Rad-Path:
HIV/AIDS & the Thorax

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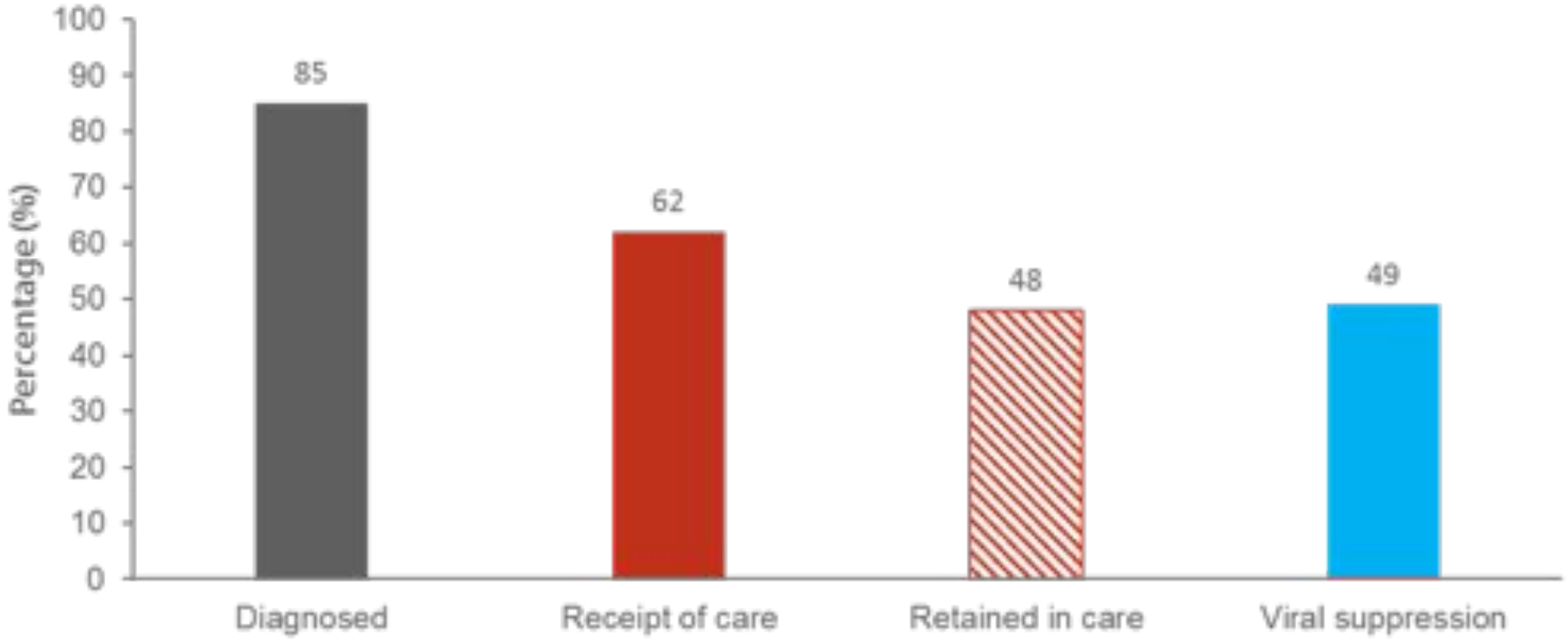
Context

Epidemiology of HIV/AIDS in the U.S.

Persons Living with Diagnosed or Undiagnosed HIV Infection

HIV Care Continuum Outcomes, 2014—United States



Note. Receipt of medical care was defined as ≥1 test (CD4 or VL) in 2014. Retained in continuous medical care was defined as ≥2 tests (CD4 or VL) ≥3 months apart in 2014. Viral suppression was defined as <200 copies/mL on the most recent VL test in 2014.

Pulmonary Disease in the HIV/AIDS Patient

- Pulmonary disease accounts for 30-40% of acute hospitalizations of HIV+ patients
- When approaching a case (CXR or CT) and formulating a differential diagnosis:
  - **First identify and categorize the key imaging findings**
  - **Incorporate clinical data, such as patient demographics, CD4+ lymphocyte count, and presenting symptoms**
  - **Take into account change of thoracic disease and clinical status in response to treatment**

Pulmonary manifestations of HIV/AIDS can now be considered to have two types of presentation

In underserved populations, the manifestations are much as they were in the 1980s: opportunistic infections & AIDS-related neoplasms

Box 6.1 HIV-associated respiratory disorders*

Infection

- Bacterial (pyogenic) pneumonia
  - *Streptococcus pneumoniae*
  - *Haemophilus influenzae*
  - *Pseudomonas aeruginosa*
  - *Staphylococcus aureus*
  - *Moraxella catarrhalis*
  - *Rhodococcus equi*
- Mycobacteria
  - *Mycobacterium tuberculosis*
  - *Mycobacterium kansasii*
  - *Mycobacterium avium* complex (MAC)
  - Other non-tuberculous mycobacteria
- Fungal infection
  - *P. jirovecii*
  - *Cryptococcus neoformans*
  - *Histoplasma capsulatum*
  - *Aspergillus fumigatus*
  - *Coccidioides immitis*
  - *Blastomyces dermatitides*
- Protozoal
  - *Strongyloides stercoralis*
  - *Toxoplasma gondii*
- Viral infection
  - Cytomegalovirus (CMV)
  - Adenovirus
  - Herpes simplex virus

Malignancy

- Kaposi sarcoma
- Non-Hodgkin lymphoma, including primary effusion lymphoma
- Lung cancer

Other disorders

- Sinusitis
- Bronchitis
- Bronchiectasis
- Emphysema
- Lymphoid interstitial pneumonia
- Nonspecific interstitial pneumonia
- Cryptogenic organizing pneumonia
- Pulmonary hypertension
- Immune reconstitution inflammatory syndrome (IRIS)

Box 6.2 HIV/AIDS in the highly effective ART era[9]

Less common

- Opportunistic infection, especially *P. jirovecii*, tuberculosis
- Kaposi sarcoma

Similar incidence

- Non-Hodgkin lymphoma

More common

- Non-AIDS-defining cancers (e.g. lung cancer)
- Immune reconstitution inflammatory syndrome (IRIS)
- Pulmonary hypertension
- Emphysema
- ART-related respiratory disease
  - Nucleoside-induced lactic acidosis
  - Increased incidence of bacterial pneumonia (enfuvirtide)
  - Hypersensitivity reactions (abacavir)

In populations with access to ART, the pulmonary manifestations of HIV/AIDS have changed

From: Hansell, D., et al. (2010). The immunocompromised patient. In *Imaging of diseases of the chest*. 5th ed. Edinburgh: Mosby/Elsevier.

Pulmonary Complications of HIV/AIDS Related to CD4+ Lymphocyte Count

- CD4+ > 500 cells/µL
  - Sinusitis/pharyngitis
  - Bronchitis
  - Lung cancer
- CD4+ < 400 cells/µL
  - Bacterial (pyogenic) pneumonia
  - Pulmonary TB
  - Cardiomyopathy
- CD4+ < 200 cells/µL
  - *P. jiroveci* pneumonia
  - Kaposi sarcoma
  - Bacterial sepsis
  - Disseminated TB
- CD4+ < 100 cells/µL
  - Disseminated MAC
  - CMV
  - Disseminated fungal infection
  - Non-Hodgkin lymphoma

From: Hansell, D., et al. (2010). The immunocompromised patient. In *Imaging of diseases of the chest*. 5th ed. Edinburgh: Mosby/Elsevier.

Radiologic Patterns of Pulmonary Diseases in Patients with HIV/AIDS

Box 6.8 Radiographic patterns in patients with HIV/AIDS*

Focal opacities
- Bacteria
- Tuberculosis (high CD4+ count)
- PCP (low CD4+ count)
- Fungi

Diffuse opacities
- PCP (low CD4+ count)
- Tuberculosis (low CD4+ count)
- Kaposi sarcoma
- Bacteria
- Fungi
- CMV

Multiple nodules
- Kaposi sarcoma ("flame-shaped")
- Tuberculosis (miliary)
- Fungi
- Septic emboli
- Non-Hodgkin lymphoma
- Lung cancer
- LIP (children)

Cavities
- Tuberculosis (high CD4+ count)
- PCP (low CD4+ count)
- *Pseudomonas* pneumonia (low CD4+ count)
- Septic emboli
- Lung cancer
- Fungi
- *R. equi*

Pneumothorax
- PCP

Mediastinal lymphadenopathy
- Tuberculosis
- MAC
- Kaposi sarcoma
- Non-Hodgkin lymphoma
- Lung cancer
- Fungi

Pleural effusion
- Bacteria
- Tuberculosis
- Kaposi sarcoma
- Non-Hodgkin lymphoma
- Lung cancer
- Cardiomyopathy

From: Hansell, D., et al. (2010). The immunocompromised patient. In *Imaging of diseases of the chest*. 5th ed. Edinburgh: Mosby/Elsevier.

Differential Diagnosis of Pulmonary Findings in HIV/AIDS Patients

TABLE 1: Differential Diagnosis of Pulmonary Findings in Patients With HIV Infection

Pulmonary Consolidation	Ground-Glass Opacity	Cystic Lesions	Peribronchovascular Opacities
Infection	Infection	PCP (CD4 < 200 cells/mm^3)	Neoplastic
Bacterial	Viral	Lymphocytic interstitial pneumonia	Kaposi sarcoma (CD4 < 200 cells/mm^3)
CD4 < 200 cells/mm^3	Atypical bacterial		Lymphoma
Mycobacterial	CD4< 200 cells/mm^3		Lymphangitic carcinomatosis
Fungal	PCP		
	CD4 < 100 cells/mm^3		Lymphocytic interstitial pneumonia
Neoplastic	Cytomegalovirus		Sarcoidosis
Lymphoma			
Lung cancer	Interstitial lung disease		
	Lymphocytic interstitial pneumonia		
	Nonspecific interstitial pneumonia		

Note—PCP = *Pneumocystis jiroveci* pneumonia.

From Lichtenberger JP 3rd, et al. (2012). AJR Am J Roentgenol.

Differential Diagnosis for Pulmonary Nodules in HIV/AIDS Patients

TABLE 2: Differential Diagnosis for Pulmonary Nodules in Patients With HIV Infection

Micronodules (< 1 cm)	Macronodules (> 1 cm)	Cavitary Lesions
Centrilobular/tree-in-bud distribution	Neoplastic	Infectious
Infectious	Lymphoma	Bacterial pneumonia or abscess
Bacterial	Lung cancer	Mycobacterial
Viral	Metastatic disease	Fungal
		Septic emboli
CD4 counts < 200 cells/mm^3	Infectious	
Mycobacterial	Mycobacterial	Noninfectious
Fungal	Fungal	Necrotic carcinoma
		Lymphoma
Noninfectious	Septic emboli	
Lymphocytic interstitial pneumonia (centrilobular nodules only)		
Perilymphatic distribution		
Sarcoidosis		
Lymphocytic interstitial pneumonia		
Lymphangitic carcinomatosis		
Miliary distribution		
Infectious		
Tuberculosis		
Nontuberculous mycobacterial		
Fungal		
Toxoplasmosis		
Noninfectious		
Metastatic disease		

From Lichtenberger JP 3rd, et al. (2012). AJR Am J Roentgenol.

Differential Diagnosis of Extrapulmonary Diseases in HIV/AIDS Patient

TABLE 1: Differential Diagnosis of Extrapulmonary Diseases in the Patient With HIV

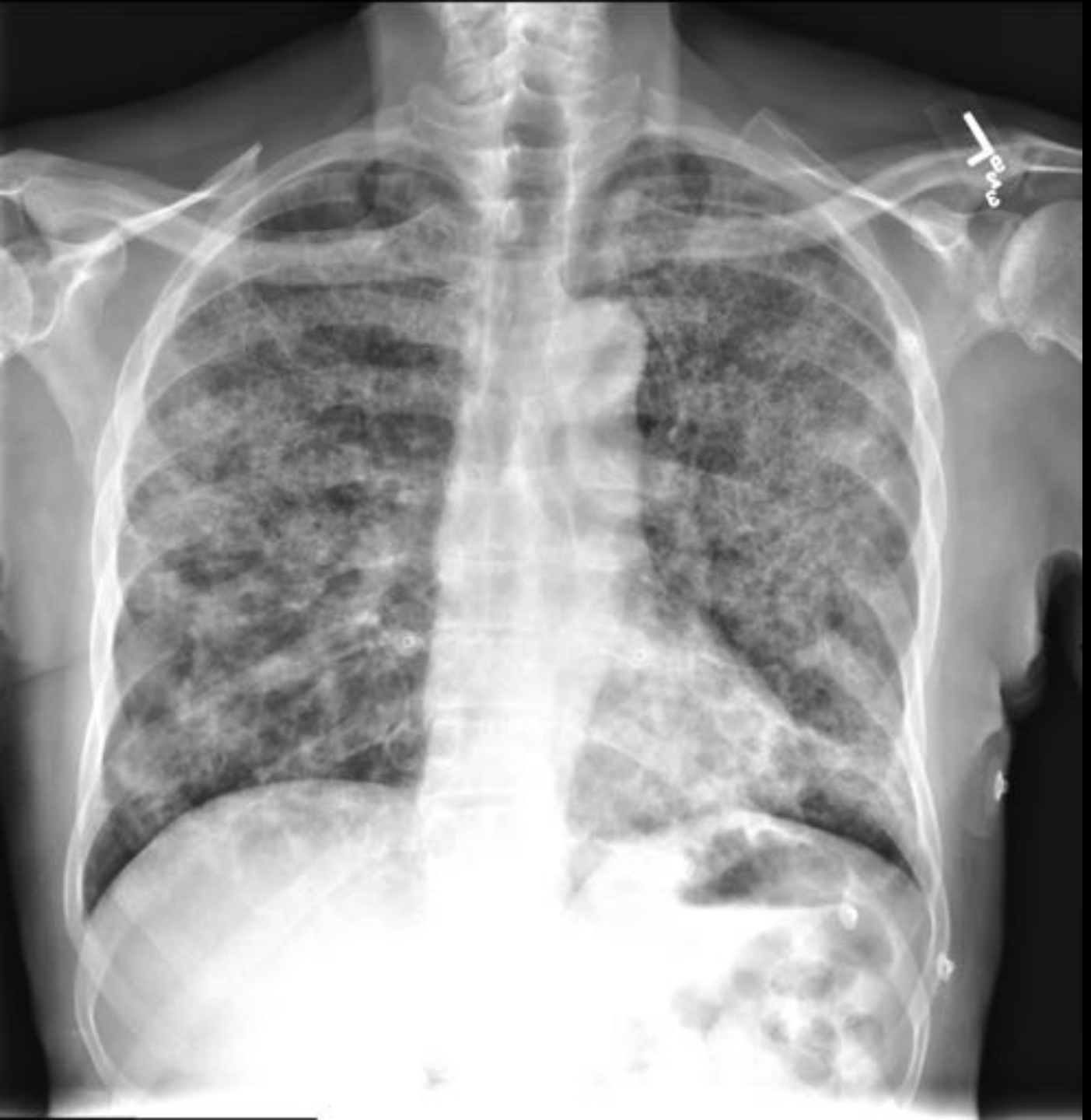
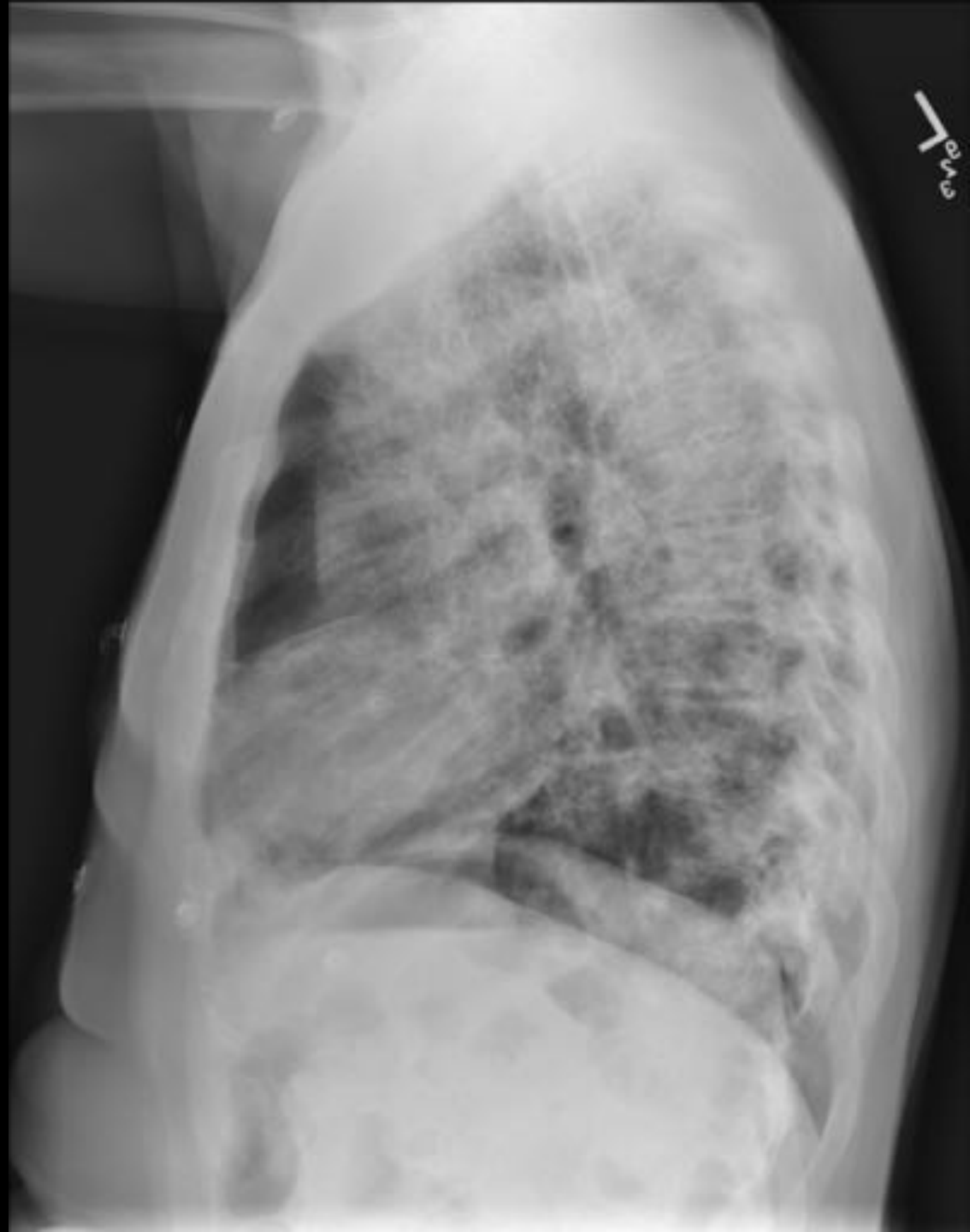
Lymphadenopathy	Cardiovascular and Pericardial Disease
Low-attenuation center	Pericardial effusion
Mycobacterial infection (greatest risk when CD4 count is < 50 cells/mm^3)	Infectious
Fungal infection	Mycobacterial
	Bacterial
Enhancing	Viral
Multicentric Castleman disease (CD4 counts < 350 cells/mm^3)	Fungal
Kaposi sarcoma	Malignant pericardial involvement
Bacillary angiomatosis	Lymphoma
	Kaposi sarcoma
Homogeneous soft-tissue density	Lung carcinoma
Infection	Heart failure
Lymphoma	Infectious myocarditis
Sarcoidosis	HIV-associated cardiomyopathy (CD4 count less than 400 cells/mm^3)
	Ischemic cardiomyopathy
	Cardiac tumor
	Lymphoma
	Kaposi sarcoma
	Pulmonary hypertension (PH)
	HIV-associated PAH
	Chronic pulmonary thromboembolism
	Chronic pulmonary diseases

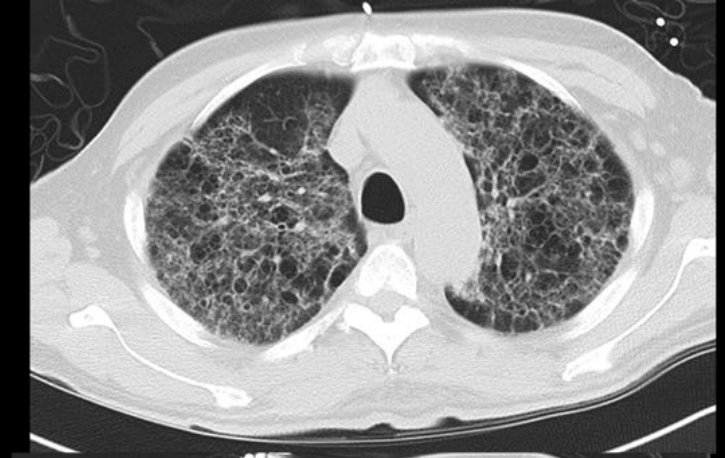
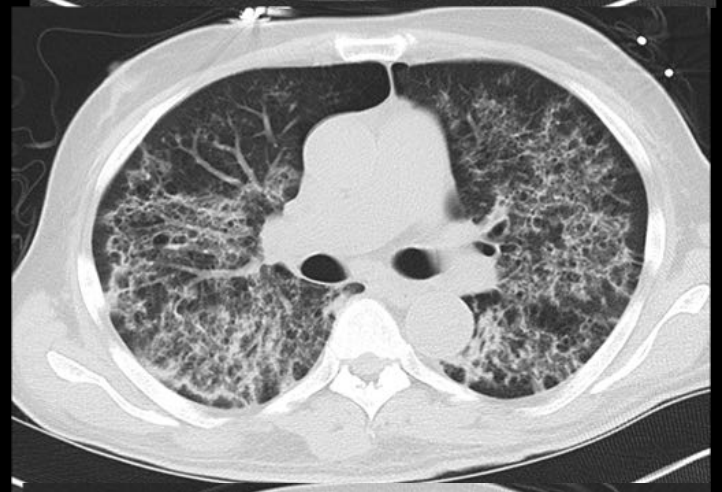
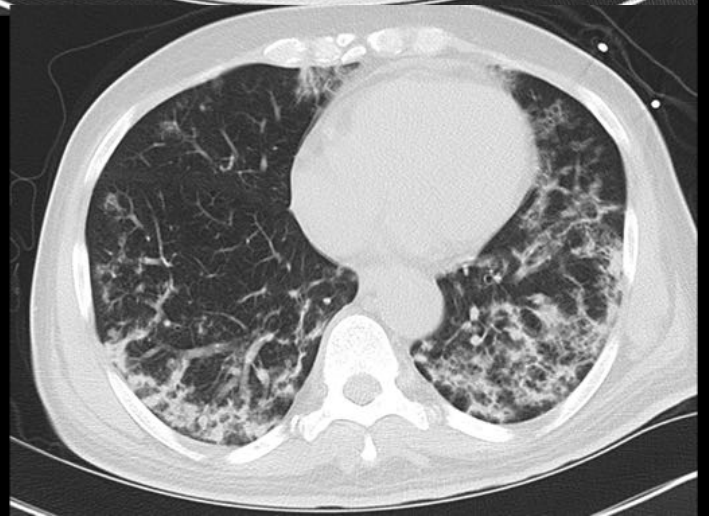
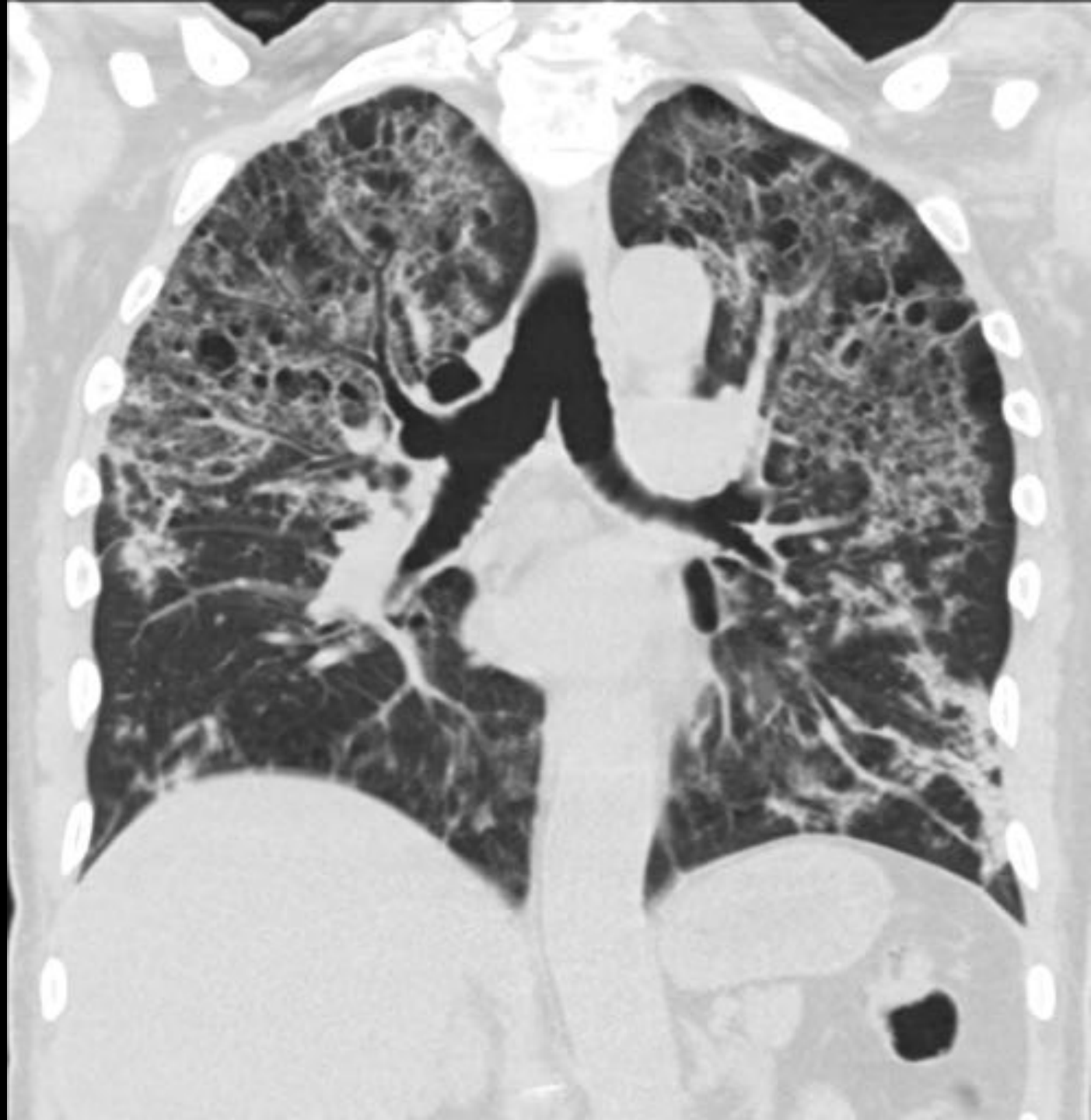
From Lichtenberger JP 3rd, et al. (2012). AJR Am J Roentgenol.

Case 1

- 61-year-old male with HIV/AIDS (diagnosed 2/2009; on ART; CD4 126, VL 15,132), who presents with dry cough, pleuritic chest pain, shortness of breath, and worsening dyspnea with exertion for 5 days.

