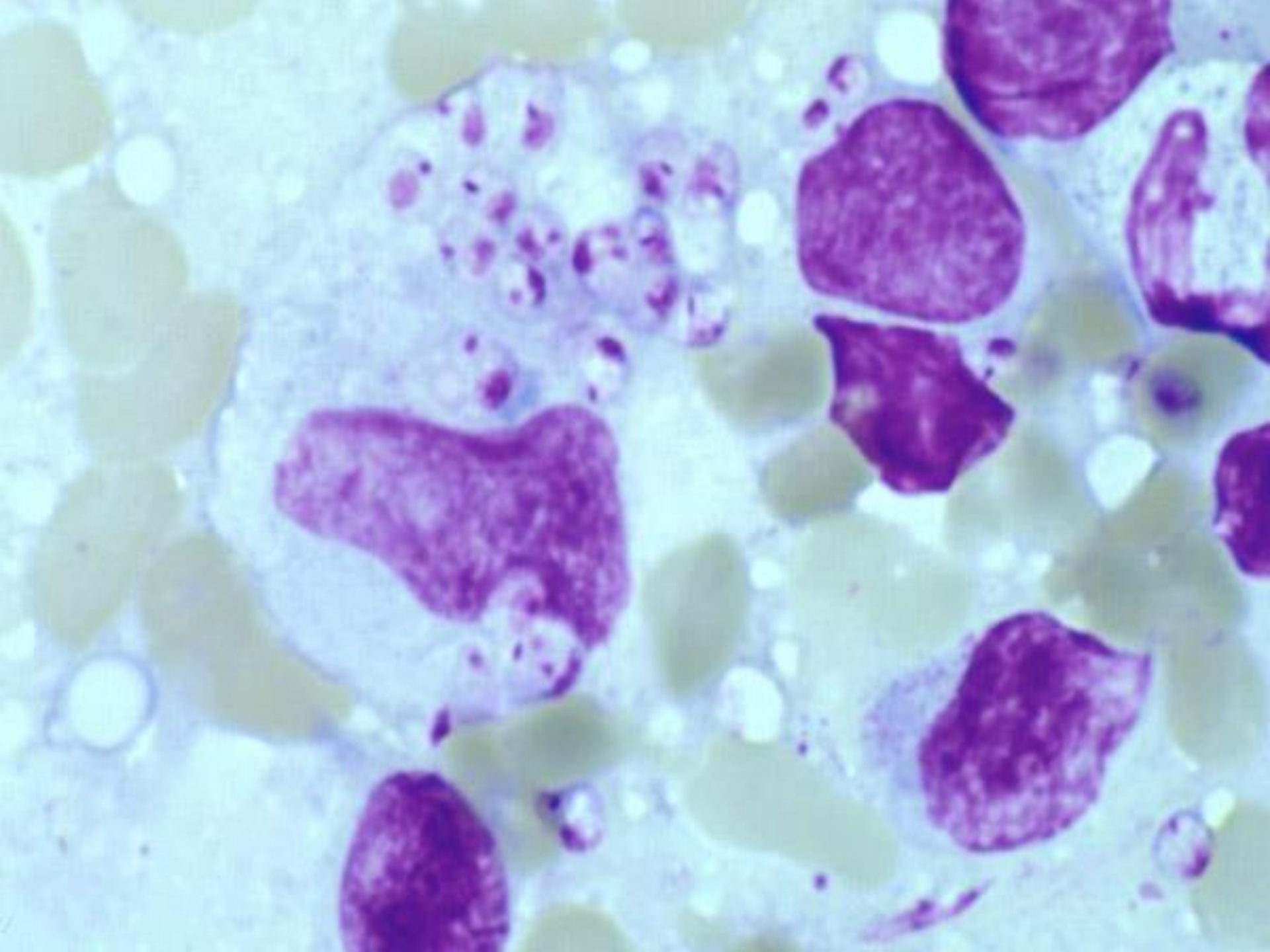












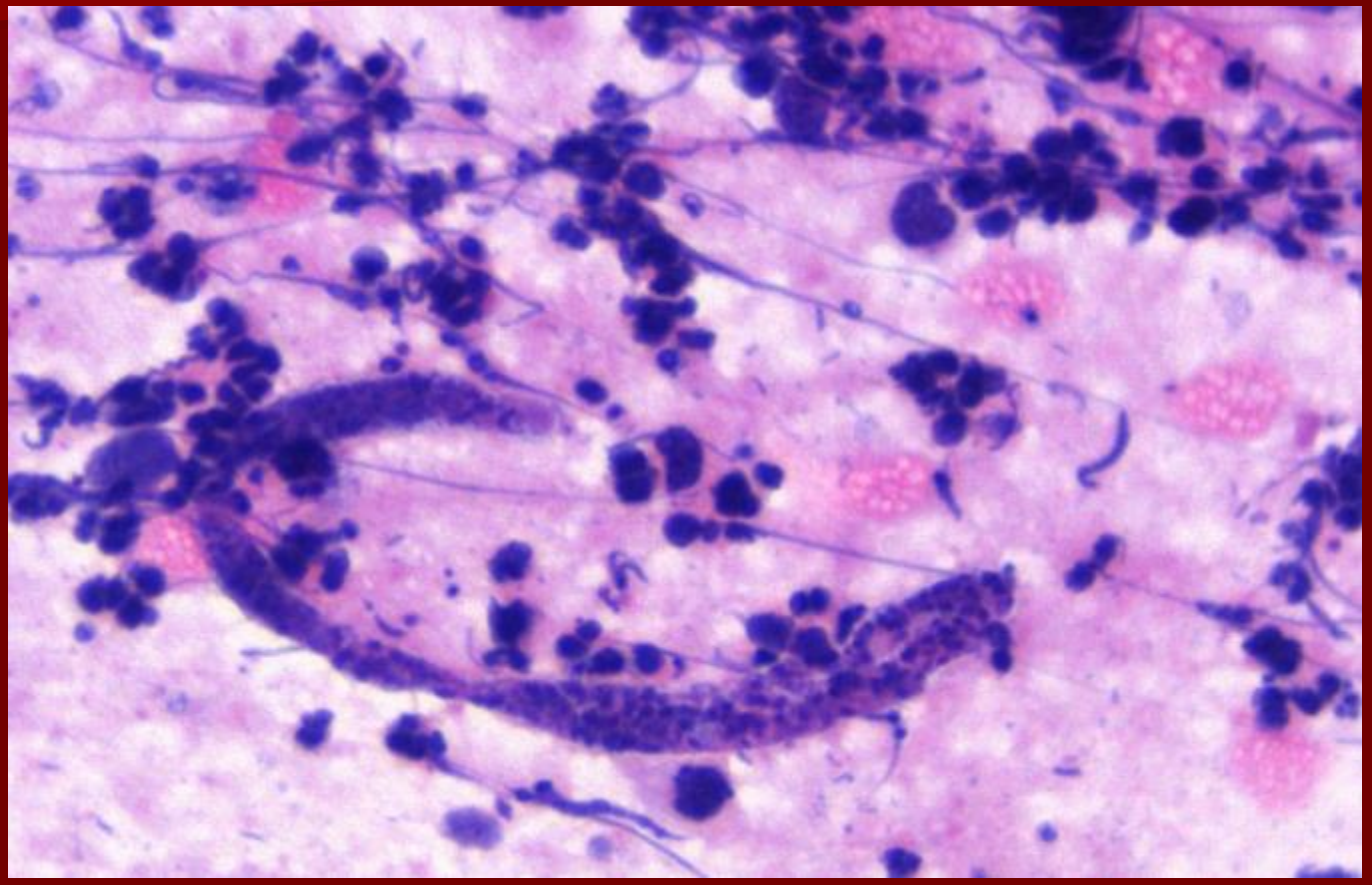
Filaria

- Wucheria bancrofti, Brugia malayi
- Adult filaria is found in dilated LN sinus or perinodal lymphatics
- No tissue reaction to living worms
- Intense reaction to dead worms (granuloma, numerous eosinophils, followed by fibrosis and calcification)

Case Illustration

- An 8 year old child presented with an enlarged, 2 x 2 cm posterior cervical lymph node with restricted mobility

Wucheria bancrofti



Multiple, coarse, discrete nuclei extending from head to tail

Lymphadenopathies

- Lymphadenopathies associated with clinical syndromes
- Iatrogenic lymphadenopathies (vaccination)
- Vascular lymphadenopthies
- Foreign body lymphadenopathies
- Lymph node inclusions

Lymphadenopathies Associated with Clinical Syndromes

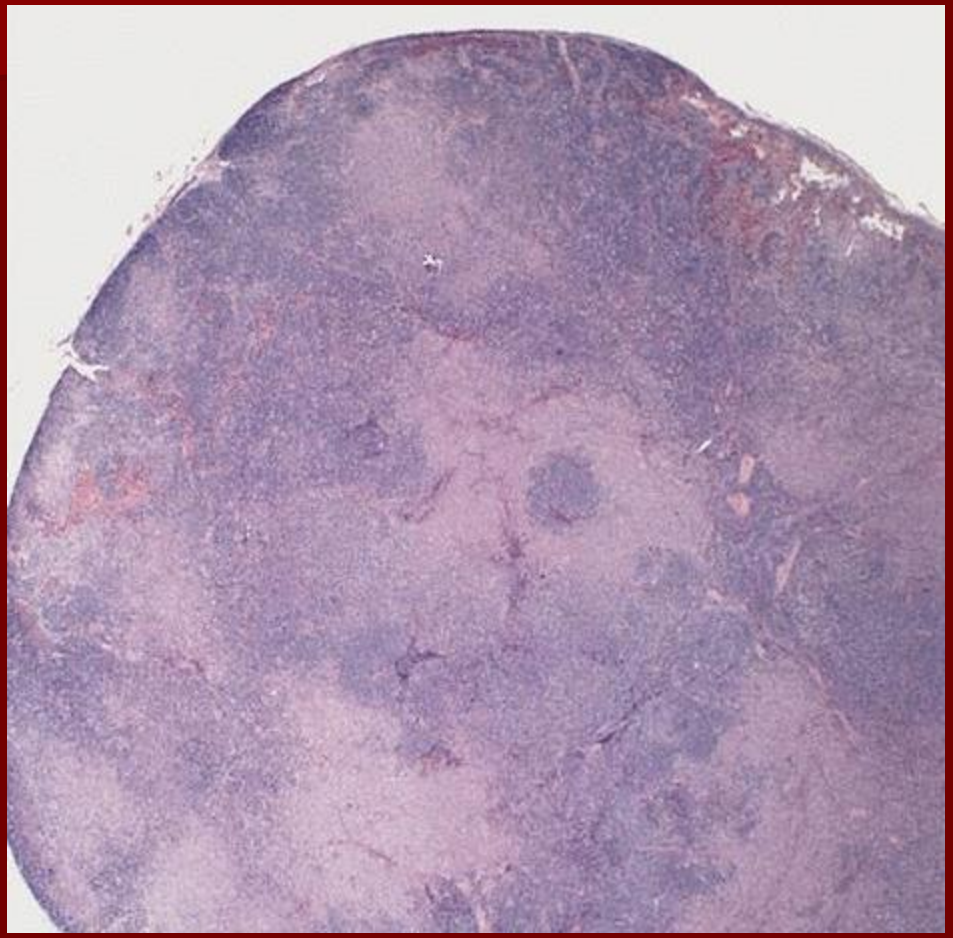
- Sinus Histiocytosis with Massive Lymphadenopathy
- Kikuchi-Fujimoto Lymphadenopathy
- Sarcoidosis
- Rheumatoid Arthritis; SLE
- Dermatopathic Lymphadenopathy
- Castleman's disease
- Tumor-Reactive Lymphadenopathy
- Sarcoidosis
- Kimura Lymphadenopathy

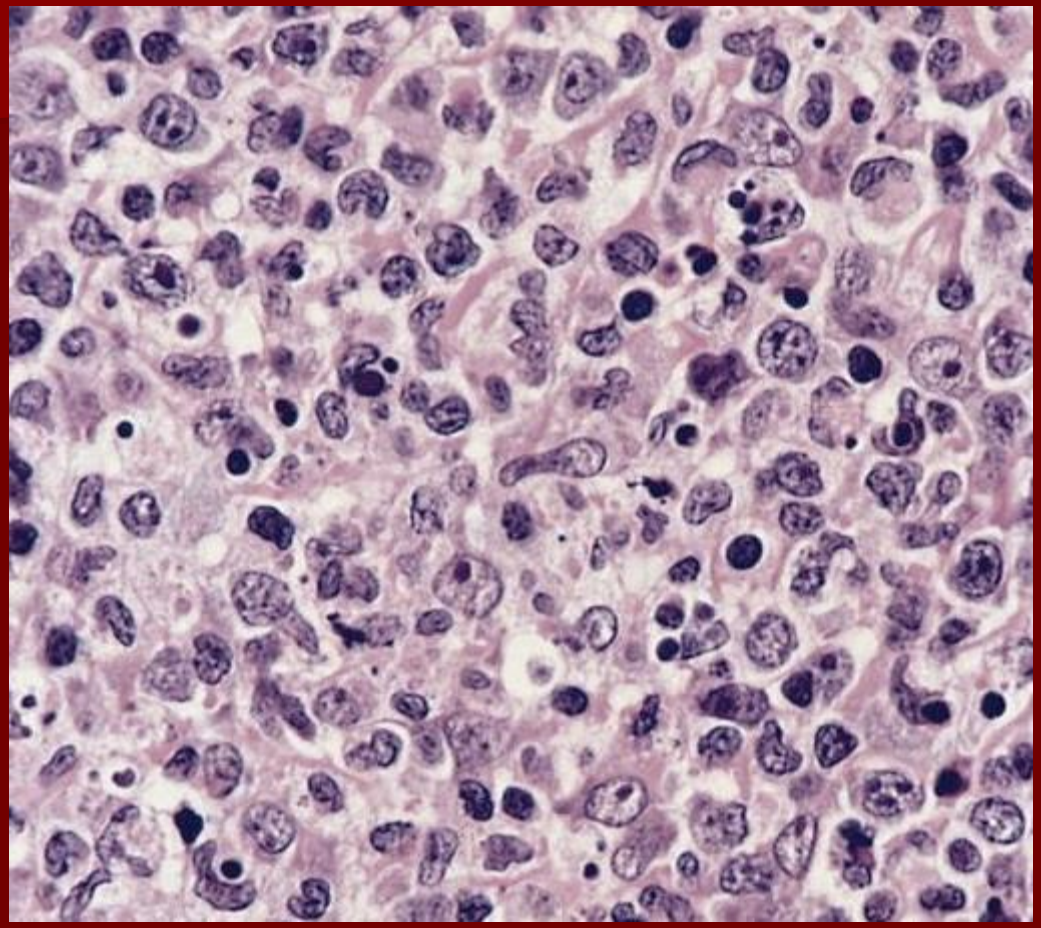
Kikuchi-Fujimoto
(Subacute necrotizing lymphadenitis)

