

대한결핵 및 호흡기학회 심포지엄

2014.7.21

이화의대 이석정



CASE

❖ **ID:** 전 0 0

❖ **Age/sex:** 50/F

❖ **CC:** Abnormal finding in chest X-ray and chest CT

CASE

❖ Present illness

특이병력 없던 분으로 2014.01 지역의원 건강검진에서 시행한 chest X-ray 에서 좌하엽 lung mass 의심되어 타원에서 chest CT 시행 후 further evaluation 위해 입원함.

CASE

❖ **Past history**

- No history of DM, Hypertension, Tb, Hepatitis, or cancer
- No history of hospitalization or operation

❖ **Social history**

- Never smoker
- Alcohol (-)
- Occupation: housemaid

❖ **Family history**

- None

CASE – Review of system

- General weakness/easy fatigue (-/-)
- Fever/Chill/Night sweat (-/-/-)

- Headache (-)
- Dizziness/Vertigo (-/-)

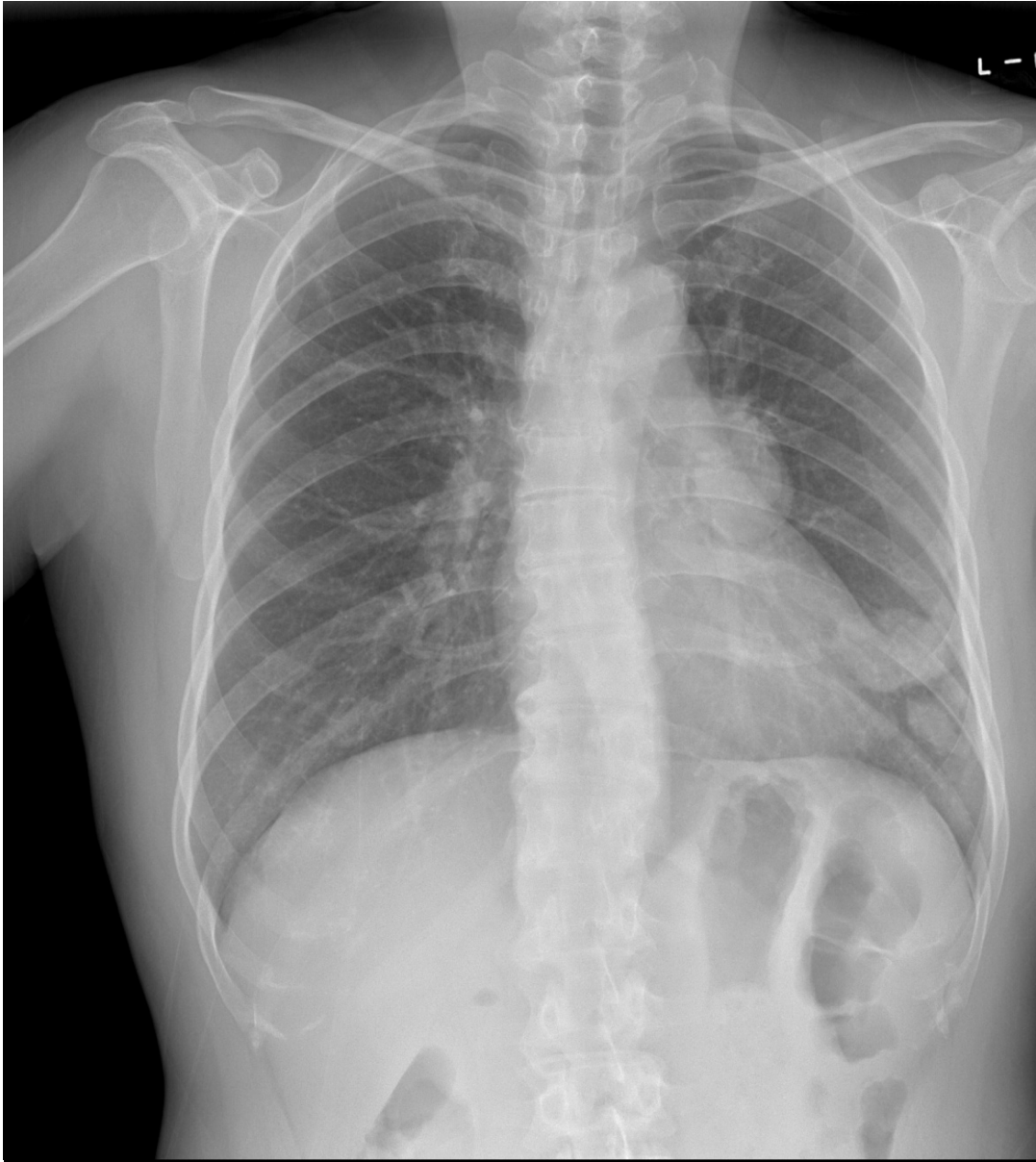
- Cough/Sputum (-/-)
- Dyspnea/Orthopnea (-/-)
- Palpitation (-)
- Hemoptysis (-)
- Chest discomfort (-)

- Anorexia/Nausea/Vomiting(-/-)
- Constipation/diarrhea(-/-)
- Abdominal pain (-)
- Melena/hematochezia (-/-)

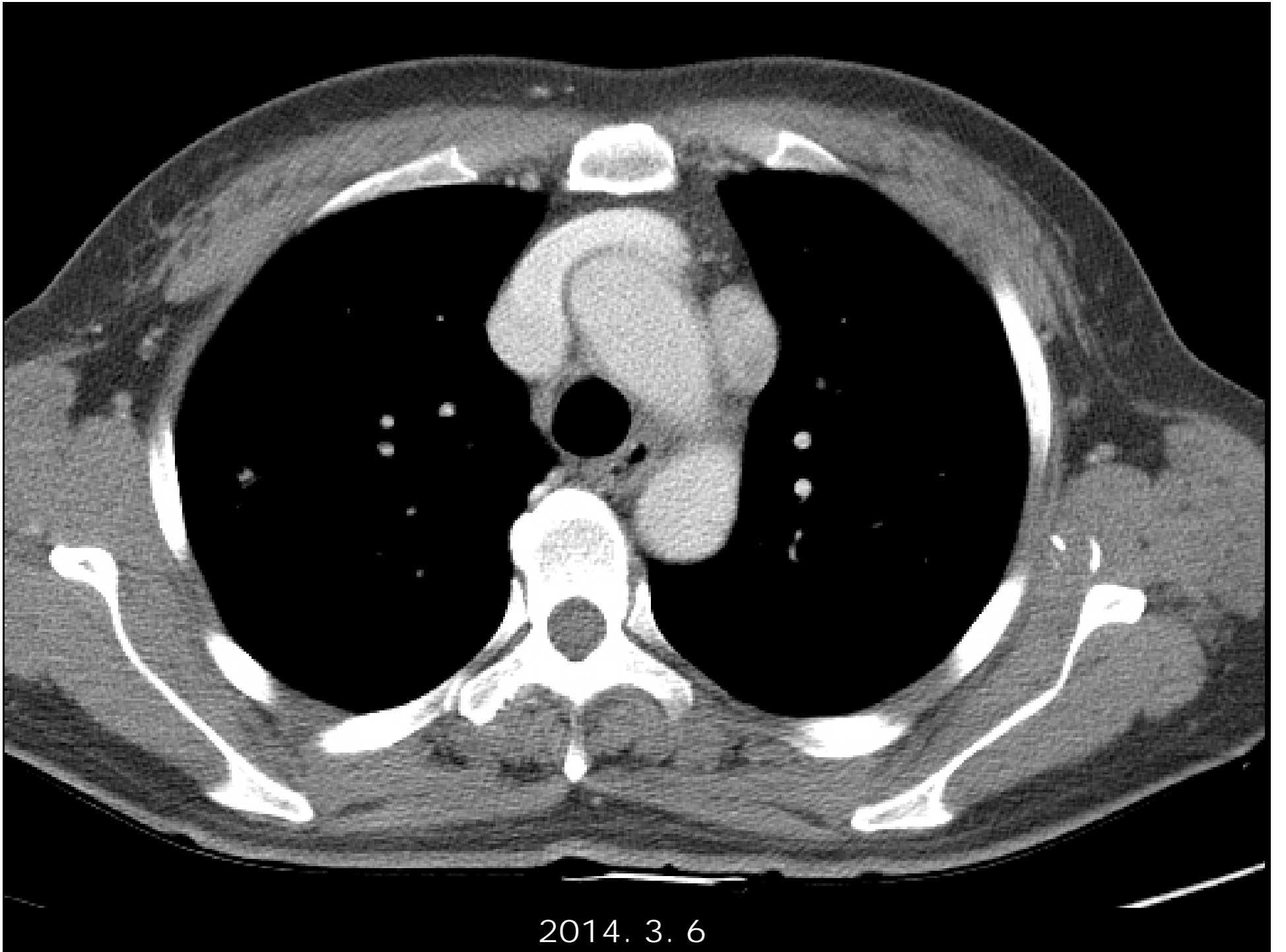
- Urinary symptom (-)

CASE – Physical examination

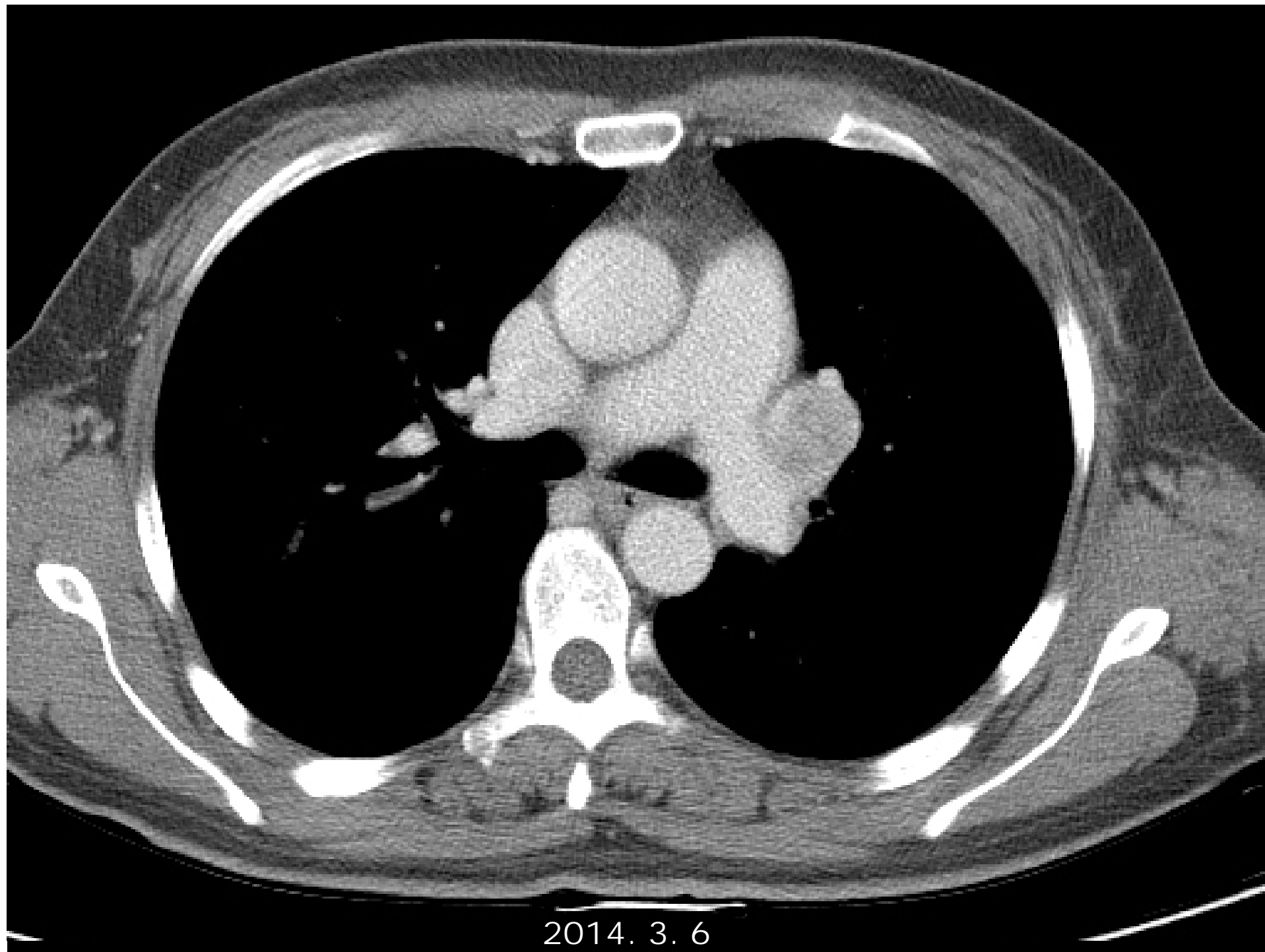
- Vital sign
 - BP 100/60 PR 80/min RR 20/min BT 36.4°C
- General appearance
 - Not so ill-looking appearance
 - Mental state: alert
- HEENT
 - Not anemic conjunctiva
 - Anicteric Sclera
 - Not injected Throat
- Neck
 - Palpable cervical lymph node (-)
 - Neck vein engorgement (-)
- Chest
 - Both symmetrical chest expansion
 - Clear breath sound without crackle
 - Regular heart beat without murmur
- Abdomen
 - Soft & Flat
 - Normoactive bowel sound
 - Direct tenderness/rebound tenderness (-/-)
 - Hepatosplenomegaly (-)