Case 1 – Radiology

Case 1 – Findings

CXR

Widespread interstitial abnormality, prominent in the upper and mid-lungs

CT

Widespread interstitial abnormality, upper- and mid-lung predominant with small cystic spaces

At the bases, more nodular opacities with some consolidation

Case 1 – Differential

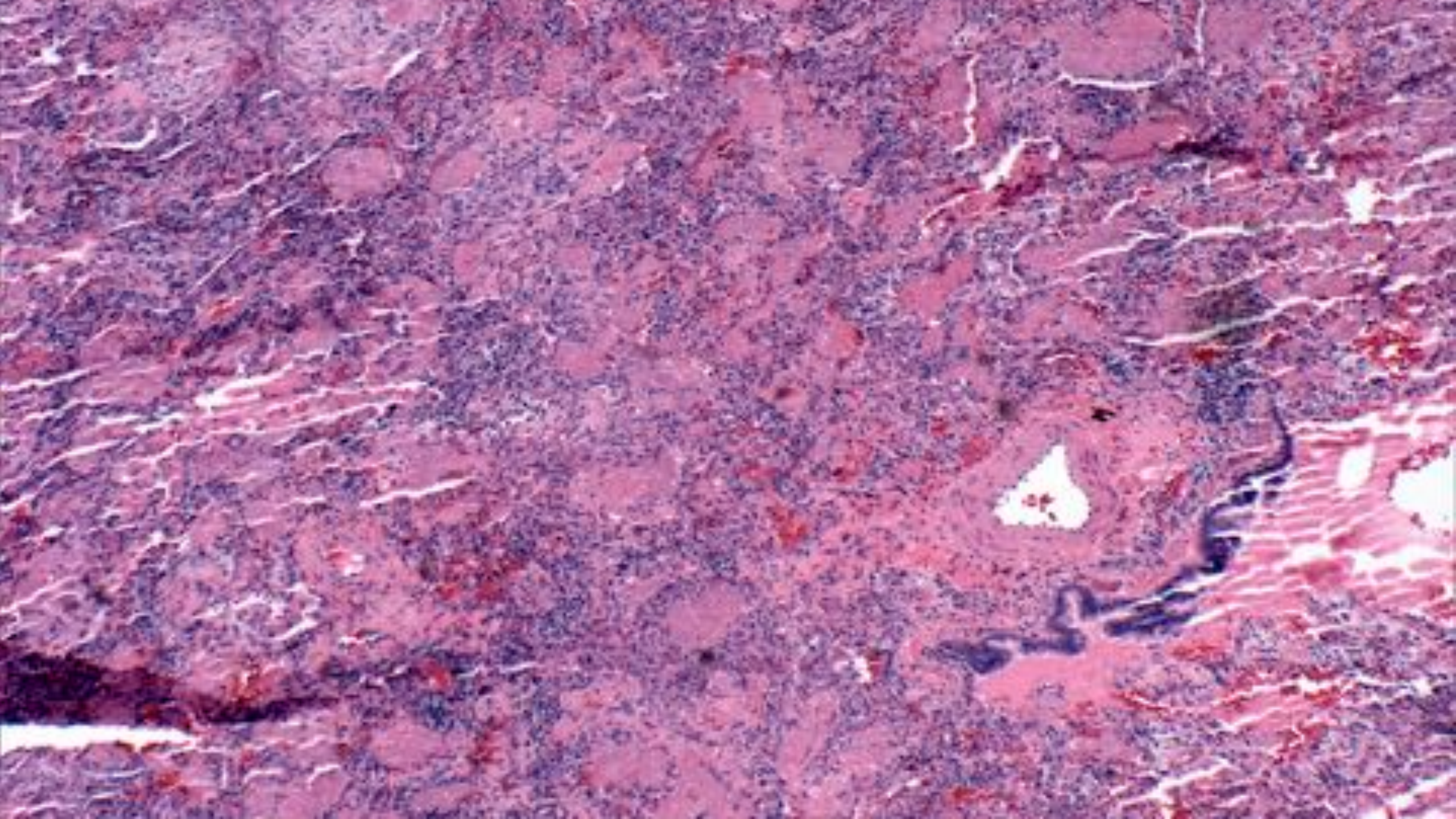
Case 1 – Differential

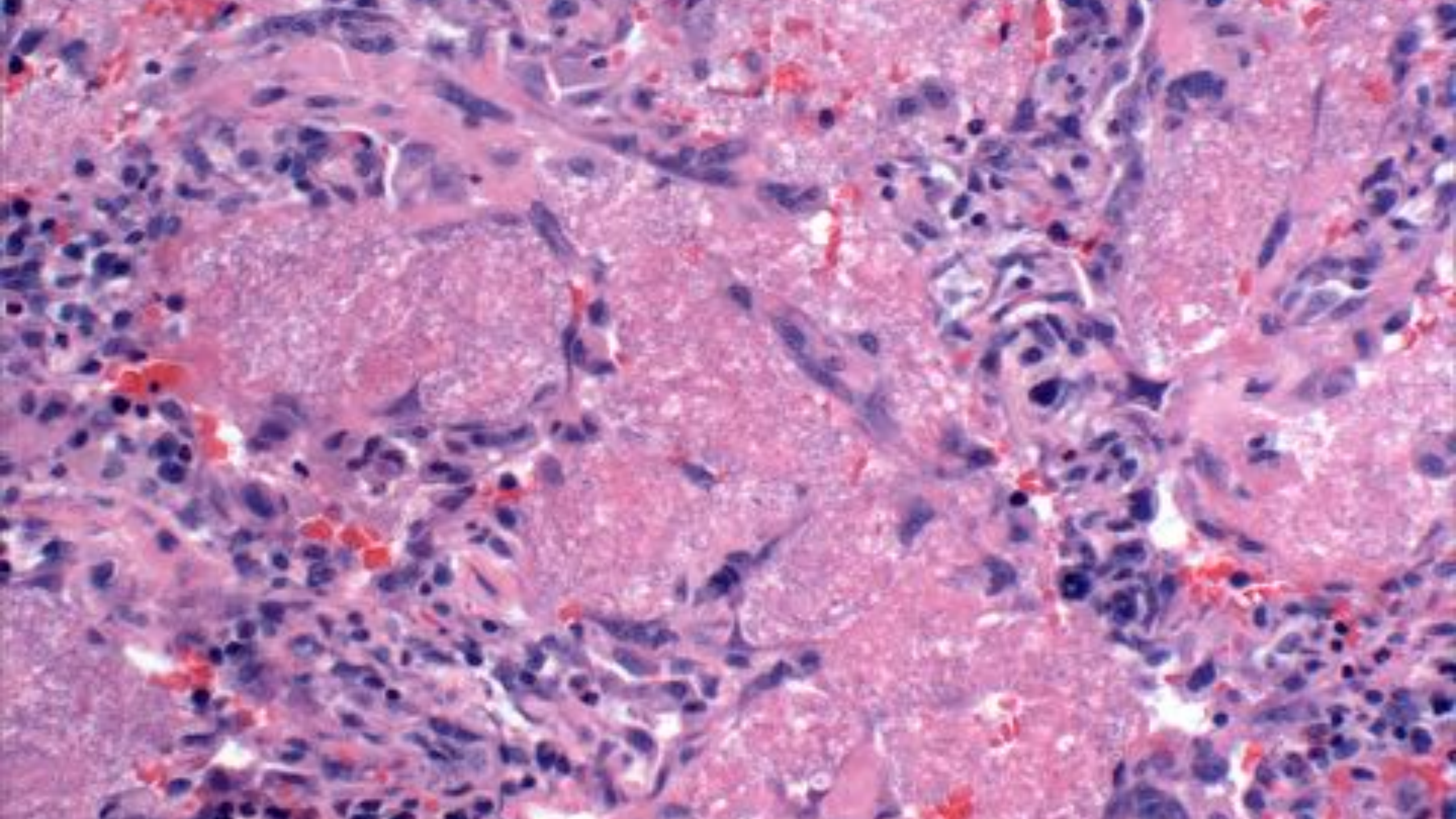
- *Pneumocystis jiroveci* pneumonia
- Viral pneumonia – not typically associated with cystic change
- Diffuse alveolar hemorrhage – not typically associated with cystic change
- Desquamative interstitial pneumonia (DIP) – predominately lower lobe groundglass opacities and cystic change
- Lymphoid interstitial pneumonia (LIP) – usually scattered cystic change and patchy groundglass opacities

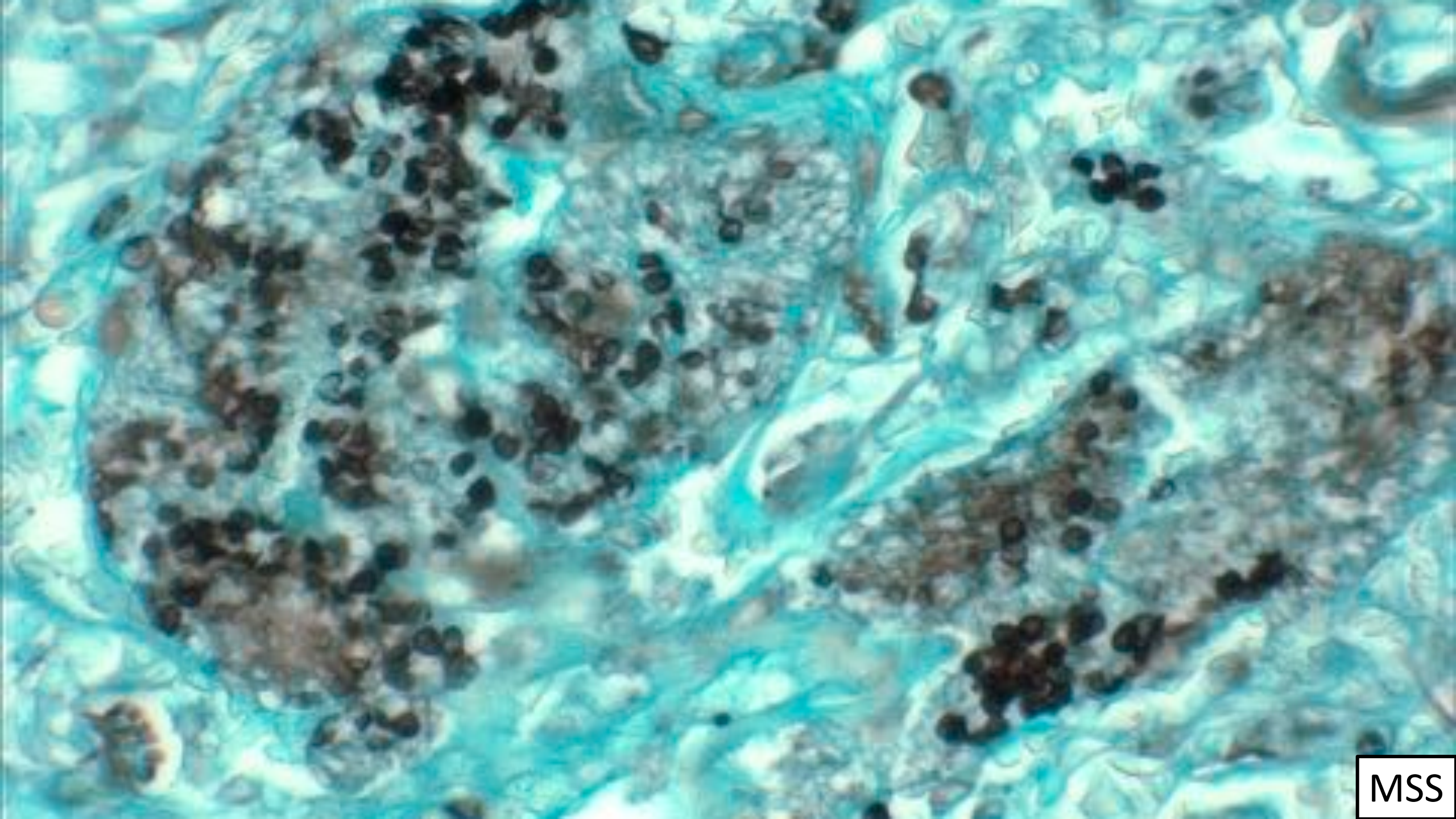
Case 1 – Pathology

Companion case for BS-09-28802

Transbronchial biopsy






MSS

TRANSBRONCHIAL LUNG BIOPSIES:
PNEUMOCYSTIS JIROVECI PNEUMONIA, see NOTE.

NOTE: The sections show a cell-poor frothy interstitial infiltrate associated with mild interstitial pneumonitis and focal organization. The organisms are highlighted by the MSS stain. No organisms are present on gram or AFB stains.

Pneumocystis Jiroveci Pneumonia

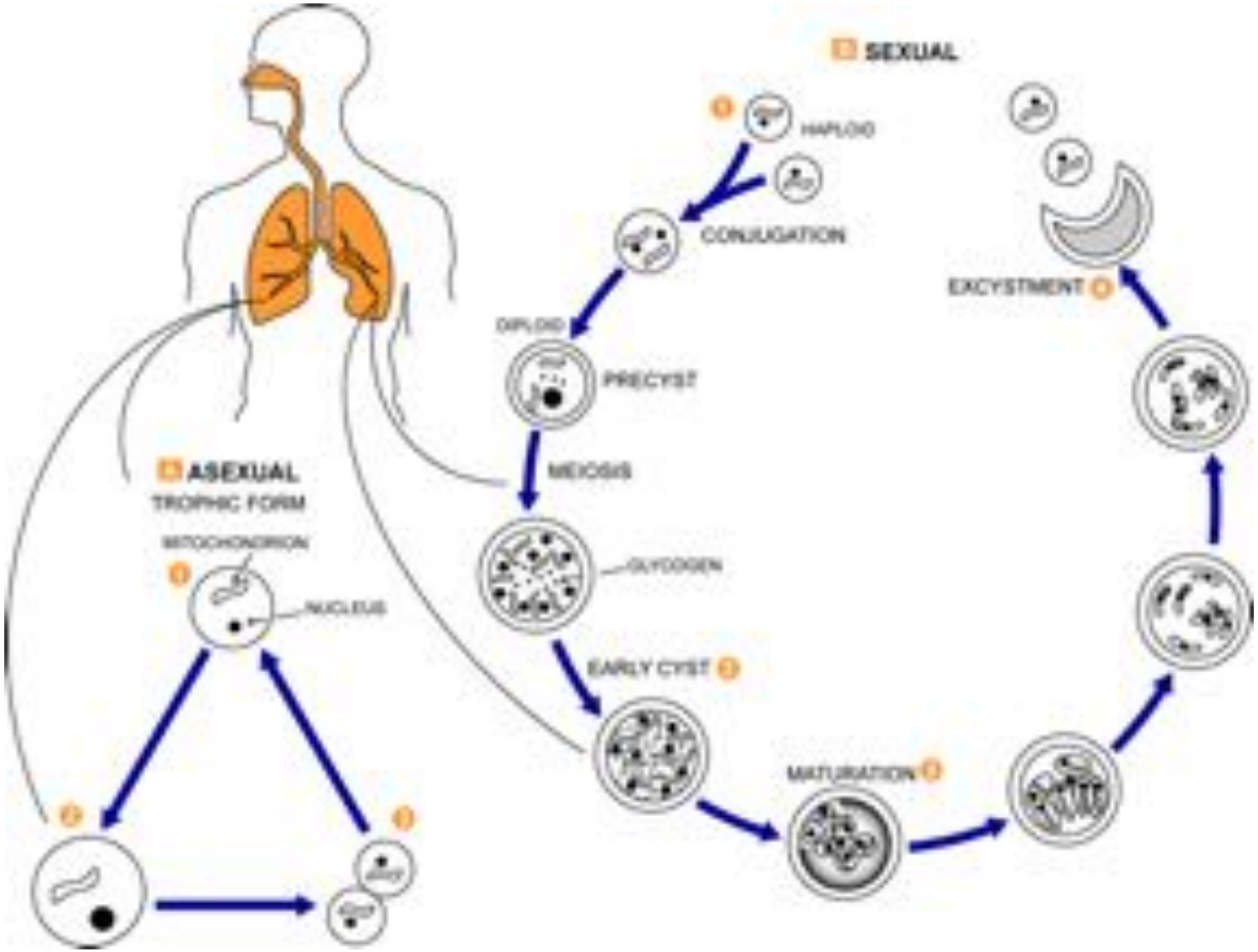
Macroscopic

- Consolidation of pulmonary parenchyma with pale-gray or tan nodular cut surface
- Nodules or cavities occasionally identified
- Small subpleural blebs or cysts often in upper lobes

Microscopic

- Alveolar exudate composed of fibrin admixed with abundant trophozoites and cysts, surfactant, and cellular debris
- Alveolar exudate may be focal or diffuse and can be accompanied by mild interstitial inflammation and type II pneumocyte hyperplasia
- *Pneumocystis* cysts are oval with collapsed or crescentic forms highlighted by MSS

Life Cycle of *Pneumocystis jiroveci*



https://www.cdc.gov/dpdx/pneumocystis/index.html

Case 1 – *Pneumocystis jiroveci* pneumonia

The what:

- Life-threatening respiratory infection occurring in immunocompromised individuals caused by fungus *Pneumocystis jirovecii*
- AIDS-defining illness

The where:

- Diffuse throughout lungs

The who:

- Consider PCP in HIV+ patients with severe immunosuppression, subacute respiratory symptoms, and bilateral ground-glass opacities
- Risk factors
  - HIV/AIDS: Common at CD4+ < 200 cells/µL . Most cases occur at CD4+ < 100 cells/µL .
  - Other risk factors: Chemotherapeutic regimens for malignancies, immunosuppression therapy, congenital immune disorders
- Most common opportunistic pneumonia in HIV+ patients
- Decreased incidence in HIV/AIDS population following effective prophylaxis (TMP-SMX) and ART, earlier recognition and more effective therapy

Case 1 – *Pneumocystis jiroveci* pneumonia

What does it look like:

CXR

- Normal or equivocal (10-39%)
- Diffuse or perihilar fine reticular and ill-defined ground-glass opacities
  - Untreated, these opacities progress to diffuse homogeneous opacification in 3-4 days
- Coarse reticular opacities

Case 1 – *Pneumocystis jiroveci* pneumonia

What does it look like:

CT

- Scattered or diffuse ground-glass opacities (92%)
  - Alveolar filling by foamy exudate (surfactant, fibrin, and cellular debris)
  - Variable distribution: Central distribution with relative peripheral sparing (41%), mosaic attenuation (29%), diffuse involvement (24%)
- Crazy-paving pattern
- Thin-walled air-containing cysts (10-34%)
  - Tissue invasion and secondary necrosis
  - Upper lobe predominance
- Diffuse consolidation
  - Secondary to disease progression or development of ARDS
- Intralobular lines and interlobular septal thickening
- Spontaneous pneumothorax
- Chronic PCP: Irregular liner opacities, traction bronchiectasis, pulmonary architectural distortion, large nodule(s)

Case 1 – *Pneumocystis jiroveci* pneumonia

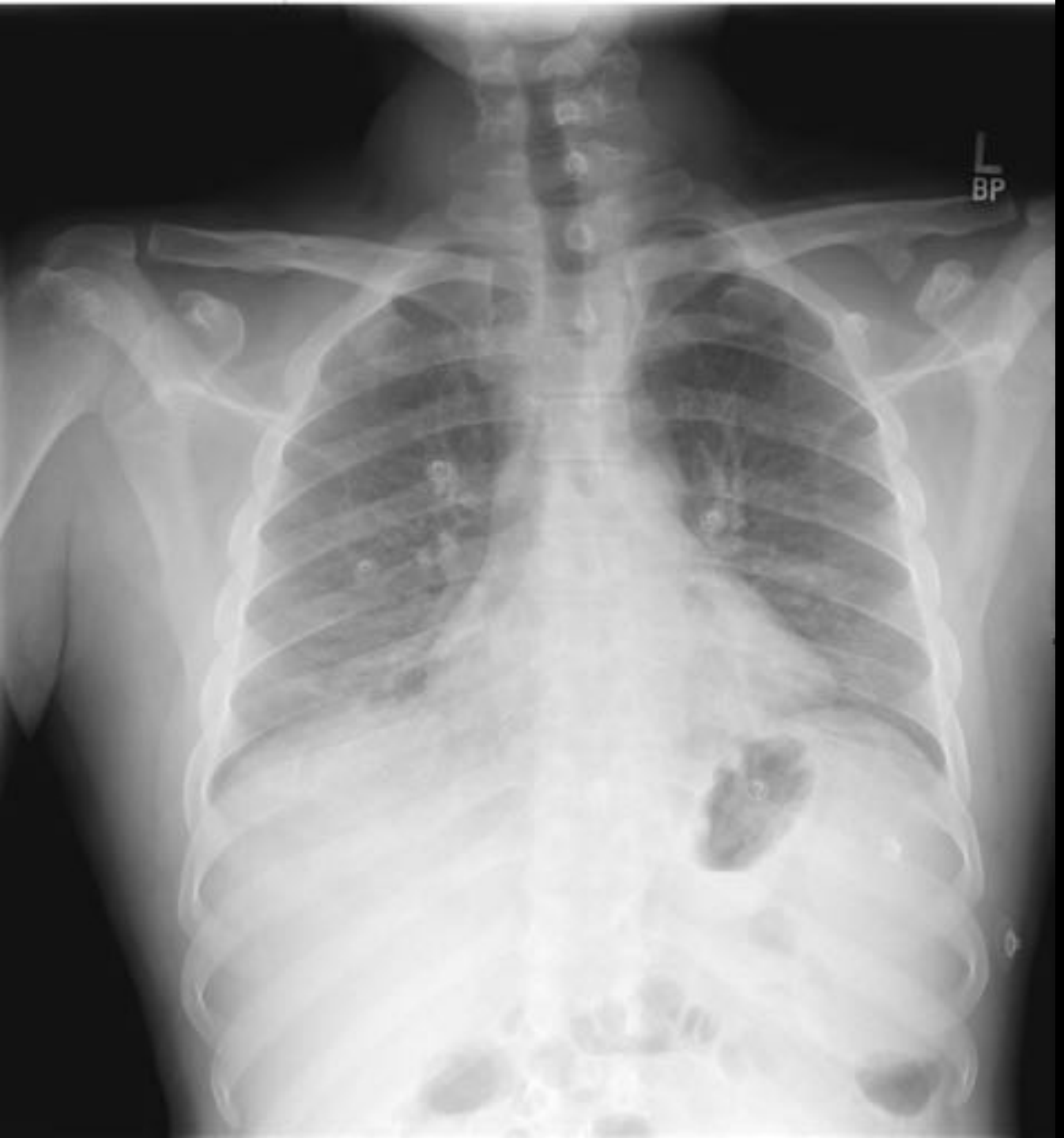
What else do you need to know:

- Clinical prodrome (from a few days to a few weeks): fever, malaise, and weight loss. Patients then develop either a nonproductive cough or a cough productive of frothy white phlegm, associated with increased respiratory rate and arterial desaturation on exertion.
- Mortality
  - Patients with HIV infection: 10-20% mortality during initial infection
  - Patients without HIV infection: 30-60% mortality
  - Greater risk of death among patients with cancer
- Treatment of choice: TMP-SMZ with adjunctive corticosteroid therapy.
- Primary prophylaxis against PCP in HIV+ patients should begin when CD4 < 200.

Case 2

- 38-year-old male with epigastric pain for 3 weeks and transaminitis on initial labs, as well as fevers, night sweats, fatigue and malaise for 2 weeks, and found to have a new diagnosis of HIV/AIDS (CD4 33, VL >650,000).

Case 2 – Radiology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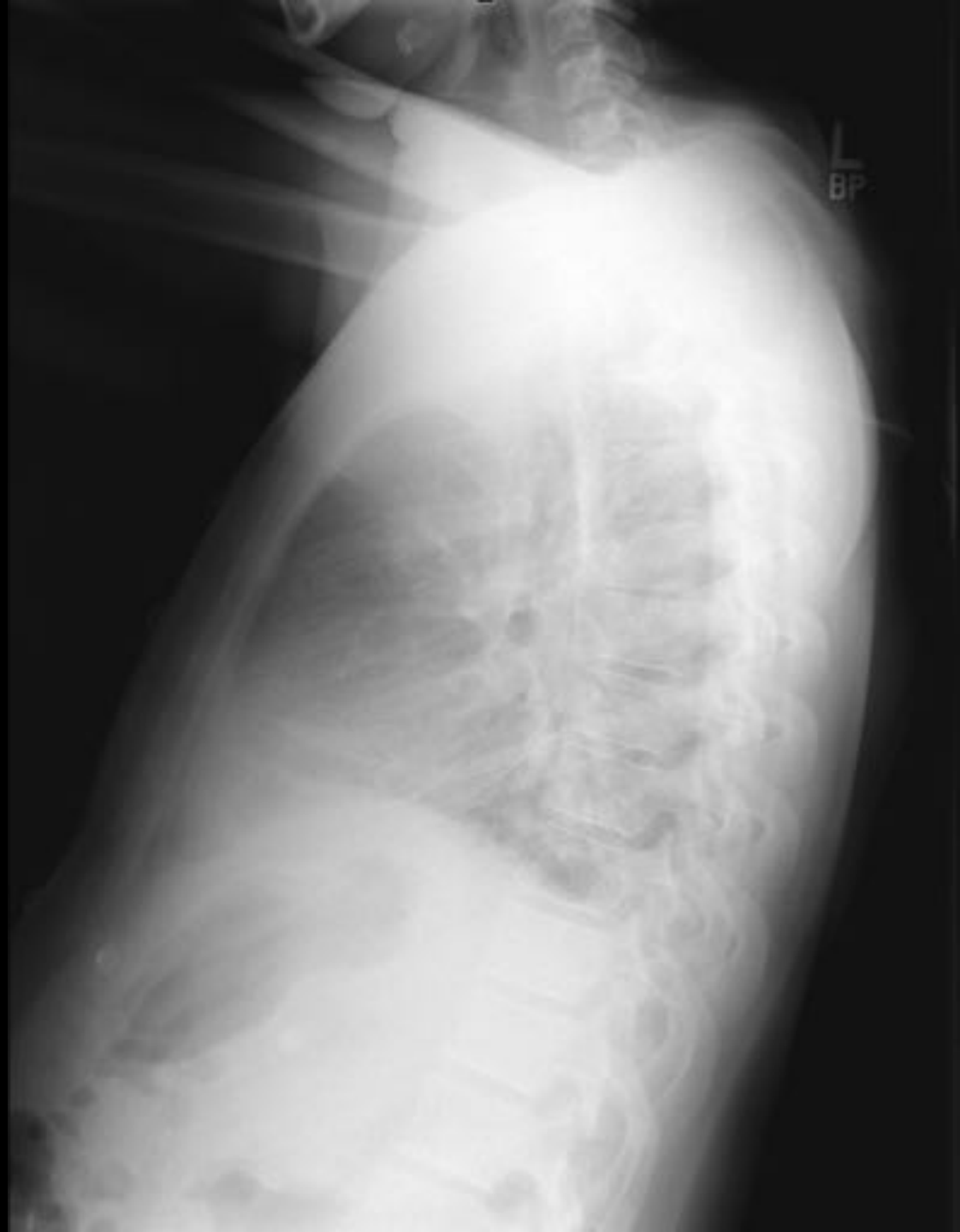
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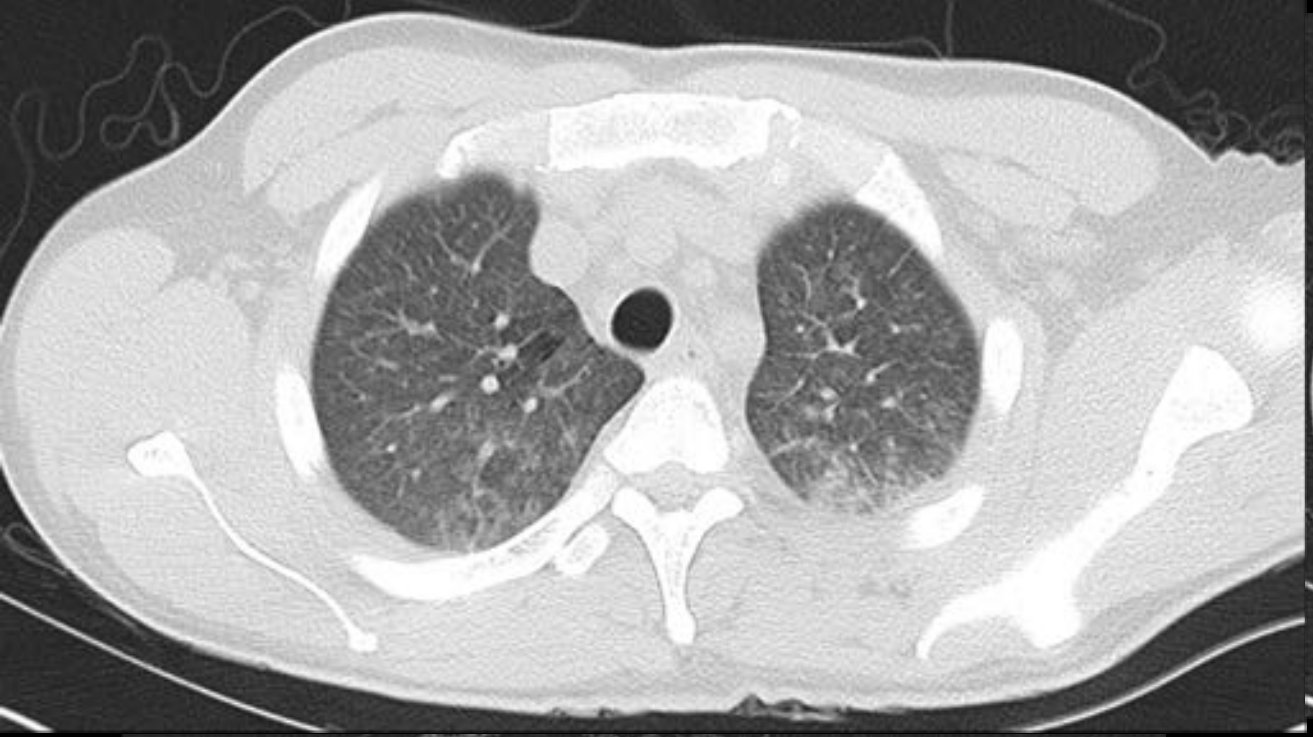
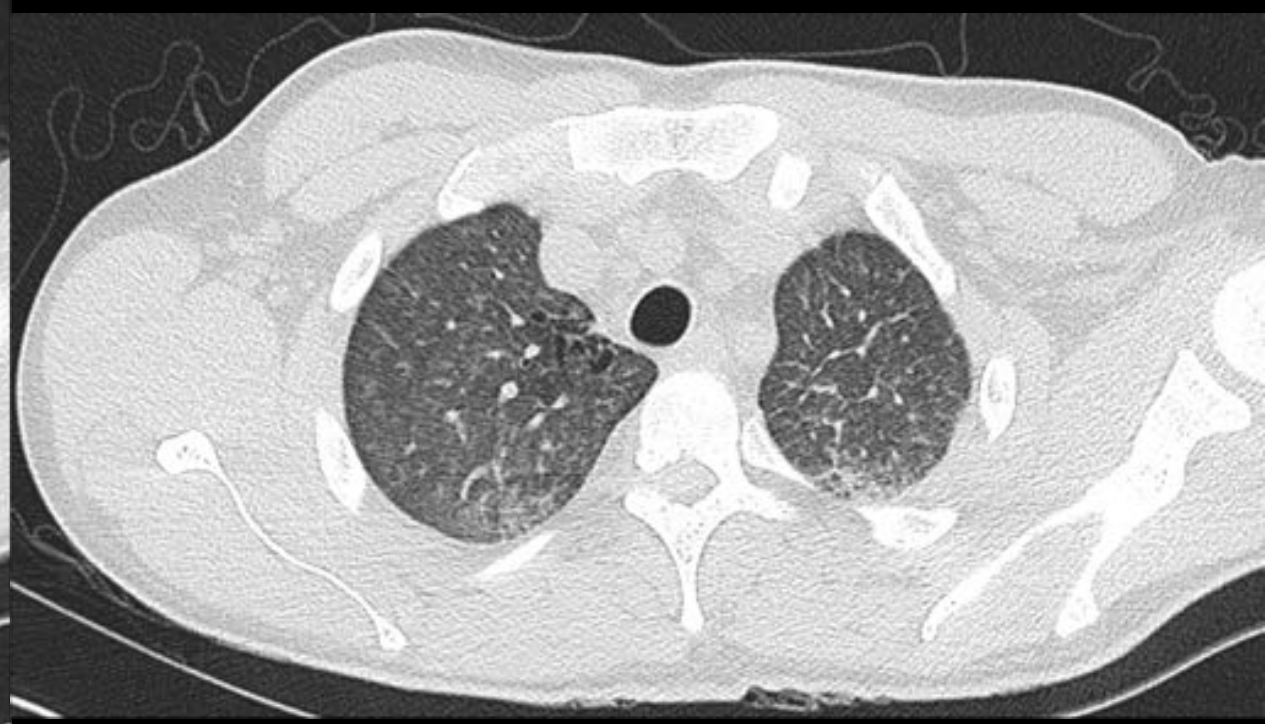
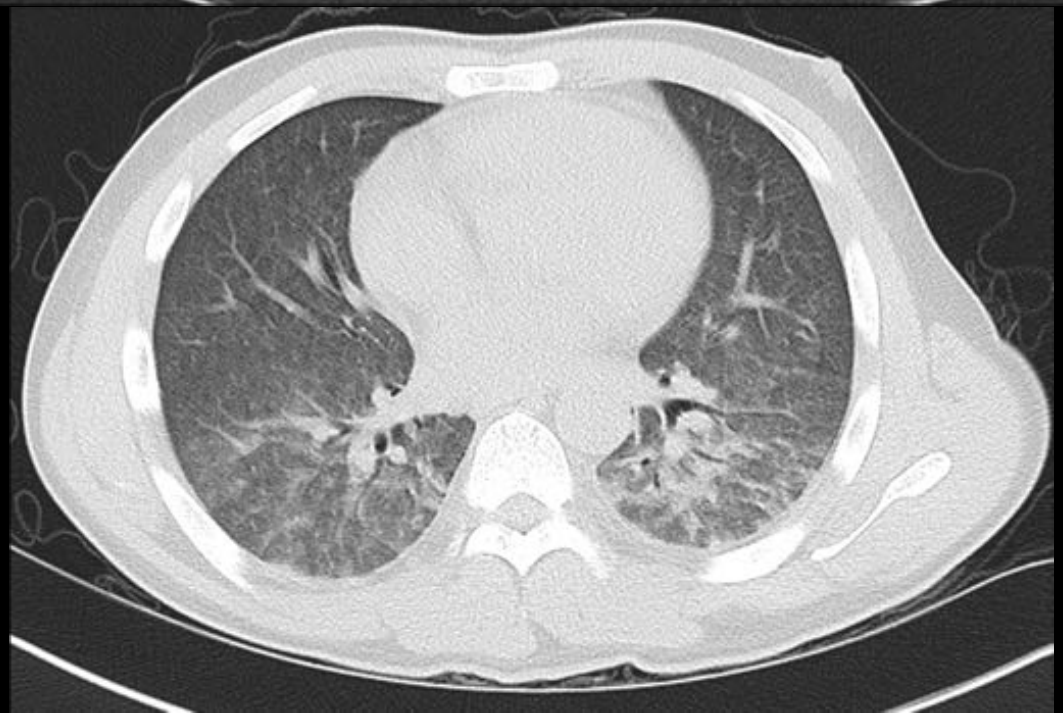
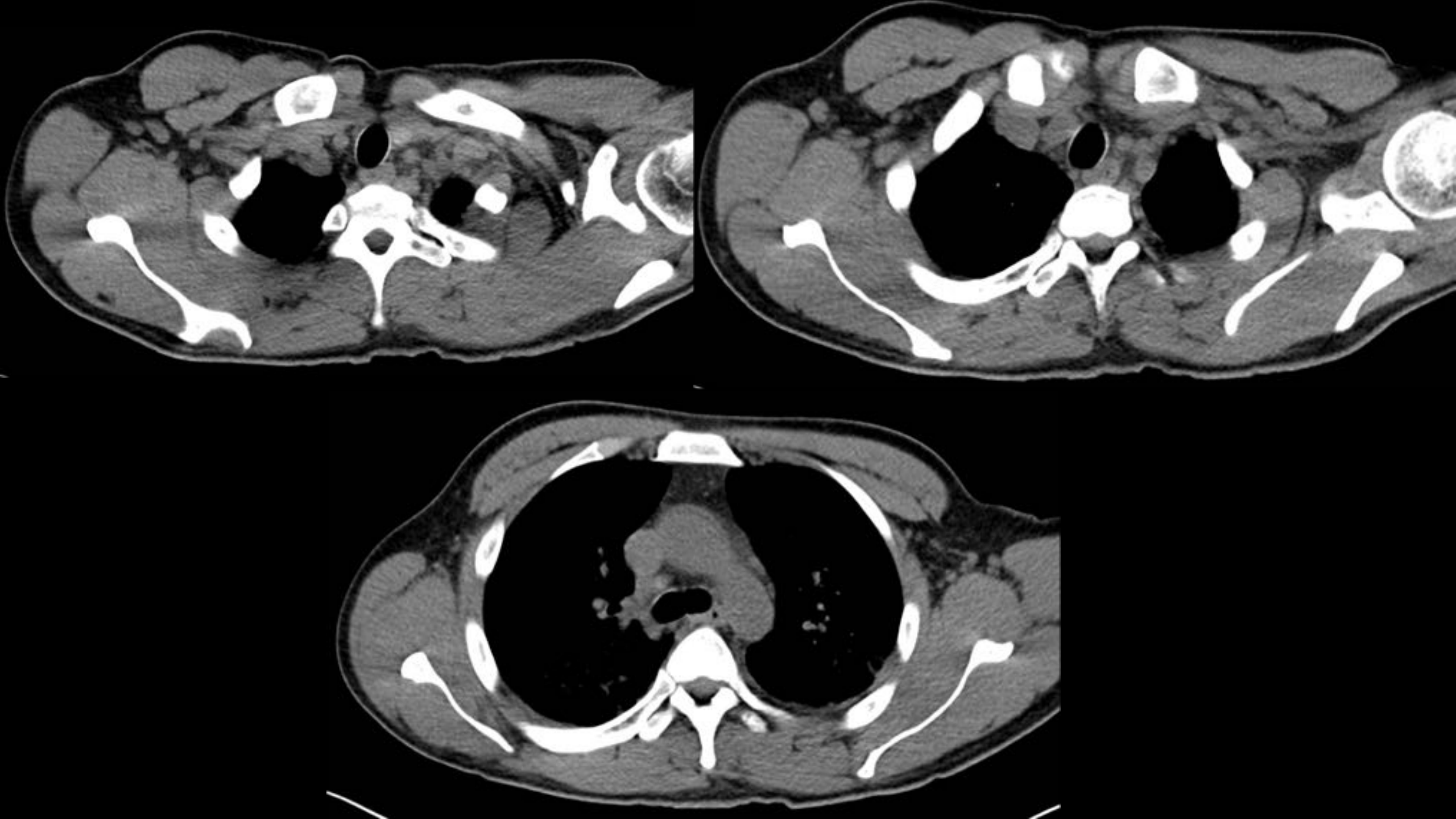
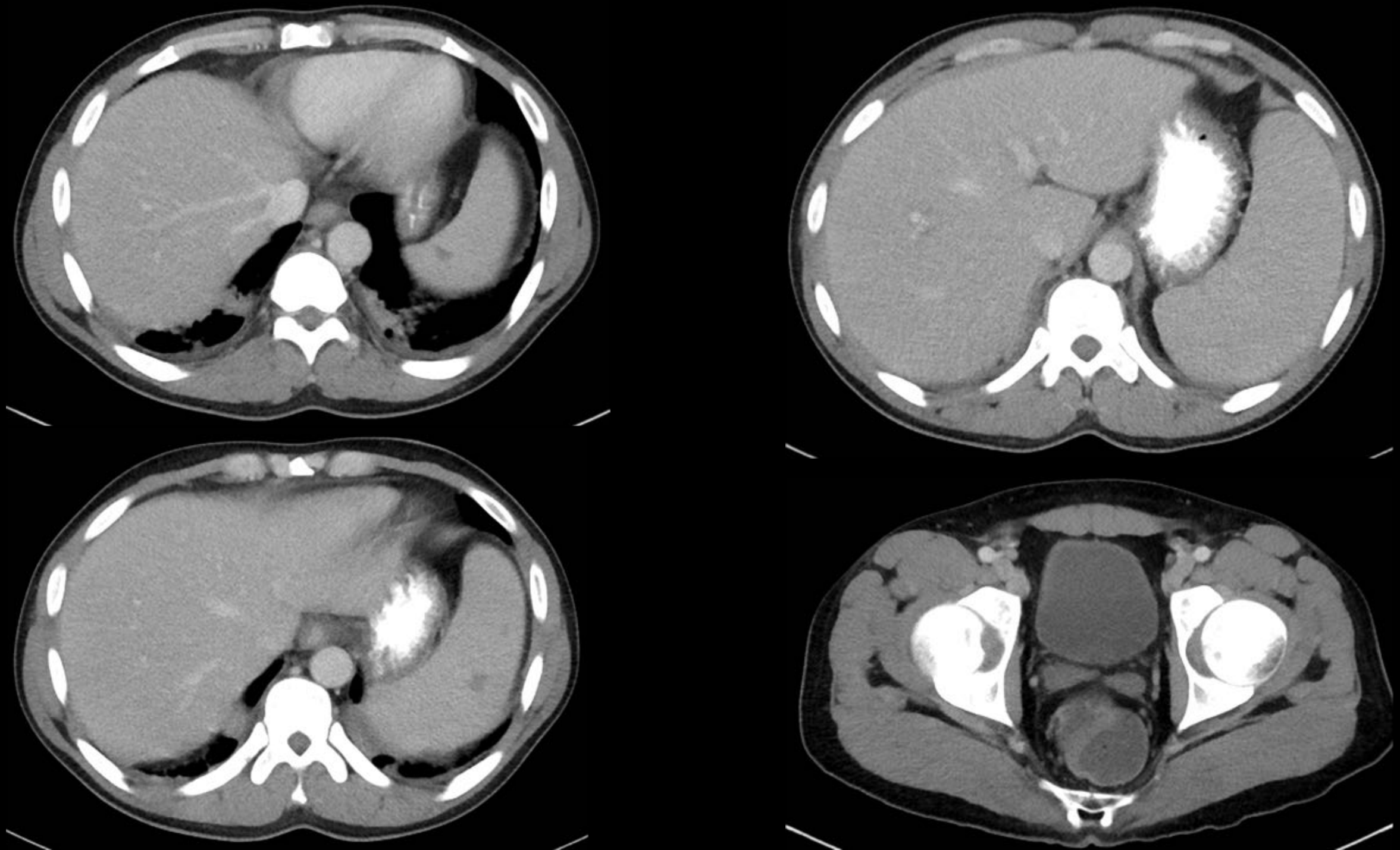