- Affects predominantly young Asians
- Females more often than males
- Benign course, spontaneous remission
- Fever, cervical lymphadenapthy
- Patchy necrosis, marked apoptosis, nuclear debris
- Aggregates of histiocytes
- Neutrophils, eosinophils absent
- Kawasaki's disease: infancy and childhood. Histology similar to Kikuchi + fibrin thrombi

Case Illustration

- 28-year-old Japanese woman with low-grade fever, fatigue, and cervical lymphadenopathy

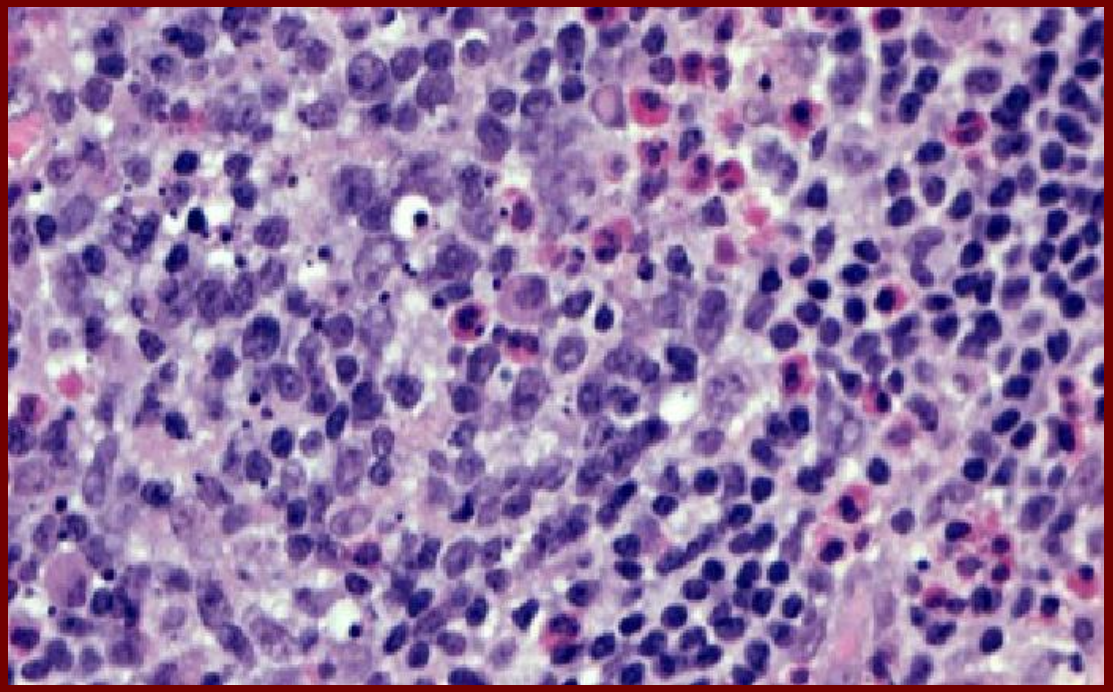




Kimura's disease

- Affects predominantly young Asian men
- Subcuntaneous tissue, salivary glands, regional LNs of the neck, increased fibrosis
- Folllicular hyperplasia, polykaryocytes (multinucleated large cells, neg for CD30) within follicles.
- Numerous interfollicular eosinophils and thin-walled blood vessels
- Surgical removal with frequent recurrence

Kimura's disease

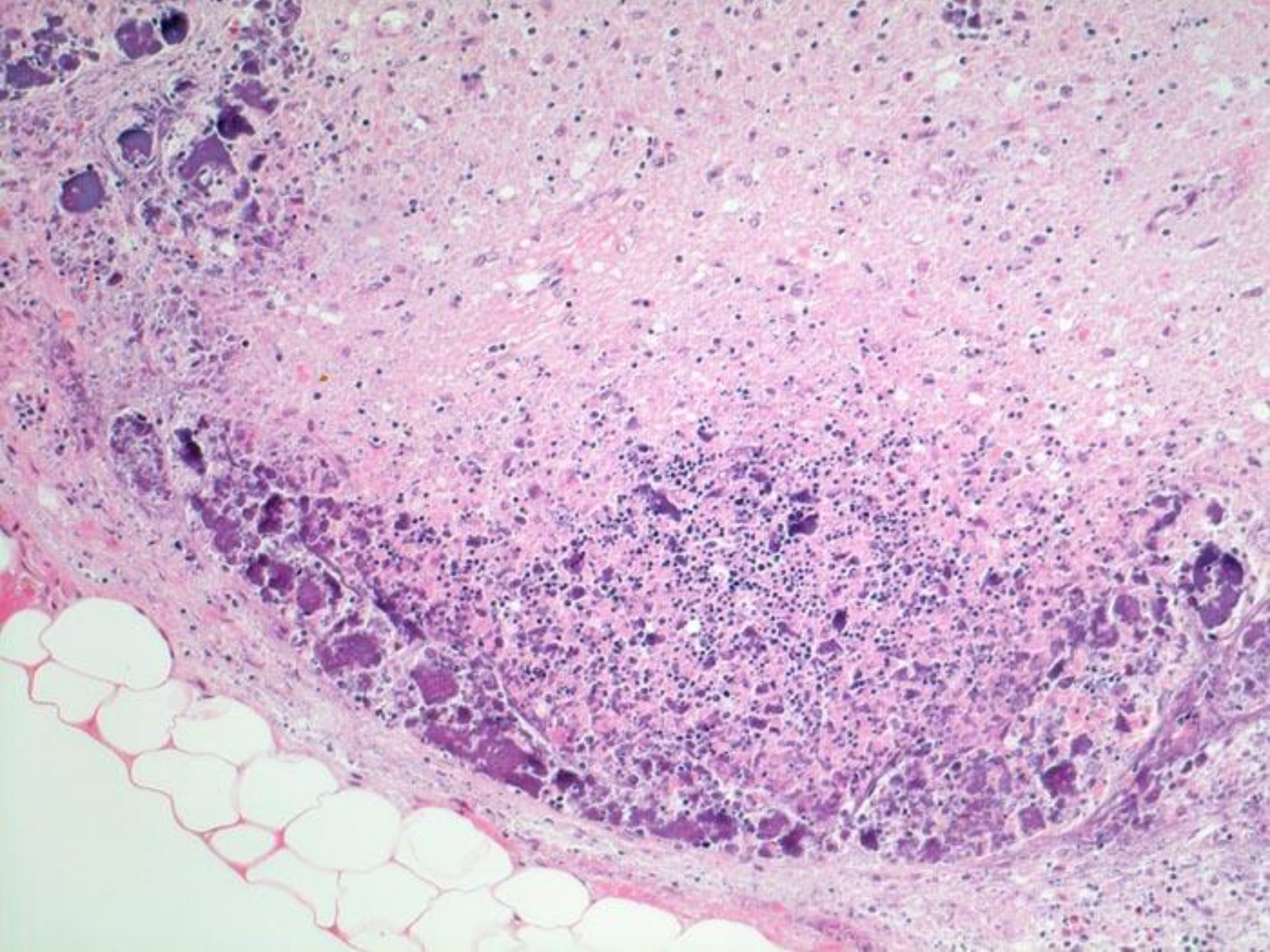


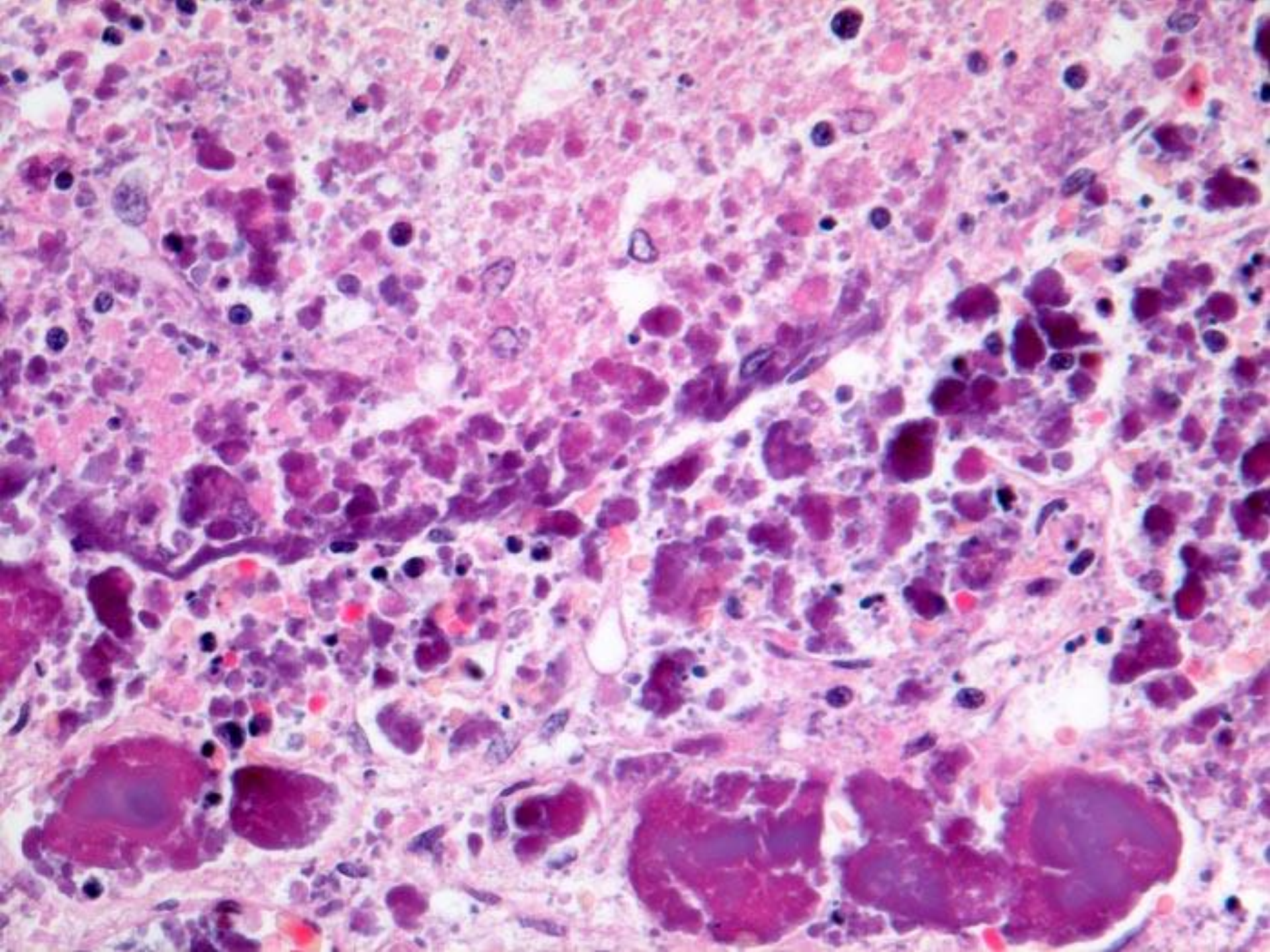
Systemic Lupus Lymphadenopathy

- Architecture effaced
- Follicles inconspicuous
- Necrosis focal or confluent
- Nuclear debris and hematoxylin bodies (basophilic masses of DNA)
- Presence of plasma cells, immunoblasts
- Vasculitis with fibrinoid necrosis
- Granulomas, neutrophils and eosinophils: absent

Case Illustration

- 25-year-old woman with fatigue, weight loss, uremia





SLE Lymphadenopathy Differential Diagnosis

- Kikuchi's lymphadenopathy
- Infectious mononucleosis
- Cat-scratch lymphadenitis
- Syphilitic lymphadenitis
- Mycobacterial lymphadenitis
- Special stains and serology helpful

Rheumatoid Lymphadeopathy

- Lymphadeopathy is frequent in rheumatoid arthritis
- Florid follicular hyperplasia, marked interfollicular plasmacytosis
- Diff DX: syphilis, HIV, Castleman disease

Sinus Histiocytosis with Massive Lymphadenopathy (Rosai-Dorfmann Disease)

