Interesting cases of pulmonary hypertension

Seol Sang-Hoon

Inje University College of Medicine,
Haeundae Paik Hospital, Busan, Korea

1. Fatal acute right heart failure
with elevated D-dimer in gastric cancer

2. Chronic ThromboEmbolic
Pulmonary Hypertension (CTEPH)

Case 1

46-year old female

- *C.C.: Dyspnea (NYHA IV)*
- *Present Illness : the patient was brought to the emergency room following a 1 week period of progressively worsening shortness of breath.*
- *Past Hx: gastric cancer – operation – 6 months ago*

  adjuvant chemotherapy – not done
- *V/S : 100/60 mmHg-116/min-28/min-36.5 ℃*

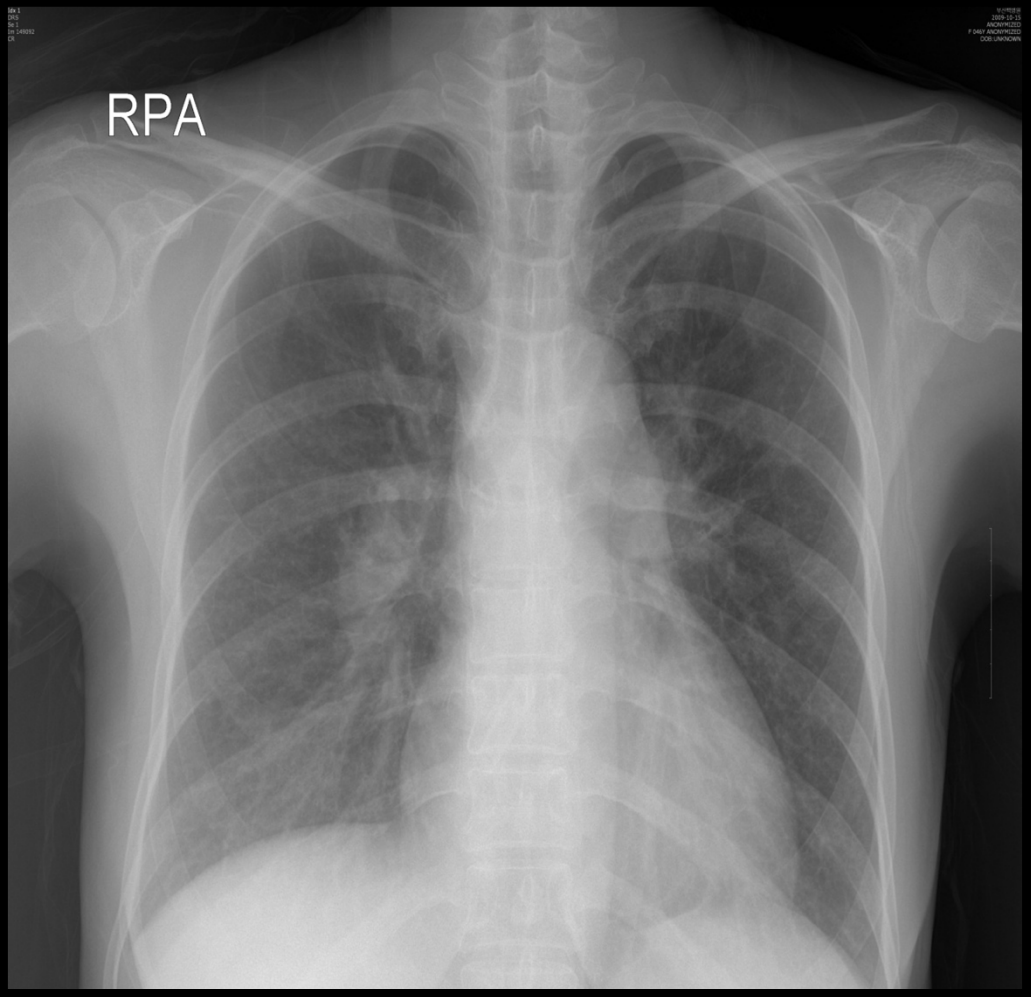
Case 1

Initial Lab

- *CBC*
  - *WBC 6410 Hb 9.6 g/dL, Hct 28%, Platelet: 111K*
- *Pro-BNP: 4263 pg/mL*
- *D- dimer : 19.1 ug/mL (normal <1.3)*
- *FDP : 30.9 ug/mL (normal <5.0)*
- *PT /PTT : WNL*
- *ABGA (room air)*
  - *pH 7.47, Actual bicarbonate 21 mmol/L*
  - *PCO_2 29 mmHg, PO_2 59 mmHg, O_2 sat 89 %*
- *ECG : sinus tachycardia*

