대한결핵 및 호흡기학회
심포지엄 증례

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김 용 현

증례

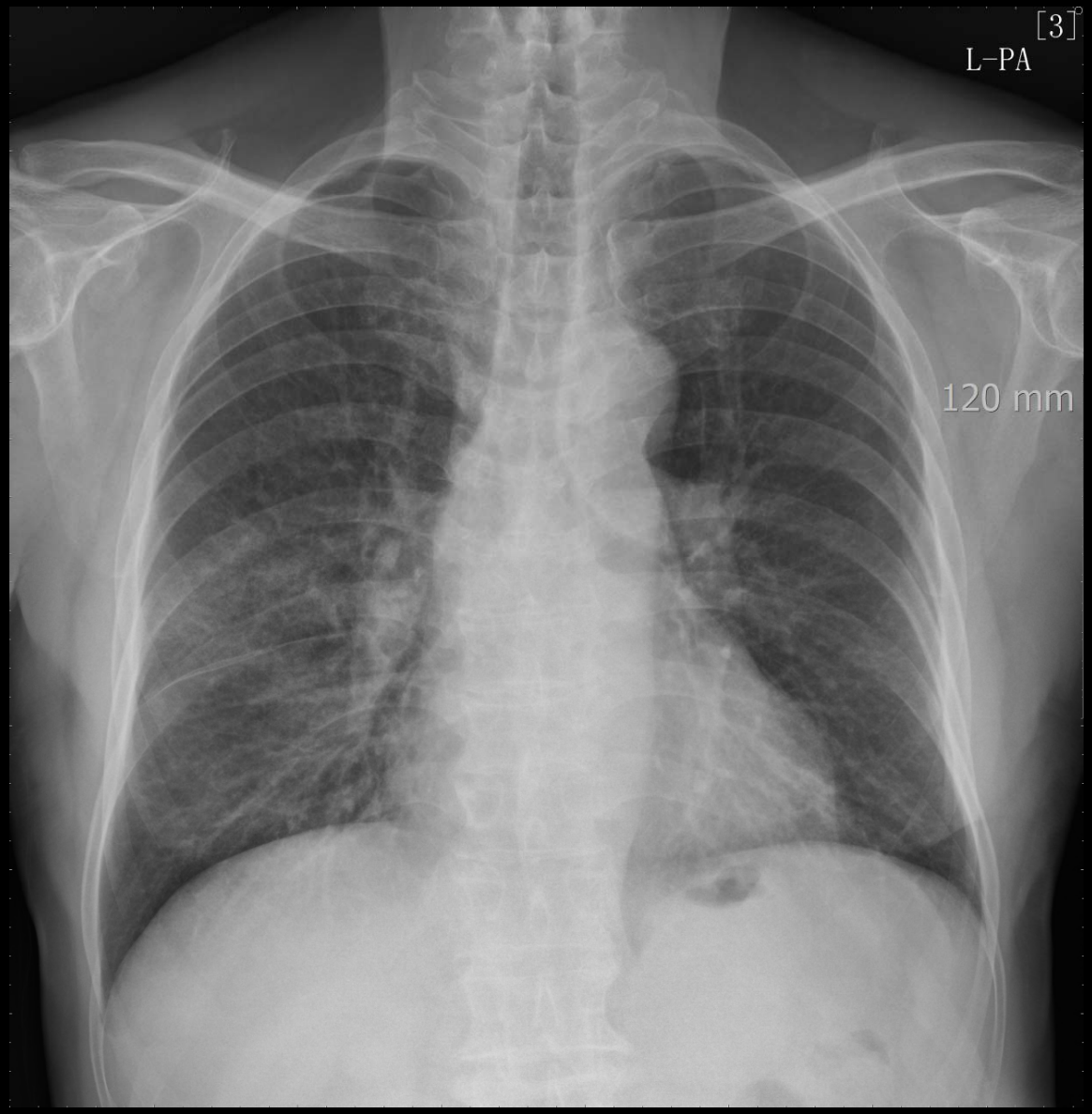
- 70세/남자
- 4주 전 부터 시작된 객혈과 호흡곤란

- 흡연력, 30 PY Current smoker
- 농부(인삼재배)
- 고혈압 (Amlodipine, carvedilol)
- 가족력, 특이 사항 없음

