Pulmonary Capillary Hemangiomatosis (PCH) associated PH

Nam Eun Kim,
Division of Pulmonology, Department of Internal Medicine
Severance Hospital, Yonsei University College of Medicine

Name : 곽 O 숙

F/53

Chief complaint: dyspnea

Onset : 10 yrs ago, aggravated 3 yrs ago

Past History

PAH associated with CTD (2017)

Systemic sclerosis

CTD-related ILD (clinical)

LC (NBNC)

r/o autoimmune hepatitis

HTN/DM/old TB/hepatitis :

-/+/-/+(autoimmune hepatitis)

Op hx

s/p cholecystectomy (2013)

s/p varicose vein op (2014)

Smoking hx : never-smoker

Alcohol hx : none

Occupation hx : none

Family hx

부(Colon cancer)

친오빠(Lung cancer)

Present illness

본 53세 여환 DM, Systemic sclerosis , r/o autoimmune hepatitis 과거력 있는 분으로 2017.05월 타병원에서 PAH associated CTD 진단받고 medication 3제 유지하던 중 (CCB, Ambrisentan, PDE-5 inhibitor) CTD related ILD progression 소견으로 cytoxan 및 high dose steroid 사용하였으나 호전 소견 보이지 않아 2019.02월 폐이식 대기자로 등록, 본원에서 수술 위해 내원함.

Review of System

Dyspnea+

DOE + , mMRC III

O2 : 3L /min (2017.12월부터 가정산소)

산소하고 평지 천천히 20m 정도 걸으면 쉬어야 함.

외출 거의 못함 (최근 1-2달)

6MWT: 108m (SpO2 80->74%)

Sicca Sx +, Raynaud -, puffy finger-

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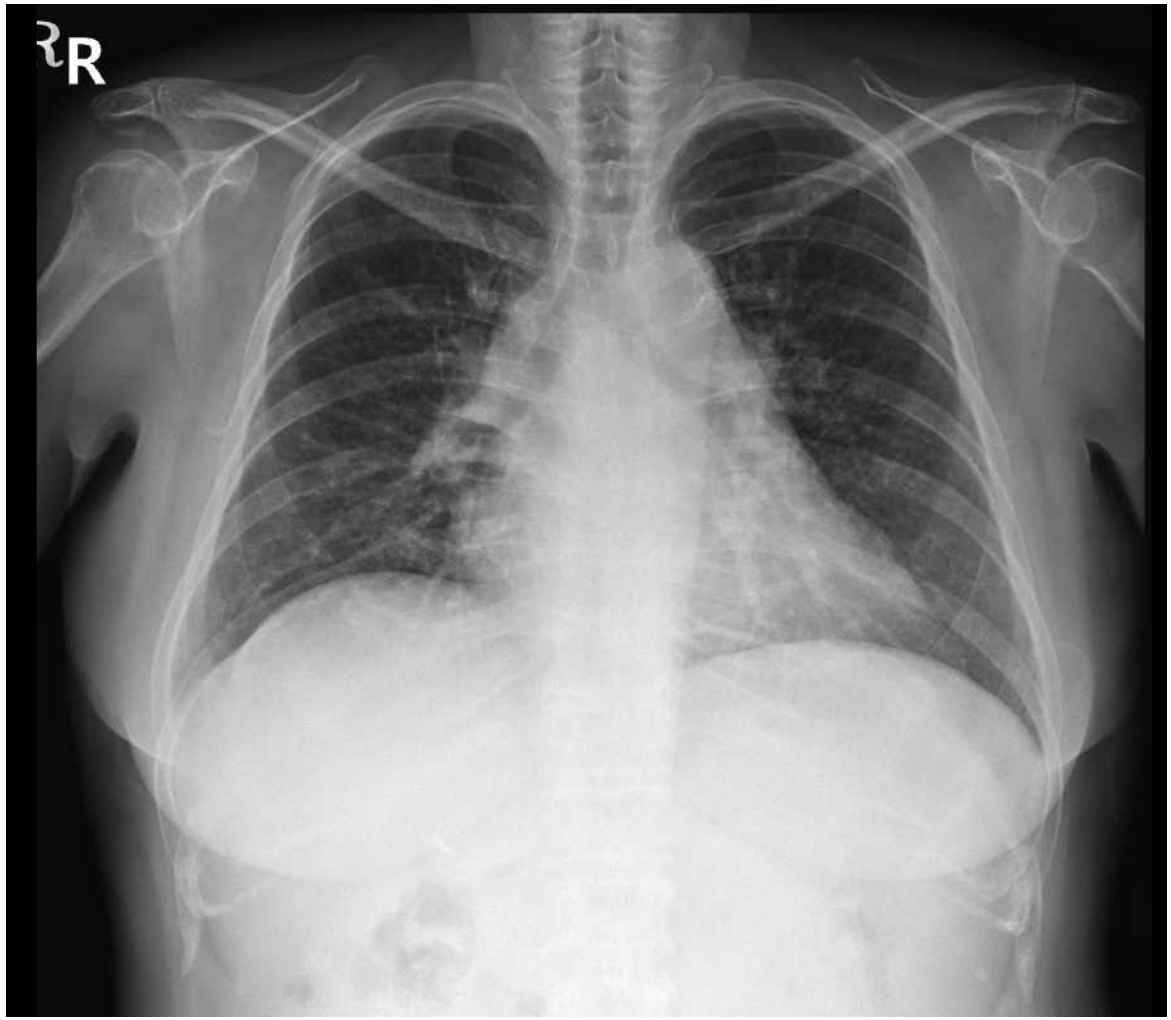
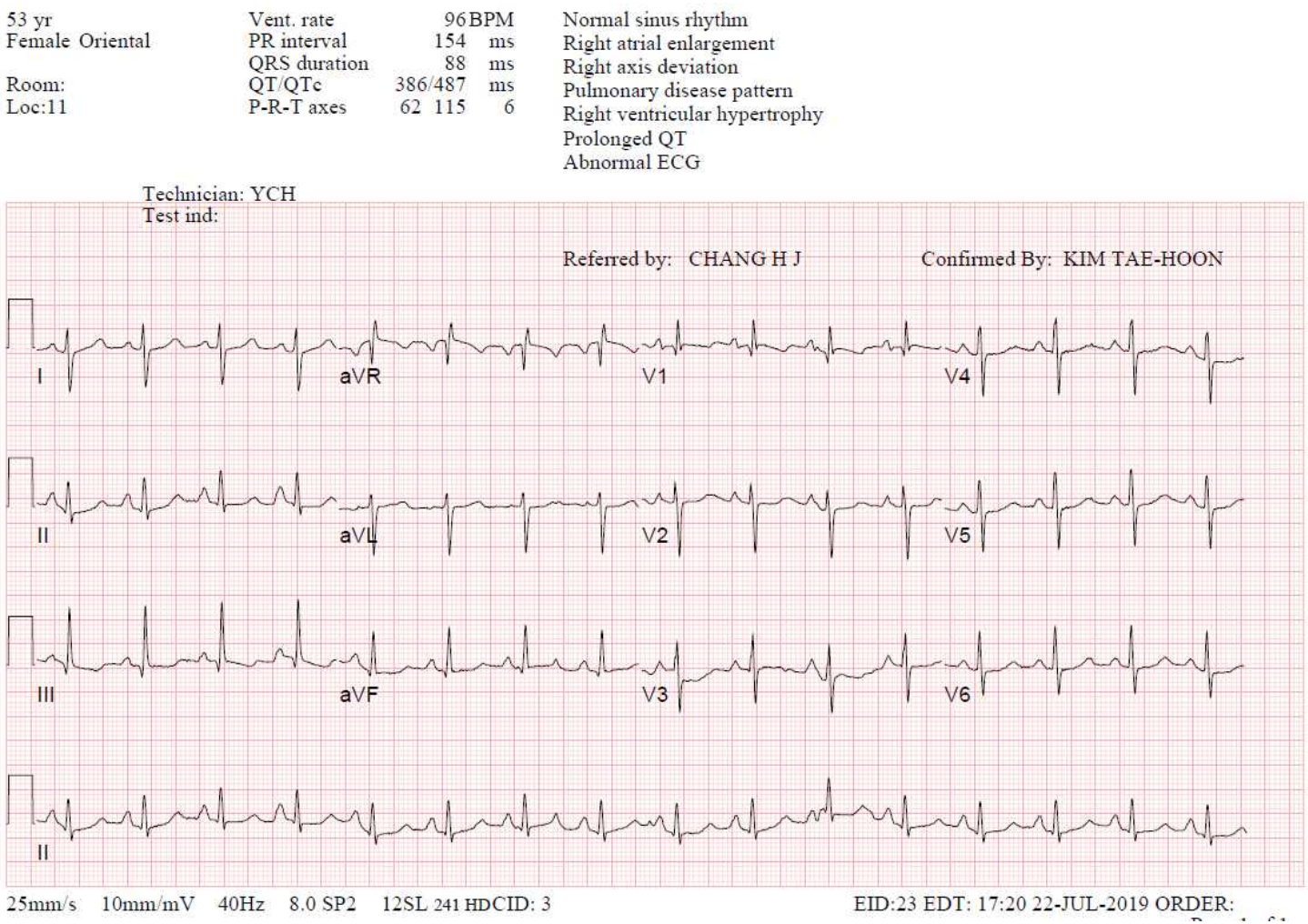
CXR (2019.07.22)



EKG (2019.07.22)



Laboratory findings

Pre-OP labs

CBC 7390>14.5<118k (seg. 78.8%)

PT/aPTT 1.00/33.6

BUN/Cr 28.8/0.94

Electrolyte 137/4.8/103

OT/PT/T.bil 16/11/1.0

ESR/CRP 5/6.5

NT-proBNP **1733**

ABGA

pH 7.45, **pCO2 27.8**, pO2 142.0, HCO3- 19.8, SpO2 99.8% (O2 3L)

ANA > 1:320, anti-centromere+

Other ENA (-)

Anti-Scl-70 (-)

Anti-DNA screening(+)

Anti-smooth muscle (+)

HBsAg Negative(0.31)

Anti-HBc Negative(2.24)

HBeAg Negative(0.433)

Anti-HCV Negative(0.033)

타병원 Cardiac catheterization

2017 06 mPAP 45, PVR 7 Wu, partial response to NO

2017 12 mPAP 38, PVR 3 WU, no acute vasodilator test

2019 02 mPAP 43, (+) vasodilator test, modereate pulmonary HTN

PCWP : 7/1**(5)**mmHg

RPA : 72/27**(45)**mmHg, SaO2 64.9%

MPA : 69/23(43) mmHg-

RVA : 74/4/8 mmHg

RA : 11/6(8) mmHg SaO2 63.9%

CO(Thermodilution) 3.96L/min

CO(Fick method) 3.45L/min

PFT (2019.05.15)

FVC 2.41L (79%), FEV1 2.03L (89%), FEV1/FVC ratio (84%), **DLCO (32%)**

ECHO

TTE (2019.05.13)