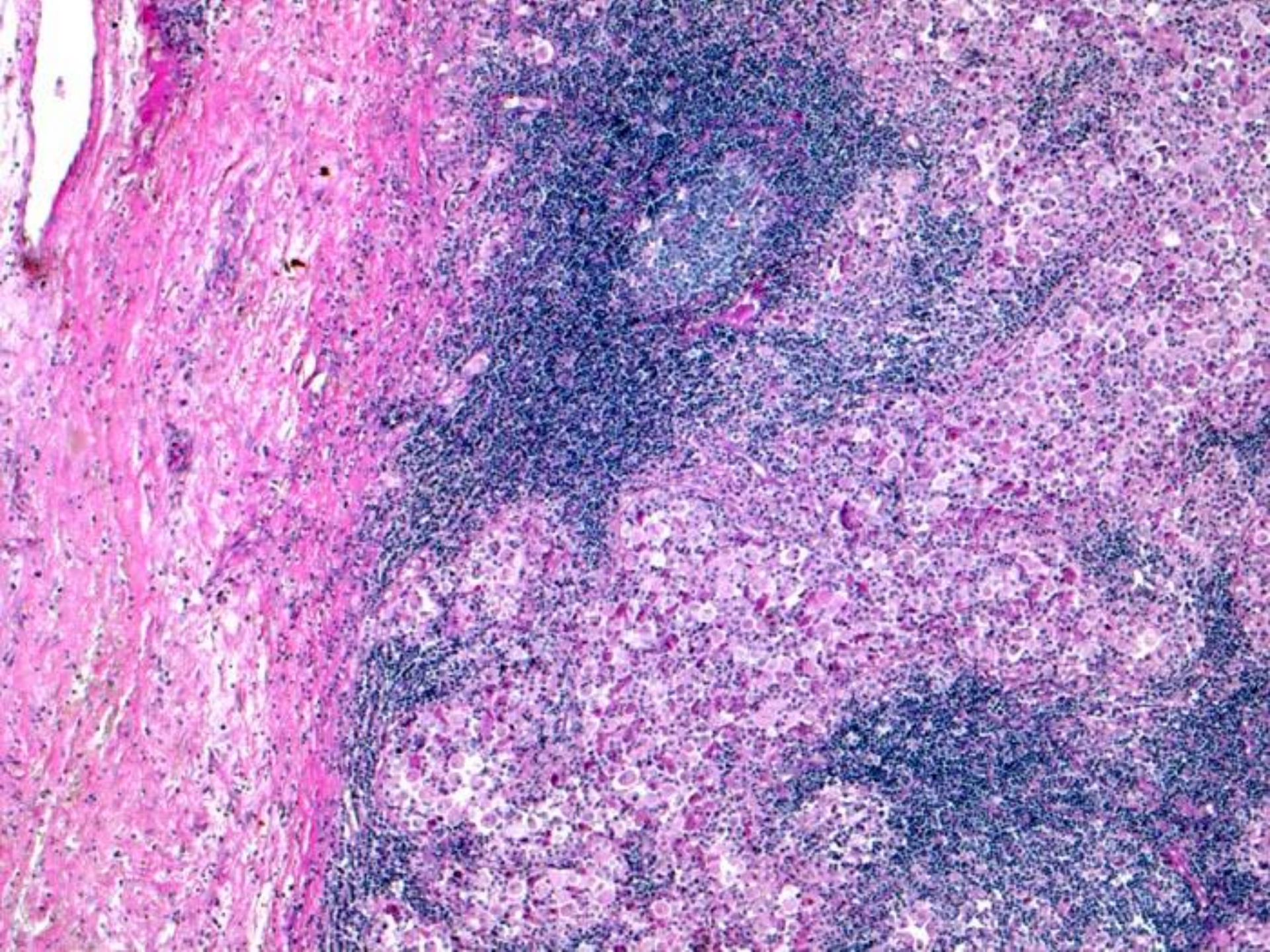
- Children and adolescents
- May have fever or no systemic symptoms
- Polyclonal hypergammaglobulinemia
- Massive lymphadenopathy; cervical lymph nodes most commonly affected
- Good general condition
- Long duration; spontaneous regression

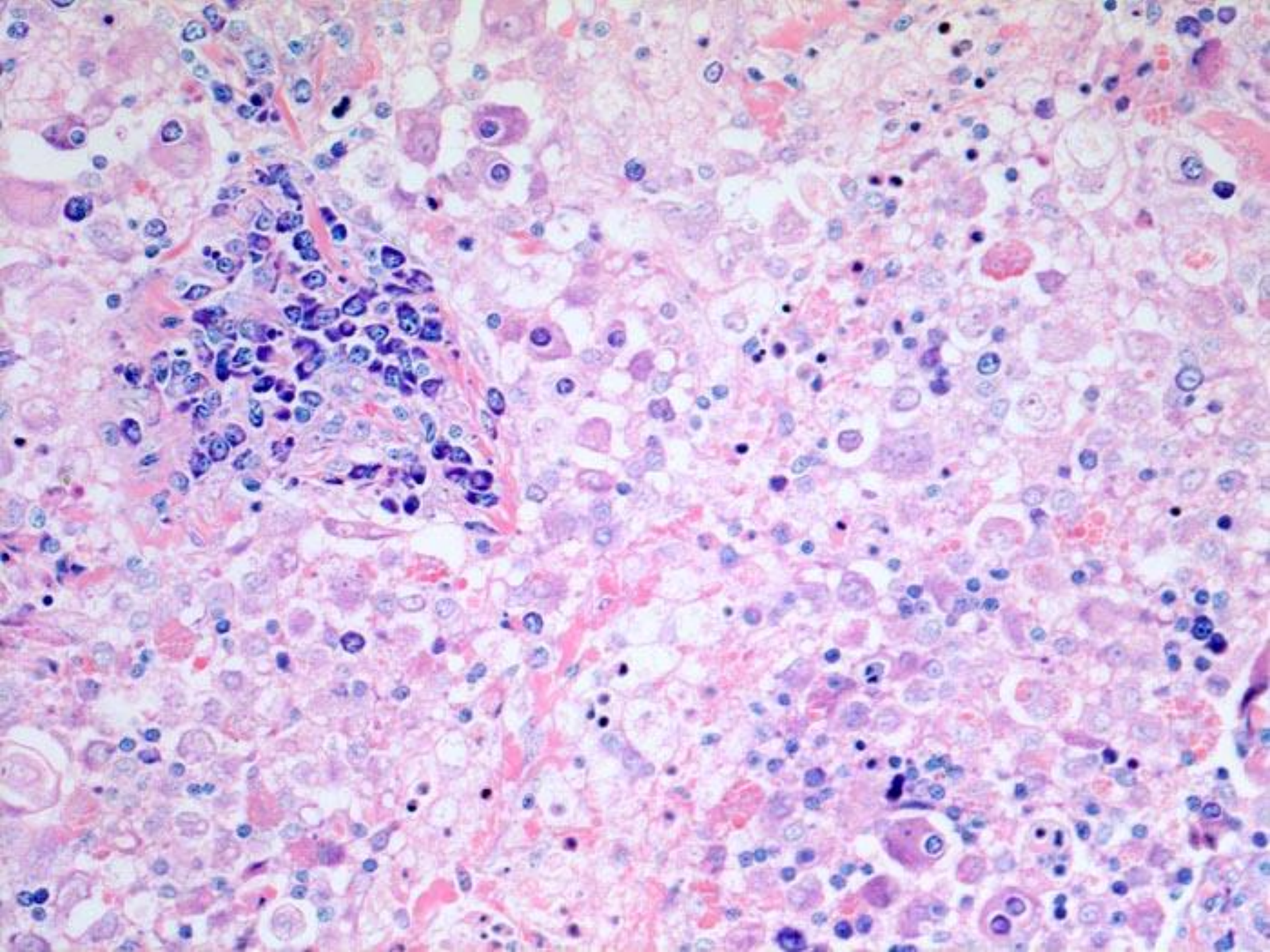
SHML-Rosai-Dorfmann Disease Histologic Features

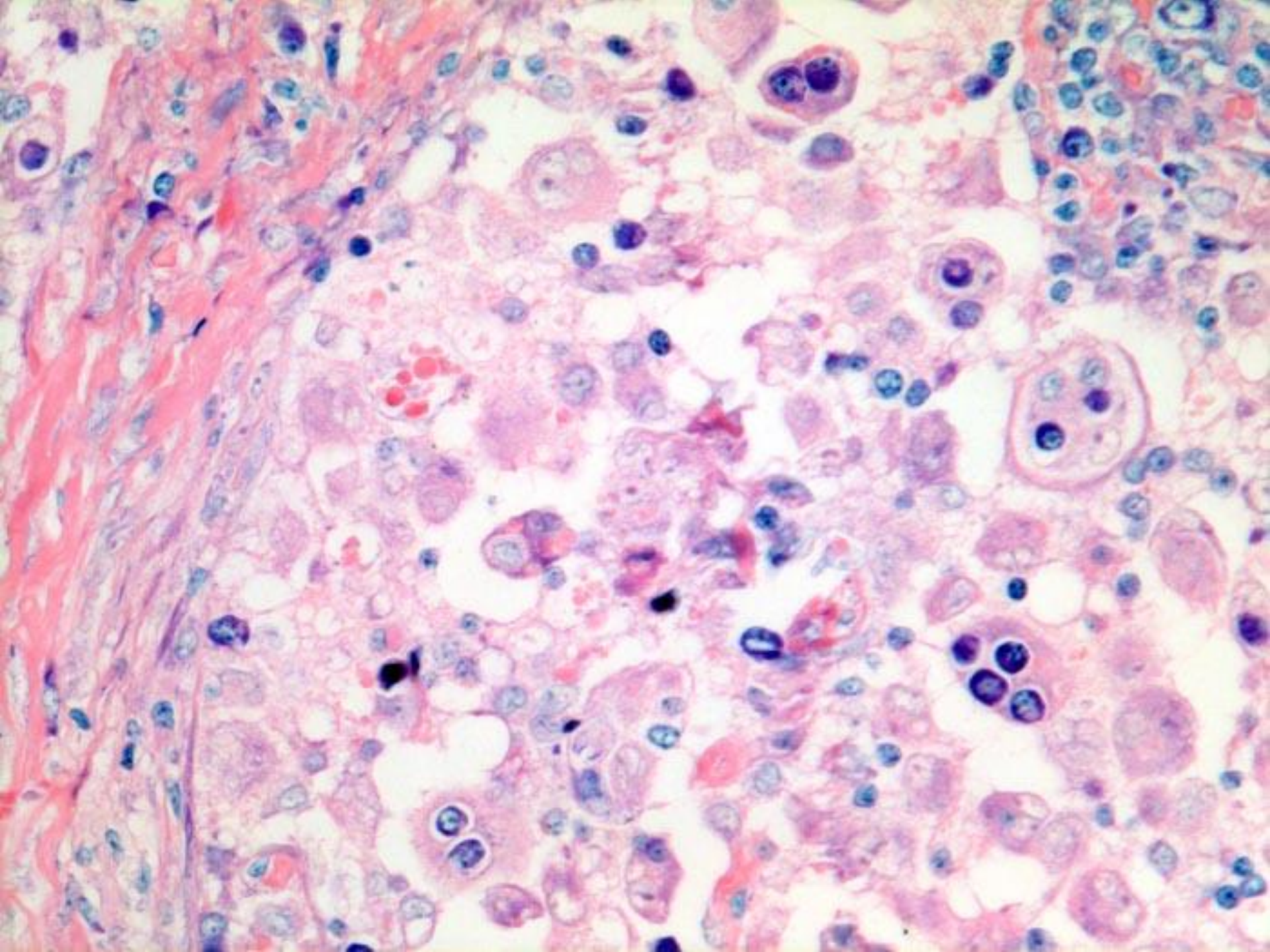
- Effacement of follicles
- Dilatation of sinuses
- Proliferation of sinus histiocytes
- Lipid-laden macrophages
- Absence of necrosis
- Lack of mitoses
- Emperipolesis (lymphocytes in histiocytes)

Case Illustration

- 9-year-old boy with bilateral cervical lymphadenopathy; otherwise healthy







Castleman Lymphadenopathy

- Hyaline-vascular type
- Plasma cell type
- Mixed type
- Multicentric

Castleman Lymphadenopathy: Hyaline-Vascular Type

- More common; younger patients
- Isolated lymph node mass; often mediastinal
- Frequently asymptomatic
- Hyaline deposits in atrophic germinal centers
- Transfixing, collagen-ensheathed ("lollipop") arterioles
- Concentric layering of lymphocytes ("target" follicles)
- Interfollicular vascular hyperplasia

Castleman Lymphadenopathy: Plasma Cell Type

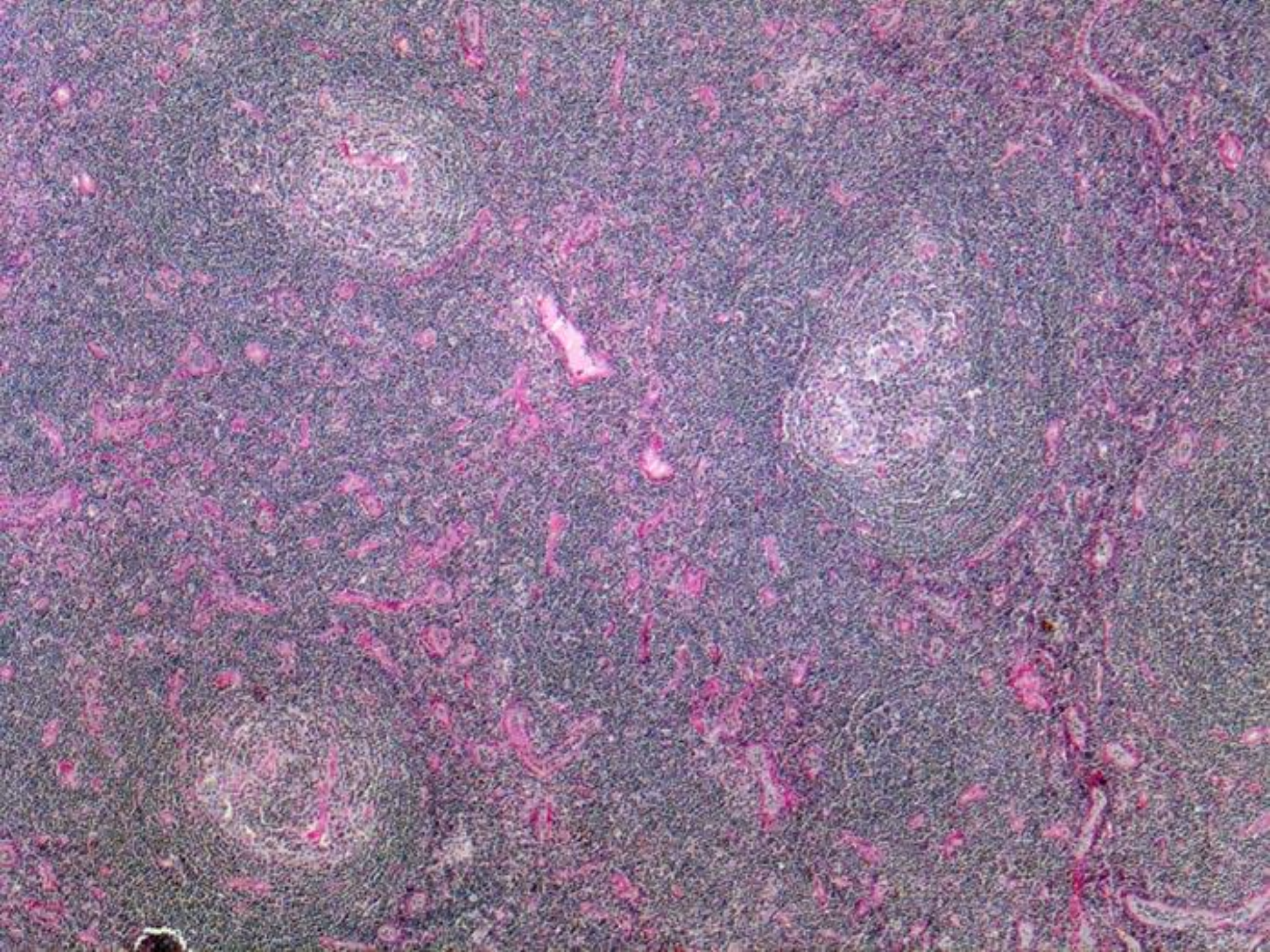
- Older patients
- Systemic symptoms
- Possible associations: polyneuropathies, organomegaly, endocrinopathy, monoclonal gammopathy, skin changes (POEMS syndrome)
- Hyperplastic lymphoid follicles with active germinal centers
- Interfollicular sheets of plasma cells