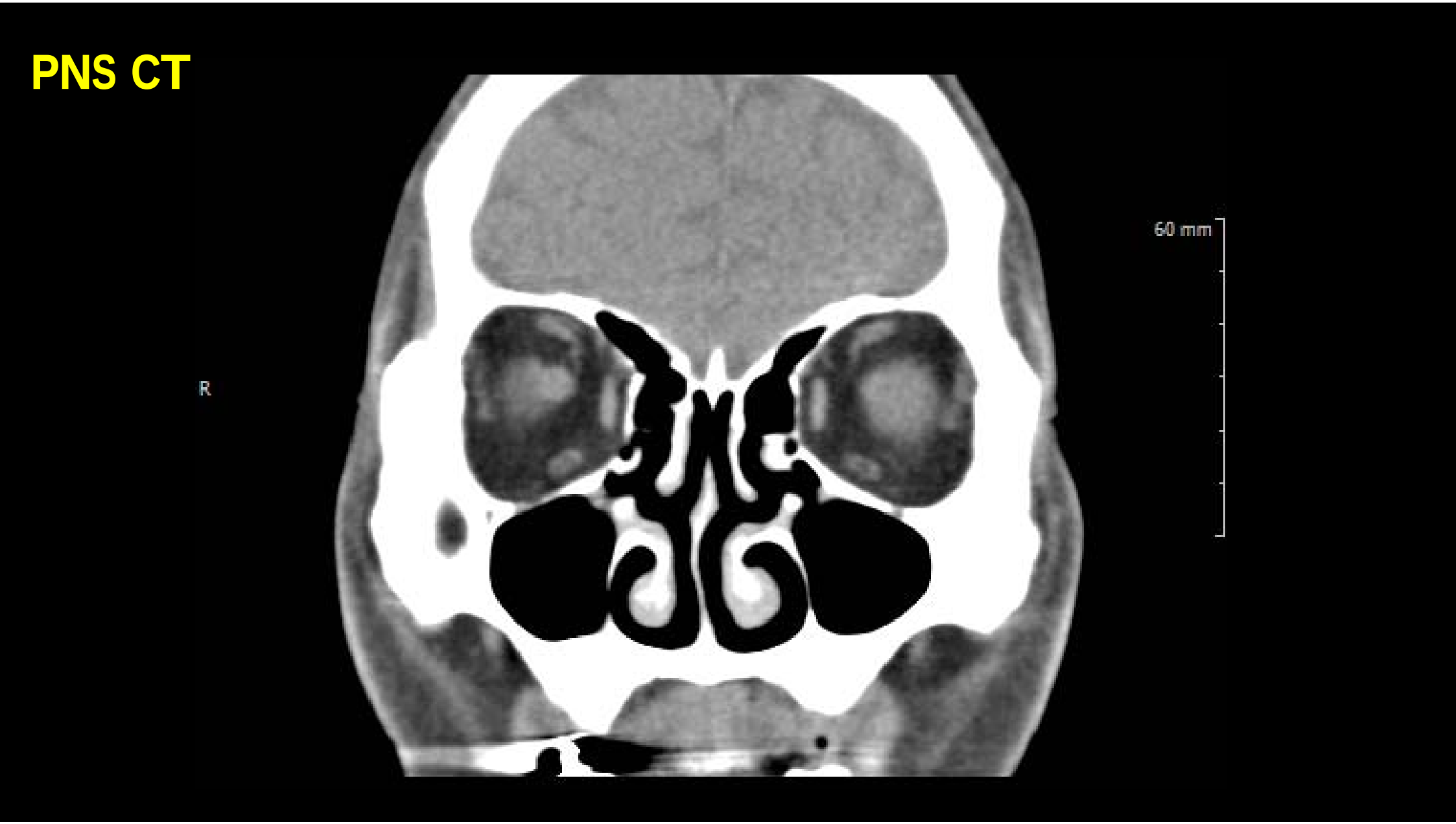
신체검사

- 활력 증후, 110/70 – 52 – 20 – 36.2
- 신경학적 검사 : 정상
- 경정맥 및 림프절, 정상
- 이비인후과 검사, 특이소견 없음
- 안과적 검사, 결막의 창백소견 이외에는 정상
- 청진 : 심음 정상/ 흡기 시 수포음
- 복부, 사지말단 및 피부 : 특이 소견 없음