1 mm slice thickness





Case 2 – Findings

CXR

Subtle parenchymal opacities present in the right lower lobe

CT chest

Diffuse groundglass opacities

Centrilobular micronodules, which are best viewed at the lung apices

Minimal septal thickening at the lung apices

Superimposed peribronchial consolidative opacities in the dependent upper lobes and dependent lower lobes, most suggestive of aspiration

Multiple small and mildly enlarged mediastinal lymph nodes

CT abdomen/pelvis

Splenomegaly

Multiple scattered low-attenuation splenic lesions

Scattered small low upper abdominal and retroperitoneal lymph nodes

Bilateral pelvic sidewall lymph nodes

Case 2 – Differential

Case 2 – Differential

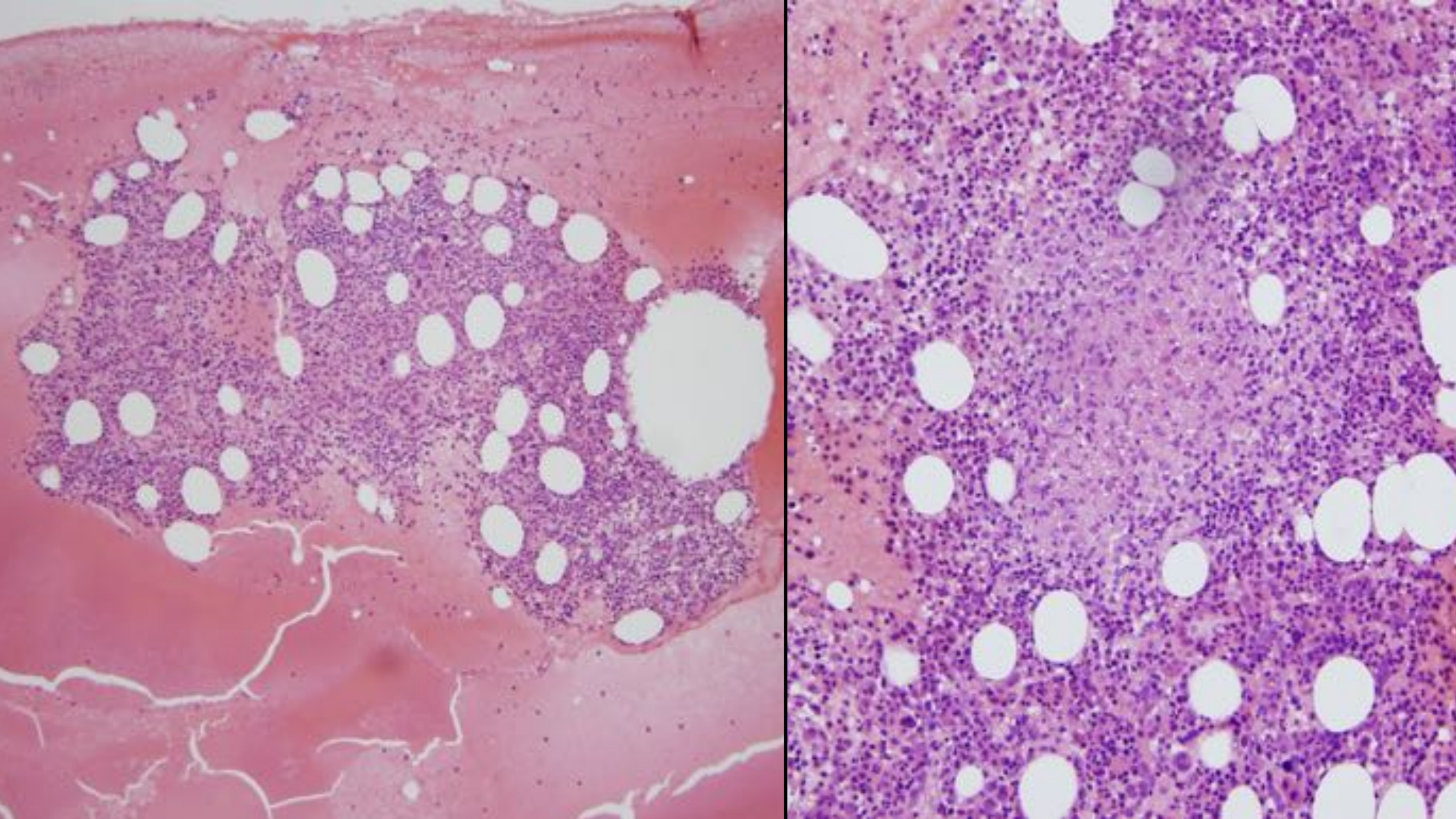
- Disseminated tuberculosis
- Disseminated nontuberculous mycobacterial disease
- Metastatic lung cancer
- *Pneumocystis jiroveci* pneumonia
- Fungal infection

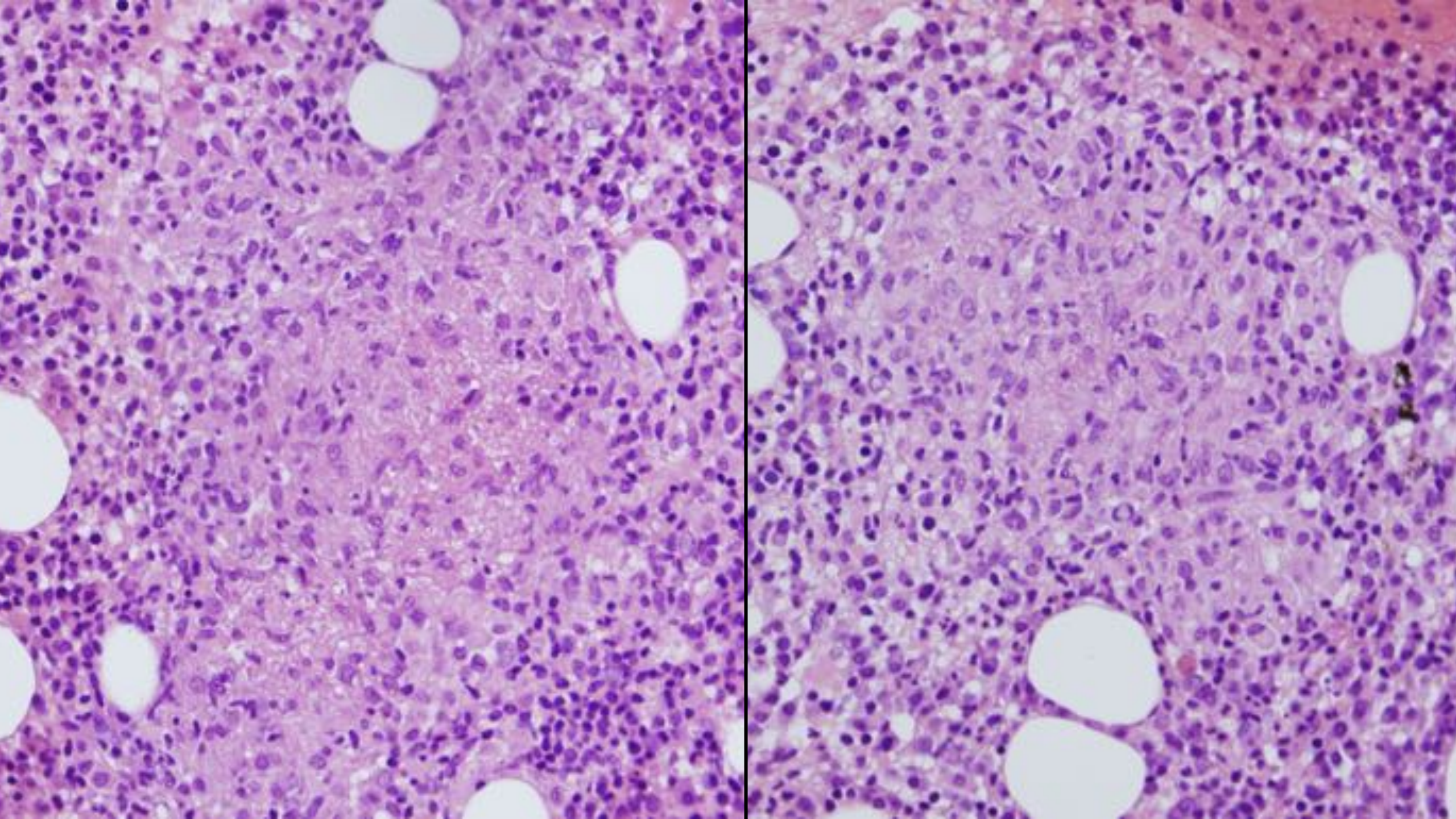
Case 2 – Pathology

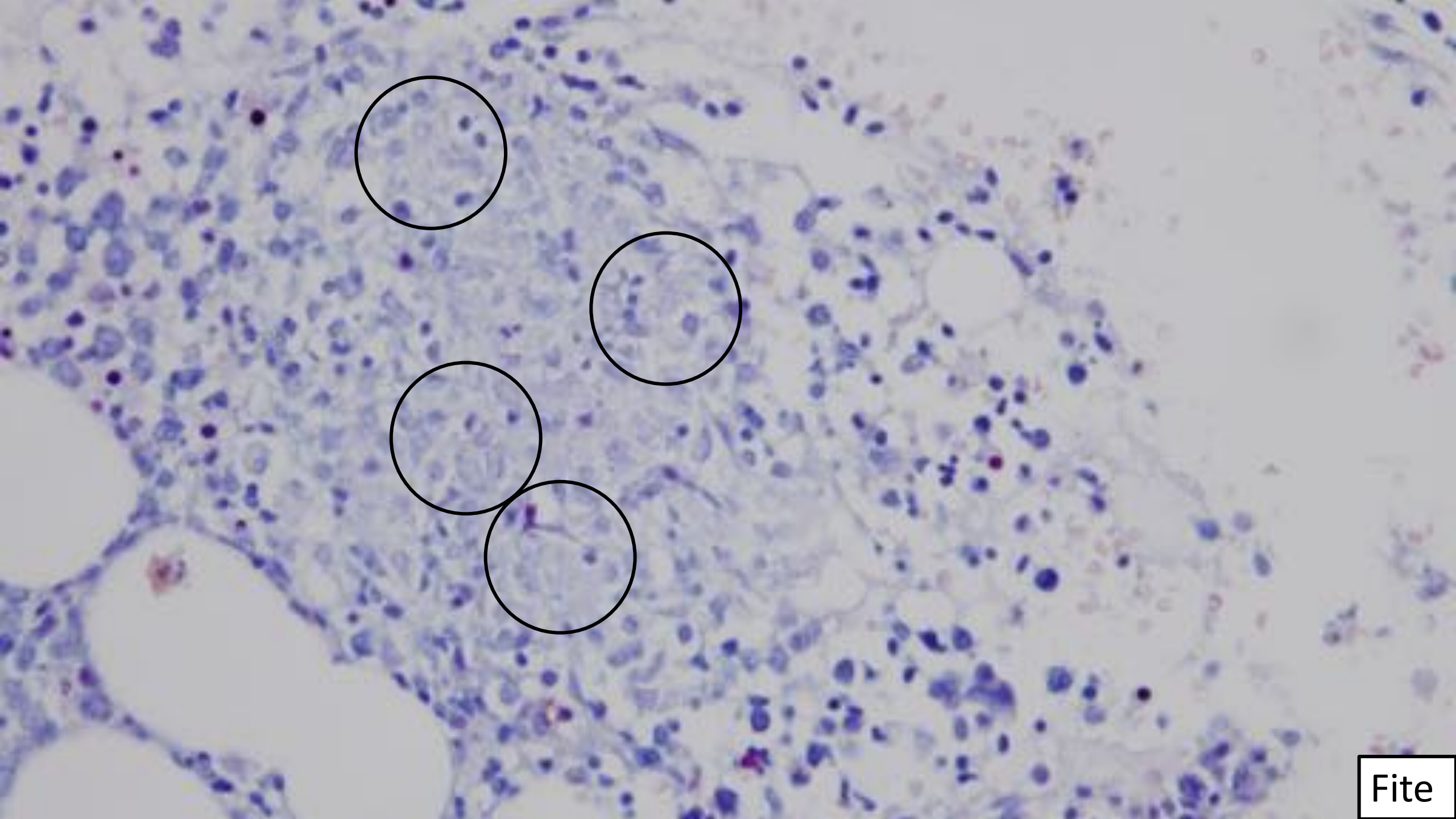
BS-17-21270

Bone marrow biopsy

Date of procedure: 4/15/2017






Fite

The findings are of a moderately hypercellular marrow with maturing trilineage hematopoiesis and multiple granulomas, consistent with DISSEMINATED MYCOBACTERIAL INFECTION, which is best demonstrated by FITE staining.
Correlation with clinical, laboratory, microbiologic, and molecular findings is advised for determination of whether the forms represent Mycobacterium tuberculosis or other type of Mycobacteria.
Diagnostic features of involvement by a lymphoproliferative disorder are not seen.

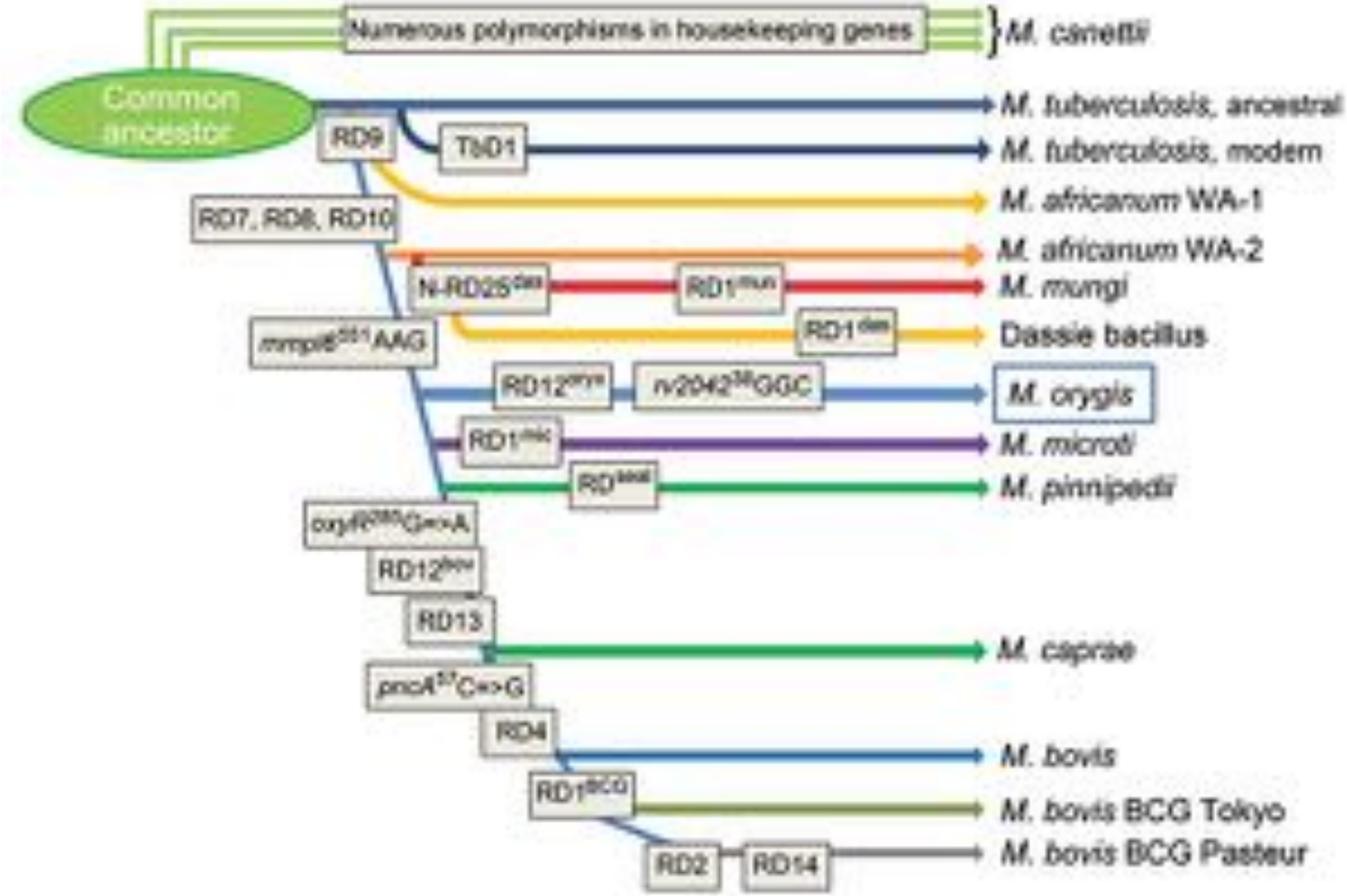
4/16/17 7:20 AM

Specimen Source/ Description INDUCED SPUTUM
SPECIAL REQUESTS None
SMEAR NO ACID FAST BACILLI (CONCENTRATED SPECIMEN)
CULTURE / TEST **MYCOBACTERIUM TUBERCULOSIS COMPLEX (*)**
CULTURE / TEST The acid fast organism was identified by MALDI-TOF.

4/16/17 7:20 AM

Specimen Source/ Description INDUCED SPUTUM
SPECIAL REQUESTS None
MTB PCR **M. TUBERCULOSIS COMPLEX DETECTED: NAAT results will be followed by confirmatory testing with conventional culture and drug susceptibility testing.**
(*)
MTB PCR RIF RESISTANCE NOT DETECTED: Rifampin resistance is unlikely but cannot be definitively excluded with this method.
MTB PCR Per BWH infection control policy, airborne precautions can be discontinued if two tuberculosis PCR tests are negative and there is no longer any suspicion for pulmonary tuberculosis. Specimens must be collected at least 8 hours apart.

Mycobacterium tuberculosis Complex

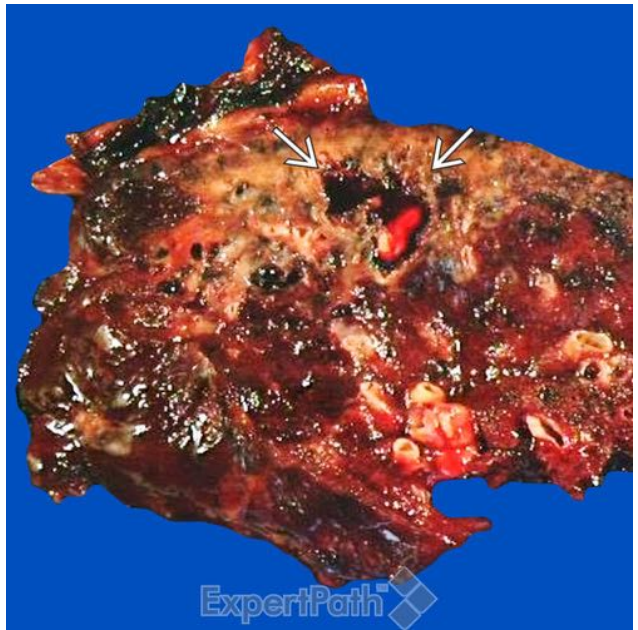


https://wwwnc.cdc.gov/eid/article/18/4/11-0888-f2

Disseminated Tuberculosis

Macroscopic

- Consolidation with areas of caseous necrosis
- Mass or circumscribed nodules with central necrosis, calcification, or fibrosis
- Miliary spread characterized by numerous small (1-2 mm) nodules diffusely distributed throughout lungs

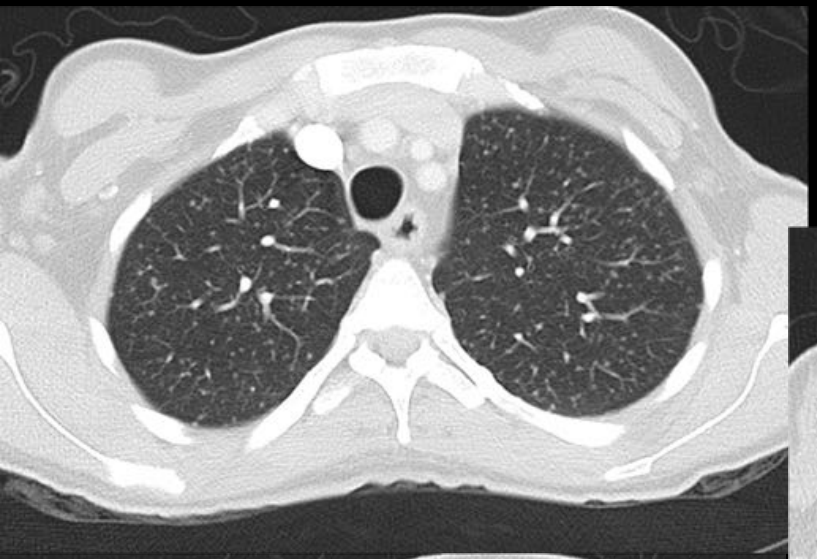


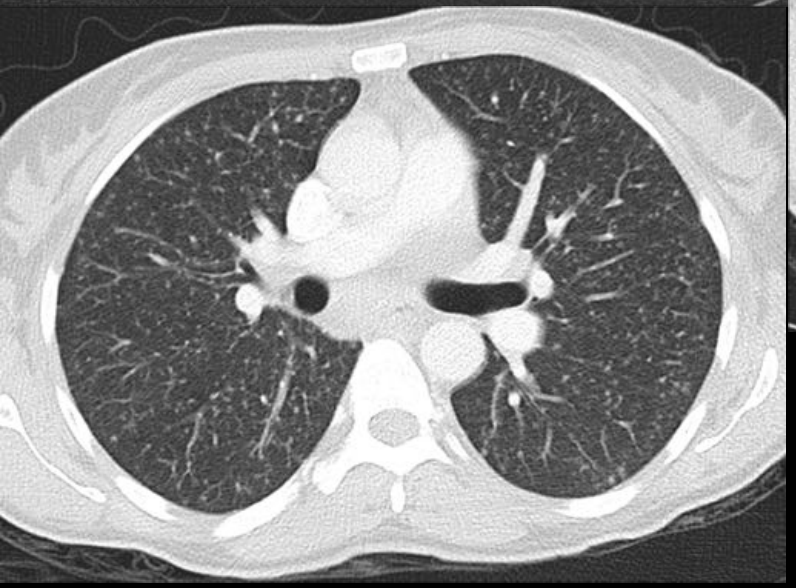
Microscopic

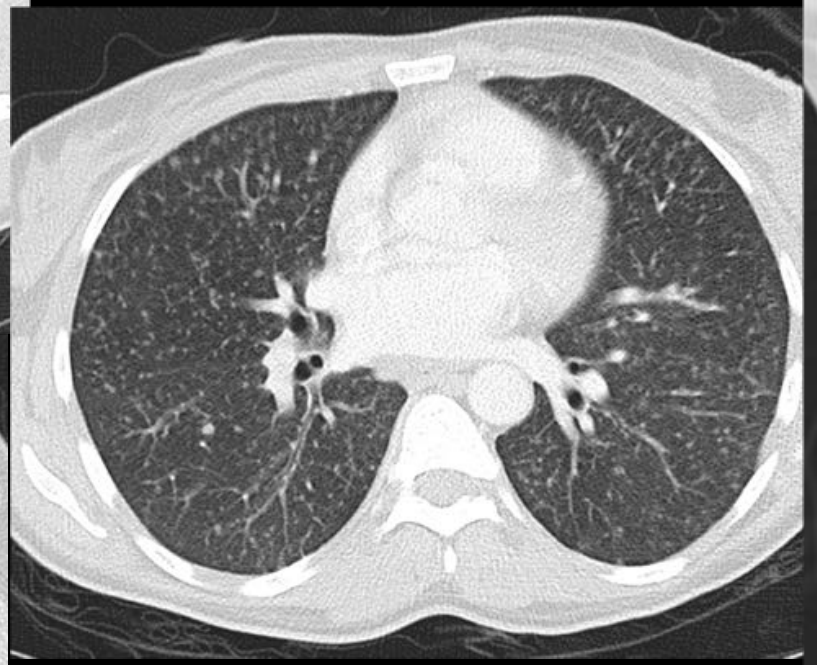
- Granulomas can be necrotizing or non-necrotizing and contain abundant epithelioid macrophages and Langhans-type giant cells
- Palisading granulomas can progress to complete fibrosis and calcification
- Necrotizing granulomas may enlarge to form cavities with central liquefaction
- *Mycobacteria* are slender rods measuring 4 µm in length, which cannot be visualized on routine histology and require special stains for acid-fast bacteria (AFB or Fite)

