Sex/Age : M/41

Chief complaint : Dyspnea

Onset : 1 week ago

Present illness

건강상 특별한 과거력 없는 남자로 한달 전부터 흉통 있어 이비인후과의원에서 투약 받았으나 호전되지 않았고 일주일전부터 가슴이 답답하고 운동시 호흡곤란 호소하여 호흡기 내과 외래 방문함.

Past medical history

Hypertension	(-)
DM	(-)
Pulmonary tuberculosis	(-)
Drug	(-)
Operation history	(-)

Social history

Smoking history	(-)
Alcoholic drinking	(-)

Family history

none

Systemic Review

Fever & Chilling	(-/-)
General weakness & Weight loss	(+/-)
Headache & Dizziness	(-/-)
Cough & Sputum	(+/-)
Hemoptysis	(-)
Dyspnea/ Chest pain	**(+/+): right side, inspiration**
Nausea/ Vomiting	(-/-)
Epigastric pain / Indigestion	(-/-)
Frequency/ Residual urine	(-/-)

Physical exam

General

Alert mental status

Vital Sign : 110/70-68-20-36.5 ℃

Relatively healthy appearance

HEENT

Not anemic conjuntivae

Anicteric sclerae

No throat injection

Not palpable cervical lymph node

Chest

Symmetric chest wall expansion

Decreased breathing sound with crackle on right lower lung field

Regular heart beat without murmur

No wheezing & No thrill

Physical exam

Abdomen

- Soft & flat abdomen
- No tenderness & no rebound tenderness
- Not palpable liver and spleen

Genitourinary

- No costovertebral angle tenderness

Back and extremities

- No digital clubbing
- No petechiae and pupura on lower limb
- No pretibial pitting edema on lower limb
- No peripheral swelling and pain

Impression

Pneumonia with pleural effusion

Pulmonary tuberculosis with TBc pleurisy

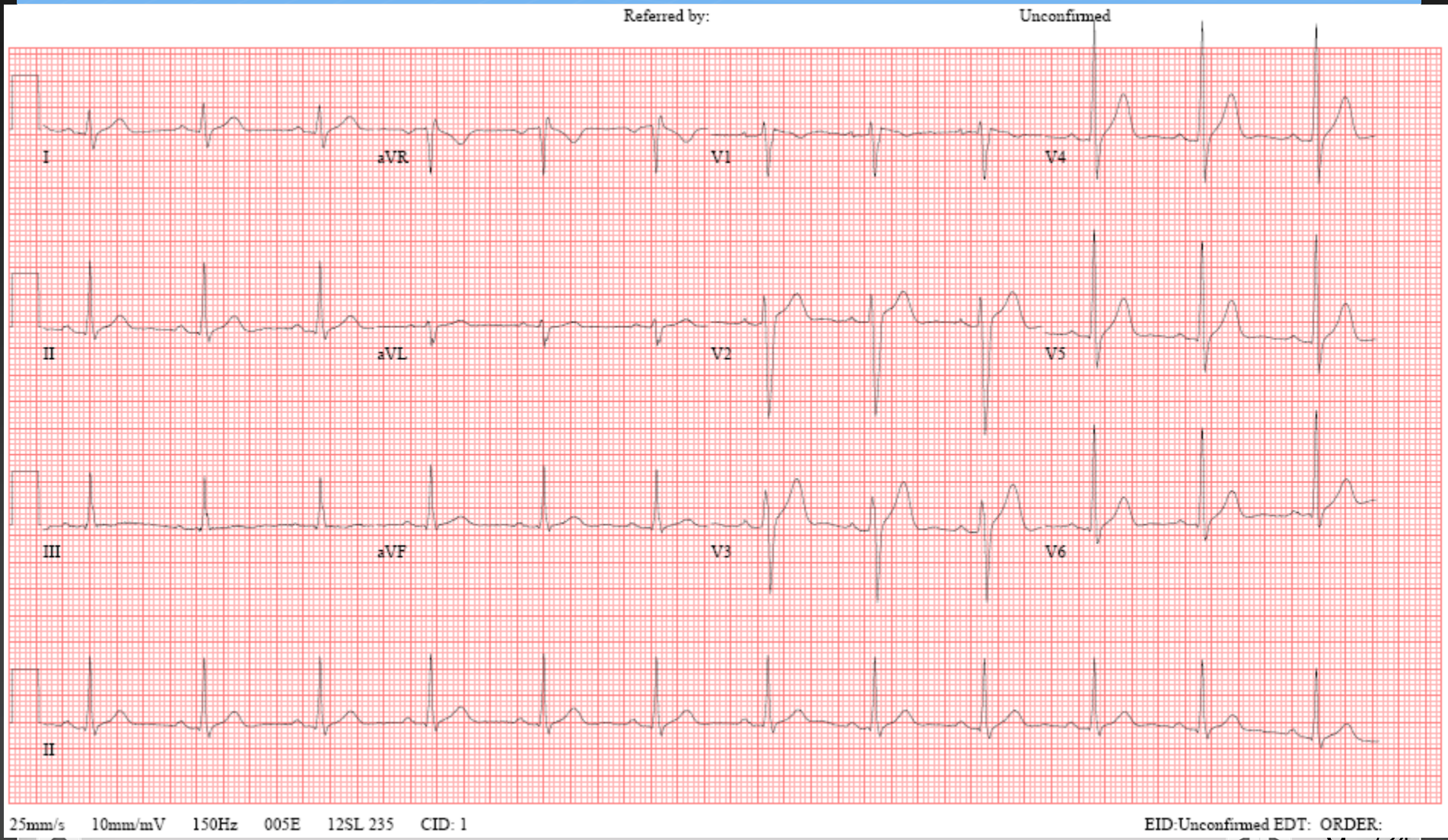
Interstitial lung disease

- Plan
  - Chest PA
  - Chest CT
  - Echocardiography with cardiac marker
  - PFT with methacholine provocation test