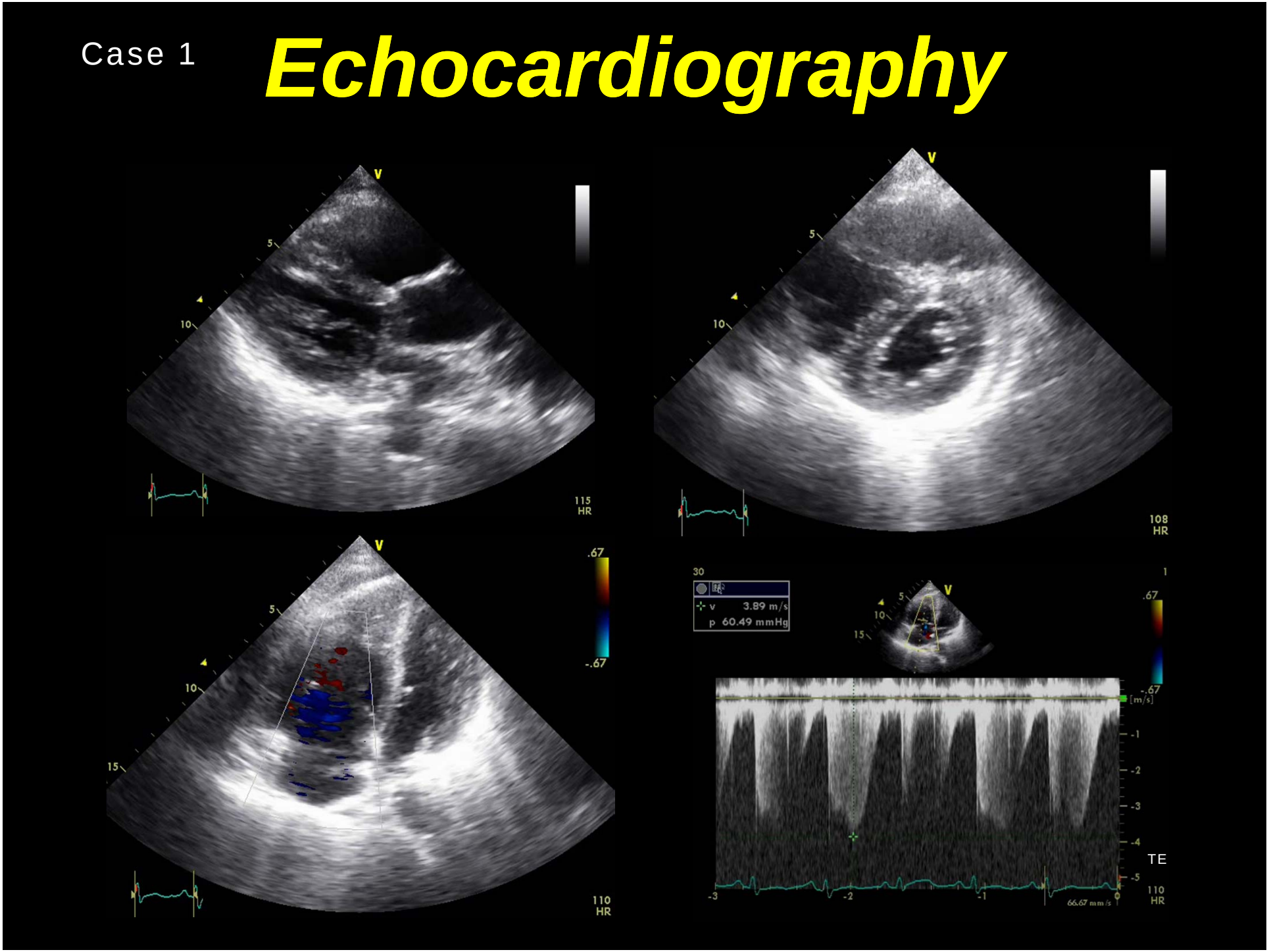
Case 1

Chest X-ray



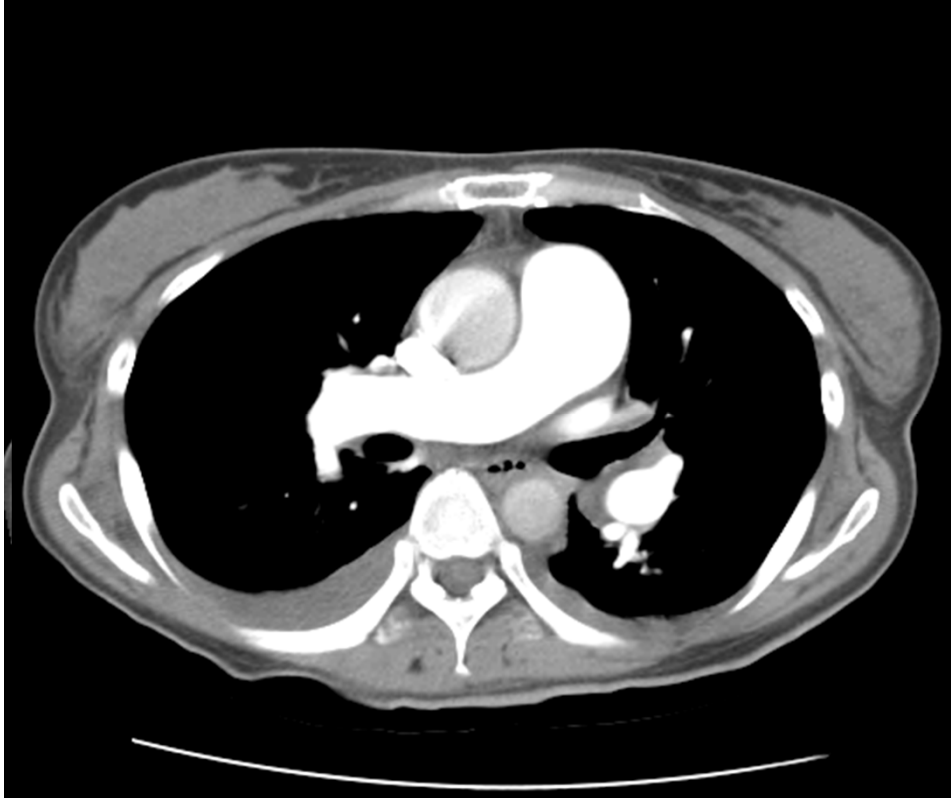
Case 1

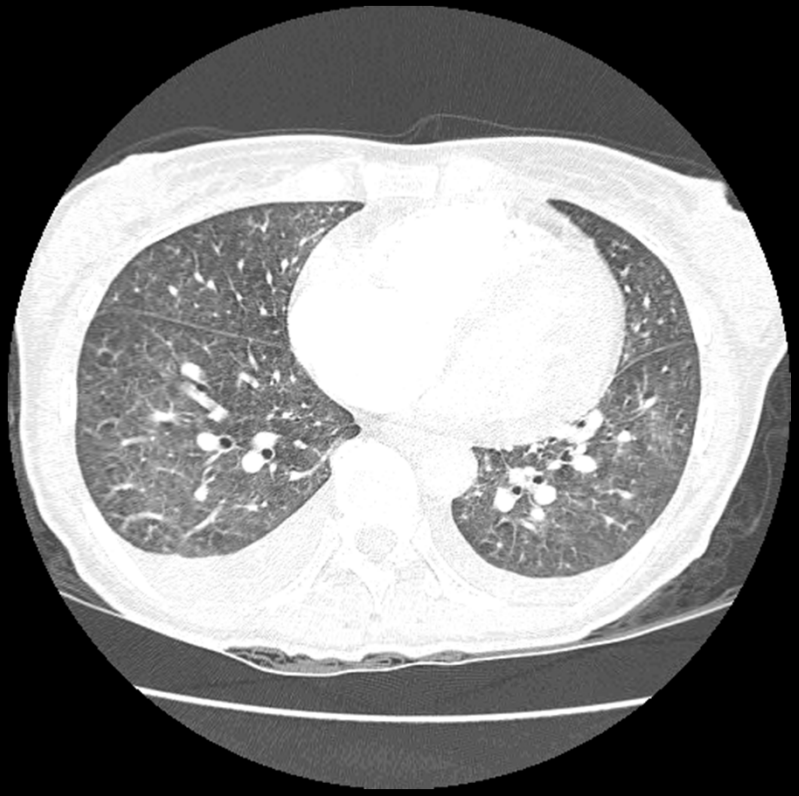
Echocardiography



Case 1

Chest CT





Case 1

Progress Note

- *She rapidly developed hypoxemic respiratory failure and desaturated 80% on 10 liters of oxygen.*
- *The patient`s condition progressively worsened and took a rapid downhill course, despite aggressive hemodynamic support.*

Progress Note

- Finally, the patient developed an intractable respiratory failure and died 14 hours after hospitalization.

- I didn`t know what the cause of her death was.

- Another patient with the same symptoms & past history came to our hospital in that day afternoon.

Case 2

48-year old male

- *C.C.: Dyspnea (NYHA IV)*
- *Present Illness : the patient was brought to the emergency room following a 2 weeks period of progressively worsening shortness of breath.*
- *Past Hx : gastric cancer – operation – 1year ago*

  adjuvant chemotherapy – done

  V/S : 90/60 mmHg-110/min-25/min-36.5 ℃

Case 2

Initial Lab

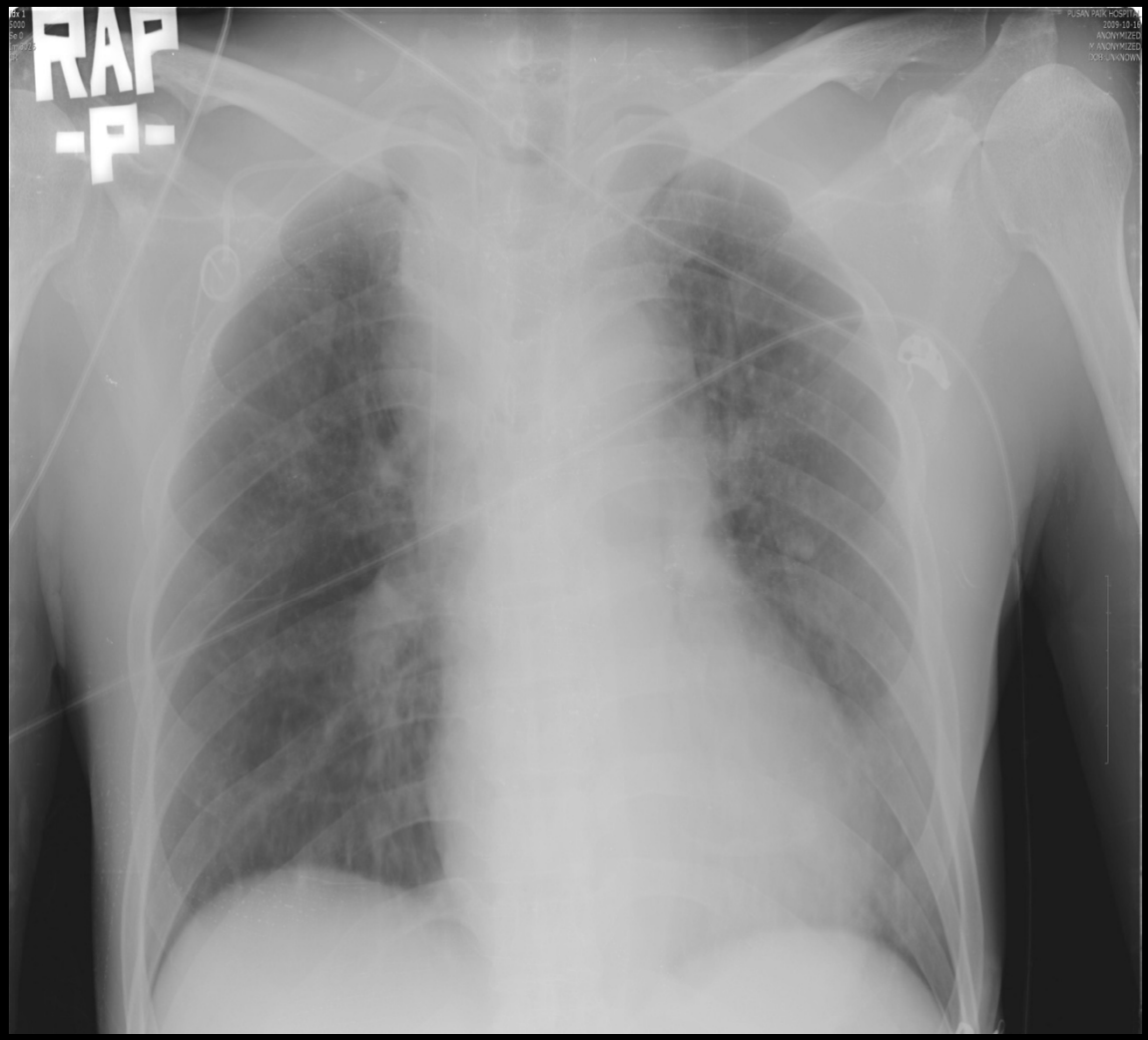
- *CBC*
  - *Hb 9.8 g/dL, Hct 31.4%, Platelet 107K*

- *BNP : 619 pg/mL (normal <100)*
- *FDP : 21.9 ug/mL (normal < 5)*
- *D- dimer : 14.7 ug/mL (normal < 1.3)*
- *PT/PTT : WNL*
- *ABGA (with room air)*
  - *pH 7.47, Actual bicarbonate 23 mmol/L*
  - *PCO_2 30 mmHg, PO_2 60 mmHg, O_2 sat 92%*