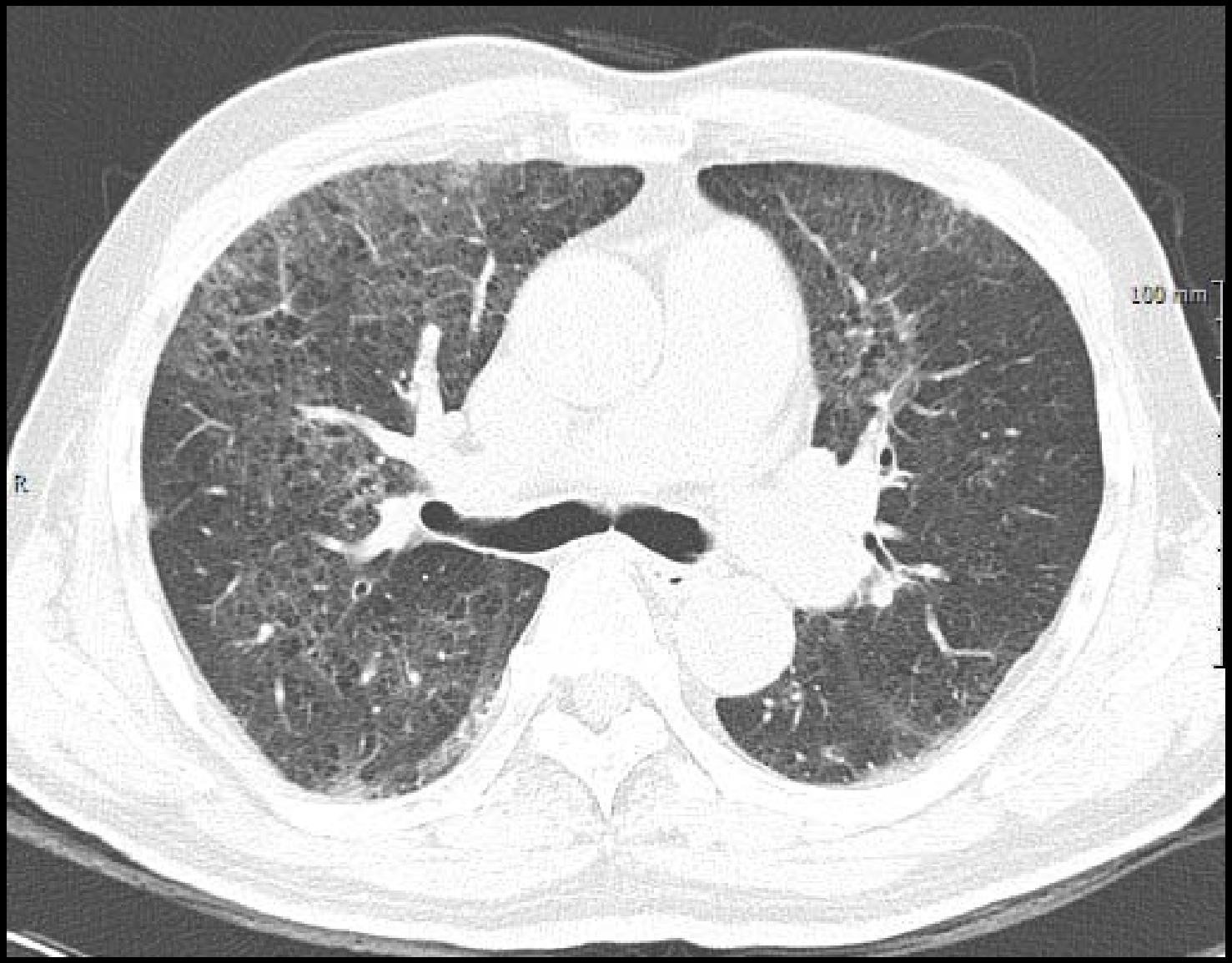
Chest x-ray



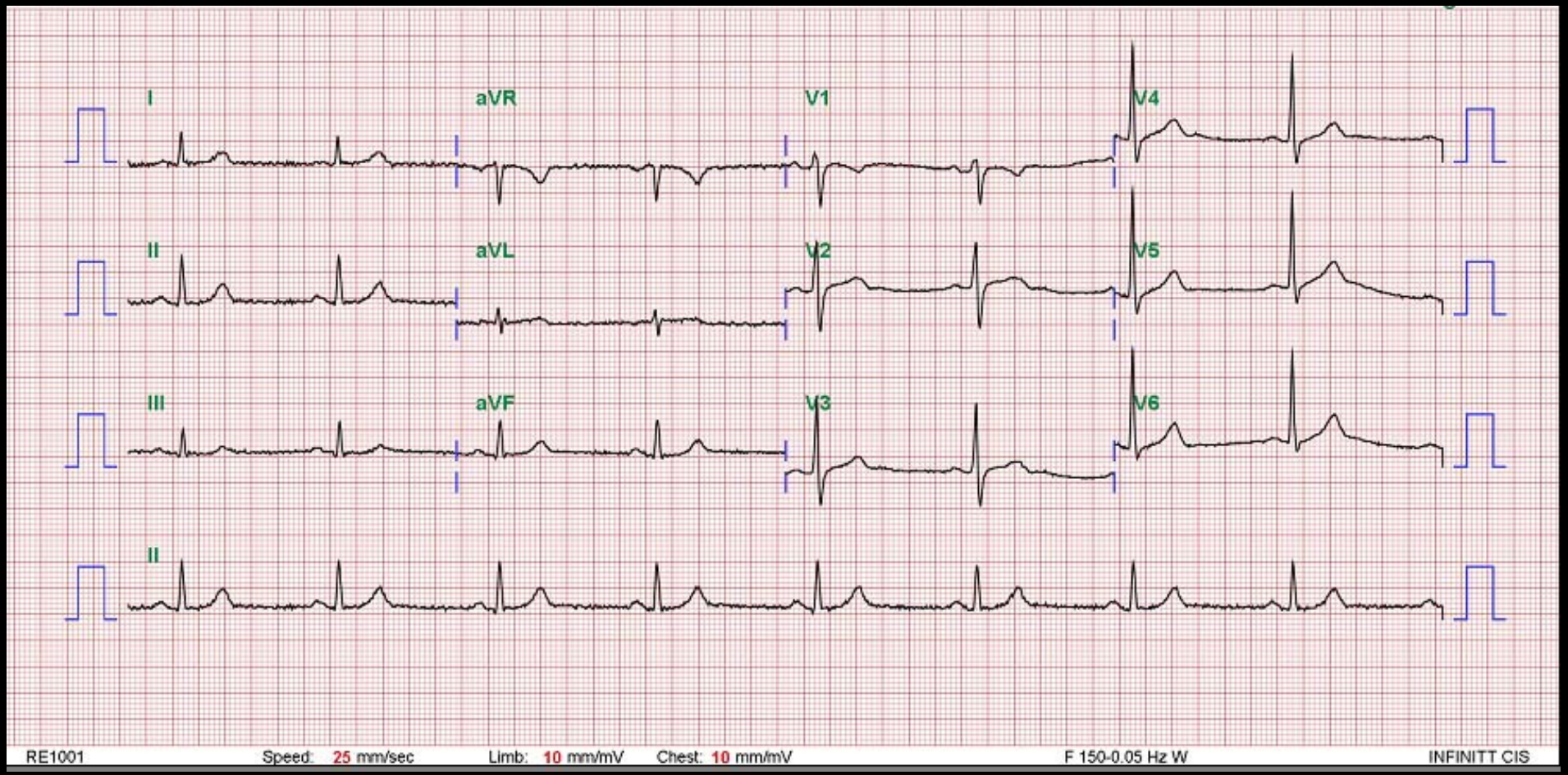
PNS CT



Chest CT



ECG


I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6
II
RE1001
Speed: 25 mm/sec
Limb: 10 mm/mV
Chest: 10 mm/mV
F 150-0.05 Hz W
INFINITT CIS

Laboratory findings

CBC		Blood Chemistry	
Hemoglobin	9.2 g/Dl	BUN / Creatinine	22.5 / 1.11 mg/dL
Hematocrit	26.4 %	AST / ALT	33/12 U/L
White blood cell	4770x 10^6/L	TP/albumin	6.7 / 3.8 g/dL
seg. neutrophil	65.9 %	Bilirubin,total	1.09 mg/dL
lymphocytes	24.5 %	LDH / CPK	579 / 104 IU/L
eosinophils	1.9 %	Ca/P/Mg	9.2/ 3.1 / 2.3 mg/dl
basophils	0.2 %	Na/K/Cl	138/ 3.8 / 104mEq/L
Platelet count	210 x 10^9/L	ESR / CRP	30 /42.25

ABGA (on room air)

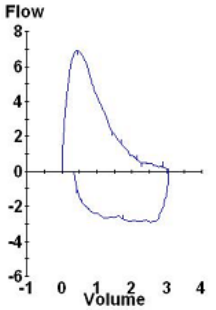
pH 7.455 pCO2 28.8 pO2 56.3 HCO3 20.5 Sat 90.8%

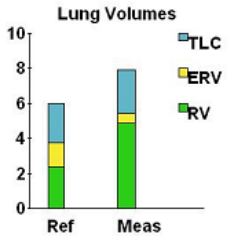
Laboratory findings

Coagulation and viral etc		Urine Chemistry	
PT and aPTT	WNL	Color	Yellow
HBsAg /Ab	- /+	Specific gravity	1.030
Anti HCV Ab	-	PH	5.5
HIV Ag/Ab	-	Protein	-
Coom's test		Glucose	-
direct /indirect	- /-	Ketone	-
Syphilis Reagin Test	-	Occult blood	-
TFT , Pro BNP	WNL	RBC/WBC	0~1/0~2