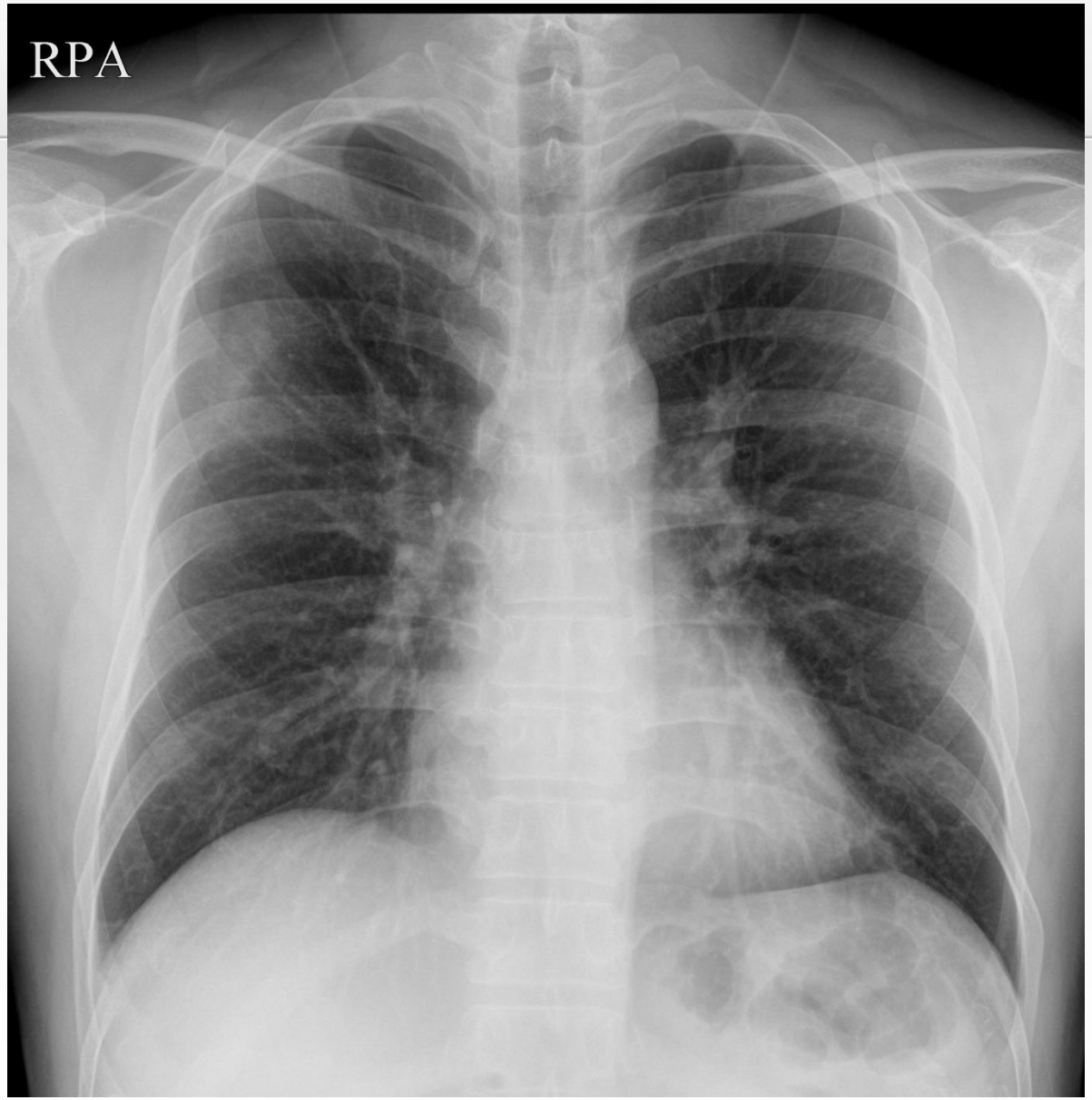
LAB

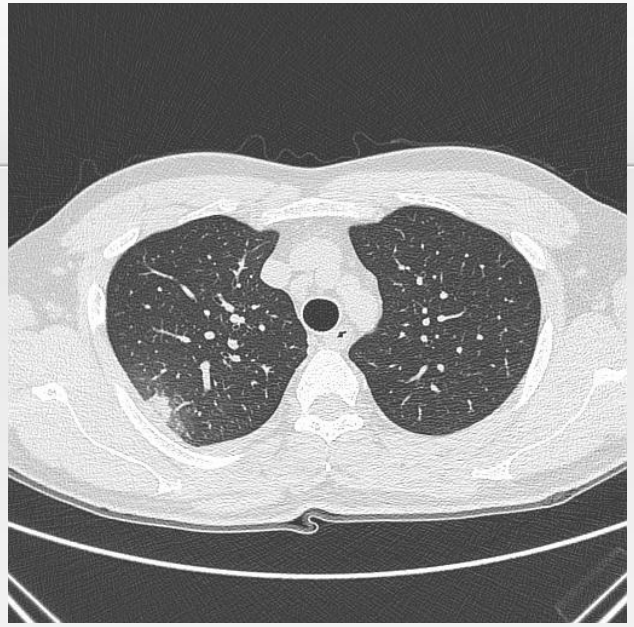
ABGA	7.412–42.3-88.4–26.2–97.3% (room air)	
CBC	4400/mL – 13.3 g/dL –37.4 % - 216 K/mL	
BUN/Creatine	12/0.9 mg/dL	
Total protein/albumin	6.8/4.4 g/dL	
AST/ALT	16/16 IU/L	
Bil T/D	0.5/0.1 mg/dl	
T-Chol/TG/HDL	140/82/40 mg/dL	
PT	97% /1.01	
aPTT/PT	40.3 sec	
Urinalysis	G/P -/-, RBC/WBC 1-4/1-4 HPF	
CK-MB/TnI:	0.28ng/ml / <0.006ng/ml	
D-Dimer	**0.8ug/ml**	**[0-0.5]**
CRP	**8.6mg/dl**	**[0-5.0]**

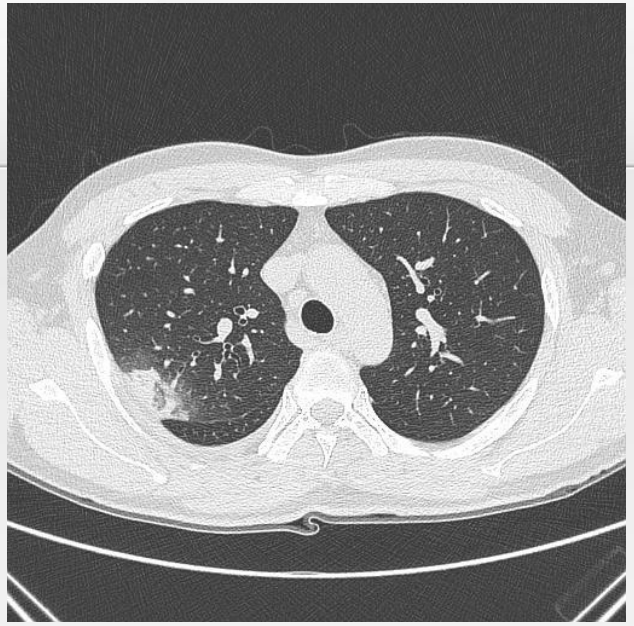
EKG

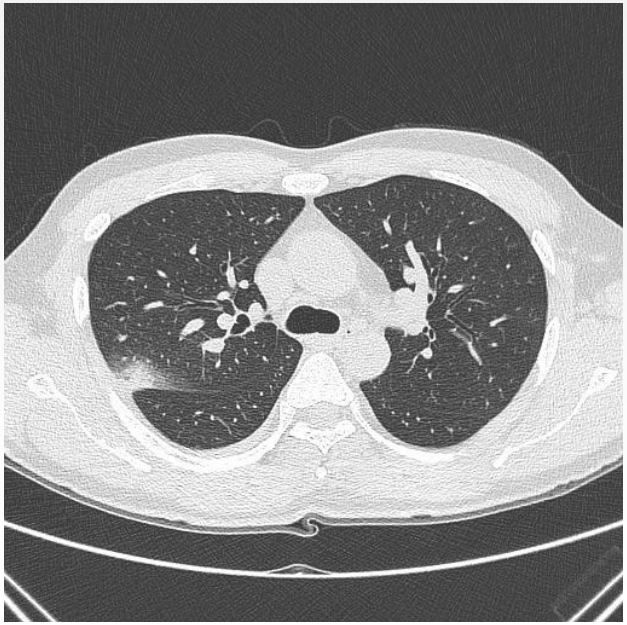

Referred by:
Unconfirmed
I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6
II
25mm/s 10mm/mV 150Hz 005E 12SL 235 CID: 1
EID:Unconfirmed EDT: ORDER:

