胸腔外科困難個案討論會:

Early thrombotic microangiopathy following lung transplantation

林口長庚胸腔外科 陳維勳

Basic data

- Name: 席XX
- Sex: Male
- Age: 59 y/o
- Occupation: Worker
- Underline disease: Type 2 diabetes mellitus
- Past surgical history: L1, L3 vertebroplasty in 2017

Chief complaint

- Dyspnea for 10 years

Clinical course

- 2014/4
  - Went to our chest clinic cough and dyspnea for 3 years.
  - Pulmonary function test: Severe lung restriction (FVC/FEV1 : 2.13/1.98)
  - Favor idiopathic pulmonary fibrosis

Clinical course

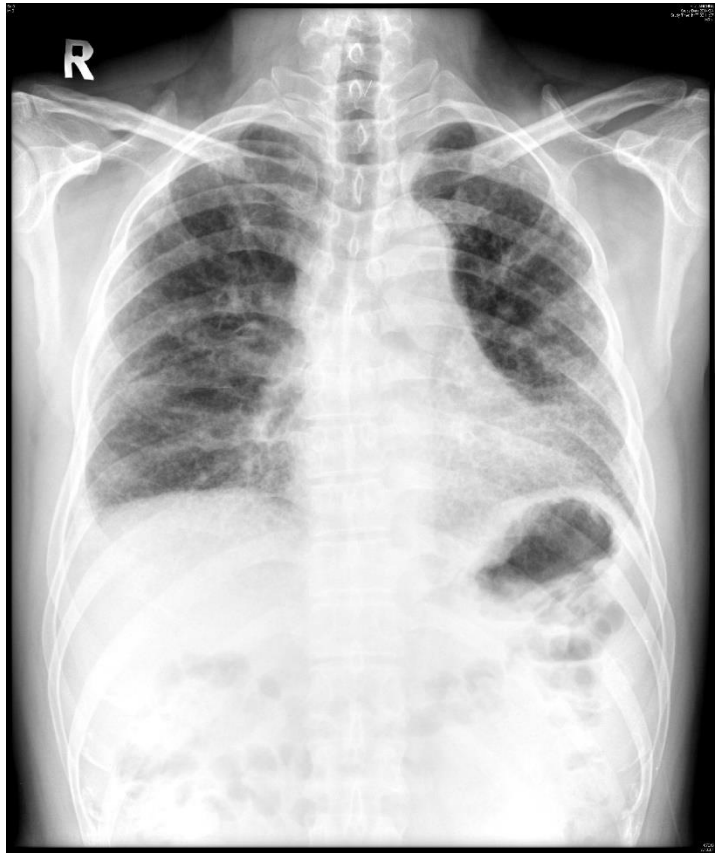
- 2015/8 AE
- 2015/9 AE
- 2015/12 AE

- 2016/12 Ofev(Nintedanib)

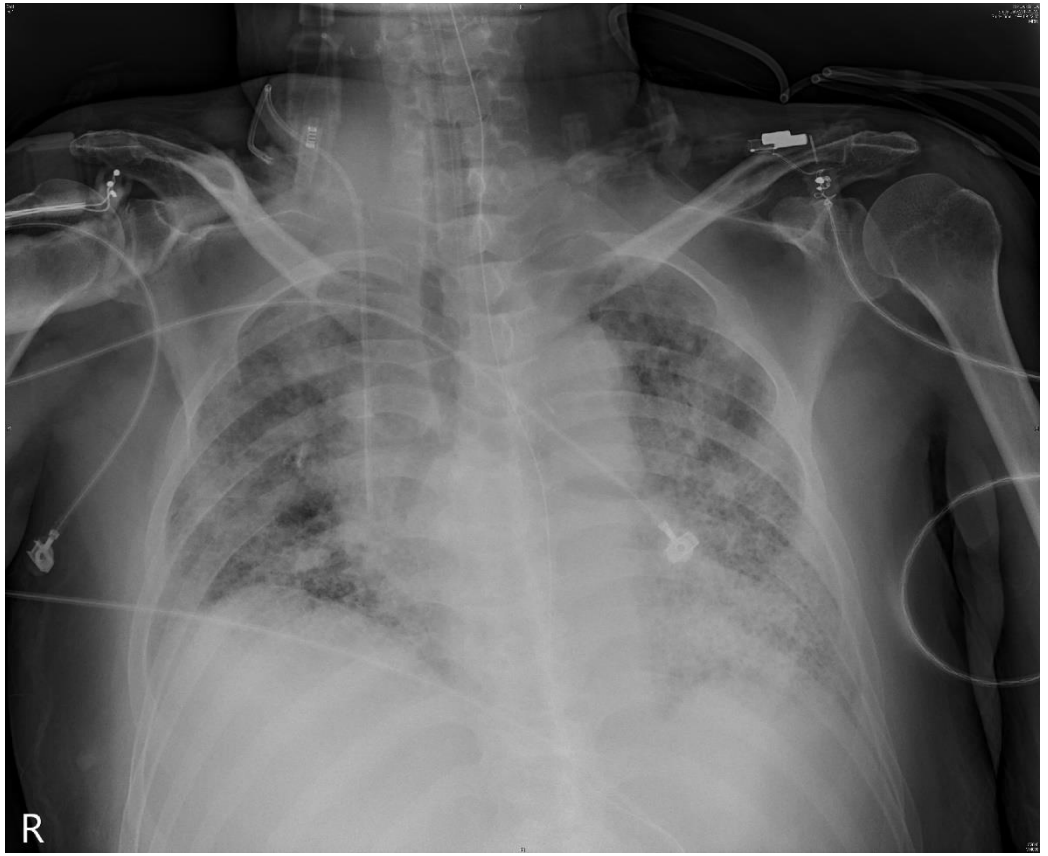
- 2017/4 AE
- 2017/12 AE

- 2018/1 Consult for lung transplantation
- 2018/8 Sequential bilateral lung transplantation