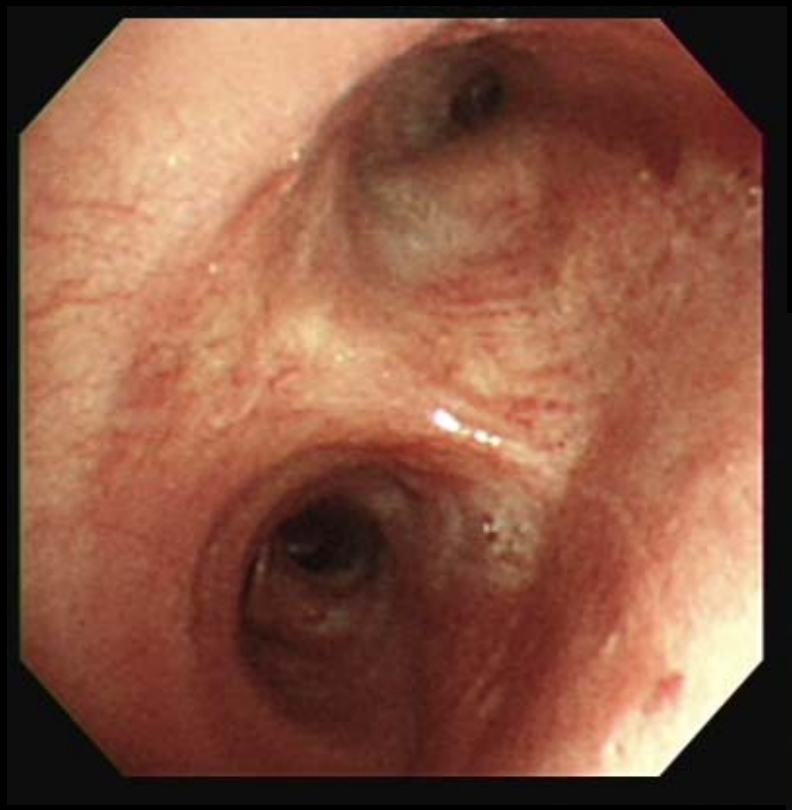
Pulmonary Function Test

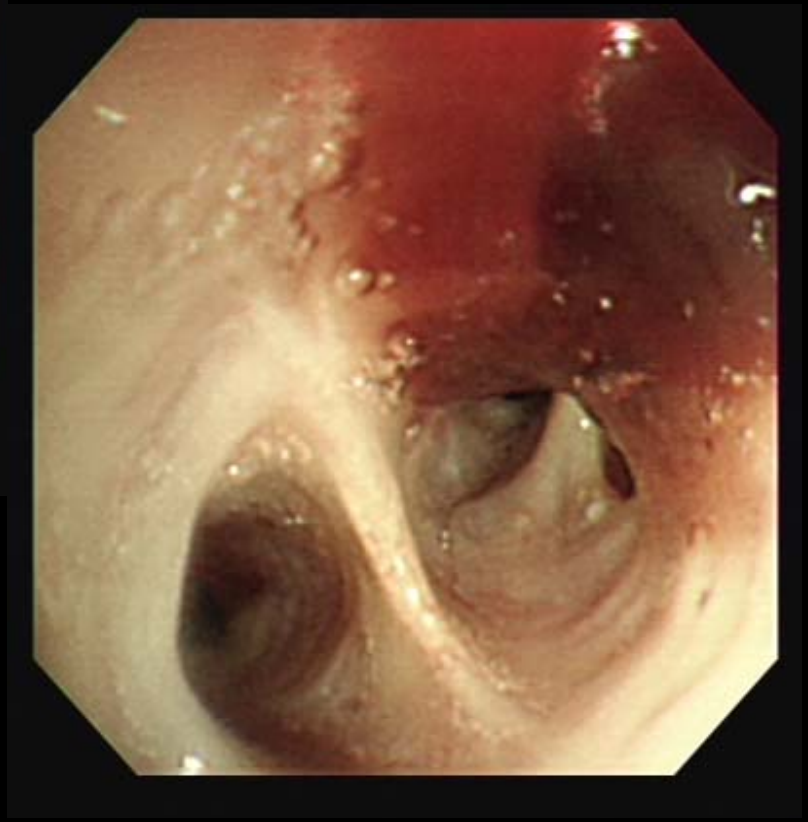
		Ref	Pre	% Ref	Post	% Ref	%Chg
Spirometry							
FVC	Liters	4.03	3.04	75			
FEV1	Liters	2.73	2.17	80			
FEV1/FVC	%	69	71				
FEF25-75%	L/sec	2.54	1.42	56			
IsoFEF25-75	L/sec	2.54	1.42	56			
FEF50%	L/sec	3.66	2.03	55			
PEF	L/sec	7.72	6.91	90			
MVV	L/min	120	69	58			
Lung Volumes							
TLC	Liters	5.96	7.92	133			
VC	Liters	4.03	3.04	75			
RV	Liters	2.38	4.88	205			
RV/TLC	%	41	62				
Diffusing Capacity							
DLCO	mL/mmHg/min	19.4	19.2	99			
DL Adj	mL/mmHg/min	19.4	19.2	99			
DLCO/VA	mL/mHg/min/L	3.66	4.22	115			
DL/VA Adj	mL/mHg/min/L		4.22				
VA	Liters	6.66	4.55	68			
Resistance							
Raw	cmH2O/L/sec	1.31	1.97	151			
Gaw	L/sec/cmH2O	0.829	0.507	61			
Vtg (Raw)	Liters		6.14				
Raw f	BPM		87				