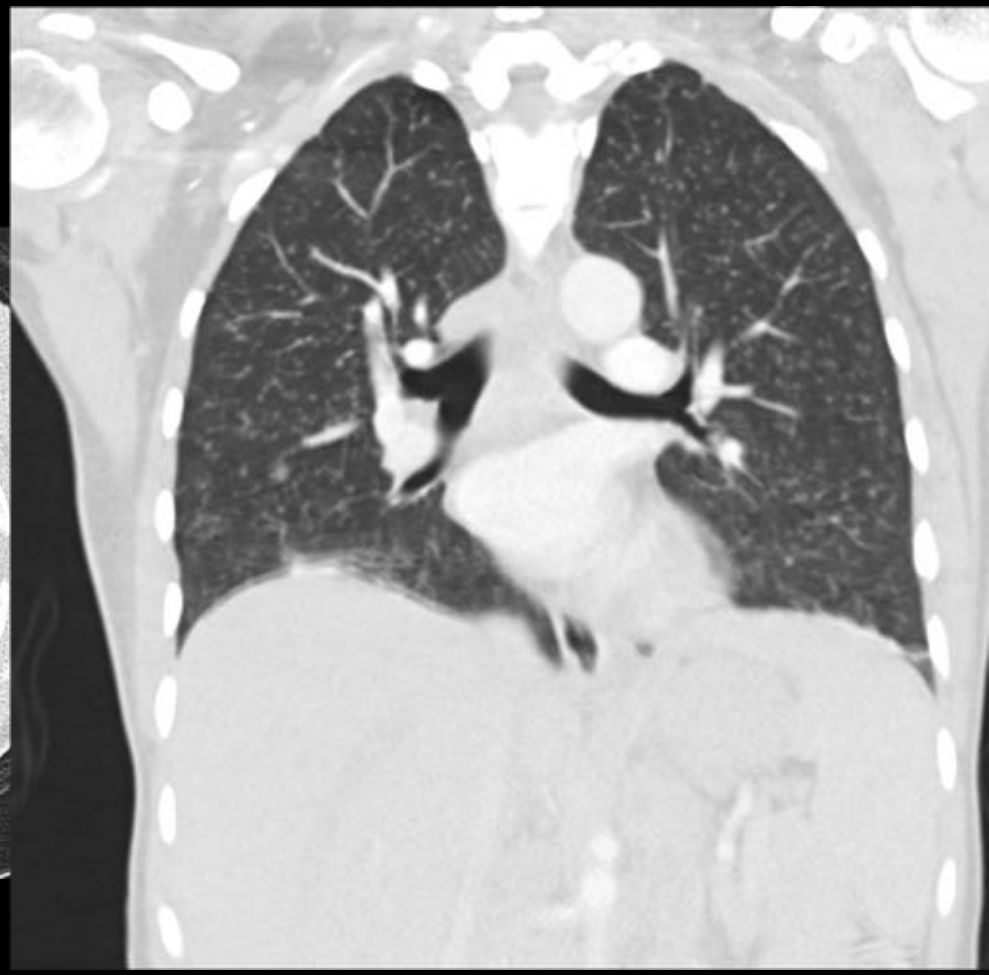
ExpertPath

Case 2 – Companion Case









Case 2 – Disseminated Tuberculosis

The what:

- Airborne infection transmitted from person to person via organism-containing droplets
- Abdominal TB is usually secondary to pulmonary TB

The where:

- Extensive lung parenchymal, extrathoracic lymph node, and extrathoracic organ involvement
- Most common sites of involvement in abdomen are lymph nodes (67%), GU tract (most common organ system), peritoneum, and GI tract
    - Also liver, spleen, biliary tree, pancreas, and adrenal glands unusual and more likely in HIV patients or patients with military TB

The who:

- Risk factors
    - Immunocompromised (HIV/AIDS, transplant recipients, immunosuppressive drugs)
    - Poverty, homelessness, alcoholism, from developing country, imprisonment

Case 2 – Disseminated Tuberculosis

What does it look like:

- Depends on CD4+ lymphocyte counts
- If CD4+ > 200 cells/µL and/or receiving ART = postprimary/reactivation pattern of disease: upper lobe linear and nodular opacities and cavitation
- If CD4+ < 200 cells/µL, cavitation less common and = focal or multifocal lobar or segmental opacities (often in atypical locations), bronchial wall thickening and centrilobular nodules (endobronchial spread), miliary nodules, enlarged hilar or mediastinal lymph nodes, and/or pleural effusion

Case 2 – Disseminated Tuberculosis

What does it look like:

CXR

Pulmonary TB

- Consolidation, nodules, &/or masses ± cavitation
- Upper lobes &/or lower lobe superior segments
- Segmental or subsegmental consolidation common in highly immunocompromised patients with TB lymphadenitis

TB lymphadenitis

- Mediastinal &/or hilar lymphadenopathy
- Common cause of isolated lymphadenopathy on CXR

Miliary TB

- Millet seed-size (< 3 mm) micronodules
- May manifest with scattered hazy opacities

Tuberculoma

Pleural TB

Case 2 – Disseminated Tuberculosis

What does it look like:

CT

Pulmonary TB

- Centrilobular nodules and branching opacities (i.e., tree-in-bud opacities) (most common)
- Cavitary nodules (20-40%), masses, &/or consolidations
- Lobular consolidation (Location: Upper lobe apical and posterior segments and lower lobe superior segments)
- Bronchial wall thickening
- Poorly defined nodules and linear opacities (25%)
- Tuberculoma (focal nodule/mass) (5%)

HIV positive

- Lymphadenopathy in several lymph node stations (typically low attenuation centers and rim enhancement)
- Consolidation in severely immunocompromised

Miliary TB

- Diffuse, random, bilateral distribution of millet seed-size nodules (innumerable, 1-3 mm micronodules)
- More frequent in reactivation TB
- Interlobular septal thickening and intralobular lines (common)
- Diffuse or focal ground-glass opacities

Other: TB lymphadenitis, Pleural TB

Case 2 – Disseminated Tuberculosis

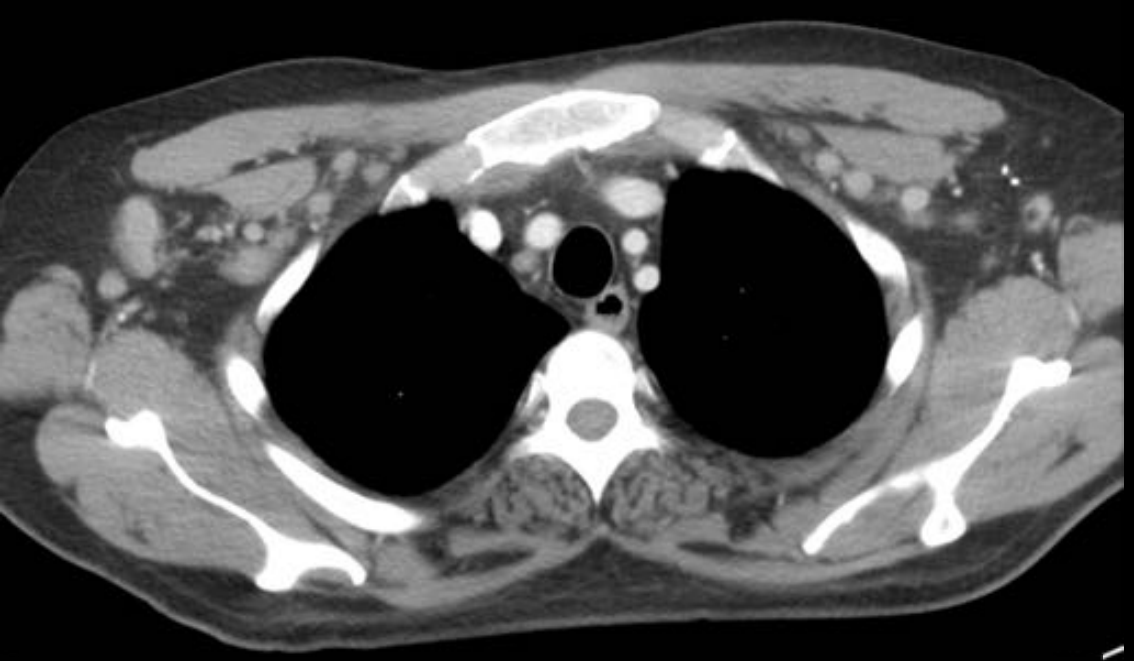
What else do you need to know:

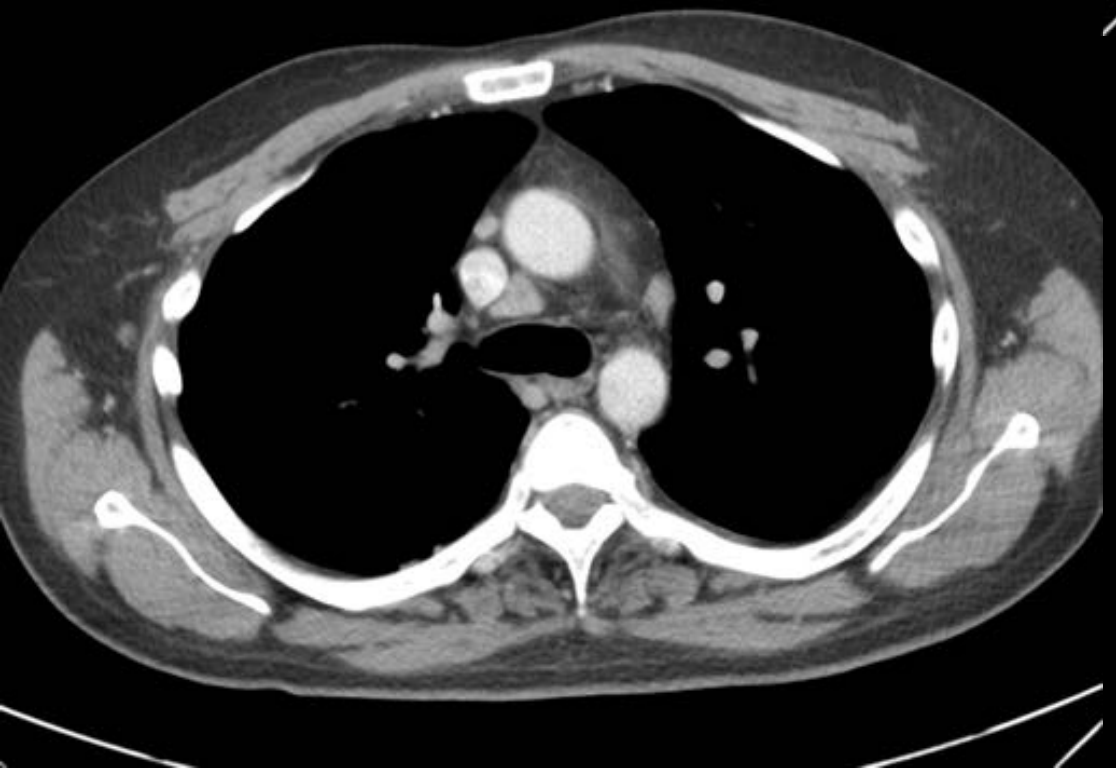
- Most common signs/symptoms
  - Chronic cough (> 3 weeks), chest pain, hemoptysis, fatigue and weight loss, fever, chills, night sweats
- Much less common if receiving ART
- Lymphadenopathy (tuberculous lymphadenitis)
  - Enlarged, centrally necrotic nodes with hypoattenuating centers and hyperattenuating enhancing rims
  - Nodes often calcify after healing
- Treatment
  - Multiple drugs based on sensitivity; preferred treatment: Isoniazid, rifampin, ethambutol, and pyrazinamide
  - Combined drugs for sufficient period of time + Directly observed therapy (DOT)

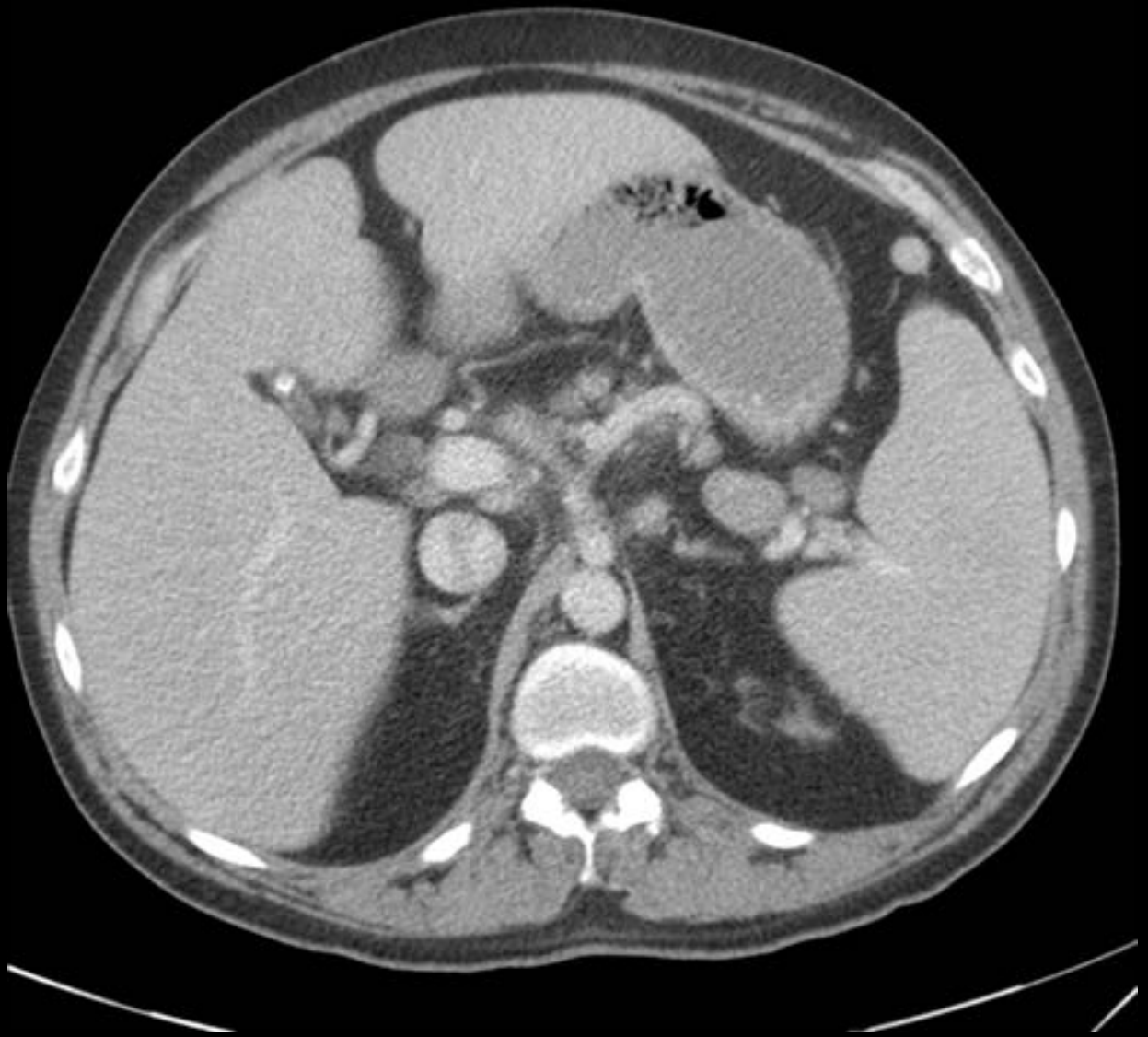
Case 3

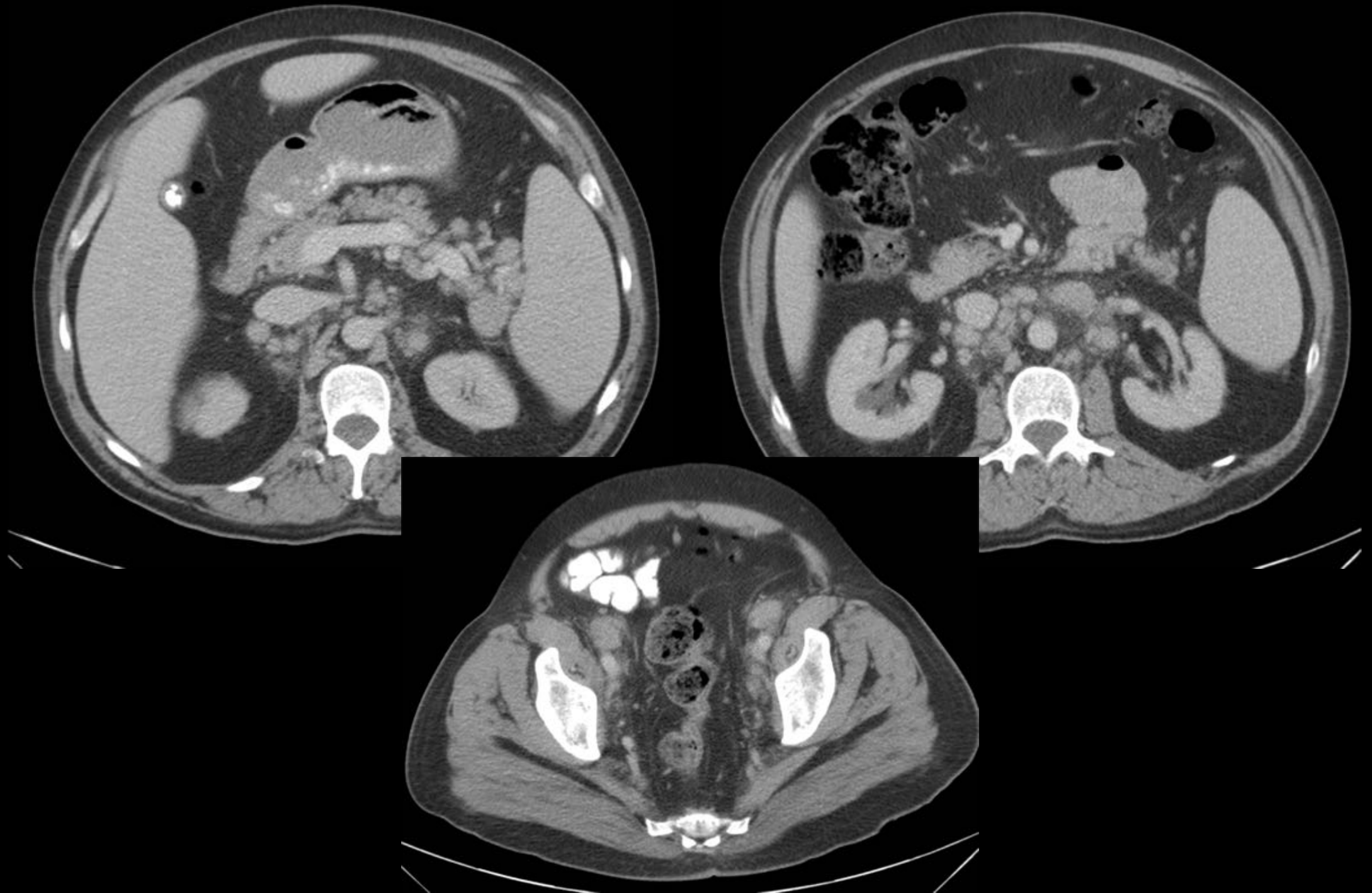
- 36-year-old male with fatigue and diffuse adenopathy, and HIV+ (on ART; CD4 >/= 350, VL undetectable).

Case 3 – Radiology









Case 3 – Findings

CT chest, abdomen/pelvis, and PET/CT

Extensive enhancing and FDG-avid lymphadenopathy within the abdomen, pelvis, chest, and neck

Multiple enlarged cervical lymph nodes at multiple stations with FDG uptake ranging from mild to moderate

Multiple enlarged mediastinal and axillary lymph nodes with FDG uptake ranging from moderate to mild

Extensive retroperitoneal, abdominal and pelvic lymphadenopathy with FDG uptake ranging from moderate to intense

Case 3 – Differential

Case 3 – Differential

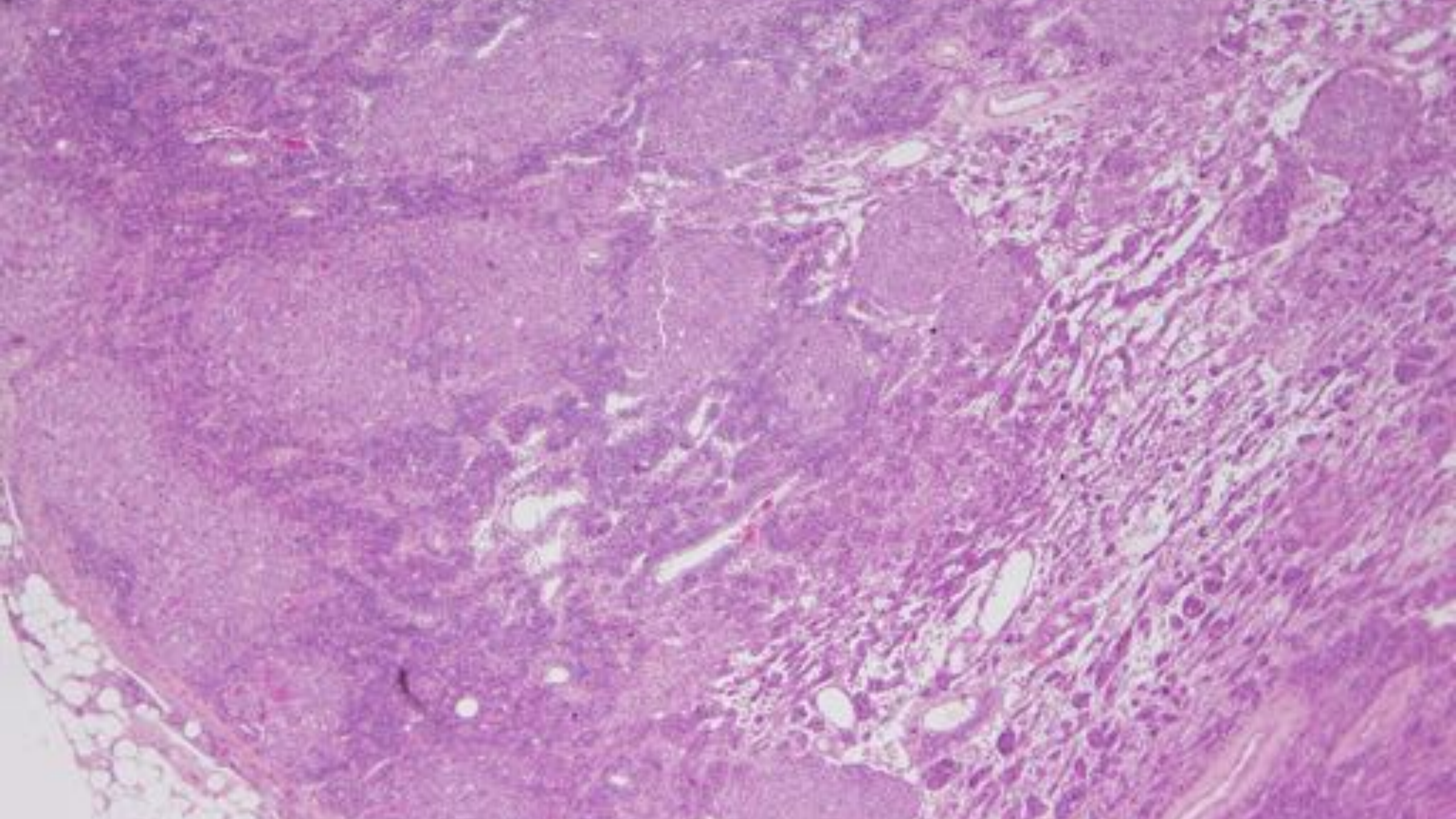
- Multicentric Castleman disease
- Metastatic lymphadenopathy – renal cell, thyroid, melanoma, sarcoma
- Lymphoma & leukemia – enhancement rare; although seen in subtypes of NHL
- Kaposi sarcoma – brisk enhancement + peribronchovascular pulmonary disease
- HIV-associated lymphadenopathy – not avidly enhancing
- AIDS-related lymphoma
- TB, MAC – would exhibit central low attenuation + lung disease