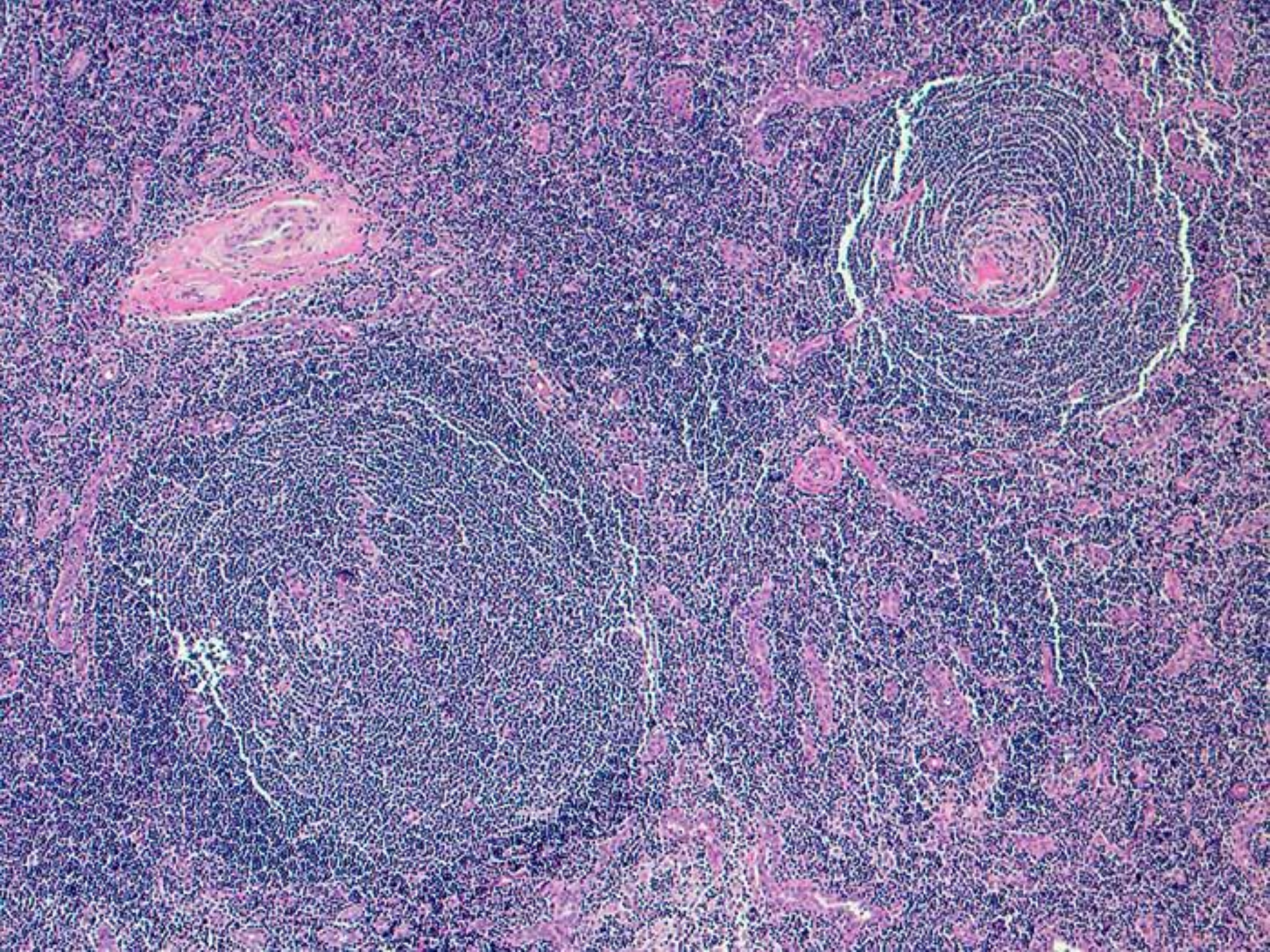
Castleman Lymphadenopathy Multicentric Form

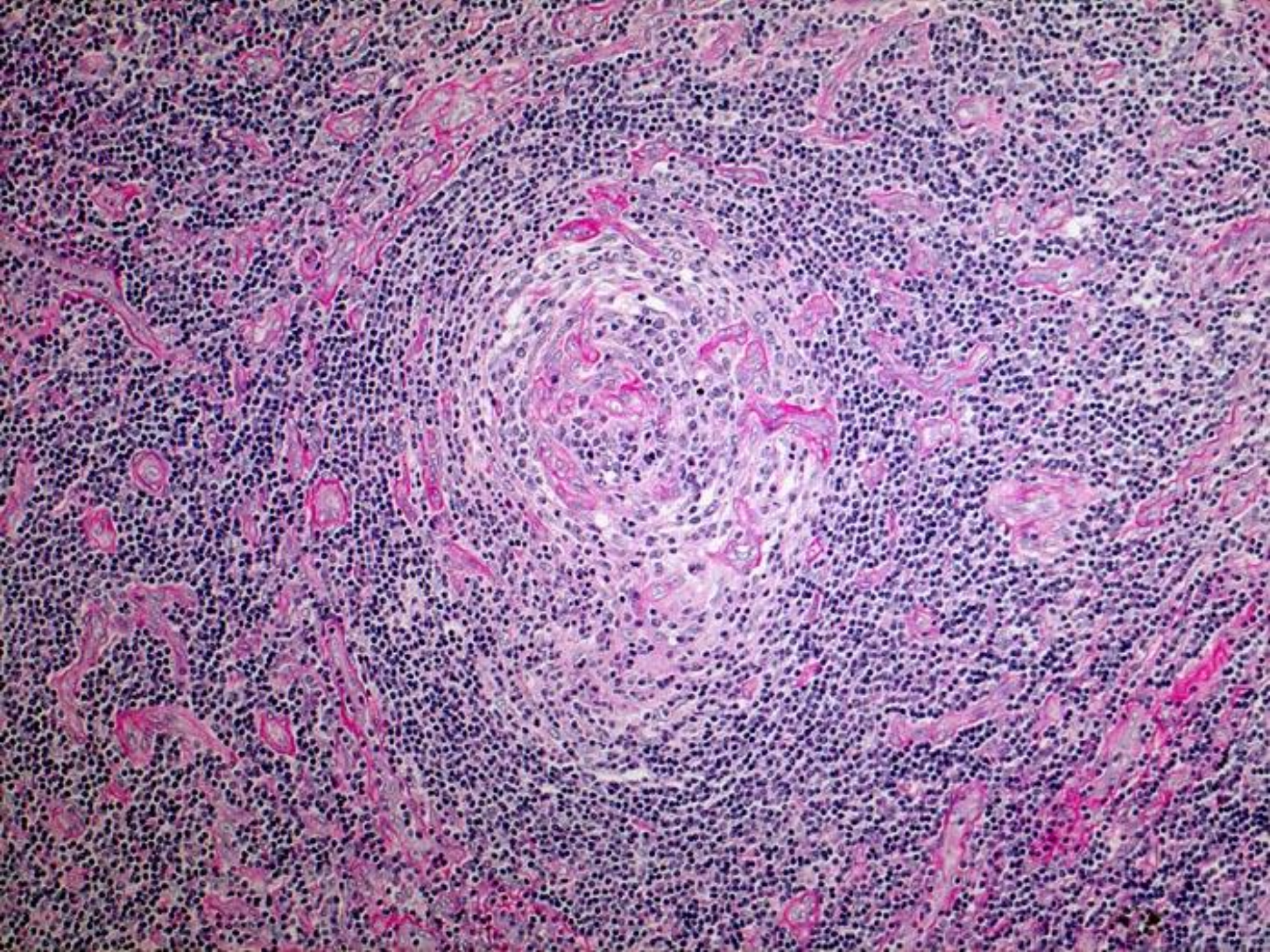
- Atypical lymphoproliferative disorder
- Most are plasma cell type or mixed type (features of both types)
- Older patients
- Severe systemic symptoms
- Multiple lymphoid organs involved
- High levels of IL-6 in lymph nodes & serum
- Kaposi sarcoma/HHV-8 often present
- HIV infection often associated