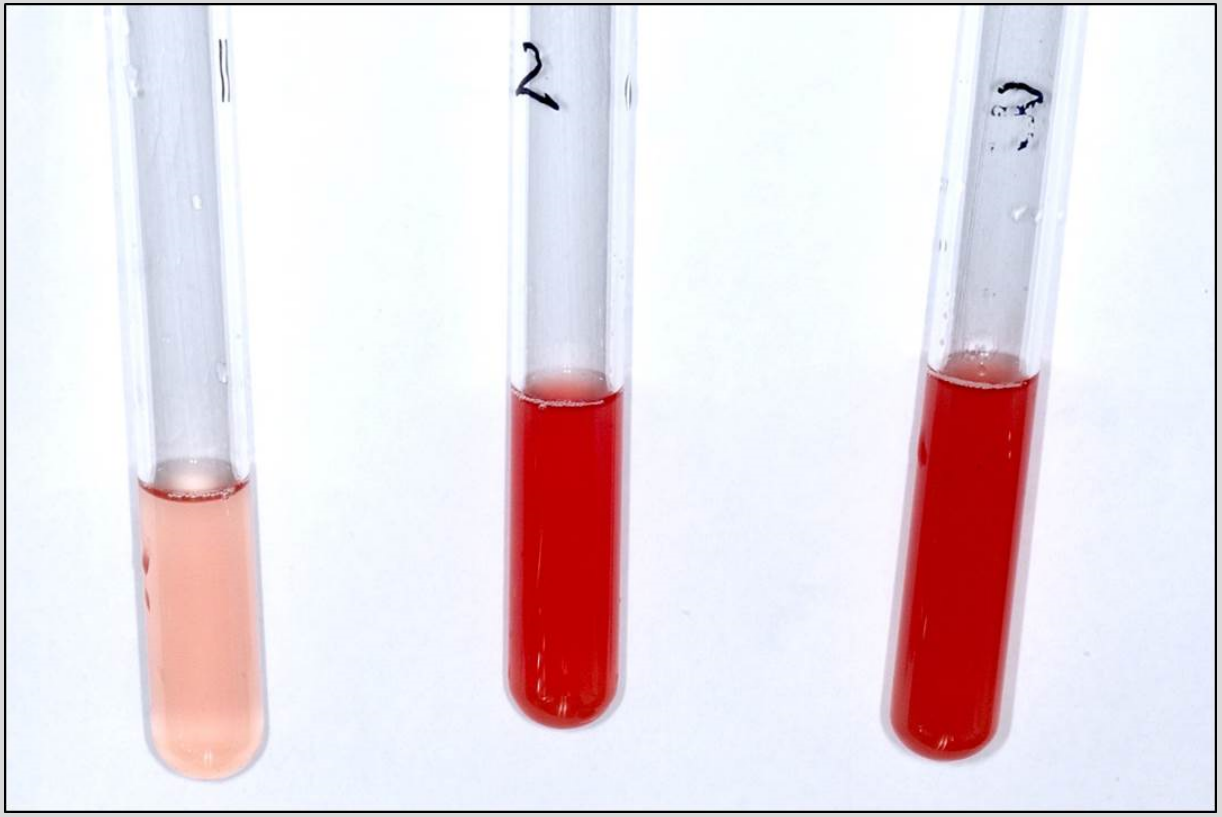


Broscopy





BAL



Hemosiderin-laden macrophages
AFB stain (-) Tbc culture (-)
M. Tuberculosis PCR (-)
BAL fluid cell count
- WBC count 290 mm^3
- RBC count 30,250
- Differential count
  Neutrophils 7% Lymphocytes 28%
  Eosinophils 3% Macrophage 62%
- CD4/CD8 74.5/13.4

점진적인 **bloody BAL fluid** 소견

Additional Result

- ANA(1:100)
- C3 98.2 mg/dl
- C4 31.6 mg/dl
- CH50 (Complement Hemolysis) ＞ 60 U/mL

- Anti-CCP Ab, Negative (0.5)
- RA Factor (Rheumatoid Factor) 8.0 IU/ml

- Immunoglobulin E 378.7 ▲IU/ml
- Immunoglobulin G 1561 mg/dl
- Immunoglobulin M 158.0 mg/dl
- Immunoglobulin A 393.0 mg/dl

- **ANCA : C-ANCA (1:160)**
  - Anti MPO Ab Negative : ＜0.2
  - Anti PR3 Ab Negative : ＜0.2

- Anti GBM Ab, negative
- Cryoglobulin, negative
- Anti-phospholipid Ab, negative
- Echocardiography : WNL

Summary, progress

- **2013. 12 월 진단**
  - prednisolone 60mg/day
- **2013. 12 – 2014. 6 월**
  - Tapering to 7.5mg/day
- **2014. 6월**
  - Recurrent activity of disease → prednisolone 20mg/day 증량 후 유지
  - Remission
- **2015.11 월**
  - AVN of femur, 정형외과 수술
- – 2015. 2 월
  - Tapering to 5mg/EOD (2.5mg/d)
- **2015. 2 월**
  - Prednisolone 중단, 치료 종결 → 2015. 8월 F/U, No disease activity

CASE REVIEW

Diffuse alveolar hemorrhage

Diffuse alveolar hemorrhage (DAH), clinically

- Diffuse alveolar infiltrates (although rarely unilateral)
- Hemoptysis (not always necessary)
- A drop in hematocrit / hemoglobin level

Usual pathological Findings in DAH

- Capillaritis (neutrophilic vasculitis of the capillaries and venules)
- Bland hemorrhage
- Diffuse alveolar damage with hemorrhage

Table 1—*Biopsy Specimen Proved Cases of Pulmonary Capillaritis

Diagnosis	No.	% of Total
Isolated pulmonary capillaritis†	14	24
Lung allograft rejection†	9	15
Microscopic polyangiitis	7	12
Wegener's granulomatosis	6	10
Idiopathic pulmonary fibrosis	4	7
Goodpasture's syndrome	2	3
Antiphospholipid syndrome	1	2
Retinoic acid toxicity	1	2
Collagen vascular disease		
SLE†	8	14
RA	3	5
Polymyositis†	2	3
MCTD†	1	2

*From 1991 to 1997 (n=58).