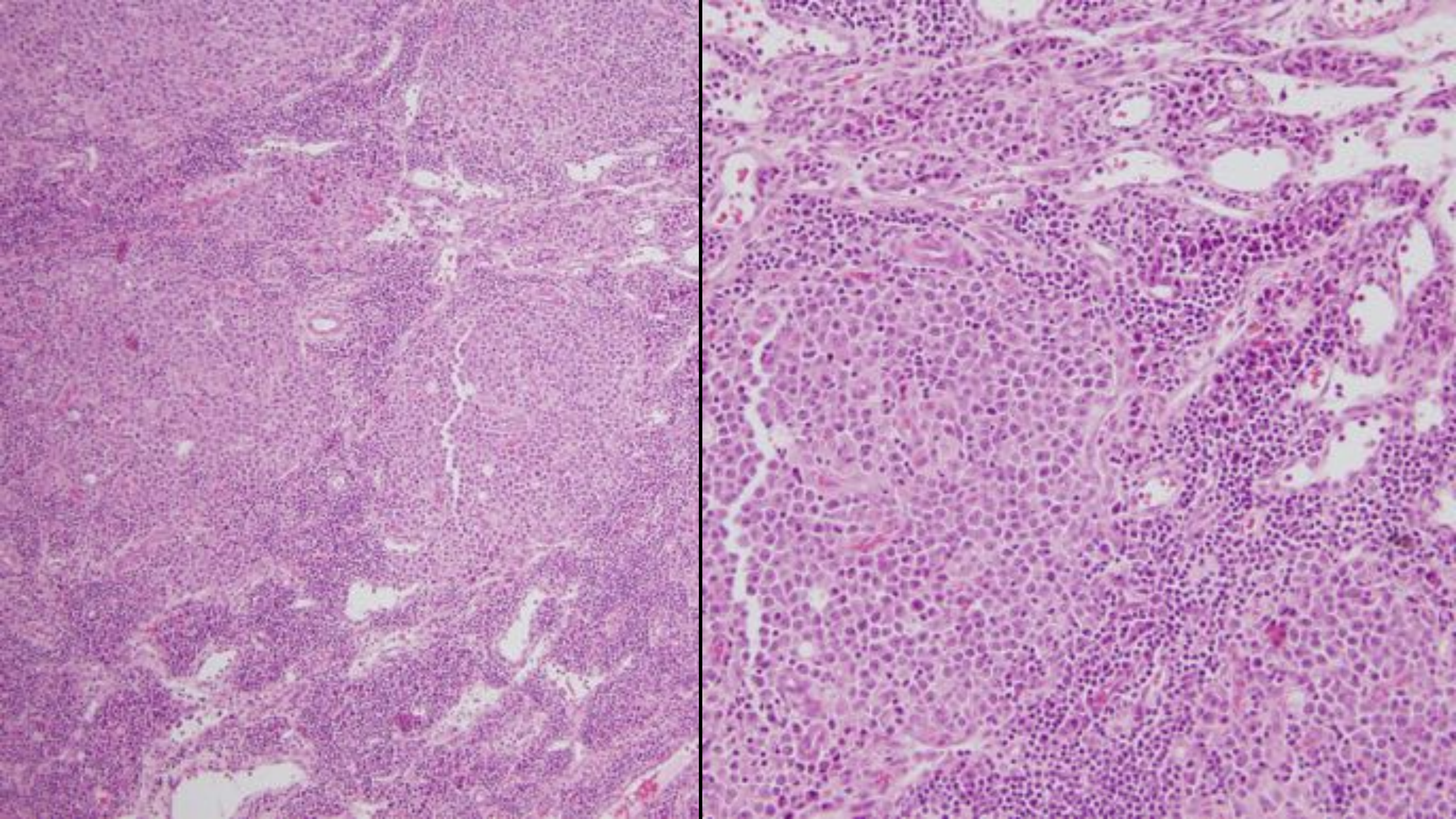
Case 3 – Pathology

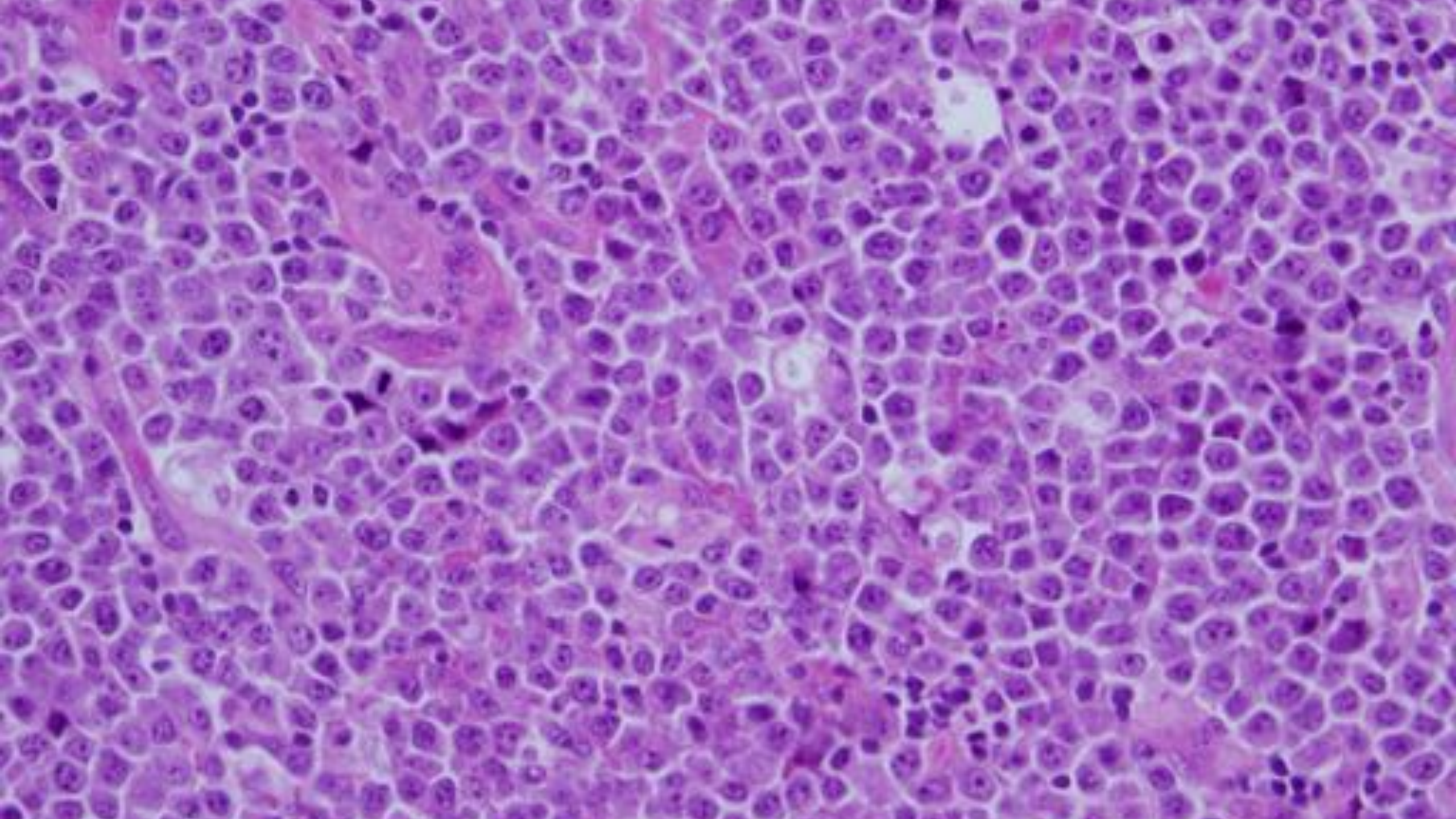
BS-10-42140

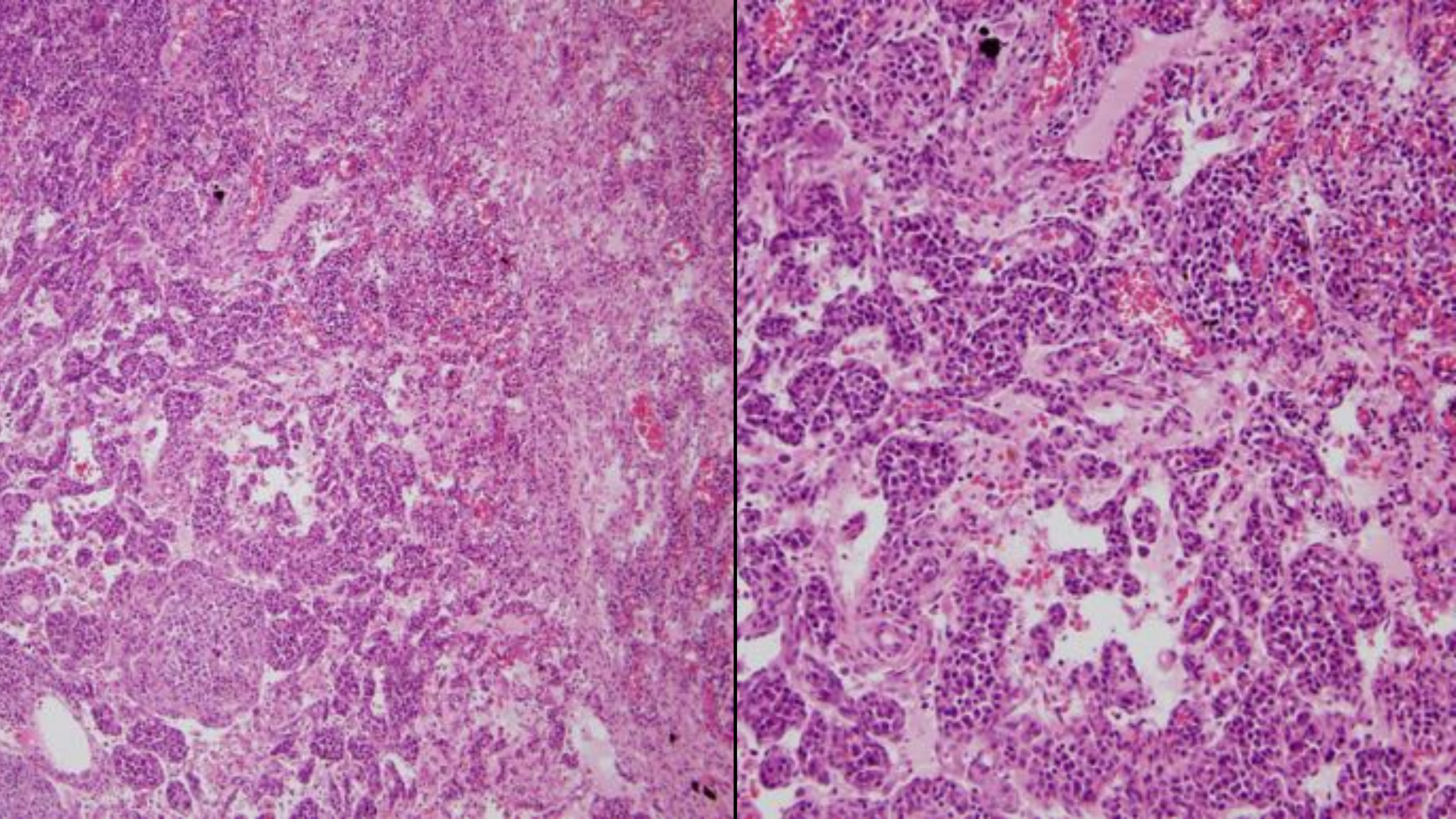
Lymph node biopsy

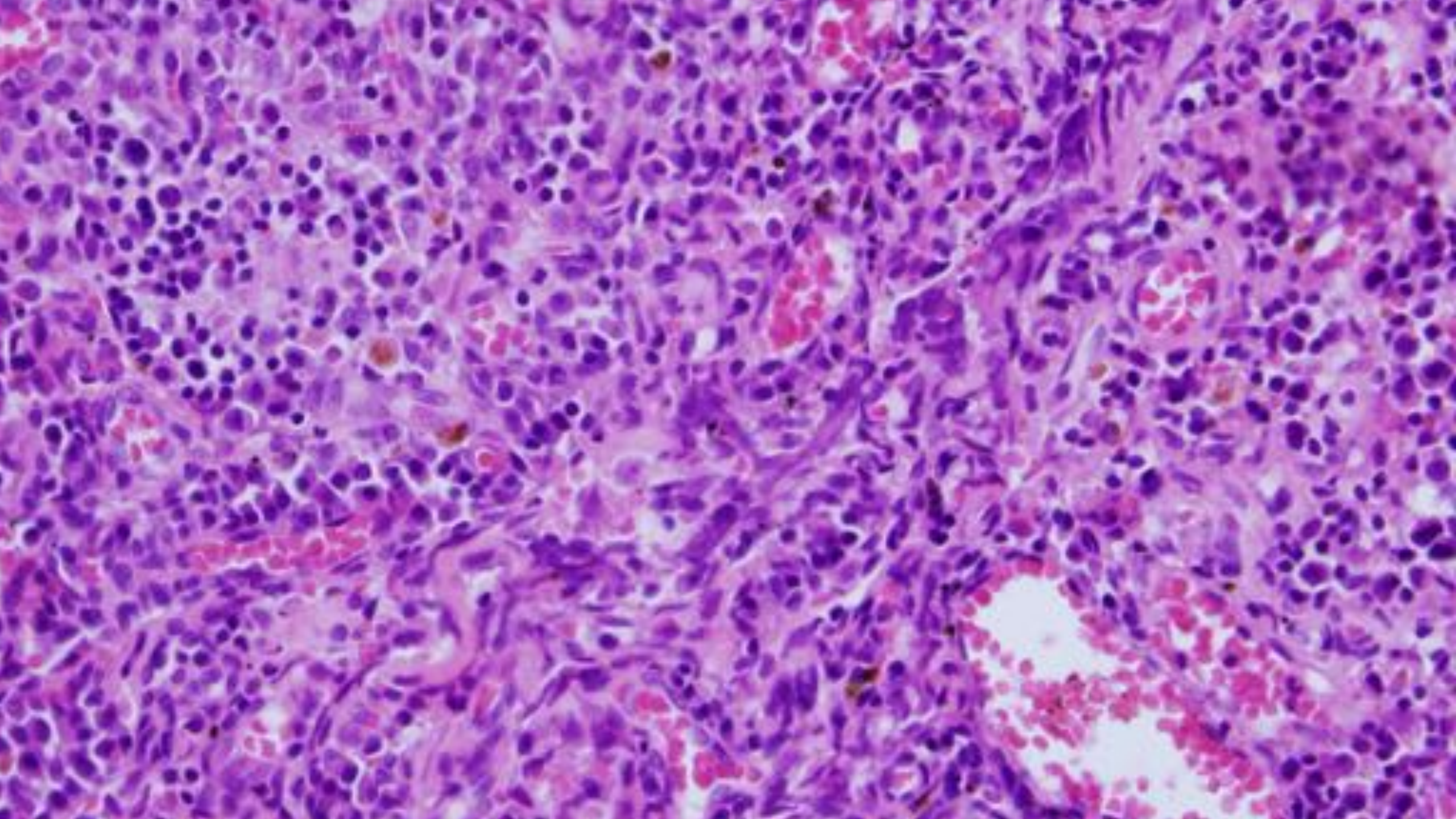
Date of procedure: 7/14/2009











RIGHT AXILLARY LYMPH NODE, BIOPSY:

The lymph node is involved by several processes:

1) HHV8-POSITIVE, EPSTEIN-BARR VIRUS POSITIVE MULTIFOCAL GERMINOTROPIC PLASMABLASTIC MICROLYMPHOMA ASSOCIATED WITH MULTICENTRIC CASTLEMAN DISEASE (see note)

2) KAPOSI SARCOMA, multifocal

Multicentric Castleman Disease (MCD)

- Most MCD cases have features of plasma cell variant
- Hyaline vascular follicles are also usually present
- Sheets of polytypic plasma cells in interfollicular regions
- Extensive vascular proliferation
- HHV8(+) cells can be small or large with features of immunoblasts or plasmablasts
- Frequently associated neoplasms: Plasmablastic lymphoma and Kaposi sarcoma
- Lymphomas evolving in background of MCD tend to initially involve the mantle zone→coalesce to form nodular aggregate (microlymphomas)→proliferate to produce frank lymphoma with sheets of plamablastic cells and effacement of nodal architecture

Case 3 – Multicentric Castleman Disease

The what:

- Rare B-cell lymphoproliferative disorder characterized by enhancing lymphadenopathy
- Unicentric vs. Multicentric (and HHV-8-associated vs. HHV-8-negative/idiopathic)
  - Human herpesvirus 8 (HHV-8) present in many patients
  - High levels of IL-6 in MCD

The where:

- Superficial, axillary, supraclavicular lymph nodes
- Less common: Mediastinal, hilar lymph nodes

The who:

- Consider in patients with multifocal enhancing lymphadenopathy, particularly those with HIV/AIDS

Case 3 – Multicentric Castleman Disease

What does it look like:

CXR

- Axillary or supraclavicular mass(es)
- Well-defined hilar or mediastinal mass(es)

Case 3 – Multicentric Castleman Disease

What does it look like:

CT

- Avidly enhancing lymphadenopathy
- Lung involvement rare
  - Enhancing pulmonary mass
  - Diffuse lung involvement may resemble lymphocytic interstitial pneumonia (centrilobular nodules, ground-glass opacities)

Case 3 – Multicentric Castleman Disease

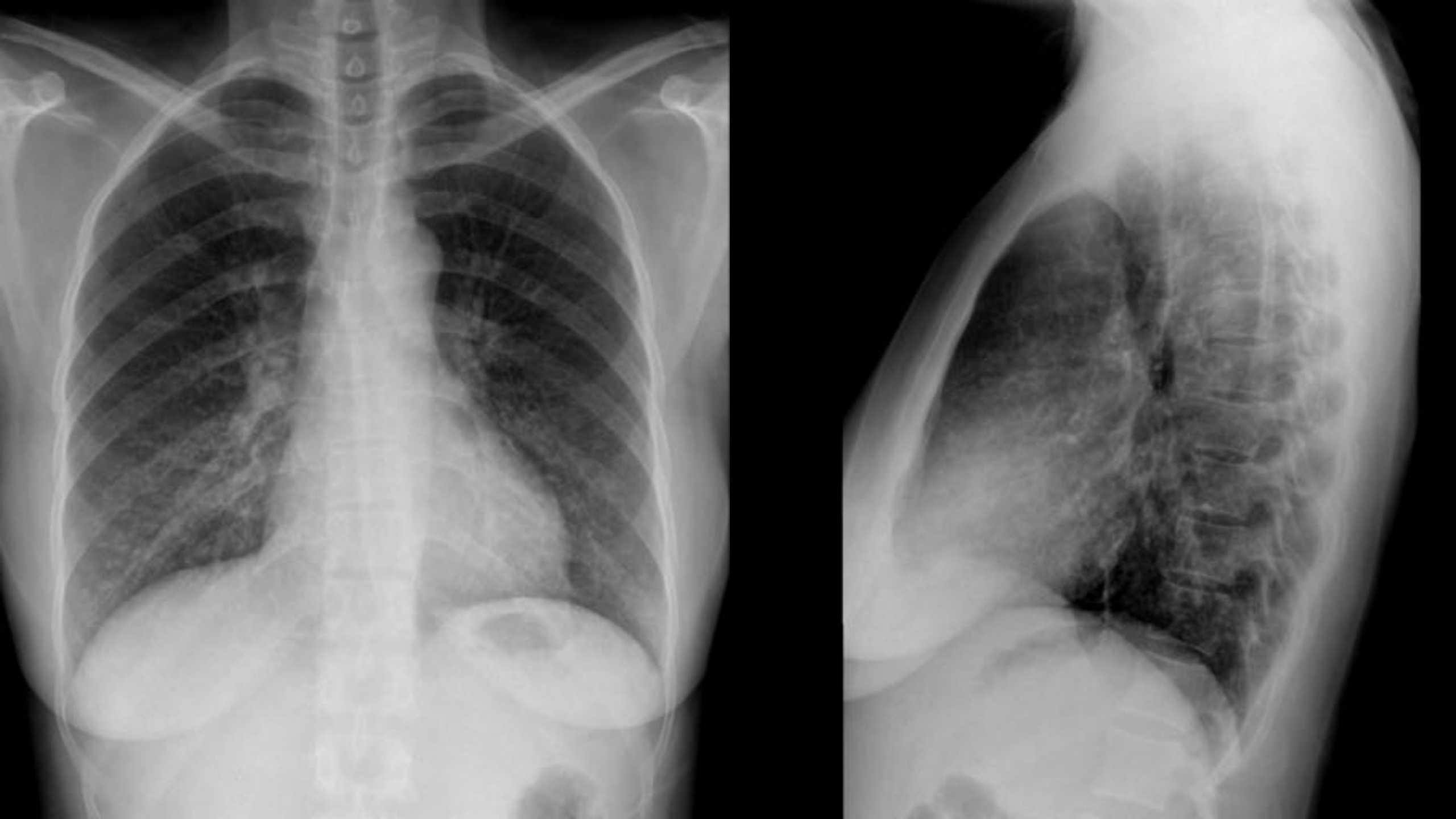
What else do you need to know:

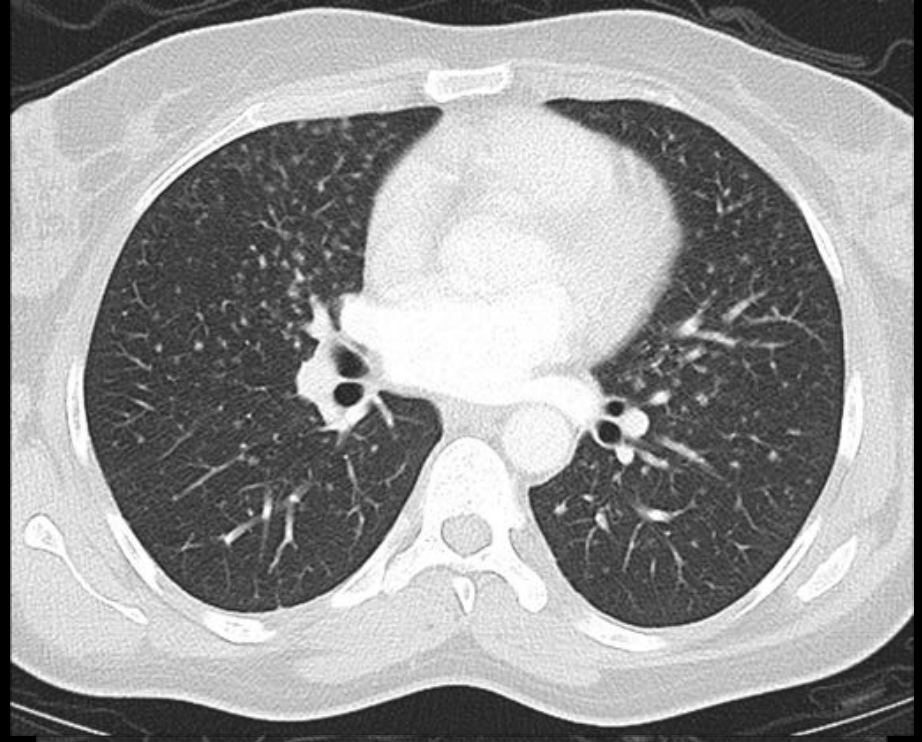
- Associated abnormalities
  - HIV/AIDS & Kaposi sarcoma
  - POEMS syndrome (polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, skin changes)
- Most common signs/symptoms
  - Constitutional symptoms: Fever, weight loss, anorexia
  - Hepatosplenomegaly
- 20% of patients with MCD develop lymphoma
- Treatment
  - Chemotherapy, corticosteroids, radiation therapy

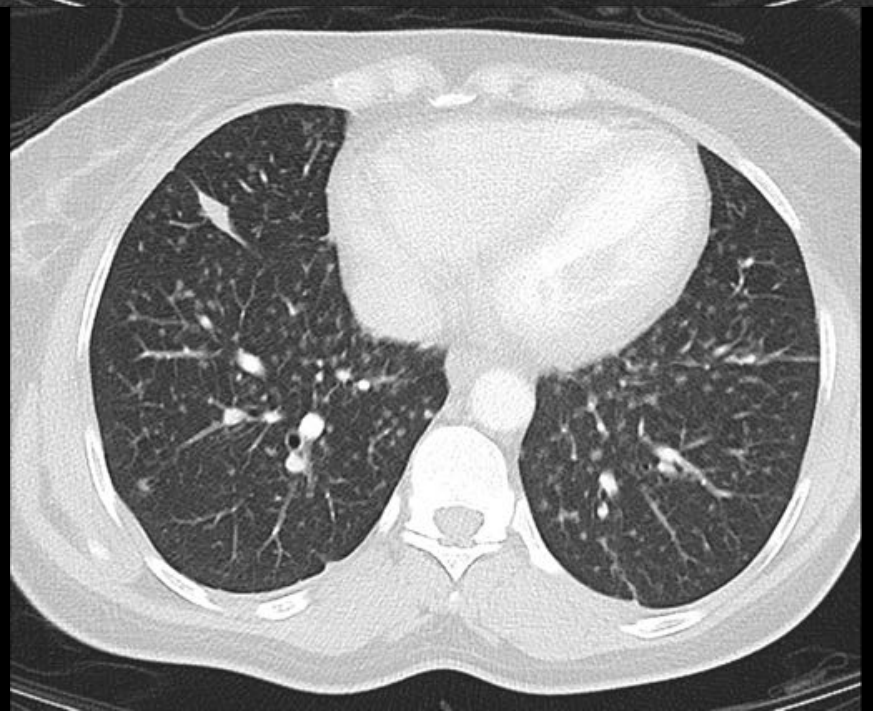
Case 4

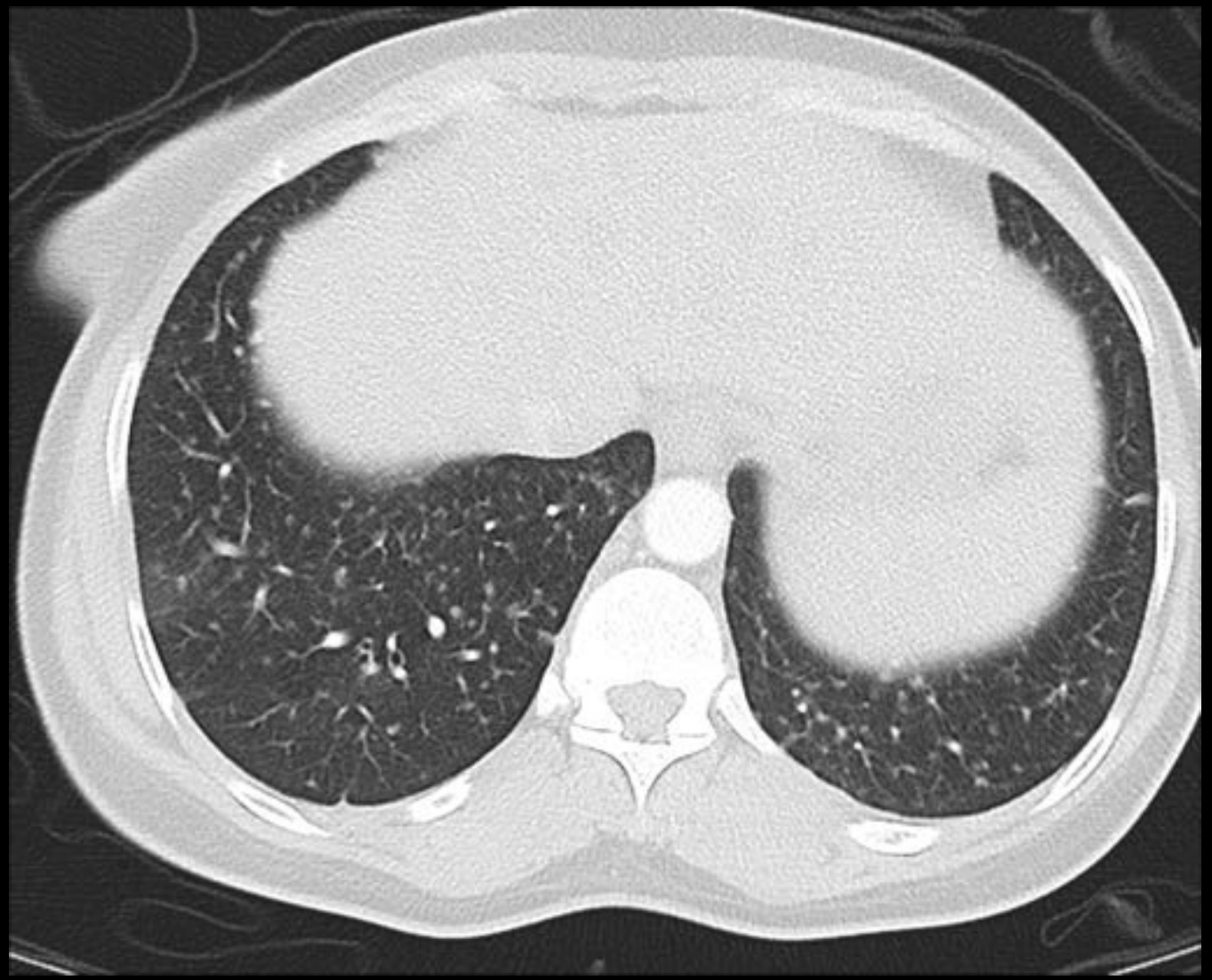
- 43-year-old female with HIV/AIDS (diagnosed 2004; sporadic adherence to ART; CD4 54, VL 121,686), who presents with fevers, abdominal and lower back pain for 2 weeks.