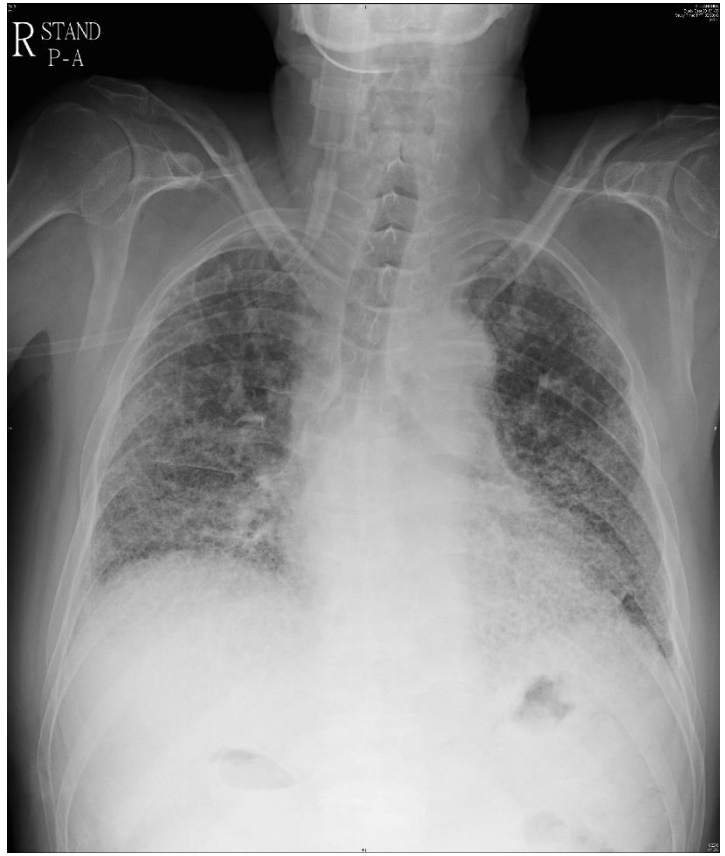
Series chest radiography



2014

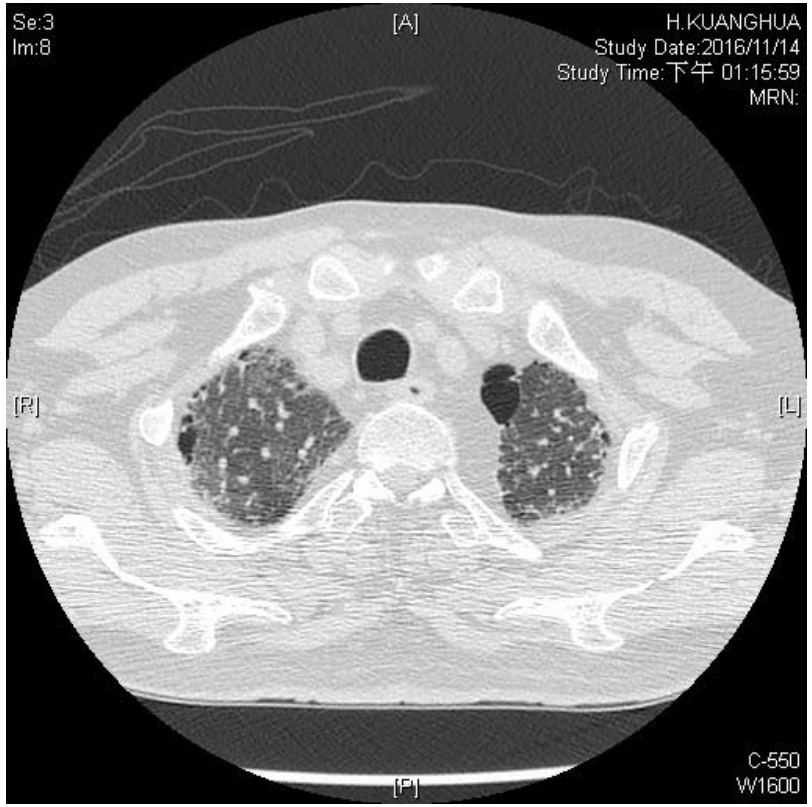


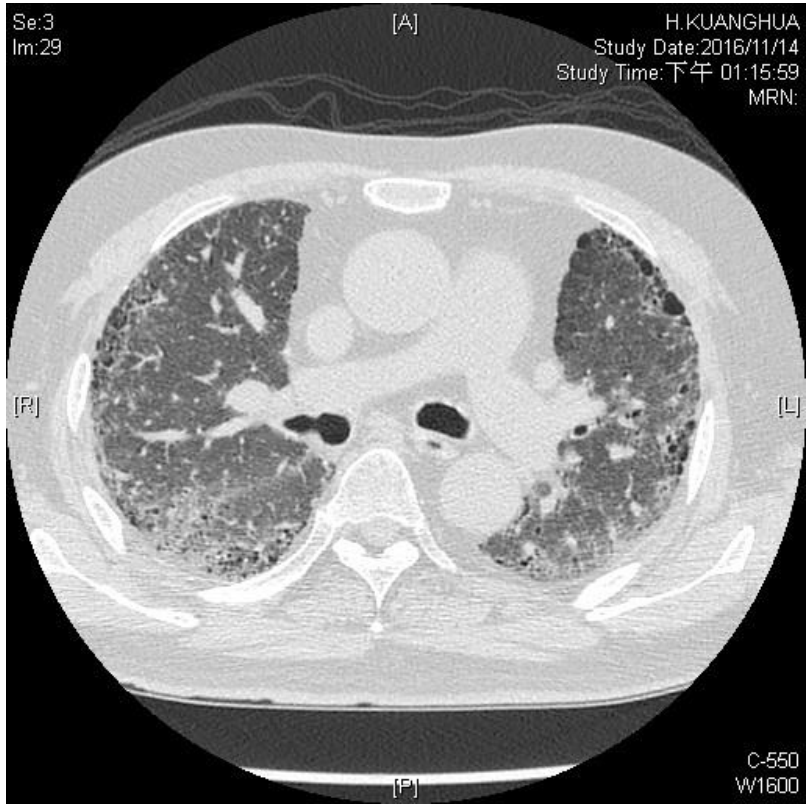
2017/12

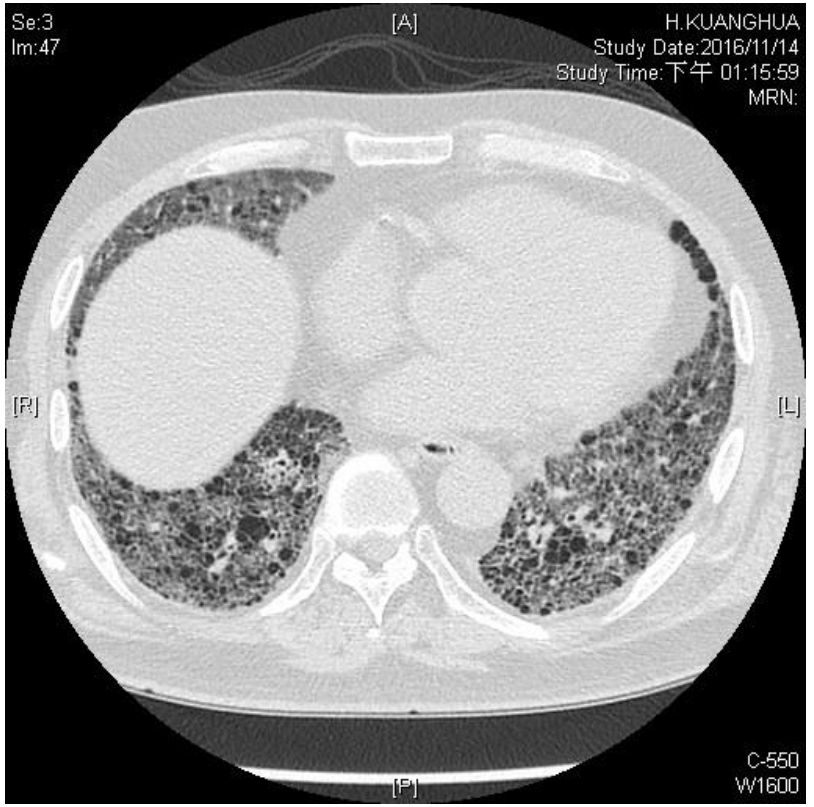


2018/2

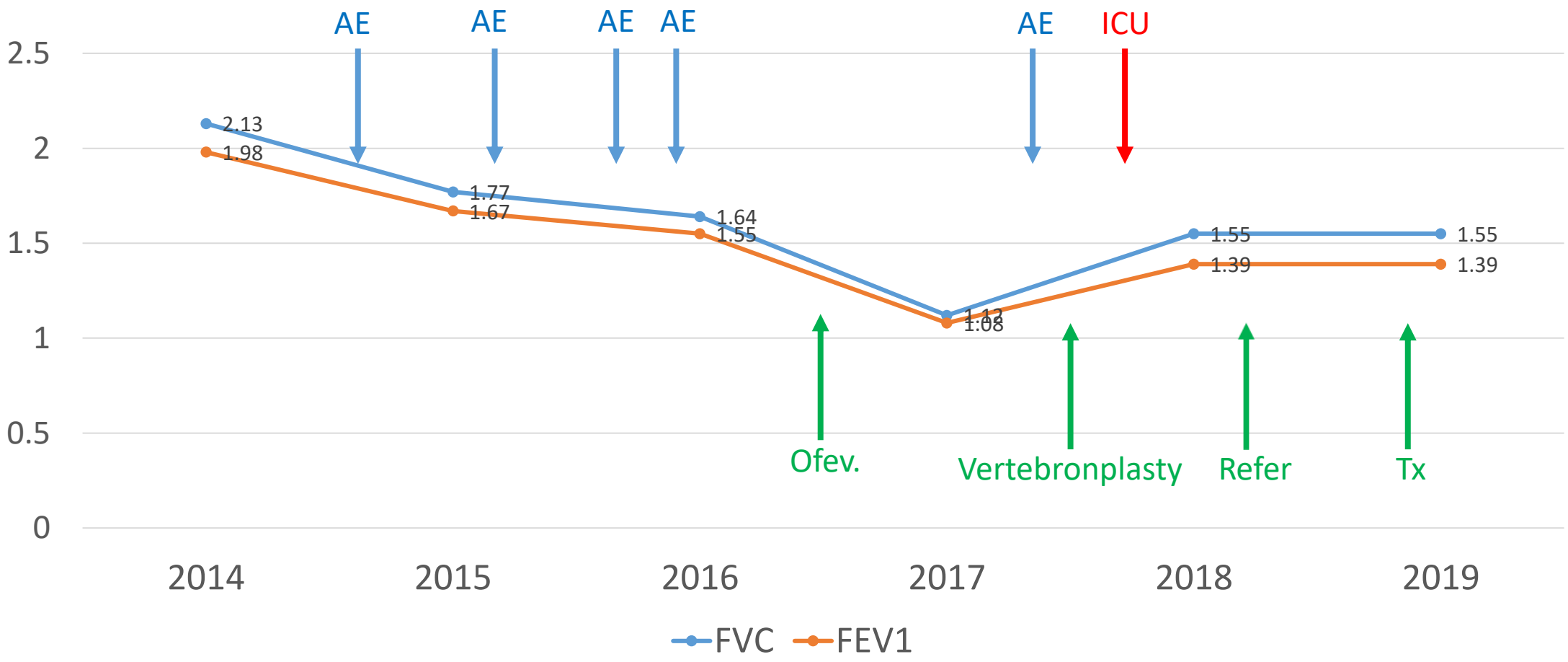
Pre-transplantation chest CT







Pulmonary Function Test



Pre-transplantation

- NYHA Class III
- Cardiac function:
  - Normal LVEF (78 %), patent coronary artery