CHEST 1998; 113:1609-15

Etiologies of DAH

Necrotizing pneumonia Inhalational injury Diffuse alveolar damage	Bone marrow transplantation Pulmonary allograft rejection Disorders of coagulation Disseminated intravascular coagulation
Isolated pauci-immune pulmonary capillaritis Wegener's granulomatosis Microscopic polyangiitis Goodpasture's syndrome Henoch-Schoenlein purpura IgA nephropathy Behcet's syndrome	Pulmonary veno-occlusive disease Pulmonary capillary hemangiomatosis Pulmonary angiosarcoma Mitral stenosis
Idiopathic pulmonary hemosiderosis	Essential cryoglobulinaemia Primary antiphospholipid syndrome
Collagen vascular disease SLE Rheumatoid arthritis Polymyositis scleroderma	Drug Penicillamine Trimellitic anhydride Propylthiouracil Diphenylhydantoin

Diagnostic studies in pulmonary Capillaritis and/or /DAH

Laboratory studies

- ANCA (p/c)
- ANA
- Anti-ds DNA antibodies
- Complement levels
- Rheumatoid factor
- Antiglomerular basement membrane antibodies
- Cryoglobulins
- Erythrocyte sedimentation
- ECG/ echocardiography

Additional studies

- Assay for circulating immune complexes
- Urinalysis with microscopic examination for erythrocyte casts
- Radiologic examination of the sinuses
- Renal biopsy for necrotizing glomerulonephritis
- Skin biopsy for leukocytoclastic vasculitis
- Lung biopsy (*frozen sections for immunofluorescence studies*)

- Clinically, pulmonary vasculitis may present in a variety of ways including alveolar hemorrhage, pulmonary nodules, cavitating lesions, or airway disease

- **Idiopathic pauci-immune pulmonary capillaritis**
  - Isolated pulmonary capillaritis without a systemic vasculitis
  - classified within the family of idiopathic, small-vessel vasculitis, despite generally being ANCA-negative

TABLE 1. CLINICAL MANIFESTATIONS OF PULMONARY VASCULITIS

Manifestations	GPA	MPA	CSS	IPIPC
Upper airway	⩾85%. May include epistaxis, destructive and ulcerating lesions, otitis, sinusitis, and mastoiditis	⩽15%	70–90%. Commonly manifests as rhinitis and sinusitis	Not characteristic
Asthma and airways	Approximately 60%. Manifestations include subglottic or tracheal stenosis, airway narrowing, ulcerations, endobronchial lesions, stenosis, or occlusion	Not characteristic	>95% present with asthma. Variable severity, but commonly steroid-requiring	Not characteristic
Nodules, cavities, and infiltrates	>80% will have focal consolidation, infiltrates, atelectasis, nodules, cavities, or other abnormalities. 40–70% will have nodules and/or cavities. Easily confused with infection or malignancy	Up to 30% will have infiltrates, often reflecting the presence of alveolar hemorrhage	70% by plain film and up to 90% by HRCT. Commonly appears as patchy, bilateral, heterogeneous disease with areas of ground-glass appearance and consolidation	Infiltrates seen in association with alveolar hemorrhage
Alveolar hemorrhage	5–10%	10–30%	Rare	100%
Thromboembolic disease	7 cases per 100 person-years. Comparable to patients with a known history of VTE	Unknown incidence	Unknown incidence	Unknown incidence
Infection	Common cause of morbidity and mortality	*See* GPA	*See* GPA	*See* GPA
Drug toxicity	Pulmonary toxicity most commonly with methotrexate but may also be seen with other immunosuppressive agents	*See* GPA	*See* GPA	*See* GPA
Extrapulmonary disease	Constitutional symptoms 50–90% GN 40–90% Cutaneous disease 45–60% Musculoskeletal disease 30–70% Ocular involvement 25–50% Cardiac involvement 5–15%	Constitutional symptoms > 90% GN 100% Musculoskeletal disease > 50% PNS 10–50% GI disease 35–45% Cardiac involvement 10–20%	Constitutional symptoms 50–90% Musculoskeletal disease > 50% Cutaneous disease 40–70% PNS > 50% GI disease 30–50% Cardiac involvement 30–50%	Generally considered a lung-limited disorder, but constitutional symptoms and other nonspecific findings may be seen

Treatment of pulmonary vasculitis

Table 2—*EUVAS Grading of Disease Severity and First-Line Treatment Options for Induction Therapy

Disease Classification	Constitutional Symptoms	Renal Function	Threatened Organ Function	Treatment Options for Induction
Limited	No	Serum creatinine < 120 μmol/L (1.4 mg/dL)	No	Corticosteroids OR methotrexate OR azathioprine
Early, generalized	Yes	Serum creatinine < 120 μmol/L (1.4 mg/dL)	No	Cyclophosphamide + corticosteroids or methotrexate + corticosteroids
Active, generalized	Yes	Serum creatinine < 500 μmol/L (5.7 mg/dL)	Yes	Cyclophosphamide + corticosteroids
Severe	Yes	Serum creatinine > 500 μmol/L (5.7 mg/dL)	Yes	Cyclophosphamide + corticosteroids + plasma exchange
Refractory	Yes	Any	Yes	Consider investigational or compassionate use agents (see text)

CHEST 2006; 129:452–465

TABLE 2. FIRST-LINE TREATMENT OPTIONS STRATIFIED BY DISEASE SEVERITY

EUVAS Classification	Clinical Features	Five Factor Score	Treatment Options
Limited	Isolated upper airway disease	0	Corticosteroids *or* methotrexate *or* azathioprine
Early generalized	End-organ involvement that lacks a clear or immediate threat to organ function. Examples include glomerulonephritis with serum creatinine < 1.4 mg/dl or the presence of minimally symptomatic pulmonary nodules. Constitutional symptoms are common	0–1	Cyclophosphamide + corticosteroids *or* methotrexate + corticosteroids (for MPA may also consider mycophenolate + corticosteroids)
Generalized active	End-organ involvement with clinically significant impairment of organ function. Examples include glomerulonephritis with serum creatinine > 1.4 mg/dl but < 5.7 mg/dl or pulmonary infiltrates with cough, dyspnea, and impaired exercise tolerance	1–2	Rituximab + corticosteroids *or* cyclophosphamide + corticosteroids
Severe	Immediate threat of organ failure or death. Examples include severe renal disease with serum creatinine > 5.7 mg/dl, alveolar hemorrhage, and heart failure/cardiomyopathy	⩾2	Plasmapheresis + corticosteroids + cyclophosphamide (or rituximab)
Refractory	Disease that has failed to respond to conventional therapy	N/A	Referral to a center of specialized expertise. Consider investigational agents
Remission (maintenance)	No evidence of ongoing vasculitic activity (BVAS = 0)	N/A	If induced with cyclophosphamide then azathioprine ± low-dose oral corticosteroids *or* methotrexate ± low-dose oral corticosteroids If induced with rituximab no additional maintenance therapy may be required or may use low-dose oral corticosteroids alone

Definition of abbreviations: BVAS = Birmingham Vasculitis Activity Score; EUVAS = European Vasculitis Study Group; MPA = microscopic polyangiitis; N/A = not applicable.