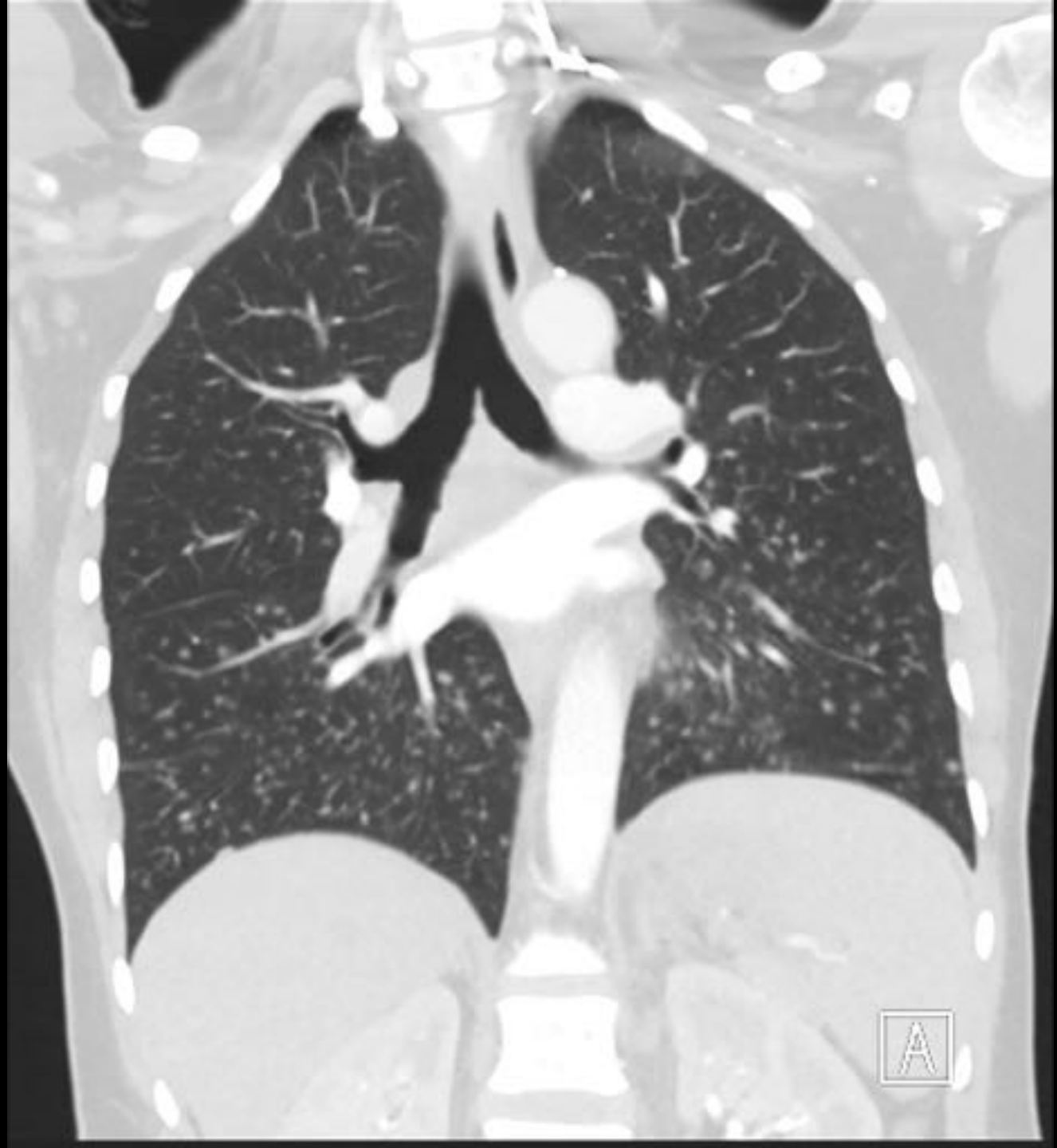
Case 4 – Radiology







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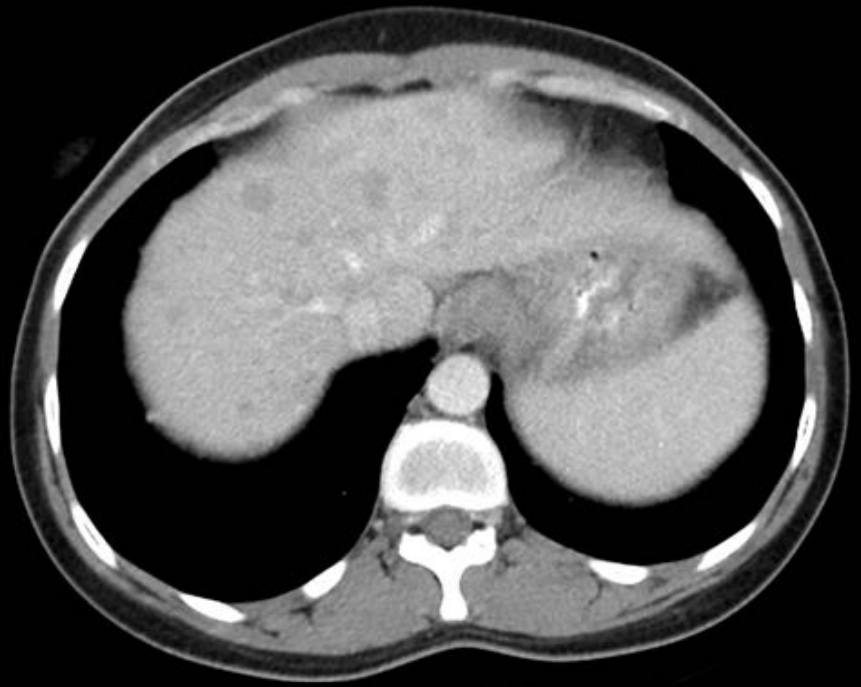
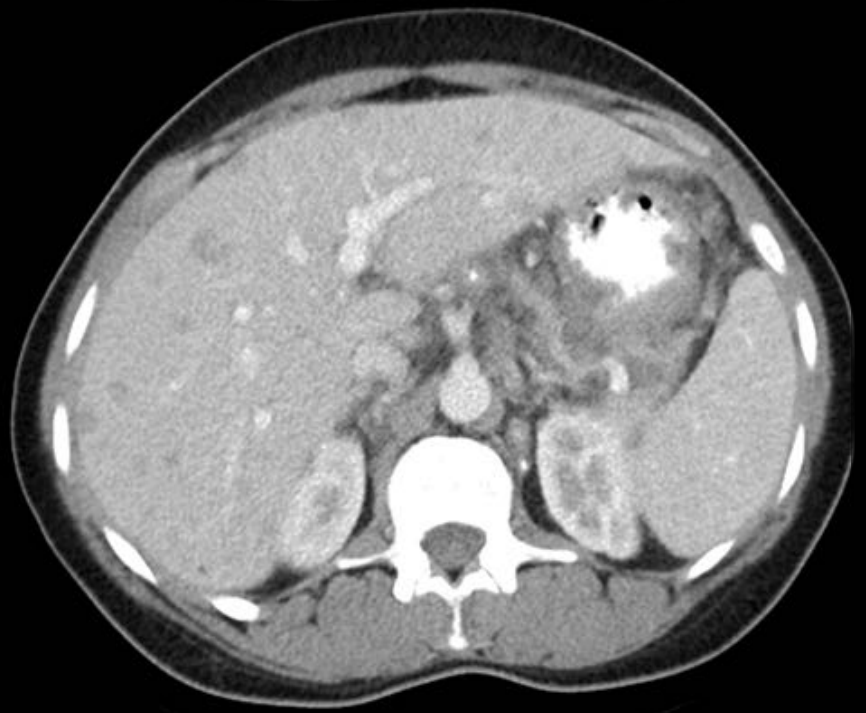
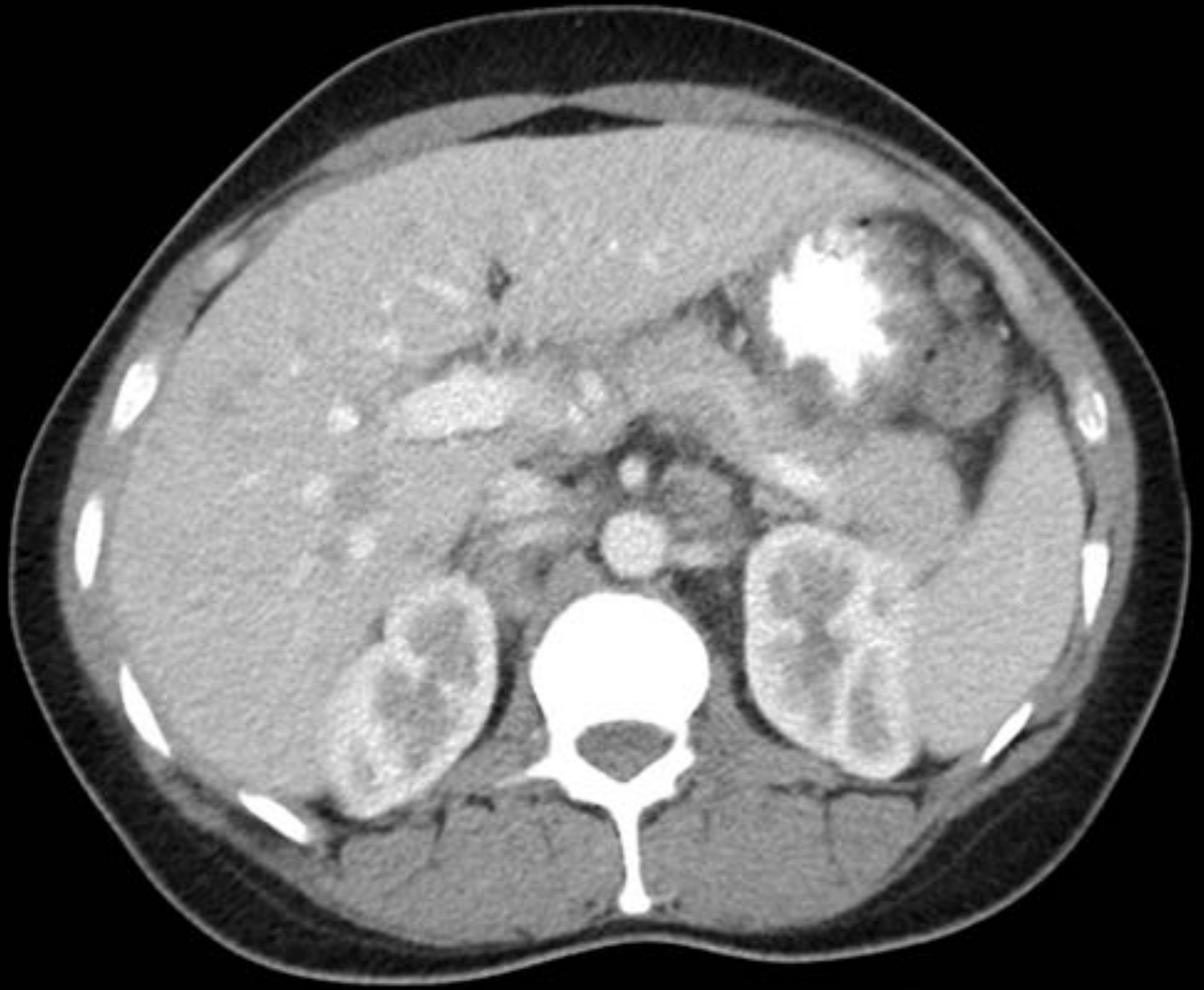
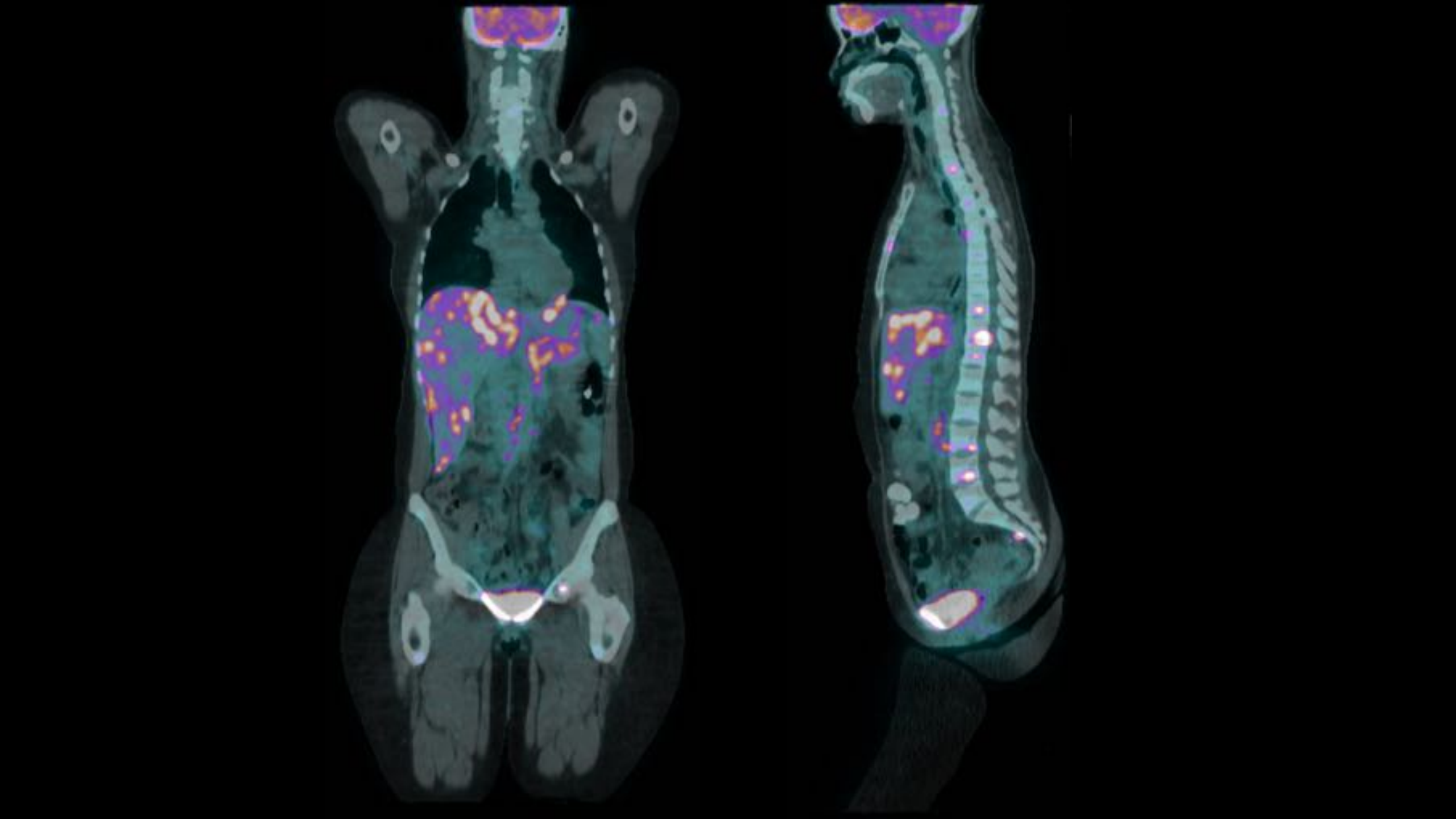








Case 4 – Findings

CXR

Diffuse ill-defined nodules at lung bases

CT chest

Innumerable sub-5 mm pulmonary nodules in both lungs

PET/CT

Diffusely scattered FDG-avid hepatic lesions

Mild FDG uptake along the scattered subcentimeter periaortic lymph nodes, and prominent gastrohepatic and gastrosplenic lymph nodes

Focal right pelvic FDG uptake may represent right pelvic lymphadenopathy and mild focal FDG uptake along the left pelvic wall

Diffusely scattered FDG-avid foci throughout the scapula, sternum, ribs, thoracolumbar spine, pelvis, and proximal bilateral femurs

Case 4 – Differential

Case 4 – Differential

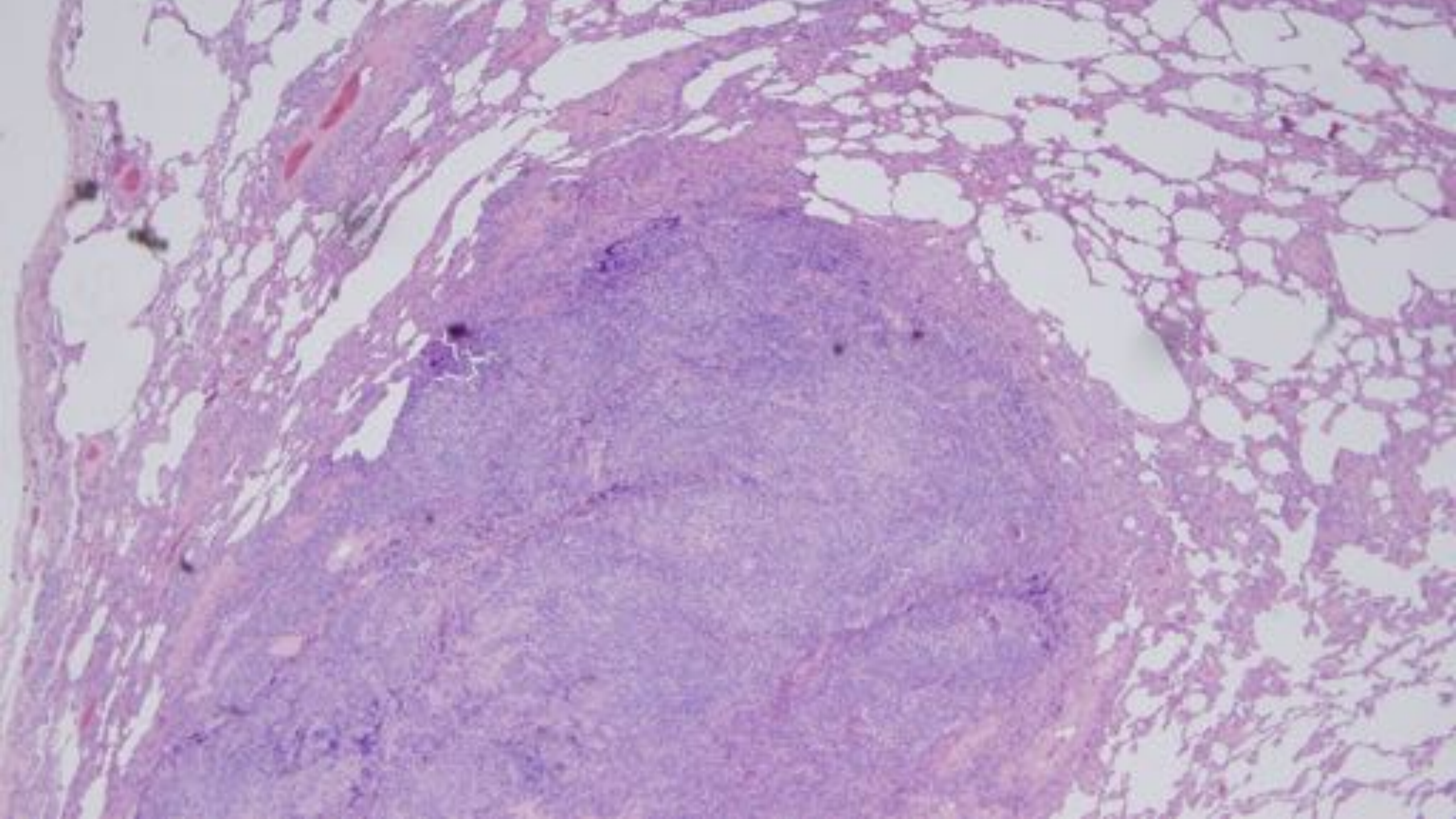
- Diffuse metastatic disease
- Lymphoma

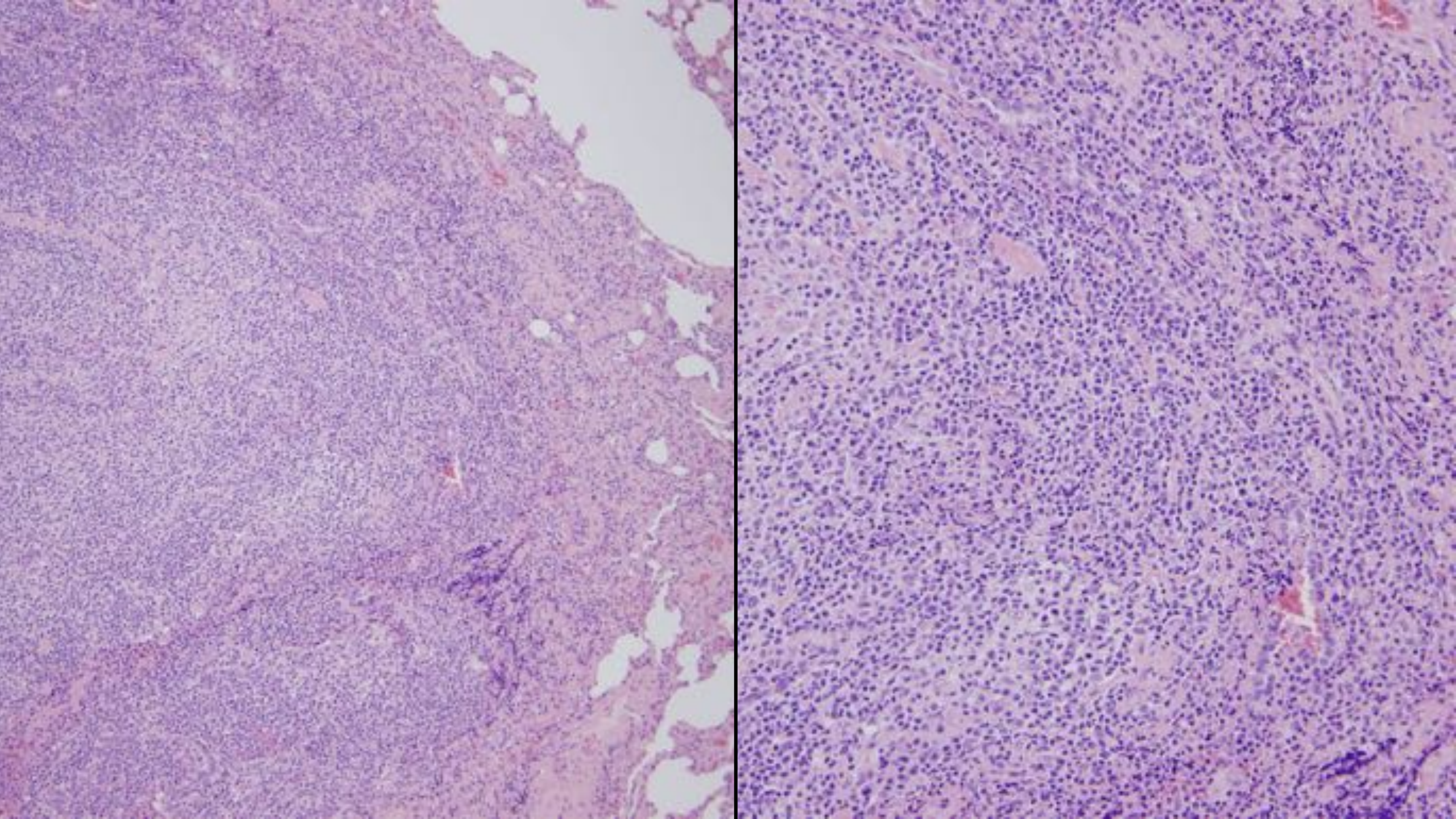
Case 4 – Pathology

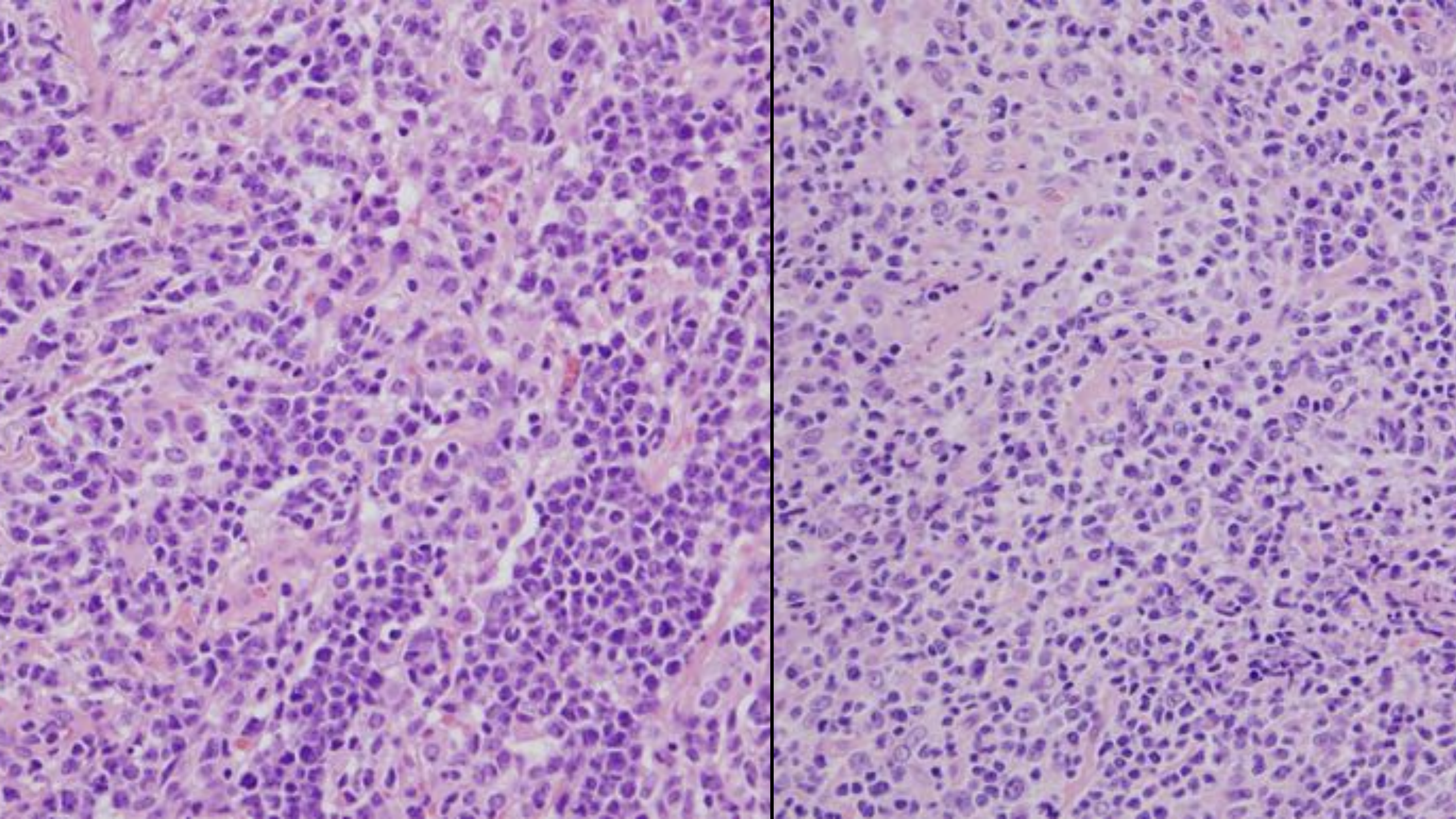
BS-17-53772

Wedge resection

Date of procedure: 9/21/2017







A. LUNG, RIGHT UPPER LOBE, WEDGE RESECTION:

Involvement by DIFFUSE LARGE B-CELL LYMPHOMA, NOT OTHERWISE SPECIFIED (see NOTE).

B. LUNG, RIGHT MIDDLE LOBE, WEDGE RESECTION:

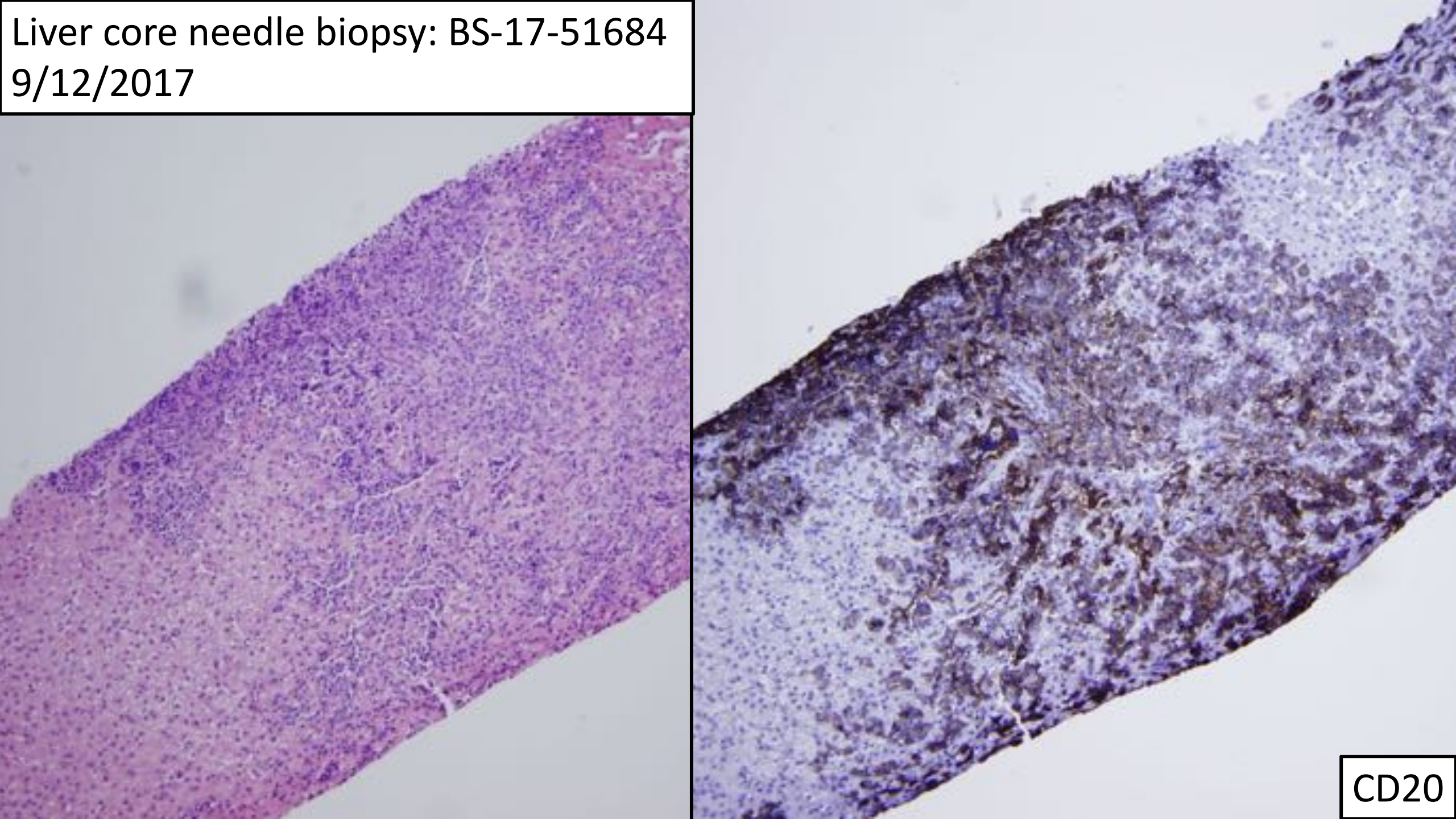
Involvement by DIFFUSE LARGE B-CELL LYMPHOMA, NOT OTHERWISE SPECIFIED (see NOTE).

C. LUNG, RIGHT LOWER LOBE, WEDGE RESECTION *:

Involvement by DIFFUSE LARGE B-CELL LYMPHOMA, NOT OTHERWISE SPECIFIED (see NOTE).

Note: The morphologic features are consistent with involvement DIFFUSE LARGE B-CELL LYMPHOMA, NOS, arising in the setting of HIV infection. Also, see liver biopsy report (BS-17-51684) for cell-of-origin classification and more detailed immunohistochemical characterization.

Liver core needle biopsy: BS-17-51684
9/12/2017

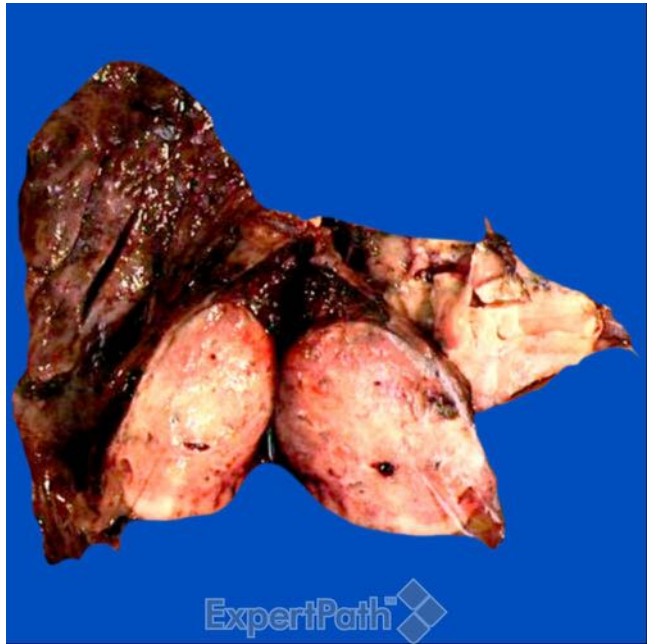


CD20

Diffuse Large B-Cell Lymphoma

Macroscopic

- Well-circumscribed, tan-white tumor mass with rubbery cut surface



Microscopic

- Sheets of large lymphoid cells with irregularly shaped, vesicular nuclei and prominent nucleoli
- Tumors show sharp interface with surrounding lung parenchyma
- Positive for CD20 and CD79-α and show kappa/lambda light chain reaction

ExpertPath

Case 4 – Diffuse Large B-Cell Lymphoma

The what:

- Most common histologic subtype of NHL (~ 30%)
- Pulmonary involvement by NHL: Hematogenous, contiguous invasion, or primary pulmonary lymphoma
  - 40-45% of NHL patients present with intrathoracic disease

The where:

- Pulmonary involvement more frequently disseminated/recurrent disease than primary lymphoma
- Perilymphatic: Along bronchovascular bundles, interlobular septa, and subpleural regions

The who:

- Consider in patients with chronic multifocal nodules, masses, or consolidations not responsive to antimicrobials
- Associated with: Solid organ transplantation with immunosuppression, HIV, Sjögren syndrome, EBV infection, environmental exposure (e.g., pesticides and solvents)

Case 4 – Diffuse Large B-Cell Lymphoma

What does it look like:

CXR

- Single or multiple lung nodules and masses
- Consolidations or ground-glass opacities
- Associated mediastinal or hilar lymphadenopathy
- Pleural effusion

Case 4 – Diffuse Large B-Cell Lymphoma

What does it look like:

CT

- Lymphadenopathy (most common)
  - Prevascular and pretracheal (75%), subcarinal (30%), hilar (20%), posterior mediastinal, paraaortic, paravertebral, and retrocrural (20%), paracardiac (10%)
- Solitary or multiple pulmonary nodules/masses of varying size
- Airspace opacity
  - Consolidation with air bronchograms
  - Ground-glass opacities ± interlobular septal thickening
  - Ill-defined opacities along bronchovascular bundles and interlobular septa
  - Atelectasis or postobstructive pneumonia from airway obstruction/compression by adjacent lymphadenopathy
- Pleural effusion (common): unilateral or bilateral, usually moderate-large

Case 4 – Diffuse Large B-Cell Lymphoma

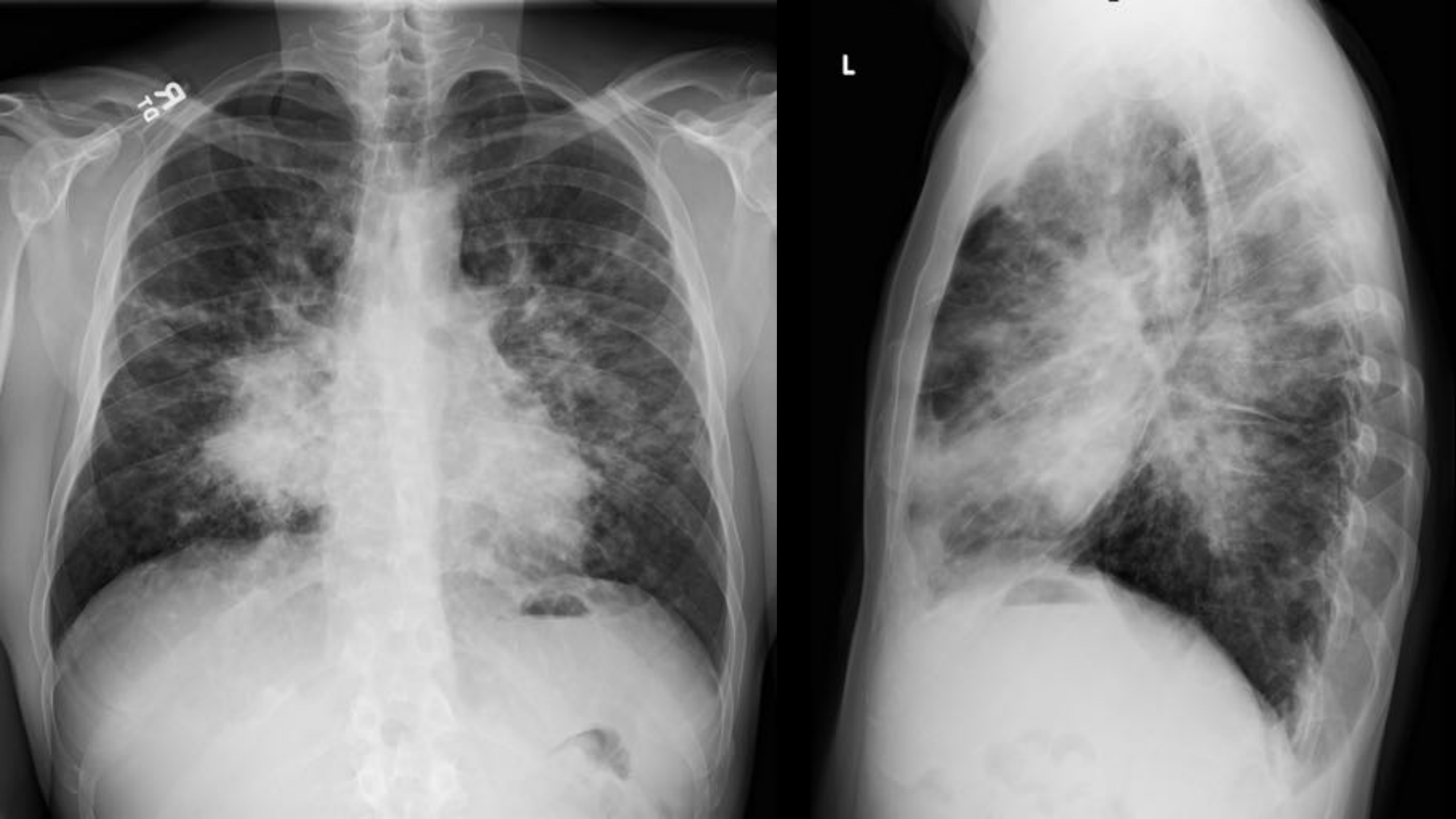
What else do you need to know:

- Symptoms/signs
  - Abdominal pain, nausea, vomiting, weight loss, fever, organomegaly, palpable lymphadenopathy
- Non-Hodgkin rather than Hodgkin lymphoma predominates in patients with HIV/AIDS, usually of high grade and of B cell or non-B–non-T cell origin
- Thoracic involvement reported in up to 40% of patients with AIDS-related lymphoma
  - Typically extranodal pulmonary involvement in the setting of disseminated disease, but primary pulmonary lymphoma has been reported
- Treatment
  - Limited-stage DLBCL: Chemotherapy with involved-field radiotherapy
  - Advanced stage DLBCL: Chemotherapy
  - Improved prognosis if receiving ART

Case 5

- 41-year-old male with HIV/AIDS (diagnosed 9/2017; on ART; CD4 40, VL <30), who presents with persistent dry cough, shortness of breath, and weight loss for 6 months.