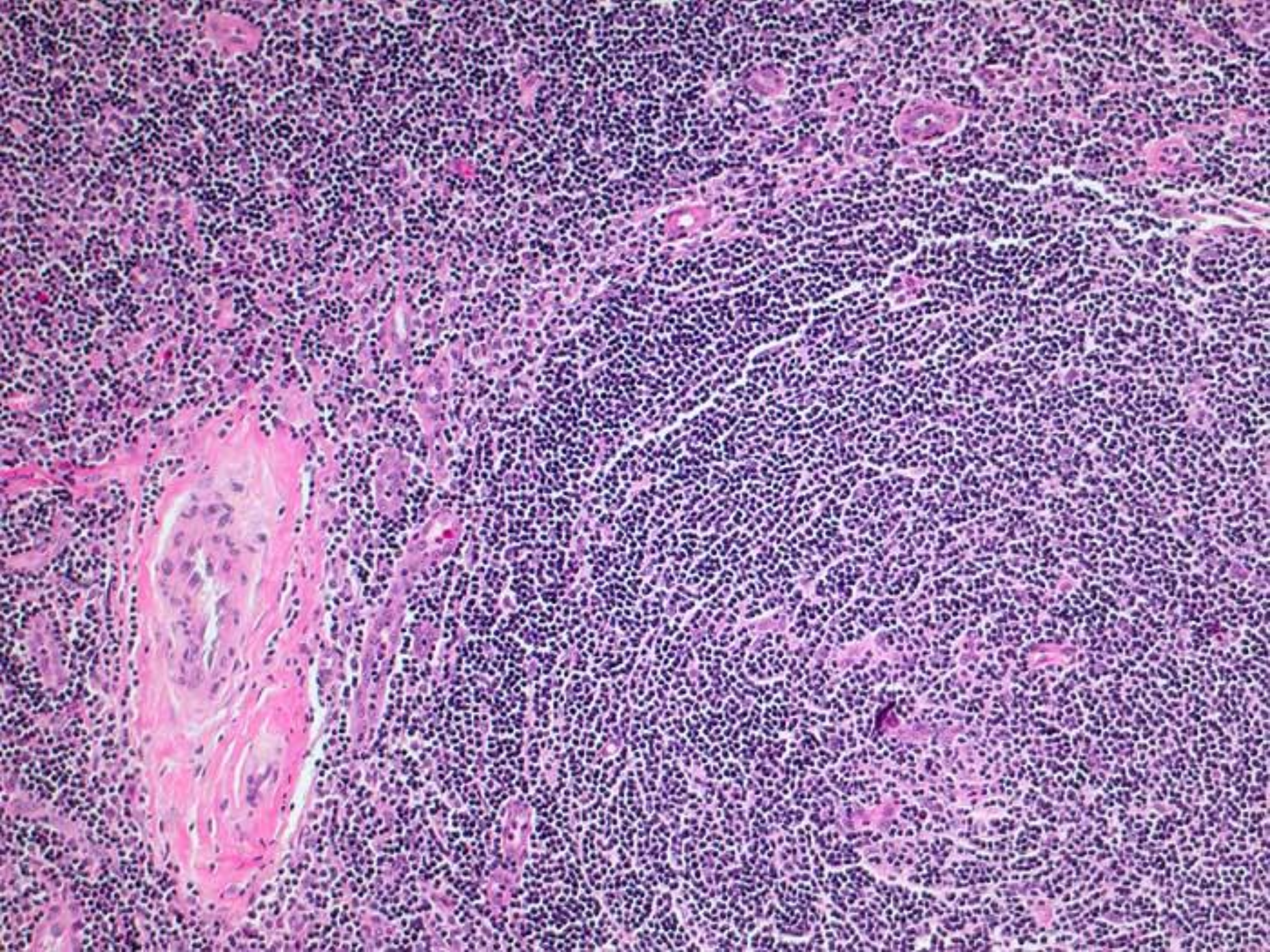
Case Illustration

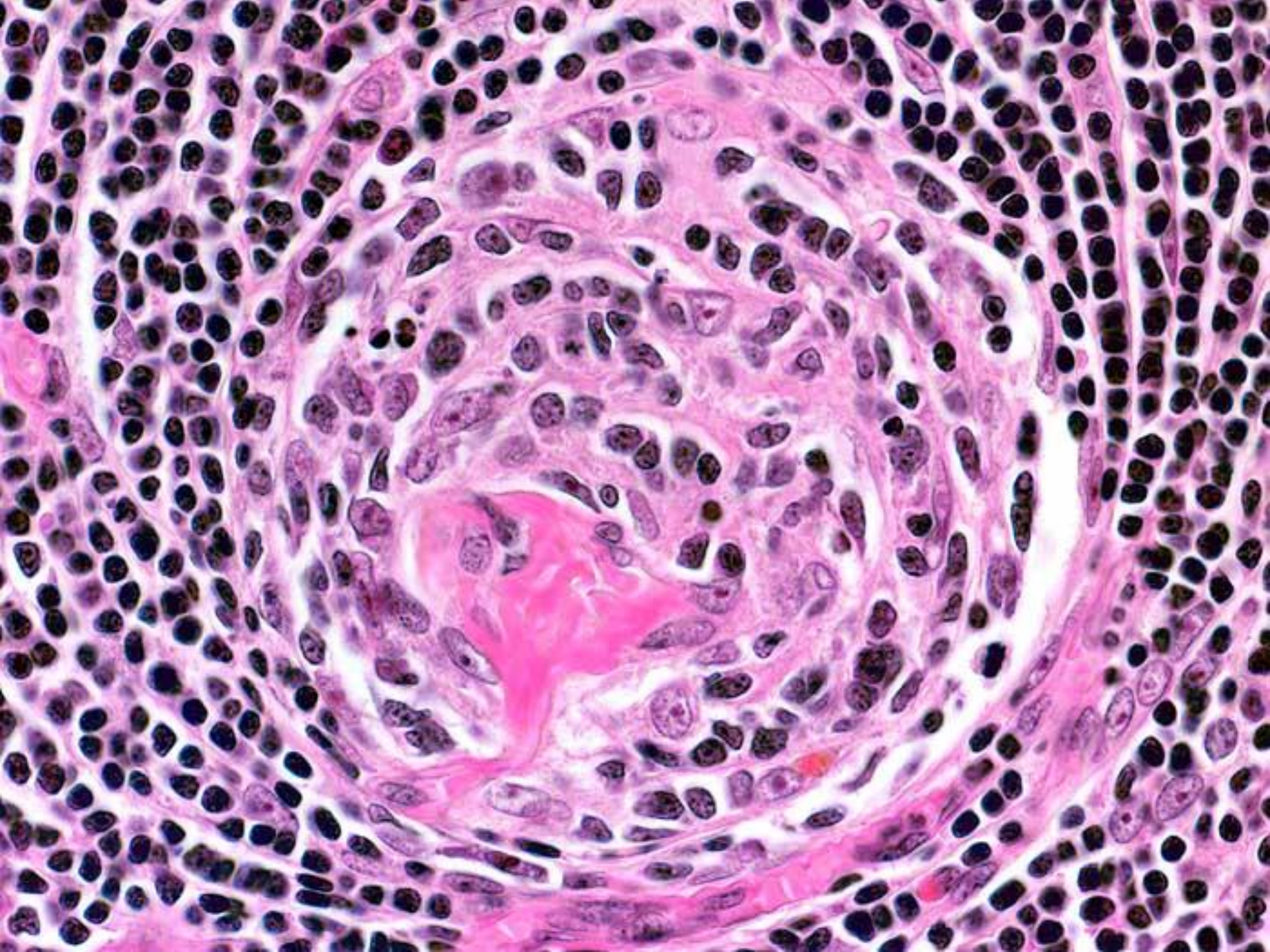
- 29-year-old man with mediastinal lymphadenopathy