- *ECG : sinus tachycardia*

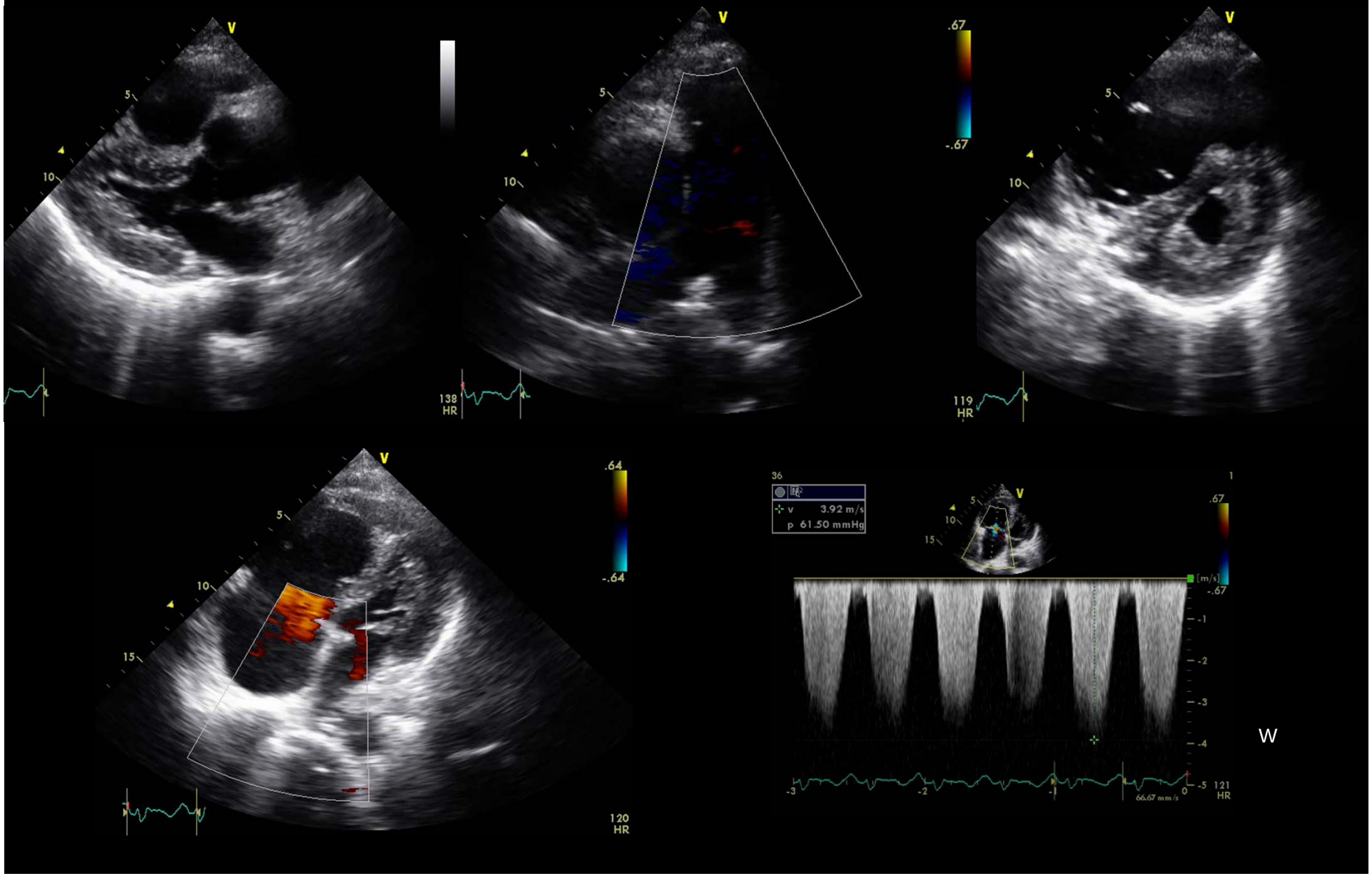
Case 2

Chest X-ray



Case 2

Echocardiography



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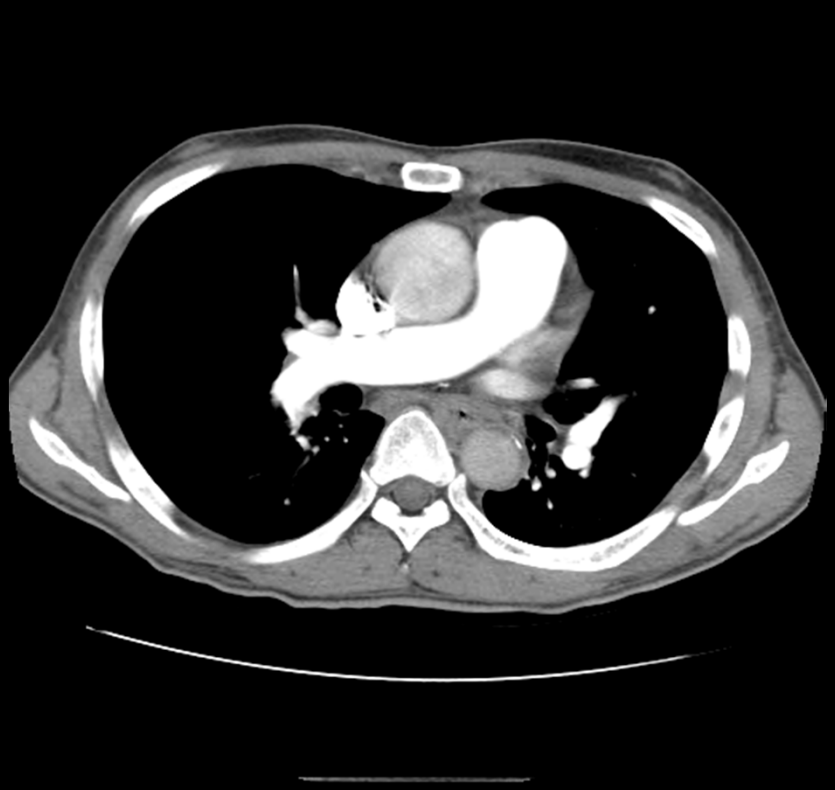
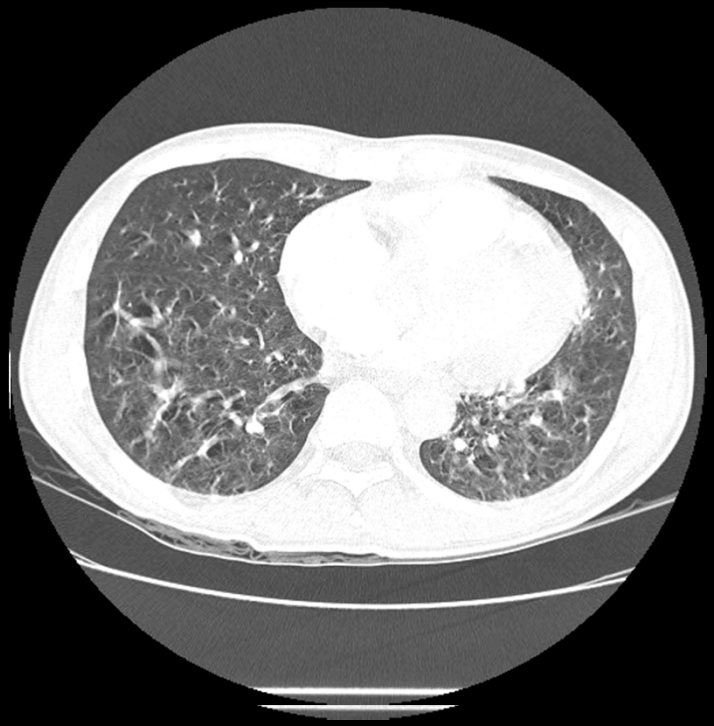
Case 2

Chest CT





Case 2

Progress Note

- *In 10 hours after hospital admission, the patient`s state rapidly deteriorated, with increasing dyspnea, peripheral cyanosis.*
- *He progressed to cardiogenic shock and had no improvement with a vasoactive drug. He had persistent hypoxemia.*
- *He died from refractory right heart failure caused by pulmonary artery hypertension.*

Summary

There are some common factors in 2 patients

- *Previous gastric cancer*
- *D - dimer level : elevation*
- *Echocardiography : pulmonary hypertension, right heart failure*
- *Chest CT: no pulmonary thromboembolism*
- *Clinical course : very rapid downhill*

Fatal acute right heart failure
with elevated D-dimer in gastric cancer

What were the causes of their death ?

The lung is a common site for the metastatic spread of malignant tumors

1. *Large tumor emboli can directly occlude the main vessel of the pulmonary tree.*

2. *Malignant cells can spread via the lymphatic channels generating carcinomatous lymphangitis.*

3. *Tumor microthromboemboli may activate the tissue factor and trigger the formation of microthrombi by stimulating the proliferation of the myofibroblasts in the intimal layer of the vessel. - PTTM*

Pulmonary tumor thrombotic microangiopathy (PTTM)

- *Pulmonary tumor thrombotic microangiopathy (PTTM) is a rare pathognomic disease with a common incidence in postmortem studies.*
- *PTTM is defined as the activation of the coagulation cascade induced by tumor cells in the lung vessel, resulting in obstructive microthrombosis and intimal fibrocellular proliferation.*
- *The most common tumor associated with PTTM is the gastric adenocarcinoma, especially that of the poorly differentiated type.*

von Herbay A.et.al. Cancer 1990;66:587-92.

Diagnosis

- *echocardiography may reveal a feature of pulmonary hypertension with severely dilated right ventricle.*
- *Chest X-ray and CT scan are usually unremarkable in the absence of lymphangitic spread.*
- *Ventilation-perfusion scanning shows multiple peripheral, subsegmental perfusion defects with a normal ventilation scan.*
- *Invasive procedures are required to conform the diagnosis These procedures include transbronchial lung biopsy or surgical open lung biopsy.*

Treatment

- *There is no specific treatment for PTTM and the prognosis is extremely poor, even when condition is diagnosed.*
- *Thrombolytic therapy is not helpful because PTTM is caused by mainly intimal fibrocellular proliferation.*
- *Nevertheless, chemotherapy is believed to reduce the burden of the tumor cells, thereby lessen the stimulus for the intimal proliferation.*

Pulmonary Tumor Thrombotic Microangiopathy

- *It has been reported the case of a patient with a history of gastric adenocarcinoma who presented with dyspnea and a dry cough.* [1]
- *The serum D-dimer level was elevated. The elevation of the D-dimer level indicates the activation of the coagulation systems. This finding is specific for PTTM.*[2]
- *The patient was early diagnosed and successfully treated with corticosteroid, anticoagulants, and oral anticancer drugs.*

1. Miyano S, Izumi S, Takeda Y, et al. J Clin Onc. 2007;25:597–599 .

2. Shigematsu H, Andou A, Matsuo K. Journal of thoracic oncology 2009;4:777-8.

Pulmonary lymphangitic carcinomatosis (PLC)

- PLC is a metastatic lung disease characterized by the lymphangitic spread of the cancer cells to the pulmonary vasculature and lymphatics.

- The most common primary sites for PLC are the bronchus, stomach, breast, pancreas and uterus.

- Pathogenesis : the tumor spreads along the paraesophageal lymphatics, hence through lung parenchyma as well as through hematogenous tumor emboli.

- Chest CT reveals thickening of interlobular septa and peribronchovascular interstitium.

- Diagnosis : Transbronchial biopsy is the procedure of choice for a definitive Dx.

-Treatment : Optimal treatment of PLC is not well defined, but a trial of chemotherapy and/or intravenous steroids may be warranted.

- Prognosis : PLC has traditionally been considered poor due to the aggressive nature of the disease and delayed diagnosis.

PTTM & PLC are a rare conditions causing severe pulmonary hypertension, and acute right heart failure in patients with cancer.

They should be suspected in patients with unexplained severe dyspnea, pulmonary hypertension, and especially in the presence of adenocarcinoma.

