

Pathology Mimics Workshop, April 27, 2023

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Erdheim-Chester Disease Global Alliance

Erdheim-Chester disease in the lung

- Frequency: Lung or pleura involvement reported in 35-50%
- Pattern: lymphangitic distribution, visceral pleura and interlobular septal thickening. Less pronounced perivascular and peribronchiolar involvement
- Histology: Infiltrate of histiocytes with eosinophilic or foamy cytoplasm, associated with variable fibrosis and minimal chronic inflammation
- Differential diagnosis: interstitial lung disease (UIP/NSIP), Rosai-Dorfman disease, Langerhans cell histiocytosis, drug reaction

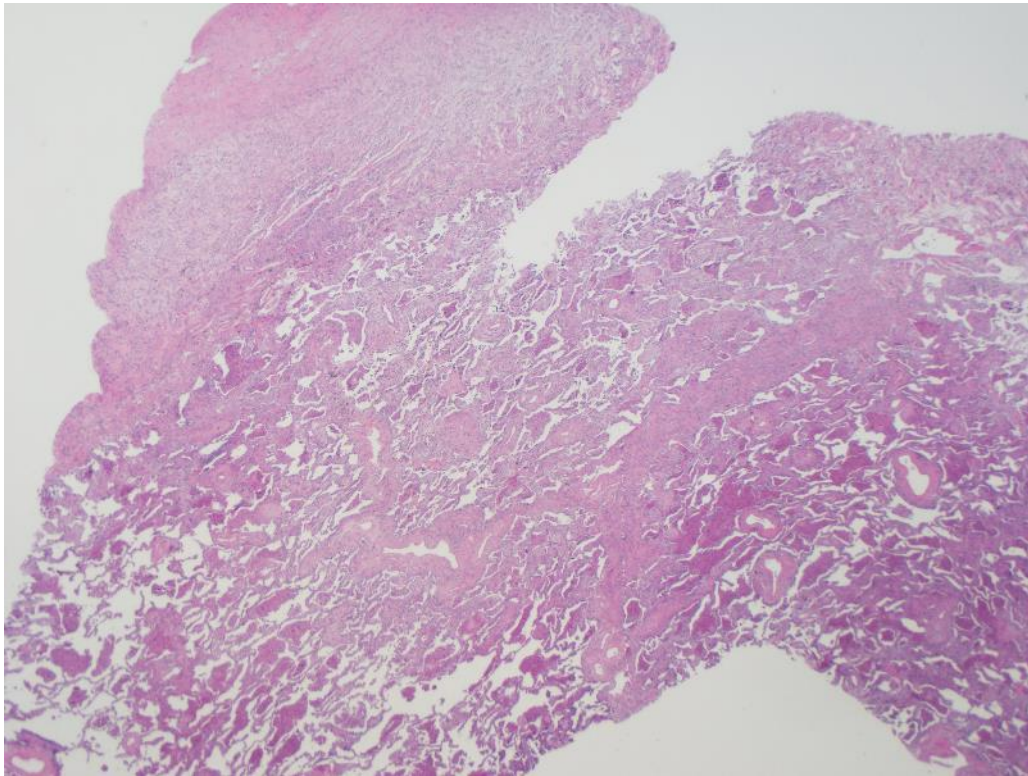
Case 1

- 71-year-old man with a history of idiopathic pleural effusions presented with shortness of breath.
- CT scan showed diffuse bilateral pleural thickening as well as some pericardial thickening. Small bilateral pleural effusions, extending into the major fissures. Diffuse bilateral irregular interlobular septal thickening, more prominent in the lower lungs. Diffuse mild ground-glass opacities throughout most of the lung parenchyma.
- Open lung biopsy performed.

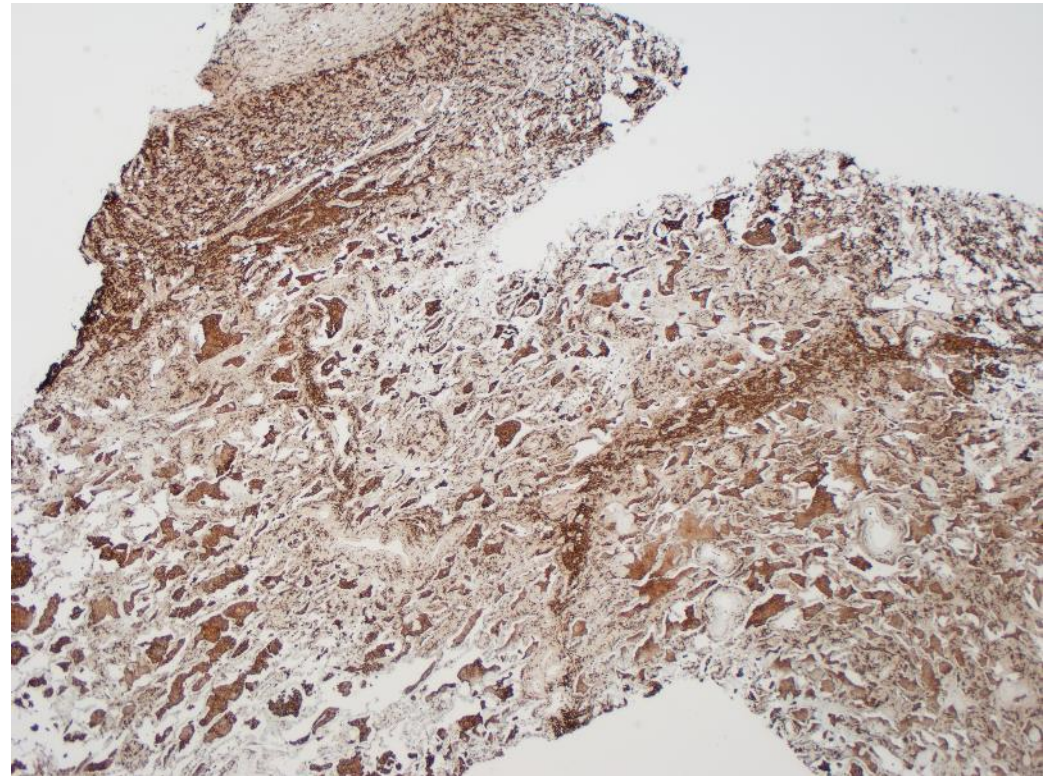
Erdheim-Chester disease

Lung biopsy

H&E 20x



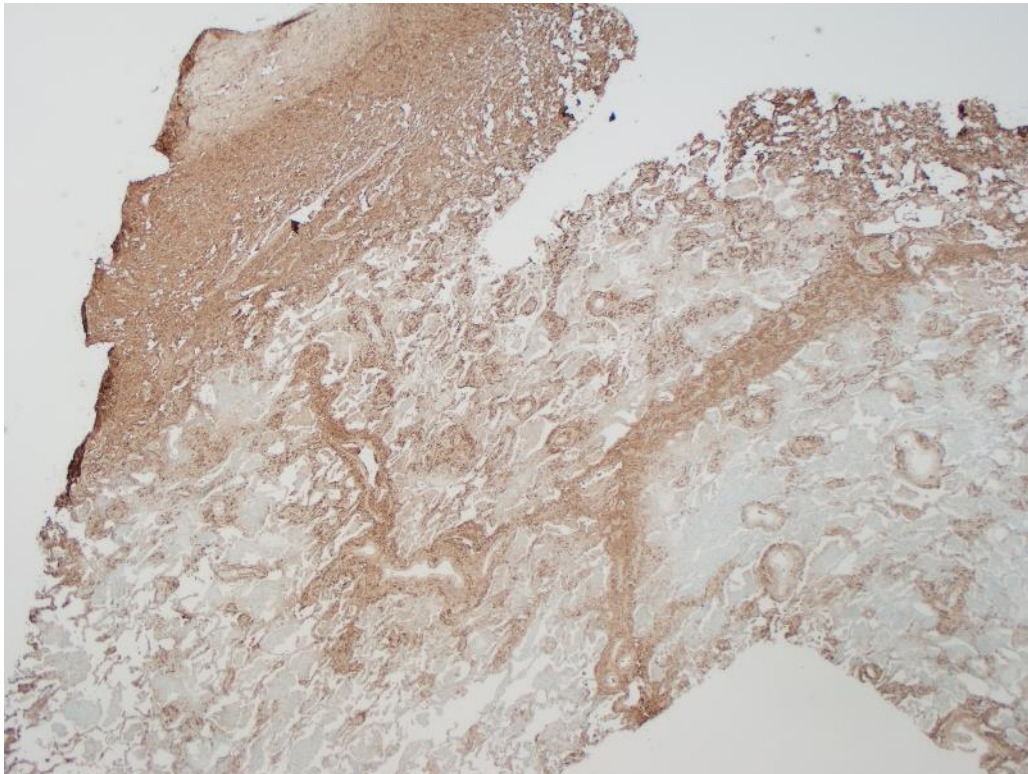
CD163 positive (20x)



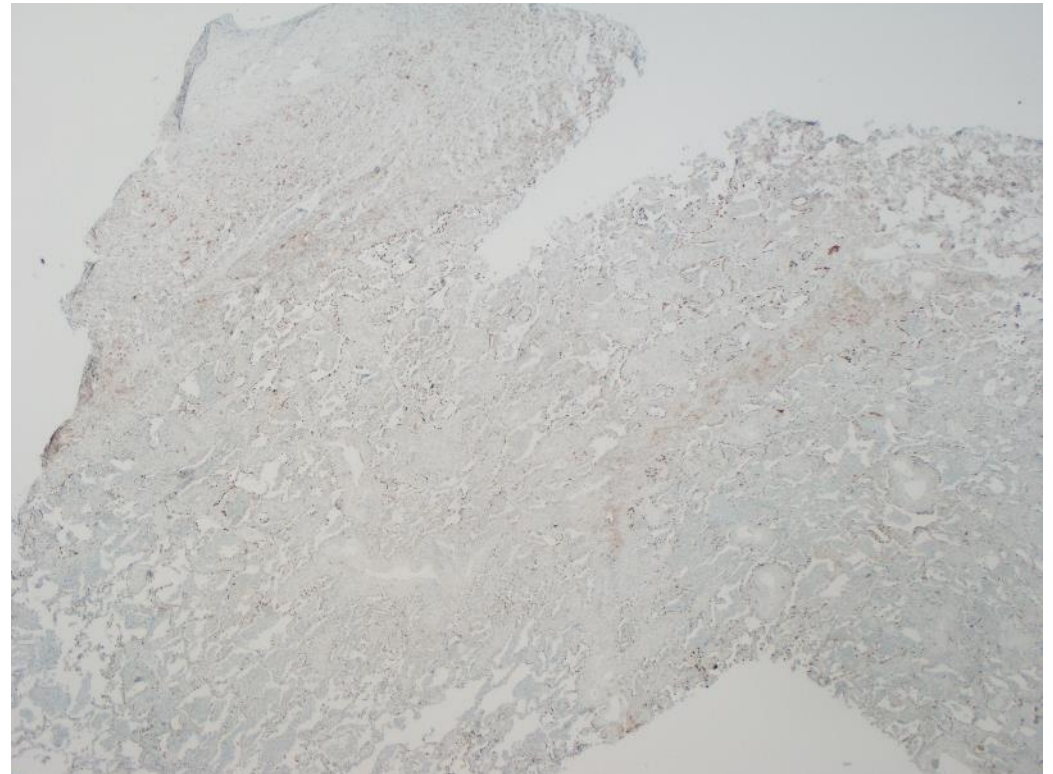
Erdheim-Chester disease

Lung biopsy

Factor 13a positive (20x)