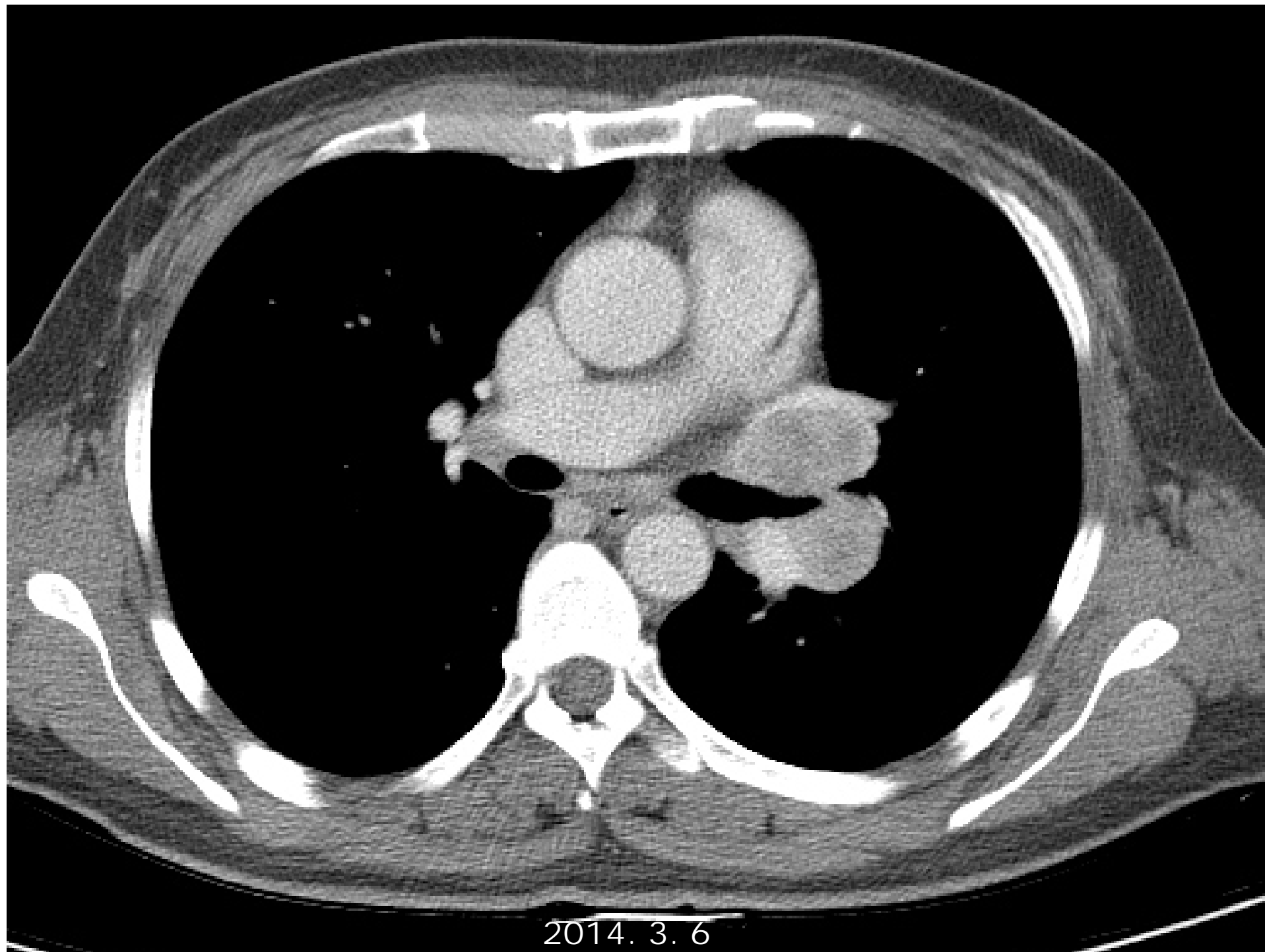


2014. 3. 6

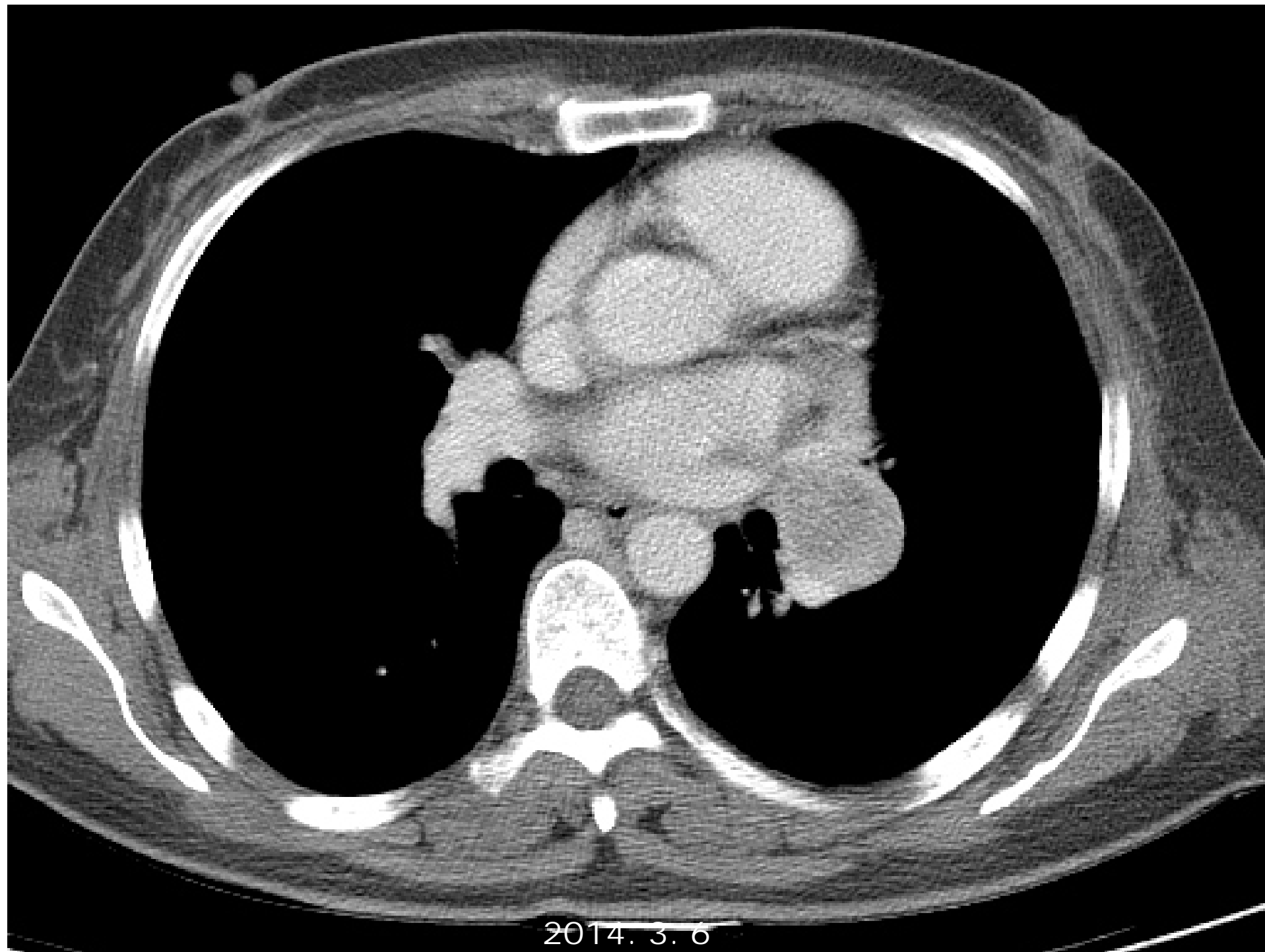


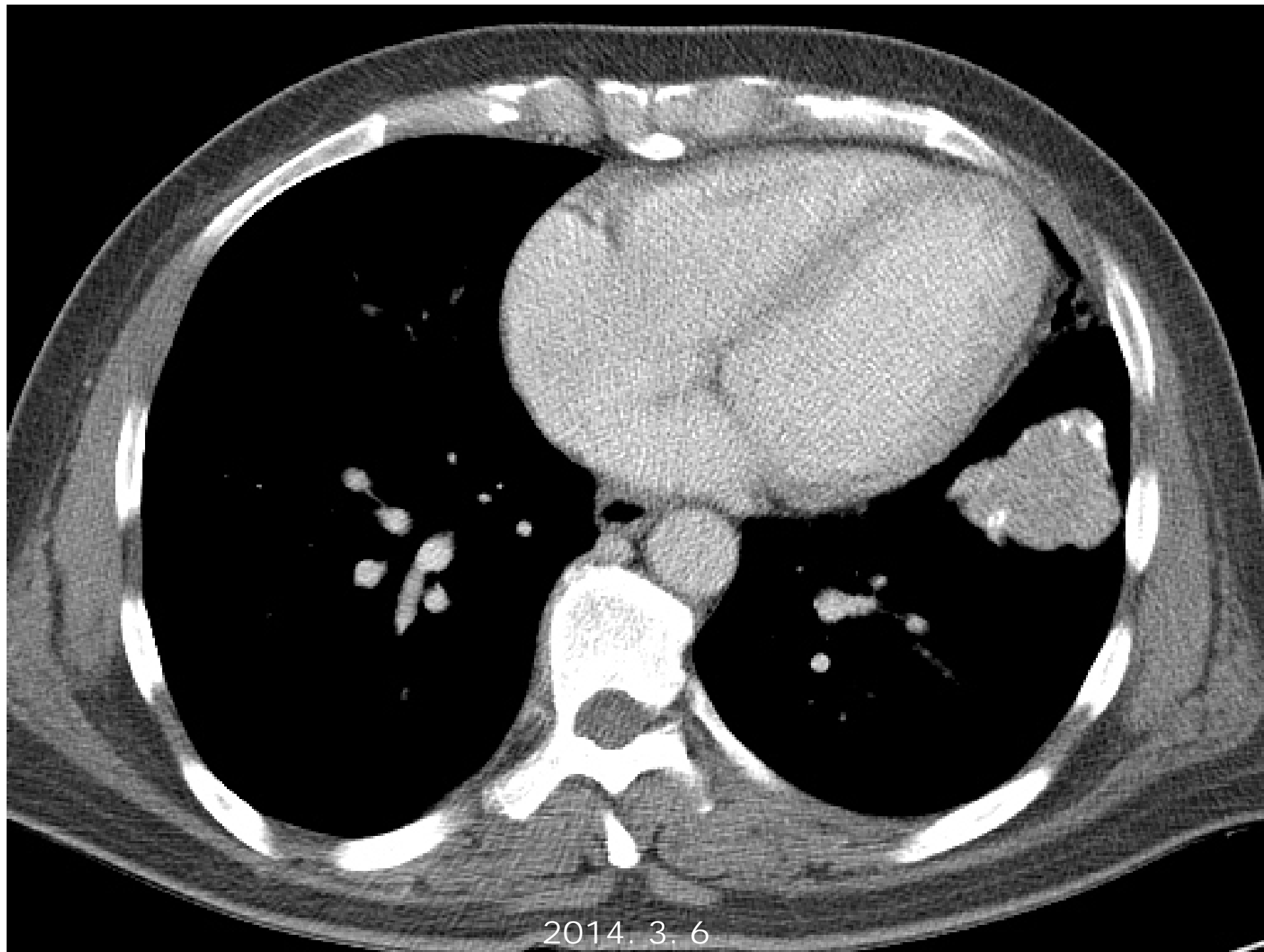
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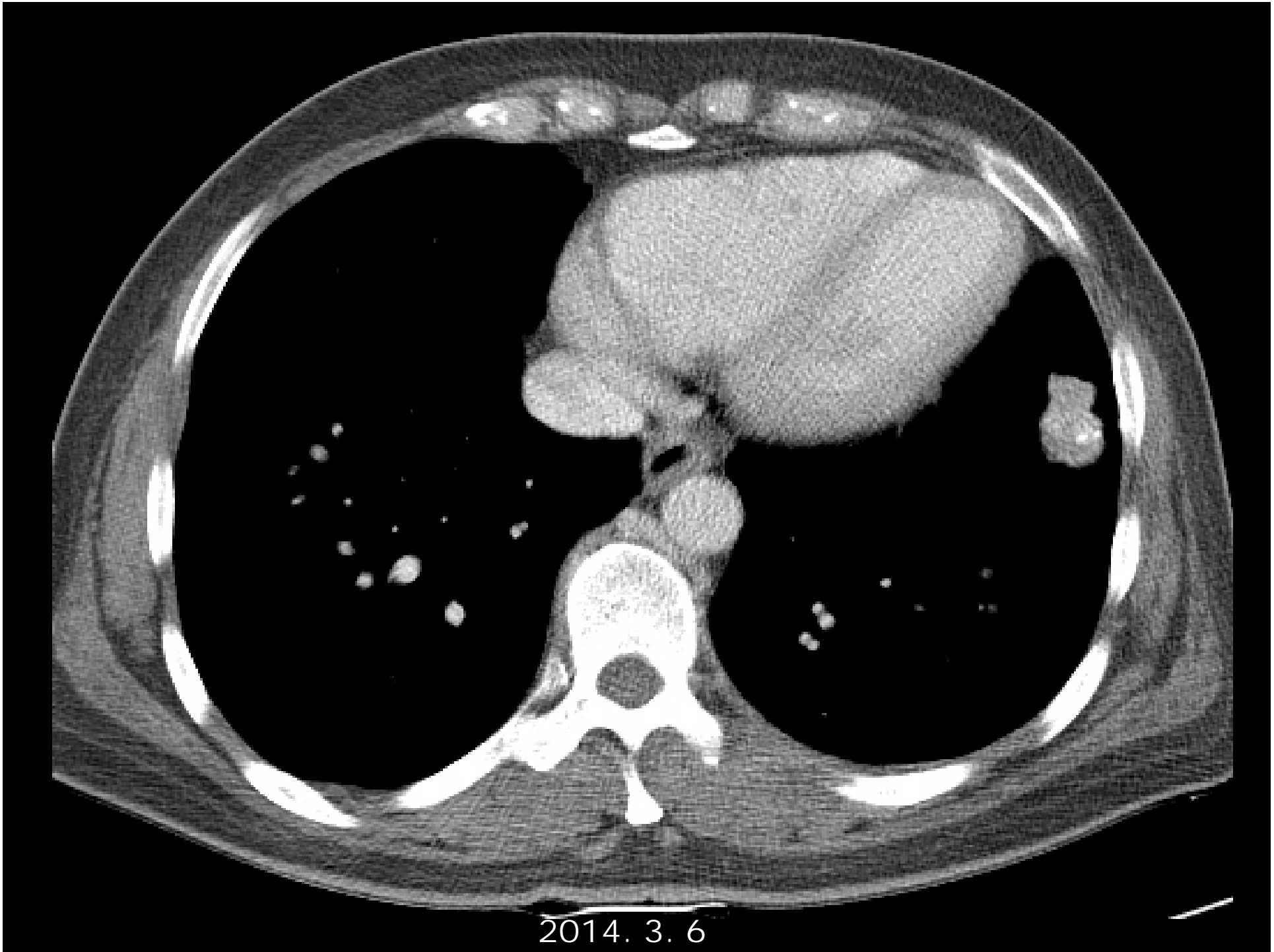


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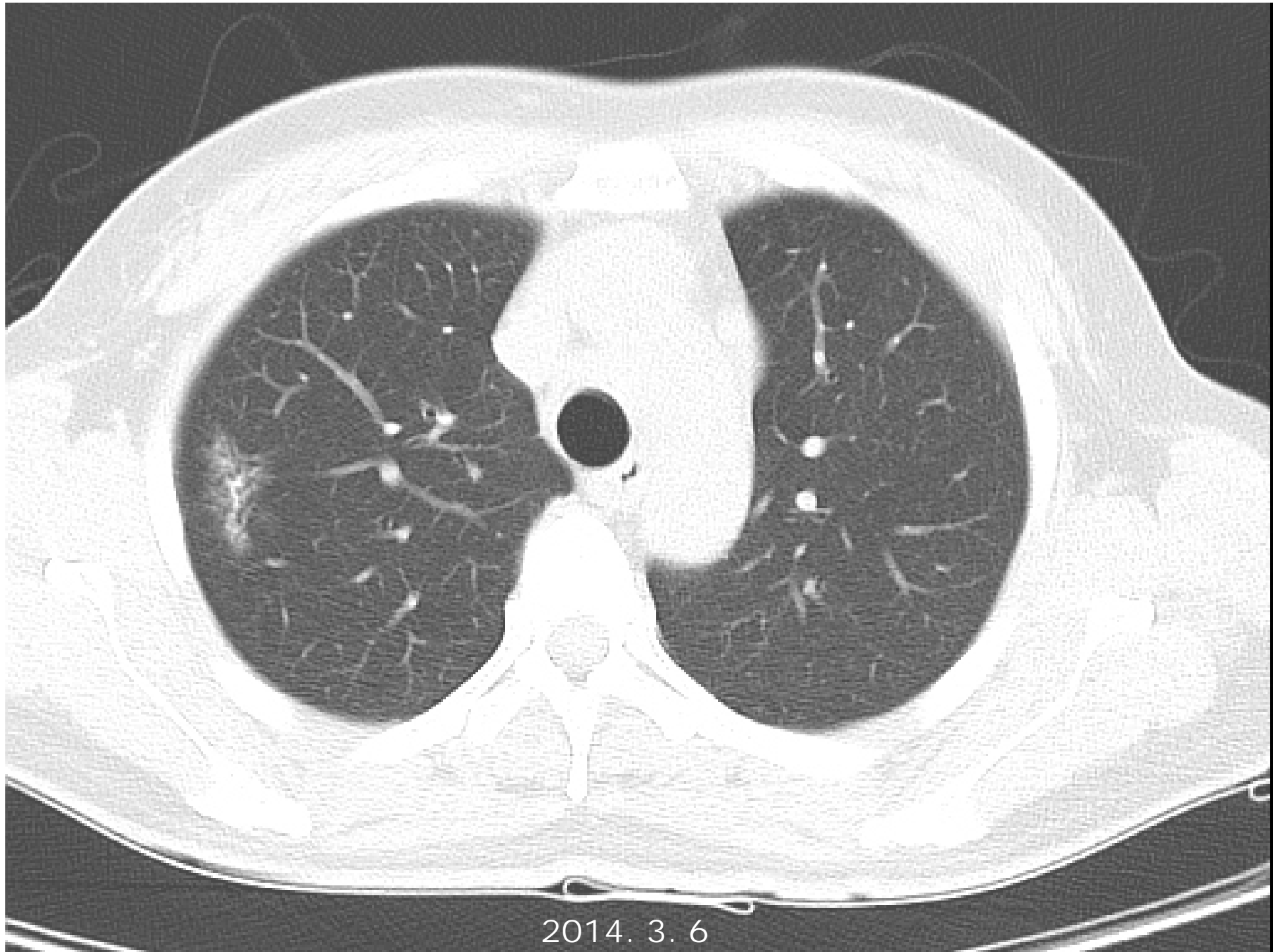