1. Severe pulmonary HTN (RVSP : 90mmHg) with poorly collapsible IVC (20mm)
2. Enlarged RV and RA with reduced RV systolic function (FAC : 11%)
3. Severe TR (G III/IV) with dilated TV annulus (39mm)
4. D-shaped LV (LVEDD/ESD : 40/22mm) with normal global LV systolic function (EF: 79%)
5. Concentric remodeling of LV and RVH (9mm)
6. Relaxation abnormality of LV filling pattern (E/e' : 11)

<Pul.HTN, complex>

1. TR V max: 4.48m/sec
2. RAP : 10mmHg
3. TR area: 11.3cm2
4. TV TDI S': 12cm/s
5. TAPSE: 1.48cm
6. RVOT acceleration time: 170.7ms
7. RVOT VTI: 15.8cm
8. LVOT VTI: 21.1cm
9. Tei-index: 0.59

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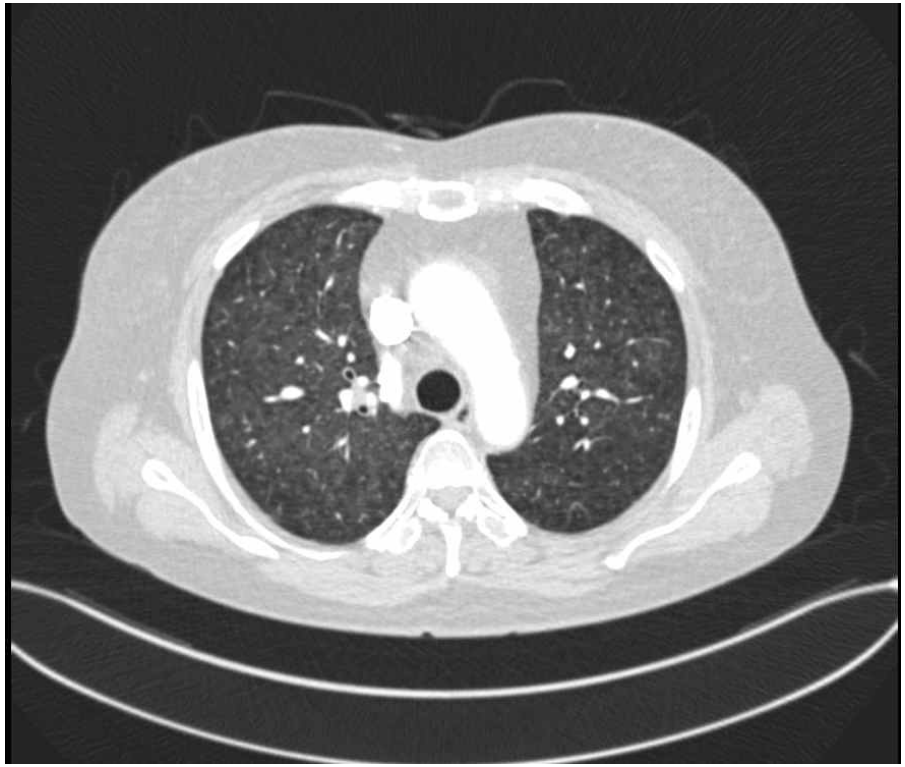
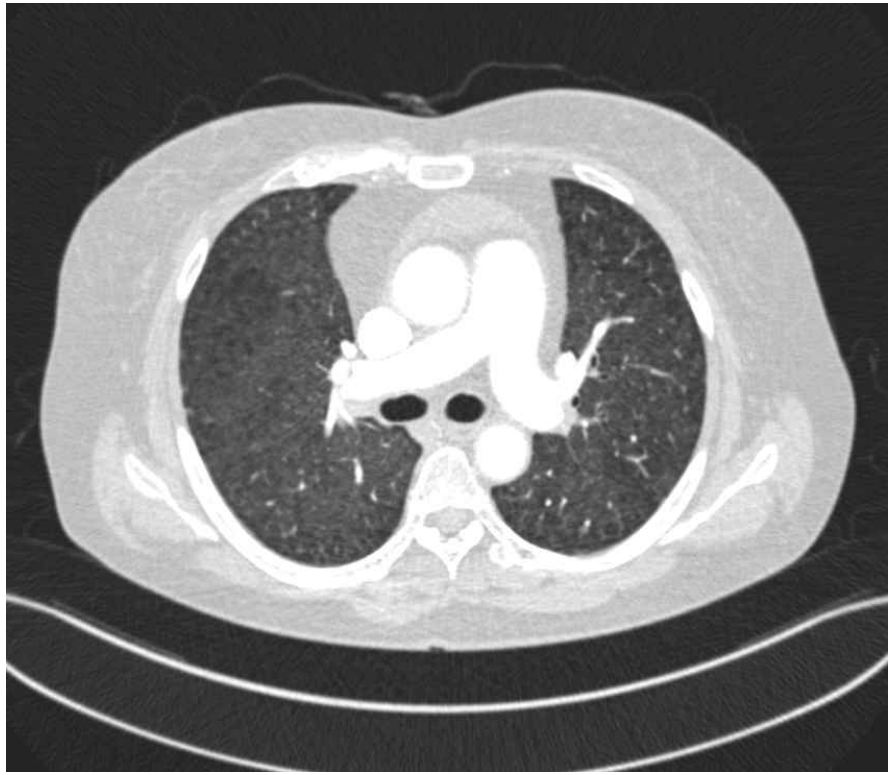
Liver fibroscan (2019.05.15)

Liver cirrhosis (F4), Mild steatosis (S1)

Chest CT(2017-06-02)





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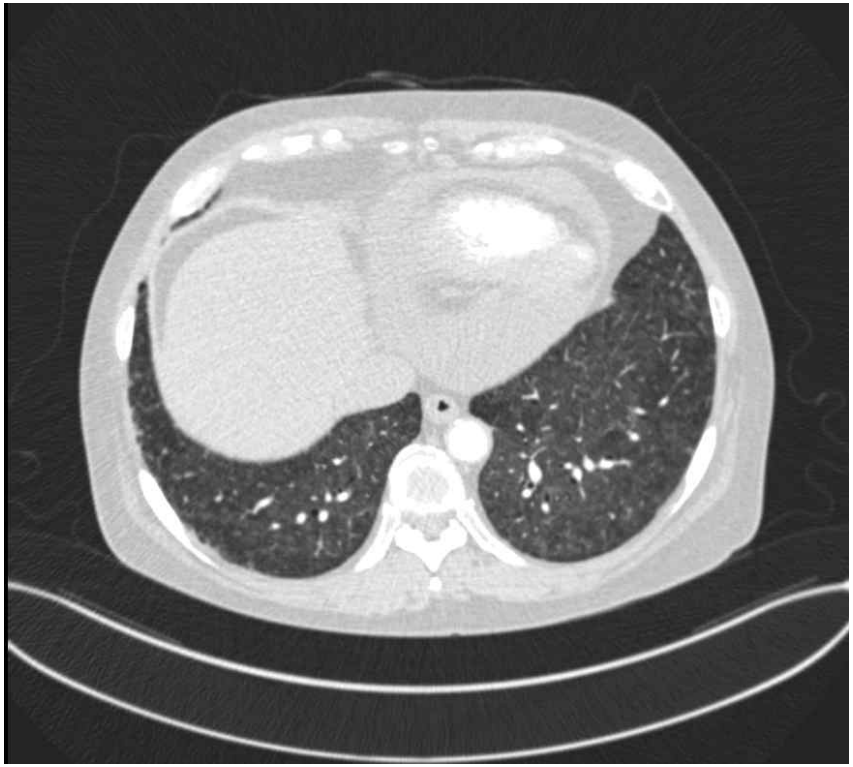
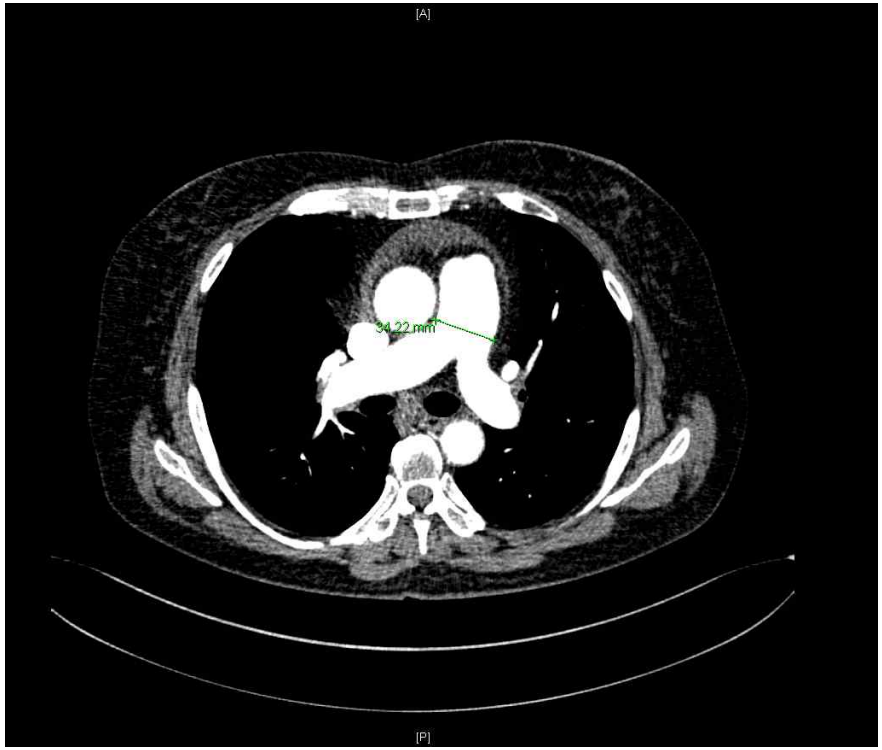
Chest CT(2017-06-02)



