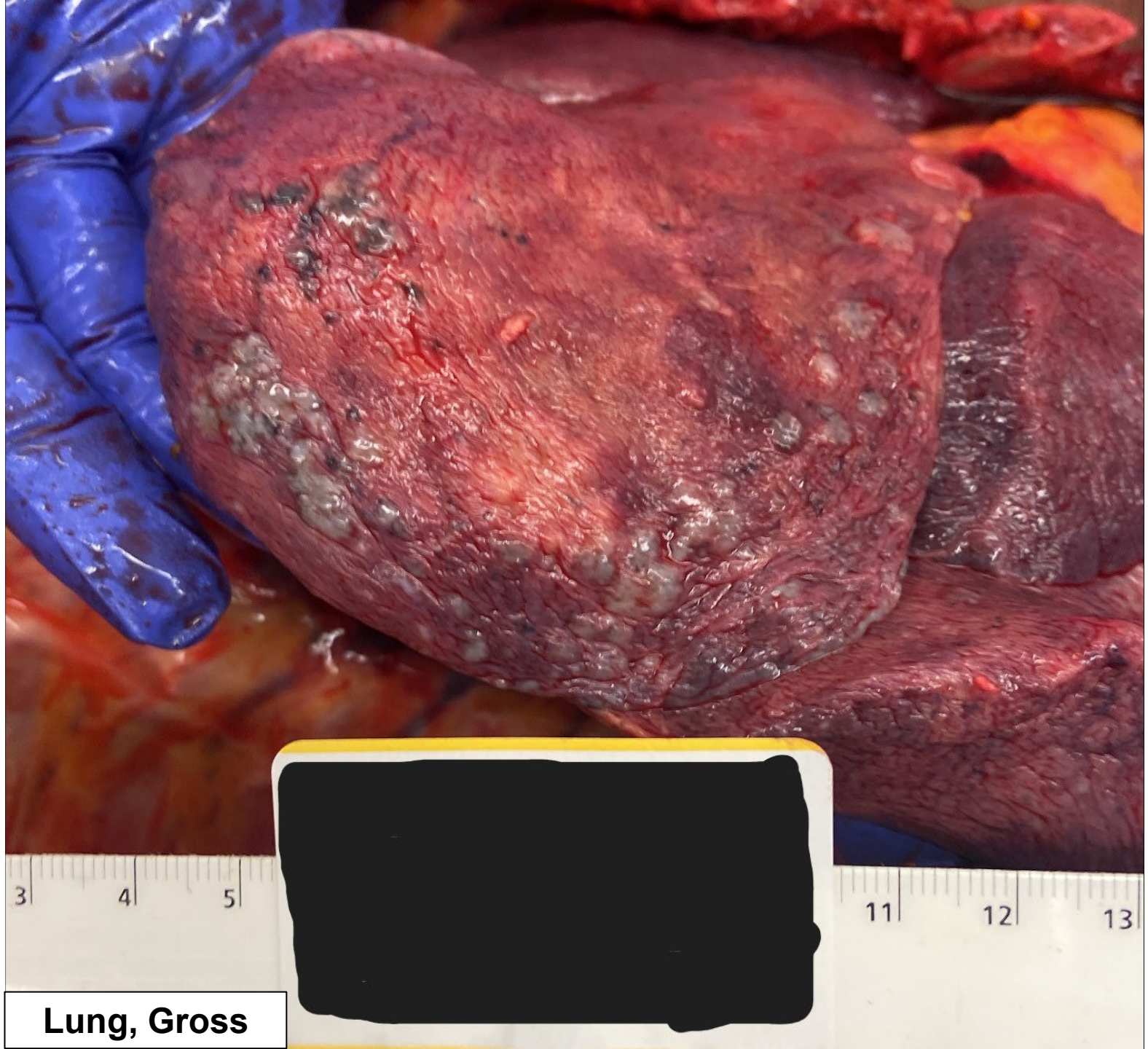
Case #143

NAME Educational Activities Committee

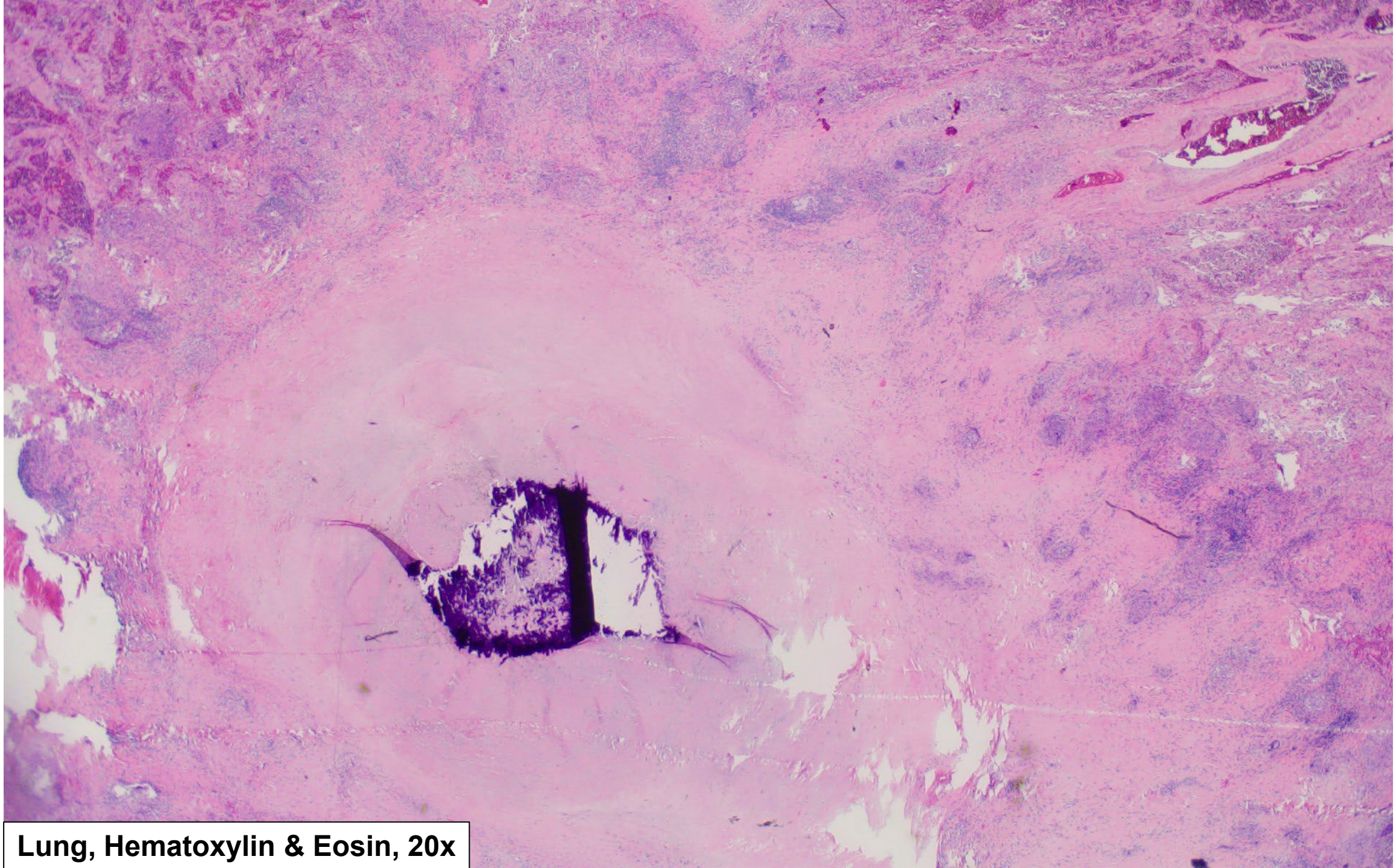
Case provided by:

Casey P. Schukow, DO (he/him)
Co-Chief Resident Pathologist (PGY3, 2025-2026 Academic Year)
Corewell Health William Beaumont University Hospital, Royal Oak, Michigan
Resident Member, National Association of Medical Examiners
Associate Member, Michigan Association of Medical Examiners