Case 3

40-year old male

- *C.C.: Dyspnea (NYHA IV) remote : 6 years ago*
- *recent : 3 months ago*
- *Present Illness : the patient was brought to the emergency room following a 3 months period of progressively worsening shortness of breath.*
- *Occupation : truck driver*
- *Past Hx: pulmonary thromboembolism – 10 years ago*

  but, only took a medication for 6 months
- *V/S : 100/60 mmHg-110/min-24/min-36.5 ℃*

Physical exam

- *Jugular venous distention*
- *Severe swelling with pitting edema – both lower extremities*
- *Pansystolic murmur : along the lower left sternal border*
- *Pulmonary rales*

Case 1

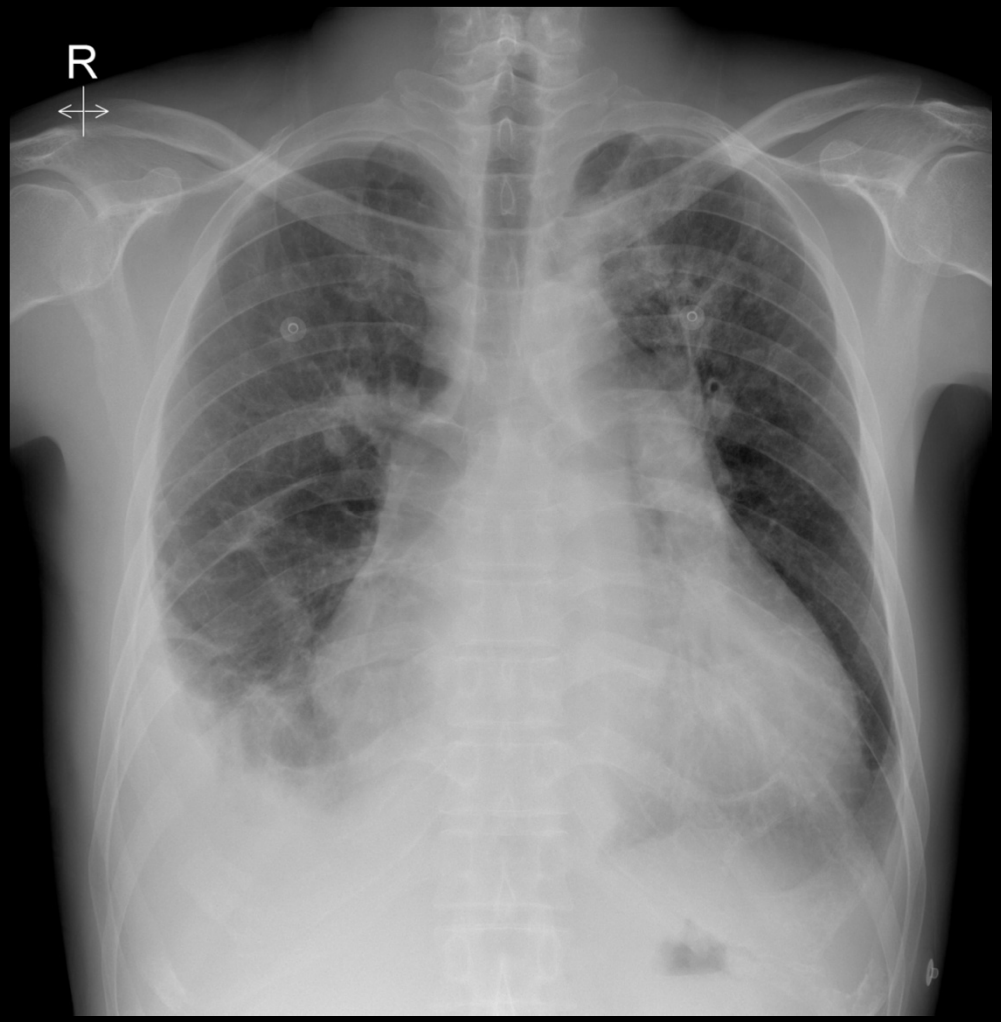
Initial Lab

- *CBC*
  - *WBC 7410 Hb 16.6 g/dL, Hct 48%, Platelet: 97K*

- *Pro-BNP: 6963 pg/mL*
- *D- dimer : 16.2 ug/mL (normal <0.55)*
- *FDP : 16.2 ug/mL (normal <5.0)*
- *PT /PTT : WNL*
- *Anticardiolipin antibodies /lupus anticoagulant(-/-)*
- *Protein C/S level: normal*
- *ABGA (room air)*
  - *pH 7.47, Actual bicarbonate 21 mmol/L*
  - *PCO_2 23 mmHg, PO_2 67 mmHg, O_2 sat 92 %*