2014. 3. 6



2014. 3. 6



2014. 3. 6

Impression

1. Lung cancer , LLL
2. AAH or AIS, RUL

Diagnostic plan

- ❖ Laboratory tests
- ❖ Abdomen and pelvis CT
- ❖ PET-CT
- ❖ Percutaneous transthoracic lung biopsy

Laboratory Tests

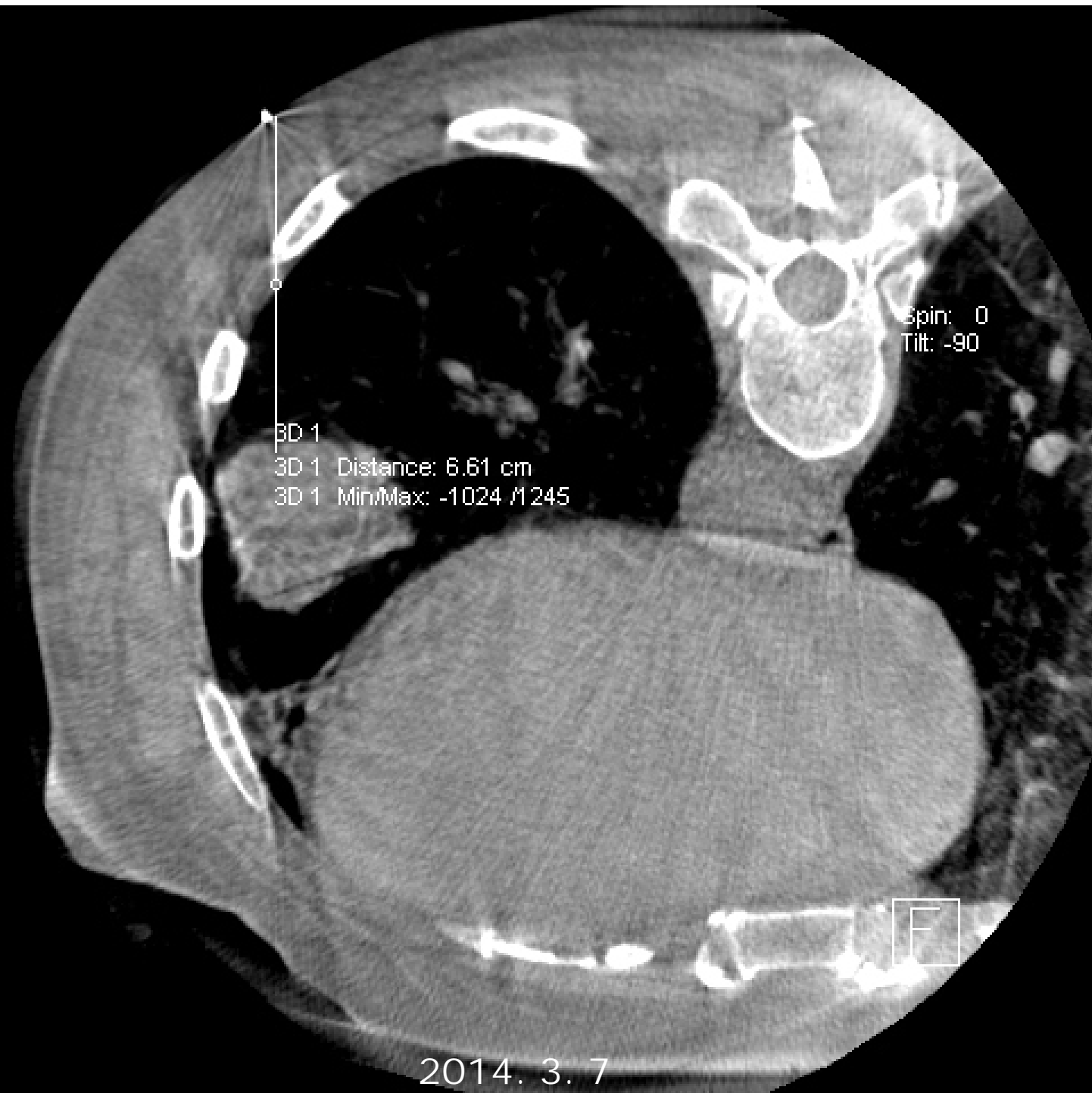
CBC	WBC (/μL)	Hb (g/dL)	Hct (%)	Platelet (/μL)
	4090	13.3	36.8	151,000

LFT	AST (IU/L)	ALT (IU/L)	ALP (IU/L)	γGT (mg/dL)
	24	16	239	10

Electrolytes	Na (mEq/L)	K (mEq/L)	Cl (mEq/L)	CO₂ (mEq/L)
	141	4.1	107	24

Renal function	BUN (mg/dL)	Creatinine (mg/dL)
	4	0.76

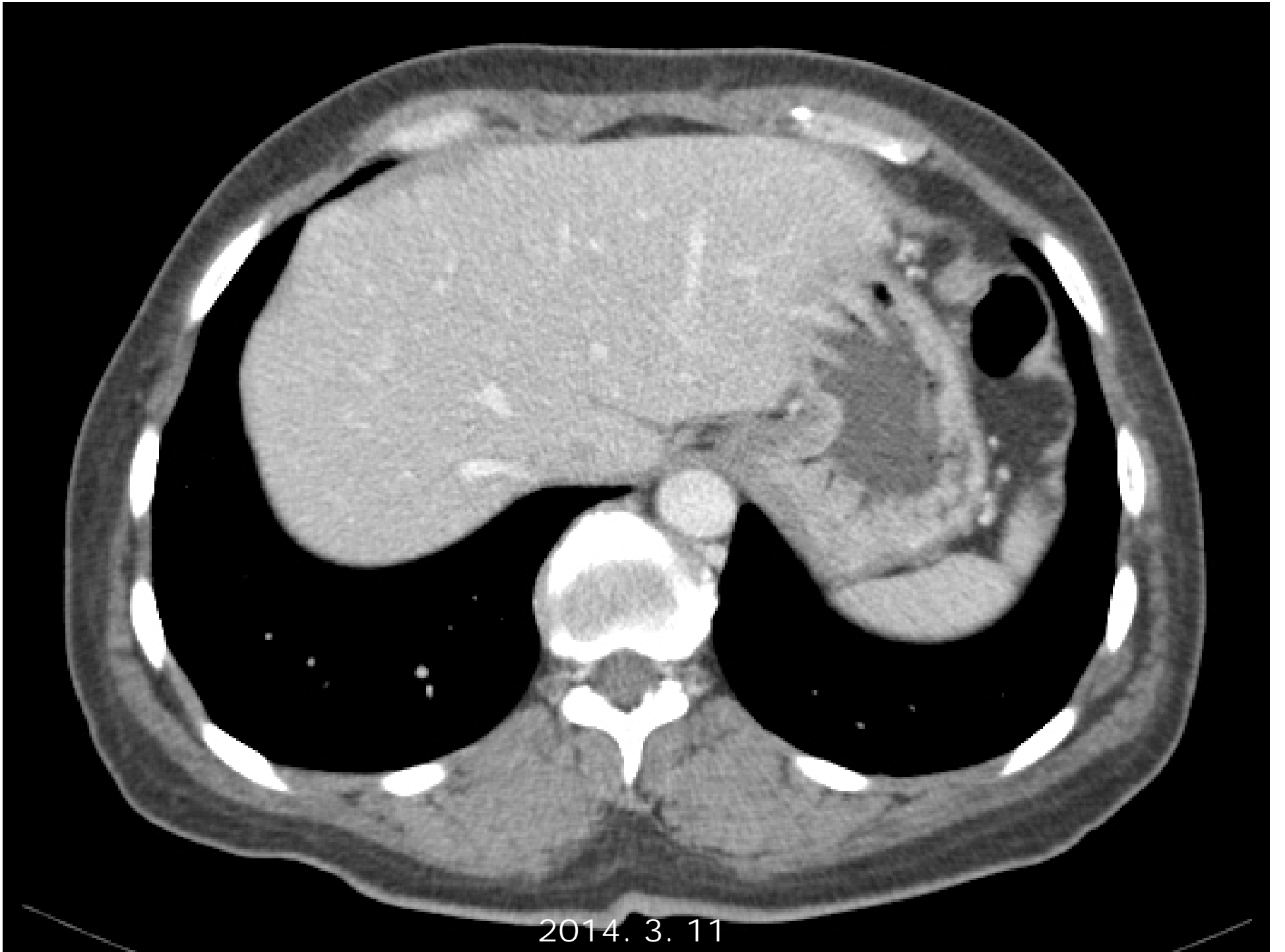
Tumor marker	CEA (U/mL)	NSE (ng/mL)
	1.2	10.8



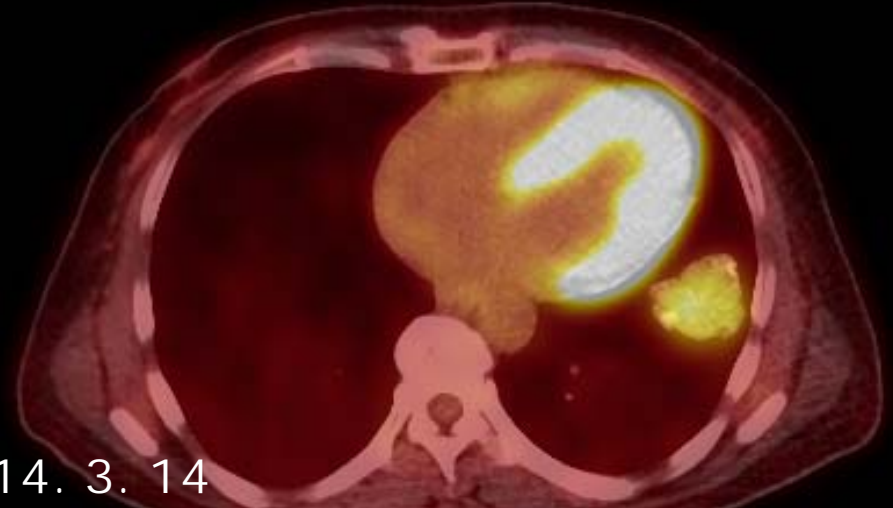
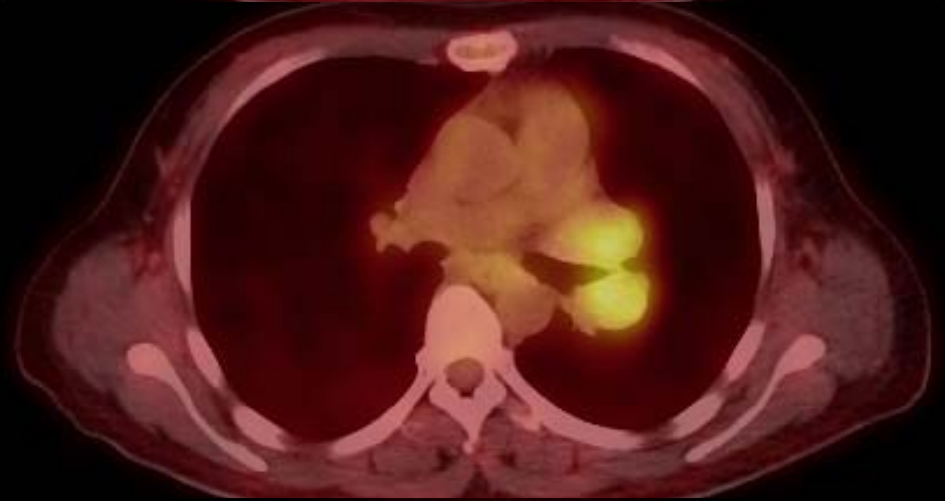
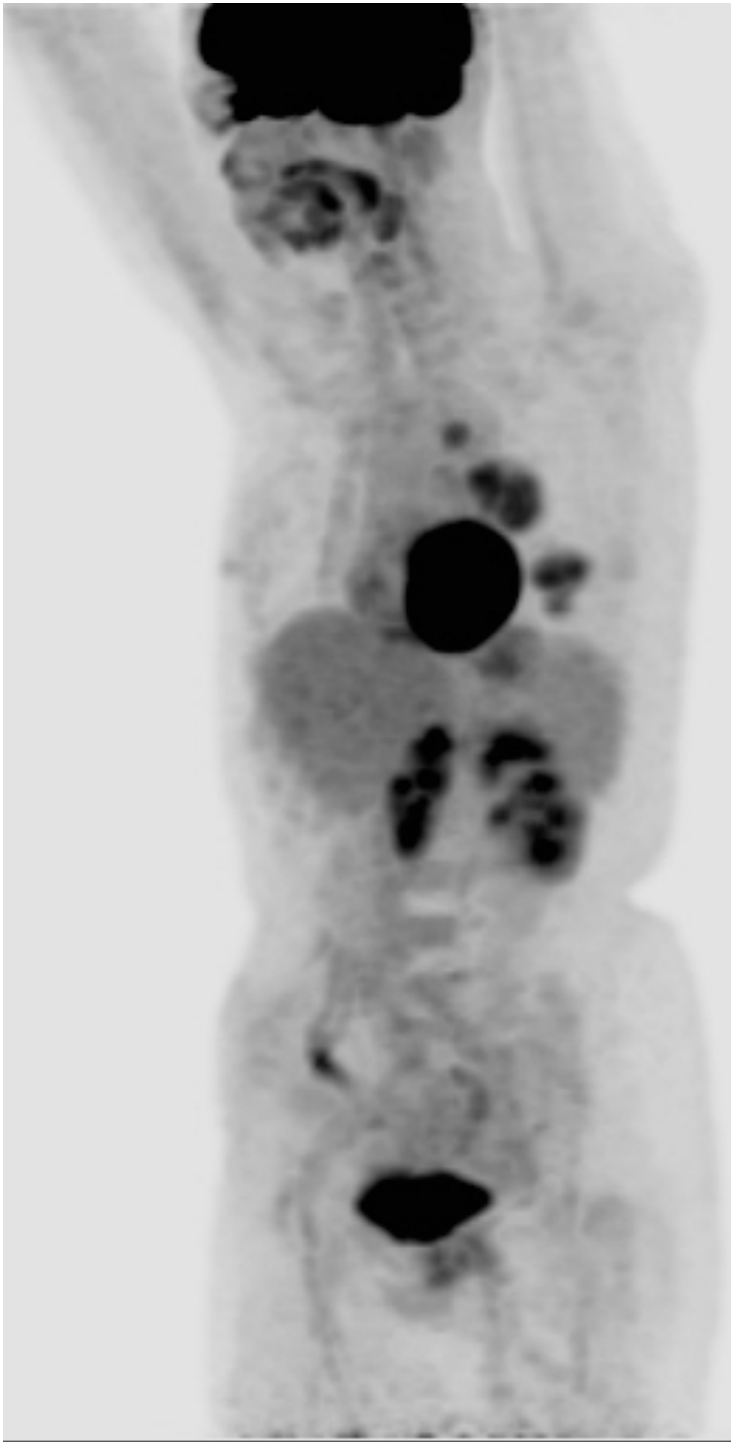
Spin: 0
Tilt: -90