  - Mild pulmonary hypertension (mPAP : 28mmHg)
- Pulmonary function:
  - Home BiPAP
  - FVC 1.55L, FEV1 1.39L, DLCO 10%pred. 6MWD: 60m.
- Normal liver function and renal function
- HBV -, HCV -, HIV -

Lung transplantation on 2019/9/21

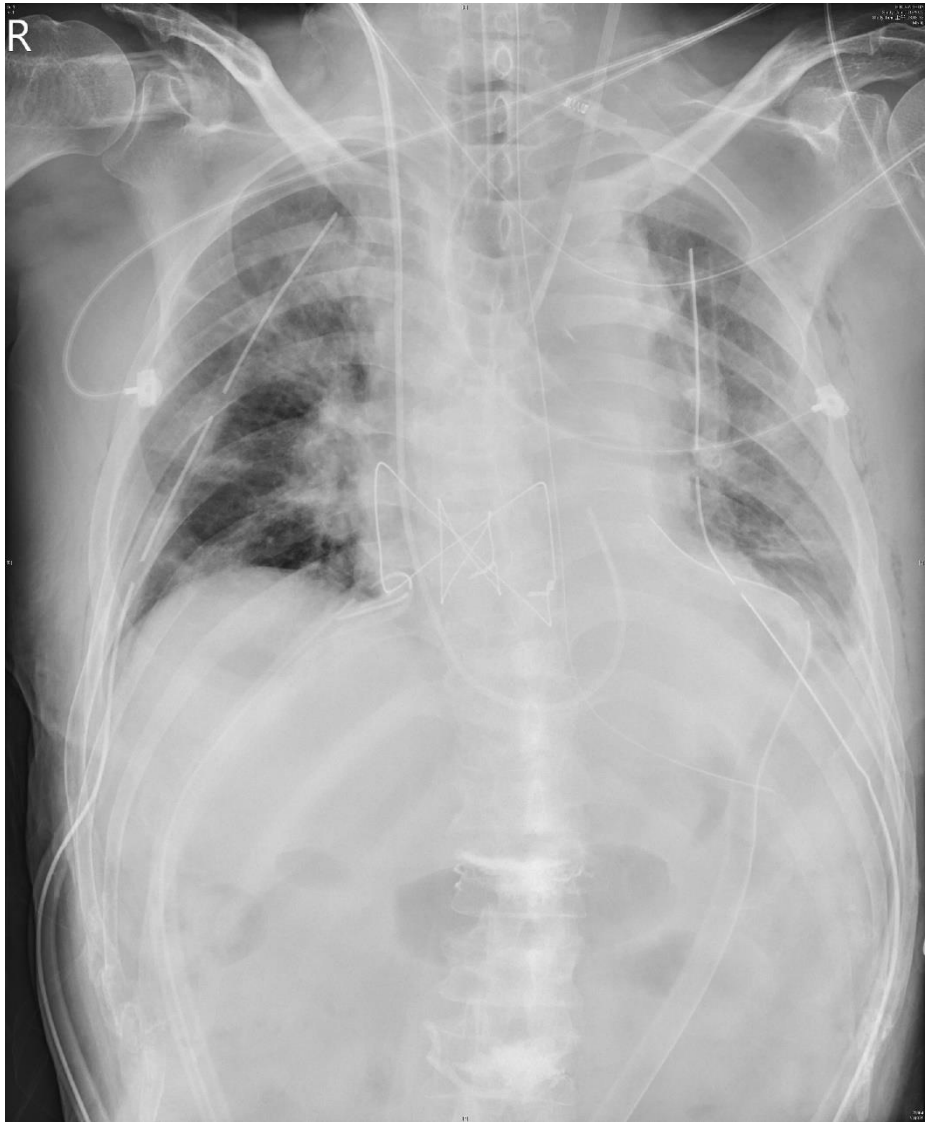
- Donor :
  - 49 y/o man brain death
  - pre-transplant PF ratio: 509 (LLL collapse)
  - Donor LLL lobectomy