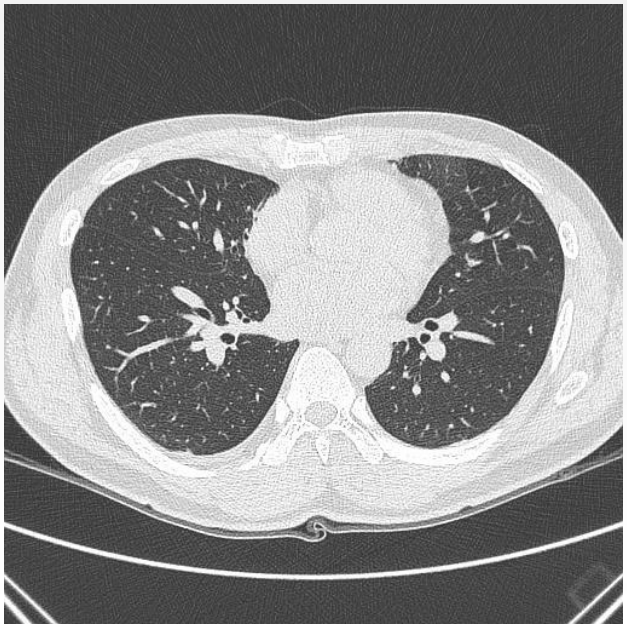
Radiologic findings

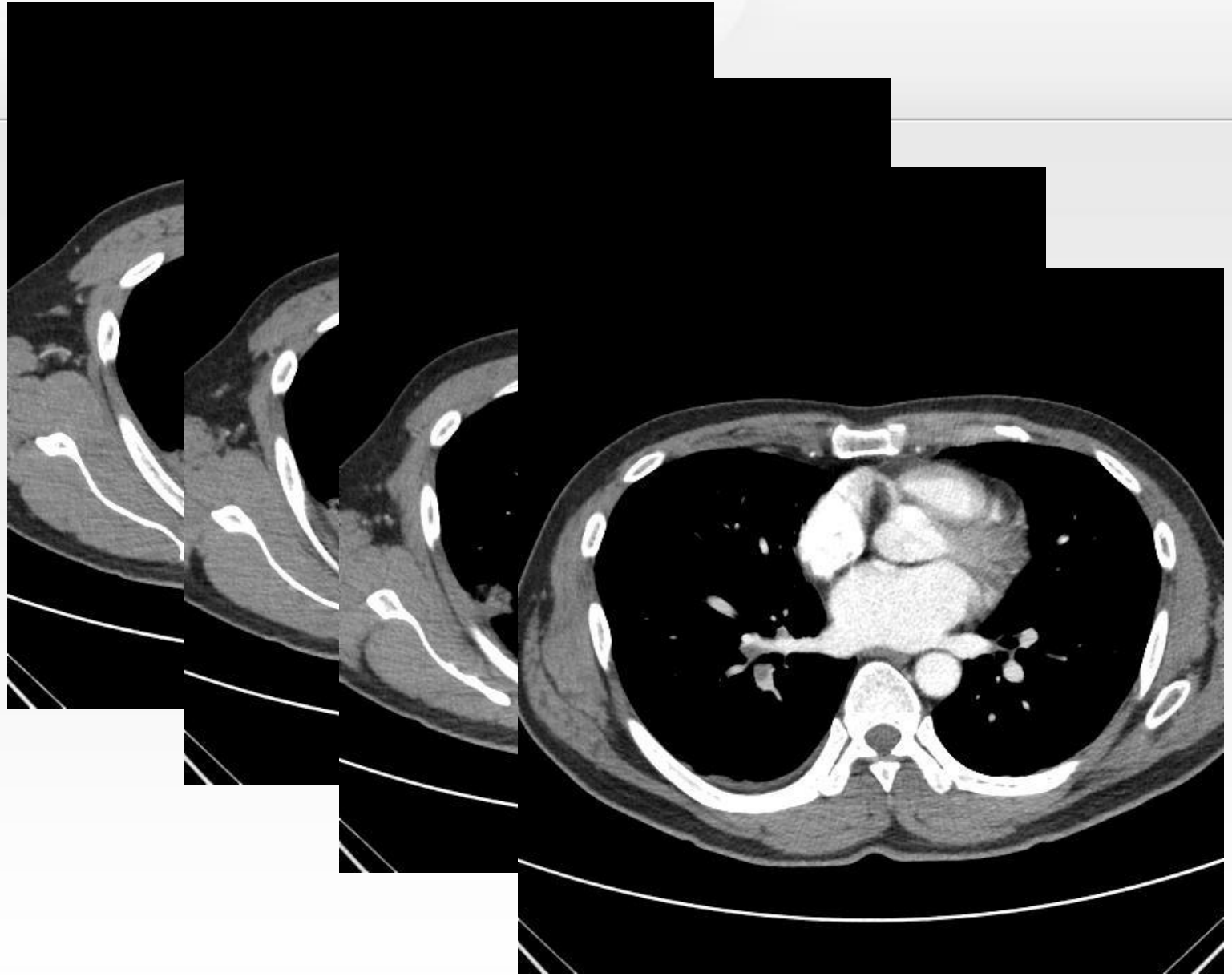

RPA











Diagnosis

Pulmonary thromboembolism

- r/o deep vein thrombosis
- r/o Hereditary thrombophilic disorders
  - antithrombin deficiency, protein C deficiency, protein S deficiency, Factor V Leiden mutation, activated protein C resistance without factor V leiden, prothrombin gene mutation, dysfibrinogenemia, plasminogen deficiency
- r/o acquired thrombophilic disorders
  - antiphospholipid antibody syndrome
  - hypercysteinemia