3D 1
3D 1 Distance: 6.61 cm
3D 1 Min/Max: -1024 /1245

2014. 3. 7



2014. 3. 11



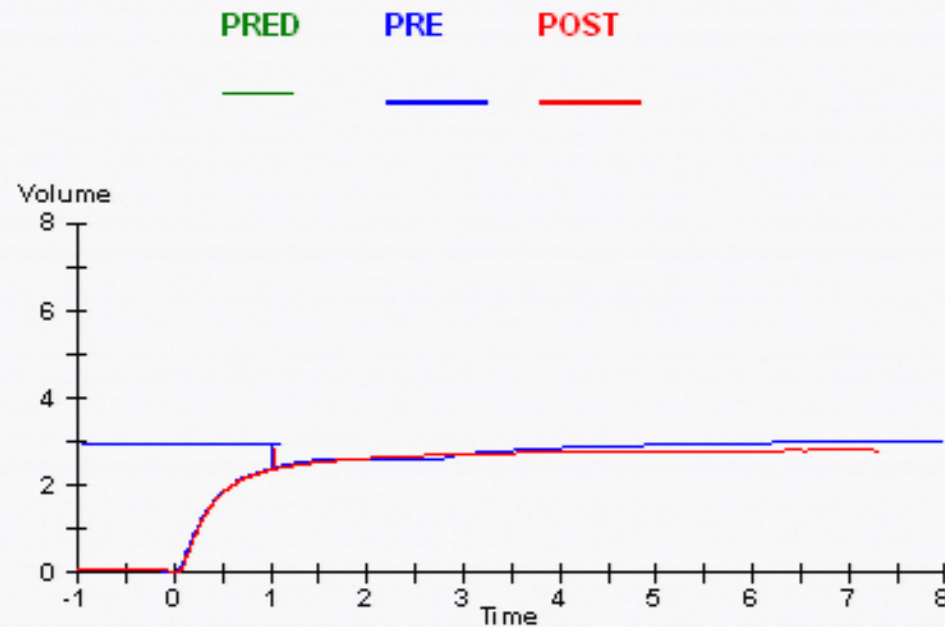
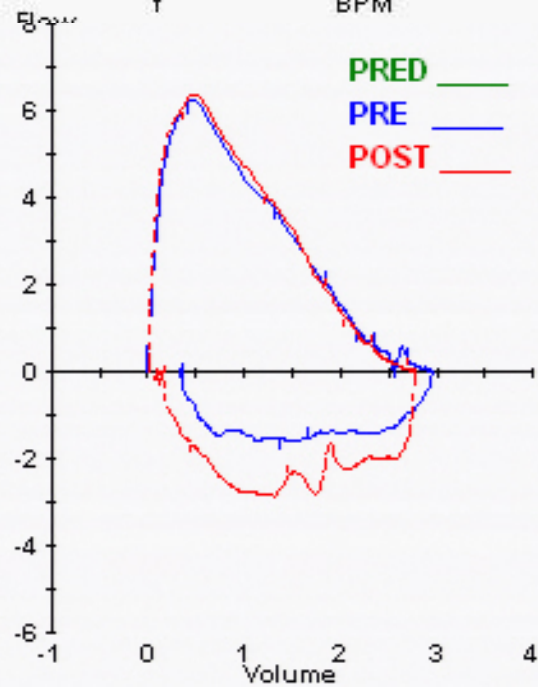
2014. 3. 14

Spirometry

	(BTPS)	PRED	PRE-RX BEST %PRED		POST-RX BEST %PRED		% CHG
FVC	Liters	3.12	2.96	95	2.78	89	-6
FEV1	Liters	2.55	2.38	93	2.36	92	-1
FEV1/FVC	%	81	81		85		
FEF25-75%	L/sec	2.65	2.40	91	2.77	105	15
IsoFEF25-75	L/sec	2.65	2.40	91	2.45	92	2
FEF75-85%	L/sec	0.77	0.57	74	0.73	94	28
PEF	L/sec	5.48	6.22	114	6.34	116	2
FET100%	Sec		8.12		7.30		-10
FIVC	Liters	2.85	2.61	92	2.71	95	4
FEV1	Liters	2.55	2.38	93	2.36	92	-1
FIV1	Liters		1.40		2.19		57
FEF/FIF50		<1.00	2.28		1.57		-31
Vol Extrap	Liters		0.03		0.01		-75
FVL ECode			001000		111000		
MVV	L/min	100					
f	BPM						

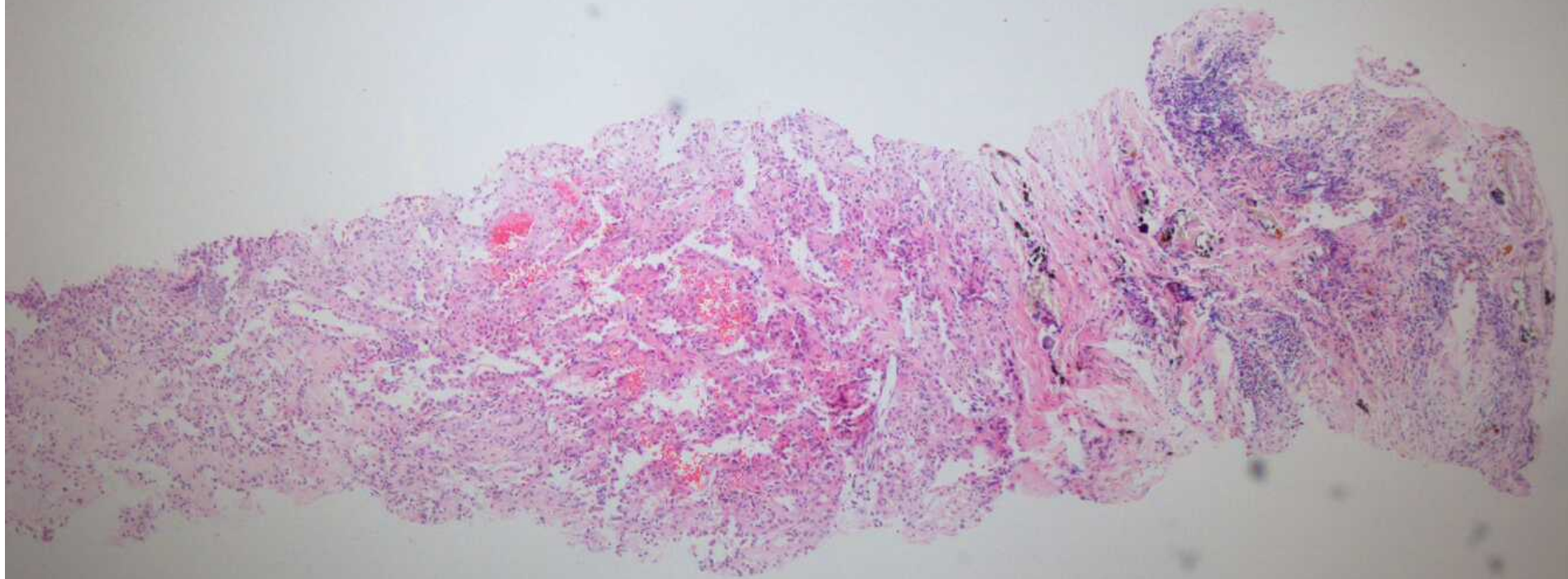
200 Pt

L:127
W:255



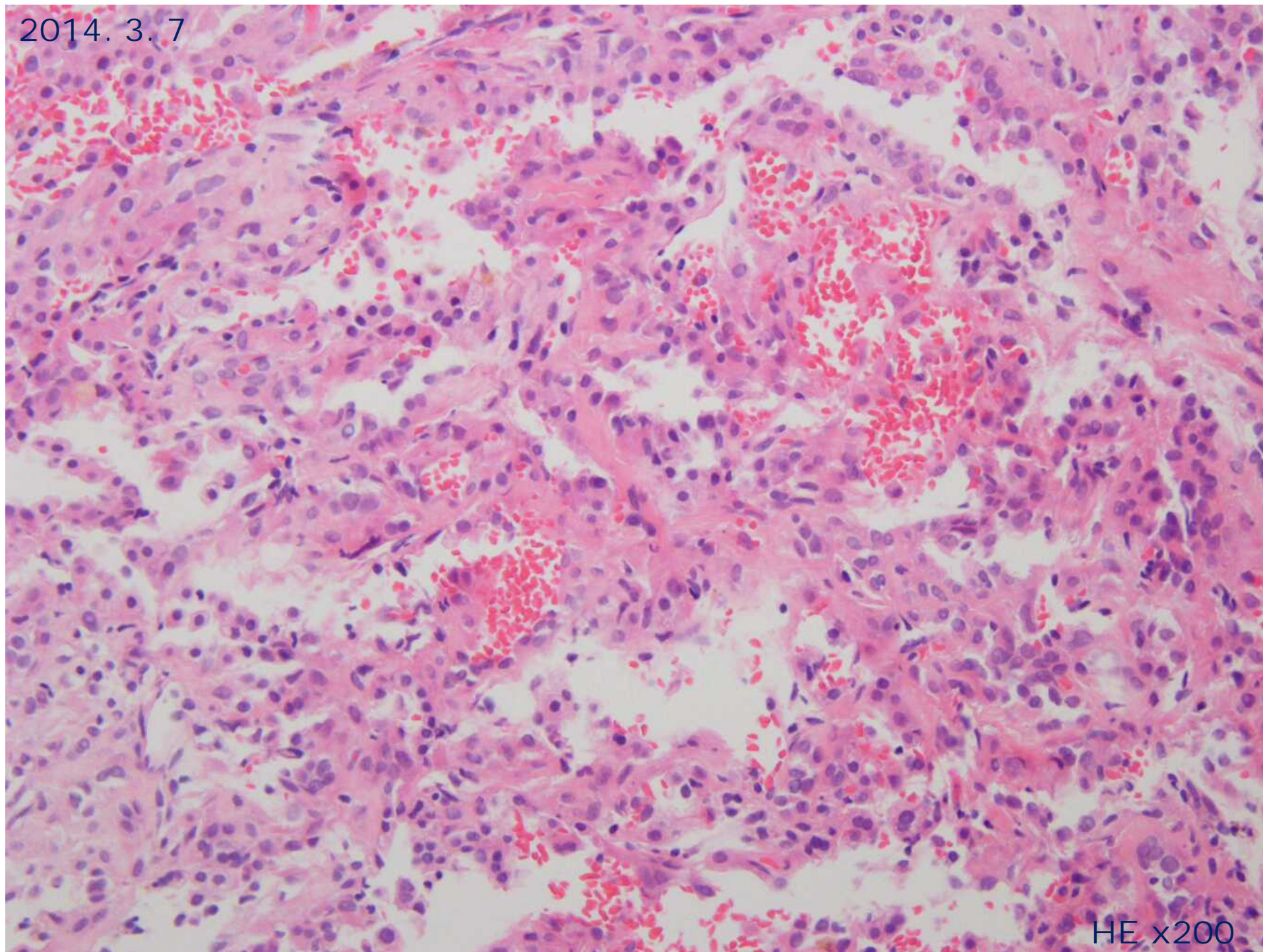
200 Pt

2014. 3. 7



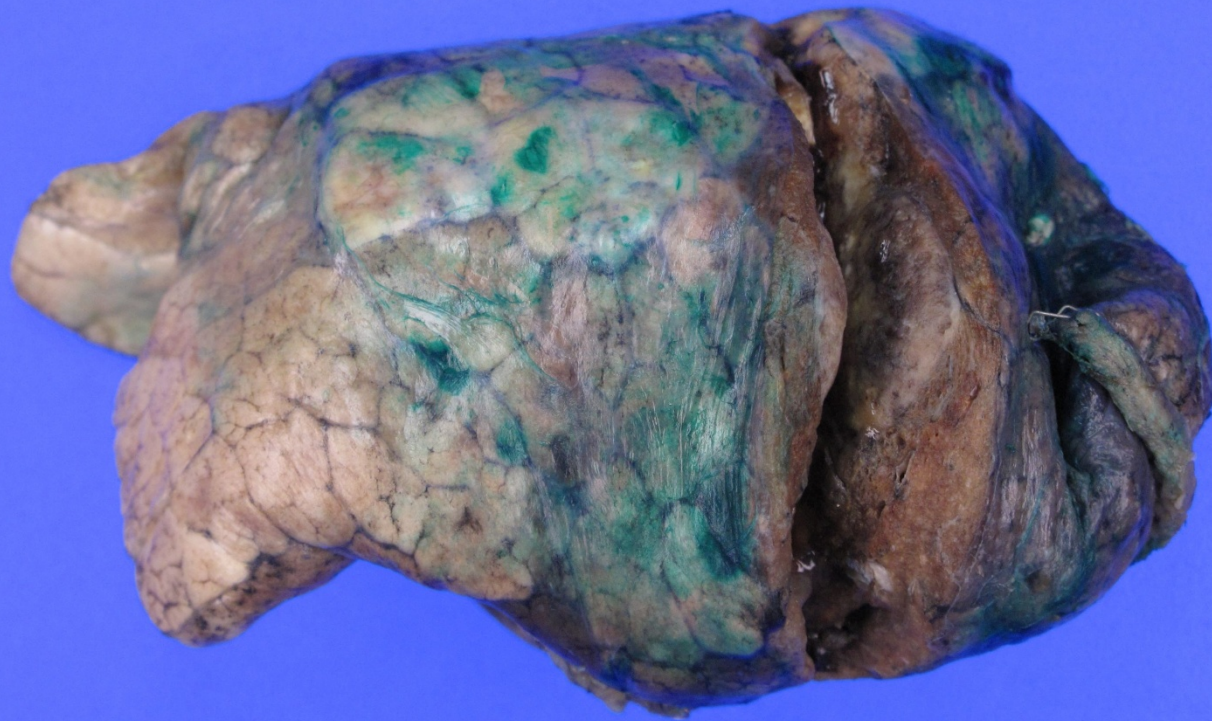
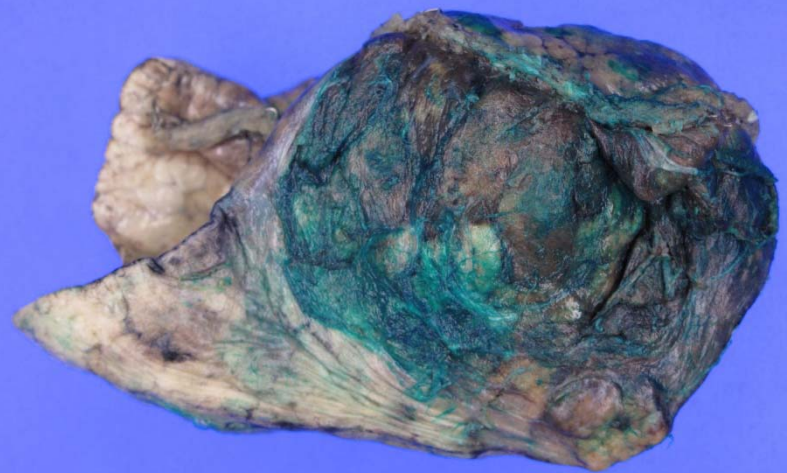
HE x40