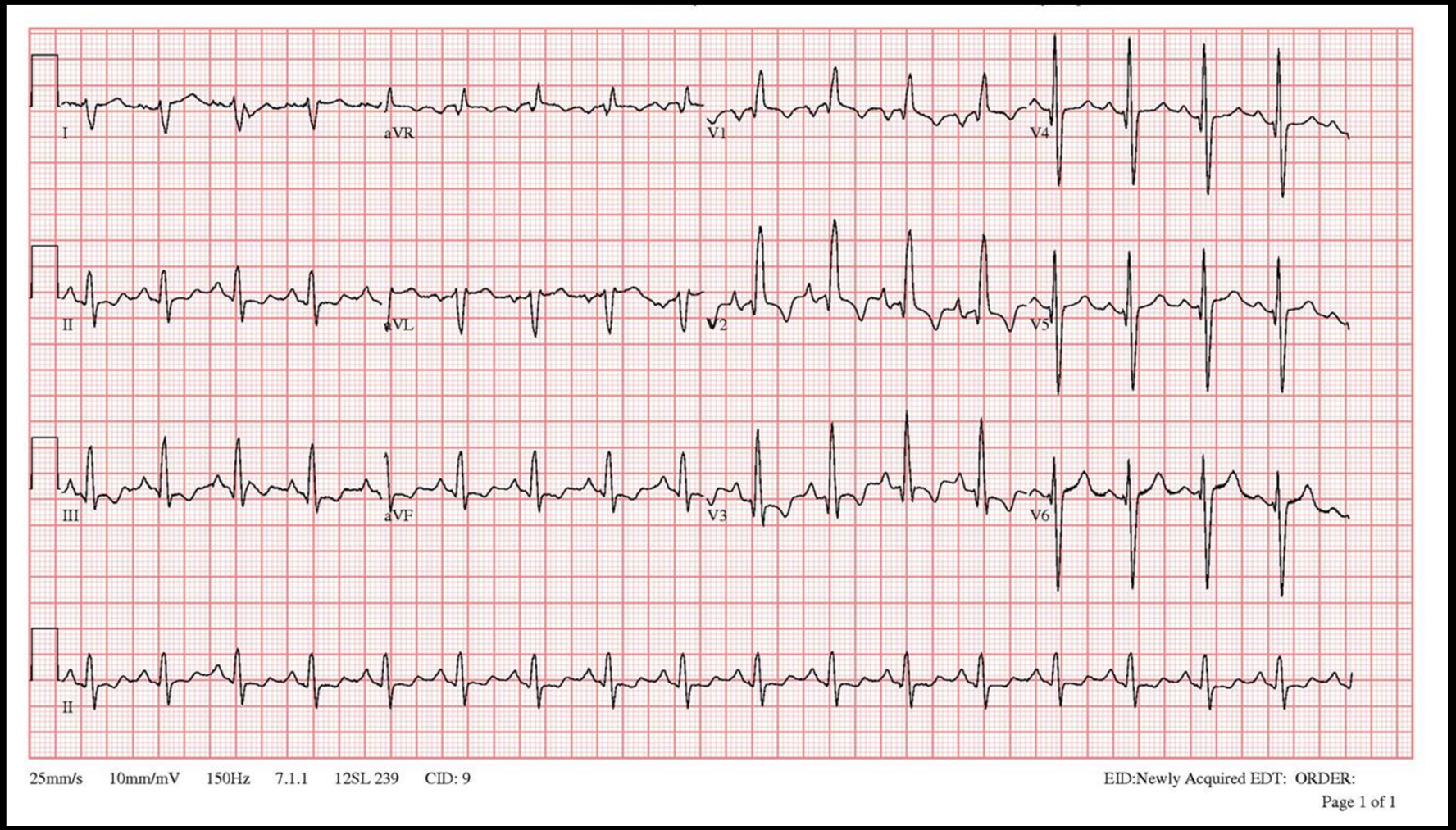
Case 3

Chest X-ray



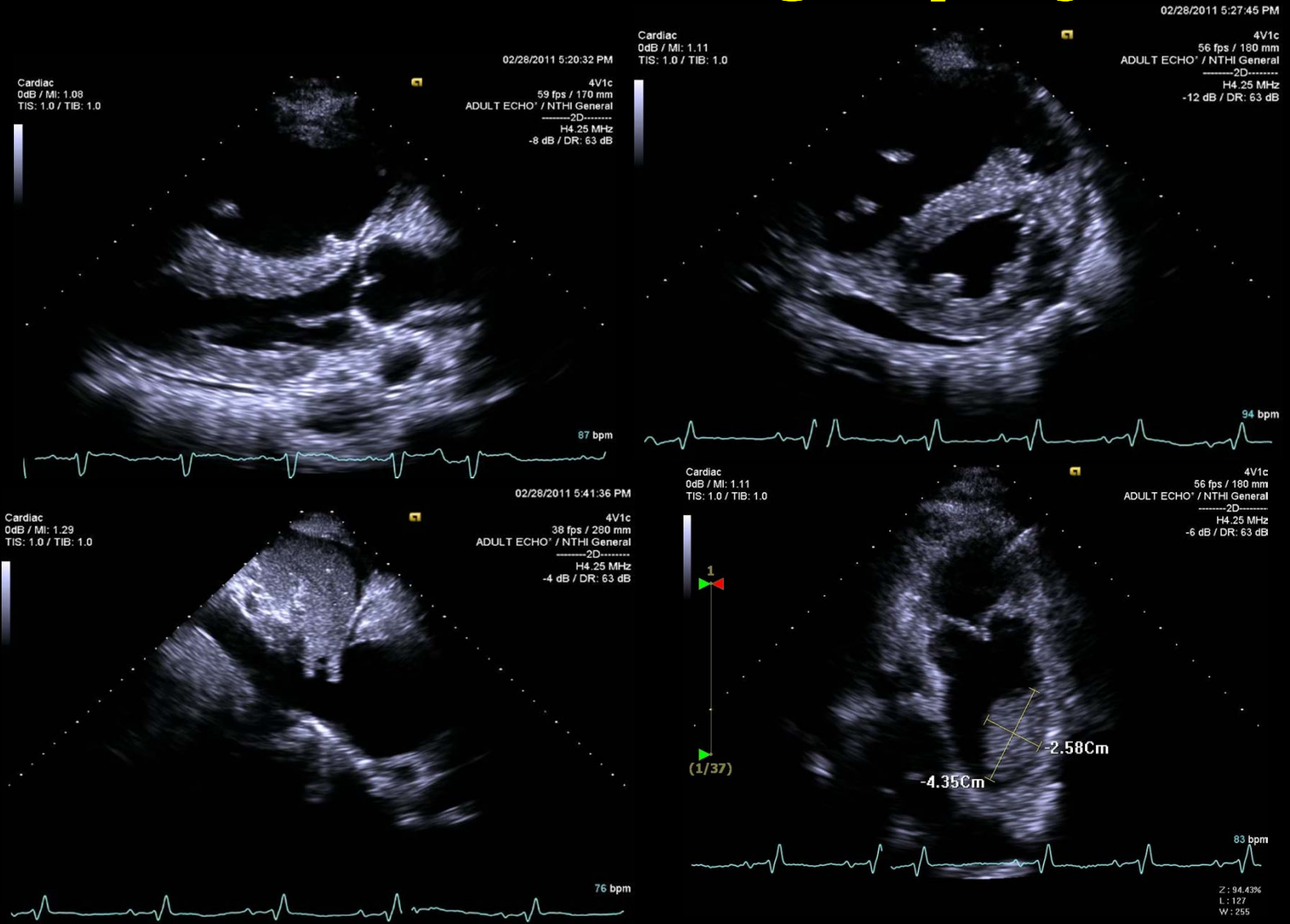
Case 3

ECG on Admission



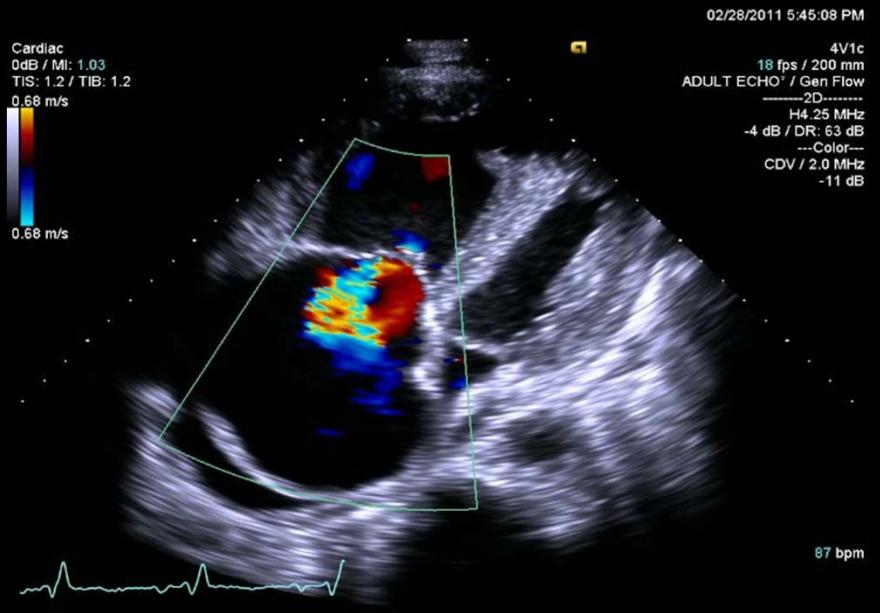
Case 3

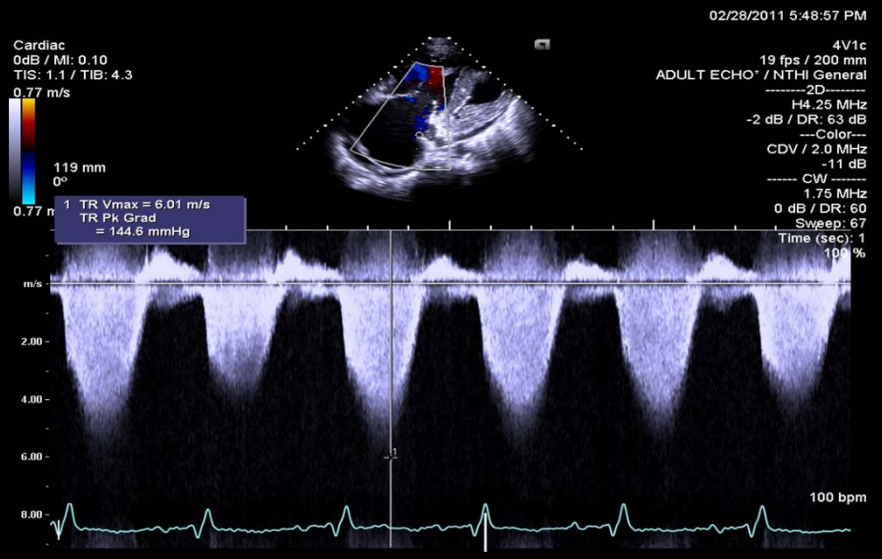
Echocardiography