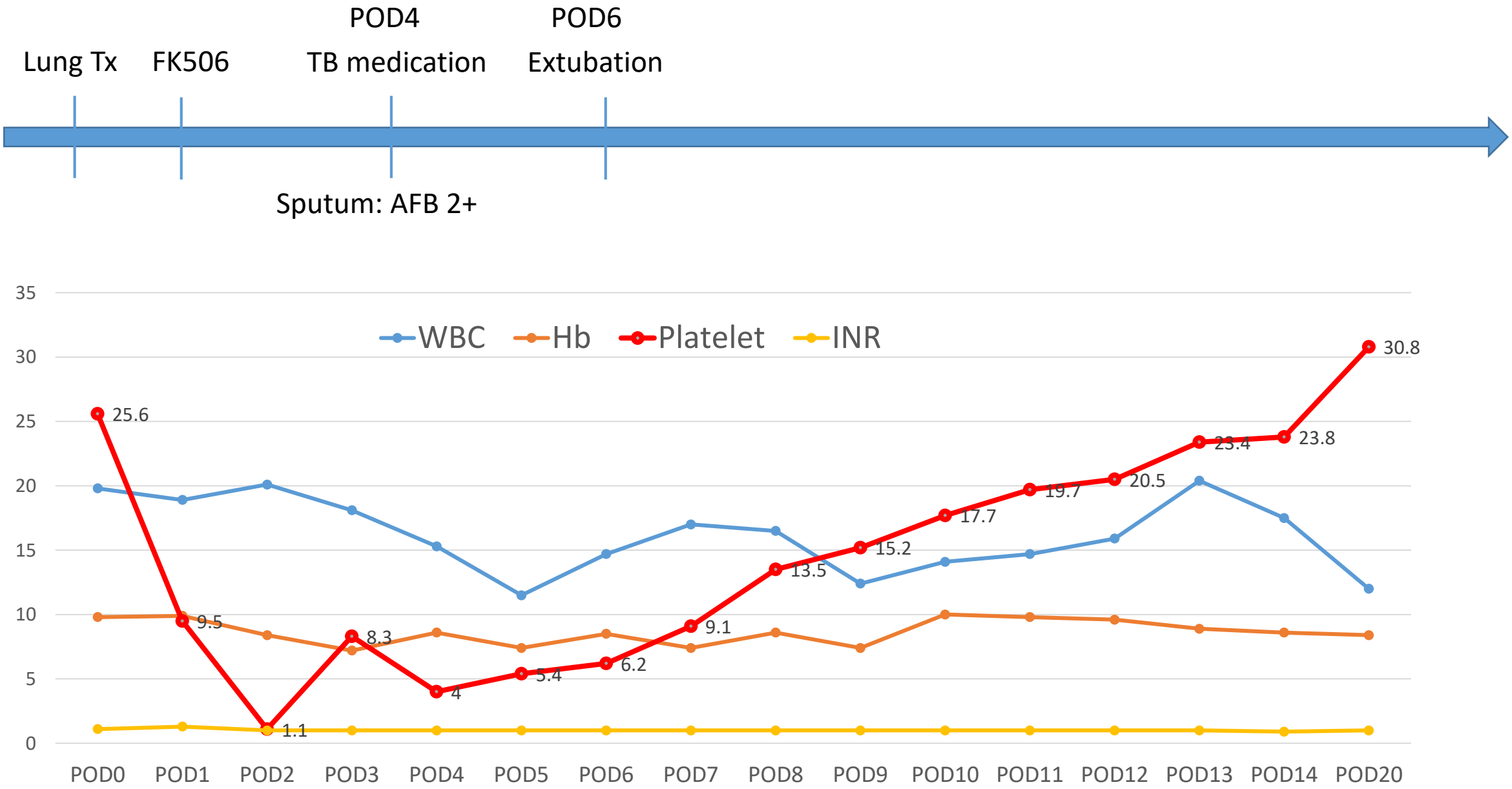
- Bilateral Sequential lung transplantation with femoral VA ECMO support (Desaturation and high PV pressure)