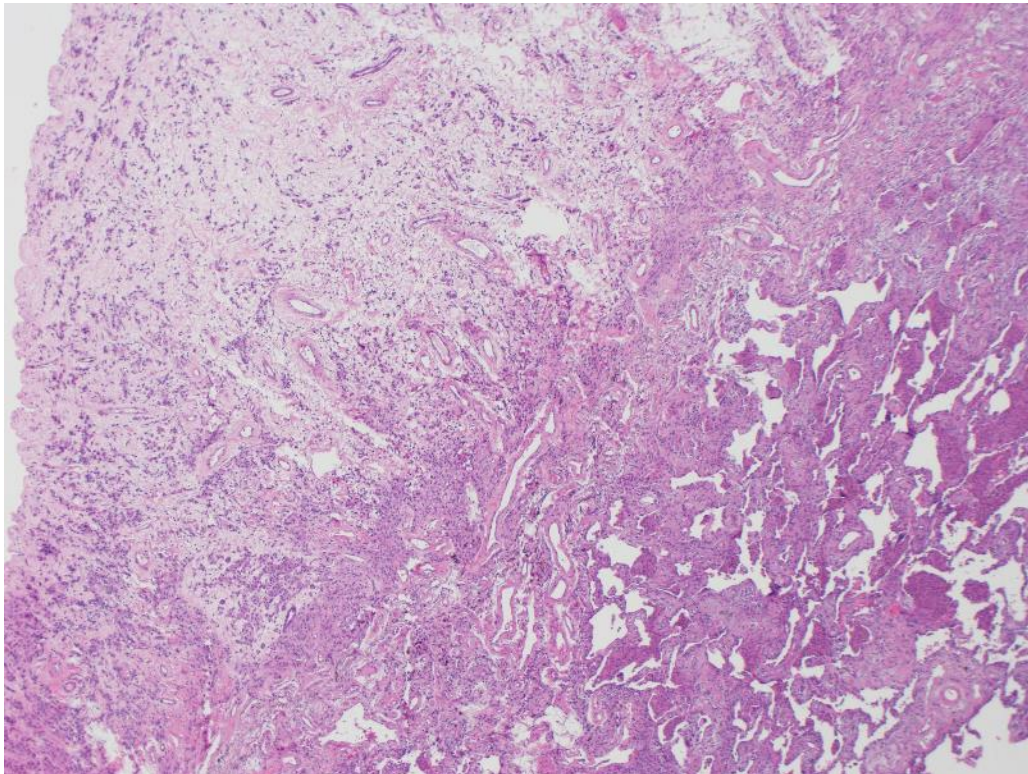
Cyclin D1 positive (20x)



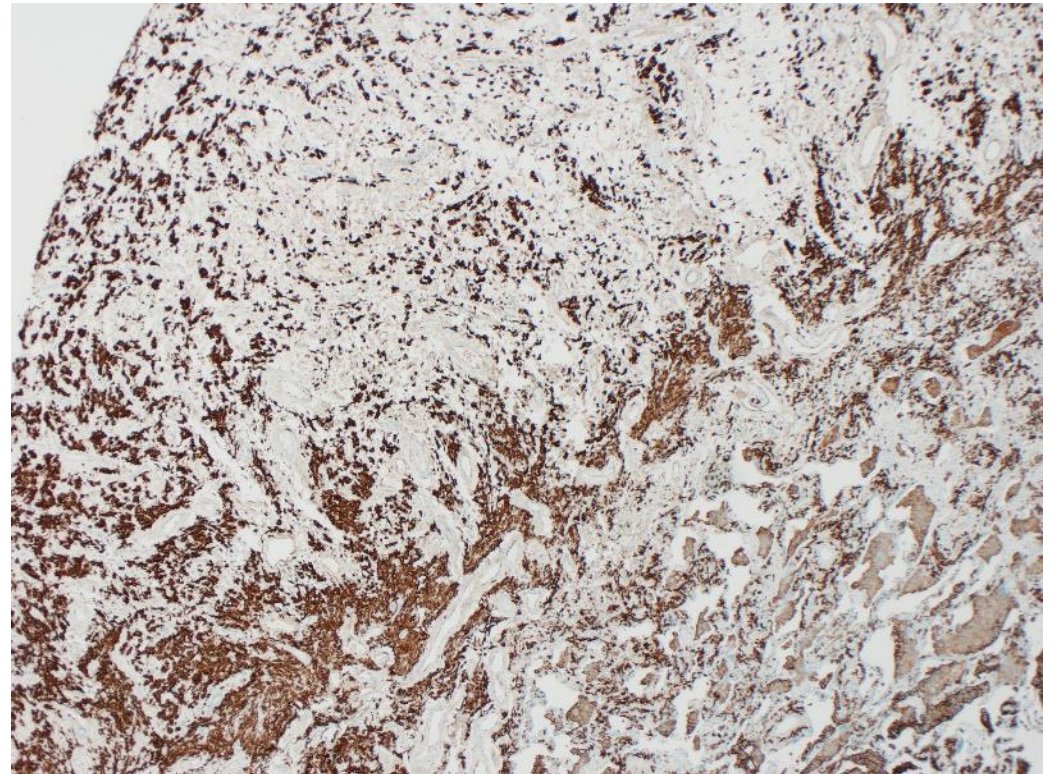
Erdheim-Chester disease

Lung biopsy

Pleura H&E 40x



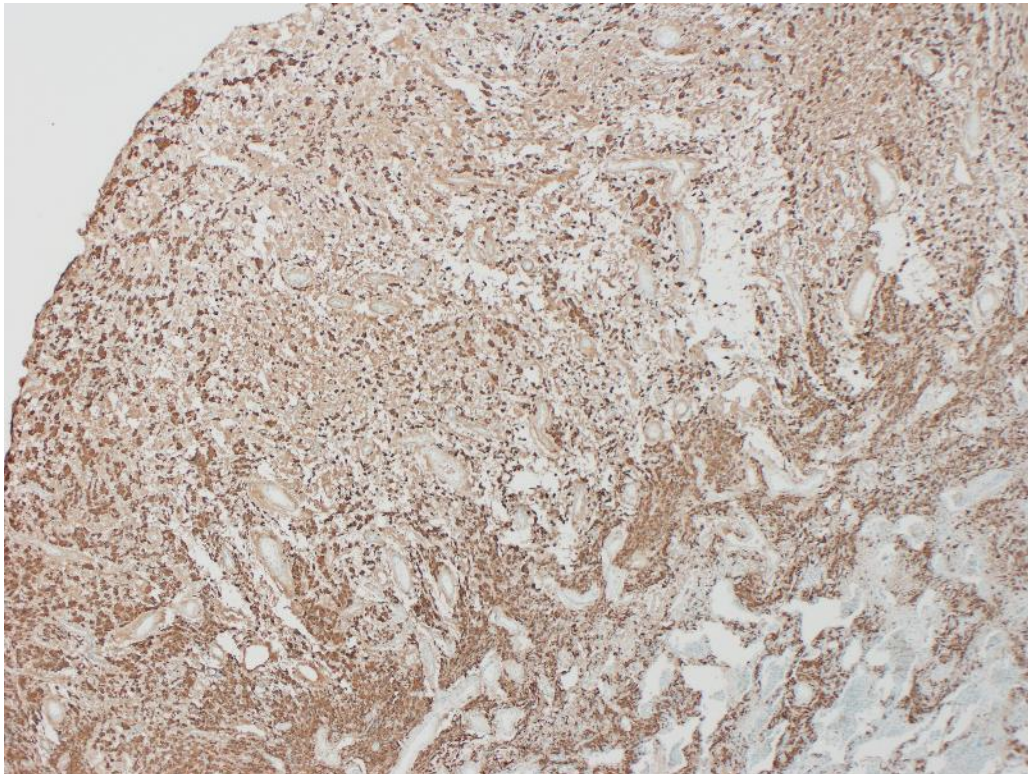
Pleura CD163 positive (40x)



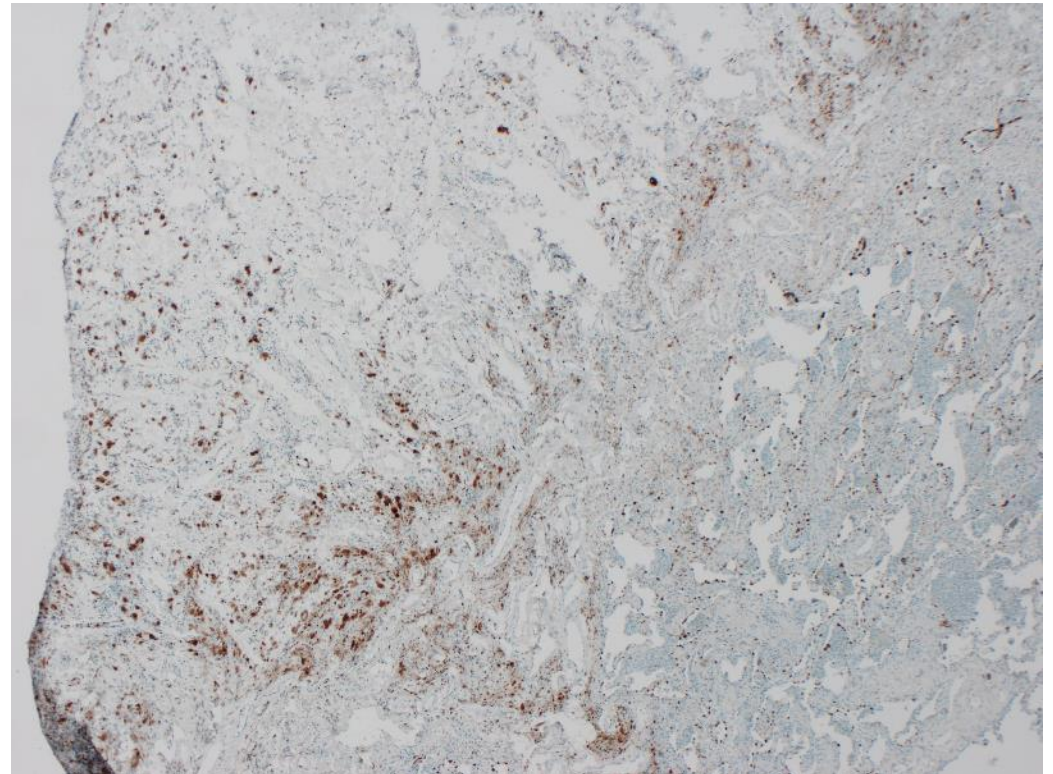
Erdheim-Chester disease

Lung biopsy

Pleura Factor 13a positive (40x)



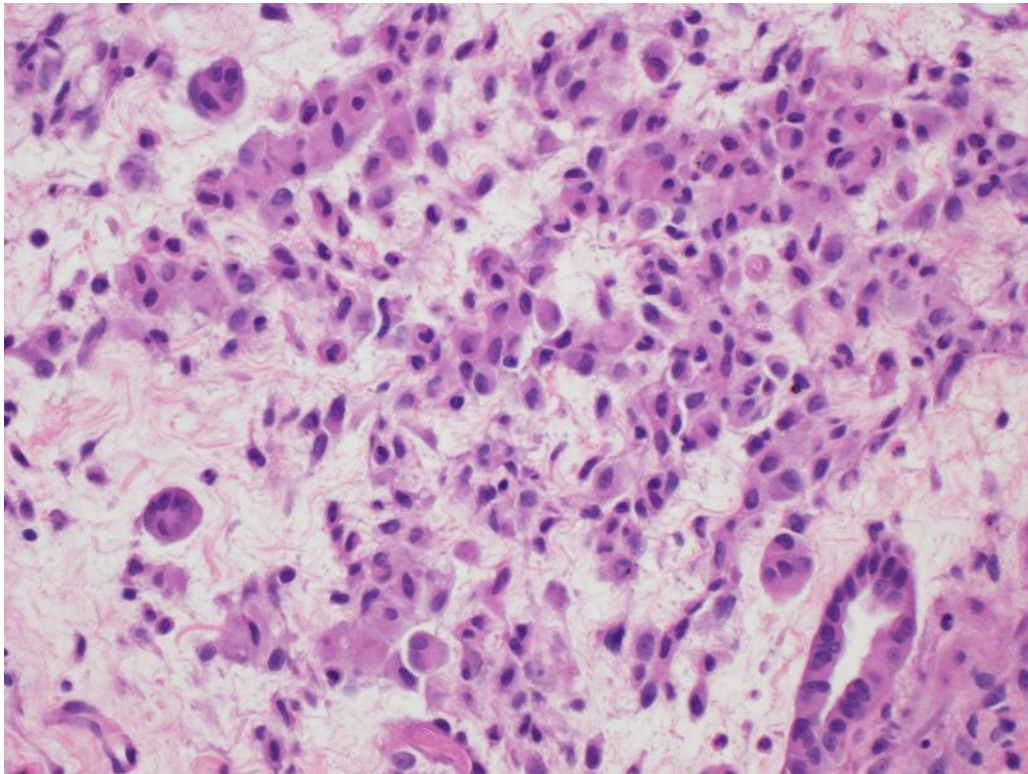
Pleura Cyclin D1 positive (40x)