Case 3

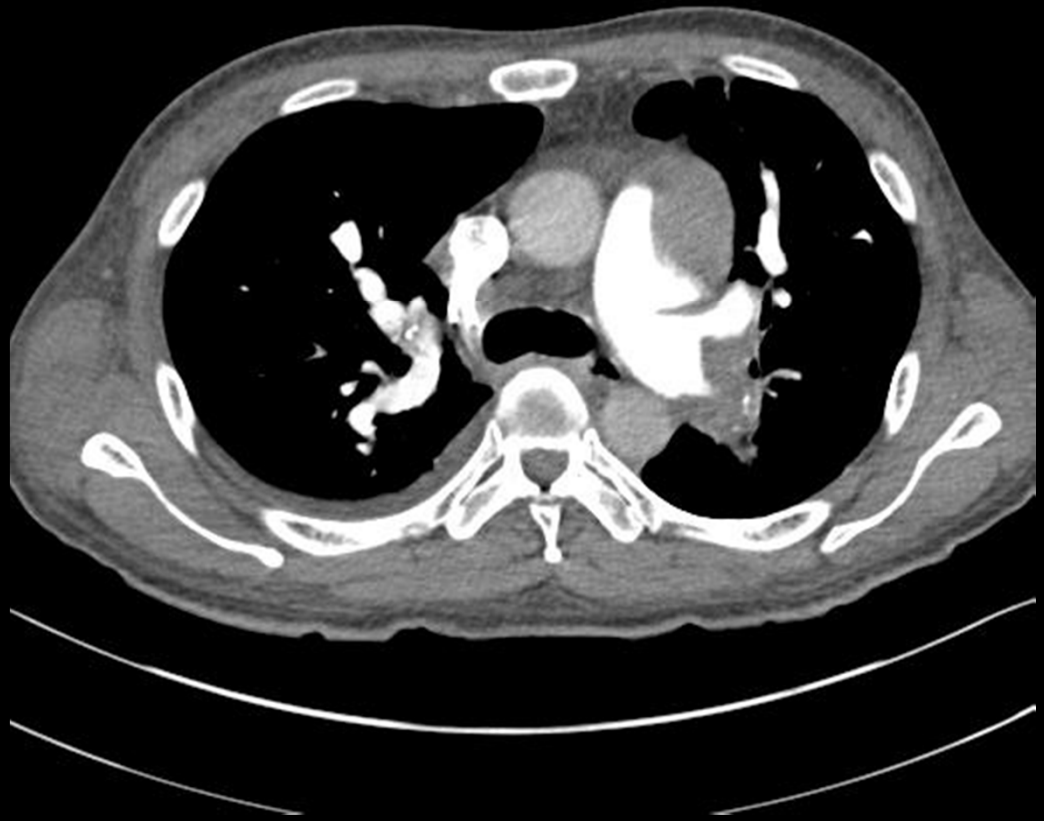
Echocardiography



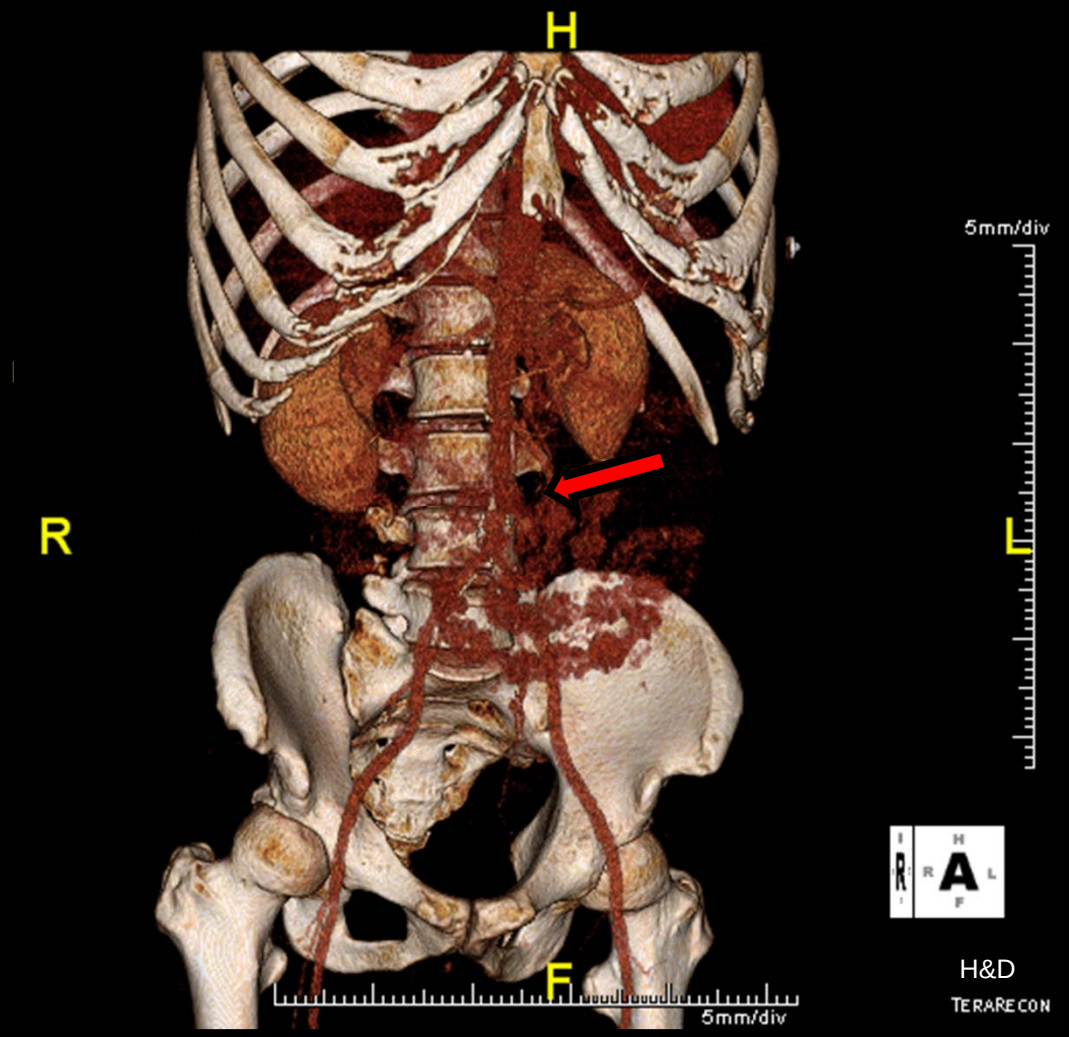


RVSP = 144 mm Hg

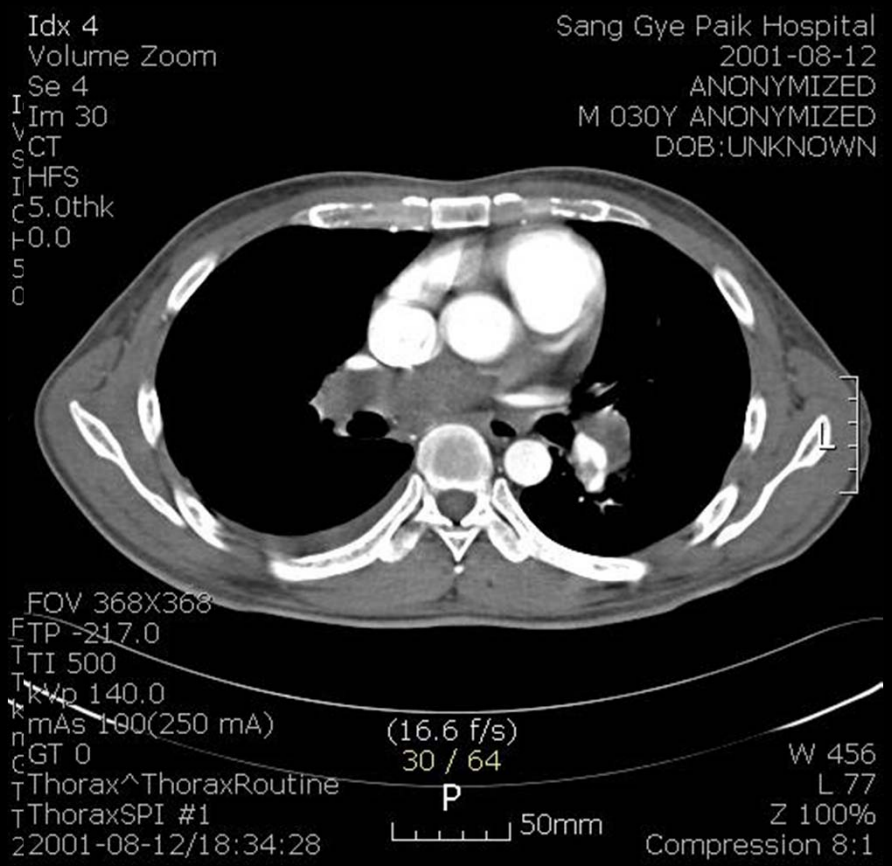
Chest CT

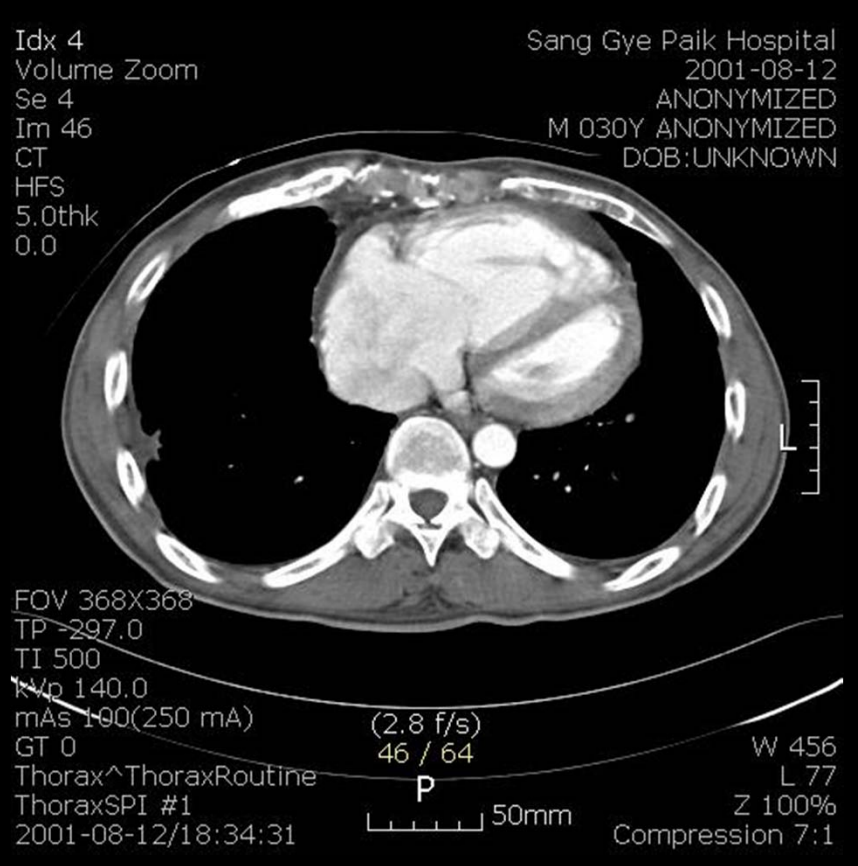


CT venogram