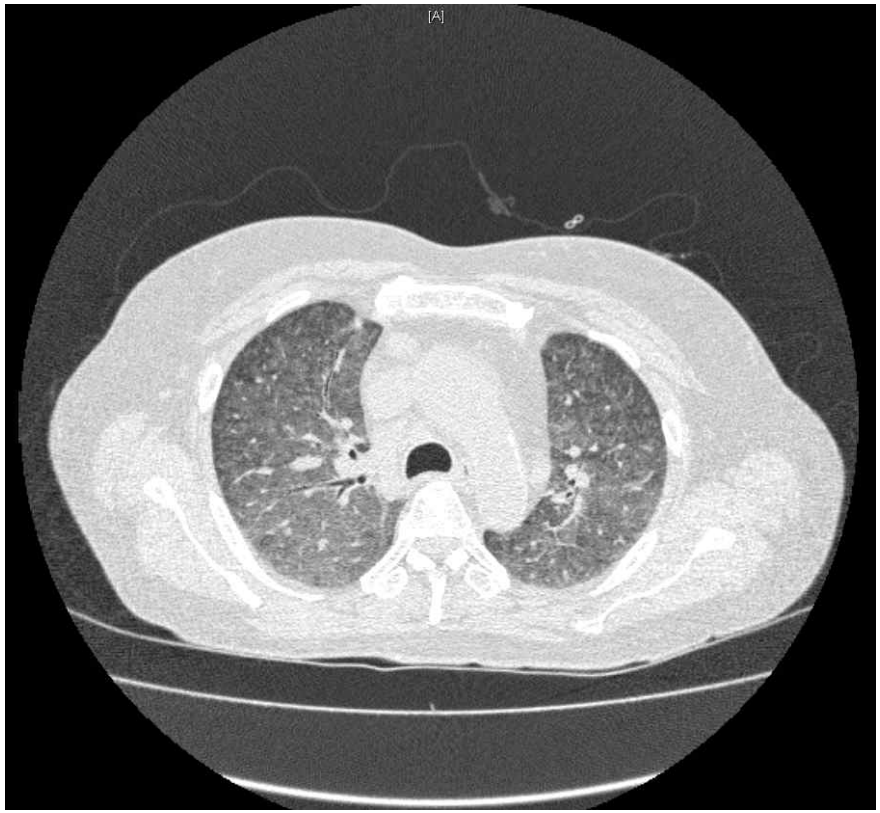


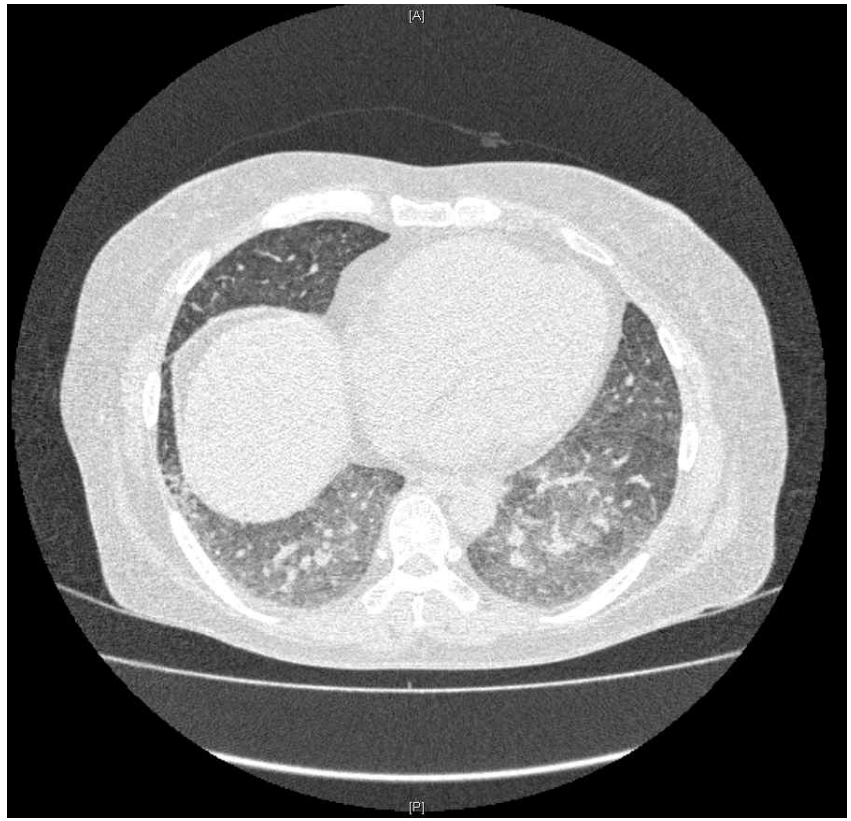
Chest CT(2017-06-02)

1. Pulmonary artery dilatation c/w pulmonary artery hypertension
2. Diffuse GGO, both lung, either central lung zone or centrilobular distribution

   -> **microangiopathy associated pulmonary artery hypertension**

Chest CT(2017-12-07)





Chest CT(2017-12-07)

1. Interval increased diffuse GGO in both lung since 2017/09

   -> **progression of CTD-associated ILD more likely** than microangiopathy due to PAH

2. No change of mild dilatation of the pulmonary artery, probable pulmonary artery hypertension

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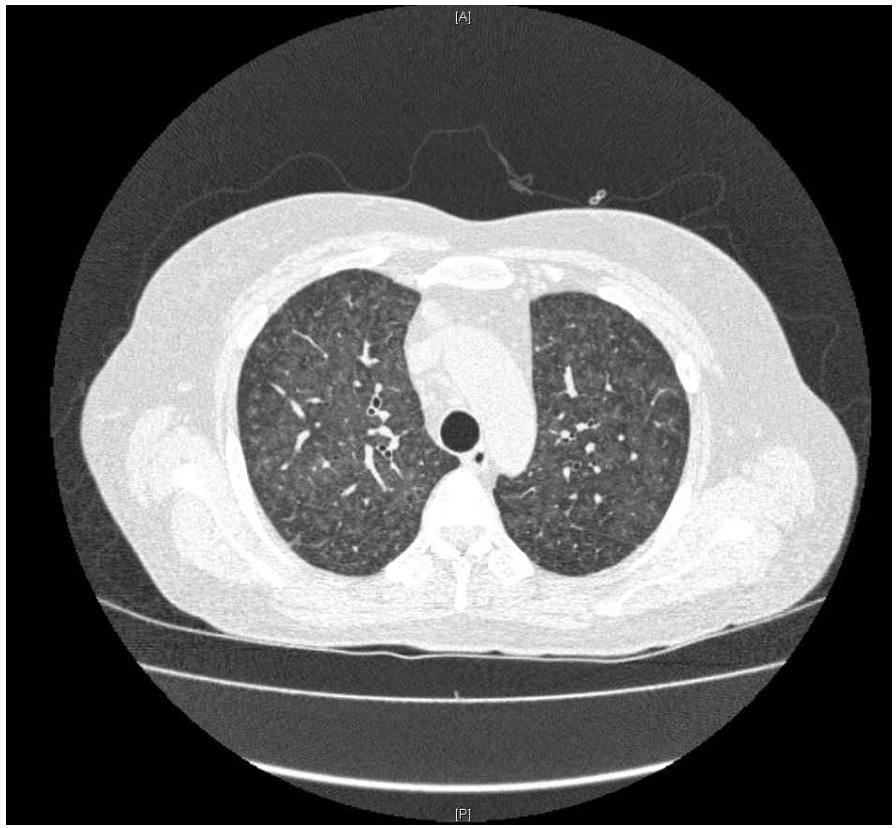
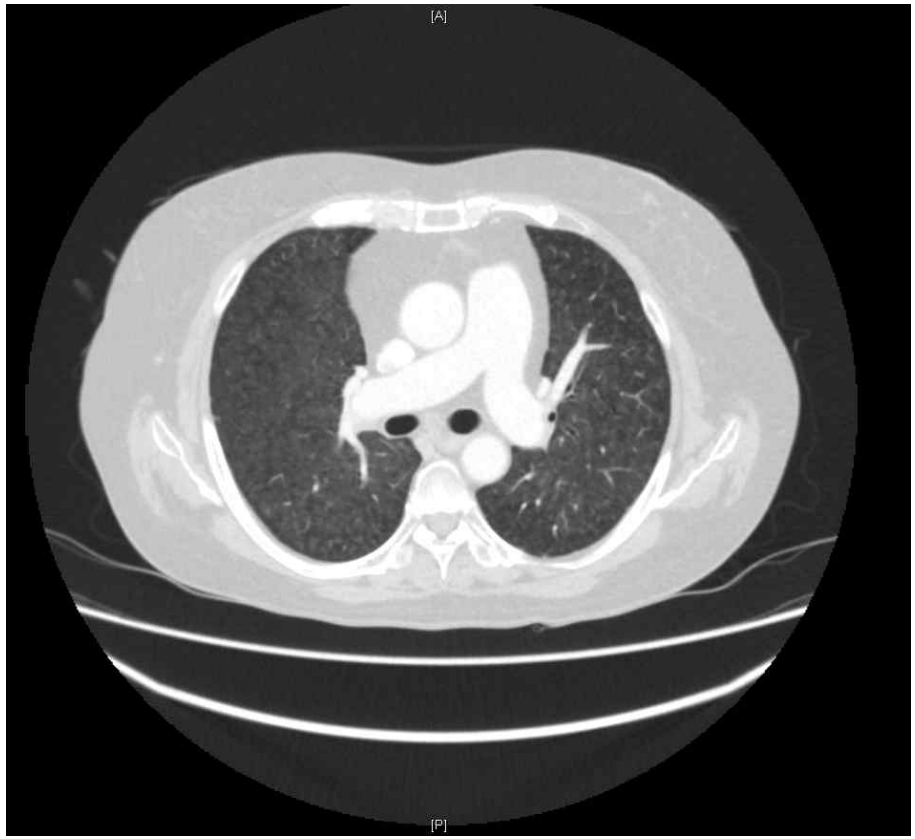
Chest CT (2019.03.08)