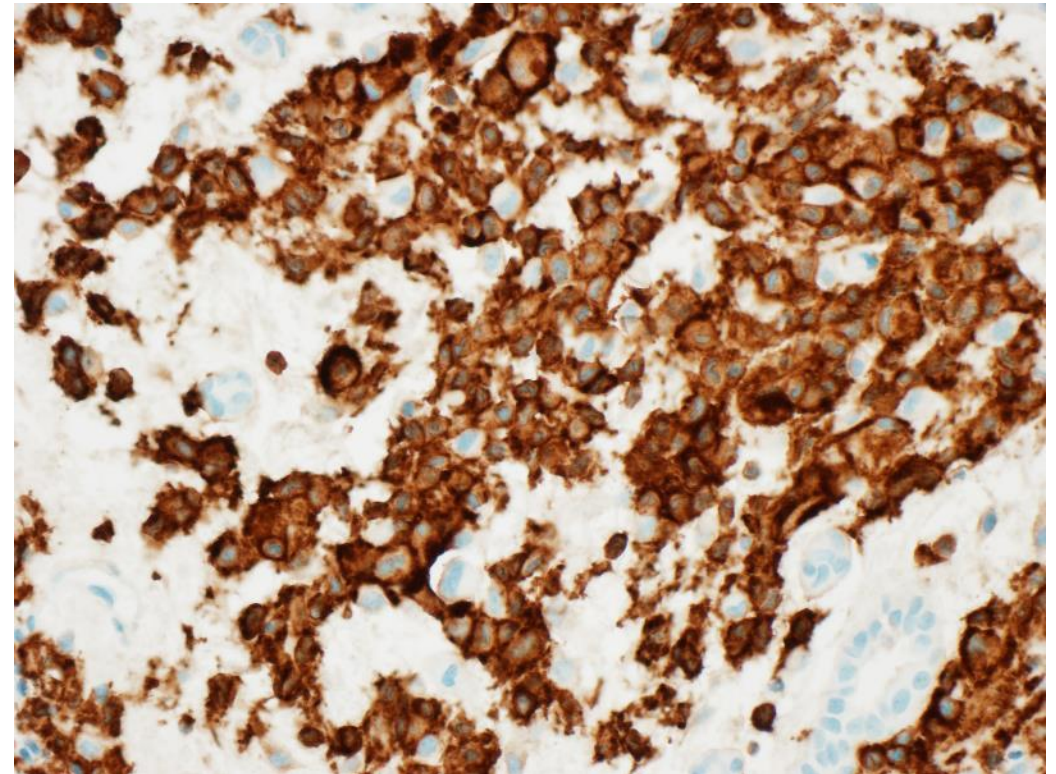
Erdheim-Chester disease

Lung biopsy

Pleura H&E 400x



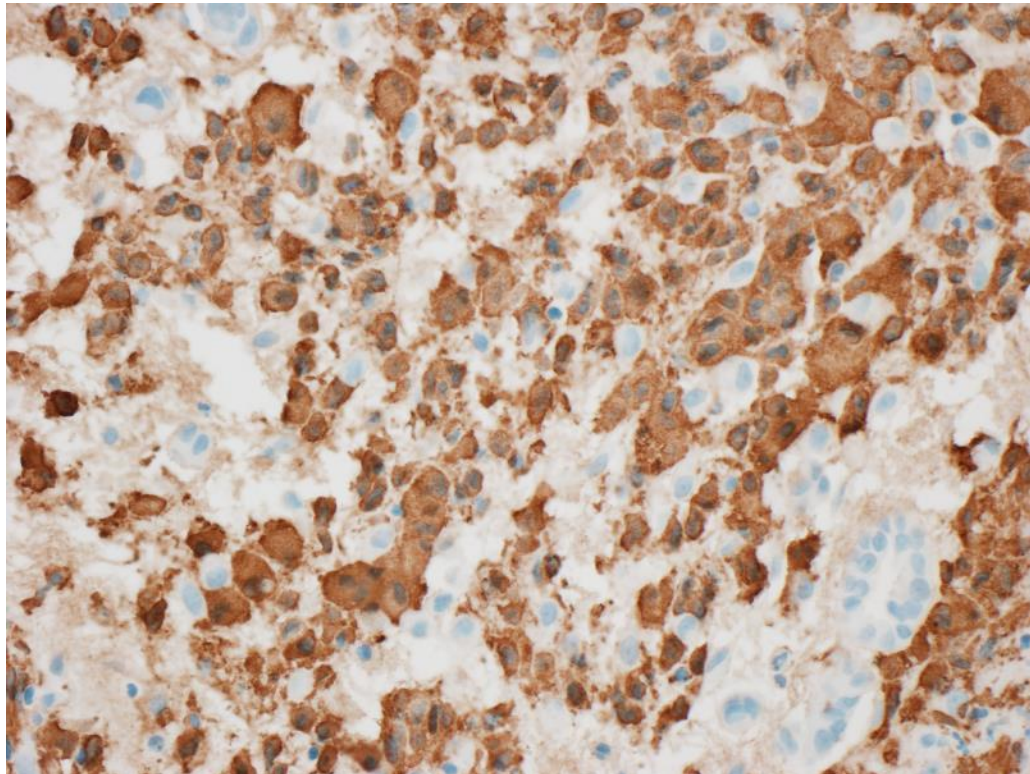
Pleura CD163 positive (400x)



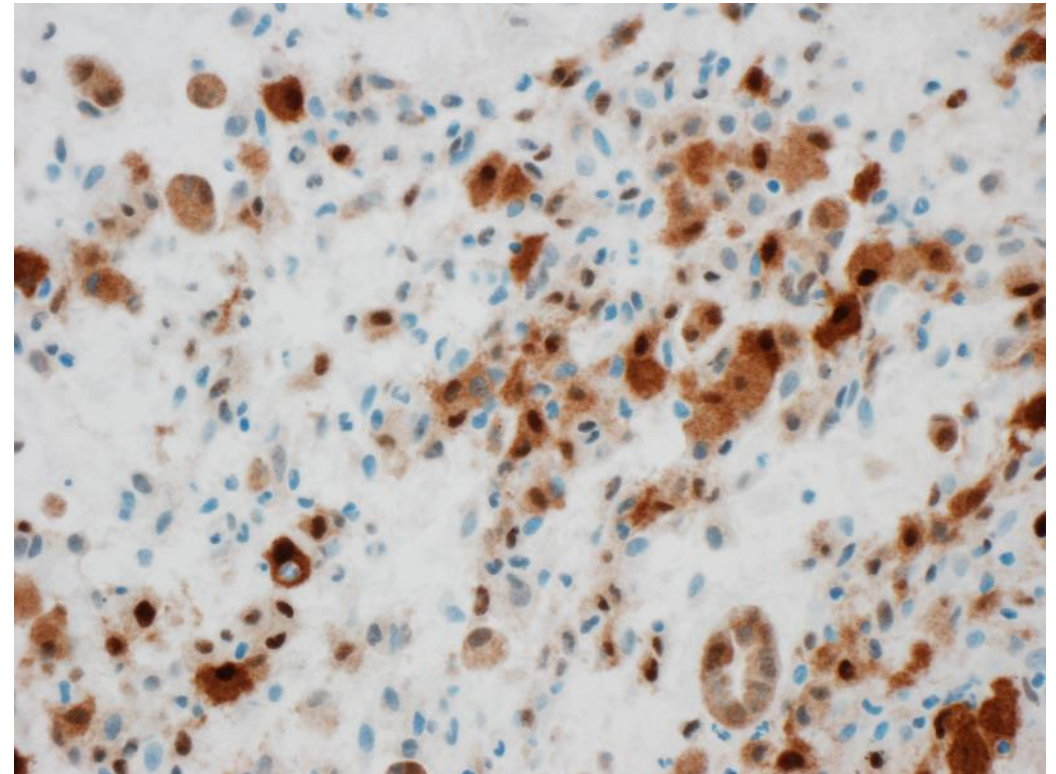
Erdheim-Chester disease

Lung biopsy

Pleura Factor 13a positive (400x)



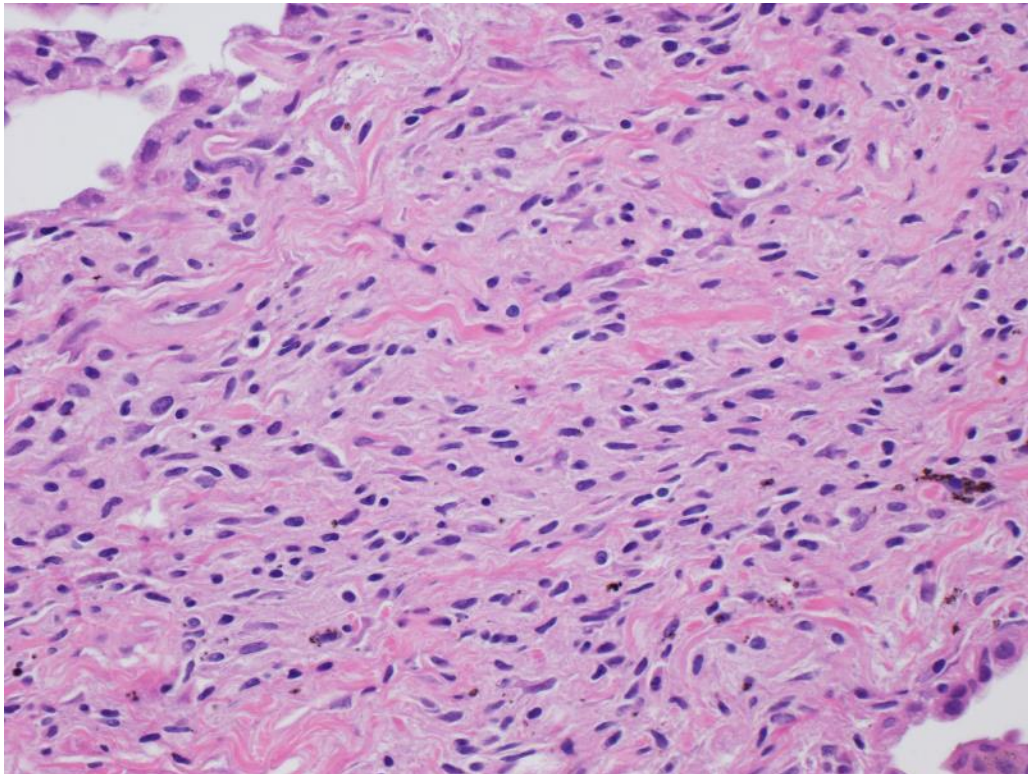
Pleura Cyclin D1 positive (400x)