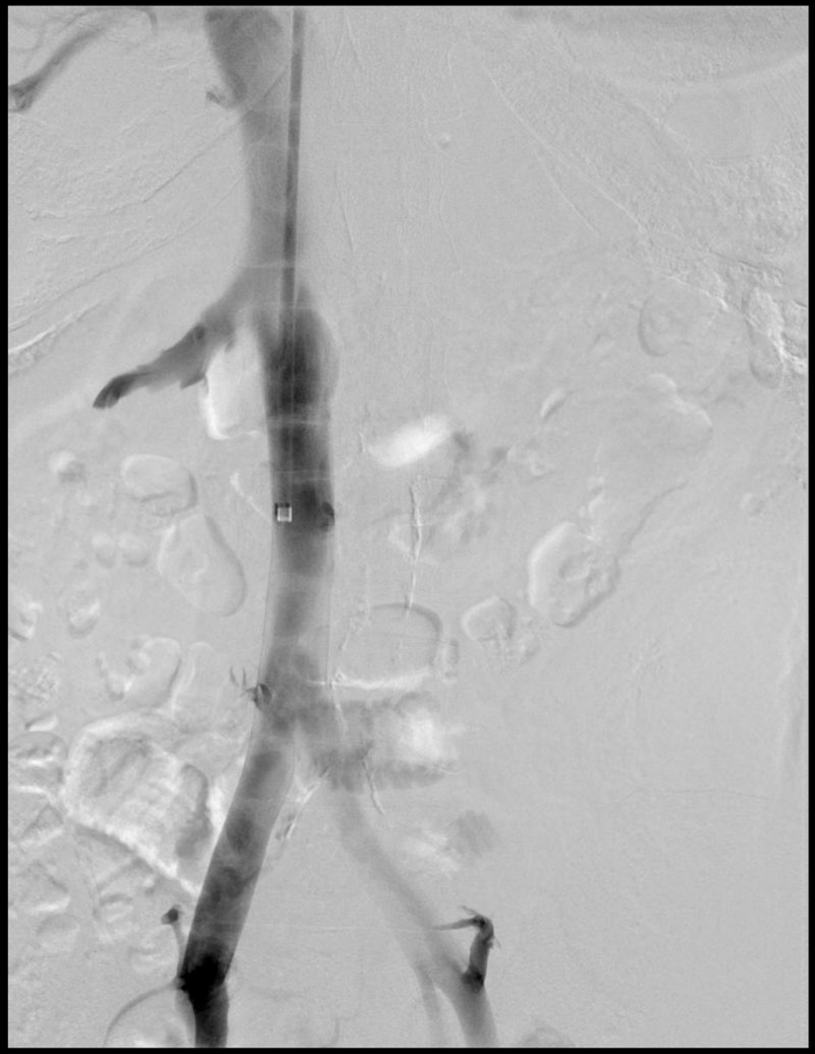


Chest CT- 10 years ago





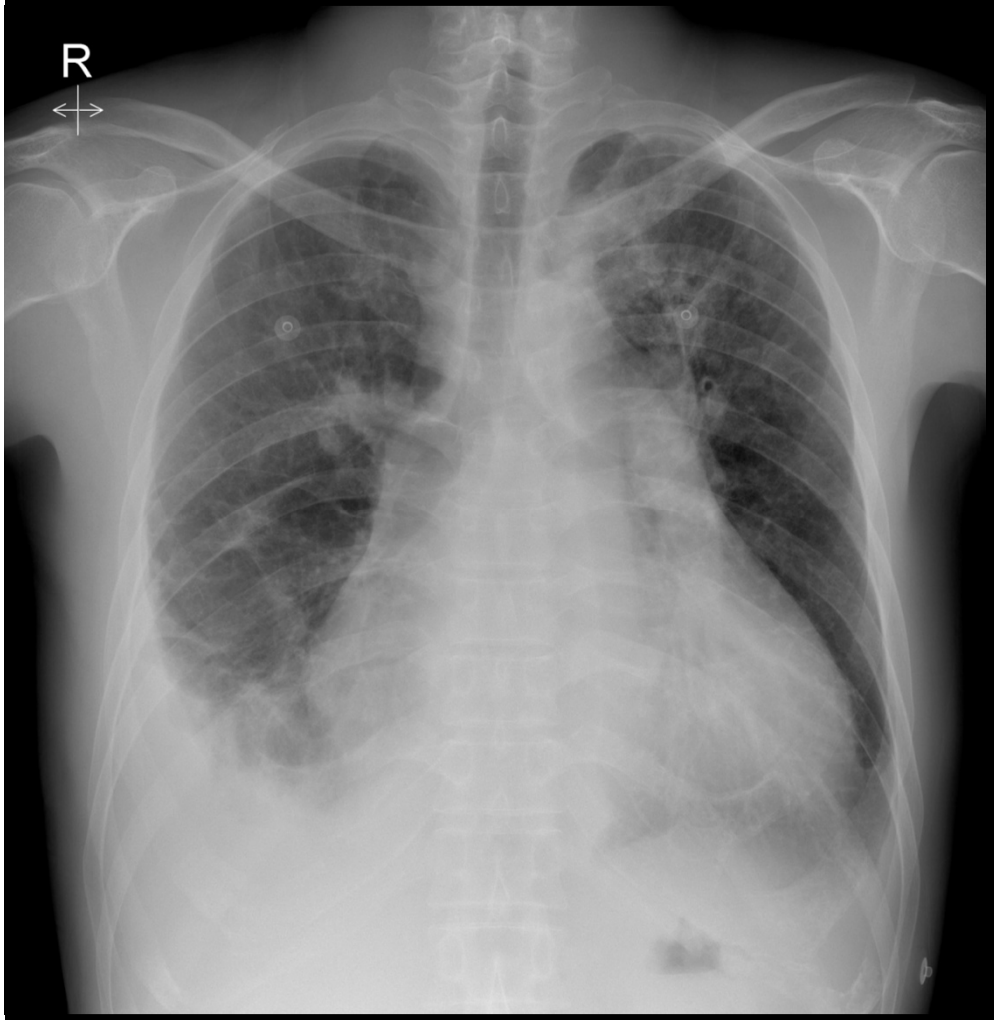
Venography- in 3 weeks



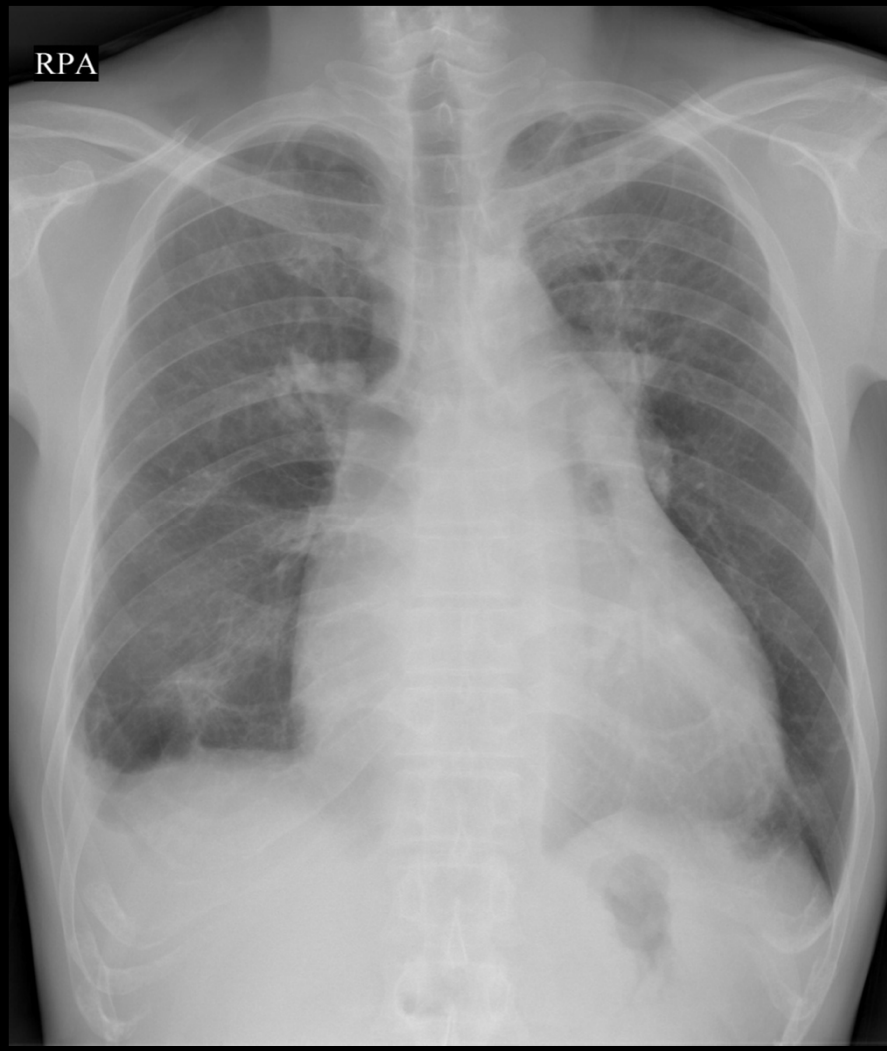
No visible thrombotic filling defects on IVC venography