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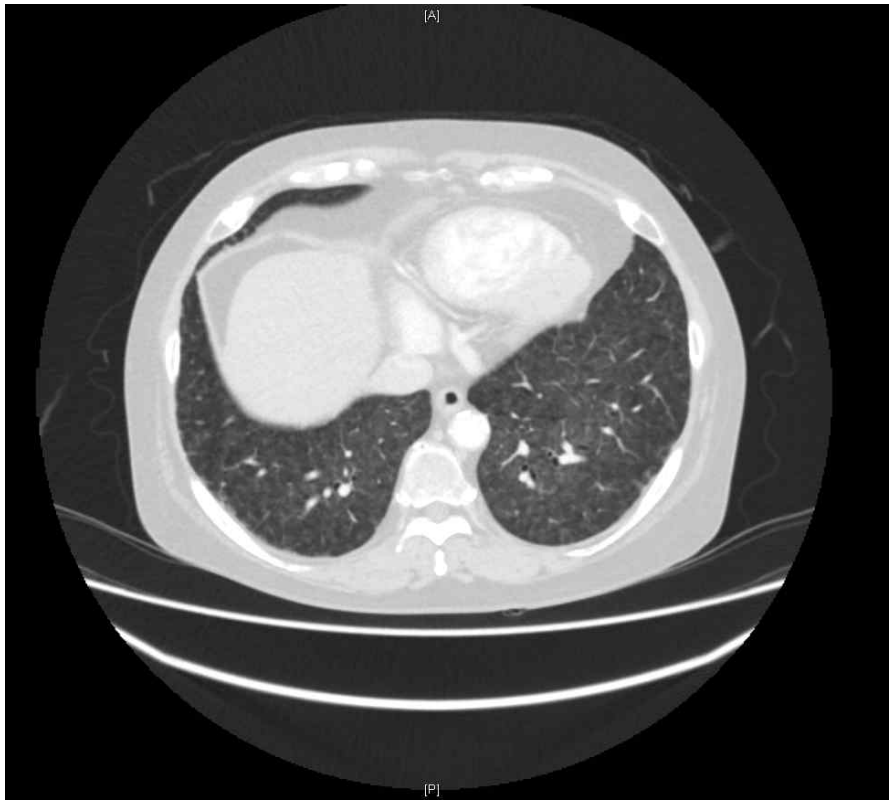
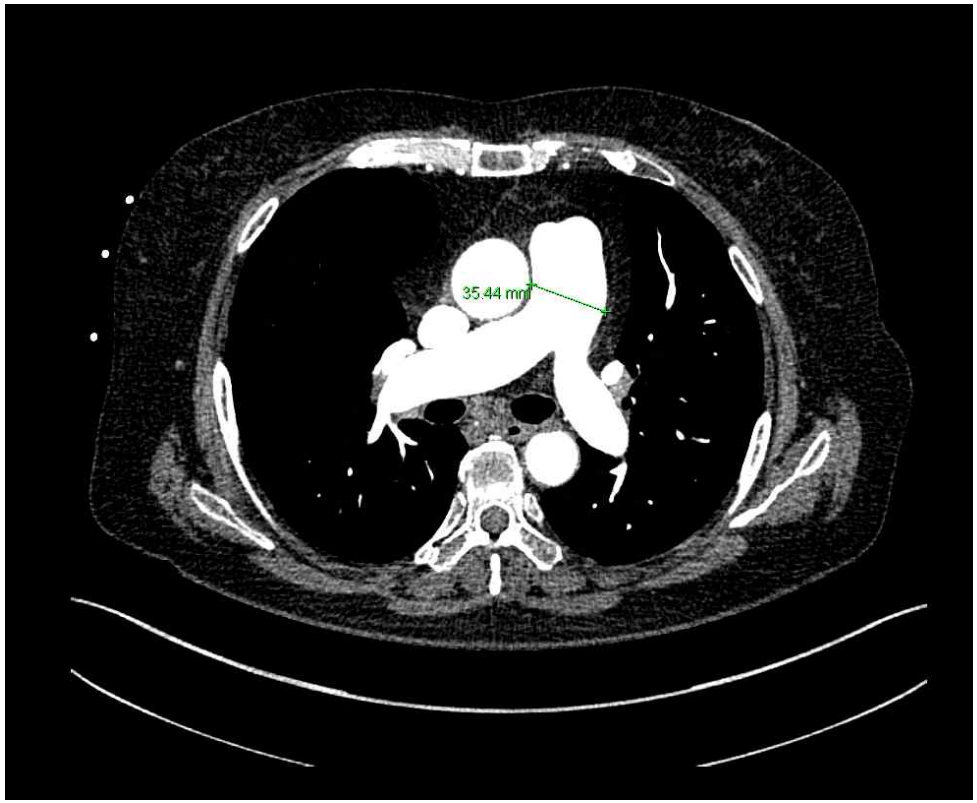
Chest CT (2019.03.08)





Chest CT (2019.02.11)

타병원 판독

Slowly progression of diffuse centri-lobular GGO with supleural sparing throughout both lungs since 2017/06, suggesting **lung parenchymal change related hypertension** rather than interstitial lung disease associated with connective tissue disease

DDX 1) capillary hemangiomatosis

2) Metabolic lung disease such as amyloidosis and sarcoidosis

3) R/O benign pneumoconiosis

본원 판독

Imp: Pulmonary arterial hypertension, **probably pulmonary capillary hemangiomatosis associated with connective tissue disease**

Operation note

Lung transplantation (2019.08.13)

Recipent

- Pulmonary HTN, SSc
- Minimal adhesion at thoracic cavity
- Uneventful anastomosis
- Anastomosis 후 bilateral lung (Rt > Lt) 에서 watery secretion 이 많았다
- Lung edematous 하며 pulmonary HTN (preop RVSP 96 mmHg) 으로 VV-ECMO 유지하고 수술 종료하였다

Pathology

Lung transplantation (2019.08.13)

[Final report]

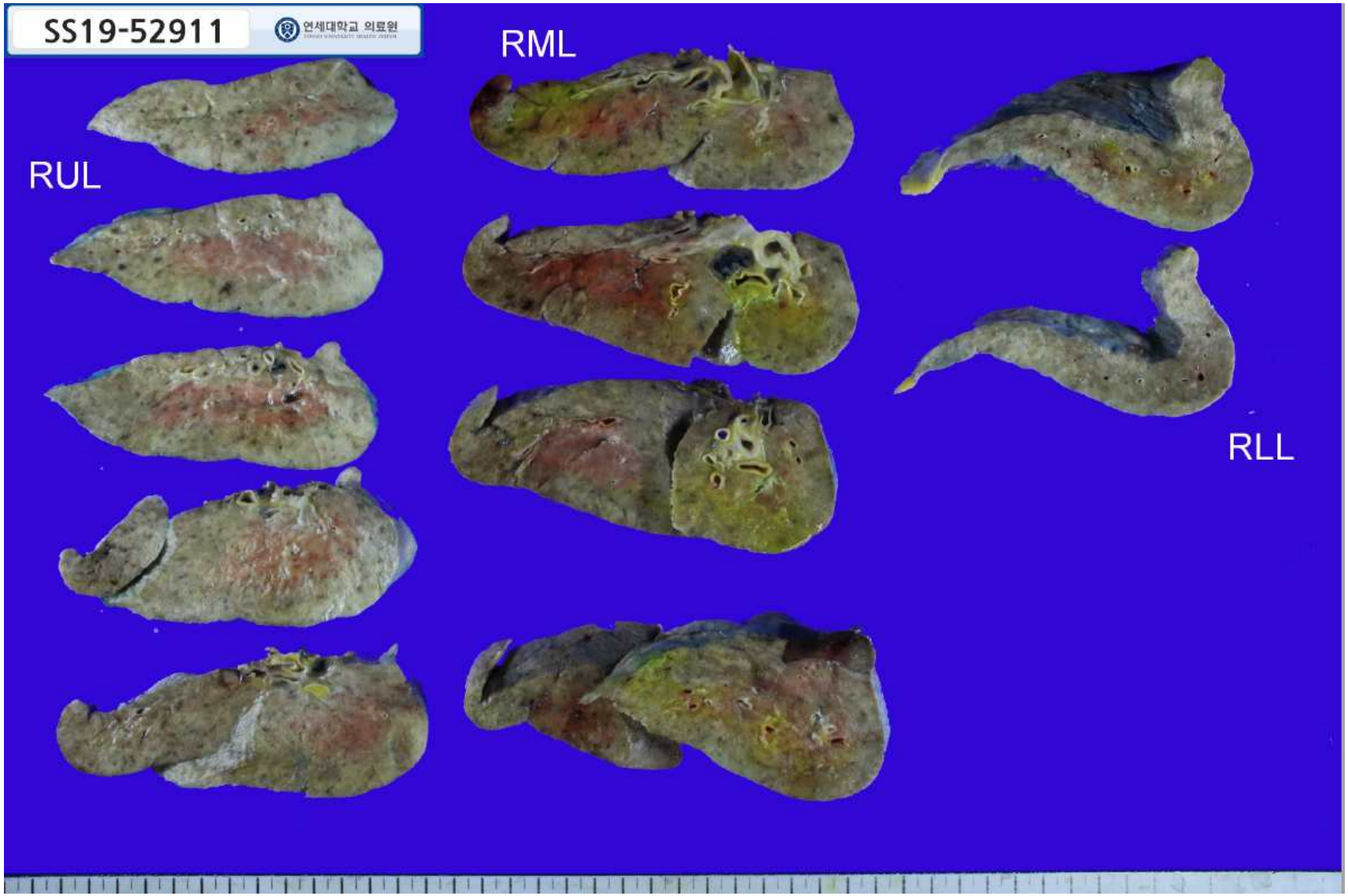
Lung, right and left:

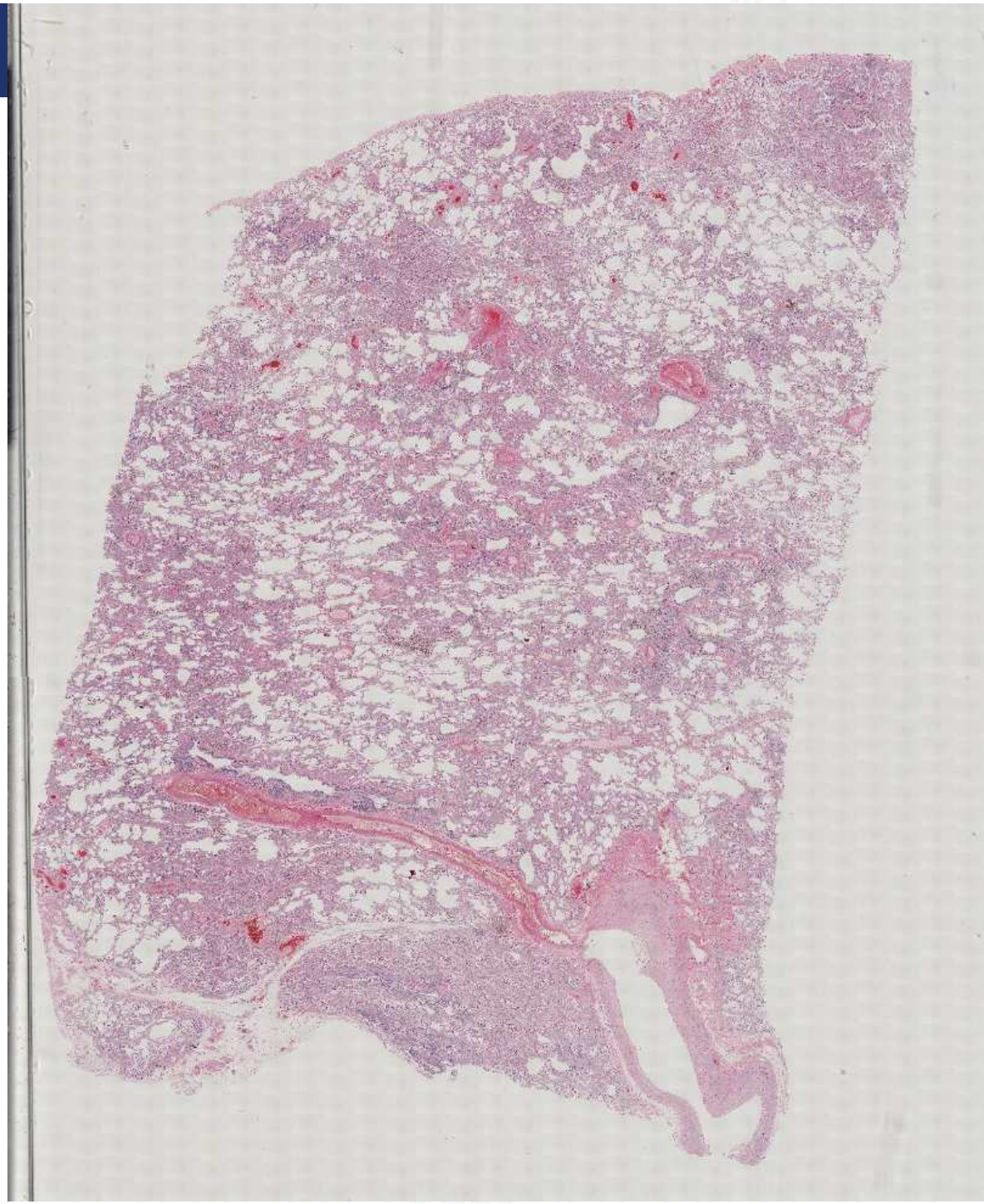
1. Multifocal thickened alveolar septae expanded by a capillary proliferation, consistent with pulmonary capillary hemangiomatosis, see note.