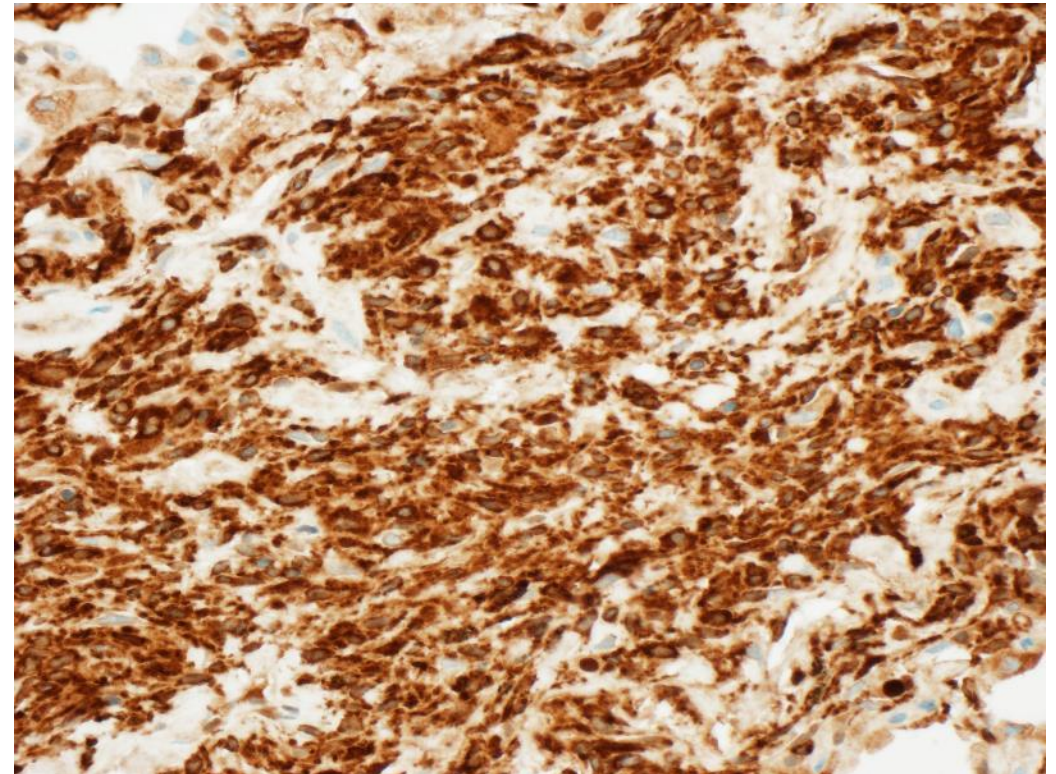
Erdheim-Chester disease

Lung biopsy

Septa H&E 400x



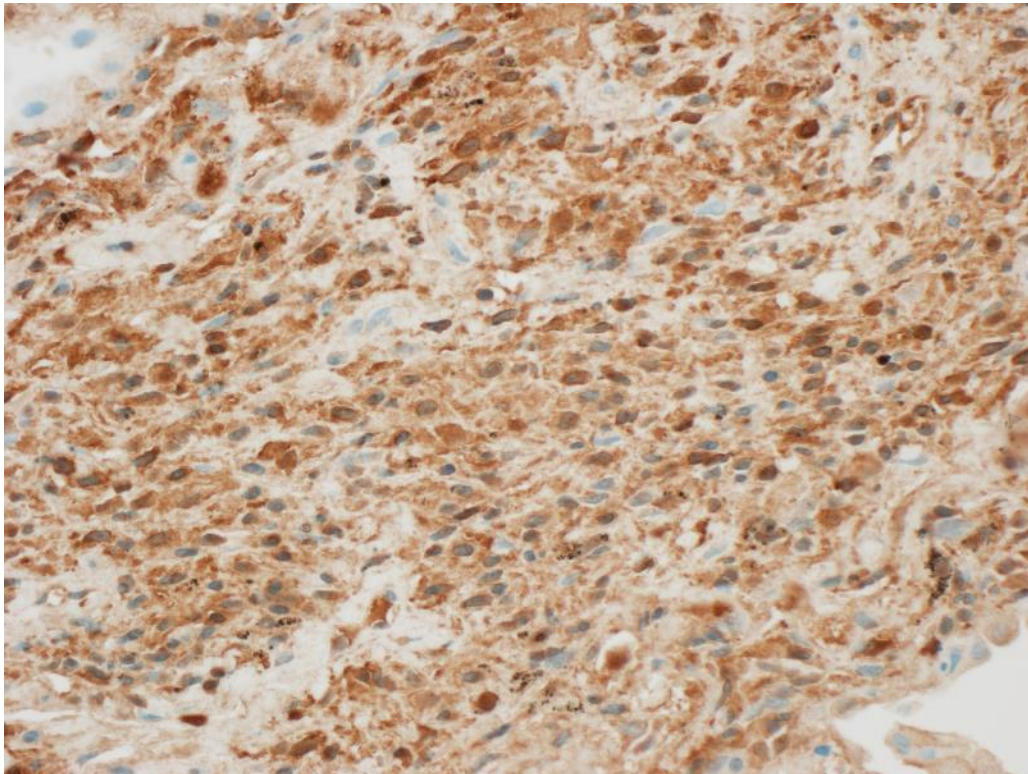
Septa CD163 positive (400x)



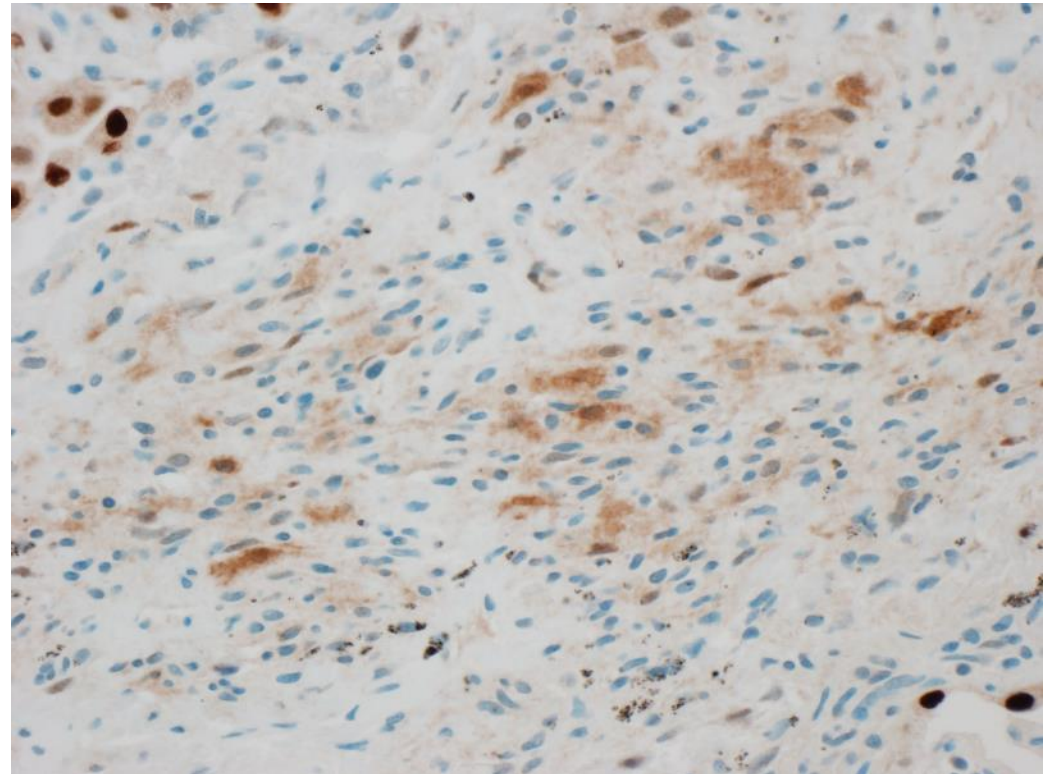
Erdheim-Chester disease

Lung biopsy

Septa Factor 13a positive (400x)



Septa Cyclin D1 weak positive (400x)

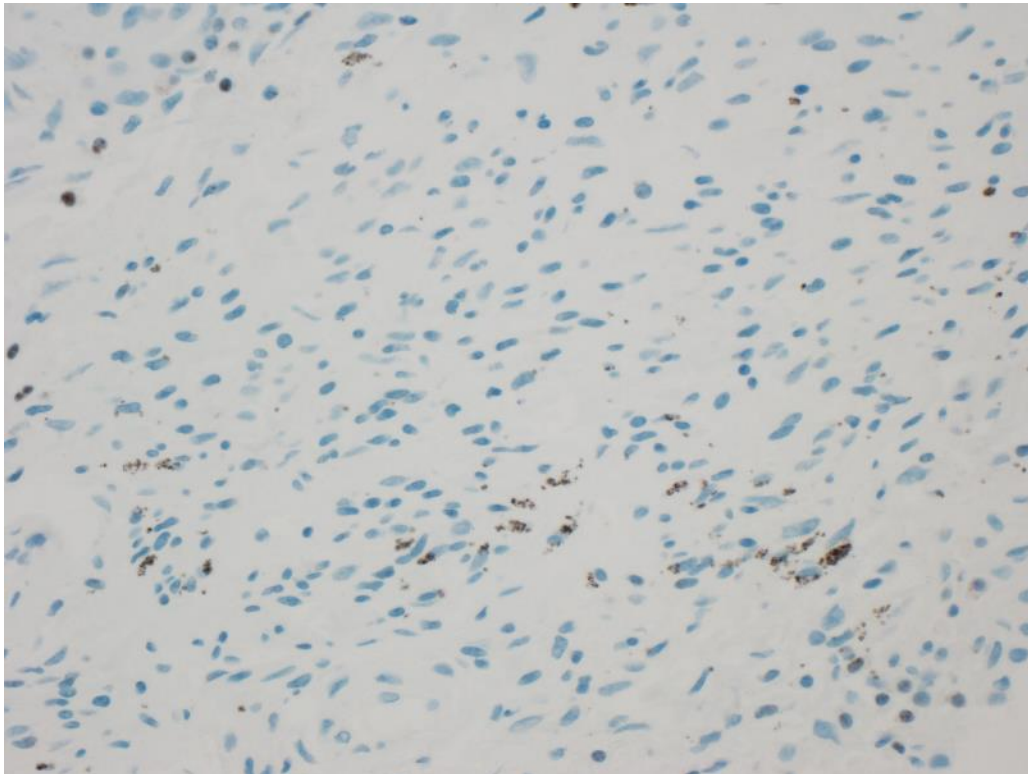


Erdheim-Chester disease

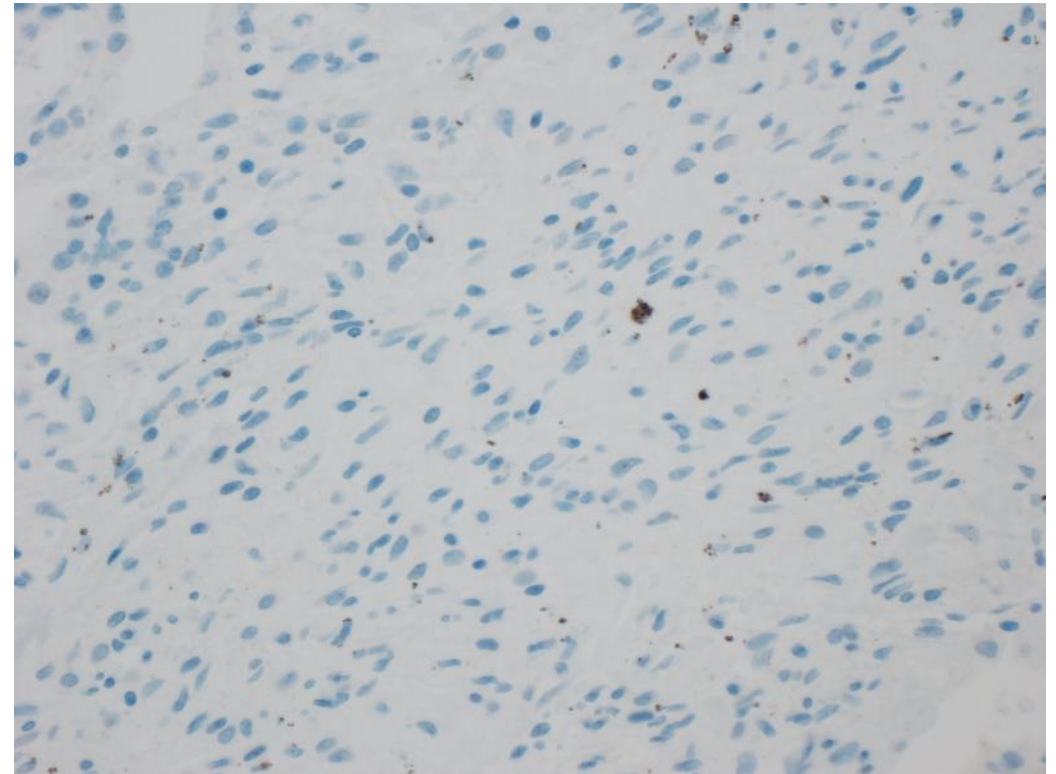
Lung biopsy

S100, CD1a, langerin negative (not shown)