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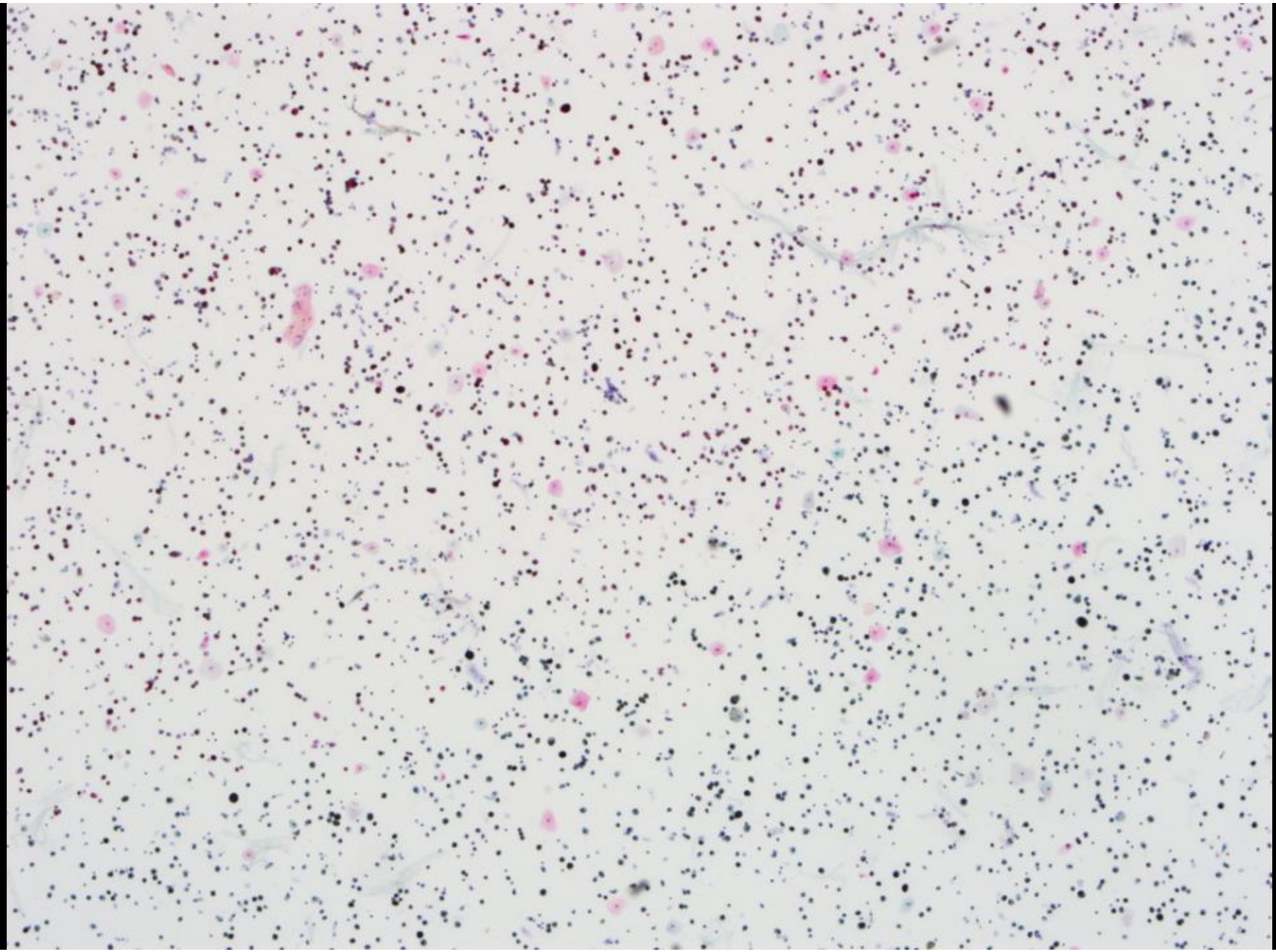