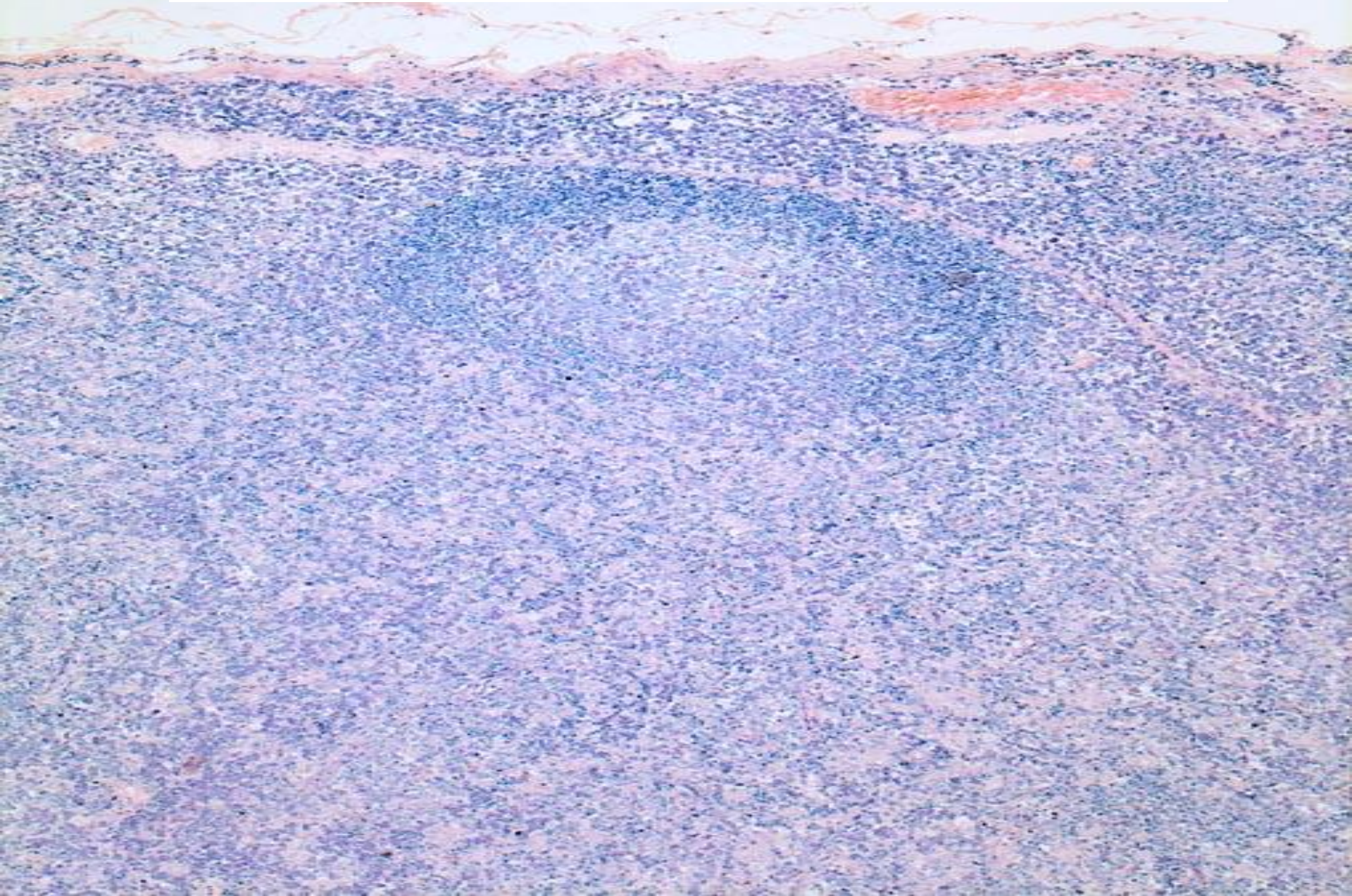


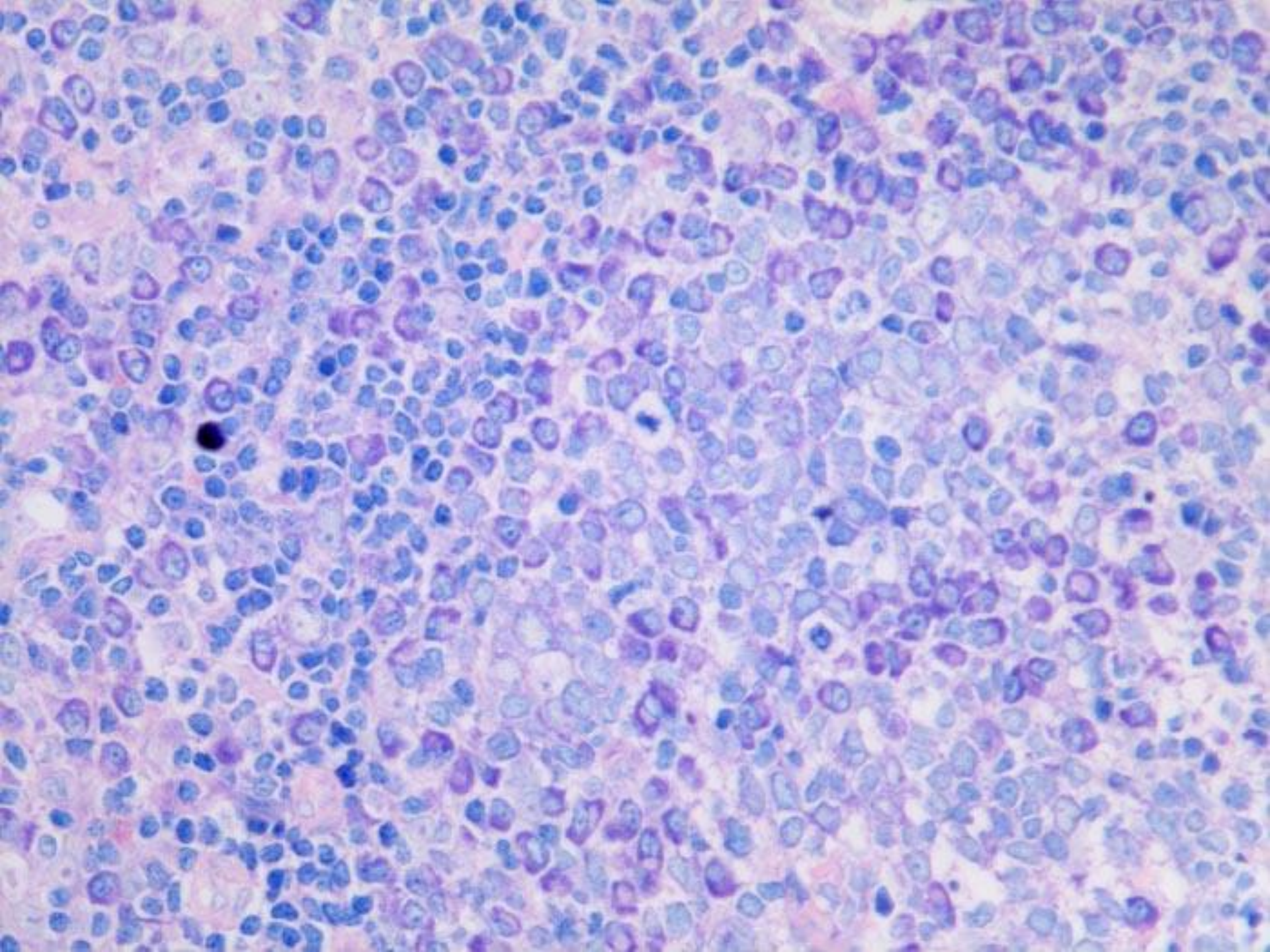






Castleman's Disease, plasma cell type



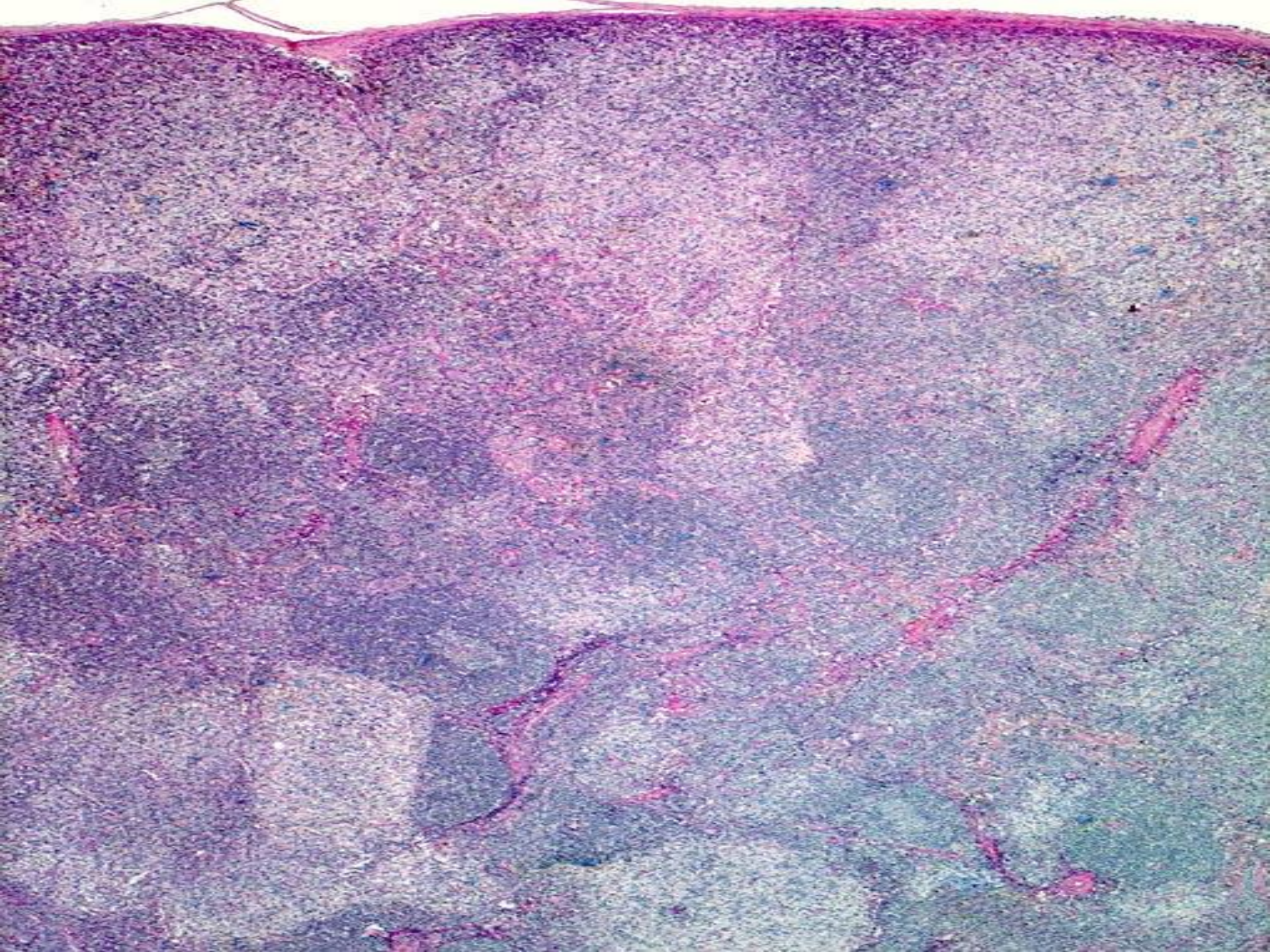


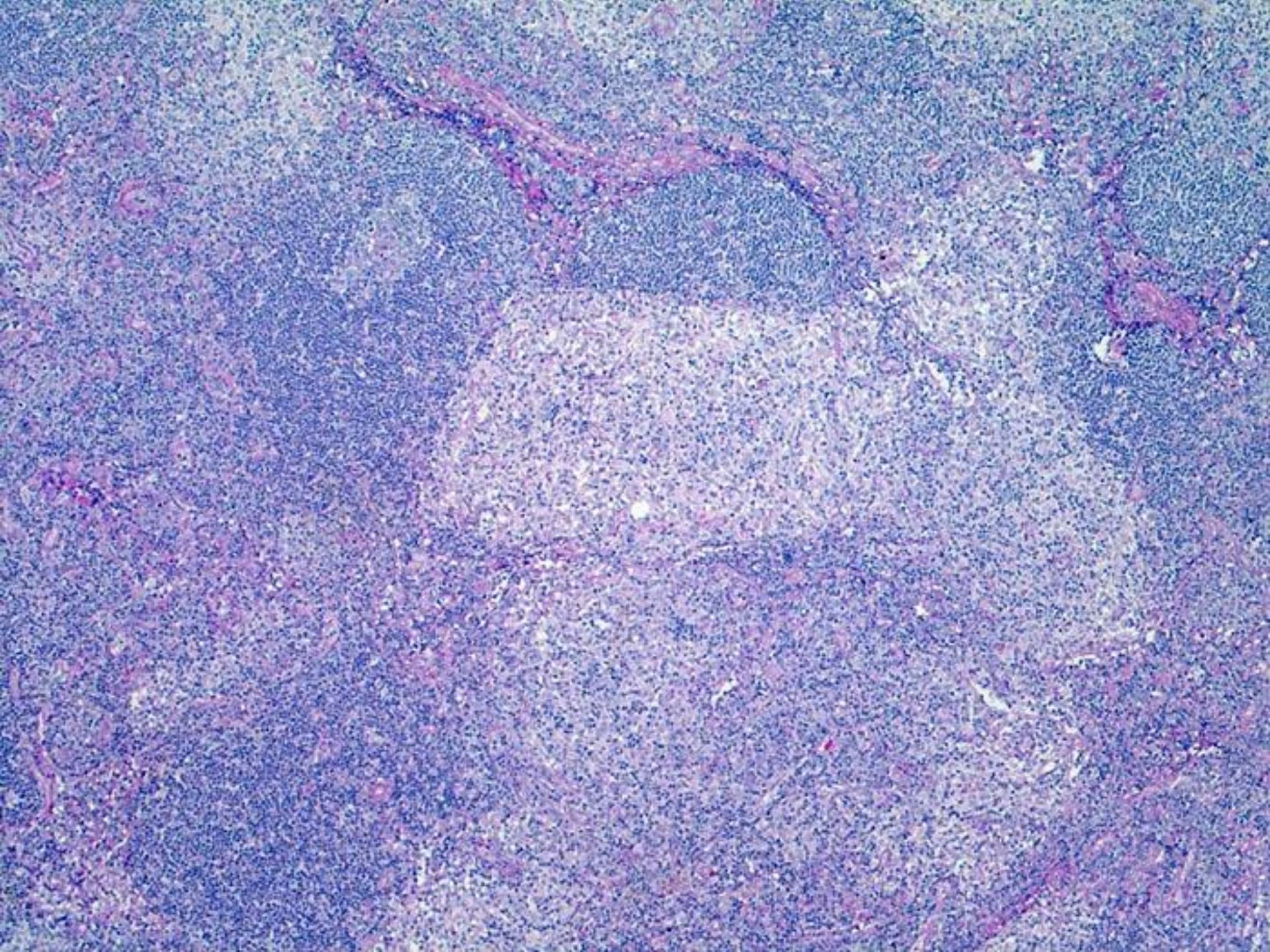
Dermatopathic Lymphadenopathy

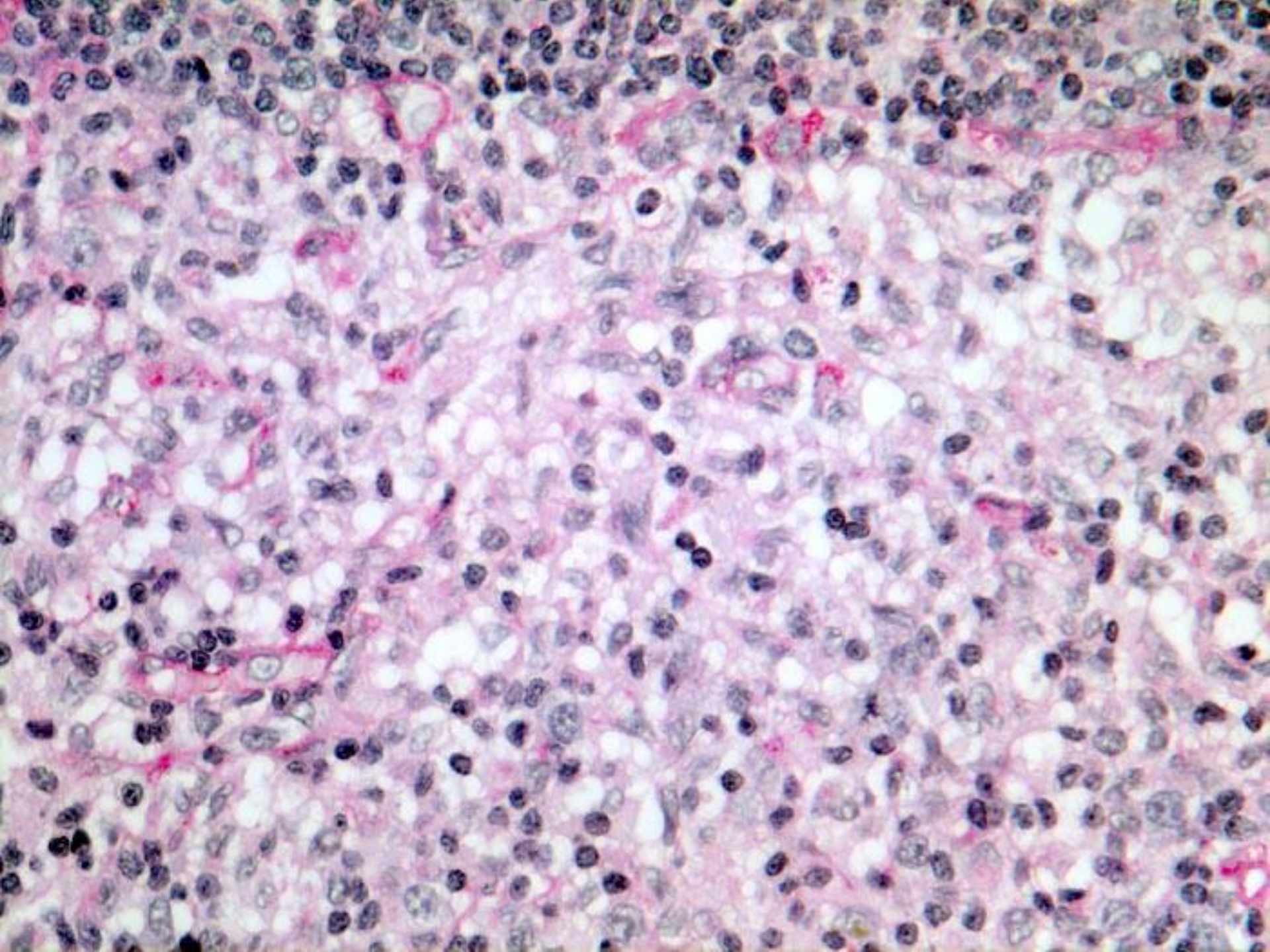
- LNs draining areas of dermatitis, also a/w cutaneous T cell lymphoma
- Pruritis, eosinophilia
- Axillary, inguinal lymphadenopathy
- Architecture preserved; follicular hyperplasia
- Paracortical, palely stained, confluent areas of histiocytes/dendritic cells, Langerhan's cells
- Melanin pigment laden macrophages
- Immuno: CD1a+ (LCs); and S100+ (IDCs and LCs)