- Antiphospholipid antibody syndrome
  - ANA : negative
  - Anti-dsDNA : negative
  - Anti-cardiolipin Ab IgM : Normal
  - Anti-cardiolipin Ab IgG : Normal
  - Anti-phospholipid Ab IgM : Normal
  - Anti-phospholipid Ab IgG : Normal
  - Lupus anticoagulant : negative
- Factor V Leiden mutation
  - Factor V leiden : G/G (정상형)
- Prothrombin gene mutation
  - Prothrombin G20210A mutation : negative
- Hyperhomocysteinemia
  - Homocystein 11.22 [3.7-13.9]
- Antithrombin III deficiency
  - Antithrombin III 92.2 [75-125]
- Protein C deficiency
  - Protein C activity 100% [70-130]
  - Protein C antigen 98% [70-160]
- Protein S deficiency
  - Protein S activity 72% [73-146]
  - Protein S antigen 58% [60-150]
  - Protein S free antigen 93% [50-150]
- Dysfibrinogenemia
  - PT(INR) 1.01 [0.85-1.20]
  - aPTT /Pt 40.3 sec [26.0-41.0]
  - Fibrinogen 392 mg/dl [140-400]

Factor 2	93 %	[60-140]
Factor 5	102 %	[60-140]
Factor 7	91 %	[60-140]
Factor 8	**28 %**	**[60-140]**
Factor 9	85 %	[60-140]
Factor Ab, 8	Negative	[Negative]
Factor Ab, 9	Negative	[Negative]
Factor 10	84 %	[60-140]
Factor 11	65 %	[60-140]
Factor 12	74 %	[60-140]
Factor 13	Normal	[Normal]
Von-Willebrand's Ag	45 %	[47-197]
Von-Willebrand's Ristocetin cofactor	46 %	[48.8-163.4]

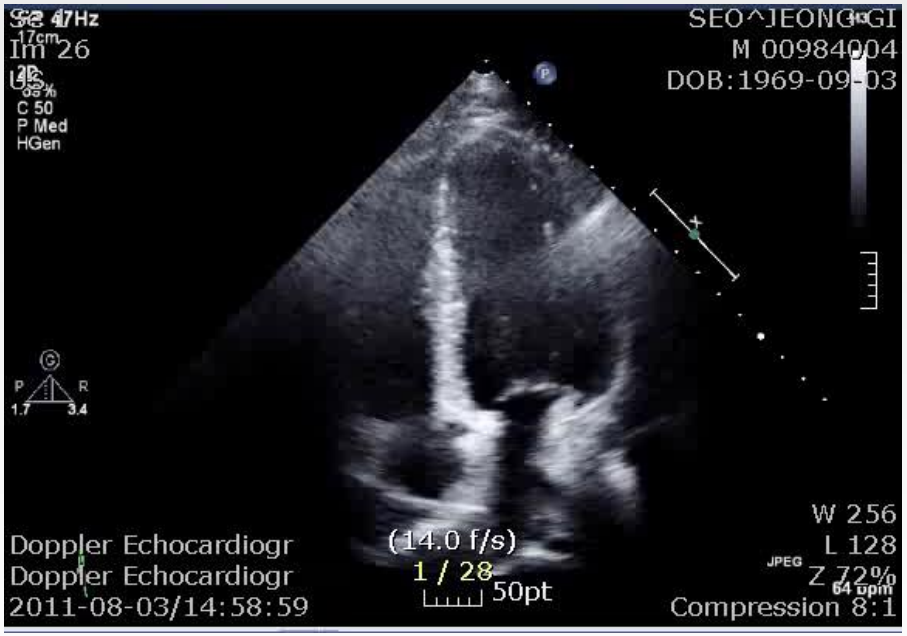
Echocardiography

Findings

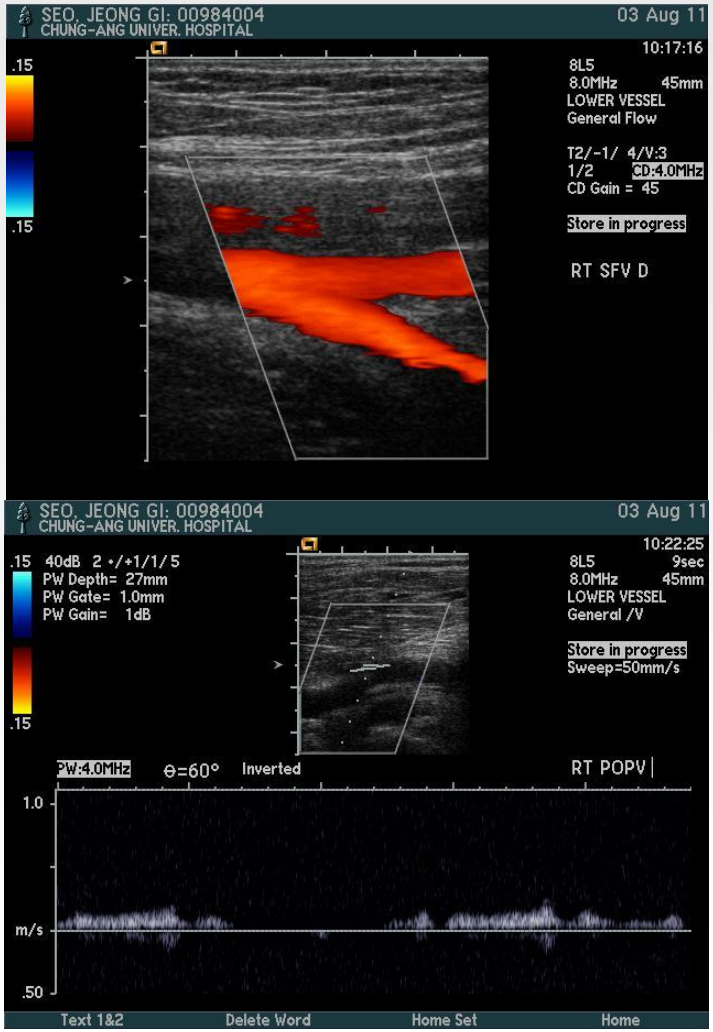
1. Borderline LA enlargement
2. Normal IVS and LVPW thickness
3. Slightly sclerotic mitral and aortic valves
4. Normal pattern of mitral inflow
5. No regional wall motion abnormality
6. No evidence of pericardial effusion
7. Normal global LV systolic function
   EF= 66%

CONCLUSION

Borderline LA enlargement
Normal global LV systolic function



Color Doppler US - Extremity (Vein)



Findings

Spectral doppler study of both common femoral and superficial femoral veins and both popliteal veins shows normal phasic pattern by respiration.
No evidence of deep vein thrombosis in these veins.

CONCLUSION

No evidence of deep vein thrombosis.