Septa OCT2 negative (400x)



Septa BRAF V600E negative (400x)

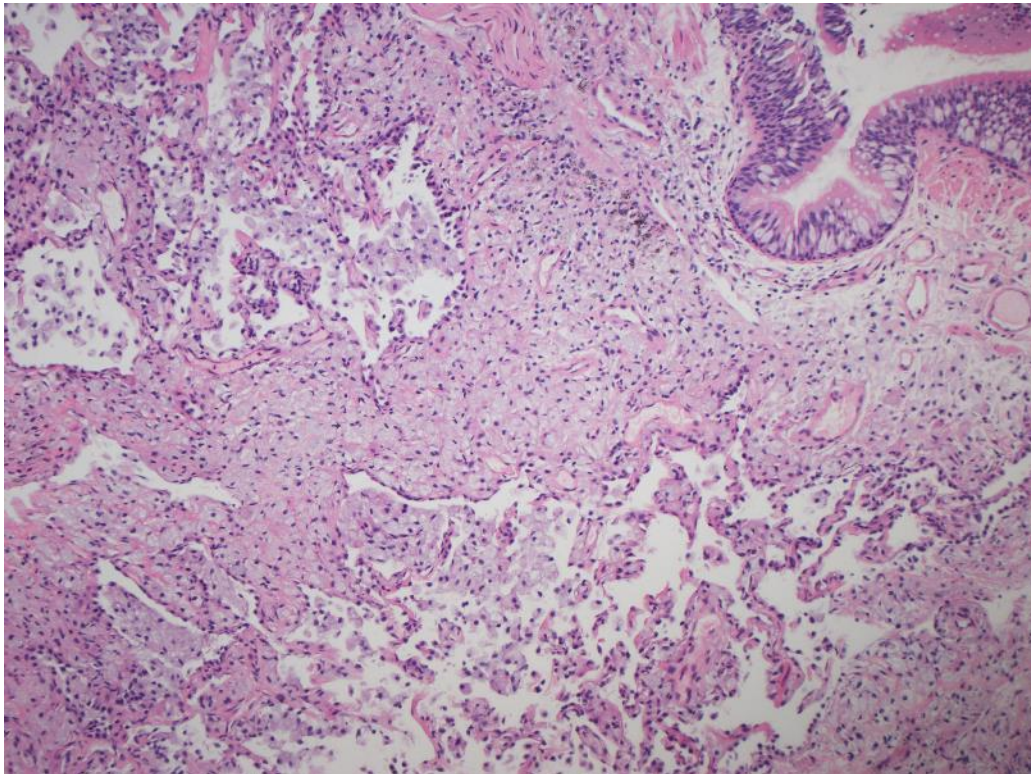


Case 2

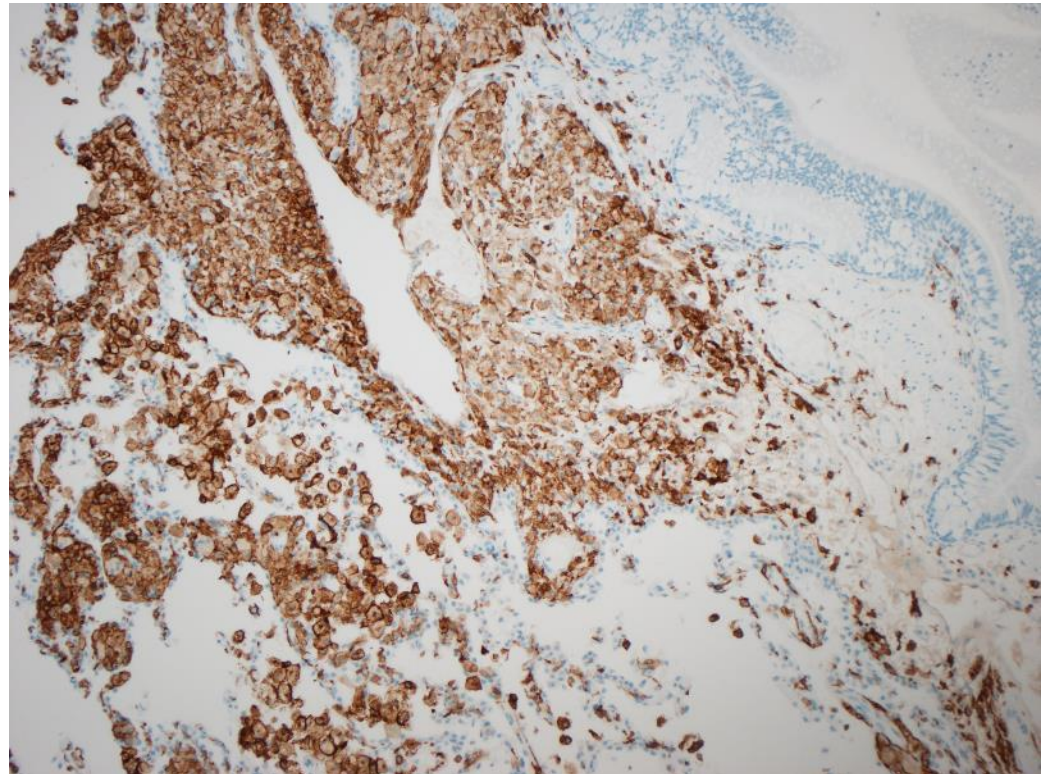
- 43-year-old man presented in 2019 with 1-2 years of shortness of breath and fevers of unknown origin. 30-35 pack-year smoking history. Significant workplace exposure to cement dust (VATS biopsy April 2019 demonstrating focal dust macules and patchy organizing pneumonia).
- CT scan showed bilateral centrilobular ground-glass opacities and upper lobe predominant emphysema.
- Open lung biopsy performed.

Case 2

H&E 100x



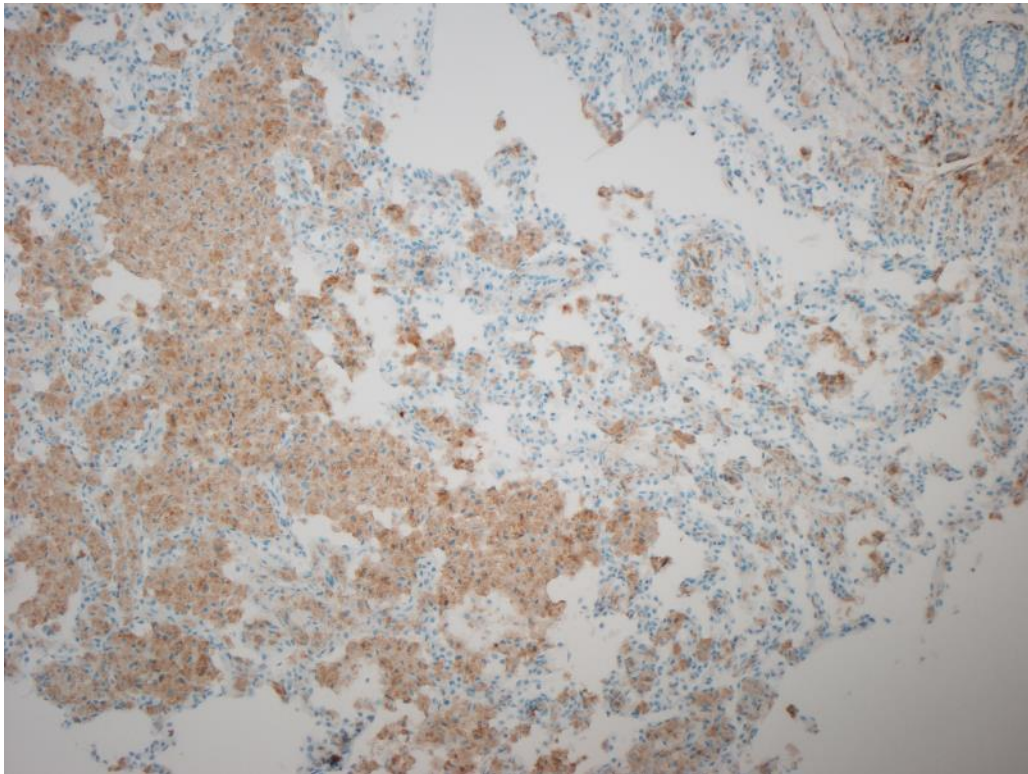
CD163 positive (100x)



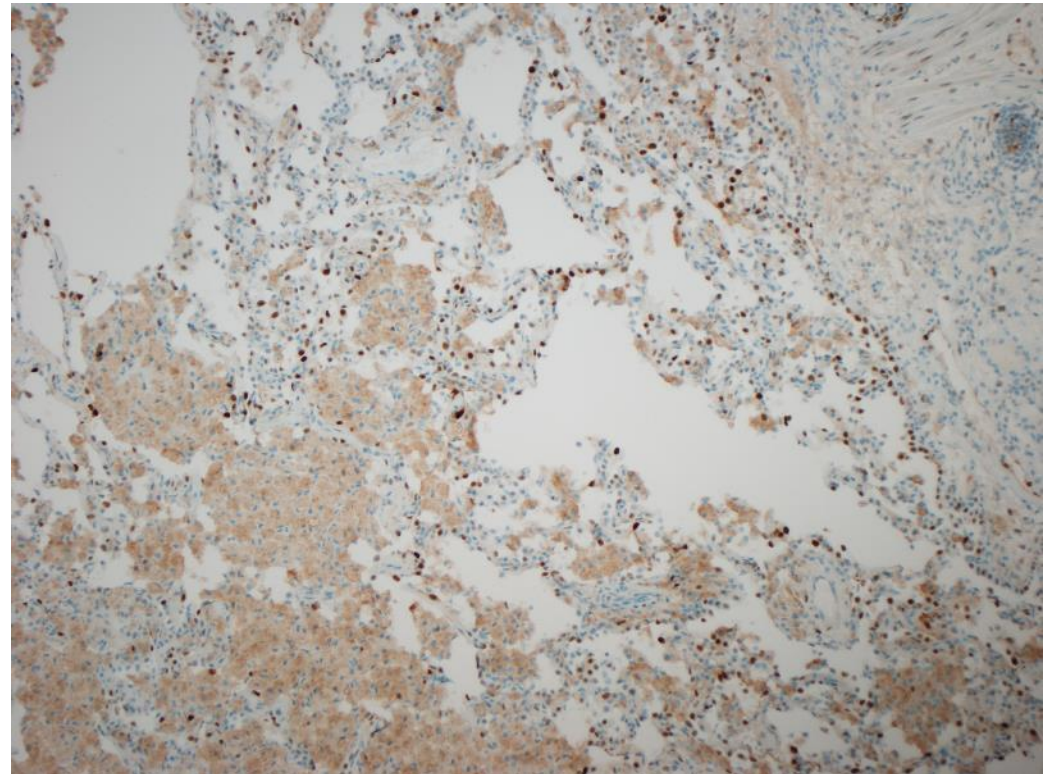
Case 2

-Negative IHC for S100, CD1a, langerin (not shown)