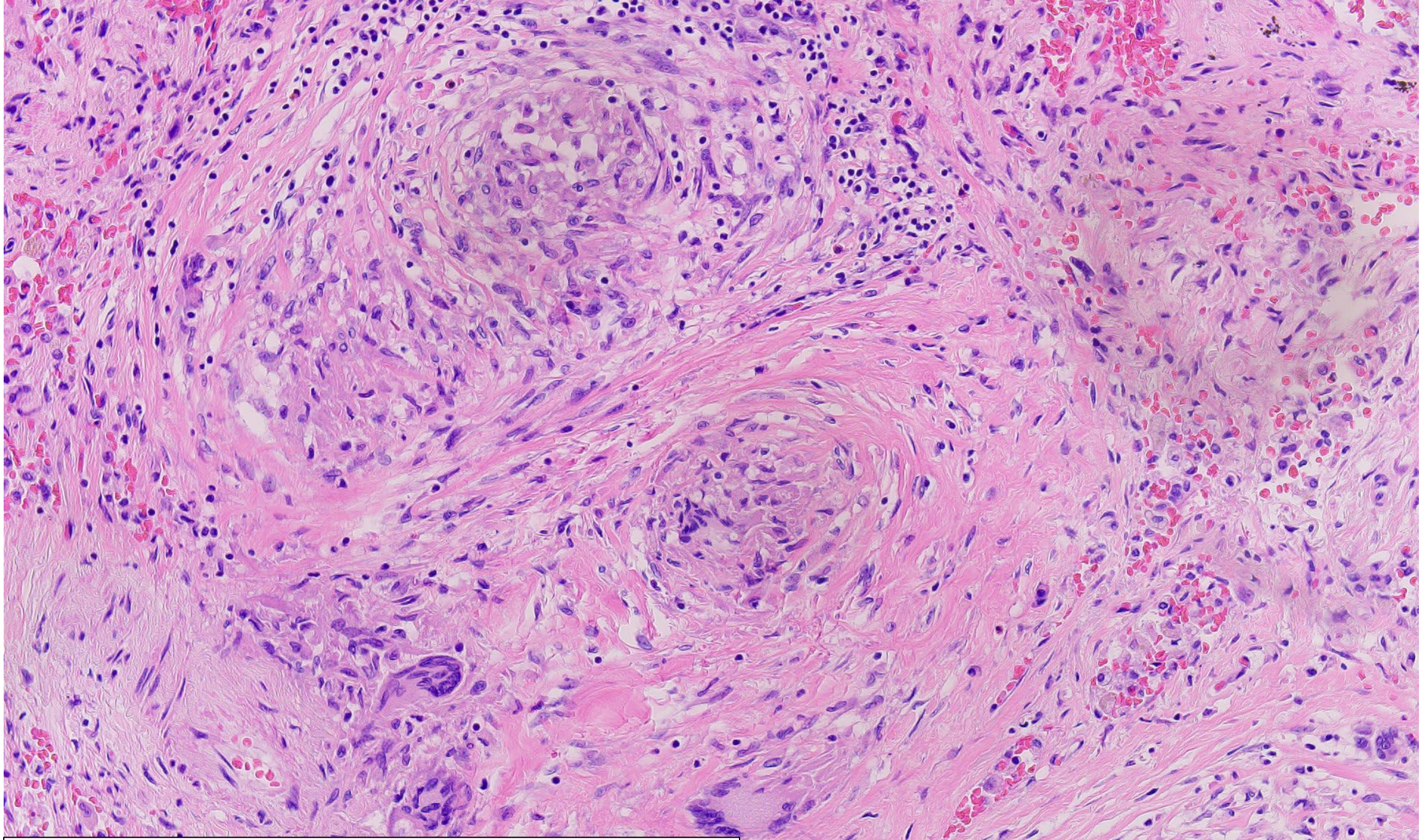
Ping L. Zhang, MD, PhD (he/him)
Faculty Pathologist
Corewell Health William Beaumont University Hospital, Royal Oak, Michigan
Member, College of American Pathologists



Lung, Gross



Lung, Hematoxylin & Eosin, 20x



Lung, Hematoxylin & Eosin, 200x, Oil Immersion

A Black female in her 70s with past medical history including end-stage renal disease, congestive heart failure, and recurrent pleural effusions presented to the emergency room with a chief complaint of shortness of breath. She was admitted for acute on chronic hypoxic respiratory failure. Pertinent clinical and laboratory parameter values are summarized in the **table**. Relevant imaging showed pulmonary edema, pleural effusions, and cardiomegaly. Her hospital stay was complicated by significant fluid overload requiring frequent hemodialysis and worsening hemodynamic stability requiring pressure support. She passed away after experiencing pulseless ventricular tachycardia despite resuscitation efforts.