Past medical history

Drug : Autologous adipose-derived mesenchymal stem cell intravenous injection 시술 받음.
3달전, 2달전, 1달전 총 3차례
(cervical herniated intervertebral disc 치료 목적)

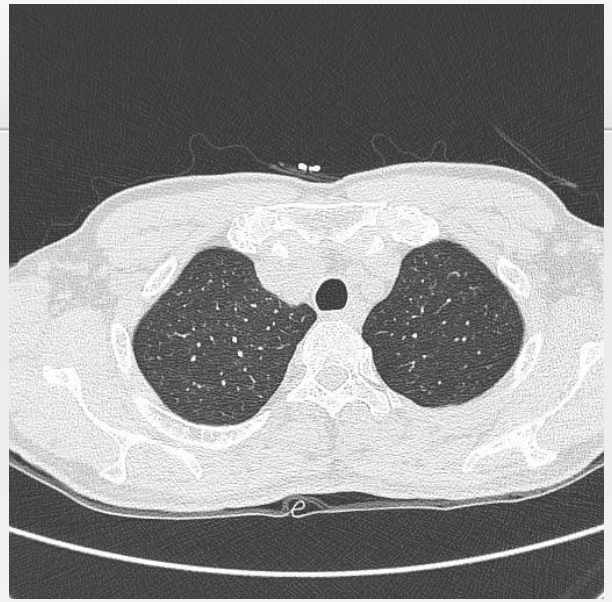
환자의 아버지와 어머니는 환자와 같은 치료를 이전에 받은 이력이 있음.

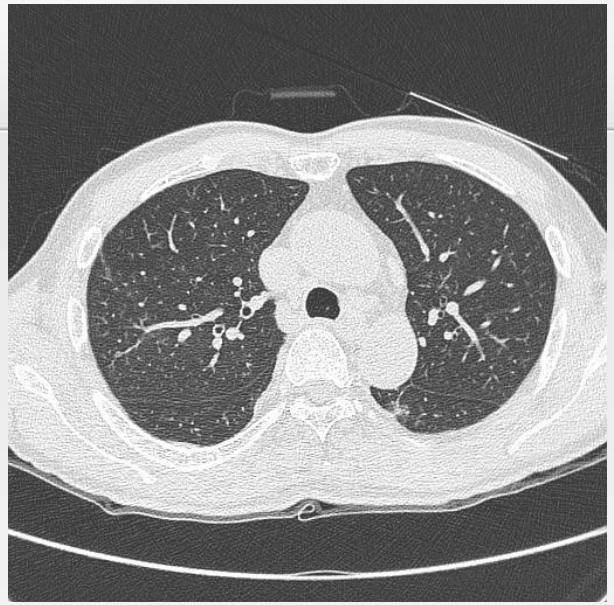
→ 호흡기내과 외래를 통해 pulmonary embolism 감별을 위한 검사 시행함.

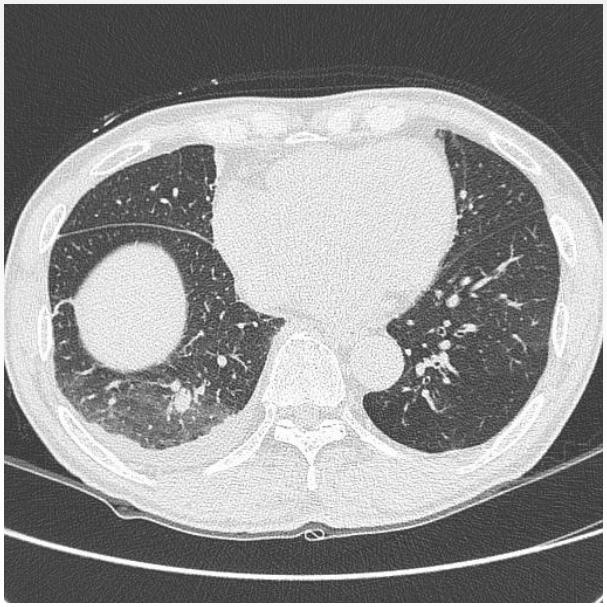
환자의 아버지

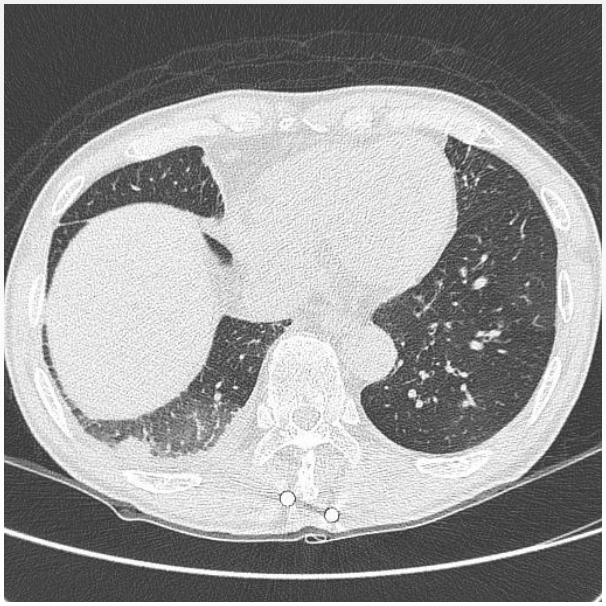
- 서 O 준 M/68
  - **2011년 2월부터 autologous hASC 총 5차례 injection**
  - **Knee osteoarthritis 치료 목적**
  - **No subjective symptom**

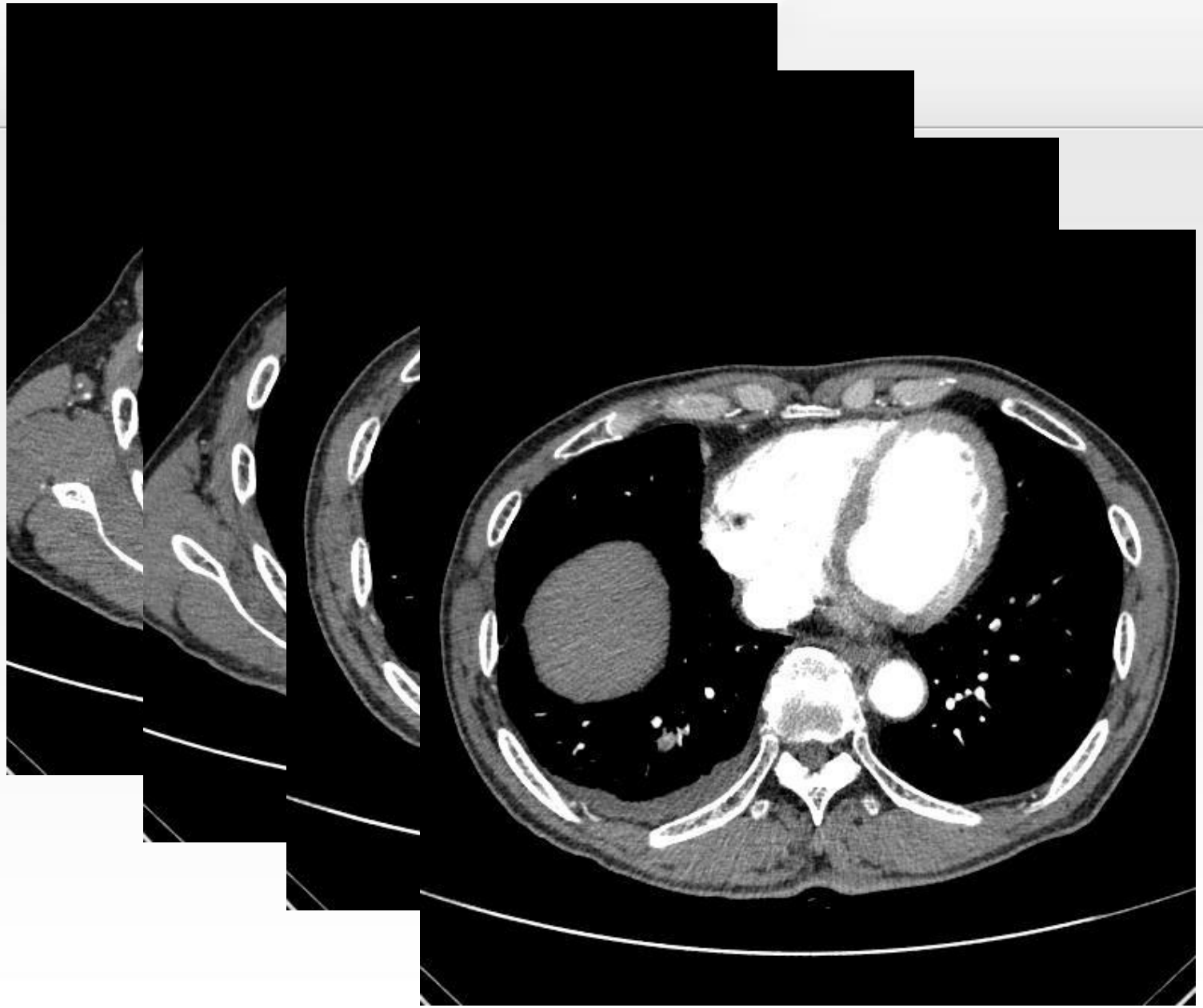
  - **D-dimer 1.0**
  - **No evidence of deep vein thrombosis on Doppler US**