Factor 13a positive (100x)

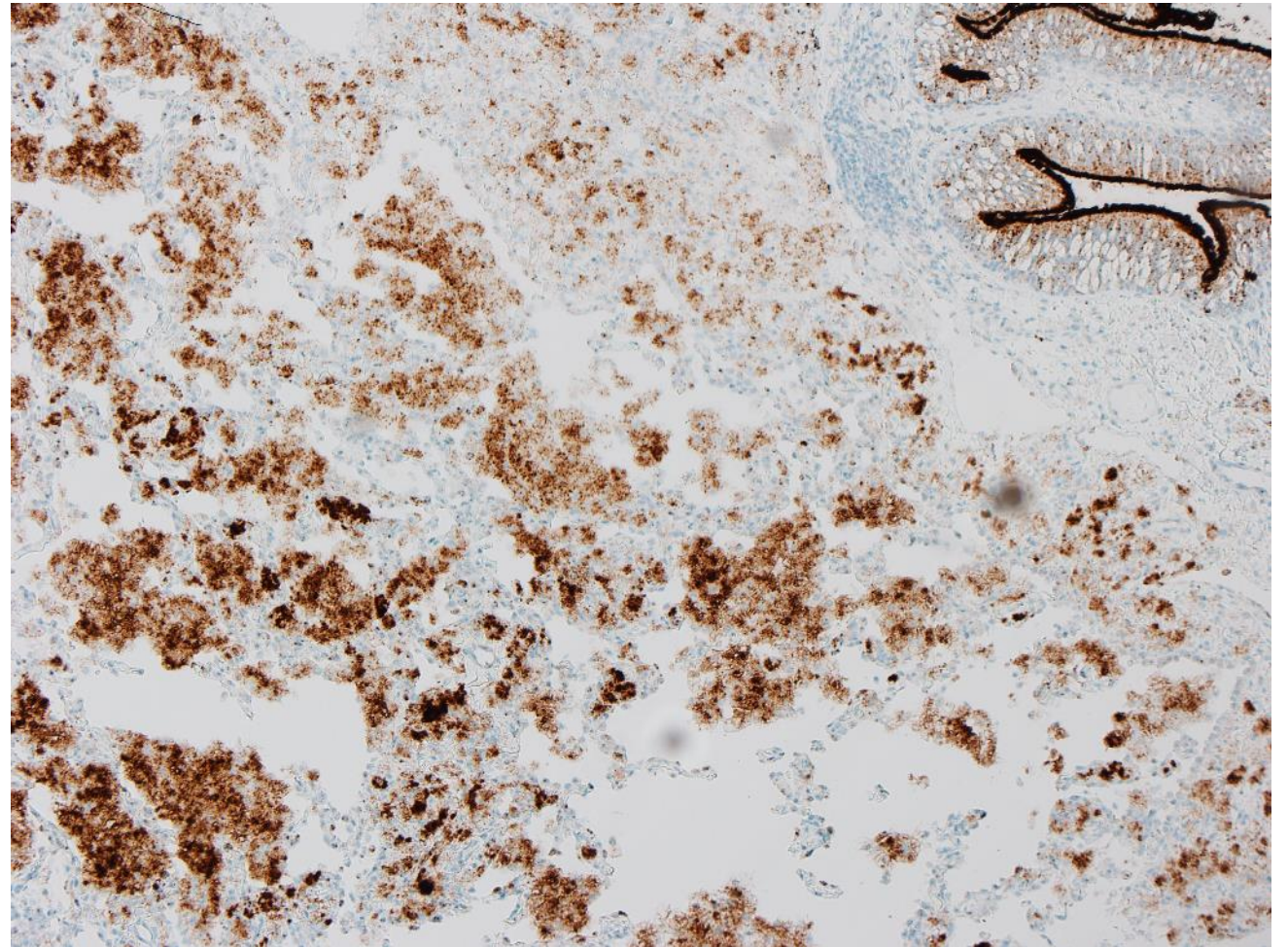


Cyclin D1 negative (100x)



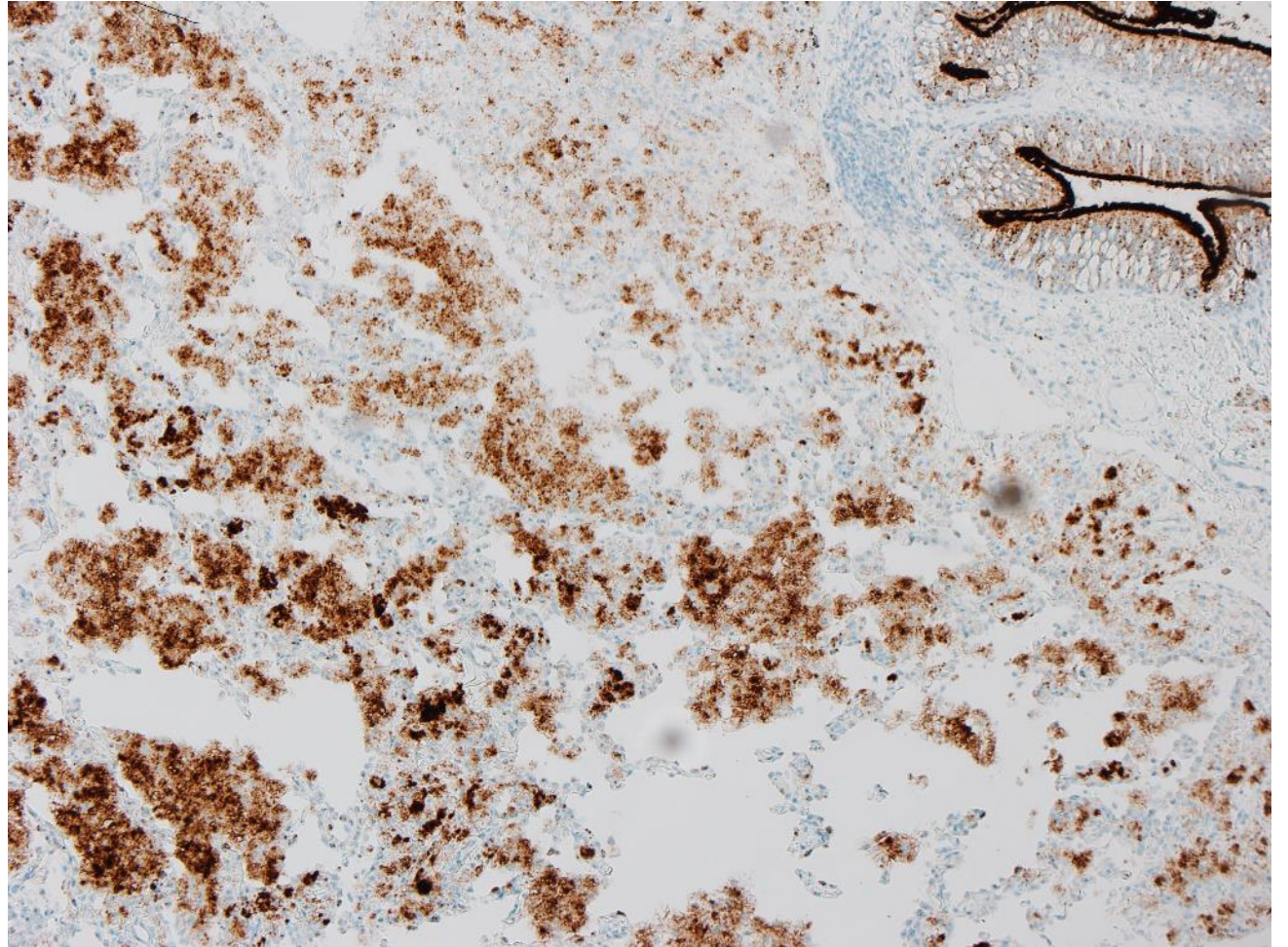
BRAF V600E (VE1) IHC

- Biopsy findings consistent with ECD
- Treated with vemurafenib
- No response



Molecular testing

- NGS negative for pathogenic mutations
- ddPCR negative for BRAF V600E/K
- False positive IHC: VE1 clone cross-reacts with ciliary proteins



Jones RT, Abedalthagafi MS, Brahmandam M, et al. Cross-reactivity of the BRAF VE1 antibody with epitopes in axonemal dyneins leads to staining of cilia. *Mod Pathol* 2015;28(4):596–606.

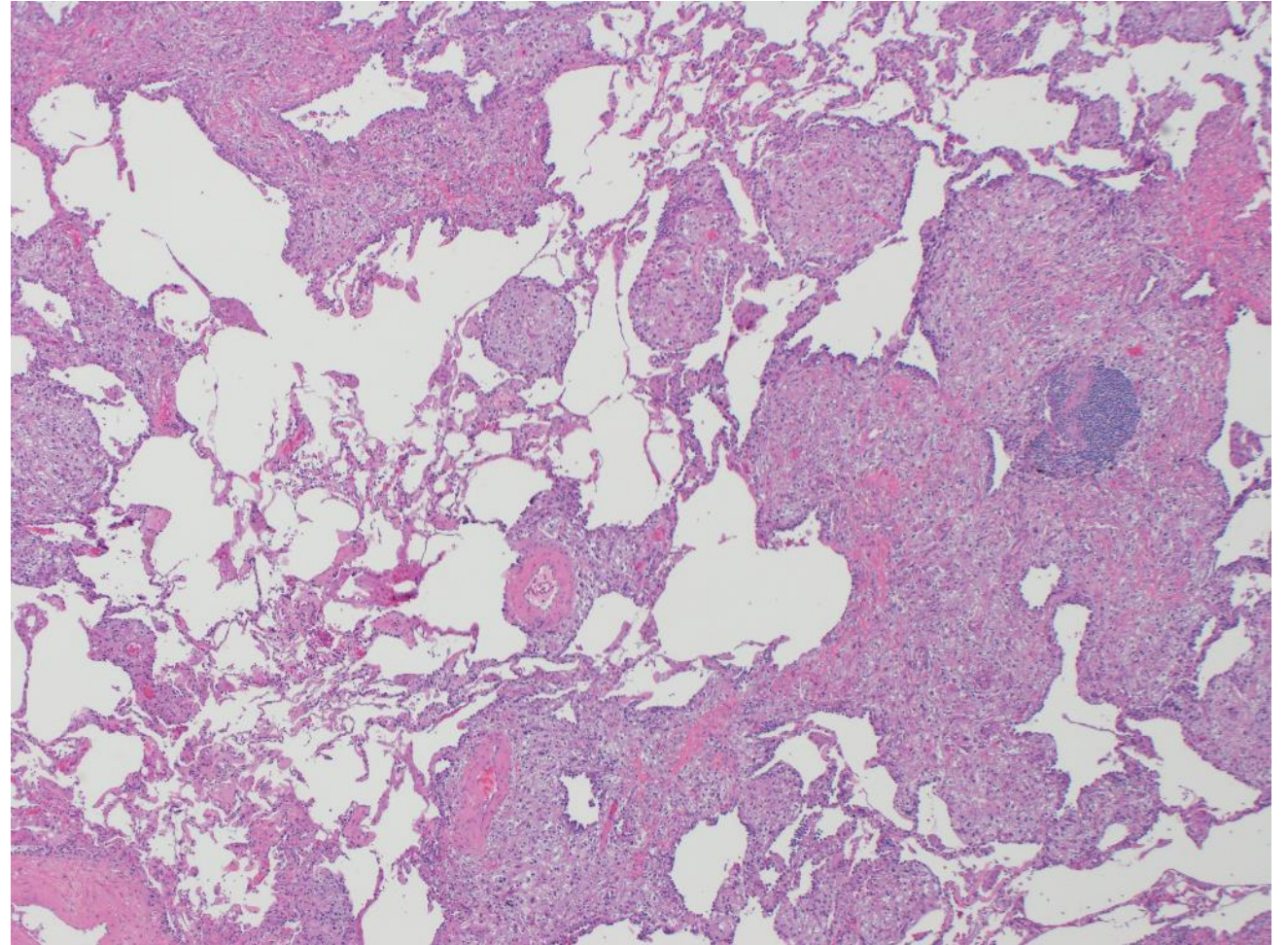
Case 3

- 64-year-old woman with diffuse rash since 1994 (biopsy reported as granuloma annulare), chronic sinusitis, elevated sedimentation rate, bronchial biopsy reported as non-necrotizing granulomas. No respiratory symptoms.
- CT scan showed bilateral pulmonary ground glass opacities with interstitial prominence and areas of nodular consolidation. Mildly enlarged lymph nodes in mediastinum, iliac and inguinal sites.
- Open lung biopsy performed in 2003.