Parameter	Value
SpO_2	92% on 6 L nasal cannula
Hemoglobin	9.8 g/dL
Creatinine	5.59 mg/dL
Serum Calcium	11.5 mg/dL
ACE level	Within normal limits

Autopsy was remarkable for enlarged paratracheal and perihilar lymph nodes (up to 6.5 cm in greatest dimension) and multiple well-circumscribed, tan-brown nodules in the bilateral lungs in each lobe (measuring up to 0.5 cm in greatest dimension). Gross and histologic images of lung findings are **shown in the photos**. Acid-Fast Bacillus (AFB) and Grocott-Gomori Methenamine Silver (GMS) stains were negative. Occupational history was non-contributory.

Which of the following statements are true regarding the most likely disease process?

A. Exposure to metal particles is critical to establishing a diagnosis.
B. Males of Indo-Asian descent are most likely to be affected by this disease.
C. Pathophysiology includes aberrant immune cell activation and genetic predisposition.
D. This disease process is often accompanied by a vasculitis.

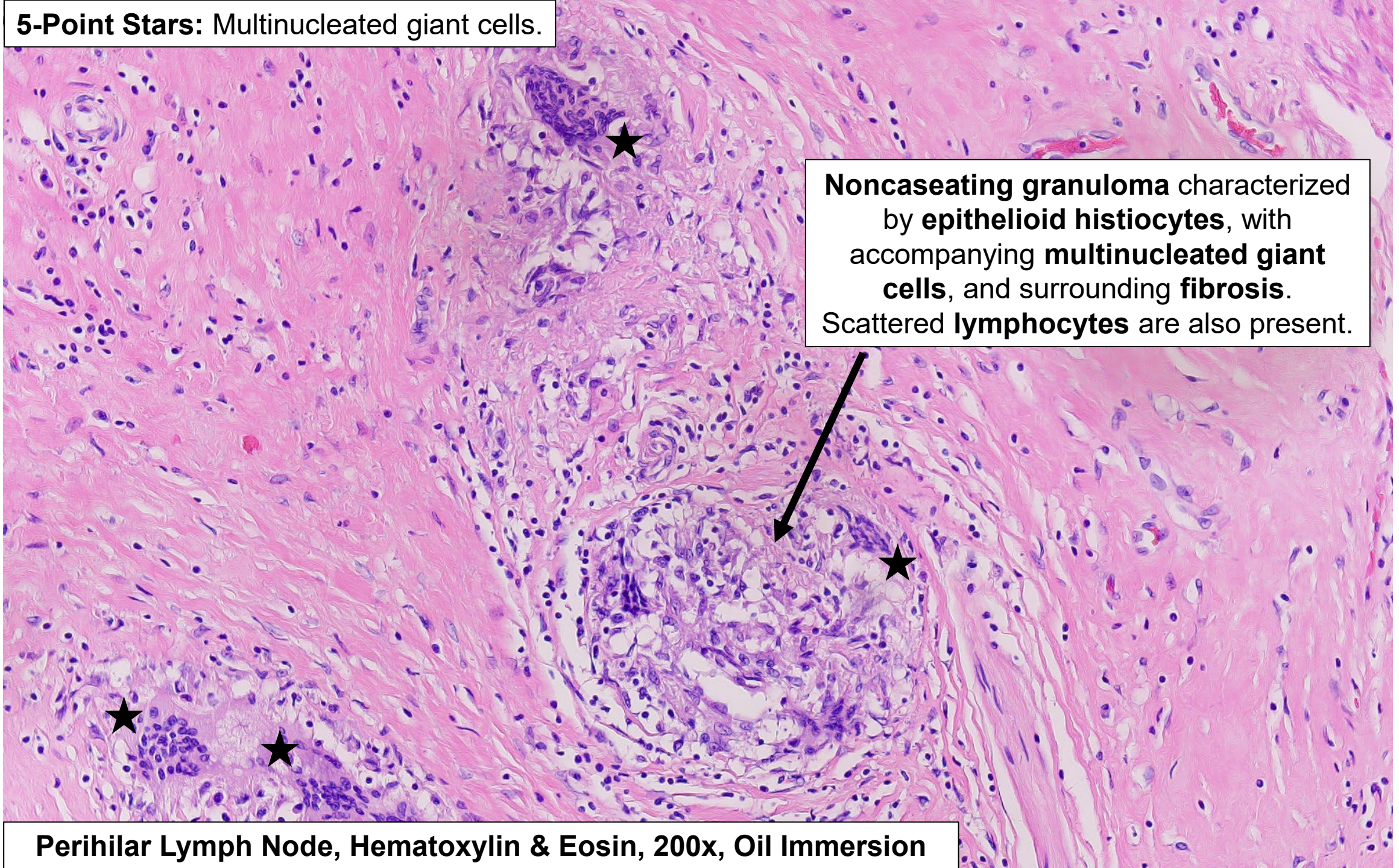
Answer...