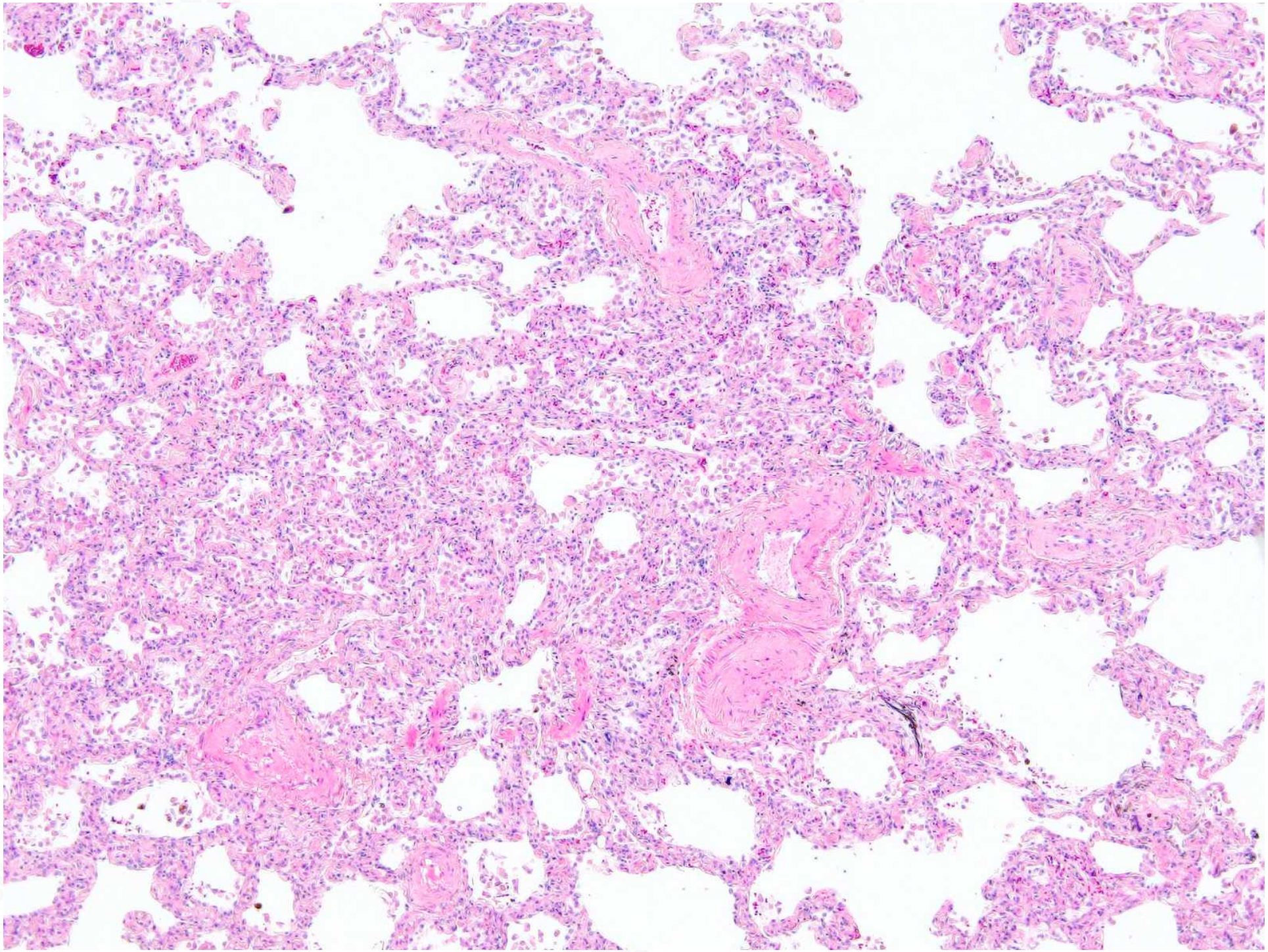
2. Intimal and medial hypertrophy of arteries and muscularization of arterioles, consistent with pulmonary hypertension

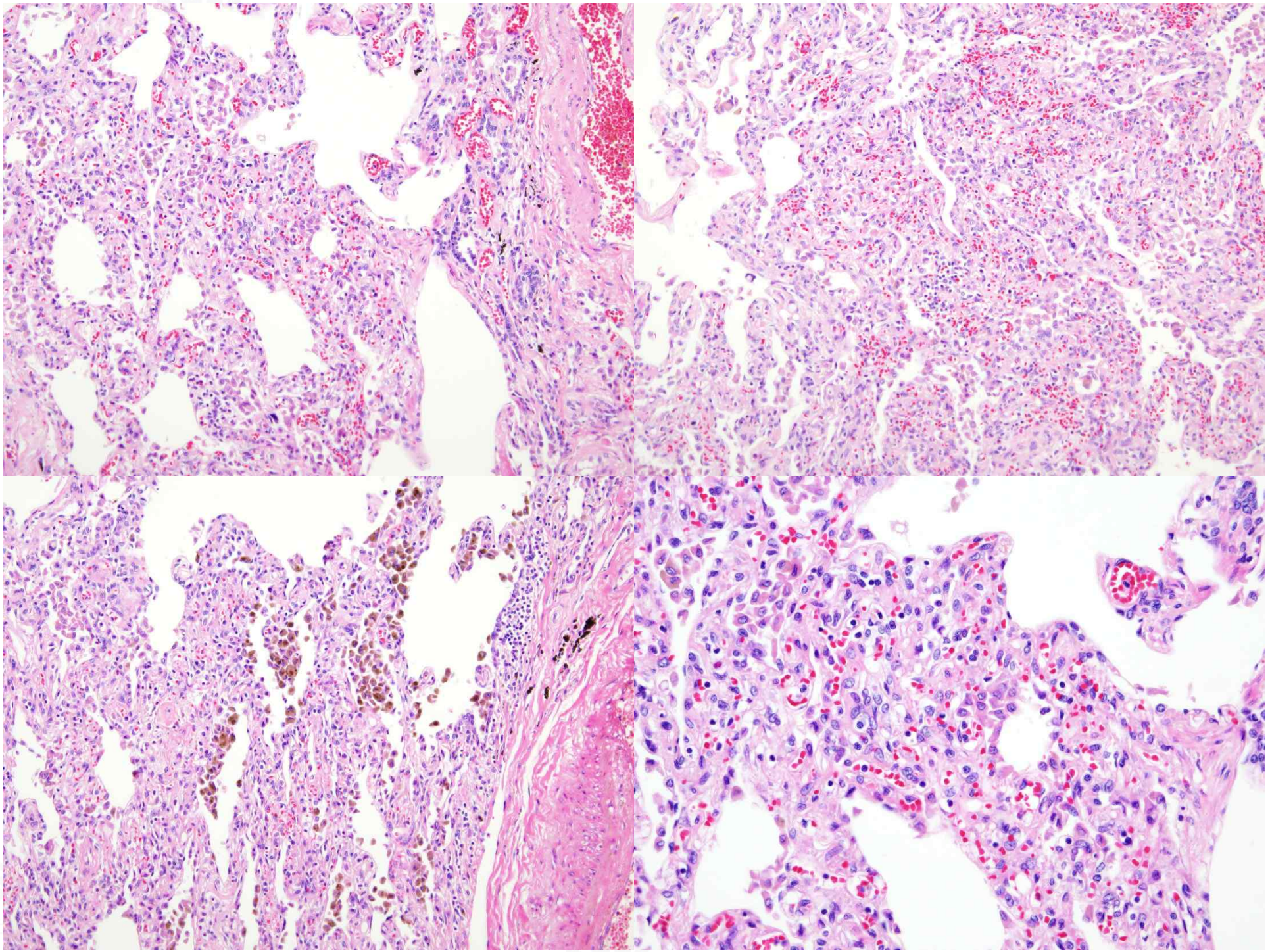
3. Multifocal hemosiderin-laiden macrophages in alveolar spaces

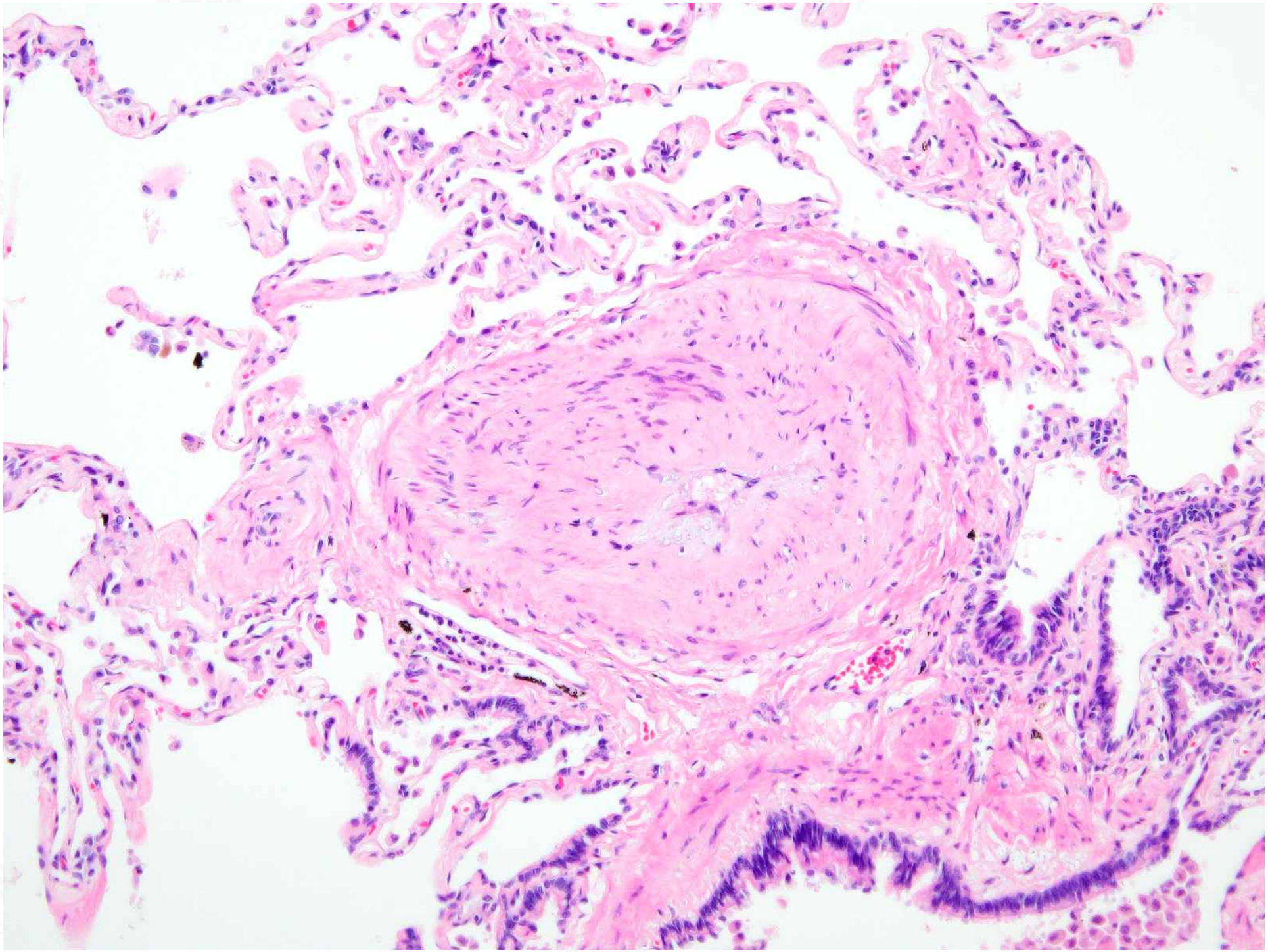
4. Focal pleural and subpleural fibrosis and peribronchiolar metaplasia