Case 5 – Radiology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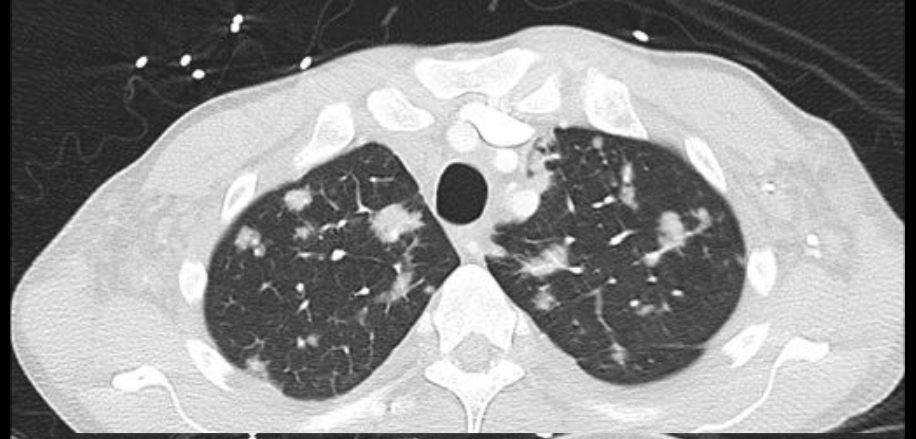
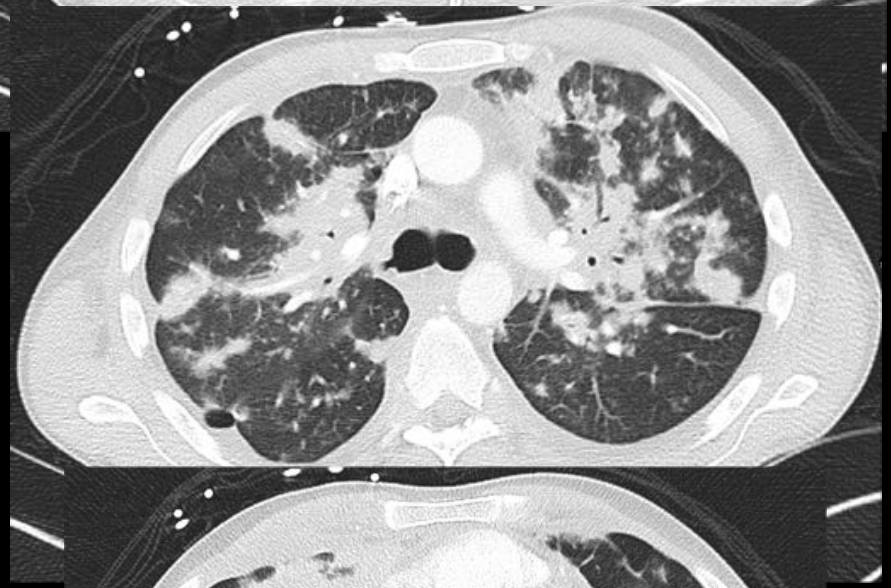
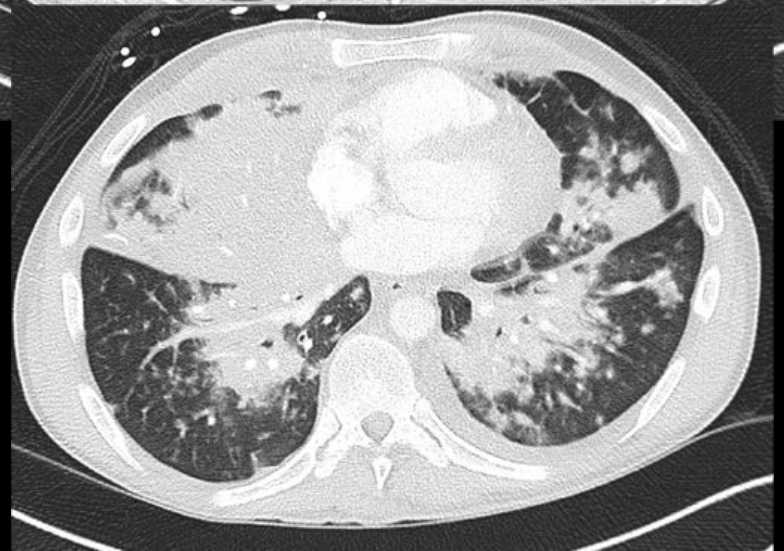
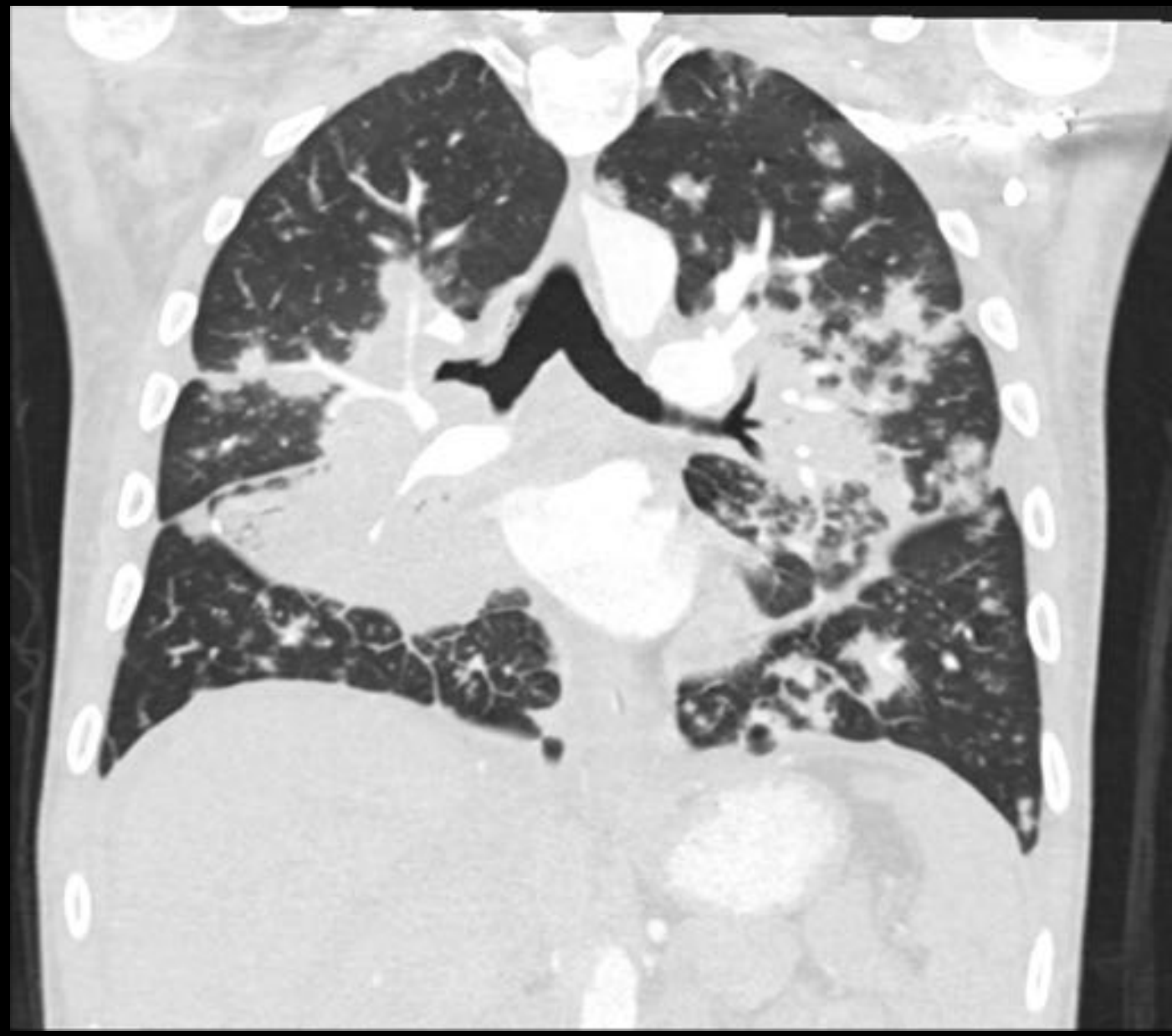
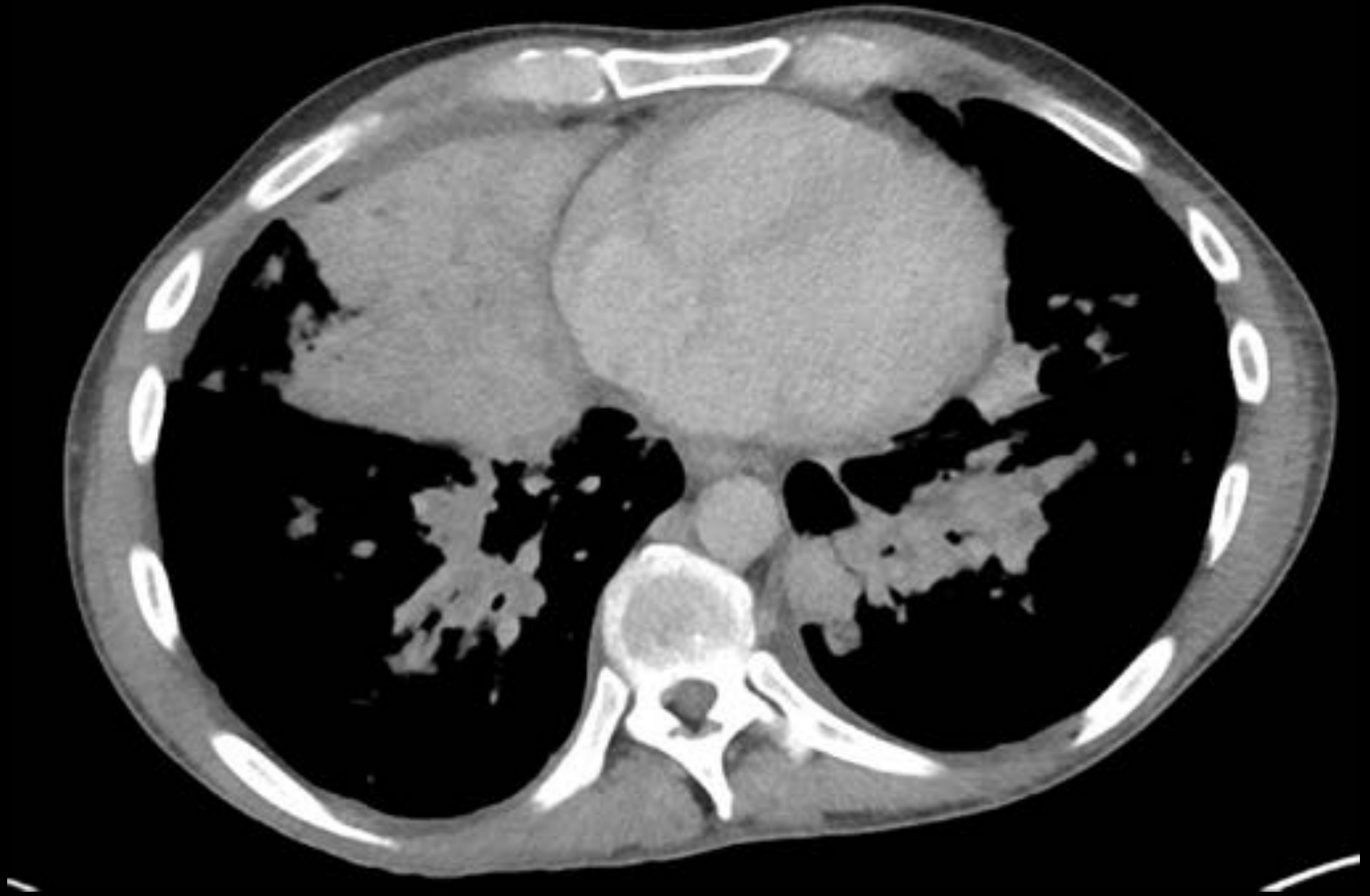










Lower lung fields on CT abdomen/pelvis

Case 5 – Findings

CXR

Diffuse, perihilar predominant nodules and confluent opacities

CT

Bilateral nodular septal thickening with soft tissue extending along the central bronchovascular bundles

Masslike consolidation in both upper and lower lobes

Bilateral ill-defined pulmonary nodules

Case 5 – Differential

Case 5 – Differential

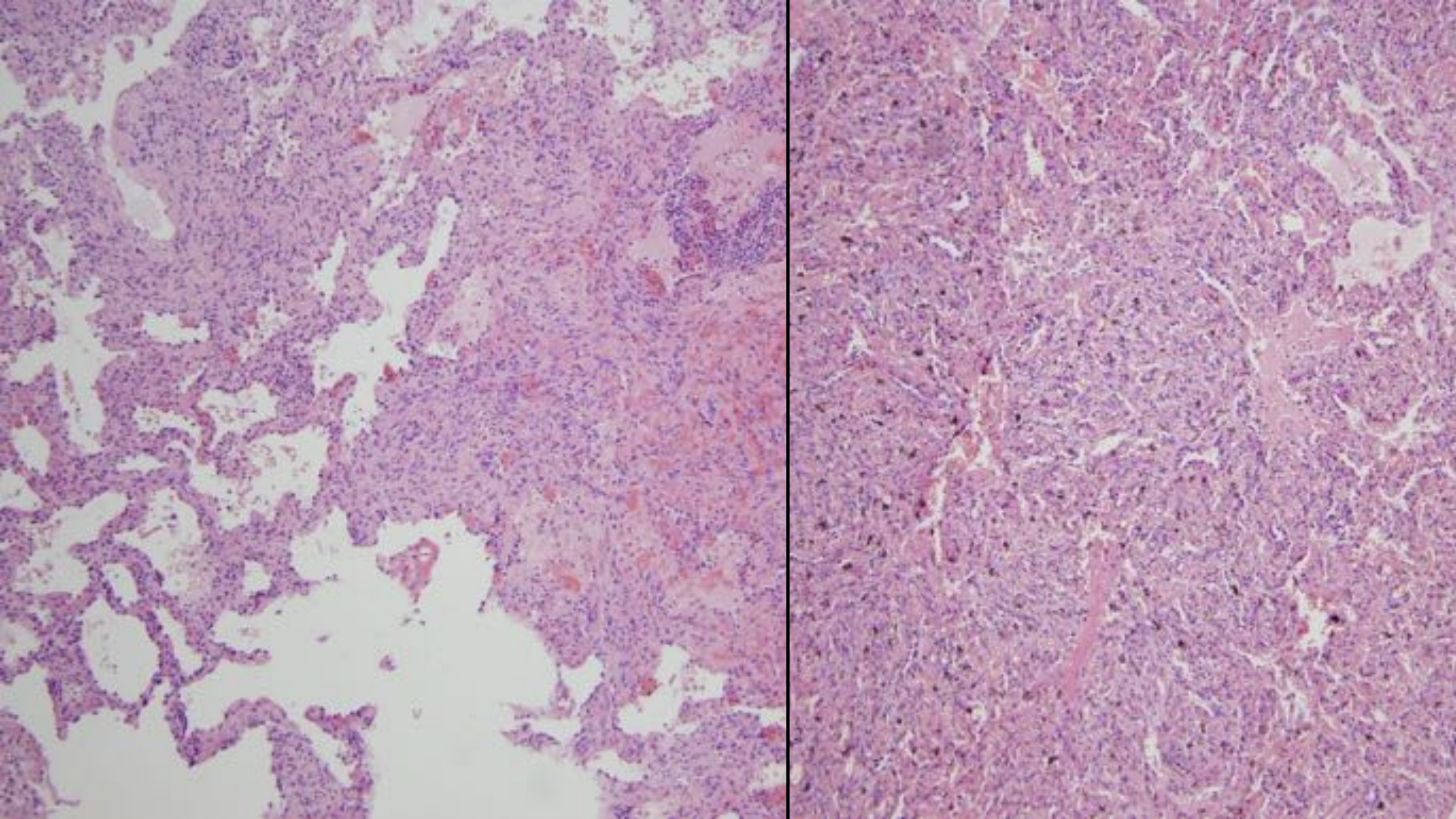
- Kaposi sarcoma
- Lymphoma – lung nodules vary in size but usually not as large as in this case, air bronchograms
- Lymphangitic carcinomatosis – unilateral distribution more likely if from primary lung cancer
- Sarcoidosis – lymphadenopathy more symmetric and does not typically enhance
- Bacillary angiomatosis – peribronchovascular thickening not as common
- Infectious bronchiolitis – nodules < 1 cm, centrilobular, tree-in-bud

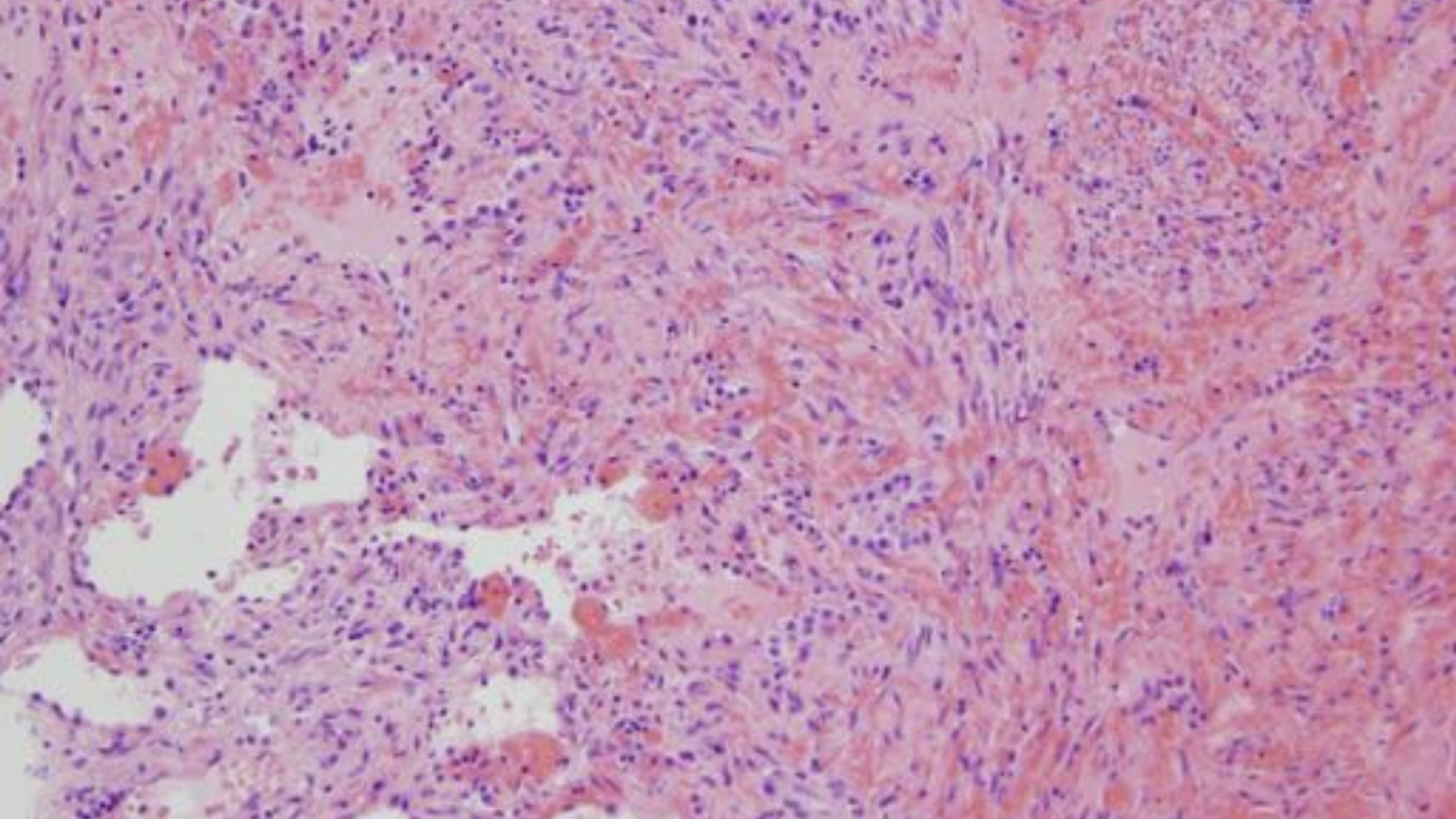
Case 5 – Pathology

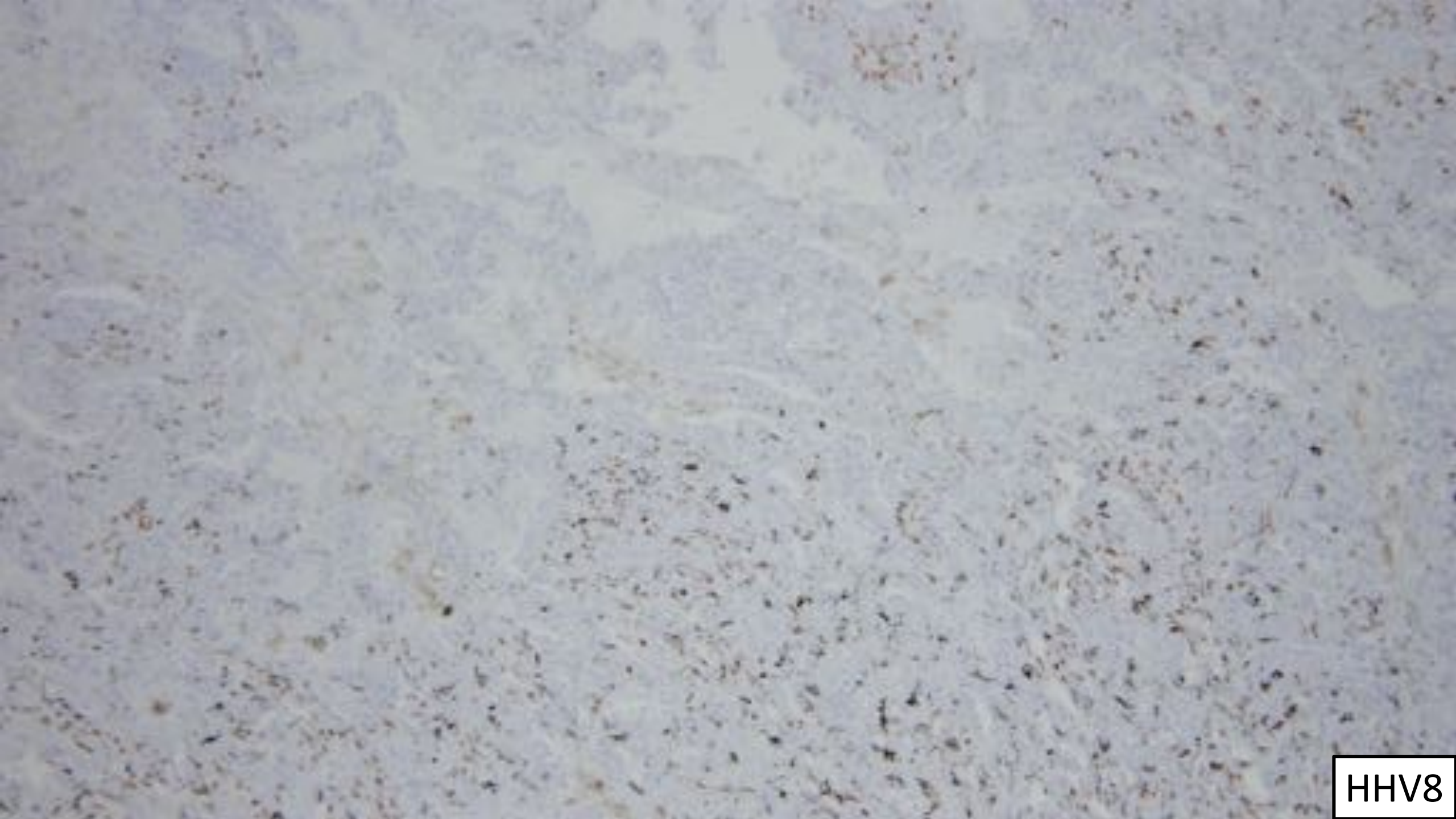
BS-18-08923

Wedge resection

Date of procedure: 1/26/2018






HHV8

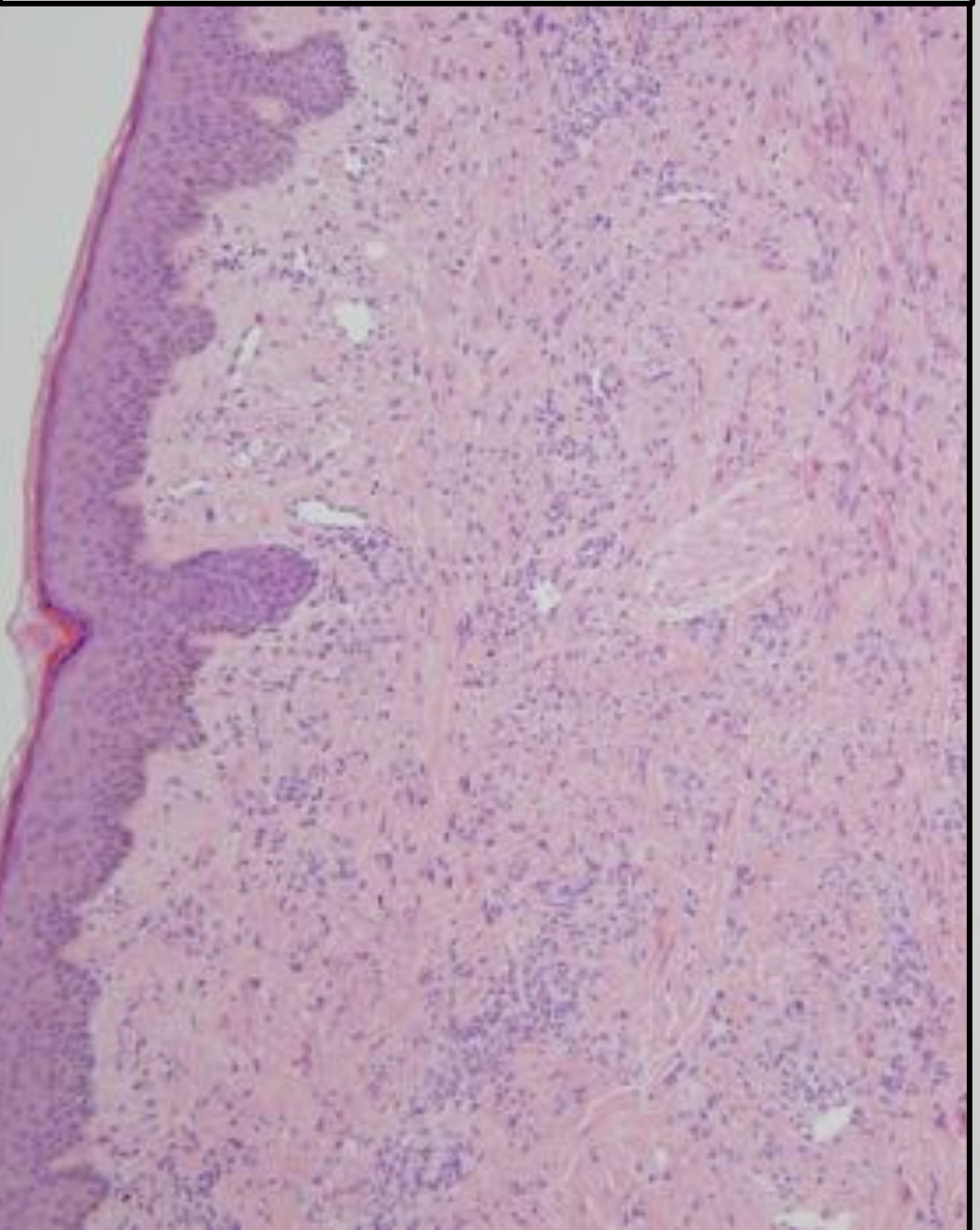
A. LUNG, RIGHT MIDDLE LOBE, WEDGE RESECTION:

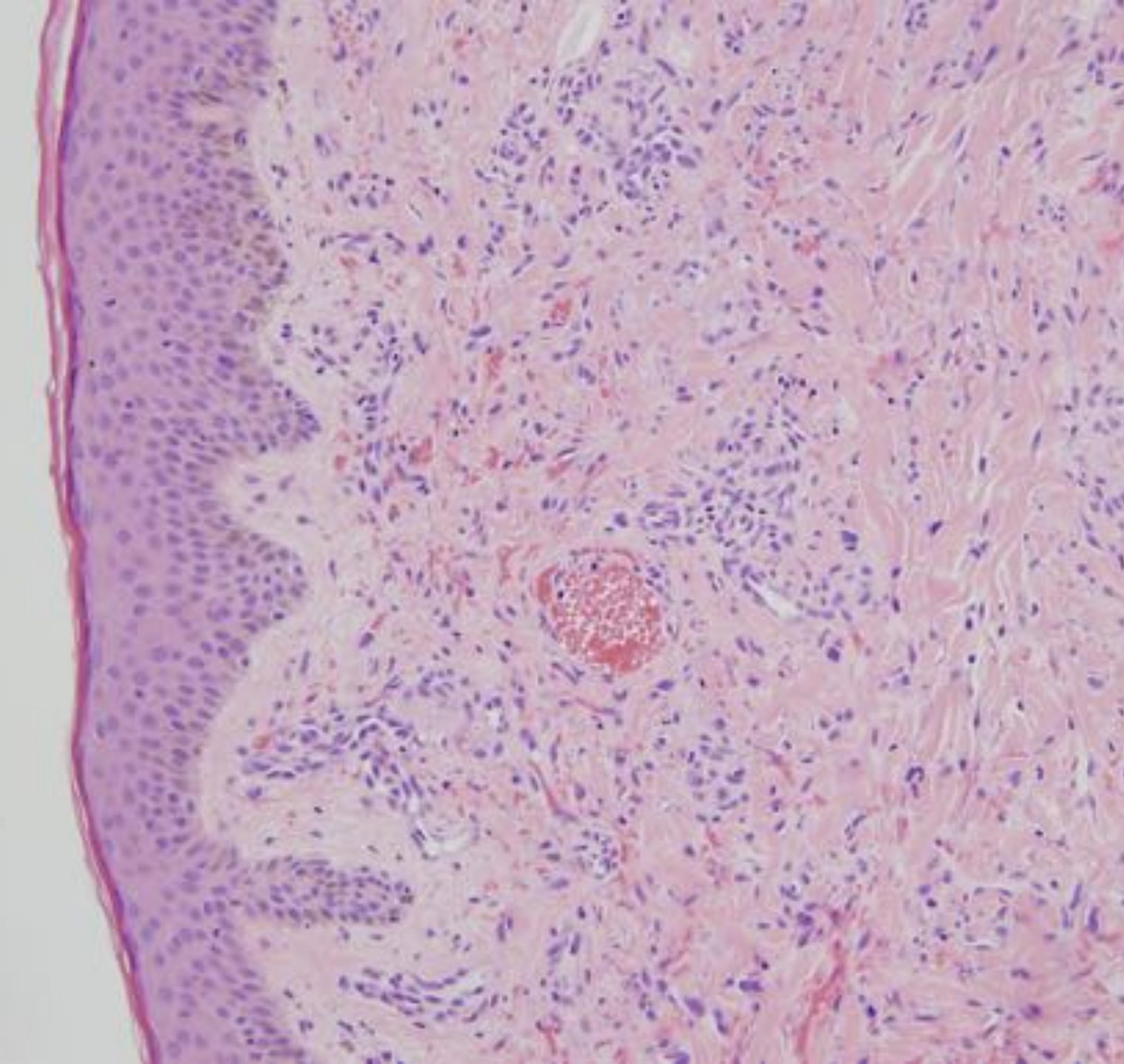
KAPOSI SARCOMA.