Lung biopsy 2003

H&E 40x

- Histiocytic infiltrate with fibrosis
- Lymphangitic, perivascular and peribronchiolar distribution
- CD68/S100 positive histiocytes
- Considered c/w ECD
- Clinical observation

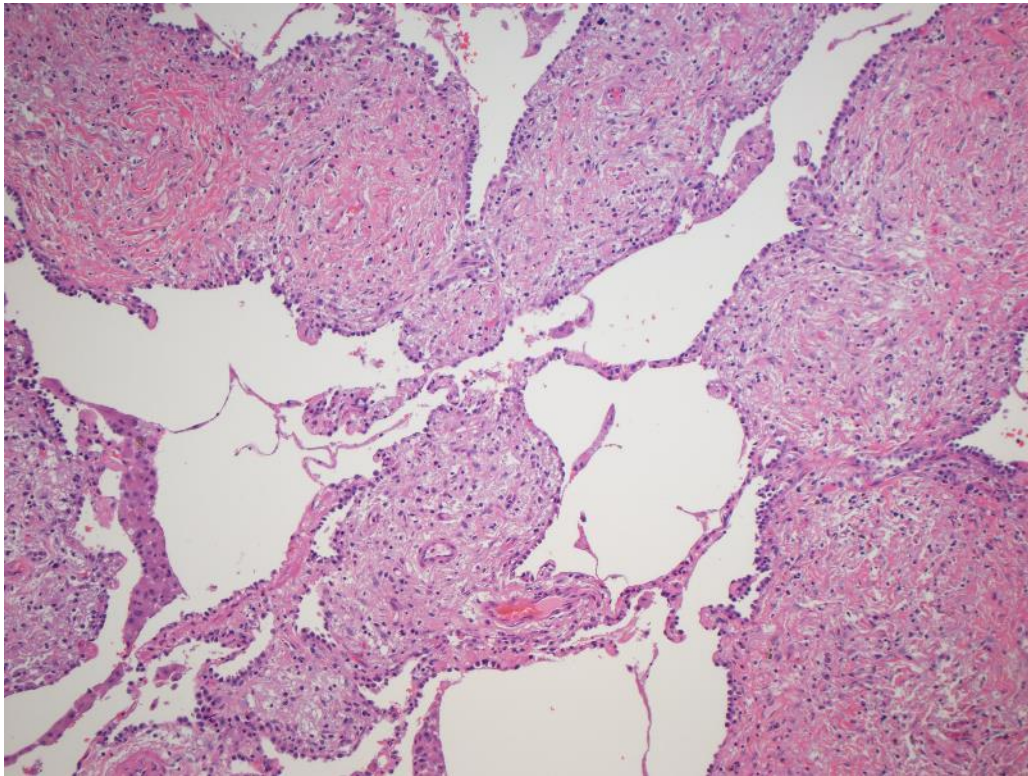


Case 3

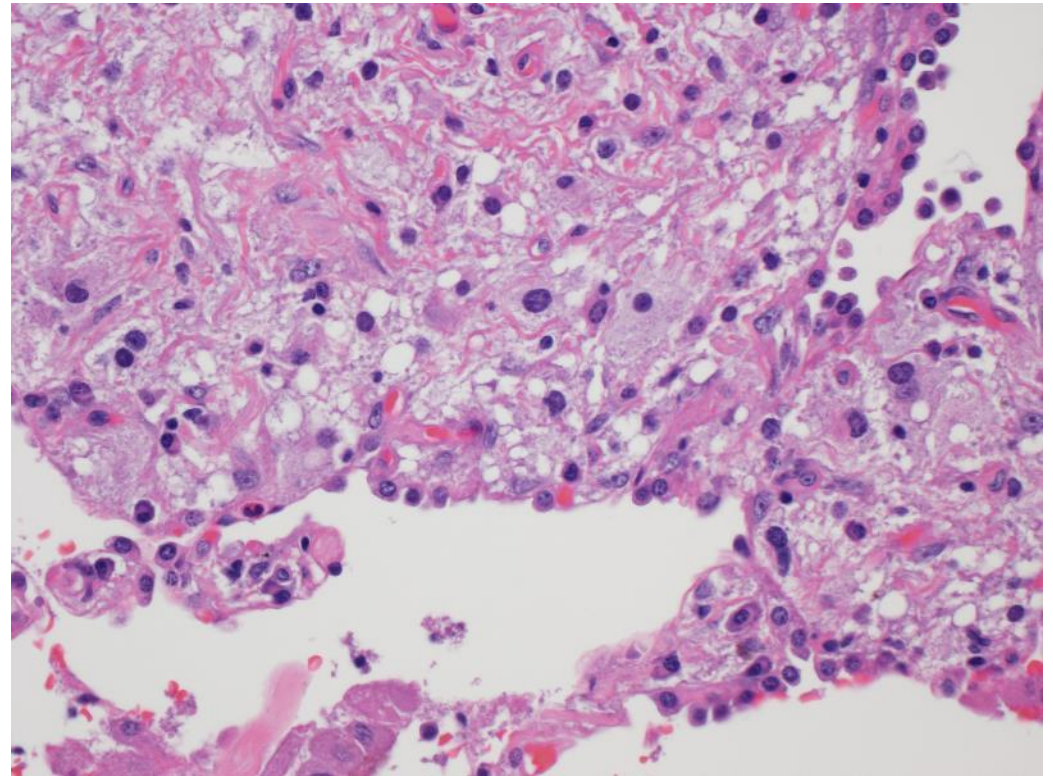
- 2014: Imaging showed persistent lung and pleural disease, bilateral perinephric soft tissue masses with stranding, bone involvement in proximal tibiae and feet.
- 2015: Urine cfDNA positive for BRAF V600E
- Treated with vemurafenib, minimal response

Case 3-second review

H&E 100x

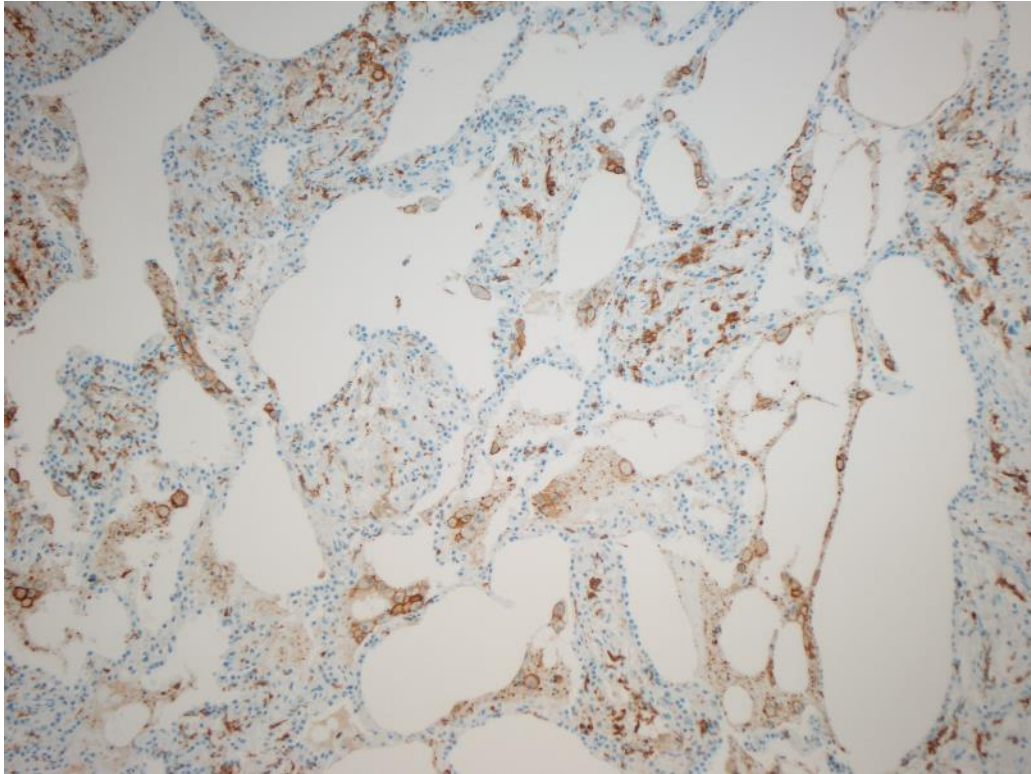


H&E 400x

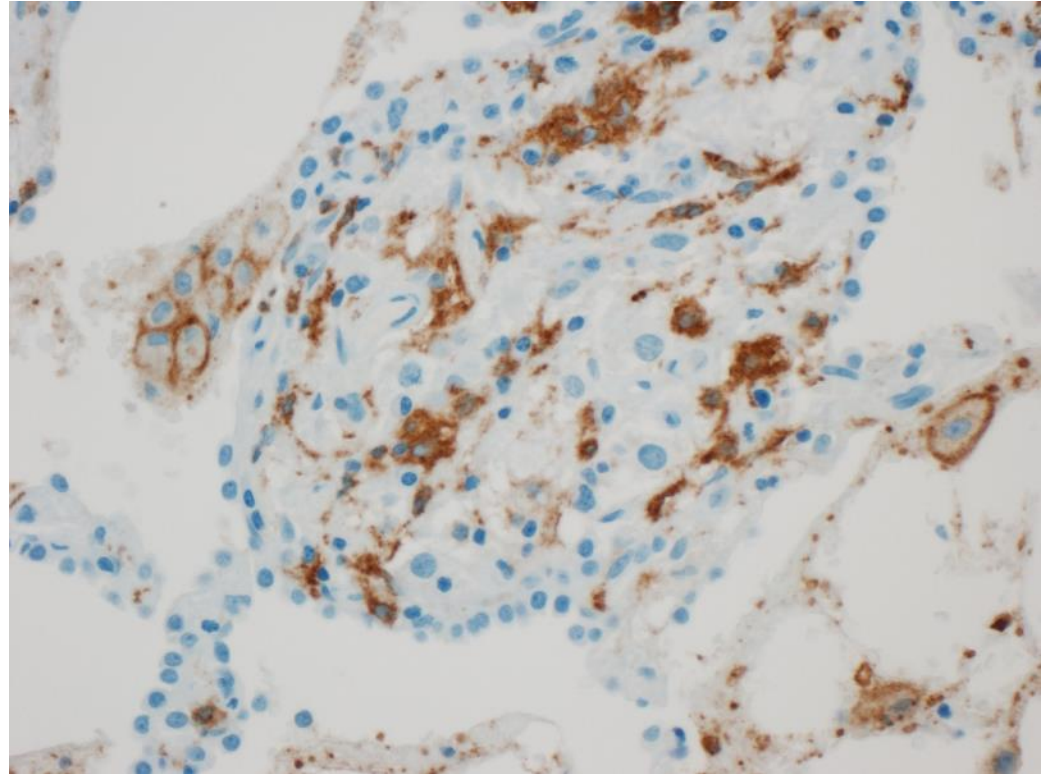


Case 3-second review

CD163 negative (100x)