환자의 어머니

- 석 O 남 M/68
  - **2011년 2월부터 autologous hASC 총 5차례 injection**
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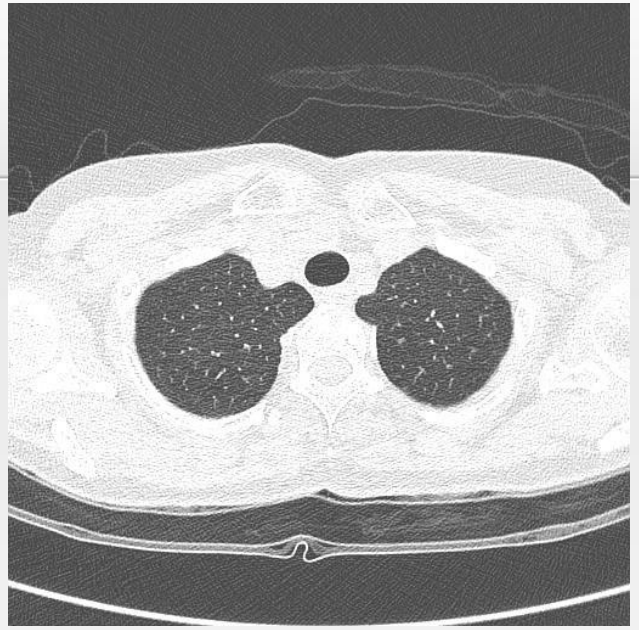
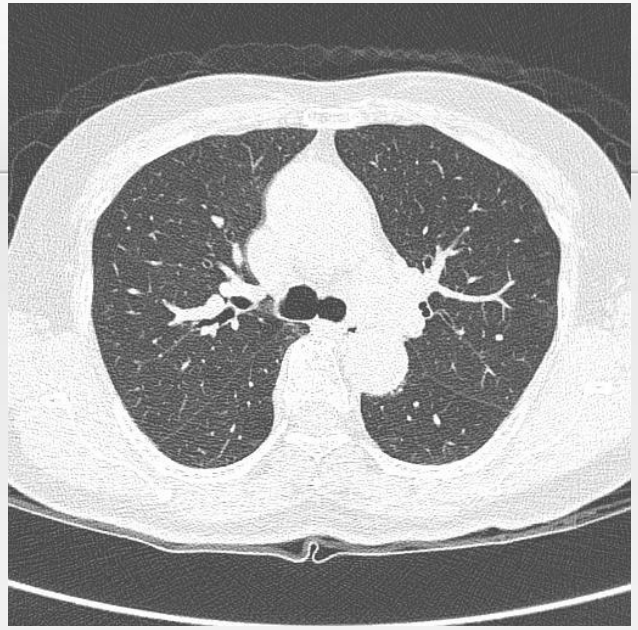
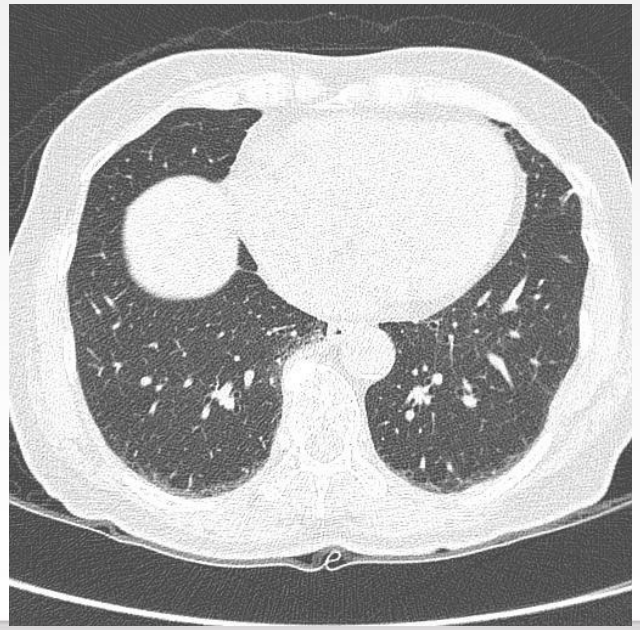
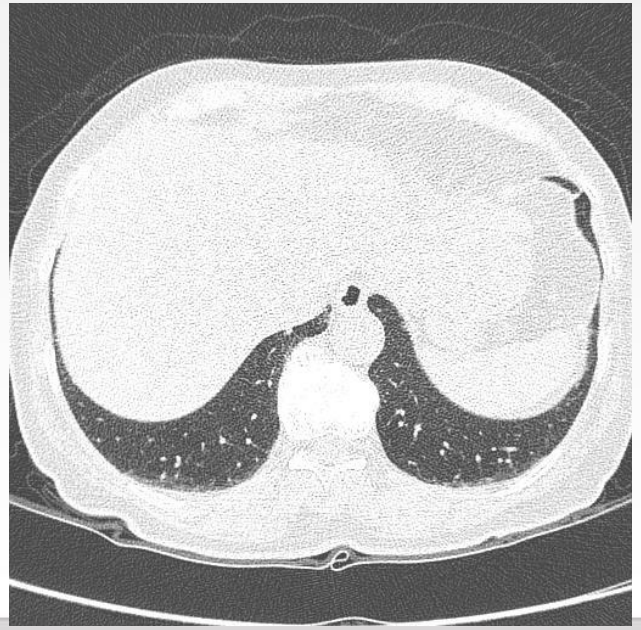
  - **No subjective symptom**