B. LUNG, RIGHT LOWER LOBE, WEDGE RESECTION:

KAPOSI SARCOMA.

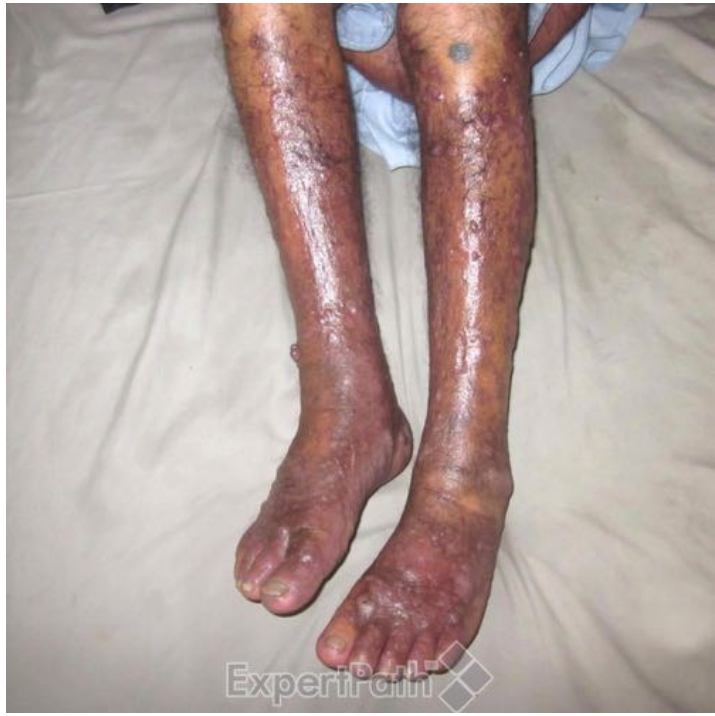
Skin, right upper back, punch biopsy: BS-18-08694
2/14/2018





Kaposi Sarcoma

- **Macroscopic**
  - Ill-defined, blueish-red intraparenchymatous nodules
- **Microscopic**
  - Monotonous spindle cell proliferation with fascicular growth pattern intersecting at right angles
  - Frequent anastomosing and slit-like vascular spaces containing abundant extravasated red blood cells
  - Scattered hyaline globules admixed with spindle cells
  - Abundant deposition of hemosiderin pigment in stroma
  - Spindle cells show mild to moderate cytologic atypia with scattered mitoses



Case 5 – Kaposi Sarcoma

The what:

- Multifocal polyclonal neoplasm, composed of a proliferation of vascular or lymphatic endothelial cells, primarily affecting skin
- Can cause disseminated disease: Lymphatic system, lungs, airways, abdominal viscera, etc.
- AIDS-KS vs. Iatrogenic KS (related to immunosuppression)

The where:

- Visceral organs affected: Lymph nodes (72%), lung (51%), GI tract (48%), liver (34%), spleen (27%)
- Thorax affected in 45% of all cases
  - Skin lesions present in 85% of patients with pulmonary involvement
- When associated with HIV/AIDS, skin lesions frequently absent

The who:

- MSM, HIV/AIDS
- Most common HIV/AIDS-related neoplasm; decreased prevalence with ART

Case 5 – Kaposi Sarcoma

What does it look like:

CXR

- Mid to lower lung zone nodular or coalescent masslike opacities in perihilar and peribronchovascular distribution
- Ill-defined pulmonary nodules
- Cavitation may occur with concomitant opportunistic infection

Case 5 – Kaposi Sarcoma

What does it look like:

CT

- Segmental, lobar-shaped, or masslike opacities due to the tumor itself, may contain air bronchograms
- Nodules
  - Bilateral, symmetric, poorly marginated, emanating from hila (flame-shaped)
  - Peribronchovascular with tendency to coalesce, usually > 1 cm in diameter
  - Ground-glass opacities surrounding nodules (CT halo sign)
  - Cavitary nodules often associated with opportunistic infection, such as *Pneumocystis jirovecii* pneumonia
- Thickened interlobular septa and fissural nodularity
- Smooth or nodular thickening of bronchovascular bundles
- Lymphadenopathy
  - Axillary, mediastinal, hilar
  - Often enhances with contrast
- Pleural effusions (common)

Case 5 – Kaposi Sarcoma

What else do you need to know:

- Most common signs/symptoms
  - Dyspnea, cough, fever, recurrent pneumonia
  - CD4+ < 150-200 cells/µL
  - Hemoptysis
- Etiology
  - Human herpesvirus type 8 (HHV8 or KS-associated herpesvirus)
    - Also associated with primary effusion lymphoma and multicentric Castleman disease
- Majority of those affected have cutaneous disease, and over half also have oropharyngeal lesions; much smaller proportion have bronchopulmonary involvement
- In most cases, cutaneous findings of KS precede visceral involvement
- Treatment
  - ART ± chemotherapy

Unknown Case Review

Unknown Case

Diagnosis?

DLBCL

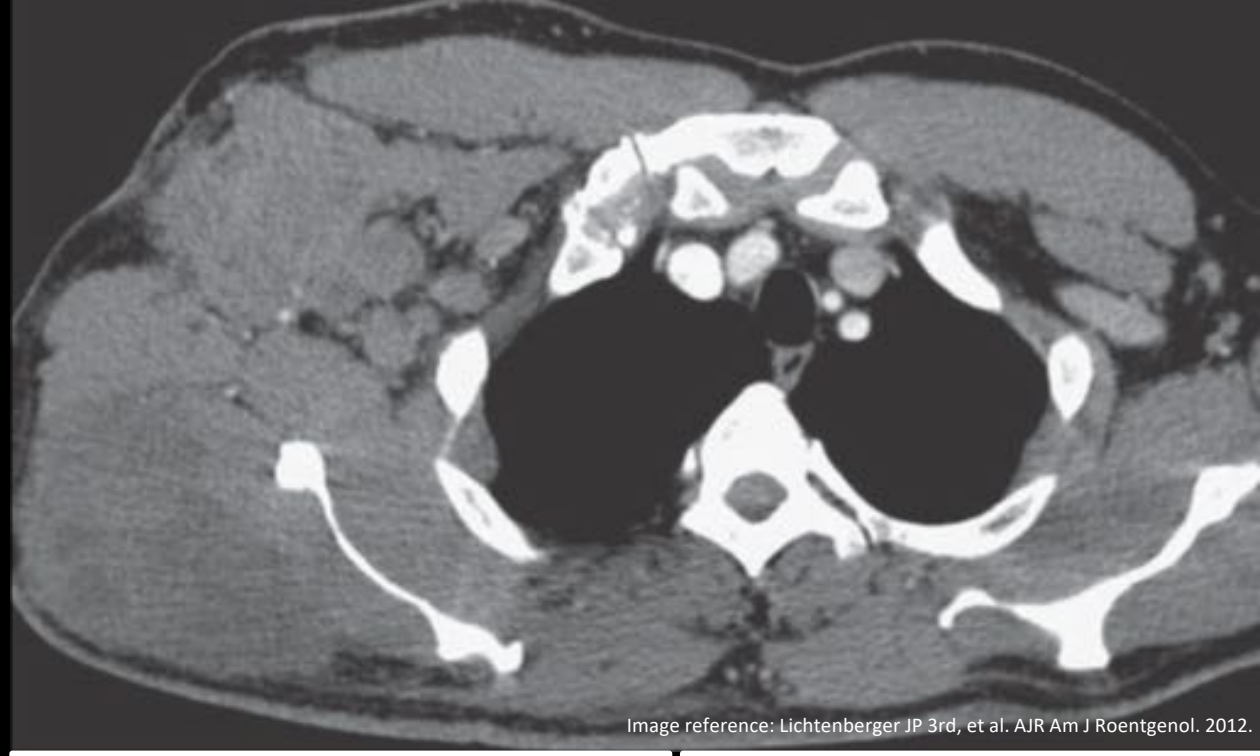
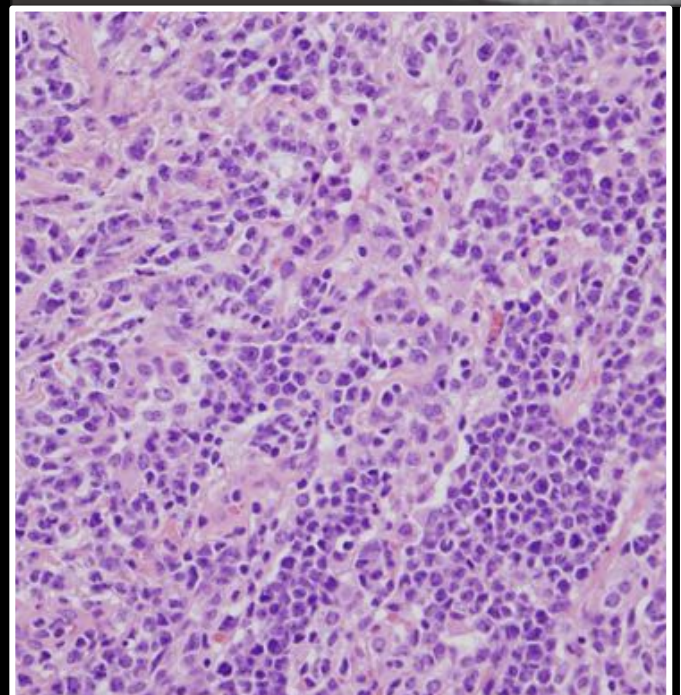
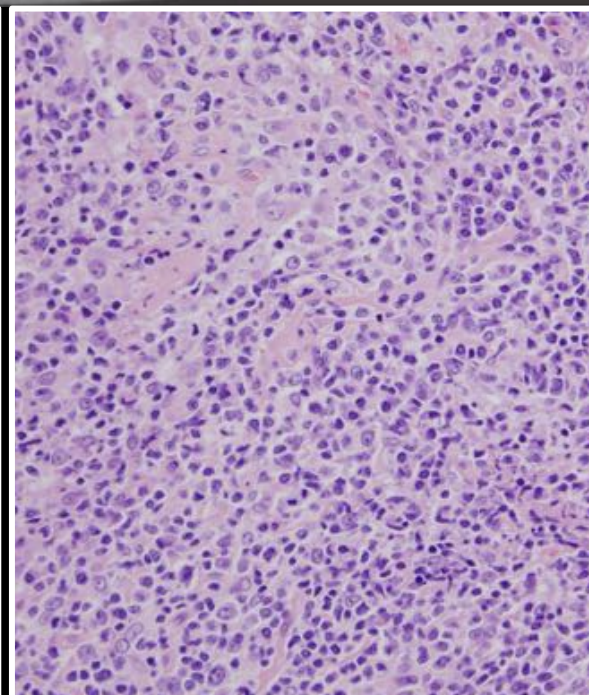


Image reference: Lichtenberger JP 3rd, et al. AJR Am J Roentgenol. 2012.

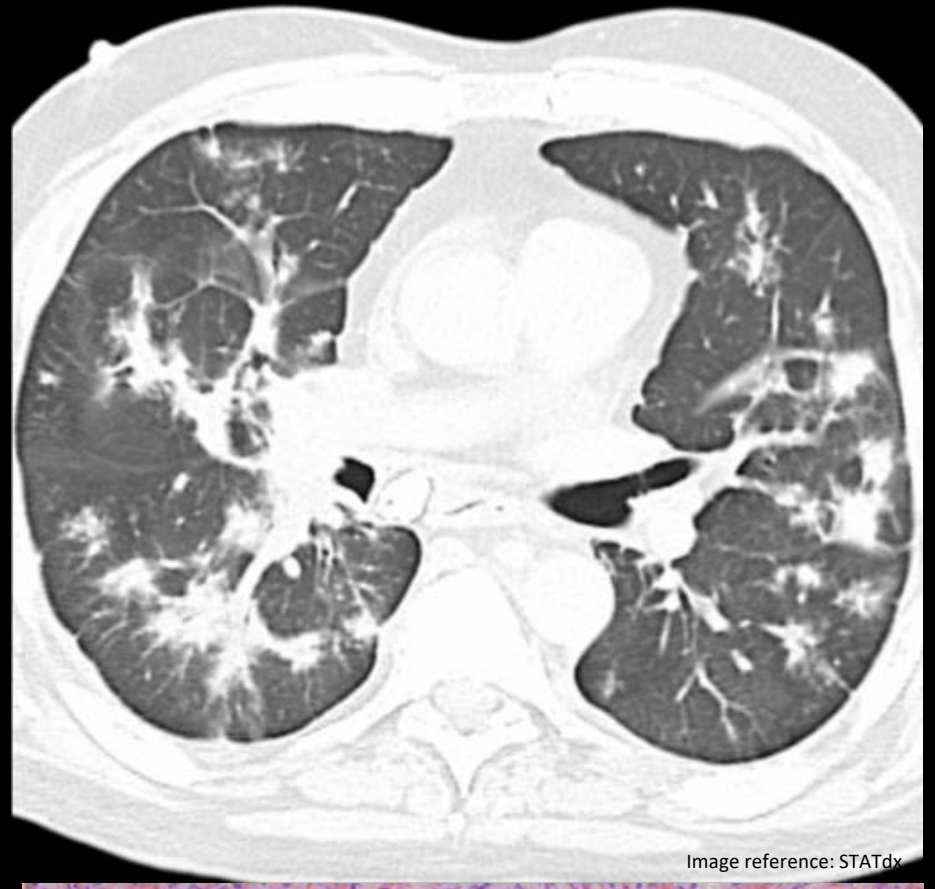




Unknown Case

Diagnosis?

Kaposi Sarcoma



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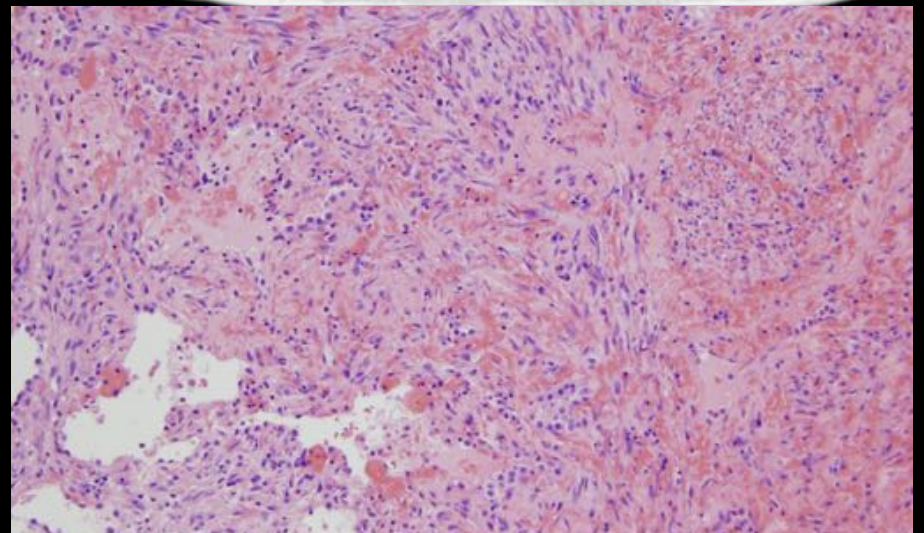
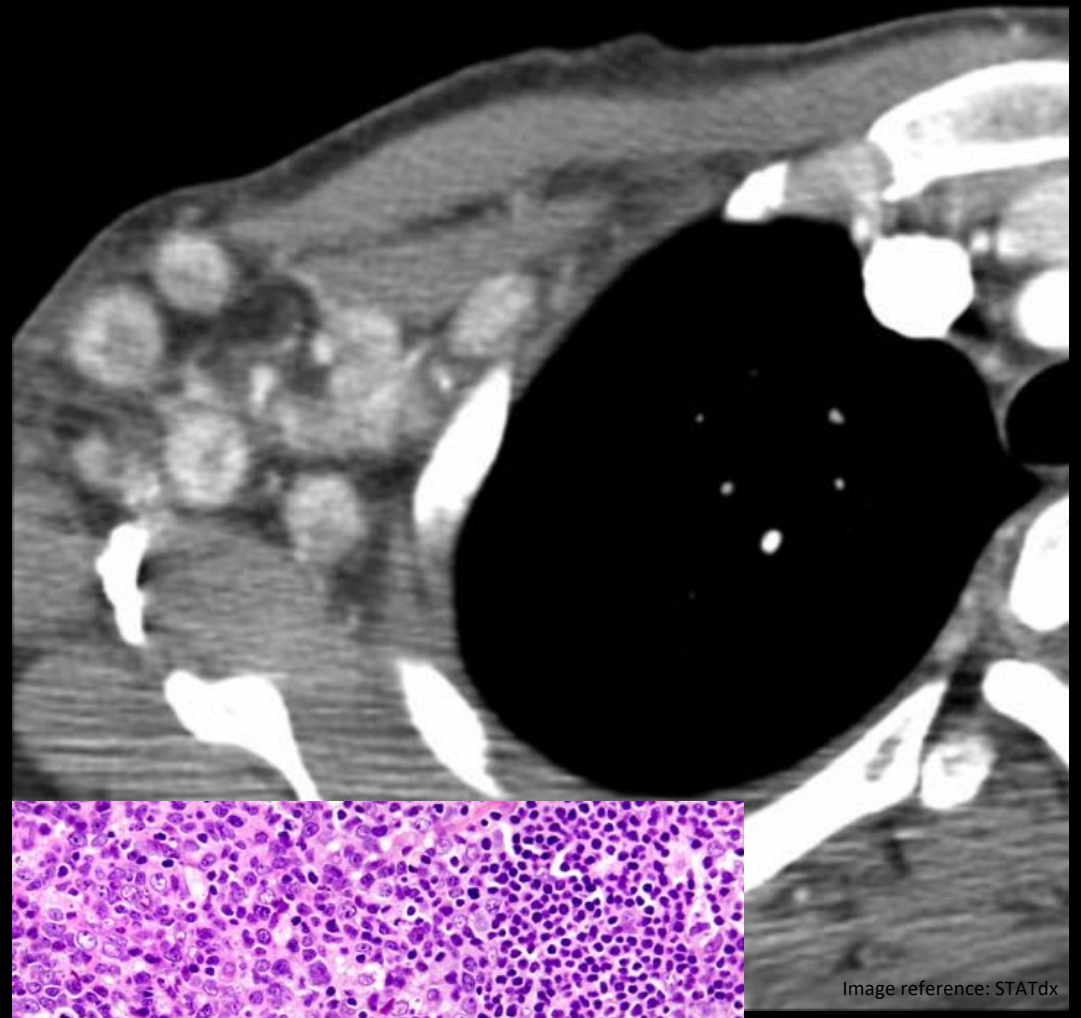


Unknown Case

Diagnosis?

Multicentric Castleman Disease



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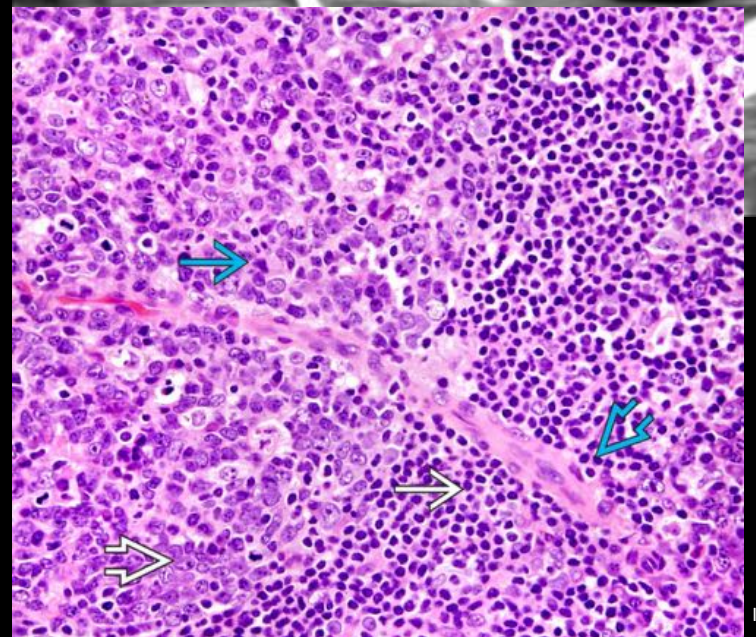
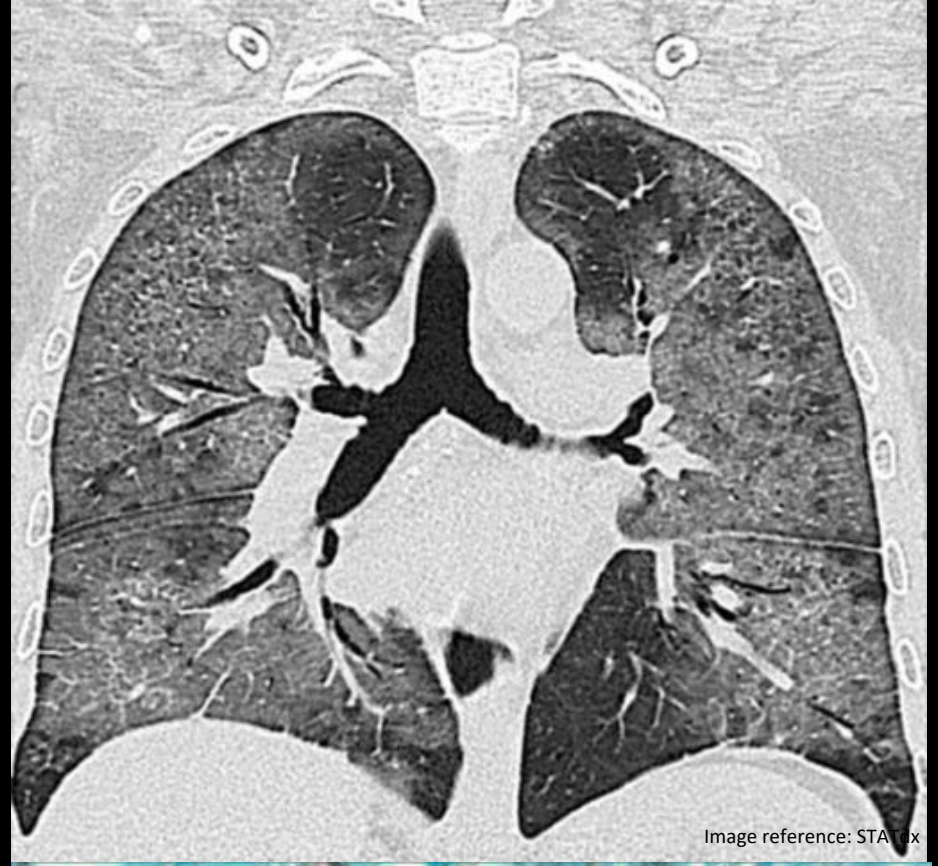


Image reference: ExpertPath

Unknown Case

Diagnosis?

PCP pneumonia



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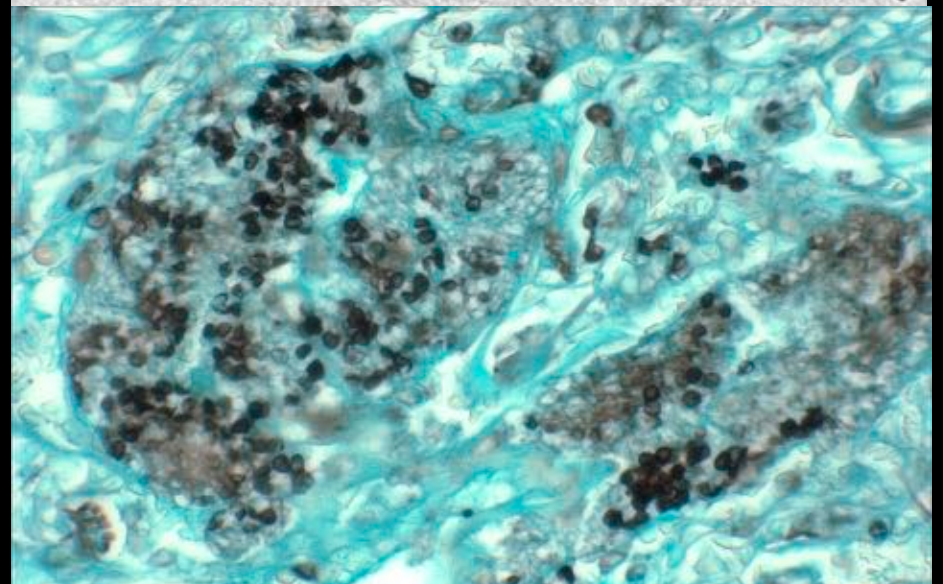
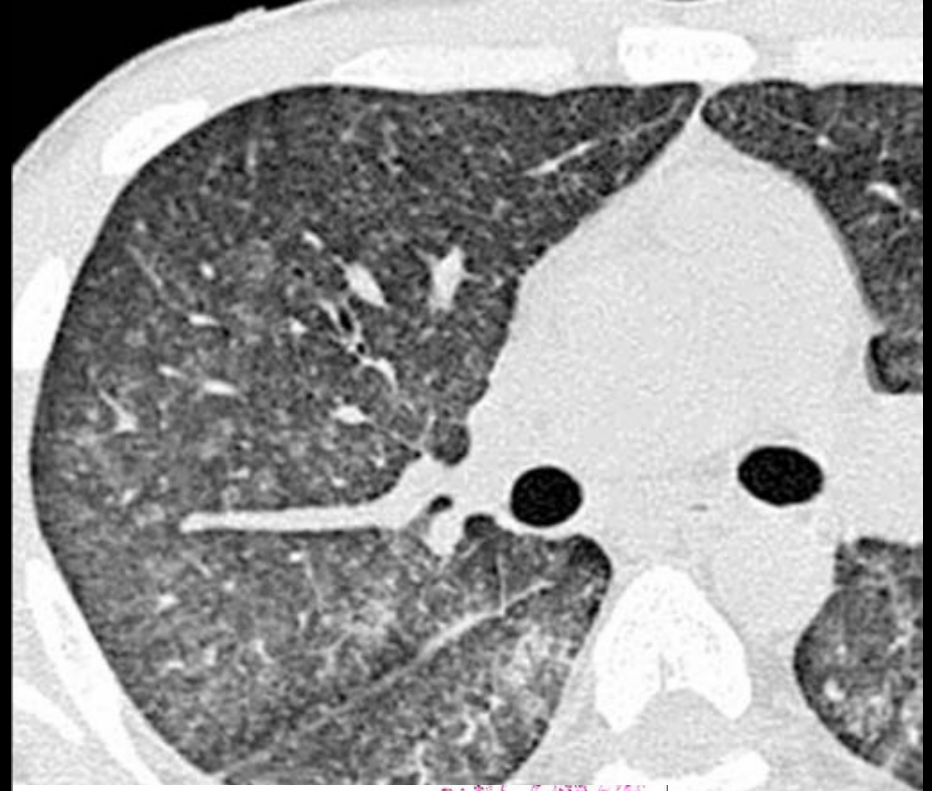


Unknown Case

Diagnosis?

TB



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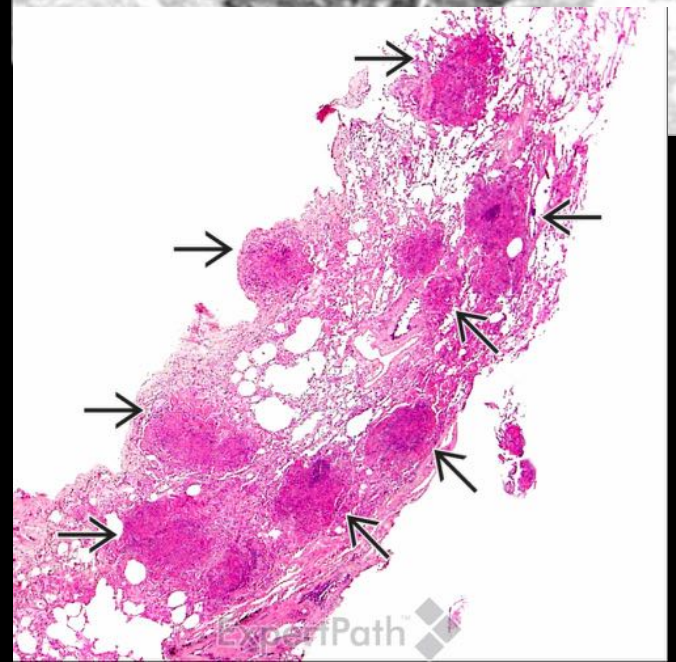

Thank you

- Rachna Madan, MD – advisor for this presentation

References

- Castañer E, Gallardo X, Mata JM, Esteba L. Radiologic approach to the diagnosis of infectious pulmonary diseases in patients infected with the human immunodeficiency virus. Eur J Radiol. 2004 Aug;51(2):114-29. Review. PubMed PMID: 15246517.
- Chou SH, Prabhu SJ, Crothers K, Stern EJ, Godwin JD, Pipavath SN. Thoracic diseases associated with HIV infection in the era of antiretroviral therapy: clinical and imaging findings. Radiographics. 2014 Jul-Aug;34(4):895-911. doi: 10.1148/rg.344130115. PubMed PMID: 25019430; PubMed Central PMCID: PMC4319520.
- Edinburgh KJ, Jasmer RM, Huang L, Reddy GP, Chung MH, Thompson A, Halvorsen RA Jr, Webb RA. Multiple pulmonary nodules in AIDS: usefulness of CT in distinguishing among potential causes. Radiology. 2000 Feb;214(2):427-32. PubMed PMID: 10671590.
- Hansell, D., et al. (2010). The immunocompromised patient. In *Imaging of diseases of the chest*. 5th ed. Edinburgh: Mosby/Elsevier.
- Lichtenberger JP 3rd, Sharma A, Zachary KC, Krishnam MS, Greene RE, Shepard JA, Wu CC. What a differential a virus makes: a practical approach to thoracic imaging findings in the context of HIV infection--part 1, pulmonary findings. AJR Am J Roentgenol. 2012 Jun;198(6):1295-304. doi: 10.2214/AJR.11.8003. Review. Erratum in: AJR Am J Roentgenol. 2013 Dec;201(6):1407. PubMed PMID: 22623541.
- Lichtenberger JP 3rd, Sharma A, Zachary KC, Krishnam MS, Greene RE, Shepard JA, Wu CC. What a differential a virus makes: a practical approach to thoracic imaging findings in the context of HIV infection--part 2, extrapulmonary findings, chronic lung disease, and immune reconstitution syndrome. AJR Am J Roentgenol. 2012 Jun;198(6):1305-12. doi: 10.2214/AJR.11.8004. Review. PubMed PMID: 22623542.
- National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, Division of HIV/AIDS Prevention, CDC. Estimated HIV Incidence and Prevalence in the United States, 2010–2015. Accessed at: https://www.cdc.gov/hiv/library/slidesets/index.html
- National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, Division of HIV/AIDS Prevention, CDC. Selected National HIV Prevention and Care Outcomes. Accessed at: https://www.cdc.gov/hiv/library/slidesets/index.html
- Rosen MJ. Pulmonary complications of HIV infection. Respirology. 2008 Mar;13(2):181-90. doi: 10.1111/j.1440-1843.2007.01167.x. Review. PubMed PMID: 18339015.
- STATdx
- ExpertPath