Case Illustration

- 45-year-old woman with psoriasis, axillary lymphadenpathy





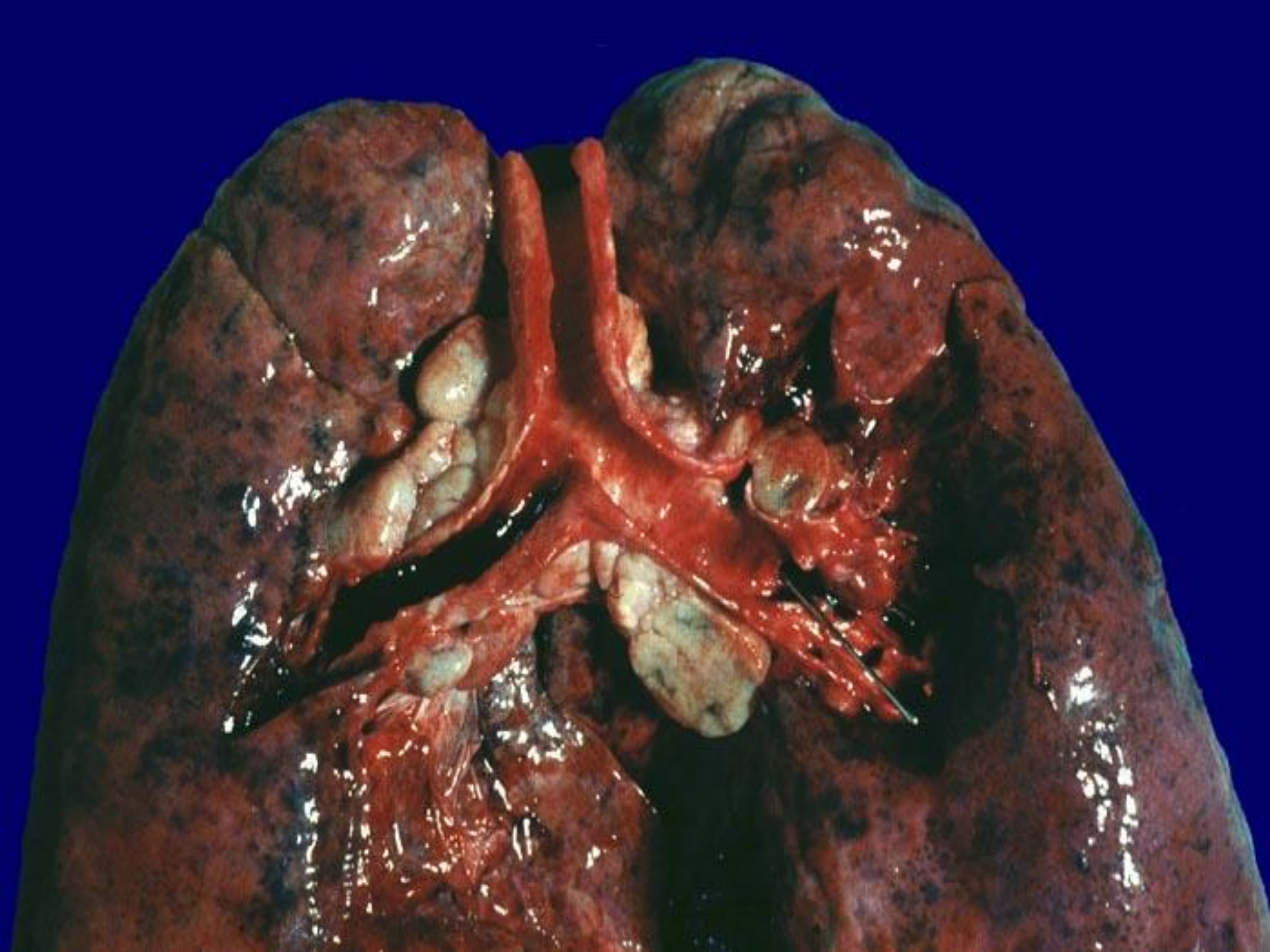


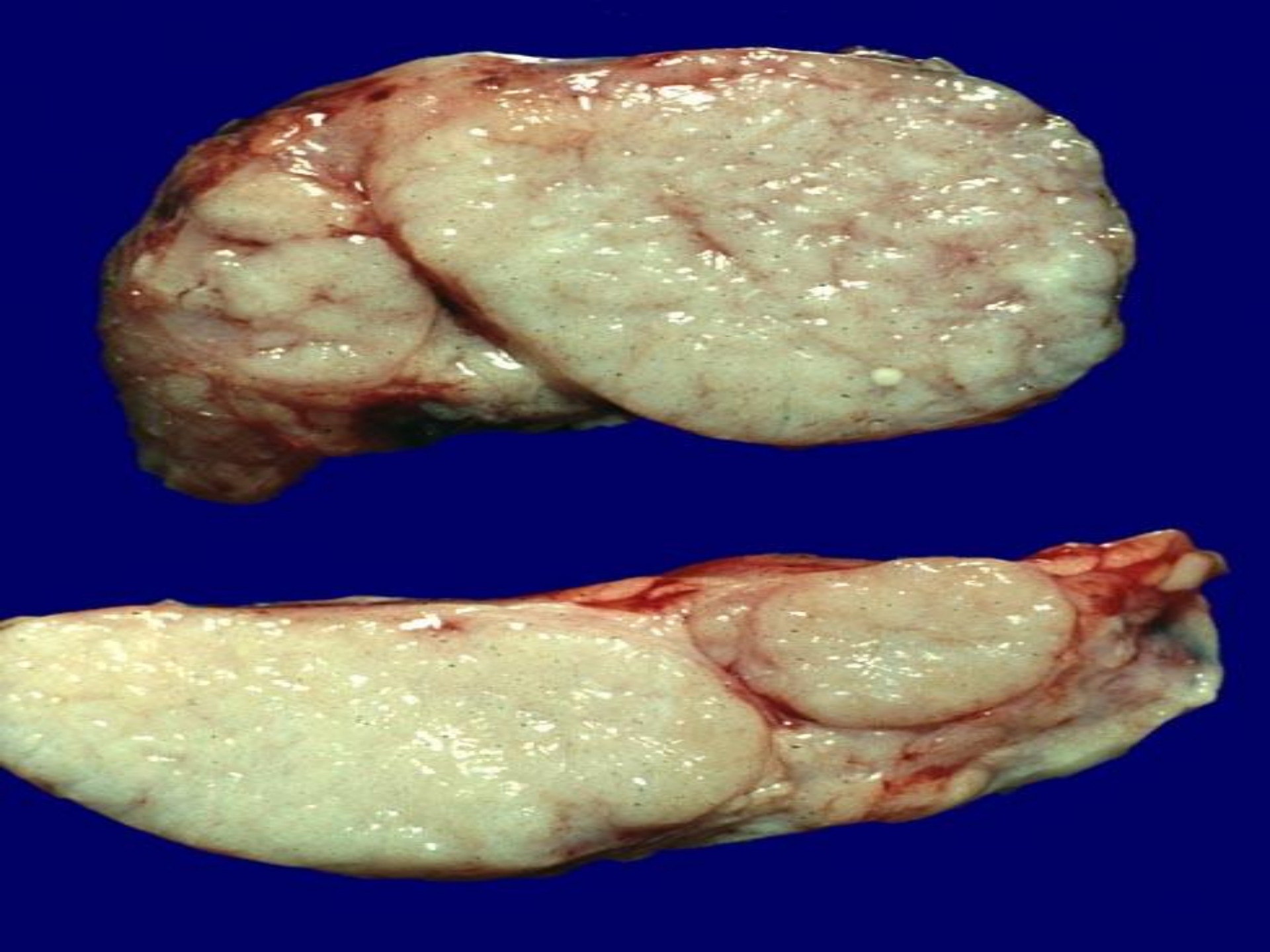
Sarcoidosis Lymphadenopathy

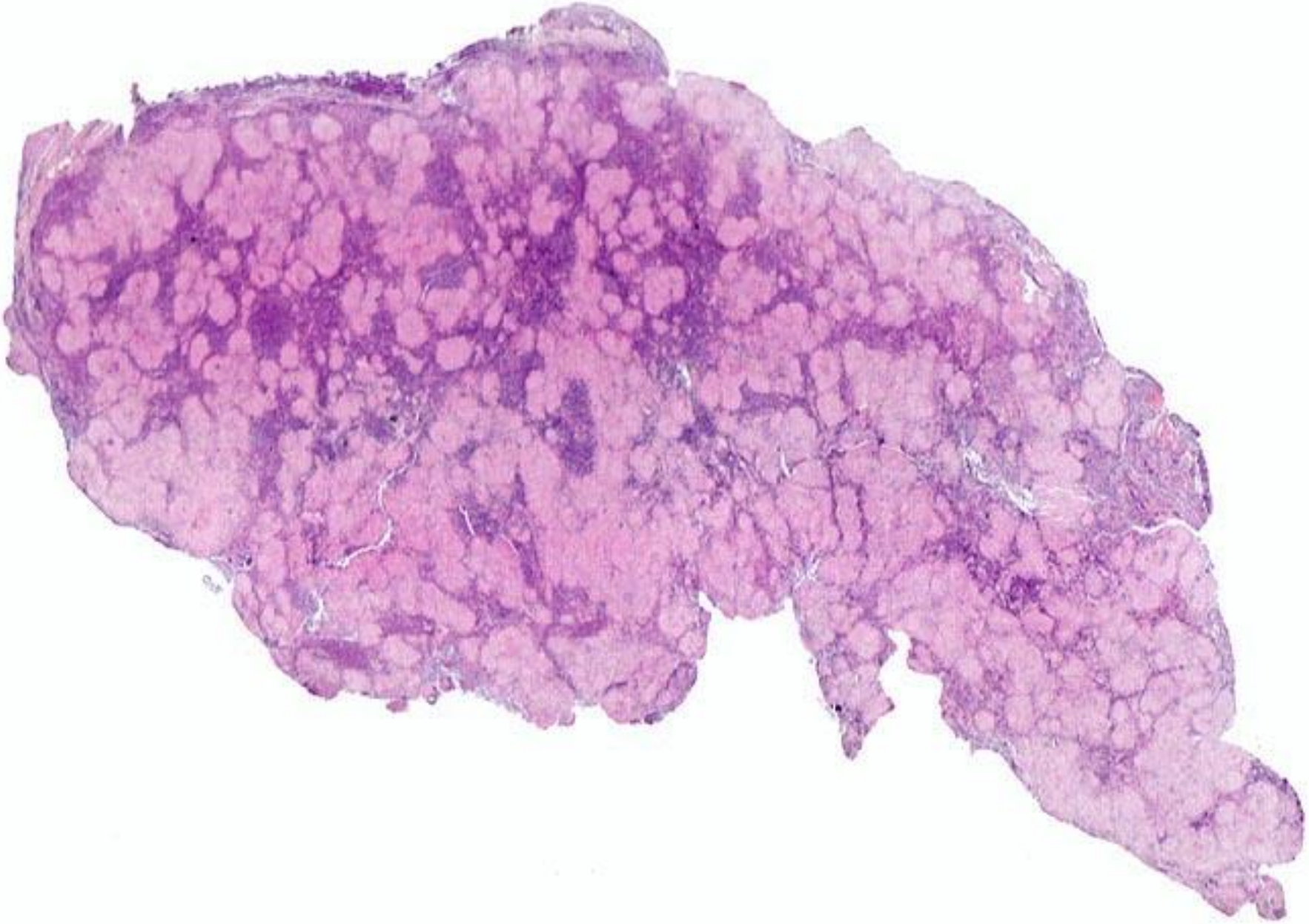
- Adults 20 to 40 years old
- Increased prevalence in blacks (10-fold) and women (twofold)
- Multisystemic (lungs, lymph nodes, skin, eyes, joints); bilateral pulmonary hilar LNs common
- Round, closely apposed granulomas; Langhans' giant cells present; noncaseating necrosis
- Asteroid bodies (stellate inclusions), Schaumann bodies (laminated inclusions)
- Special stains negative for organisms
- Fibrosis late in course

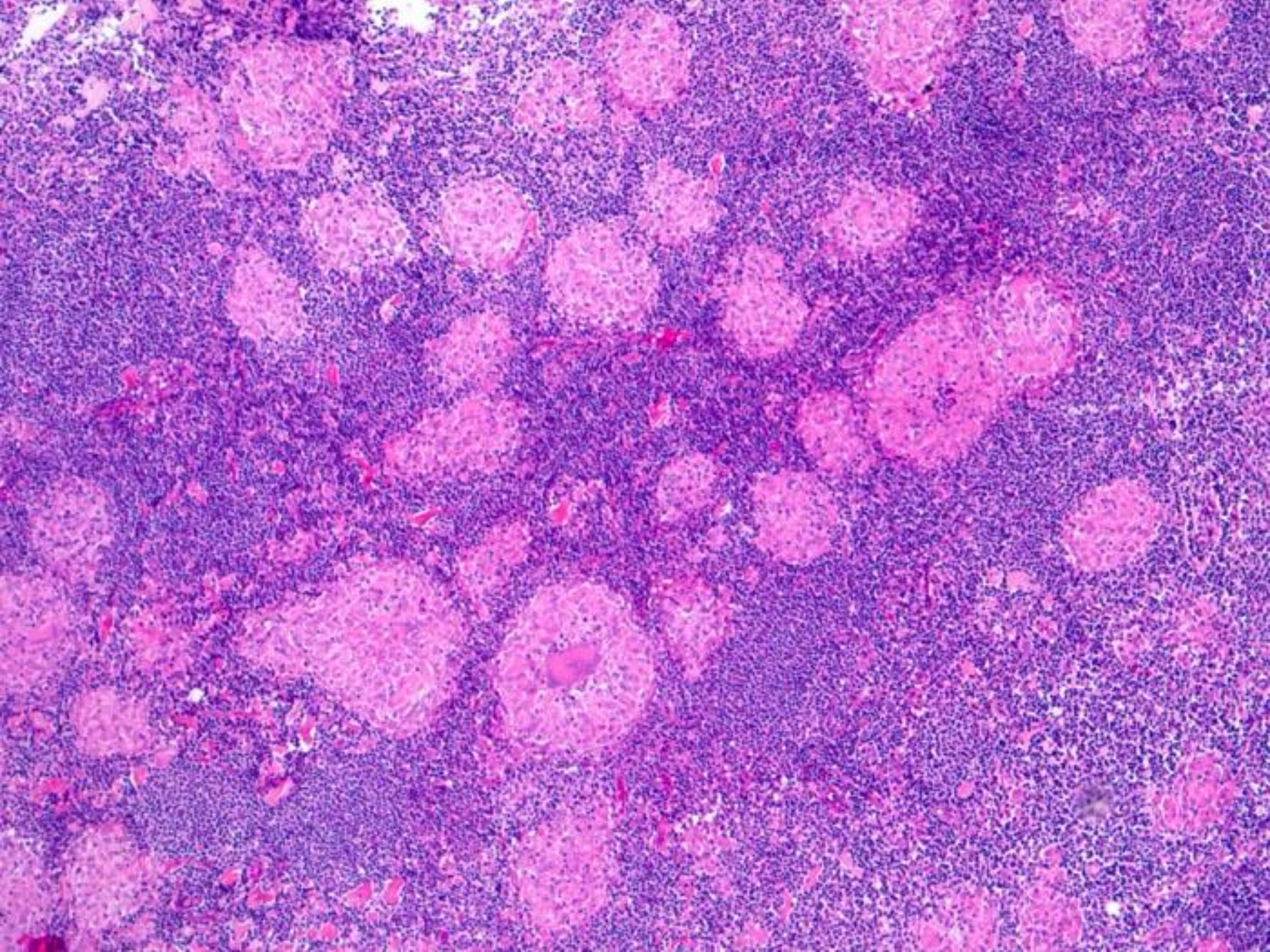
Case Illustration

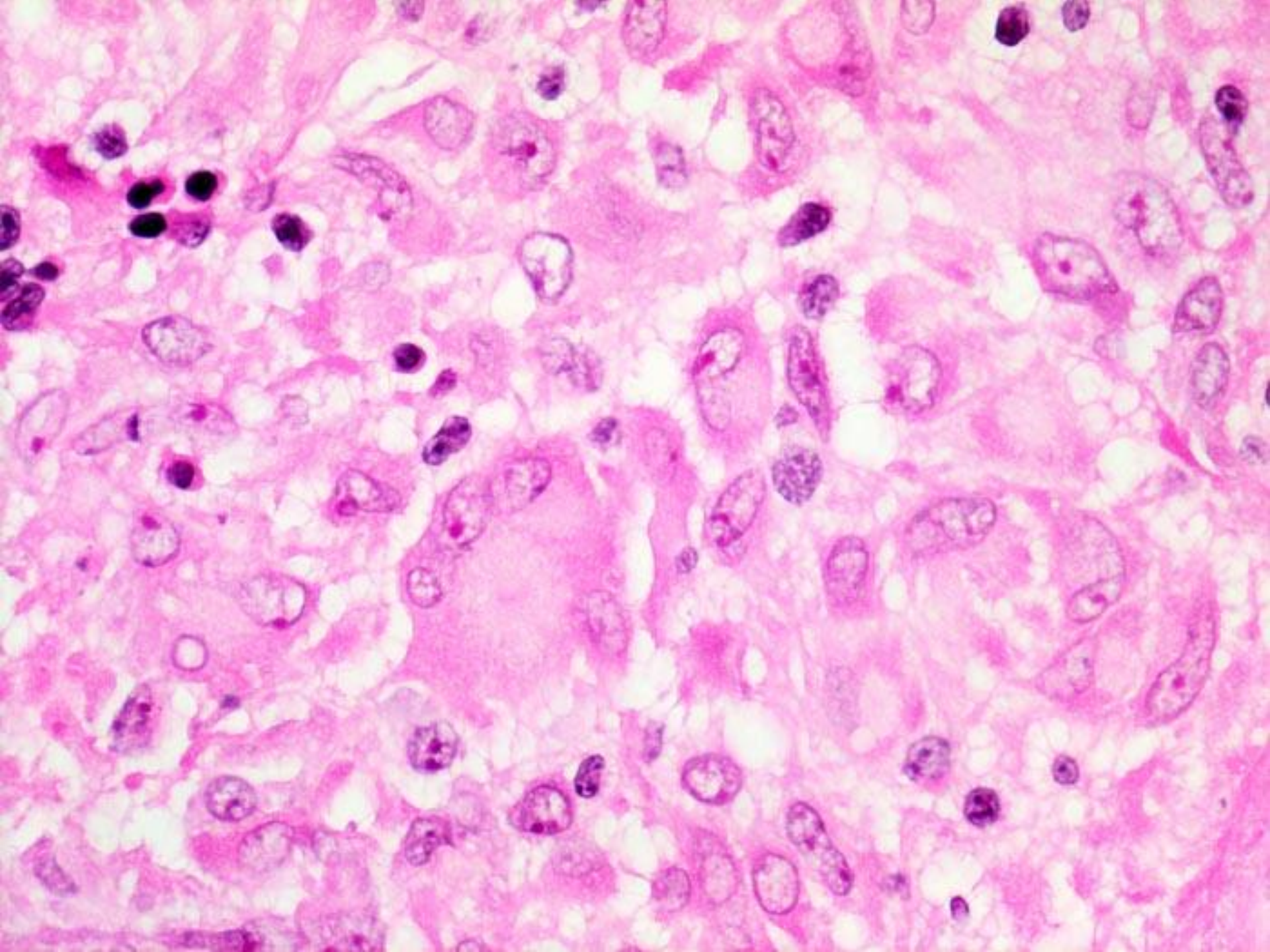
- 36-year-old man with hilar, mediastinal and supraclavicular lymphadenopathy