- Blood loss: 2200ml

Immediate post transplantation

- Post-transplant PF radio: 206
- Stable hemodynamics
- No significant bleeding




POD4
POD6
Lung Tx
FK506
TB medication
Extubation
Sputum: AFB 2+
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WBC
Hb
Platelet
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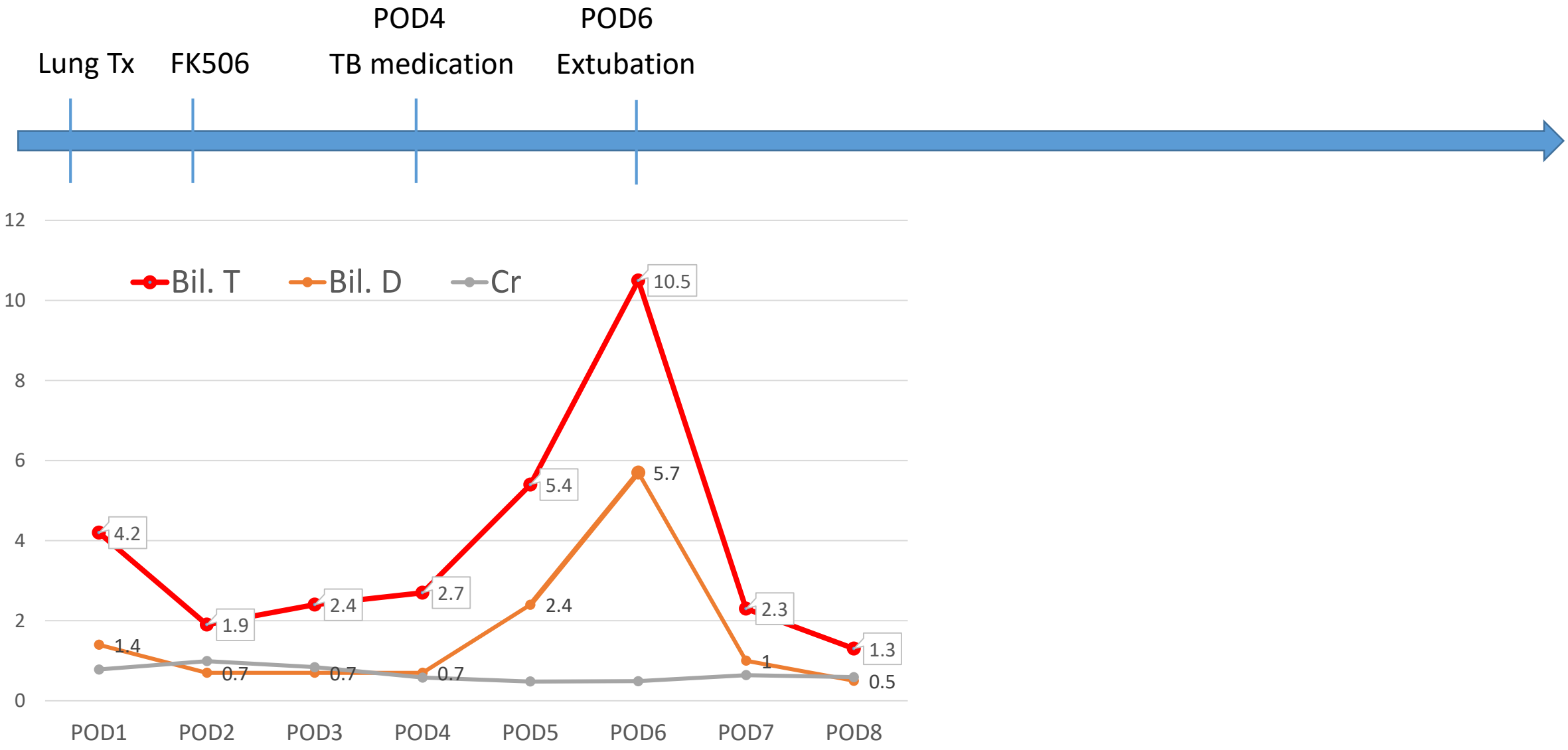
POD20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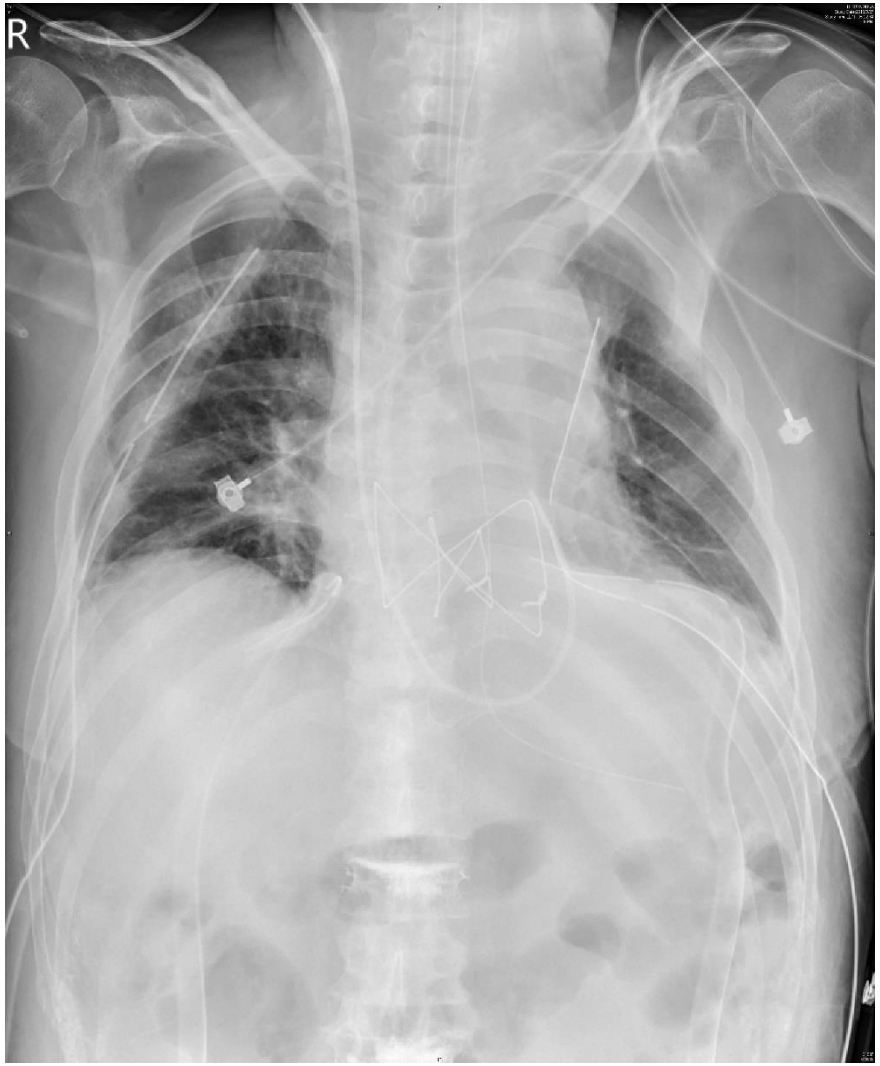
POD5
POD6
POD7
POD8

Clinical presentation , POD6

- Clear consciousness
- Stable hemodynamics, no fever
- Normal urine output
- Good oxygenation

Lab:

- Elevated Bilirubin
- Anemia
- Thrombocytopenia
- Elevated LDH
- Normal AST, ALT
- Mild leukocytosis
- Normal procalcitonin



Post-lung transplantation hyperbilirubinemia

- Common cause
  - Drug toxicity
  - Biliary tract stone
  - Sepsis
  - Bleeding
  - Liver failure

- Rare cause
  - Hemophagocytic lymphohistiocytosis (HLH)
  - Thrombotic microangiopathy (TMA)
  - Ischemic cholangiopathy