Case 3

Chest X-ray F/U

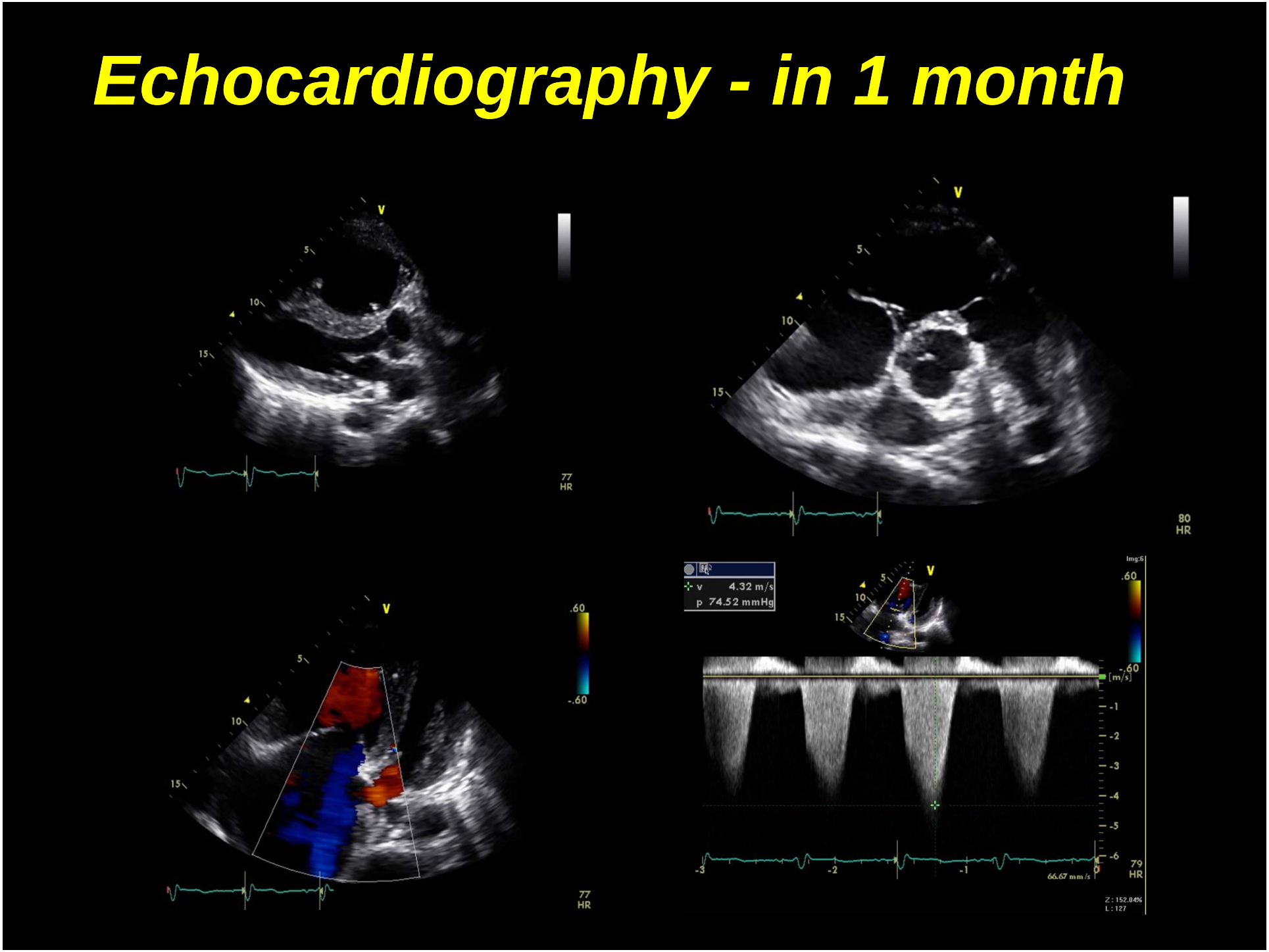


Initial

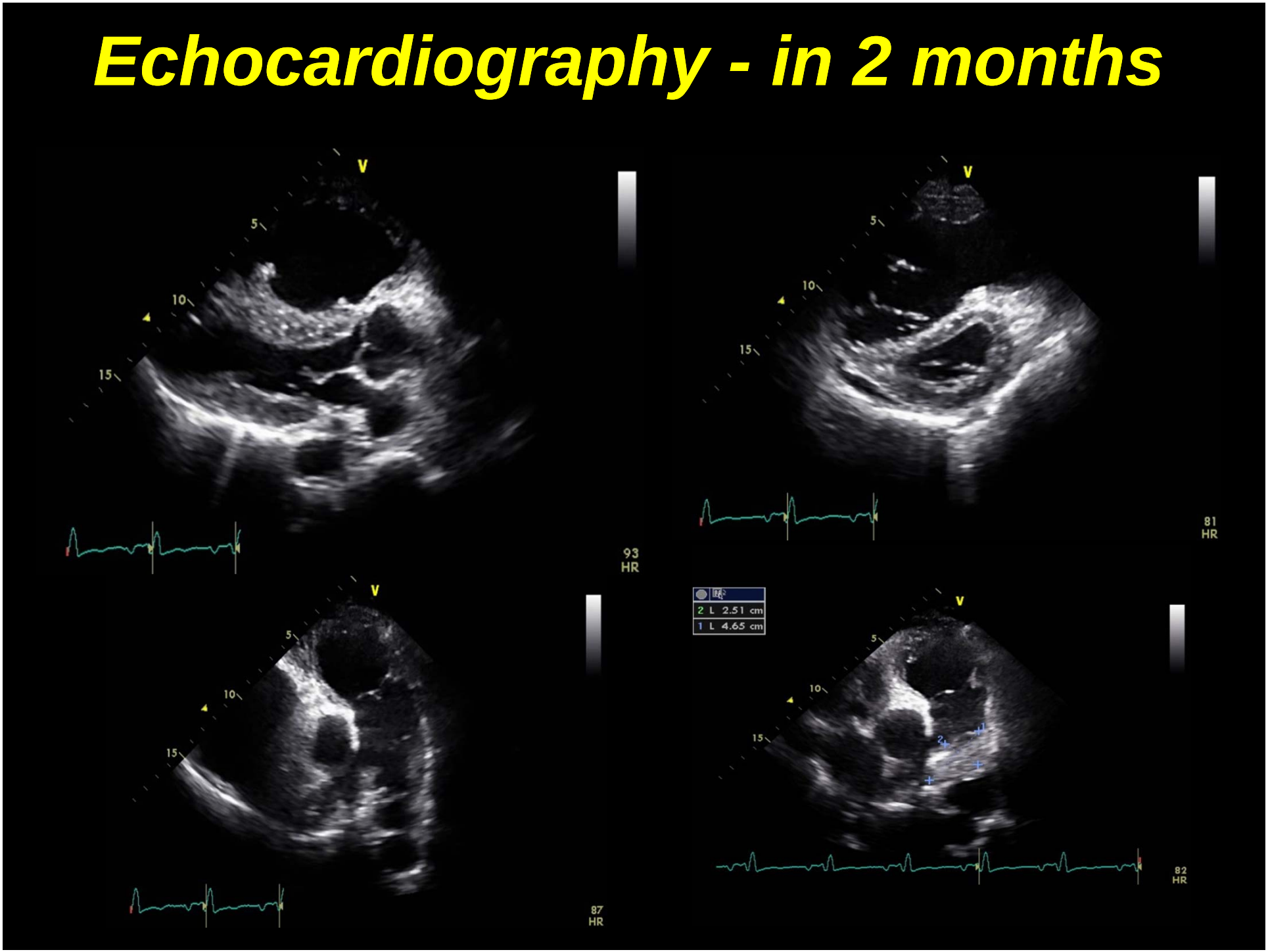


In 1 month

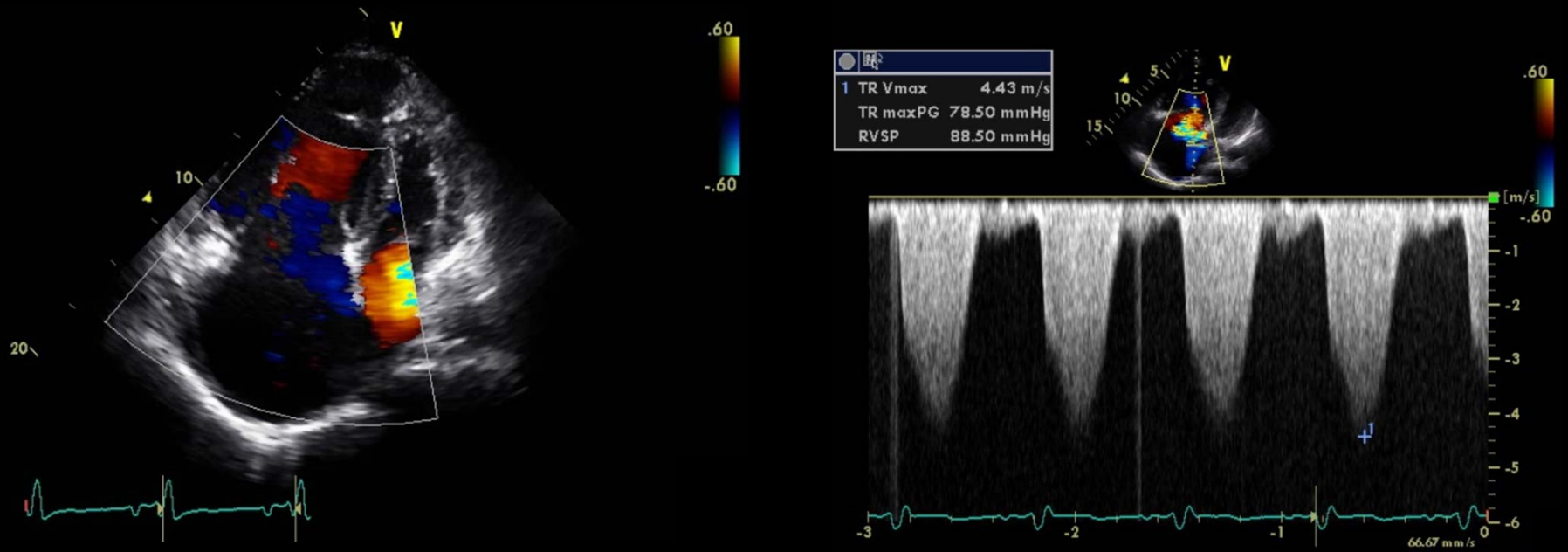
Echocardiography - in 1 month



Echocardiography - in 2 months



Echocardiography - in 2 months



- *He still had severe pulmonary hypertension (88 mmHg) at the end of 2 month follow-up.*
- *The patient`s symptom was mildly improved and continued taking oral anticoagulation therapy & prostacyclin analogues(Berasil®).*

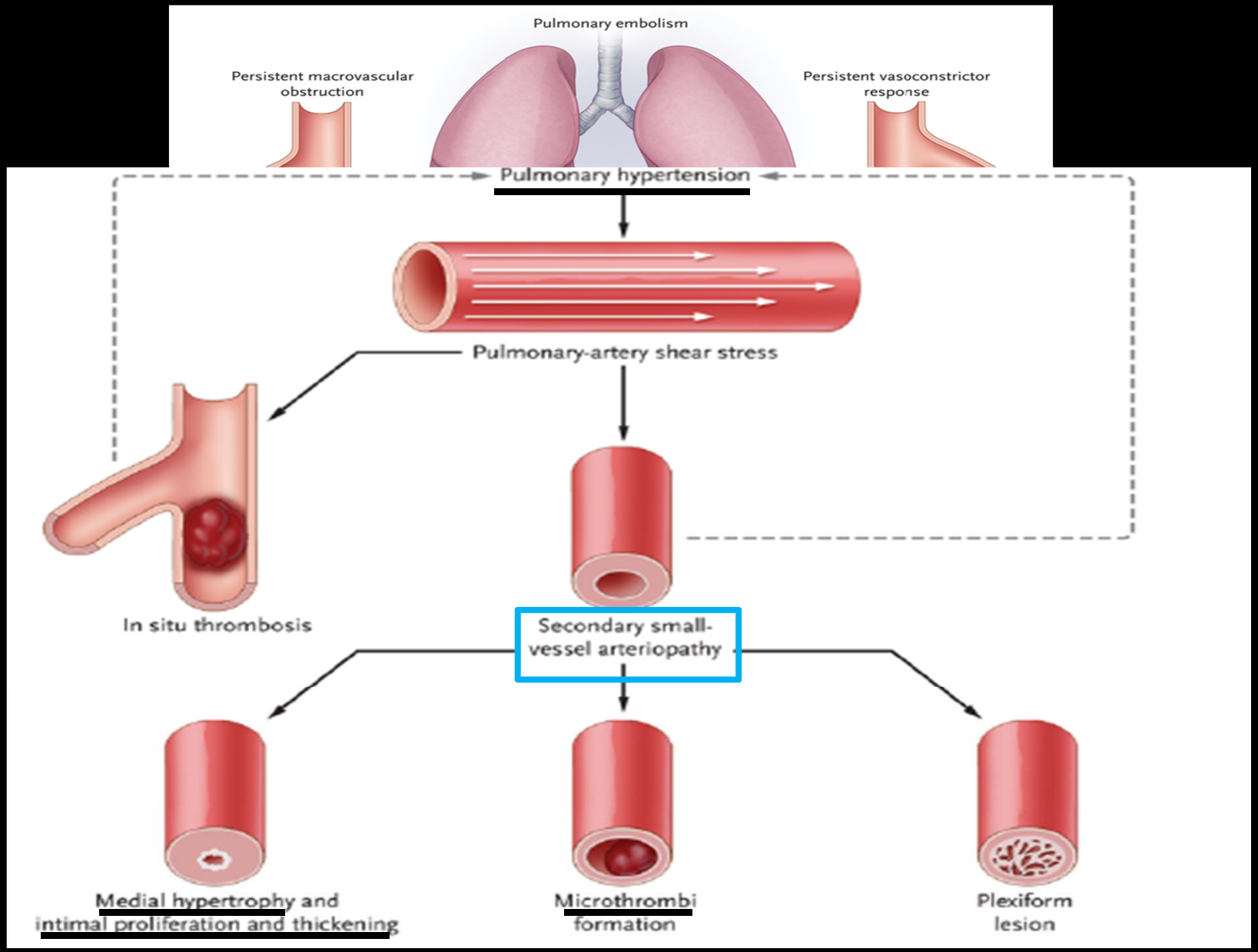
Chronic ThromboEmbolic Pulmonary Hypertension(CTEPH)

- Diagnosis : Mean pulmonary-artery pressure > 25 mm Hg that persists 6 months after pulmonary embolism

- The 2008 World Symposium on Pulmonary Hypertension emphasized the importance of CTEPH, which occurs in 2 to 4% of patients after acute pulmonary embolism.

Pengo V et.al. N Engl J Med 2004;350:2257-64.

Pathophysiology of the Pulmonary Vasculature in CTEPH



Echocardiography

- Doppler echocardiography is sensitive for the detection of pulmonary hypertension and right ventricular dysfunction.

- Common echocardiographic findings:

1. right ventricular dilatation, hypertrophy, and hypokinesis
2. right atrial enlargement
3. D-shaped LV : suggested by right ventricular pressure overload
4. tricuspid regurgitation

- The treatment of choice for CTEPH is surgical pulmonary endarterectomy .

- The preoperative pulmonary vascular resistance >1100 dynes/ second/ cm^5 and a mean pulmonary artery pressure > 50 mm Hg predicted a higher operative mortality.

Hartz RS.et.al. Ann Thorac Surg 1996;62:1255–9.

- Death is usually due to progressive pulmonary hypertension culminating in right ventricular failure.

- Prognosis without treatment is poor in cases of CTEPH; the 2 year survival was only 30% in cases where pulmonary arterial hypertension was above 30 mmHg.

Chronic ThromboEmbolic Pulmonary Hypertension(CTEPH)

- *What is the best treatment of this patient?*

  - operation or medical treatment

Thank you for your attention !

The measurement of right ventricular function is difficult for many reasons, in part because of the interplay between intrinsic myocardial performance and right ventricular loading conditions.

TABLE 2. Markers of Right Ventricular Dysfunction Associated With Clinical Status and Prognosis

Right ventricular ejection fraction (echocardiography, radionuclide angiography or thermodilution) [28,29,31,33,35-38,77]
Right ventricular ejection fraction response to pulmonary vasodilation[65]
Right ventricular dilation[78]
Degree of right ventricular dilation compared with left ventricular dilation[32]
Tricuspid annular velocity (systolic and/or diastolic) or excursion, or echo right ventricular descent (shortening)[30,34,79-81]
Right ventricular index of myocardial performance[80,82,83]
Doppler-estimated dP/dt[84]
Tricuspid regurgitation[85-87]
Doppler echo-derived right ventricular tissue displacement and strain[88]
Right atrial size[85,89]
Radionuclide angiographic, invasive angiographic, or echo/catheterization pressure-volume or pressure-area loops[90-92]
Brain natriuretic peptide level[15-19]
Heart rate variability[93]

The extent to which any of these parameters are useful as outcome measures in clinical research or practice remains unclear.