2014. 3. 7

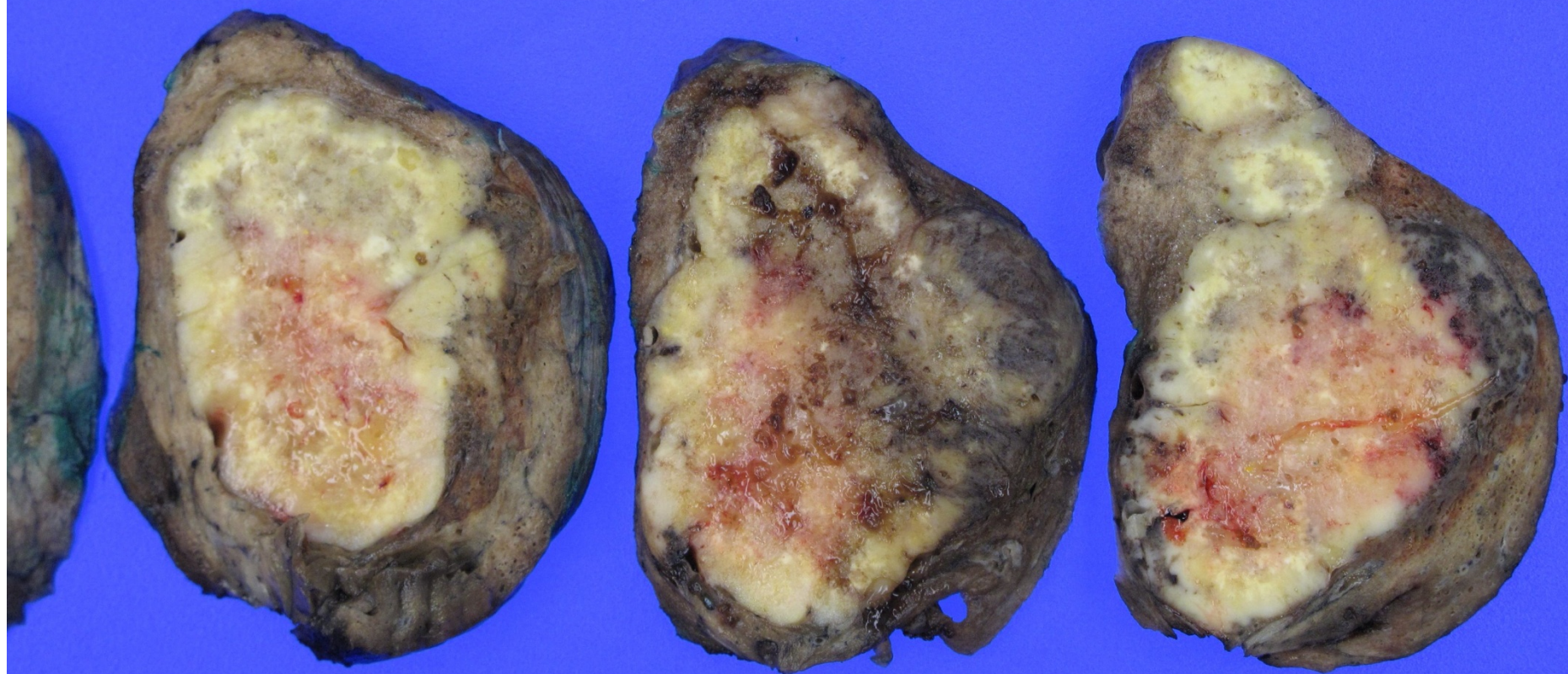


HE x200

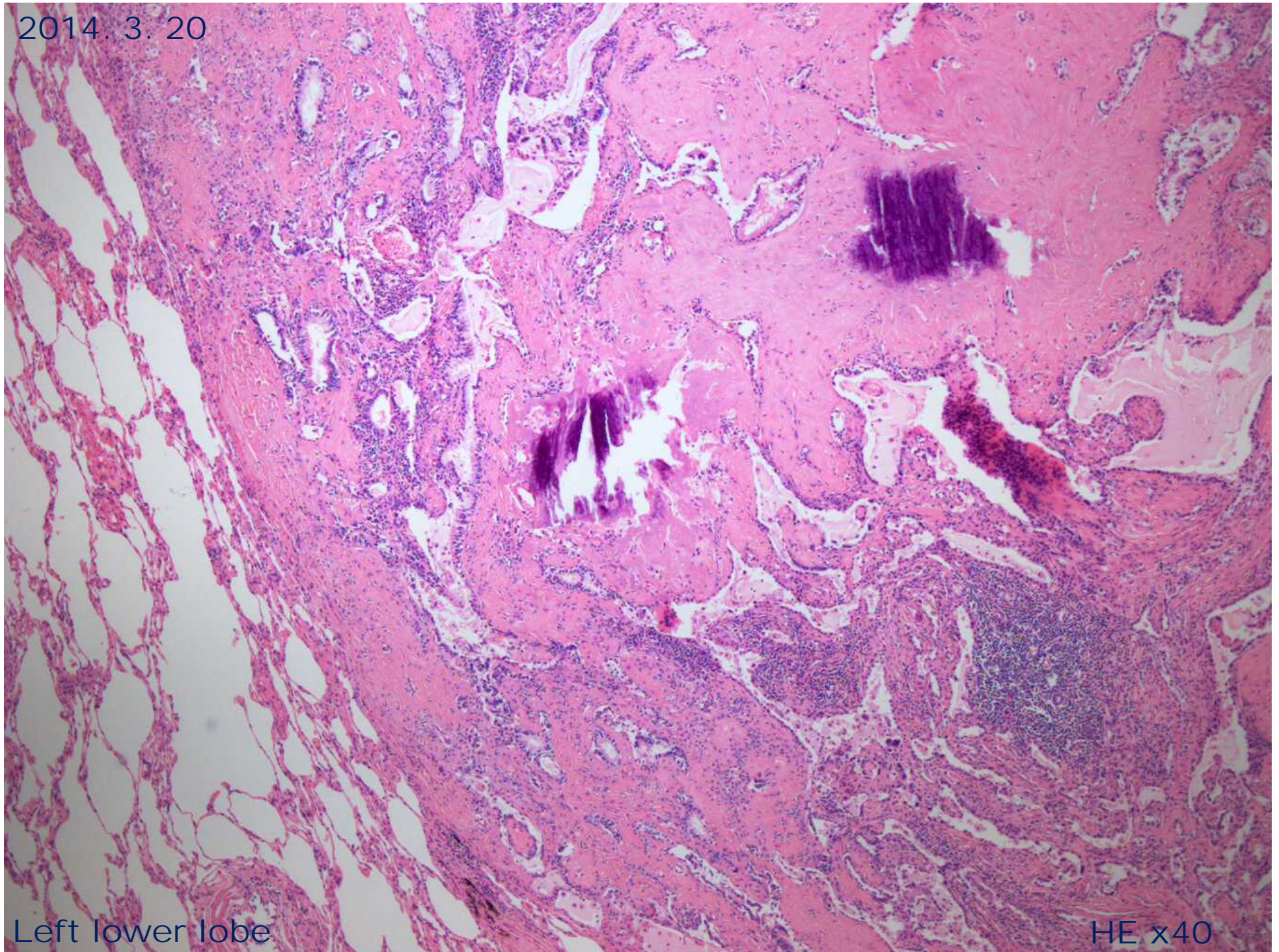
2014. 3. 20



2014. 3. 20



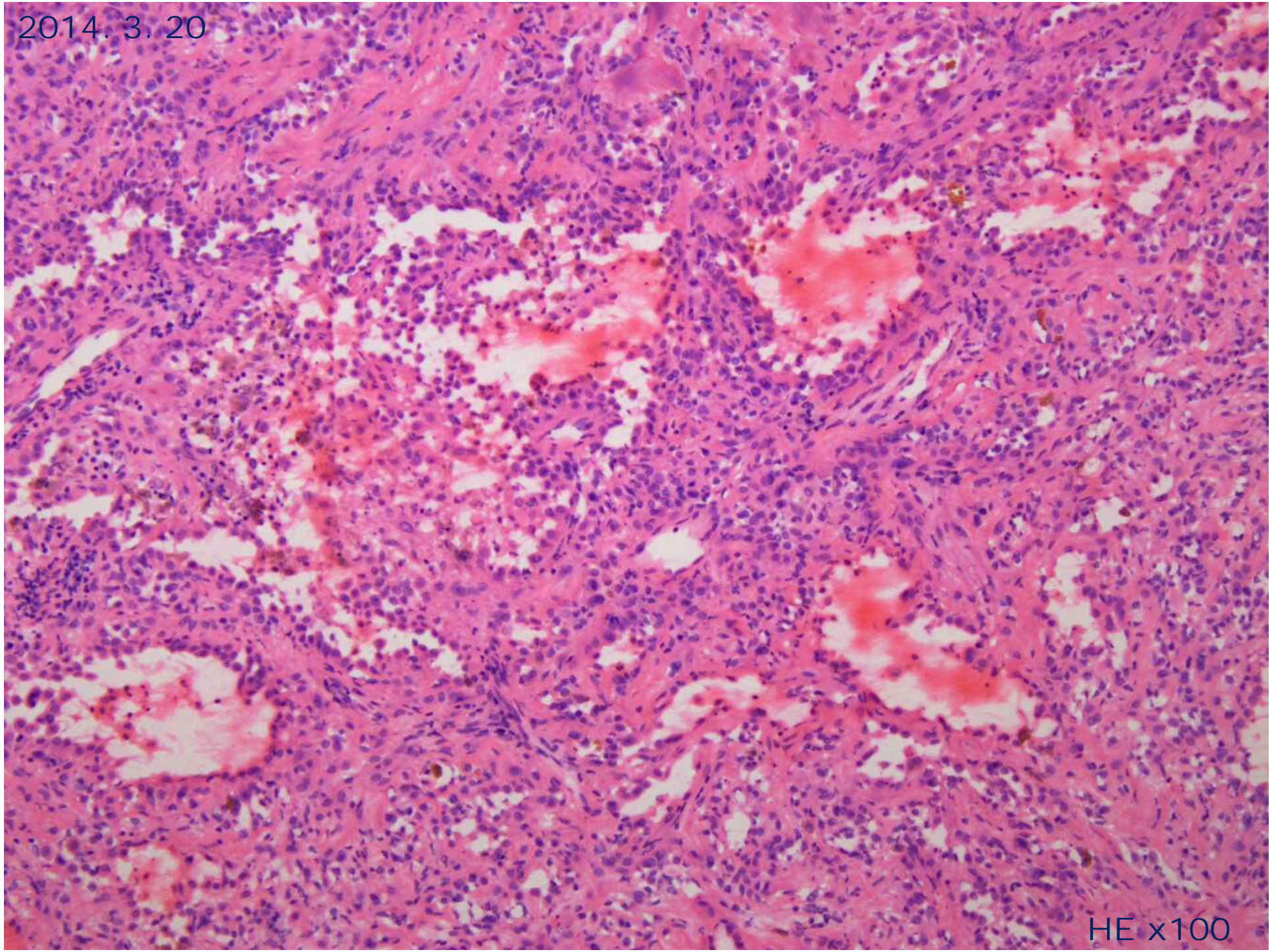
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Left lower lobe

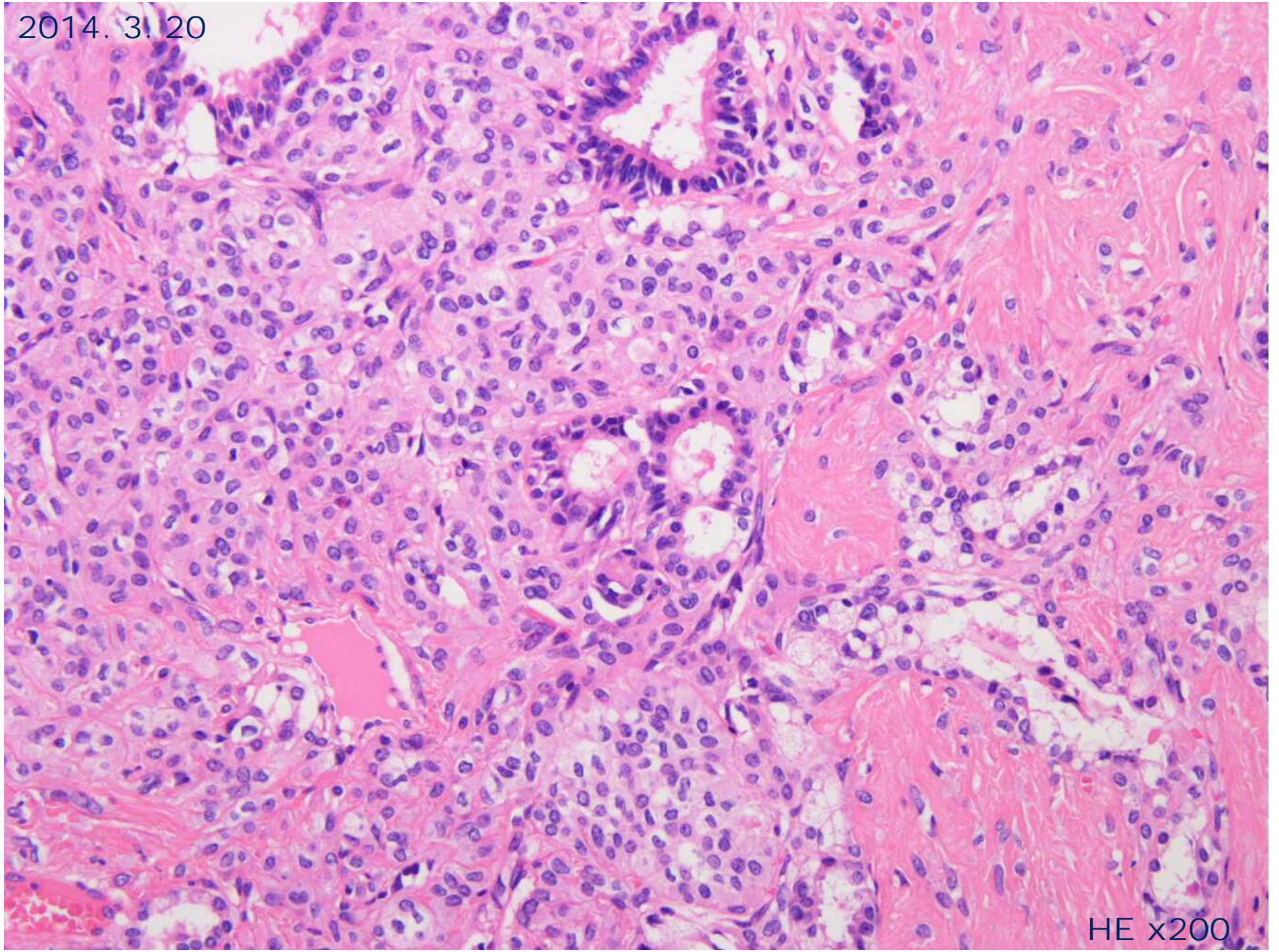
HE x40

2014. 3. 20



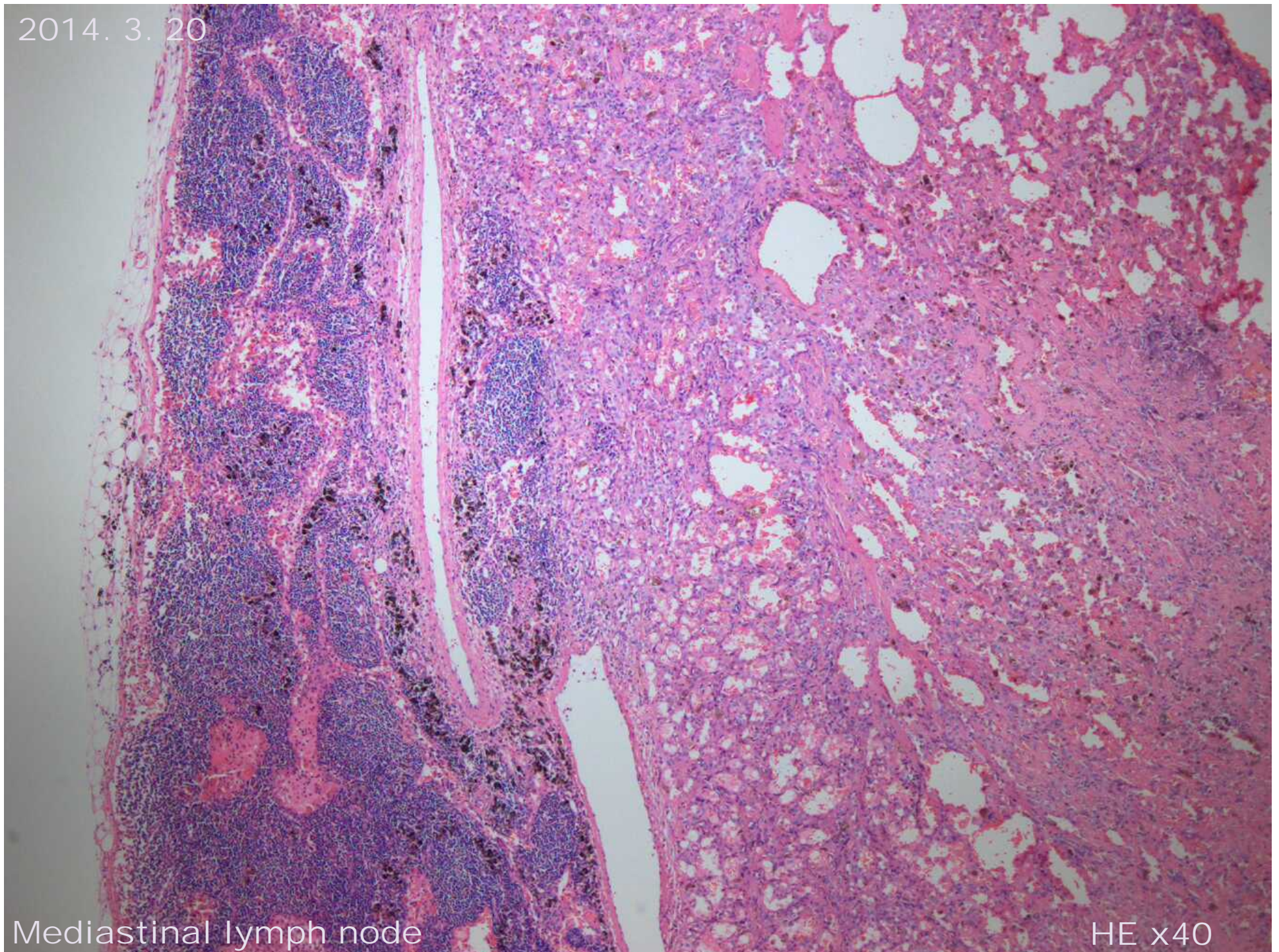
HE x100

2014. 3. 20



HE x200

2014. 3. 20



Mediastinal lymph node

HE x40

Immunohistochemical stains

IHC	Reaction
TTF-1	Diffuse
EMA	Diffuse
CK 7	Focal
CK20	-
CD31	-
CD34	-
HMB-45	-
ER	Focal weak
PR	Focal weak

Diagnosis

**Sclerosing hemangioma of lung
with lymph node metastasis**

Sclerosing hemangioma of lung



Introduction

❖ History

- 1956, First report of sclerosing hemangioma (SH) of the lung by Liebow
- Similar histologic features with SH of the skin
- Mesenchymal? Mesothelial? Neuroendocrine?
- 1972, Epithelial characteristic in EM proposed by Hill
- 1981, Tumor-like lesion by WHO
- 1999, Miscellaneous tumors by WHO classification

Introduction

❖ **Uncertain characteristics :**

- Morphologically polymorphic tumor with various cytohistologic patterns: solid, papillary, angiomatous (hemorrhagic), sclerotic
- Various cell components with different ultrastructural features and immunophenotypes
- Controversy in origins; epithelial differentiation cf. endothelial, mesothelial, mesenchymal, NE
- Truly neoplastic?