2017 JTD, Rare causes of hyperbilirubinemia after lung transplantation: our experience at a single center

Unconjugated hyperbilirubinemia: Differential diagnosis

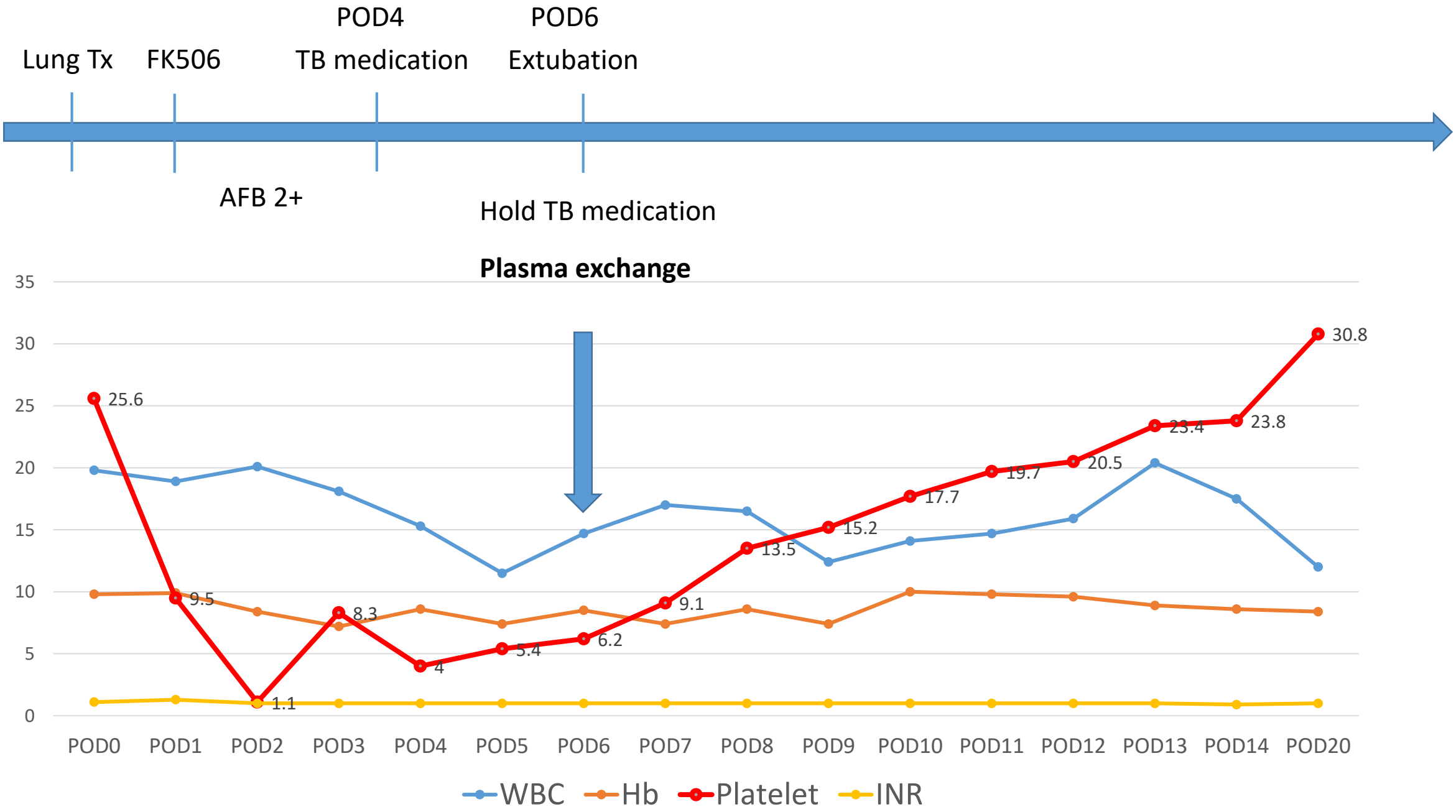
- Conjugation defect
  - Hyperthyroidism
  - Advanced cirrhosis
- Reduced uptake
  - Portosystemic shunt
  - Drugs
- Overproduction
  - Hemolysis
  - Extravasation

- Abdominal echo: no bile duct dilatation, no hepatomegaly or splenomegaly
- Normal endocrine parameters
- Hold TB medications (9/25~9/27)
- PB smear: anisopoikilocytosis with many RBC fragmentation and marked thrombocytopenia
- Coombs test: negative

De novo TMA ?

- Medication review by pharmacist
  - Hold TB medication (favor NTM)