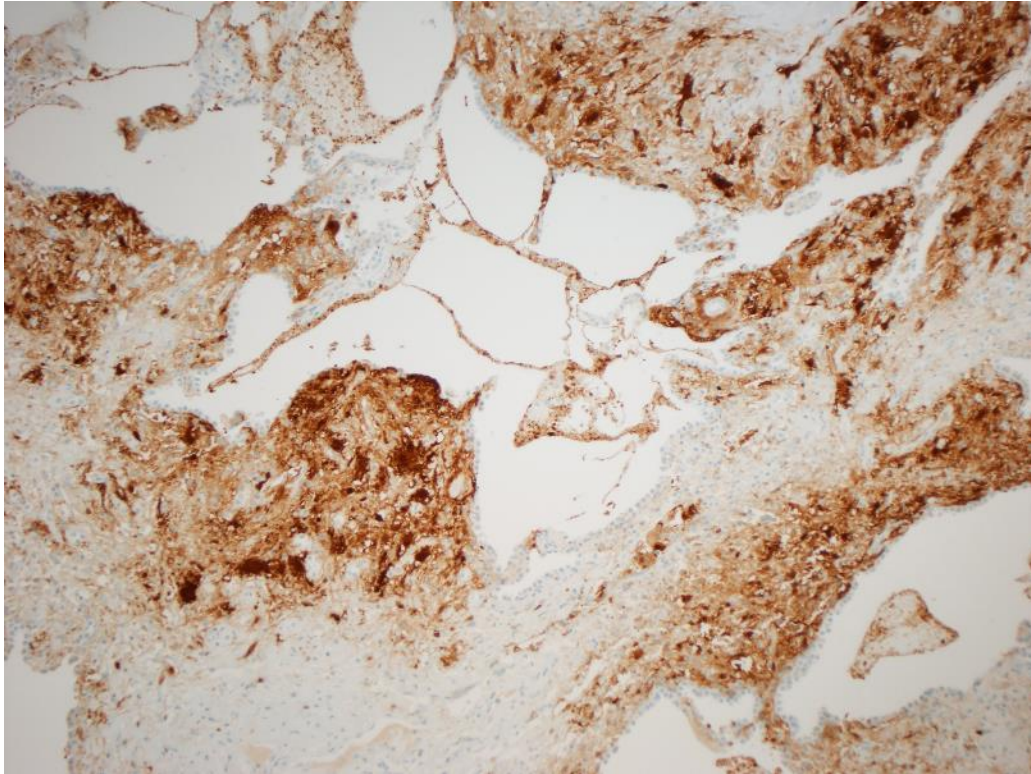


CD163 negative (400x)

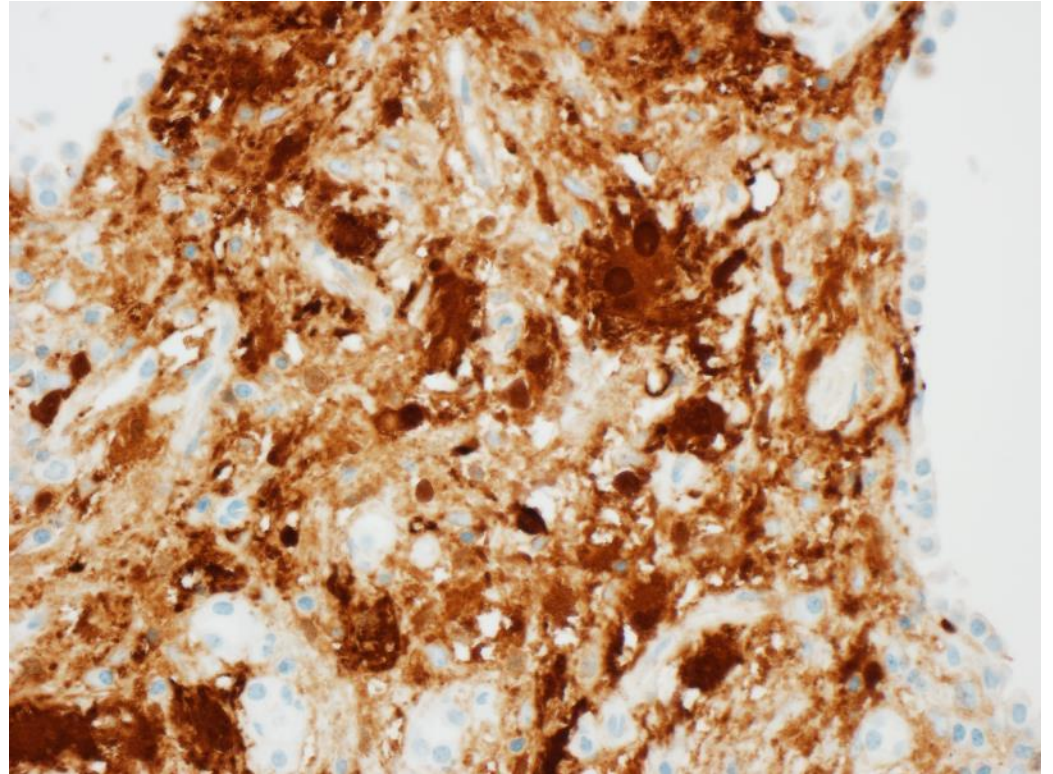


Case 3-second review

S100 positive (100x)

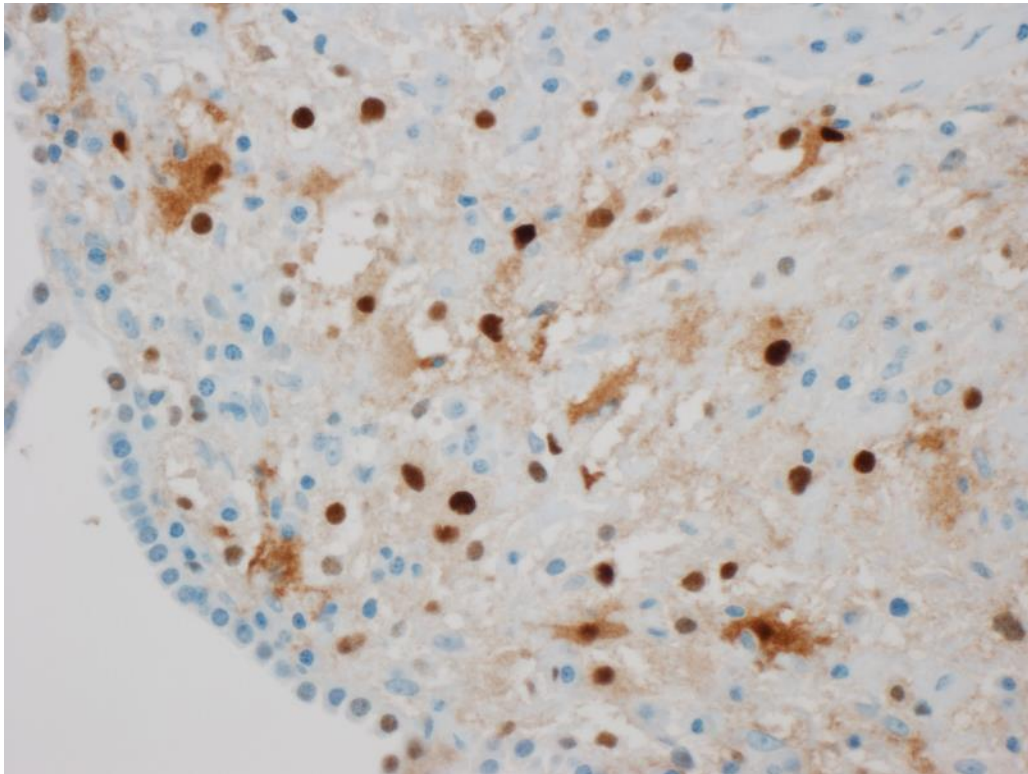


S100 positive (400x)

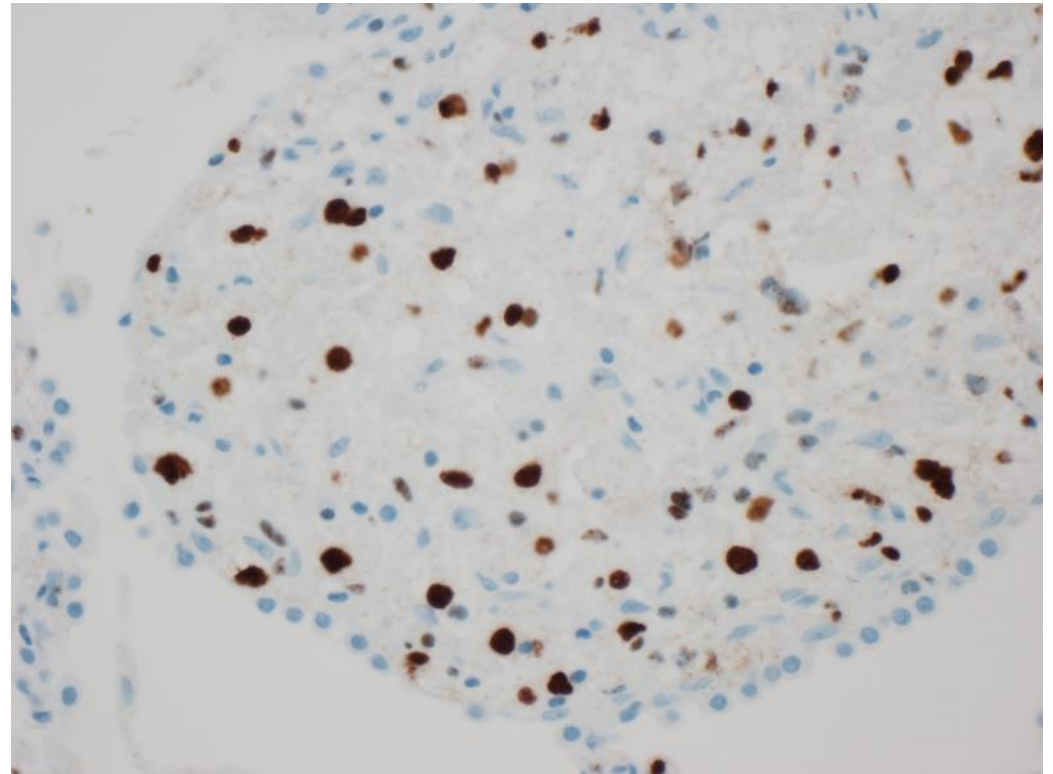


Case 3-second review

Cyclin D1 positive (400x)



OCT2 positive (400x)



Rosai-Dorfman disease versus Erdheim-Chester disease in the Lung

- Frequency of lung involvement: RDD 10-20% vs ECD 35-50%
- Lymphangitic pattern similar with RDD and ECD
- Involvement of lung, skin, sinuses, kidney, bone seen in both diseases
- Lymphadenopathy more characteristic of RDD than ECD
- RDD phenotype: CD163 negative (10% of cases), S100 positive, cyclin D1 positive, OCT2 positive
 - Ravindran A, Goyal G, Go RS, Rech KL; Mayo Clinic Histiocytosis Working Group. Rosai-Dorfman Disease Displays a Unique Monocyte-Macrophage Phenotype Characterized by Expression of OCT2. *Am J Surg Pathol*. 2021;45(1):35-44
- BRAF V600E very rare in RDD
 - IHC and plasma cfDNA negative for BRAF V600E
 - Urine cfDNA false positive