Clinical features

❖ **Epidemiology**

- F:M=7:1~5:1
- Far east
- Middle-aged (11-83 years)

❖ **Presentation**

- Asymptomatic, hemoptysis, persistent cough, chest pain
- LN metastasis, recurrence after surgical excision
- Multiple tumors in 3-4% of cases
- Combination with other tumors (carcinoid, neuroendocrine carcinoma, adenomatous hyperplasia)

Radiologic features

❖ **Chest radiographs**

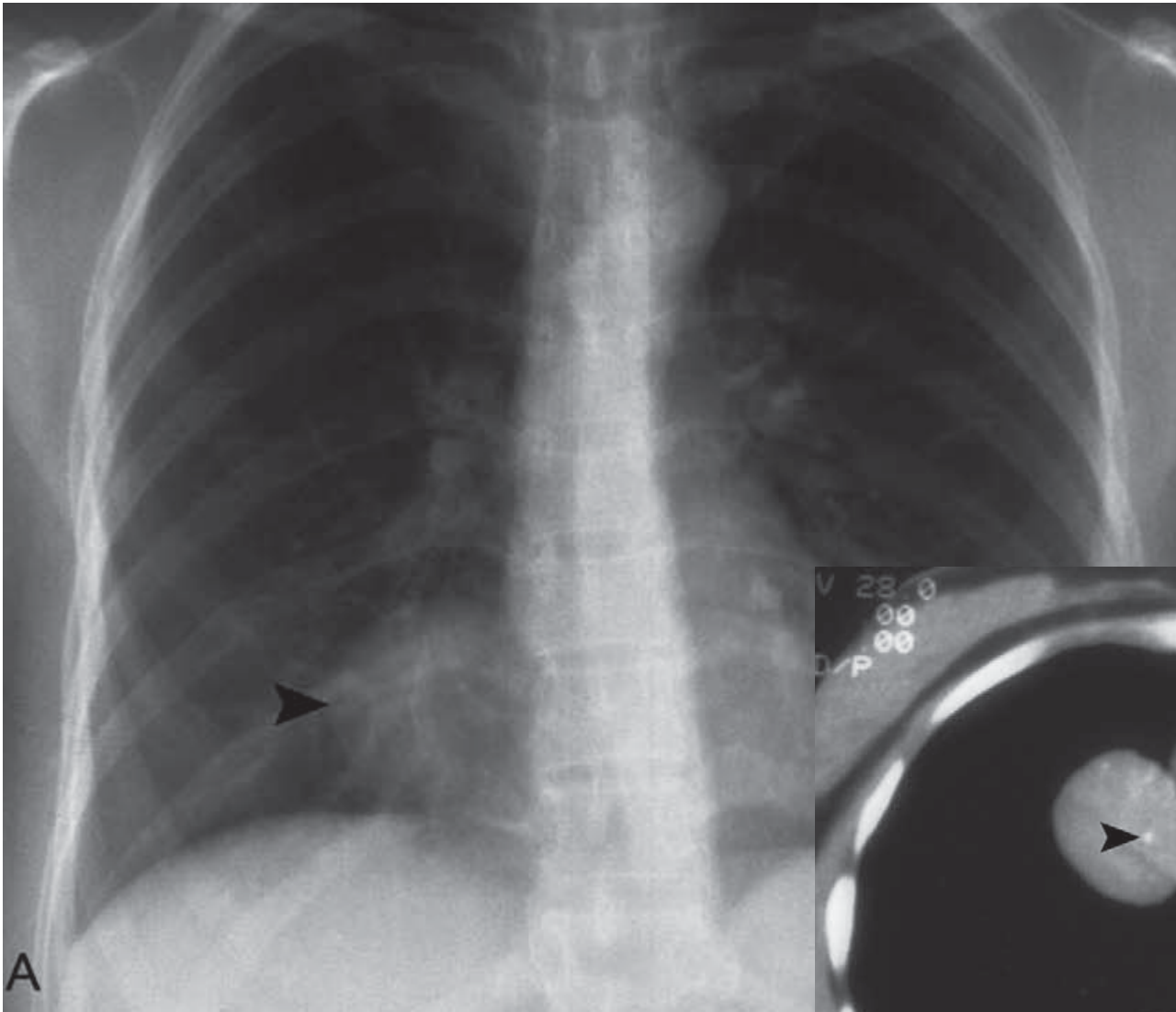
- A peripheral, solitary, well-defined, homogeneous nodule or mass without predilection for a particular lobe
- (-) cavitation

❖ **CT**

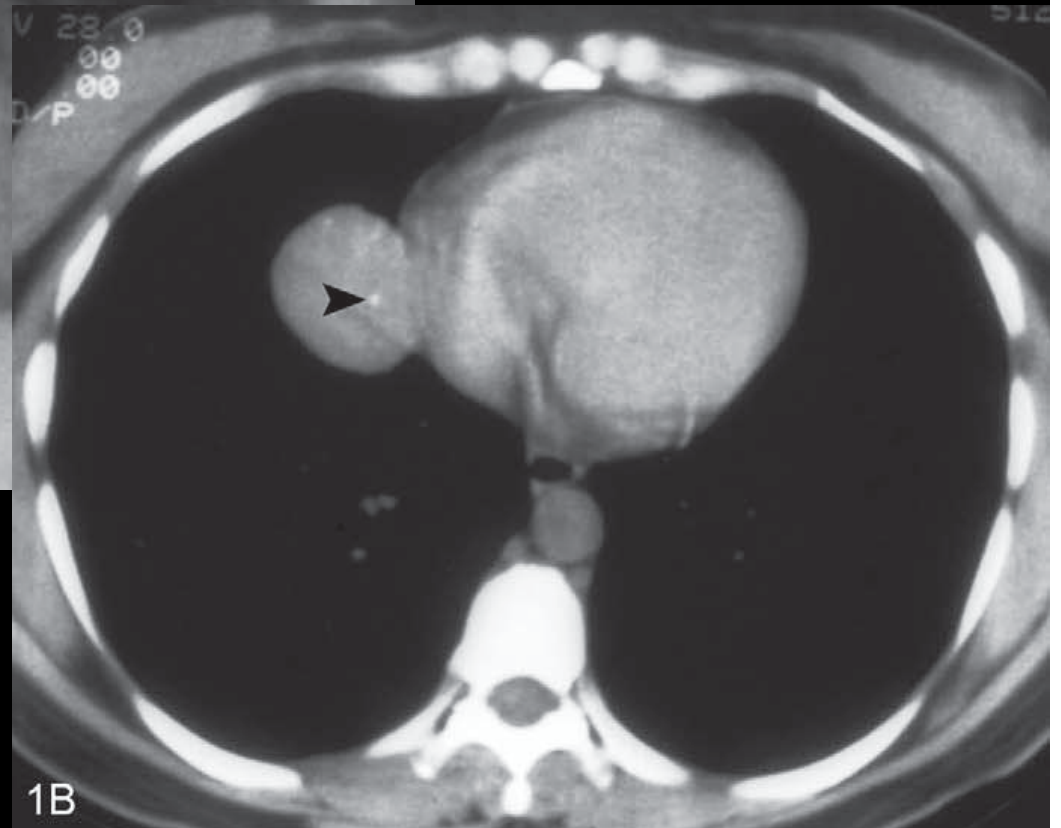
- A round to oval nodule or mass with smooth margins that enhances following injection of contrast
- (+) Calcification in 1/3
- A benign process

❖ **PET using 18F-FDG**

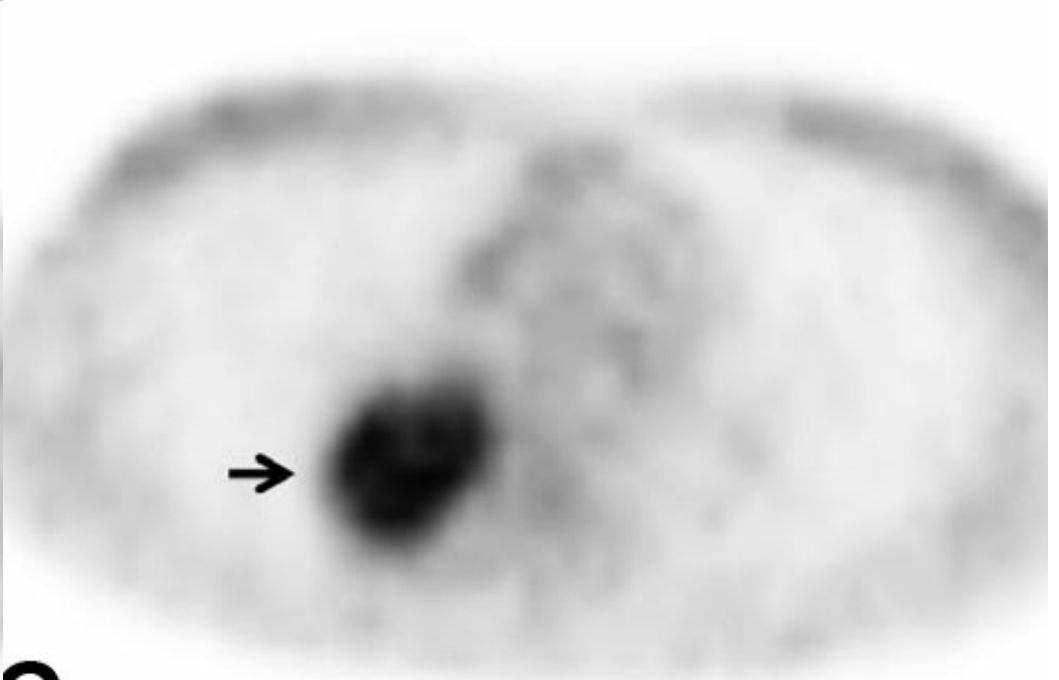
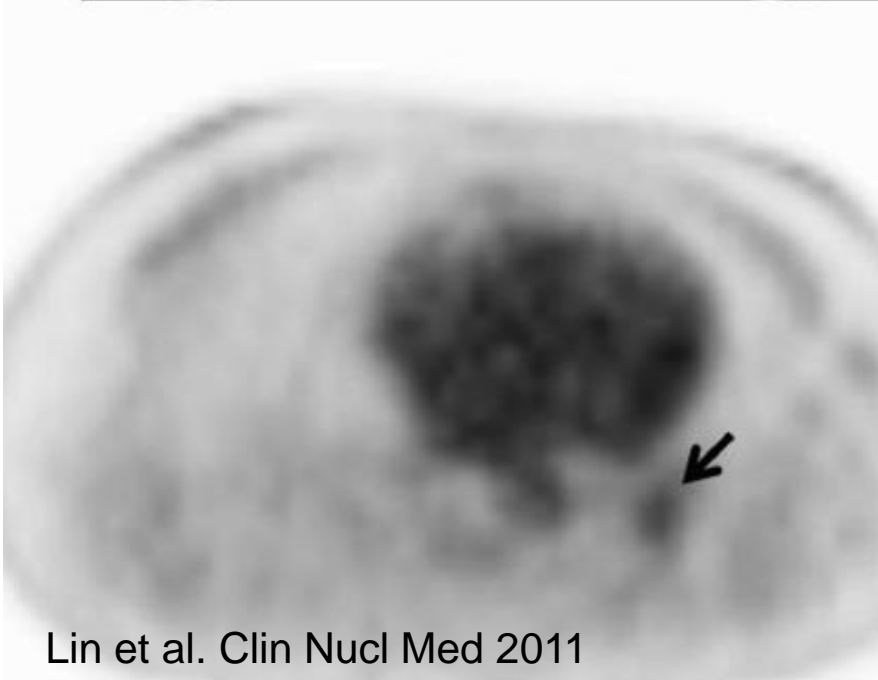
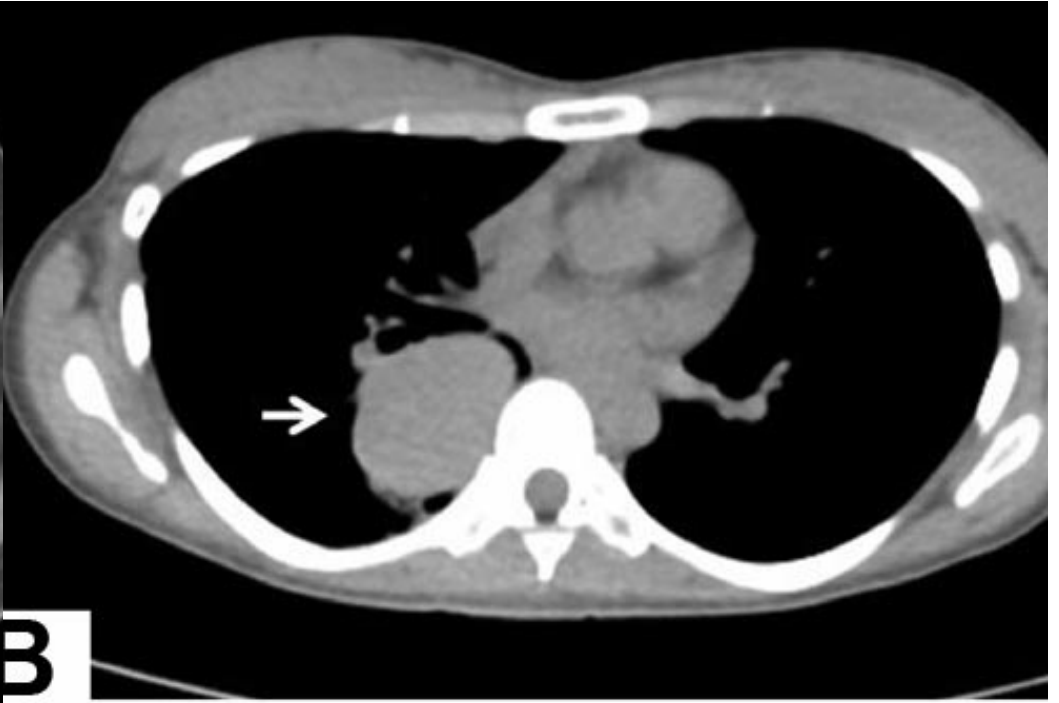
- Increased uptake in majority of SH
- Varying intensity of FDG uptake: tumor size or histology