- Consult nephrologist
  - ADAMTS13(vWF cleaving protease) deficiency
  - Presence of anti-ADAMTS13 antibody
  - Arrange urgent plasma exchange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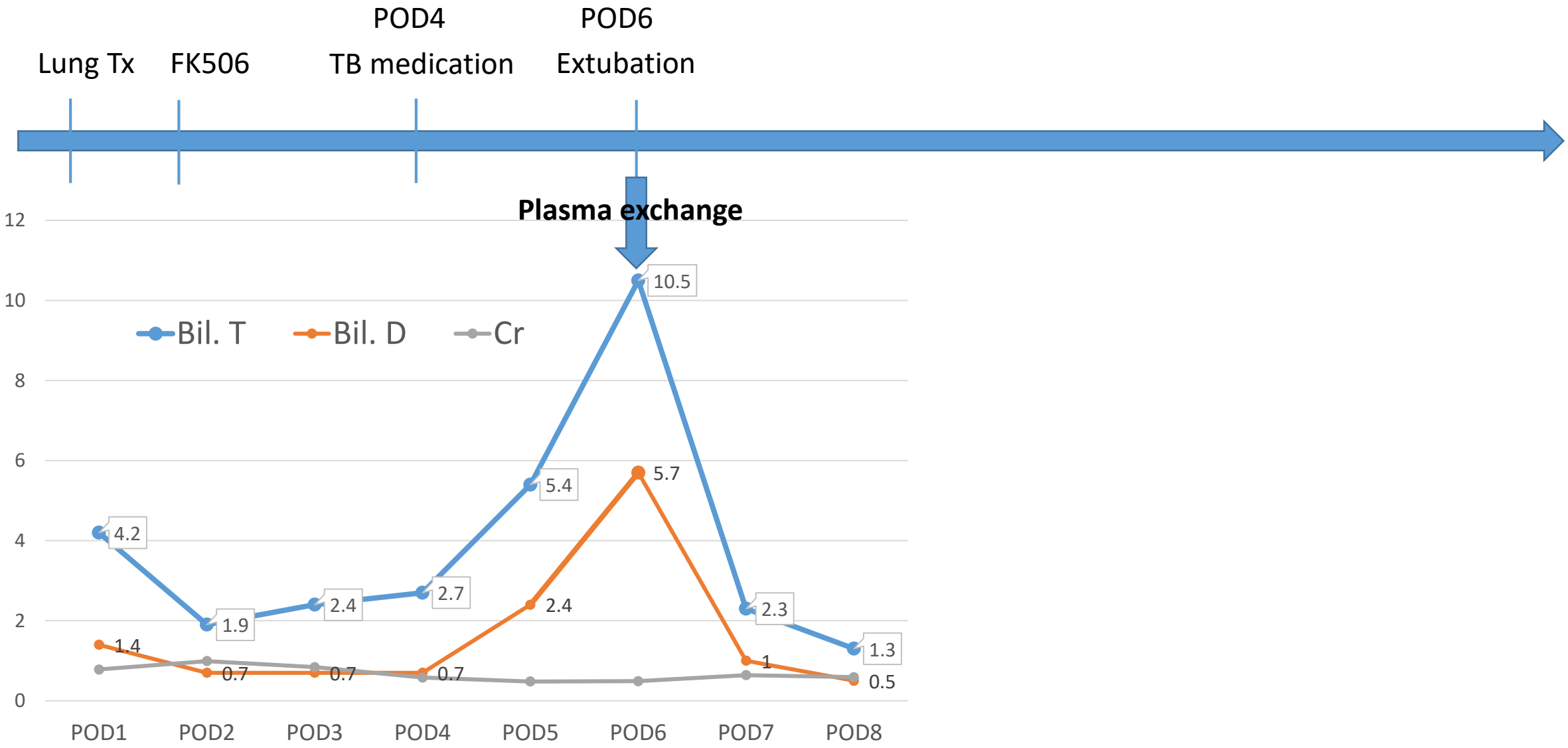