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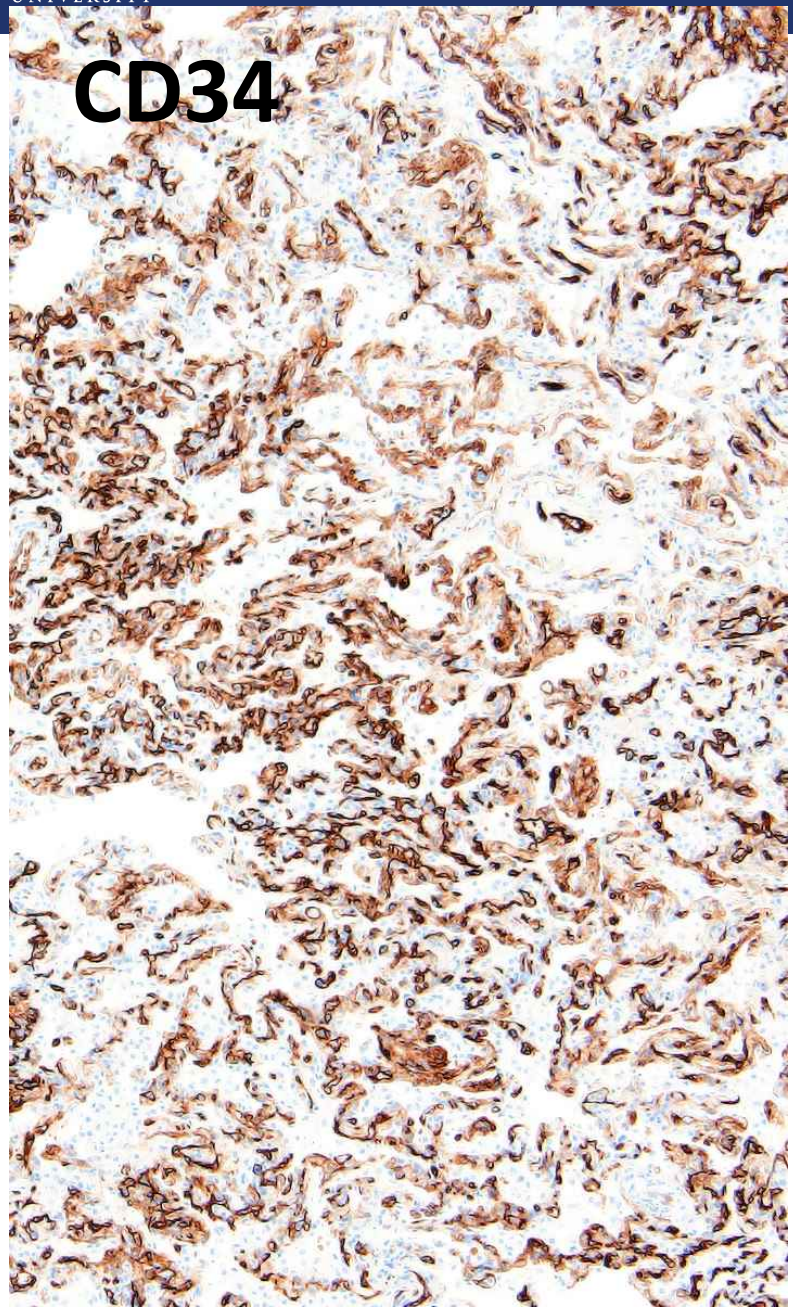
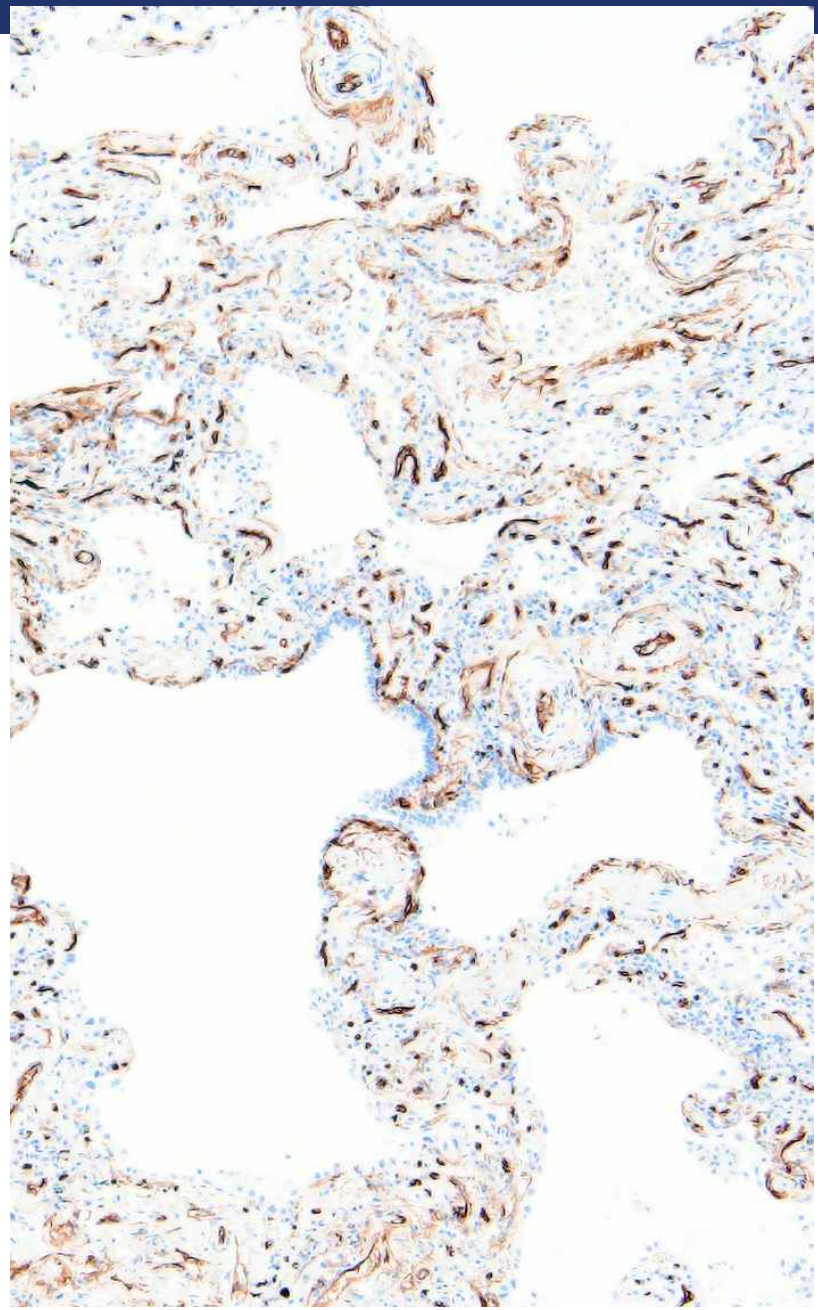
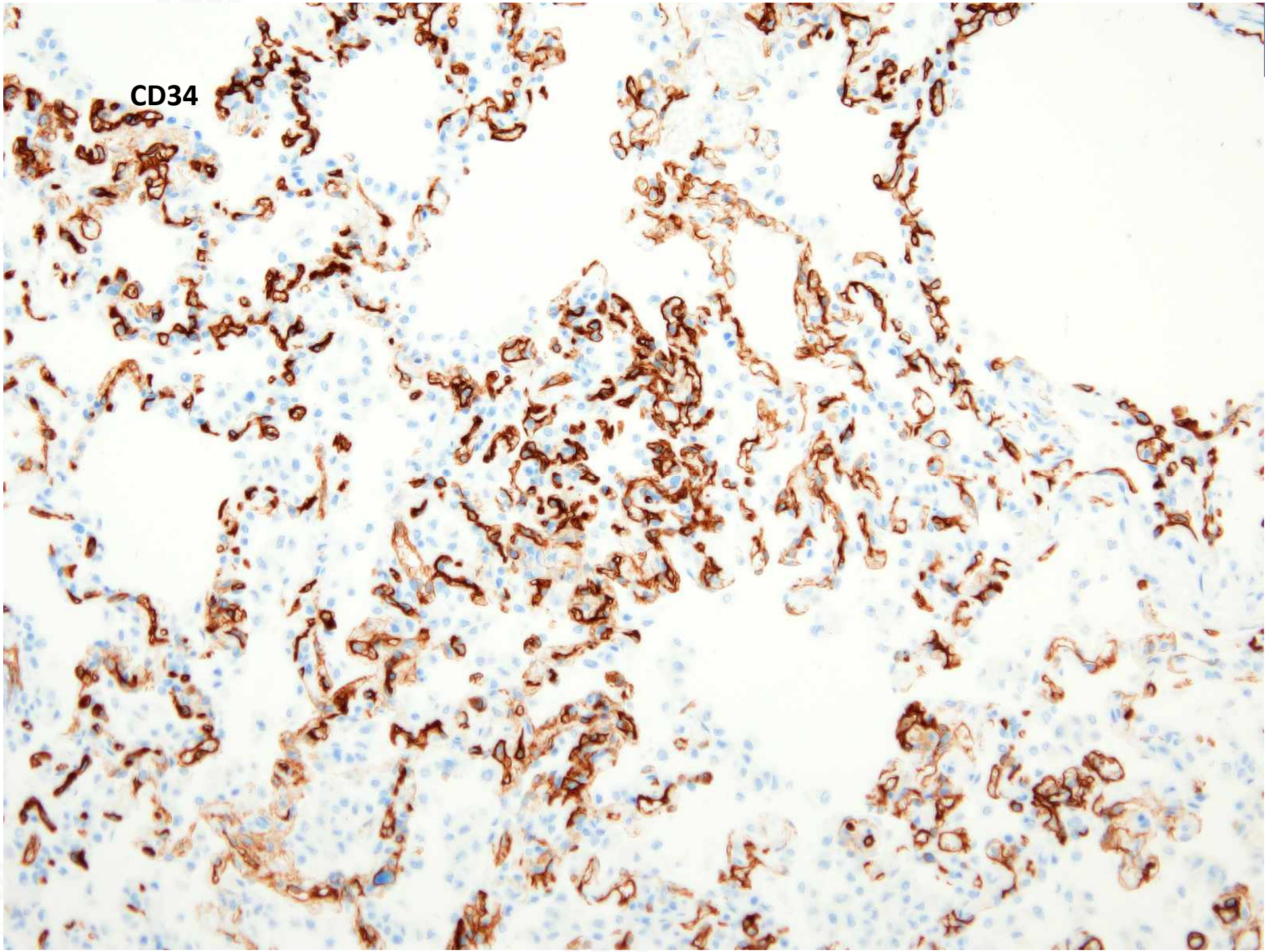
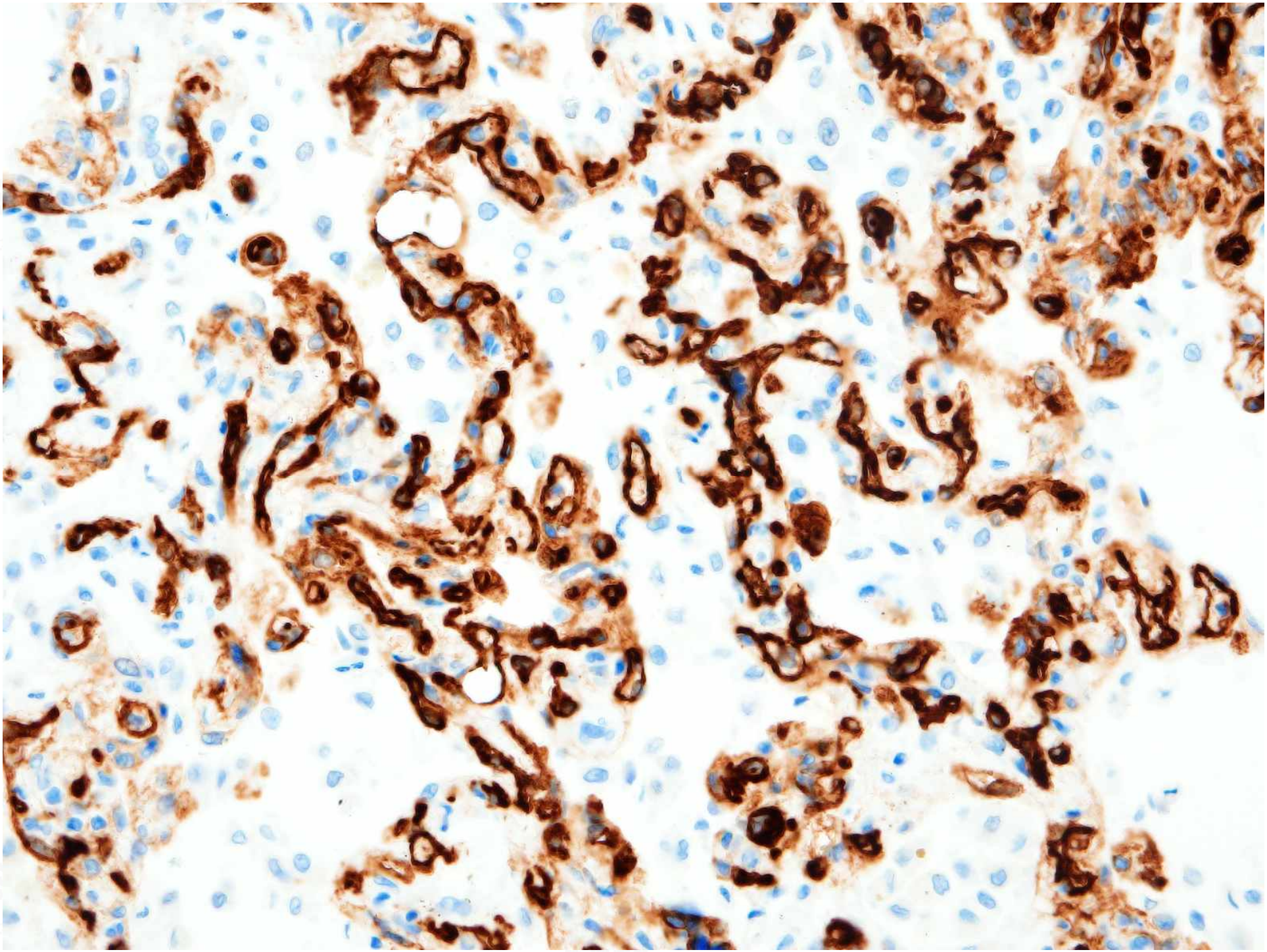
CD34