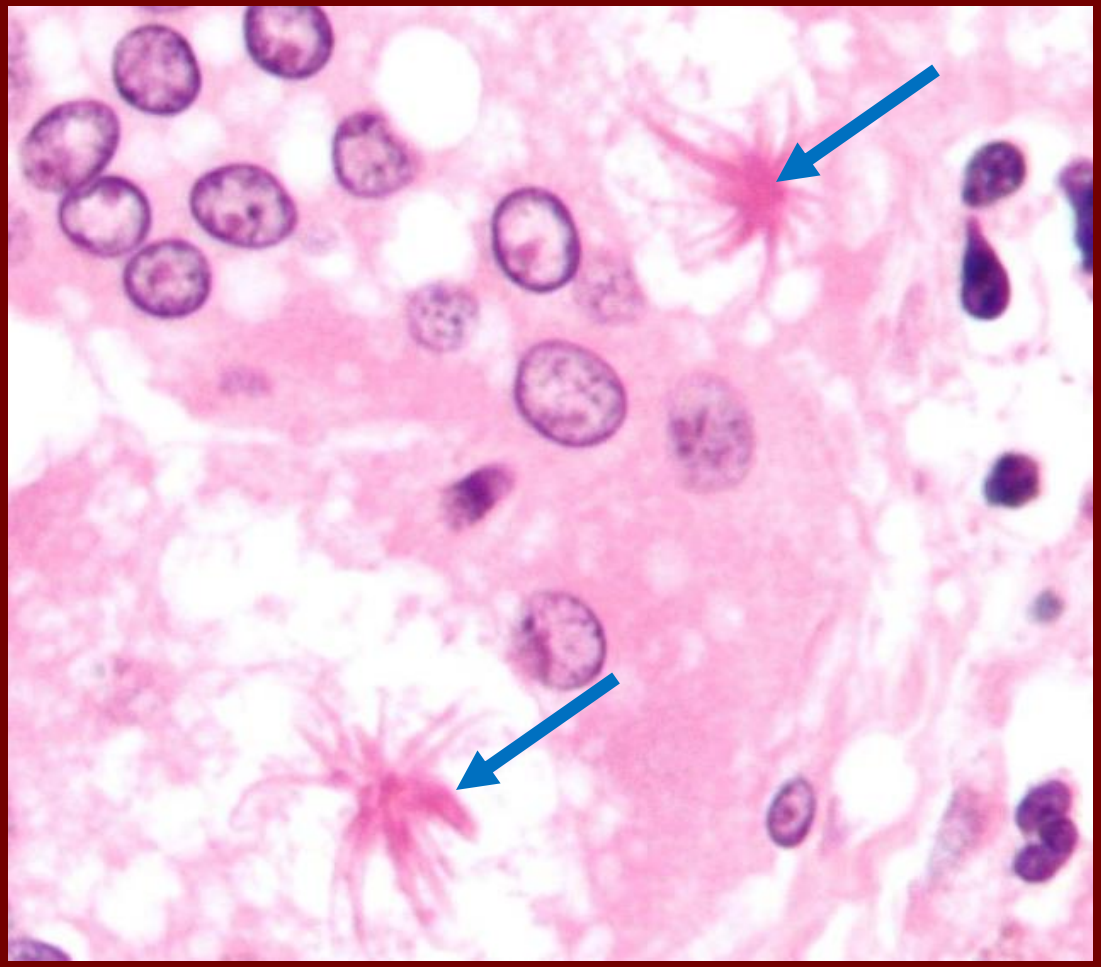






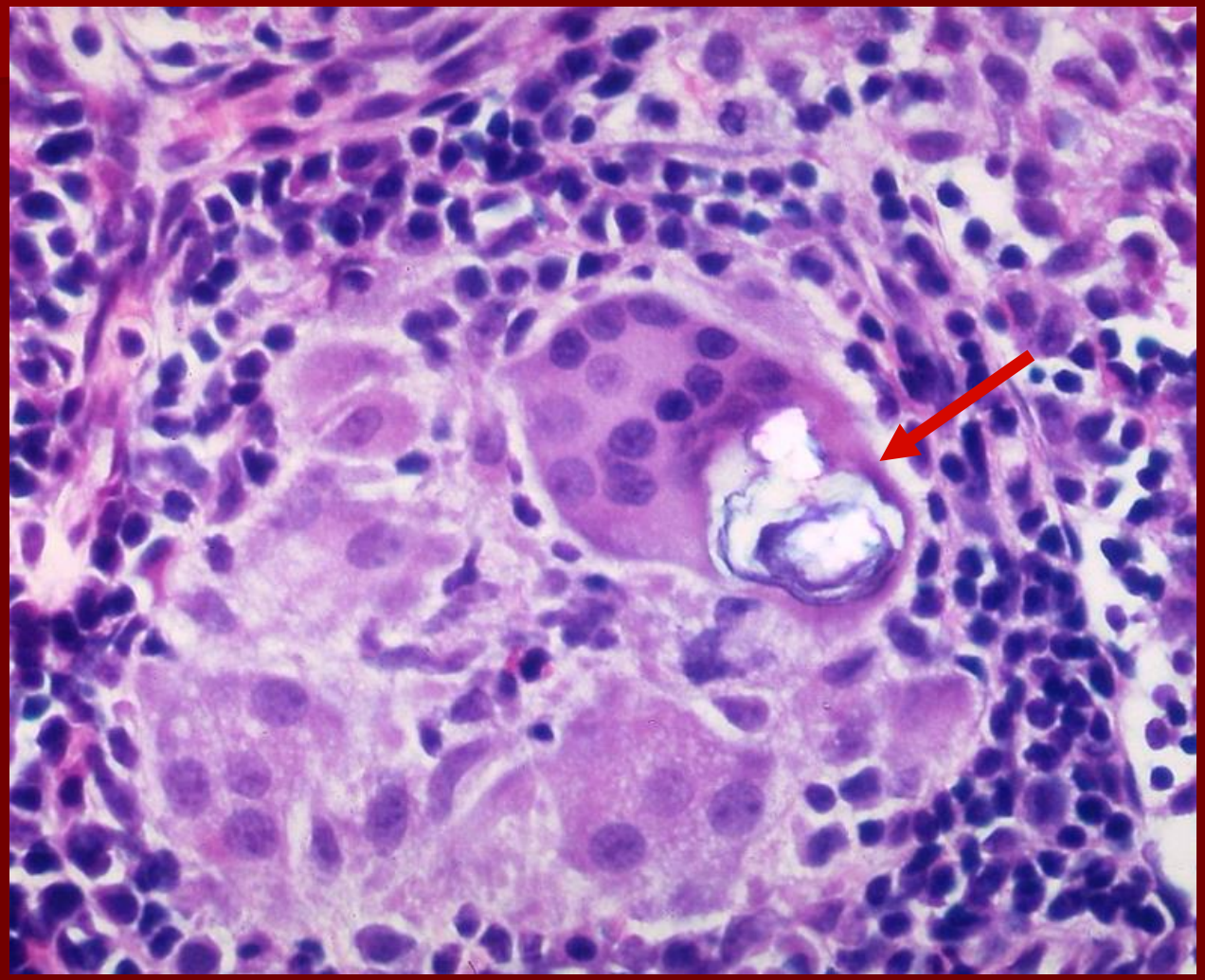
Asteroid body

(Star-like cytoplasmic pattern,
contain calcium, phosphorous, silica, aluminum)



Schaumann body

(Calcium and protein inclusions inside Langhans giant cells)



Drug-induced hypersensitivity lymphadenopathy

- Common meds: ampicilin, dilantin
- Paracortex: expanded (immunoblasts, many eosinophils) and hypervascular
- Follicles: may be involuted or hyperplastic

Postvaccinal lymphadenopathy

- Common cause: smallpox, measle vaccination
- Paracortex: expanded (immunoblasts), mottled or moth-eaten, vascular proliferation
- Follicles: hyperplastic in later phase

Lymph Node Inclusions- Epithelial Cells

- Due to development abnormalities or benign transport
- Upper cervical: salivary gland acini and ducts
- Lower cervical: colloid-containing thyroid follicles
- Axillary: nodules of mammary ducts, cysts and myoepithelial cells
- Mediastinal: glandlike structures of pleural cell origin
- Mesenteric and peritoneal: benign glandular inclusions
- Pelvic: glands lined by salpingeal or ovarian epithelium

Epithelial Inclusions

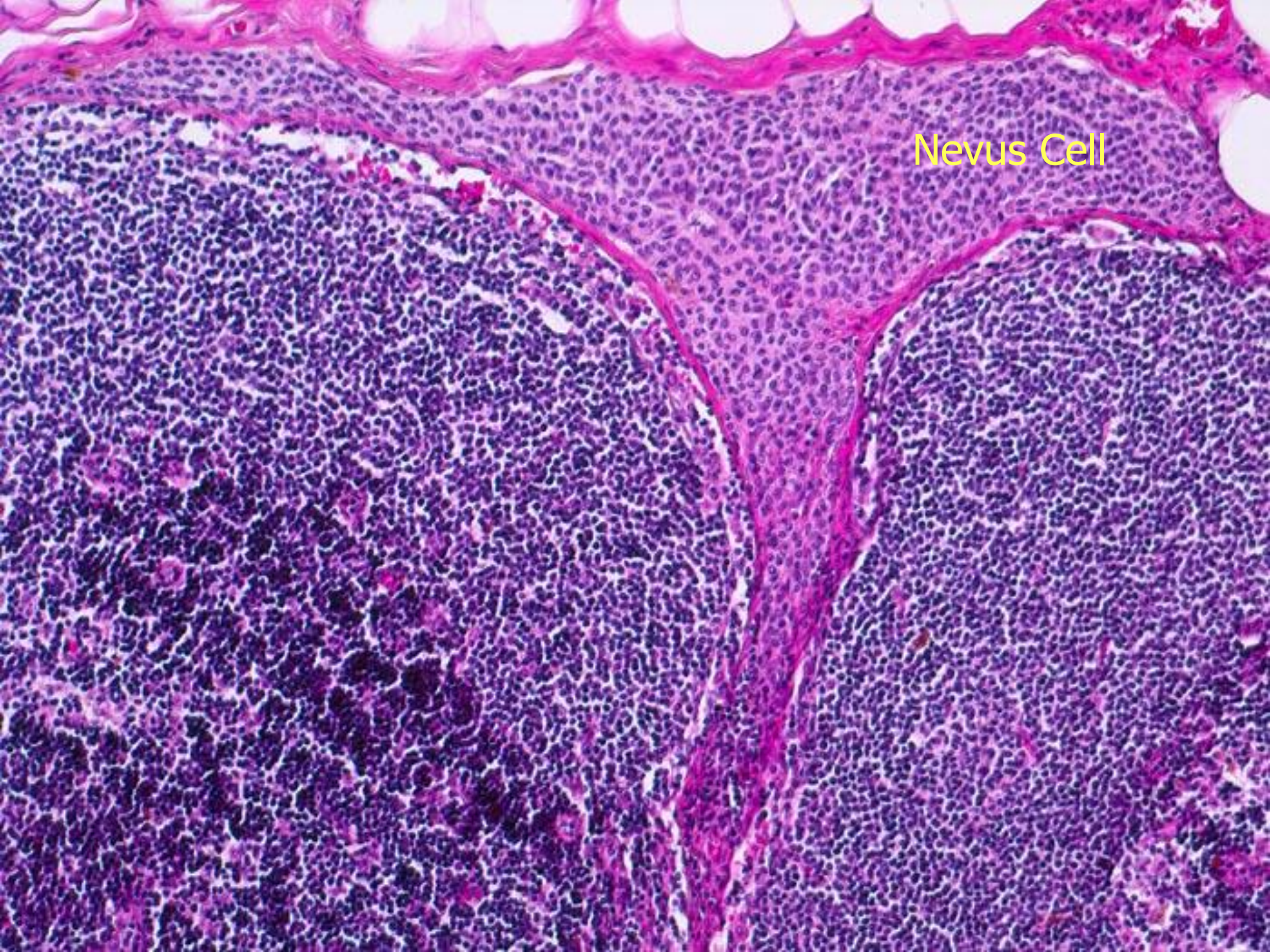
- Aggregates in capsular or cortical sites
- Benign histologic appearance
- Lack of nuclear pleomorphism and mitoses
- Lack of vascular, lymphatic and sinus invasion

Nevus Cell Inclusions in Lymph Nodes

- Aggregates of nevus cells in the lymph node capsule, hilum, or trabeculae
- Marginal sinus not involved; parenchyma very rarely involved
- Monomorphic cell population
- Lack of nuclear pleomorphism and nucleolar prominence
- Absence of mitoses
- Pos for S-100, Neg for keratin (r/o CA met)

Case Illustration

- 45-year-old woman with enlarged axillary lymph node


Nevus Cell