A



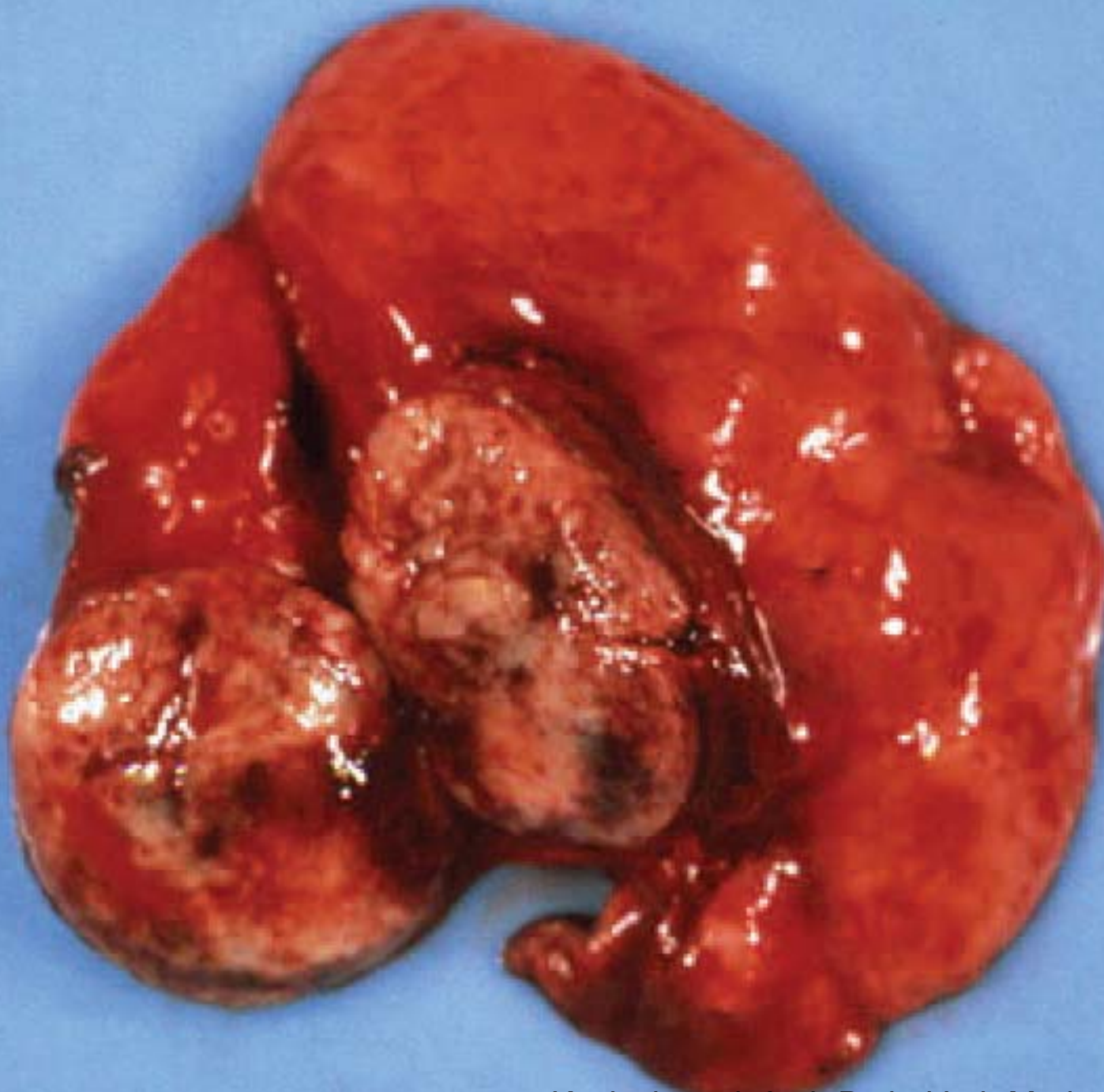
1B



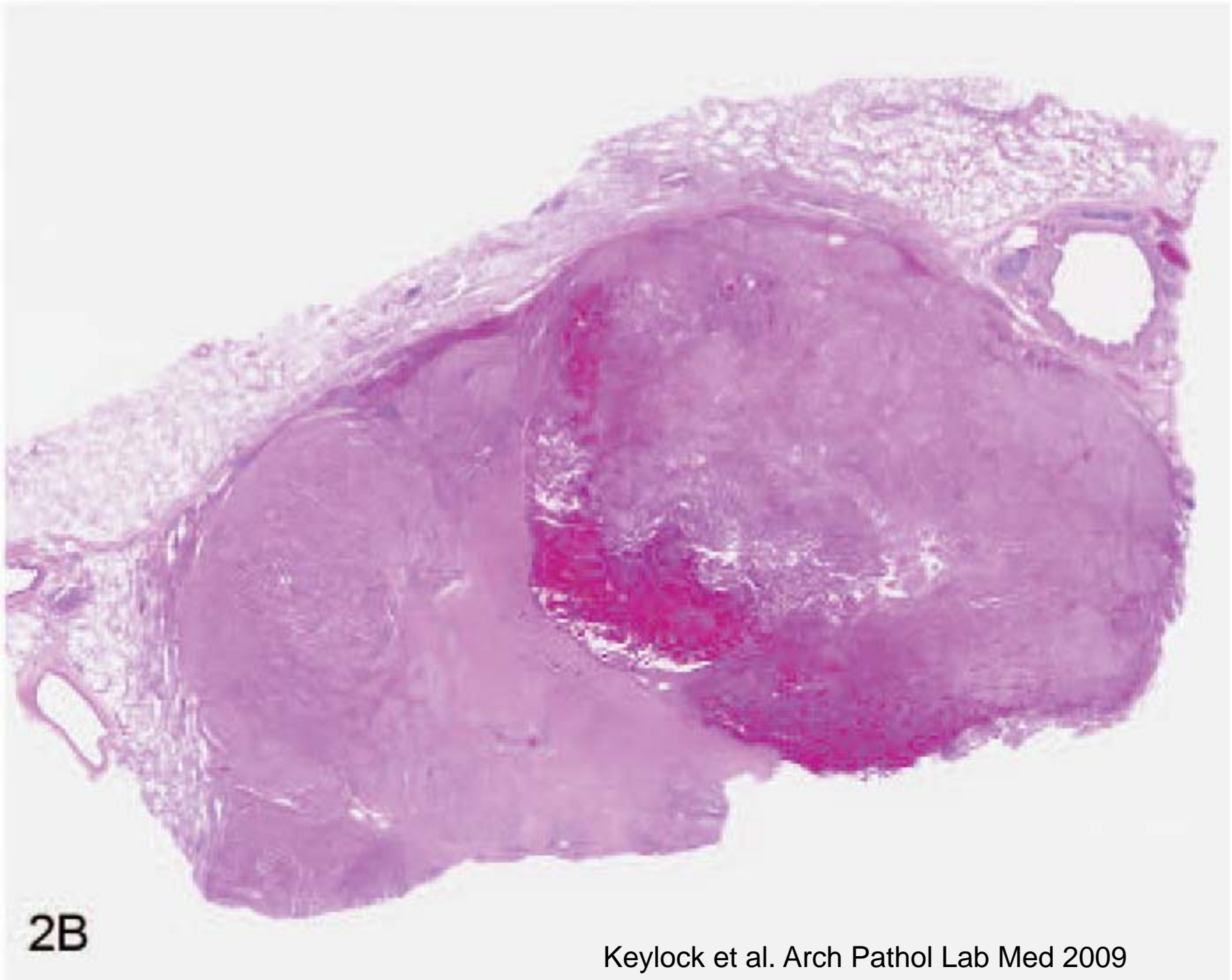
Pathology

❖ **Gross pathology**

- Well circumscribed, 0.3-8cm
- Solitary in most cases, cf. multifocality, bilateral involvement
- Periphery of lung parenchyma, cf. subpleura, centrally, intramediastinal, endobronchial polypoid
- Tan to gray, solid and firm with some cystic change, and possible focal to diffuse hemorrhage



Keylock et al. Arch Pathol Lab Med 2009



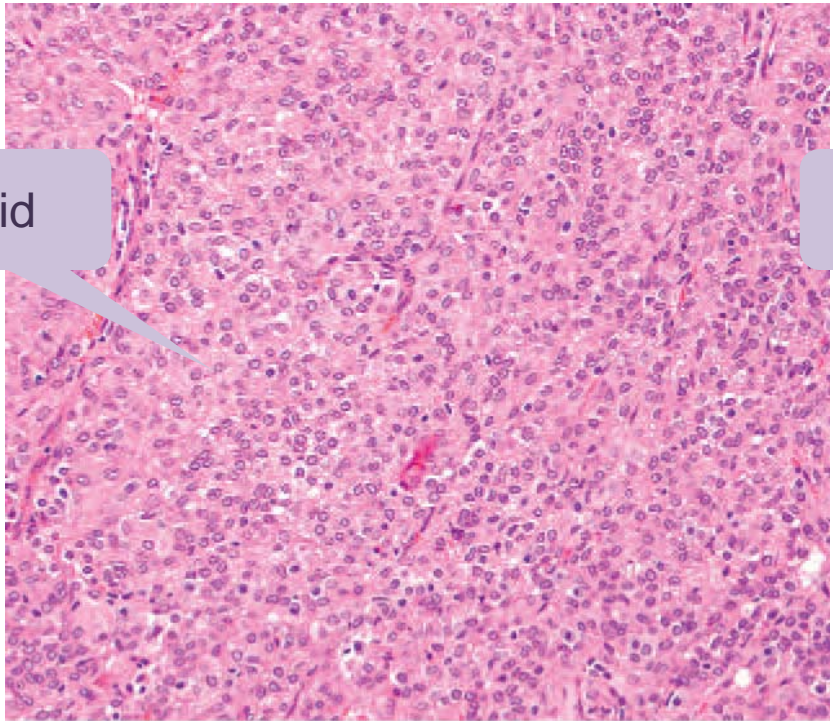
2B

Keylock et al. Arch Pathol Lab Med 2009

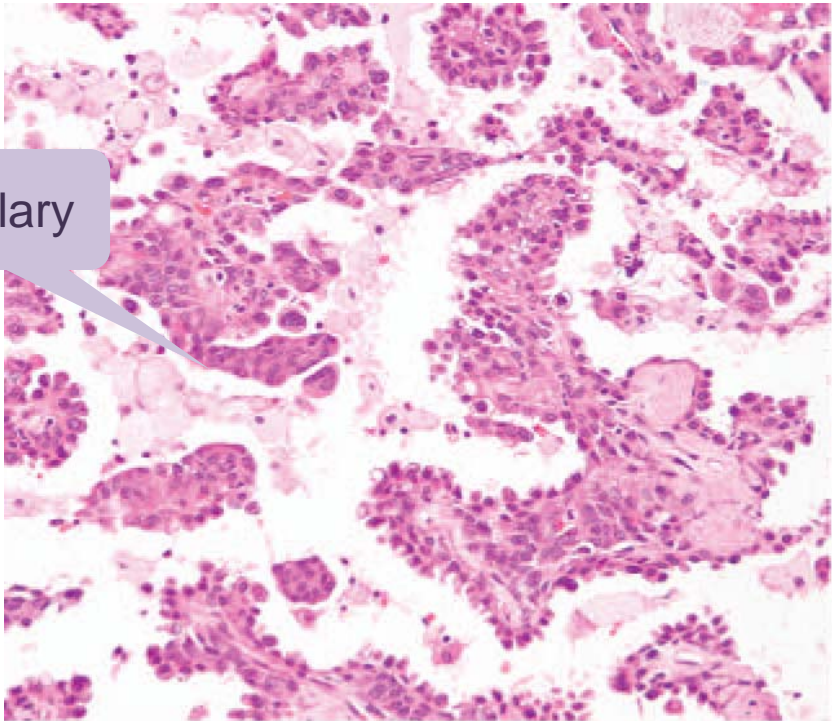
Pathology

❖ Histology

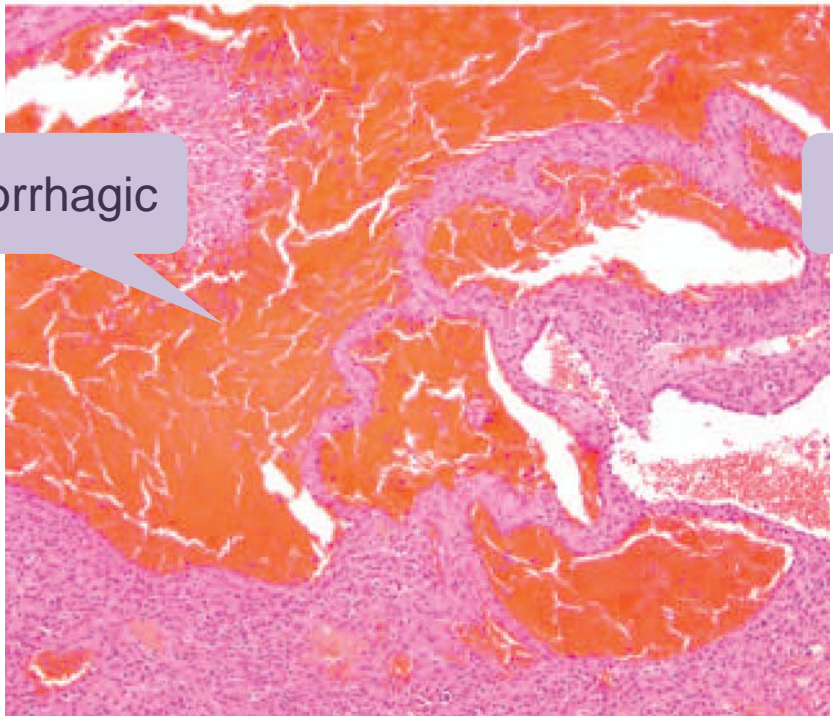
- Pure or mixed (solid, papillary, hemorrhagic cystic, sclerotic)
- Two distinct cellular components
 - ✓ Round or polygonal or stroma cells: abundant clear to eosinophilic cytoplasm, cellular atypia, nuclear pleomorphism with clumped nuclear chromatin and prominent nucleoli, rare mitotic activity
 - ✓ Cuboidal or surface cells: lining papillary structure, small, with bland nuclei and dense chromatin