Pathology

The immunohistochemical stain result:

CD31 and CD34 stains highlight exuberant septal capillary proliferation, with multiple layers of capillaries

Pathologic diagnosis

1. Consistent with pulmonary capillary hemangiomatosis

2. Intimal and medial hypertrophy of arteries and muscularization of arterioles, consistent with pulmonary hypertension

Progress note

2019.08.13 Lung transplantation

POD #3 (2019.08.16) ECMO weaning

POD #8 (2019.08.21) general ward out

POD #37(2019.09.20) Respiratory arrest로 4min CPR 후 ROSC, ICU 입실

hemolytic anemia(Reti ↑) thrombocytopenia, Ferritin ↑, LDH ↑ , TG ↑ , coomb's test(+)로 으로 r/o TTP, r/o HLH imp하에 Bone marrow bx 시행, hematologic malignancy 소견 보이지 않아 secondary HLH imp 하에 plasma pheresis 및 steroid 치료 함. 이후 경과 호전되어 weaning try 중임

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Book review

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Pulmonary Capillar

- PCH
  - Proliferati
  - vessel int
  - rare cause

1. Pulmonary arterial h

- **Idiopathic PAH**
- **Heritable**
  - **BMPR2**
  - **ALK1, endoglin**
  - **unknown**
- **Drugs and toxins ind**
- **Associated with:**
  - Connective tissue dise
  - HIV infection
  - Portal hypertension
  - systemic to pulmonar
  - Schistosomiasis
  - Chronic haemolytic ar

1'Pulm. veno- occlusiv pulmonary capillary h

2. Pulmonary hyperter disease

- **Systolic dysfunction**
- **Diastolic dysfunctio**
- **Valvular disease**

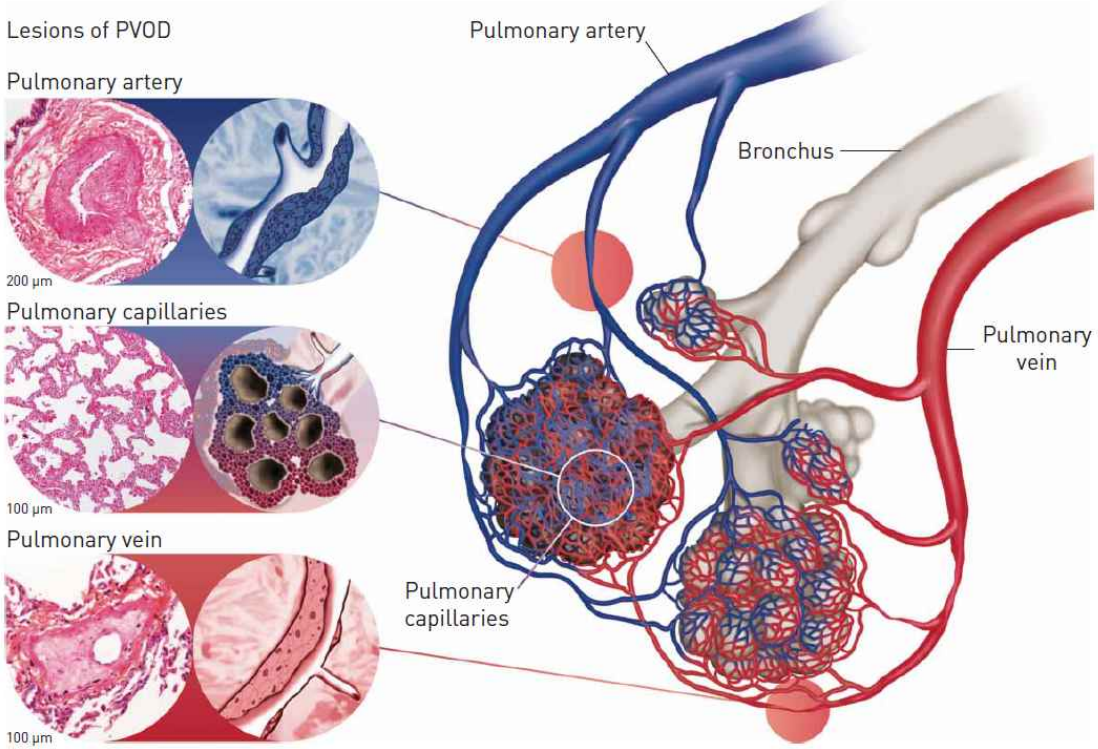
TABLE 1

Classification of pulmonary hypertension according to European Society of Cardiology/European Respiratory Society Guidelines

1 Pulmonary arterial hypertension
1.1 Idiopathic
1.2 Heritable
1.2.1 *BMPR2* mutation
1.2.2 Other mutations
1.3 Drugs and toxins induced
1.4 Associated with:
1.4.1 Connective tissue disease
1.4.2 HIV infection
1.4.3 Portal hypertension
1.4.4 Congenital heart disease
1.4.5 Schistosomiasis
1' Pulmonary veno-occlusive disease and/or pulmonary capillary haemangiomatosis
1'.1 Idiopathic
1'.2 Heritable
1'.2.1 *EIF2AK4* mutation
1'.2.2 Other mutations
1'.3 Drugs, toxins and radiation induced
1'.4 Associated with:
1'.4.1 Connective tissue disease
1'.4.2 HIV infection
1'' Persistent pulmonary hypertension of the newborn