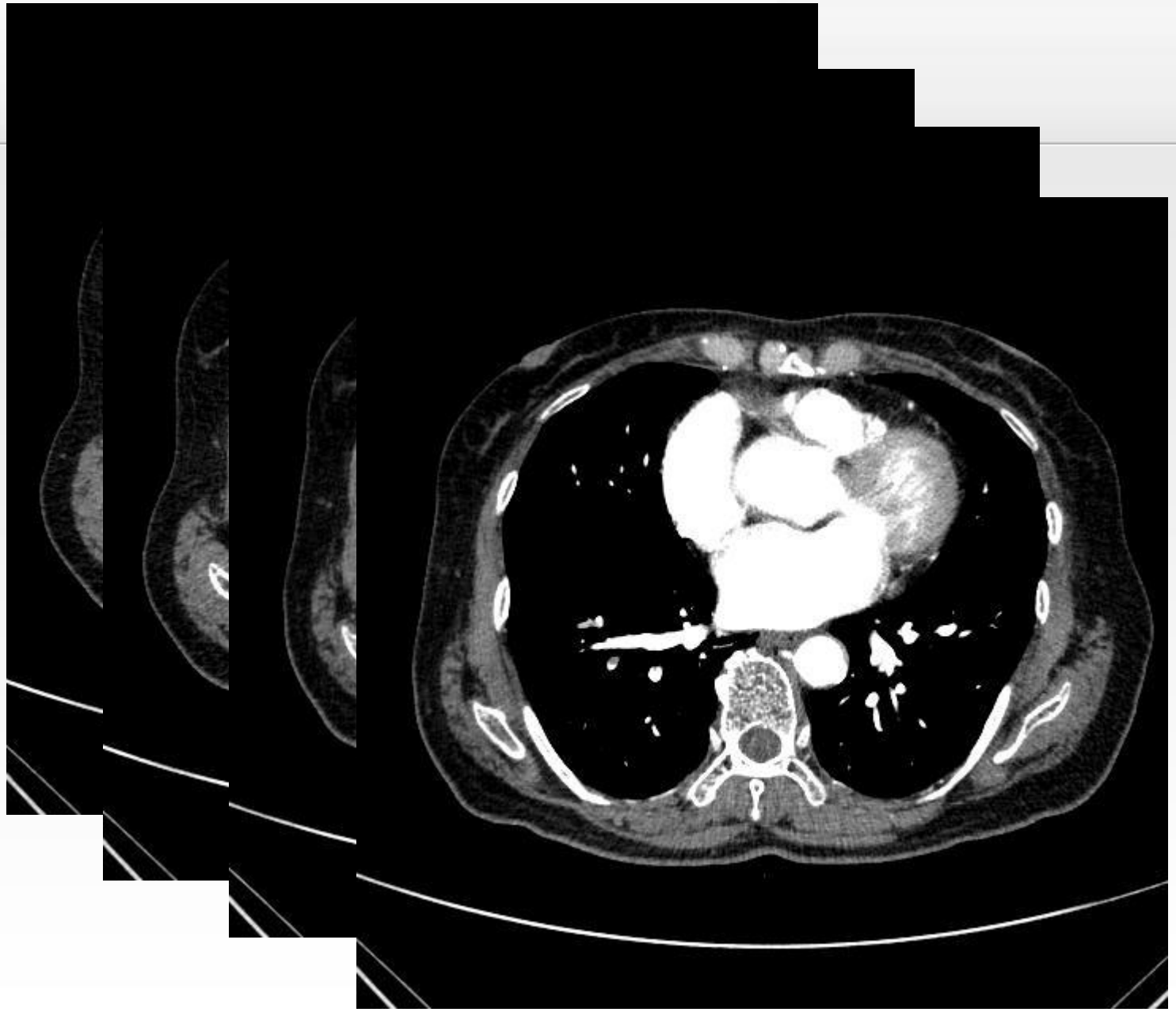
  - **D-dimer 1.1**
  - **No evidence of deep vein thrombosis on Doppler US**











Treatment

- Low molecular heparin

  → Enoxaparin 40mg twice/day SC

Warfarin overlapping : 5mg qd INR(2.0~3.0)

- Follow-up chest CT taken three month later showed disappearance of pleural effusion (index patient and his father) and pulmonary emboli (all of them).

Human adipose tissue-derived stem cells (hASC)

- **Adult human adipose tissue**

: originates from the embryonic mesoderm

: represents an abundant and less invasive source of mesenchymal stem cells

- **Human adipose tissue-derived stem cells (hASC)**

: can secrete multiple growth factors and cytokines that exert beneficial effects on organ or tissue injury

: can be easily isolated from routine liposuction and reconstructive surgery waste materials

Activated Stem Cells Now Used for Joint Pain

Harvest

1 A small amount of fat - 40cc is taken from the waist area.

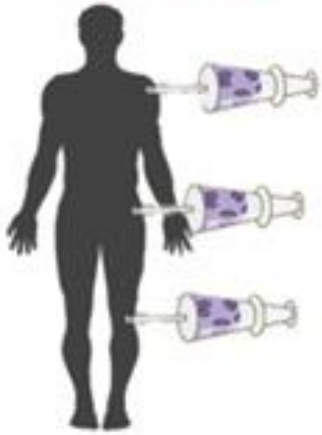
Separate

2 Stem Cells are separated from fat cells.

Activate

3 The Stem Cells are activated with AdiLight™- 2.

Treat



4 The activated Stem Cells are injected into the joint.

Cell Transplantation, Vol. 20, pp. 727–739, 2011

Comparative Study of Methods for Administering Neural Stem/Progenitor Cells to Treat Spinal Cord Injury in Mice

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Chikako Miyauchi Hara,† Hirotaka James Okano,† Atsushi Miyawaki,§¶
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To investigate potential cures for spinal cord injury (SCI), several researchers have transplanted neural stem/progenitor cells (NS/PCs) into the injured spinal cord by different procedures, including intralesional (IL), intrathecal (IT), and intravenous (IV) injection. However, there are no reports quantifying or comparing the number of cells successfully transplanted to the lesion site by each procedure in vivo. The purpose of the present study was to determine the optimal method of cell transplantation to the SCI site in terms of grafted cell survival and safety. For this purpose, we developed mouse NS/PCs that expressed a novel Venus-luciferase fusion protein that enabled us to detect a minimum of 1,000 grafted cells in vivo by bioluminescence imaging (BLI). After inducing contusive SCI at the T10 level in mice, NS/PCs were transplanted into the injured animals three different ways: by IL, IT, or IV injection. Six weeks after the transplantation, BLI analysis showed that in the IL group, the luminescence intensity of the grafted cells had decreased to about 10% of its initial level, and appeared at the site of injury. In the IT group, the luminescence of the grafted cells, which was distributed throughout the entire subarachnoid space immediately after transplantation, was detected at the injured site 1 week later, and by 6 weeks had gradually decreased to about 0.3% of its initial level. In the IV group, no grafted cells were detected at the site of injury, but all of these mice showed luminescence in the bilateral chest, suggesting pulmonary embolism. In addition, one third of these mice died immediately after the IV injection. In terms of grafted cell survival and safety, we conclude that the IL application of NS/PCs is the most effective and feasible method for transplanting NS/PCs into the SCI site.