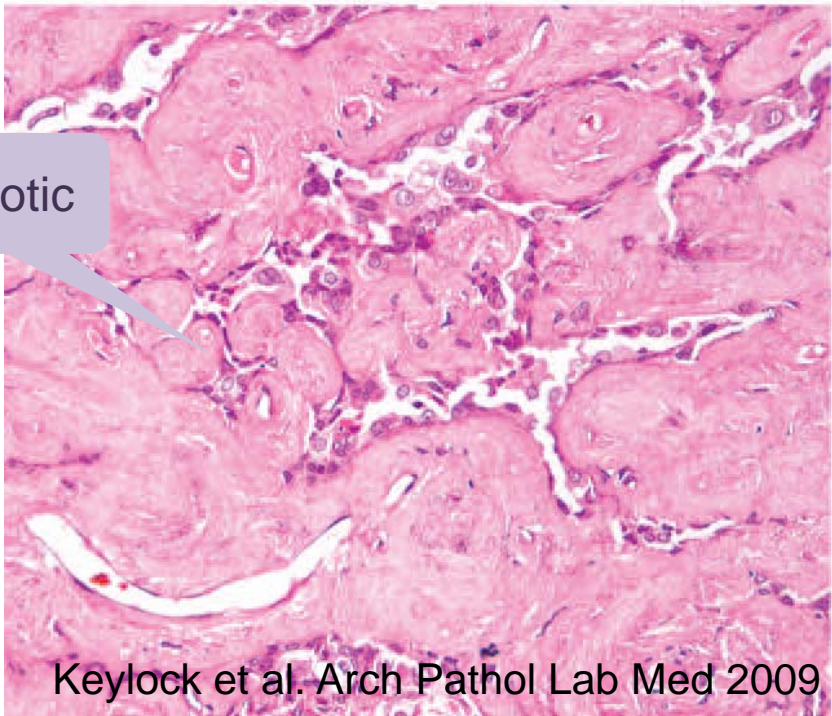
solid



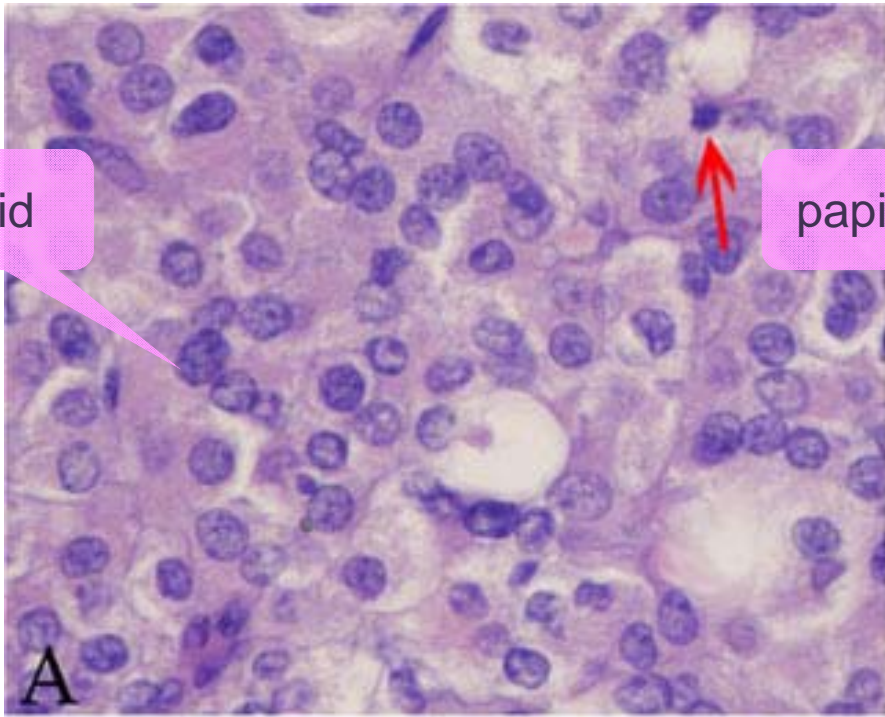
papillary



hemorrhagic

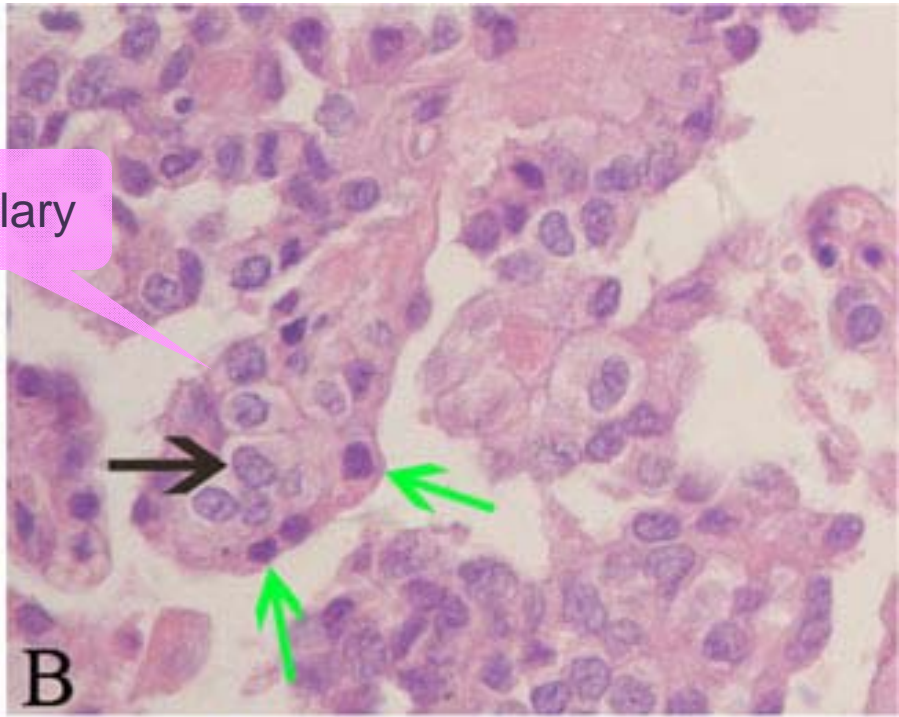


sclerotic



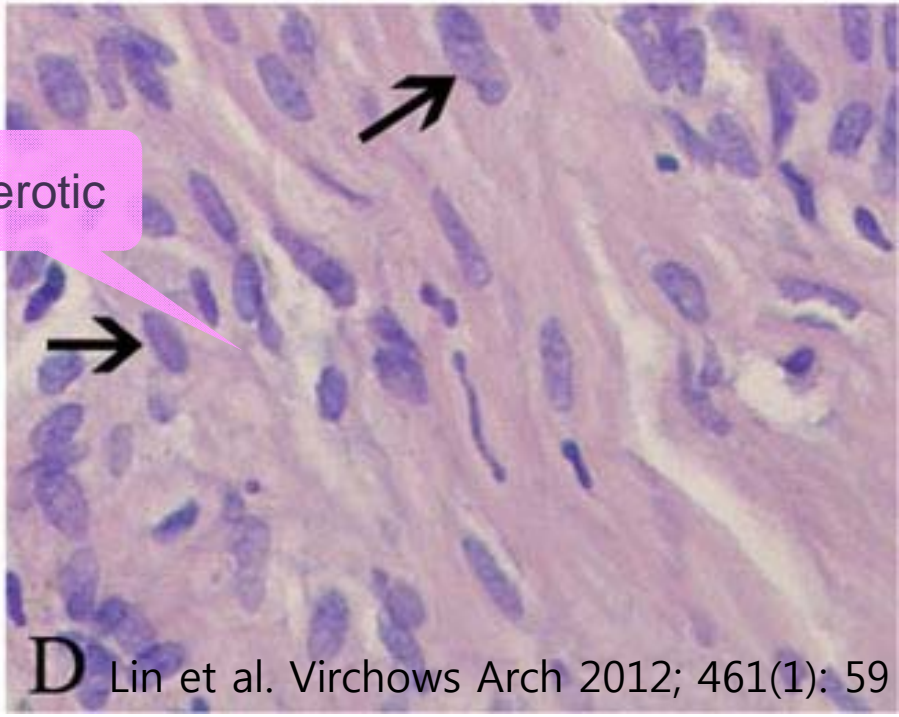
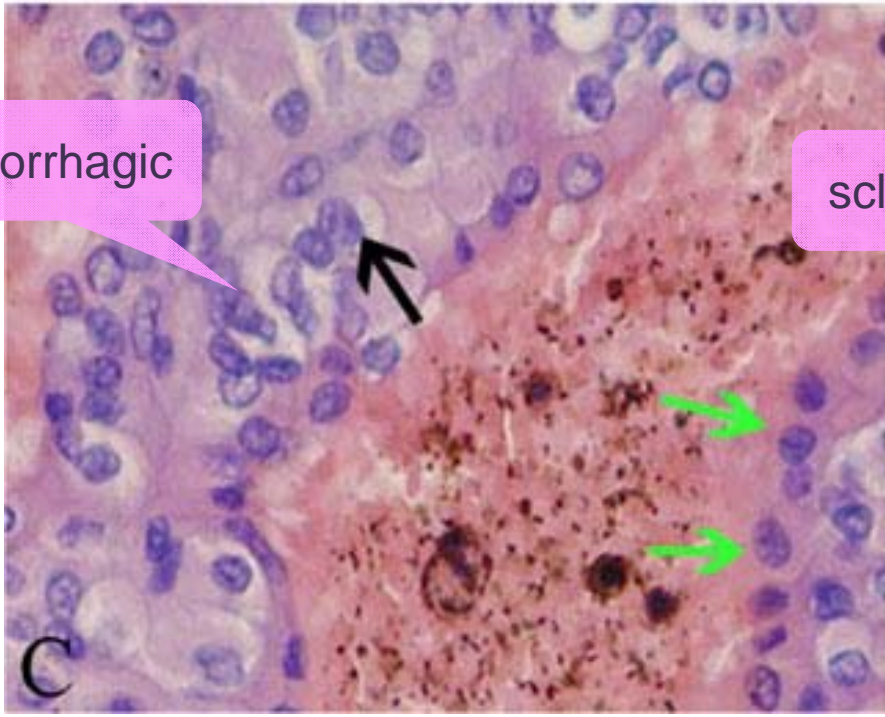
solid

papillary



hemorrhagic

sclerotic



Pathology

❖ Cytology

- Depending on the tumor pattern in the sampled area
 - ✓ Papillary structures, blood spaces, sclerotic area, or a mixture
 - ✓ Round cells: amphophilic cytoplasm with round to oval nuclei and dispersed chromatin
 - ✓ Surface cells: eosinophilic cytoplasm and small round nuclei
 - ✓ Foamy macrophages, hemosiderin-laden macrophages, calcifications, and orange lamellar concretions
- DDx: well-differentiated adenocarcinoma, well-differentiated neuroendocrine carcinoma (carcinoid tumor)

Pathology

❖ Immunohistochemistry

- (+) EMA and TTF-1 in both round cells and surface cells
- (-) factor VIII, S100, SMA, calretinin, CK 5/6, synaptophysin, chromogranin
 - ✓ cf. infrequent and focal expression for NE markers
- Keratin
 - ✓ (-) pan-keratin, occasionally focally (+) CK7, CAM5.2 in round cells, diffusely (+) in surface cells
- Sex hormone receptor
 - ✓ (-) ER & PR in surface cells, (+) PR up to 60% (cf. ER <10%)
- Pneumocyte marker other than TTF-1
 - ✓ Surfactant proteins A & B and Clara cell protein in surface cells

Immunohistochemical studies of SH

Study	EMA		Pan-K		TTF-1		Surf		Fac VIII		CK903		CK7	
	SC	RC	SC	RC	SC	RC	SC	RC	SC	RC	SC	RC	SC	RC
Yoo et al. (2005) ³⁵	+	+	+	+	+	+	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Iyoda et al (2004) ¹⁶	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Kim et al. (2004) ¹⁷	+	+	+	-	+	+	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Nicholson et al. (2002) ³⁶	+	+	+	-	+	+	-	-	n/a	n/a	n/a	n/a	n/a	n/a
Illei et al. (2001) ³⁷	+	+	n/a	n/a	+	+	+	±	n/a	n/a	n/a	n/a	n/a	n/a
Devouassoux- Shishehboran et al (2000) ¹⁰	+	+	+	-	+	+	+	-	-	-	-	-	+	±
Chan et al. (2000) ³⁸	+	+	+	-	+	+	+	-	n/a	n/a	n/a	n/a	n/a	n/a
Fukayama et al (1988) ²⁰	+	+	+	-	n/a	n/a	n/a	n/a	-	-	n/a	n/a	n/a	n/a
Leong et al. (1995) ¹¹	+	+	+	±	n/a	n/a	+	-	-	-	n/a	n/a	n/a	n/a
Nagata et al. (1987) ¹²	+	+	n/a	n/a	n/a	n/a	+	±	n/a	n/a	n/a	n/a	n/a	n/a
Haimoto et al. (1985) ³⁹	+	+	+	±	n/a	n/a	n/a	n/a	-	-	n/a	n/a	n/a	n/a
Nagata et al. (1985) ⁴⁰	n/a	n/a	n/a	n/a	n/a	n/a	+	±	-	-	n/a	n/a	n/a	n/a

Pan-K indicates pan-keratin; Surf, surfactant apoprotein; Fac VIII, Factor VIII; CAM, 5.2, low molecular SC, surface cells; RC, round cells; n/a, not applicable.

Pathology

❖ **Monoclonality**

- Separated Cells by microdissection → DNA extraction → clonal analysis
- Round cells and cuboidal cells derived from the same cells
- SH is caused by monoclonal expansion of cells

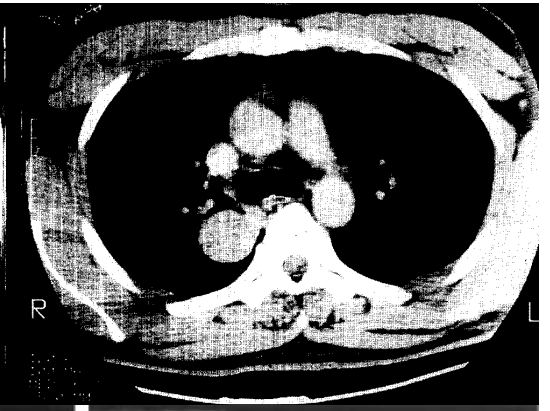
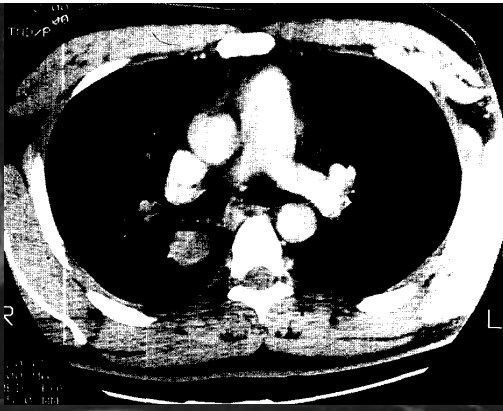
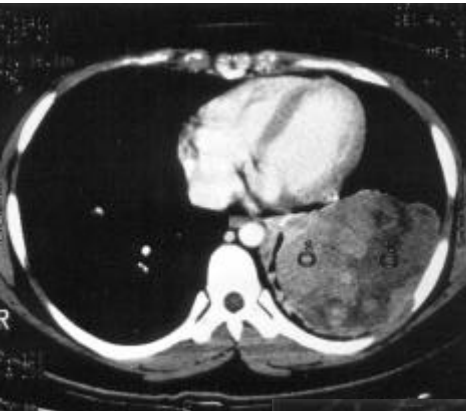
Treatment

❖ **Operation**

- Types of operation
 - ✓ Enucleation, wedge resection, lobectomy
- No adjuvant therapy

❖ **Prognosis**

- No reports of tumor-related mortality



Year, author	nation	Sex/age	Sx	Site	Size (cm)	Dx and Tx	IHC	Node (cm)	f/u
2013, Kita	Japan*	F/38	Asx	LLL(S6)	3.9	Segmentectomy of LS6 (frozen: low-grade malignancy)		Interlobar	
2009, Vaideeswar	India	M/23	hemoptysis	RUL(p)	9x7x5 3 setellite nodules	(-)B-cytology Bx: R/O bronchiolo-alveolar tumor Lobectomy	No IHC	Hilar	NA
2007, Jiang	China*								
2005, Katakura	Japan	M/32	ASx	LLL(S6)	3	(-)Broncho Bx Lobectomy (frozen: epithelial tumor)	(+)EMA, CAM5.2, CK7, TTF-1 (-)factorVIII, CD34	No.7	18 m
2004, Kim	Korea	F/37		LLL	2	Lobectomy		Peribronchial (focus: 0.1cm)	5.7 y
2003, Miyagawa-Hayashino	Japan	F/10 F/45 M/45 F/56	Flulike Flulike Asx Asx	RML RUL LLL LLL	4.7 2.5 3.7 1.5	Lobectomy CTx after op (Dx as ADC)	-	3 hilar 1 1 1 (0.5-1.2cm)	4.7 y (2.3-10)
2003, Chan	Canada	M/19	Chest pain, productive cough	LUL, lingular division	3	(-)B-brunshing FNA:possibly ADC Resection of lingular div (frozen: neg)	(+)CK(AE1/3, CAM5.2), EMA, vimentin, progesterone, PAP, TTF-1 (-)S100, CEA, CD34	1 intraparenchymal & 1 interlobar	1 y
2003, Kim	Korea	F/19	cough	LLL	12x9.7x7.8 2 daughter nodules	Lobectomy & CTx (EC)	(+)pankeratin, EMA, TTF-1, CK, vimentin, PR (-)synaptophysin, chromogranin, S100, NSE, SMA	5 Hilar, 2 interlobar, 4 intrapulmonary (-2 cm)	2 y

LN involvement in sclerosing hemangioma of lung

❖ **19 cases**

- 8 Japan, 3 Korea, 3 China (1HK), 2 UK, 1 India, 1 US, 1 Canada

❖ **Age and Sex**

- 10-67 yr, F:M=9:7

❖ **Number, size, and site of involved LN**

- 1-11, 0.5-2 cm, 3 cases with mediastinal LN metastasis

❖ **Diagnosis**

- 1 case: diagnosed in needle biopsy
- 4 cases: R/O malignancy in needle biopsy or FNA

❖ **Treatment and Prognosis**

- 2 cases: postoperative chemotherapy
- During 1-10 y, 1 case with recurrence, no recurrent LN metastasis

Summary

- ❖ **SH is a rare benign pulmonary tumor with significant female predilection**
- ❖ **A misnomer**
- ❖ **An indolent behavior with no reported mortality in the literature**

List of proposed names for SH

Author	Proposed name
Liebow and Hubbell ¹	SH
Dubilier et al (1968) ⁴¹	Histiocytoma (Fibrous xanthoma of the lung)
Kennedy ³⁰	Papillary pneumocytoma
Chan et al. ⁹	Benign sclerosing pneumocytoma
Ng and Ma ¹⁵	Alveolar mixed tumor
Katzenstein et al ³¹	Benign epithelial mesothelioma
Fukayama et al (1988) ²⁰	Sclerotic hemorrhagic alveolar-cell tumor of the lung
Xu at al ³³	Benign neuroendocrine tumor of the lung