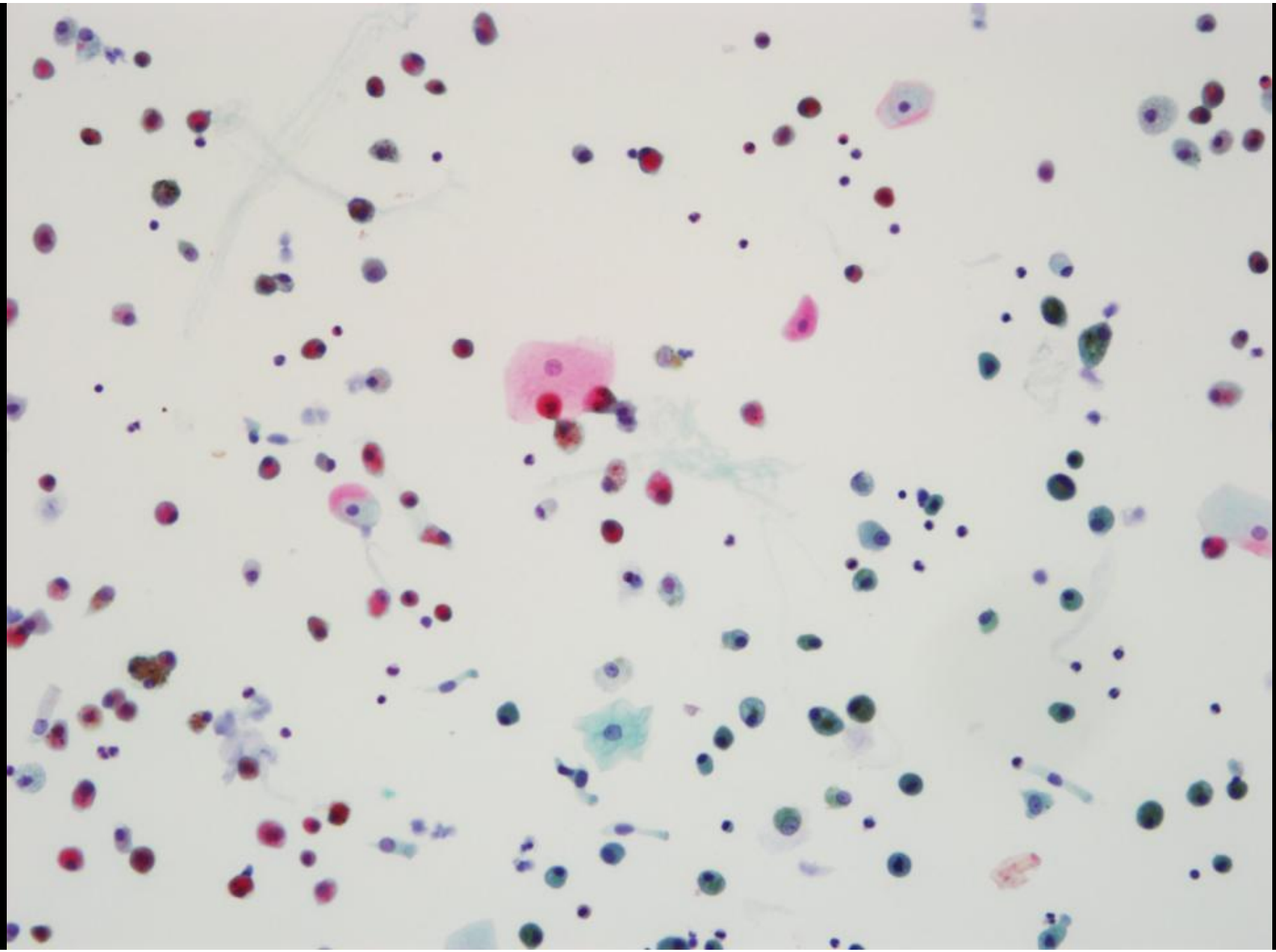
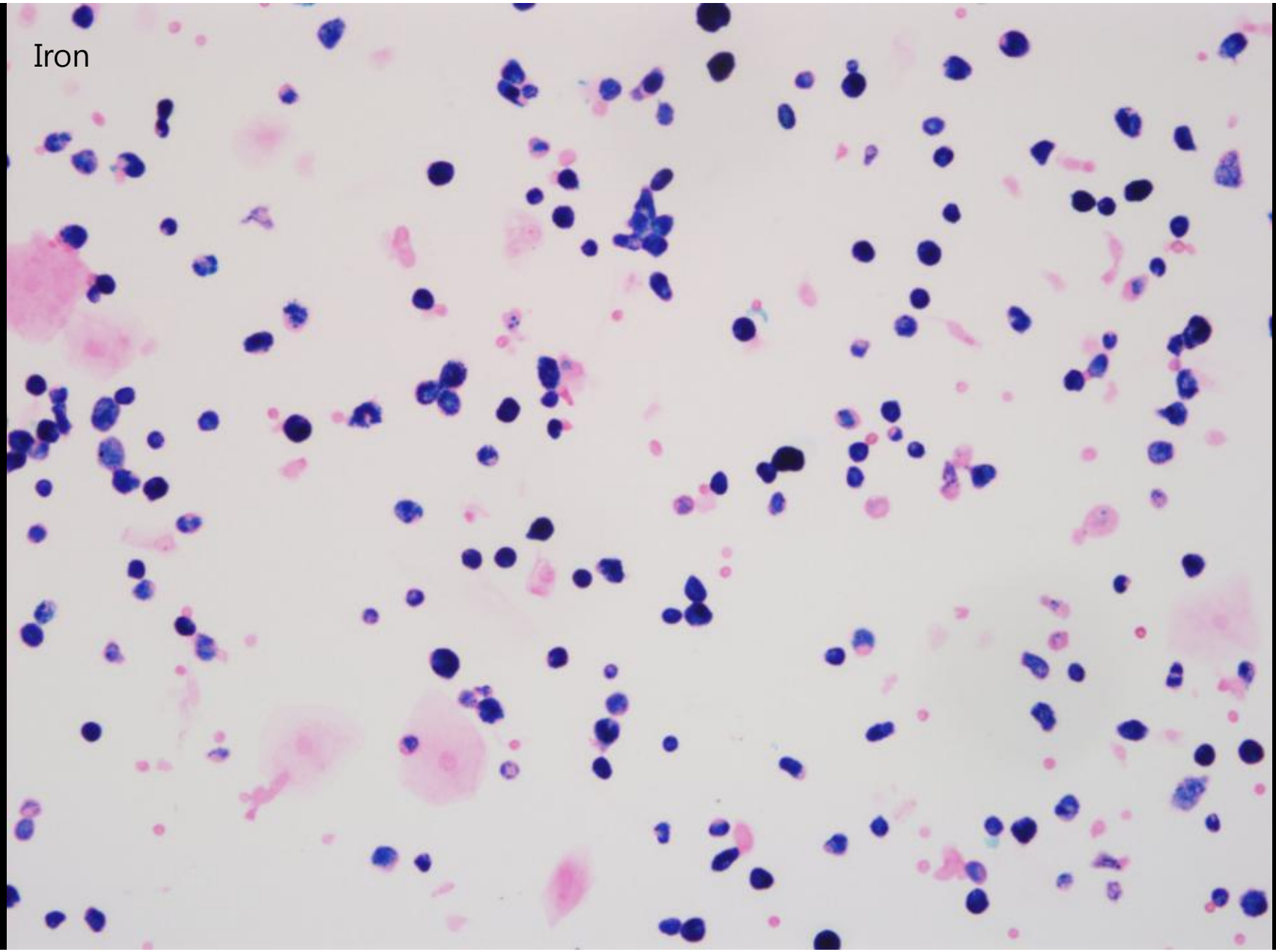
Histopathology






Iron