Key words: Spinal cord injury (SCI); Transplantation; Neural stem/progenitor cells (NS/PCs); Bioluminescence imaging (BLI)

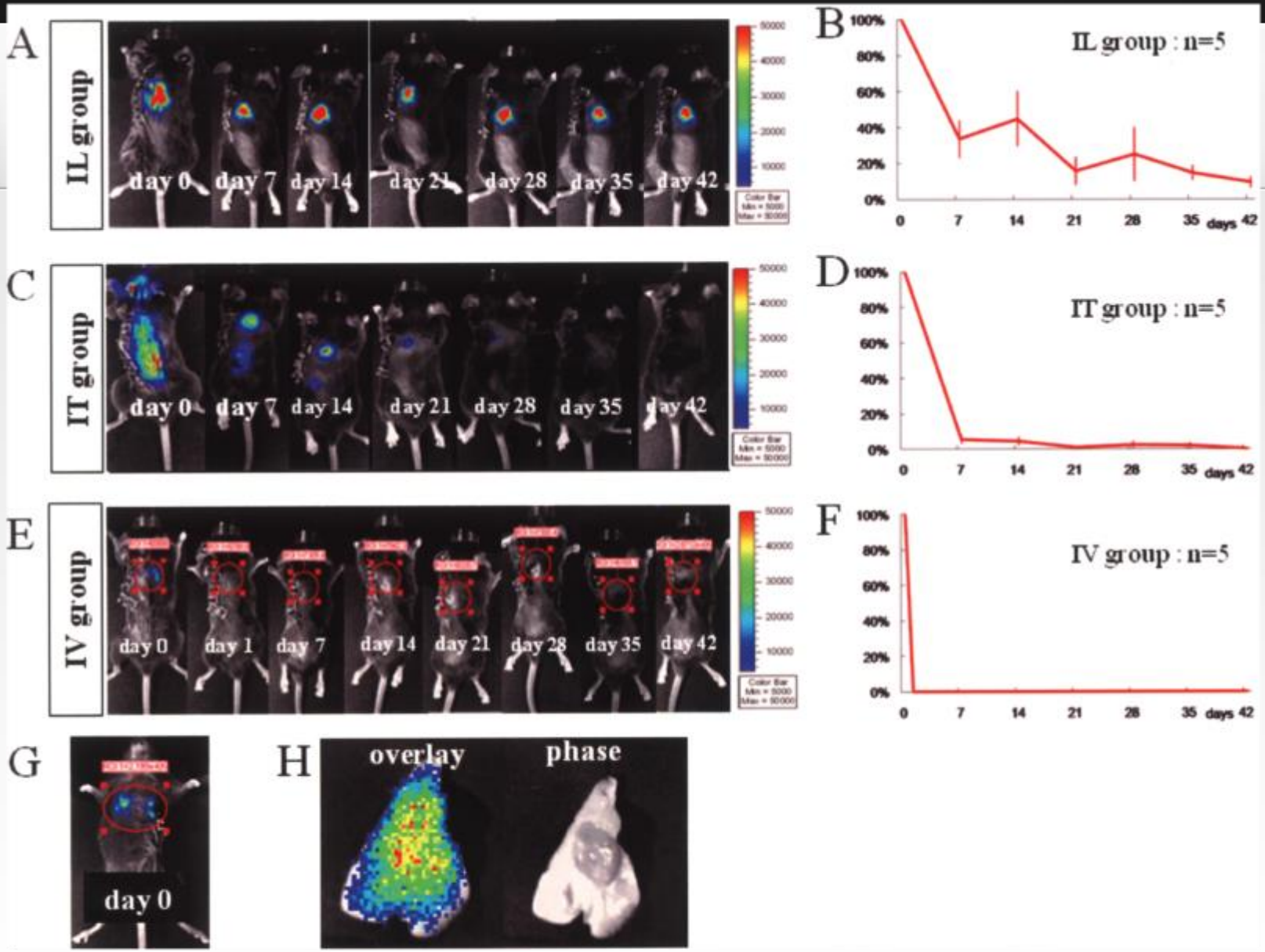

Figure 3. (A, C, E) Representative in vivo images of NS/PCs transplanted by the three application methods: (A) IL group, (C) IT group, and (E) IV group. (B, D, F) Quantitative analysis of the photon counts of the grafted NS/PCs in the IL group (B), IT group (D), and IV group (F). Data are the mean ± SEM; $n = 5$. (G) Strong luminescence was observed in the bilateral chest immediately after transplantation in all 10 animals of the IV group. (H) A resected lung from the IV group showed strong luminescence from the transplanted cells.

STEM CELLS AND DEVELOPMENT
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Safety of Intravenous Infusion of Human Adipose Tissue-Derived Mesenchymal Stem Cells in Animals and Humans

Jeong Chan Ra,[1] Il Seob Shin,[1] Sang Han Kim,[2] Sung Keun Kang,[1] Byeong Cheol Kang,[3,4] Hang Young Lee,[1] Youn Joung Kim,[1] Jung Youn Jo,[1] Eun Ji Yoon,[1] Hyung Jun Choi,[3,4] and Euna Kwon[4]

Adipose tissue-derived mesenchymal stem cells (AdMSCs) represent an attractive and ethical cell source for stem cell therapy. With the recent demonstration of MSC homing properties, intravenous applications of MSCs to cell-damaged diseases have increased. In the present study, the toxicity and tumorigenicity of human AdMSCs (hAdMSCs) were investigated for clinical application. Culture-expanded hAdMSCs showed the typical appearance, immunophenotype, and differentiation capacity of MSCs, and were genetically stable at least 12 passages in culture. Cells suspended in physiological saline maintained their MSC properties in a cold storage condition for at least 3 days. To test the toxicity of hAdMSCs, different doses of hAdMSCs were injected intravenously into immunodeficient mice, and the mice were observed for 13 weeks. Even at the highest cell dose (2.5×10^8 cells/kg body weight), the SCID mice were viable and had no side effects. A tumorigenicity test was performed in Balb/c-nu nude mice for 26 weeks. Even at the highest cell dose (2×10^8 MSCs/kg), no evidence of tumor development was found. In a human clinical trial, 8 male patients who had suffered a spinal cord injury >12 months previous were intravenously administered autologous hAdMSCs (4×10^8 cells) one time. None of the patients developed any serious adverse events related to hAdMSC transplantation during the 3-month follow-up. In conclusion, the systemic transplantation of hAdMSCs appears to be safe and does not induce tumor development.