C. Pathophysiology includes aberrant immune cell activation and genetic predisposition (correct answer – 75.29% of responses)

Pulmonary sarcoidosis is a multisystem granulomatous disease of uncertain etiology, most commonly involving the lungs(~90% of cases). The pathophysiology is not completely well-understood, but it is believed to **reflect aberrant immune cell activation in genetically predisposed individuals exposed to some unidentified antigen**. Antigen-presenting cells (e.g., macrophages, dendritic cells) activate Th1-polarized $CD4^+$ T cells, resulting in **local release of pro-inflammatory cytokines** (IFN-γ, IL-2, TNF-α, IL-12, IL-18) and recruitment of additional macrophages and lymphocytes. This leads to formation of **noncaseating epithelioid granulomas**, typically distributed along bronchovascular bundles and pleura in a **lymphangitic pattern**. Impaired down-regulation of this immune response, possibly from dysfunctional regulatory T cells, contributes to granuloma persistence and eventual **fibrosis** or hyalinization. Occasional **multinucleated giant cells** may be seen, with or without **Asteroid** (stellate cytoplasmic inclusions) or **Schaumann** (concentric, laminated, calcifications) bodies.

Clinically, patients may be asymptomatic or present with dry cough, dyspnea, and chest discomfort, sometimes with constitutional symptoms (e.g., fatigue, fever, weight loss). Chest imaging often shows **bilateral hilar lymphadenopathy** with or without parenchymal infiltrates, and pulmonary function tests reveal a **restrictive pattern**. Diagnosis requires compatible clinical/radiologic findings, **noncaseating granulomas on biopsy**, and exclusion of mimics (see next slide). **Serum ACE, soluble IL-2 receptor, or hypercalcemia may support the diagnosis but are nonspecific (ACE levels were normal during this patient's admission).** Prognosis varies from spontaneous remission to progressive pulmonary fibrosis and respiratory failure. At autopsy, pulmonary sarcoidosis may be an unexpected finding (however, in this case, we did not mention that the decedent had a known clinical history of pulmonary sarcoidosis).

Careful evaluation of the lungs, hilar nodes, and heart is essential, as **cardiac involvement is a recognized cause of sudden death**. Even though the patient had other co-morbidities such as heart failure and kidney disease, we did not identify any granulomas present in these or other tissues.


5-Point Stars: Multinucleated giant cells.
Noncaseating granuloma characterized by **epithelioid histiocytes**, with accompanying **multinucleated giant cells**, and surrounding **fibrosis**. Scattered **lymphocytes** are also present.
Perihilar Lymph Node, Hematoxylin & Eosin, 200x, Oil Immersion

Other responses…

A. Exposure to metal particles is critical to establishing a diagnosis (2.66% of responses).
Beryllium is an **alkaline metal** often used in industries like **aerospace** and **electronics**. Chronic beryllium disease can mimic sarcoidosis both clinically and histologically (noncaseating granulomas). However, **occupational exposure history** (aerospace, electronics, manufacturing) is key for diagnosis (which was non-contributory here); positive **beryllium lymphocyte proliferation test (BeLPT)** is also helpful.

B. Males of Indo-Asian descent are most likely to be affected by this disease (4.18% of responses).
Sarcoidosis most commonly affects **young Black females** beginning between the ages of 20 and 40 years.

D. This disease process is often accompanied by a vasculitis (17.87% of responses).
Granulomatosis with polyangiitis (GPA) is an **anti-neutrophil cytoplasmic antibody (ANCA)-positive disease** that is well-known for **pulmonary and renal involvement with rapid progression**. However, this is less likely given the absent of vasculitis present on the sections examined as well as lack of acute respiratory or renal presentation without hemoptysis or hematuria, respectively.

REFERENCES

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