Pulmonary Capillary Hemangiomatosis

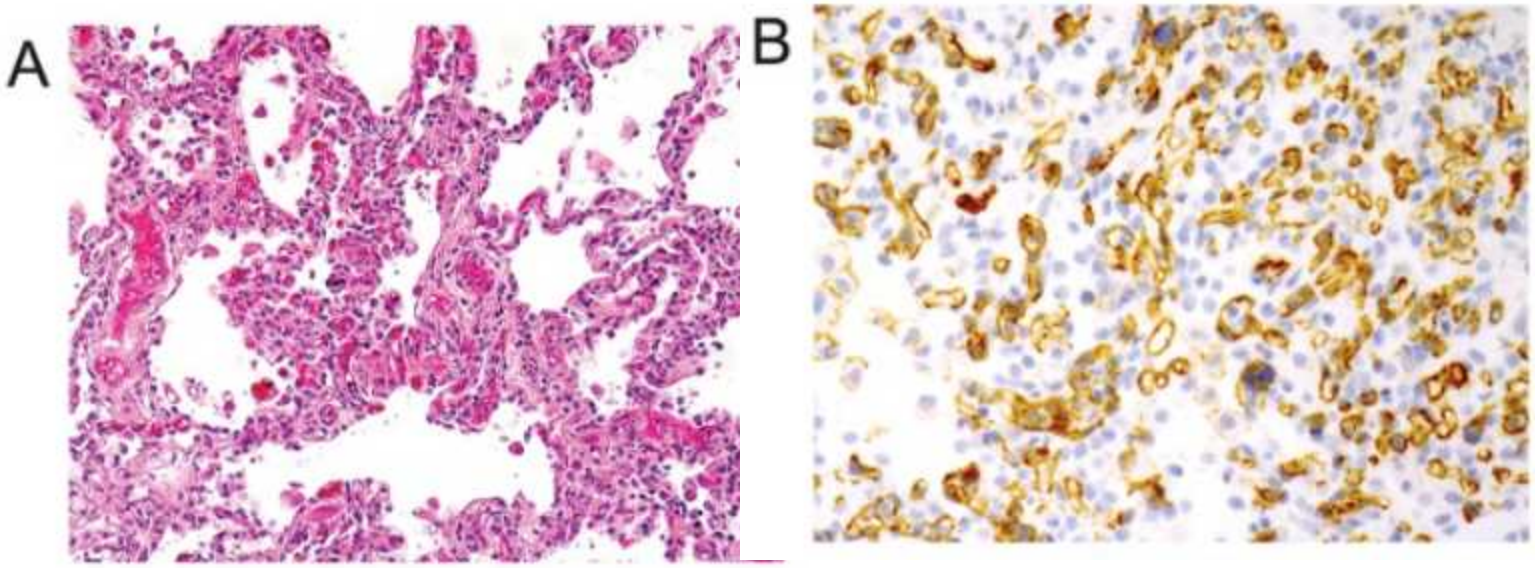
- Incidence
  - first reported in 1978, 100 by 2011
  - general population inc
  - In autopsy series, 6%
  - 7 cases : CTD with PHT
    after lung transplantat
    (Annals of Dia pathology :V19(20



- Clinical feature
  - Progressive dyspnea
  - hemoptysis
  - Cough, fatigue
  - Chest pain

Pulmonary Capillary Hemangiomatosis

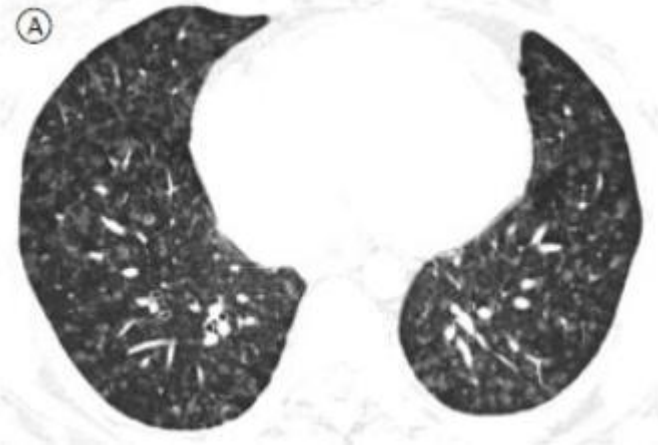
- histologic feature
  - proliferation of pulmonary capillaries
    - Interstitial, bronchial(alveolar walls and alveolar space) , vascular structures of the lung(pulmonary veins, arteries)
  - CD31, CD34 immunohistochemistry can help distinguish capillary proliferation from congestion

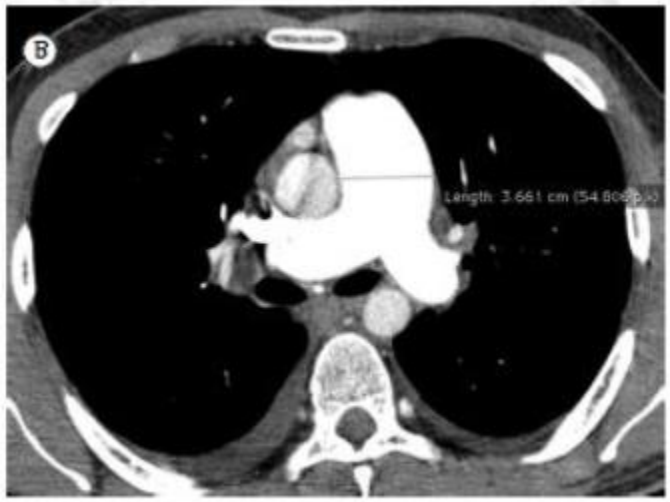


Pulm Circ. 2015 Sep; 5(3): 580-586

Pulmonary Capillary Hemangiomatosis

- Radiologic feature
  - Non-specific
  - CXR : diffuse reticulonodular opacity
  - Chest CT: Enlarged pulmonary arteries (main PA>3cm) + centrilobular GGO





J. Bras.pneumol; June 2013 : V(39) 203~204

Pulmonary Capillary Hemangiomatosis

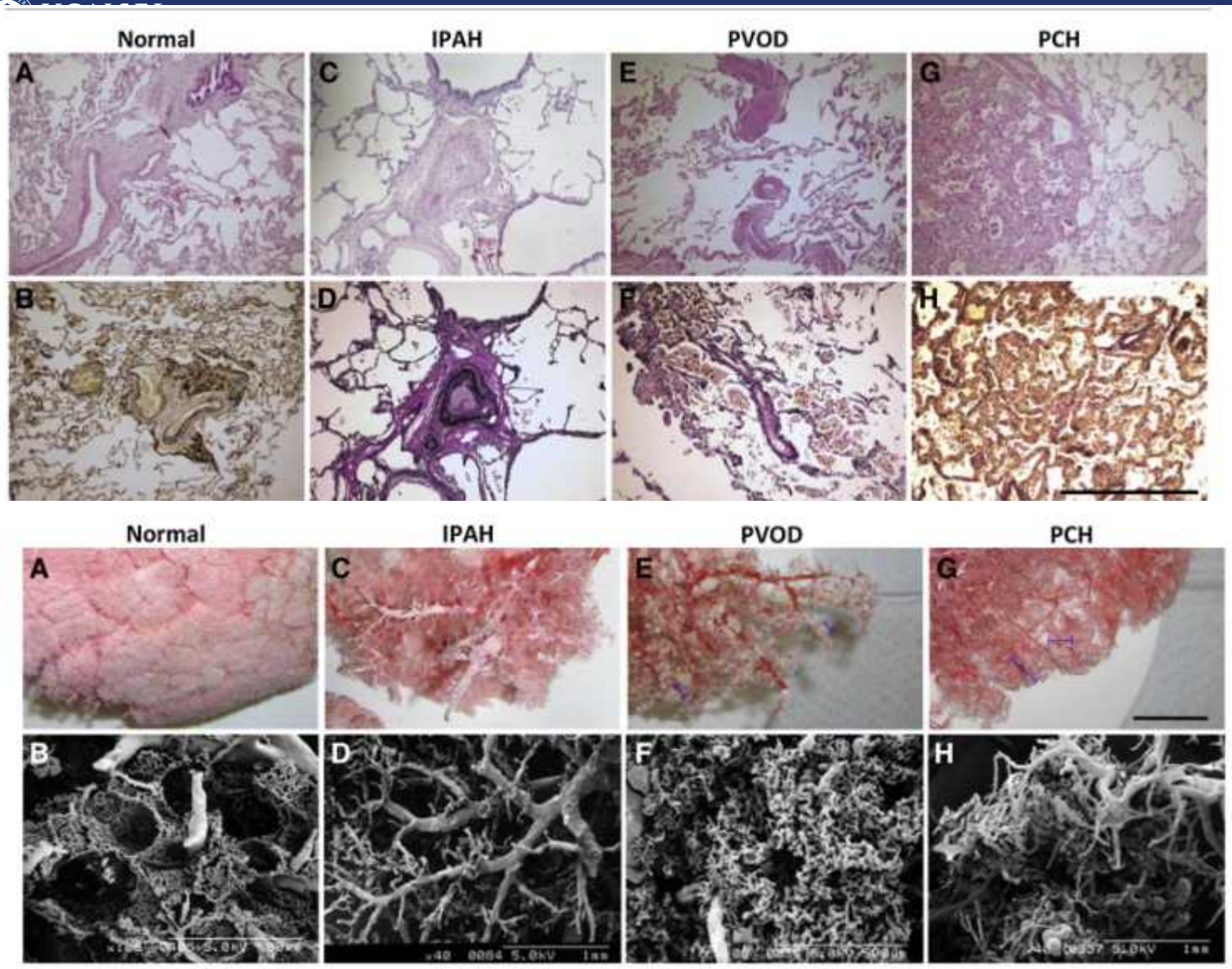
- Diagnosis
  - lung biopsy is essential (risky in patients with severe pulmonary arterial hypertension)
  - after lung transplantation
  - autopsy, after death

- Different diagnosis
  - idiopathic pulmonary arterial hypertension
  - pulmonary veno-occlusive disease
  - atypical interstitial lung disease

Differential diagnosis

- PCH vs Pulmonary hypertension
  - PCH (group 1`) is linked to but not PAH (group 1)
  - Different histologic abnormalities
    - PCH -capillary proliferation
    - PAH- affects small arteries

- PVOD vs PCH
  - Share clinical, genetic, hemodynamic background with PCH
  - *EIF2AK4* represents a clear link between PCH and PVOD
    - eukaryotic translation initiation factor
  - PVOD-post capillary venous pulmonary vessel



IPAH : intimal, medial hypertrophy , pulmonary artery stenosis, capillary defecient

PVOD: narrow pulmonary vein, obliteration venous vessel, capillary swallen

PCH : capillary proliferation, resemble tumorous clustere

Cardiovascular pathology : Aug 2013; 22(4); 287-293

Pulmonary Capillary Hemangiomatosis

- Treatment
  - Lung transplantation (curative treatment)
  - Recombinant interferon alpha-2 (ex. Imatinib, case-report, bridging treatment)
  - Doxycycline (case report, angiogenetic therapy)
  - Pulmonary vasodilator -> contraindication
    - Worsening pulmonary edema, death have been report
- Prognosis
  - symptoms appear, course is fulminant and fatal
  - Median survival after diagnosis is usually 3 yrs

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