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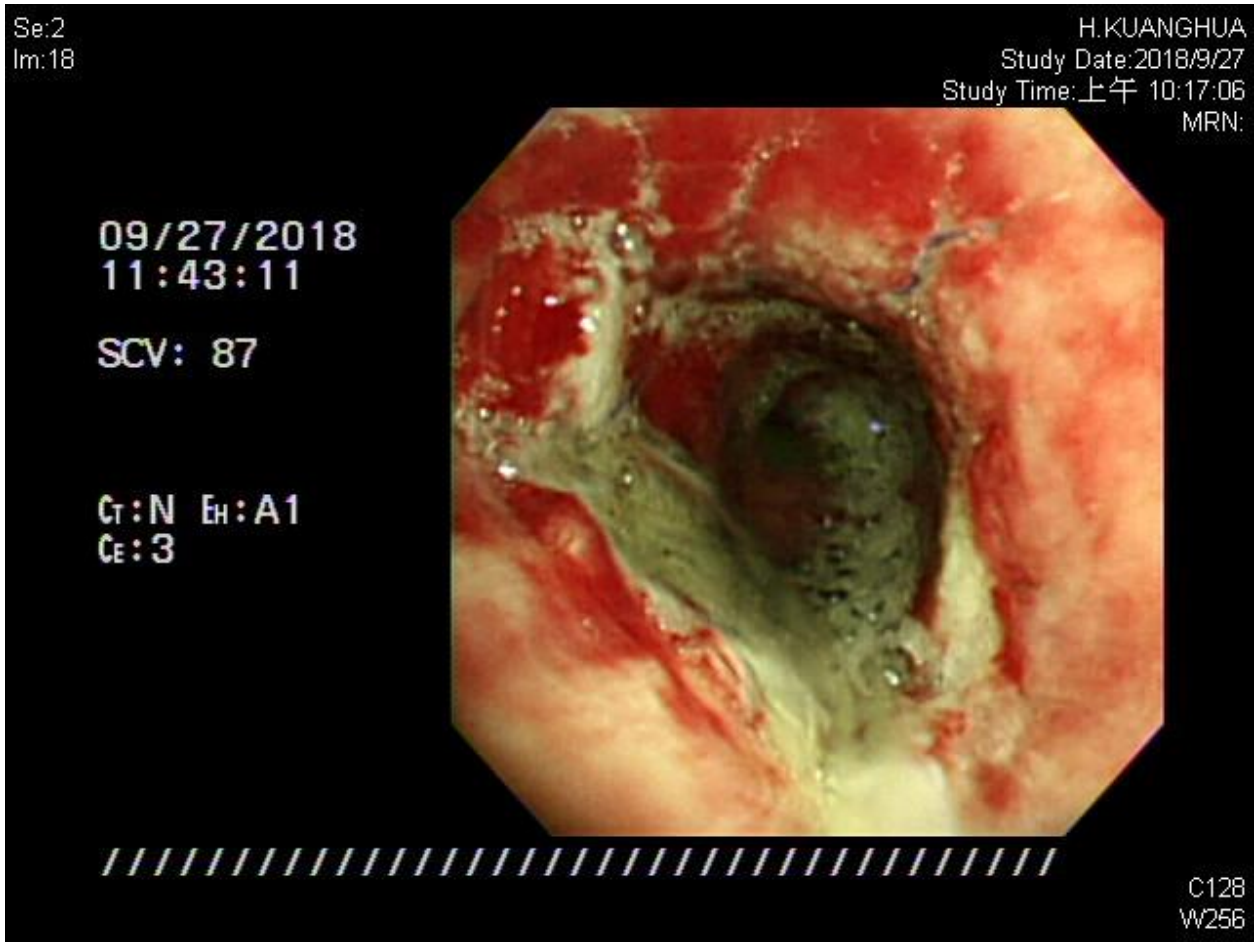
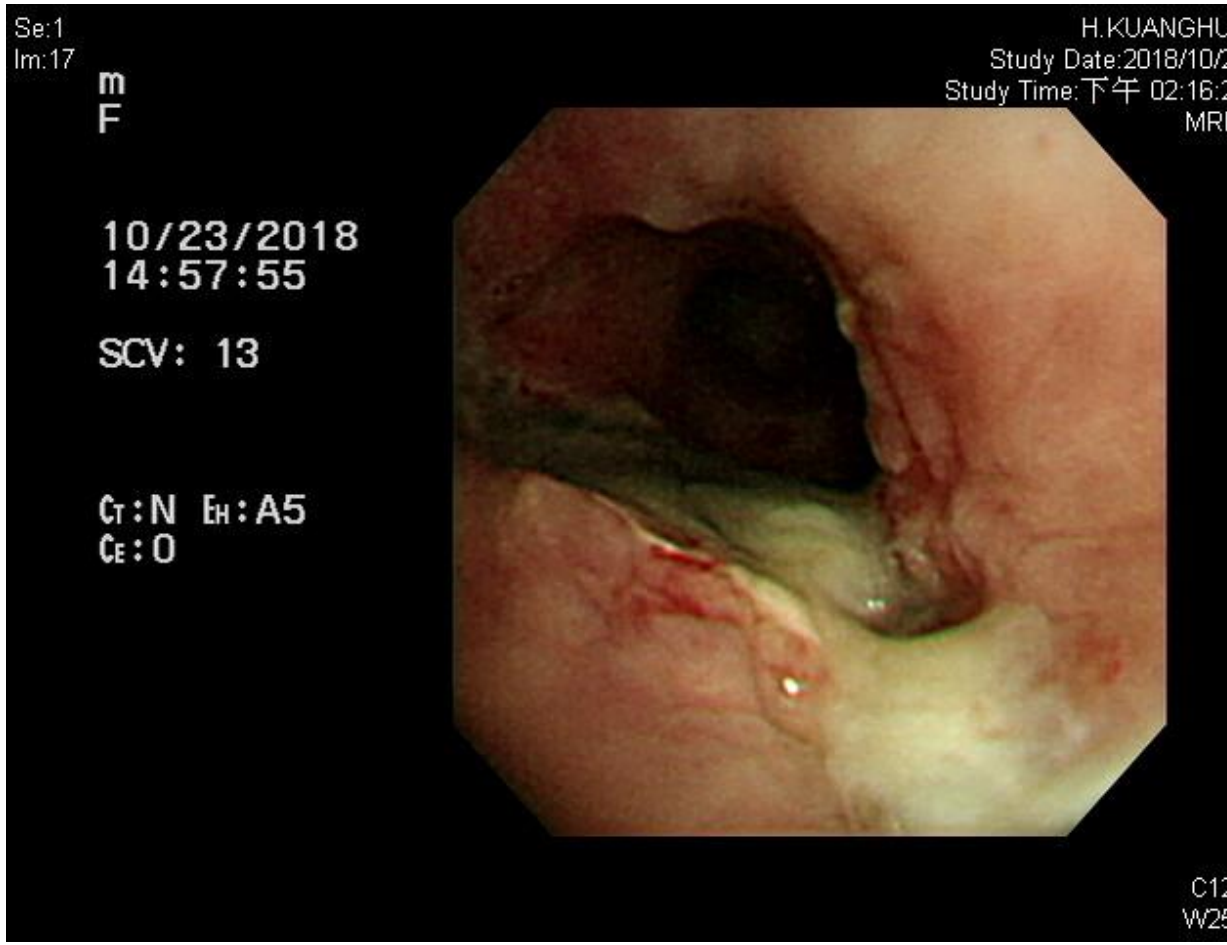
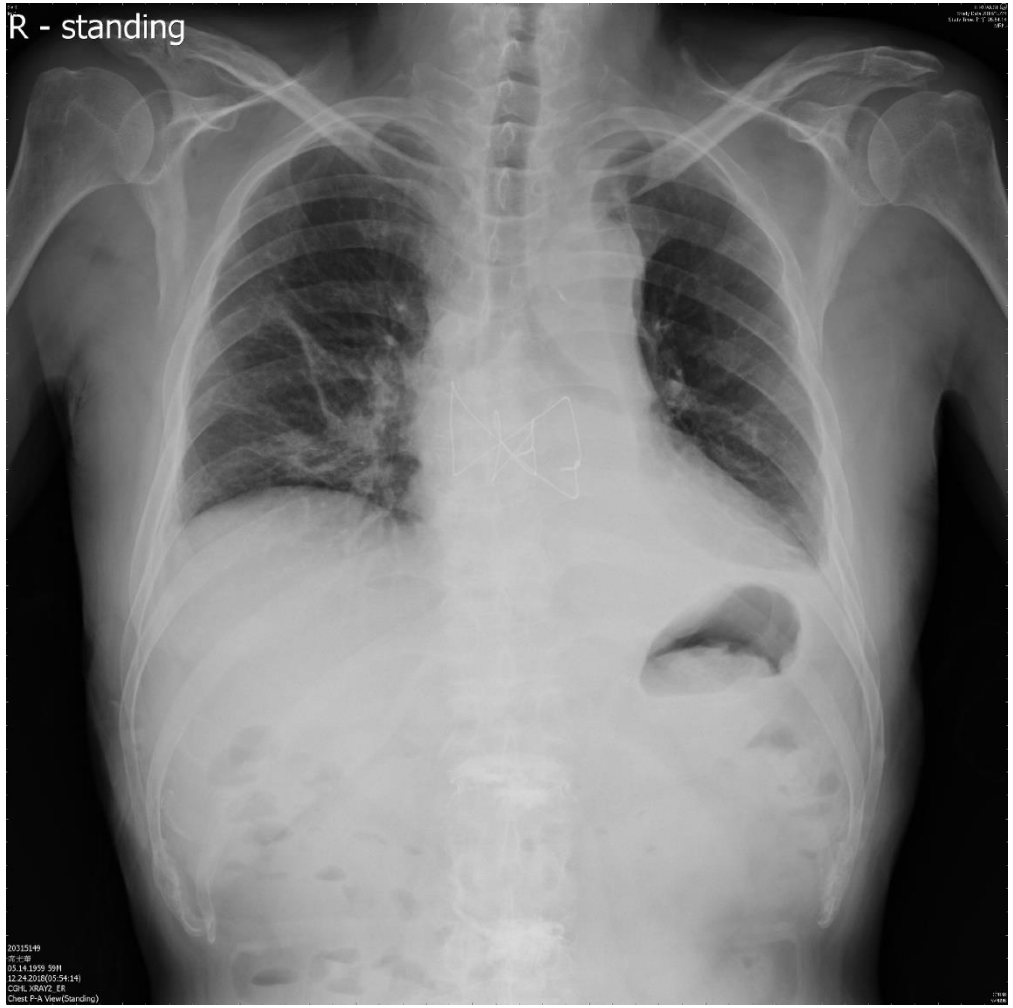
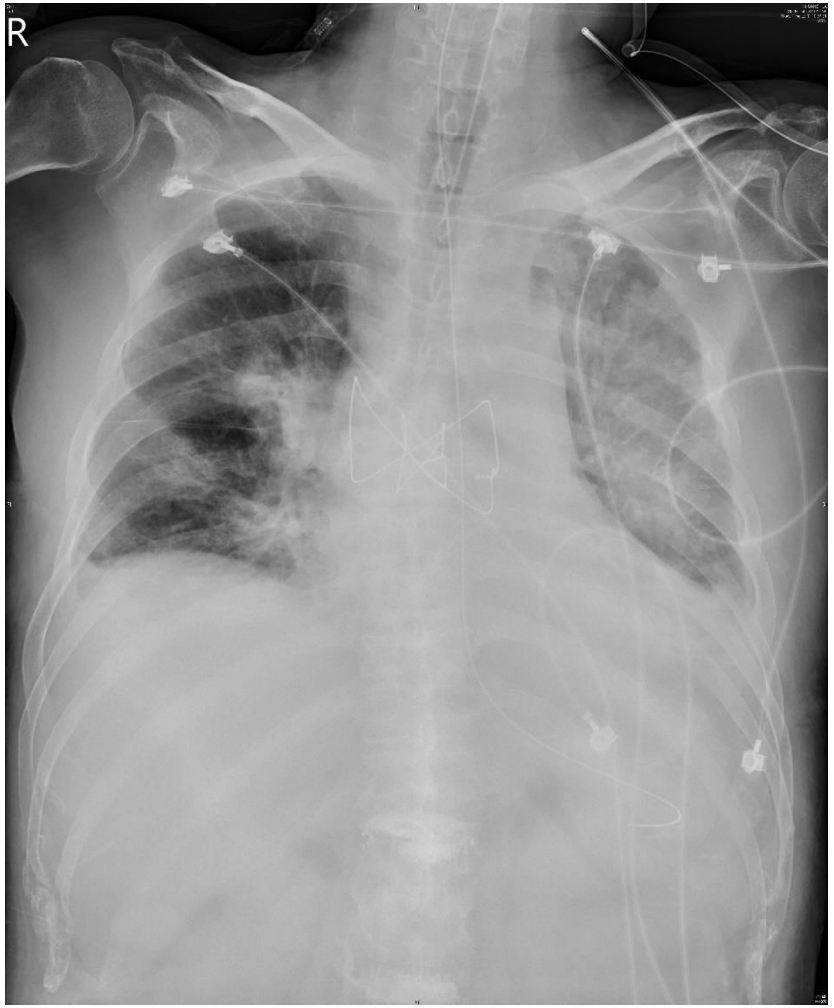
Bronchial anastomosis dehiscence



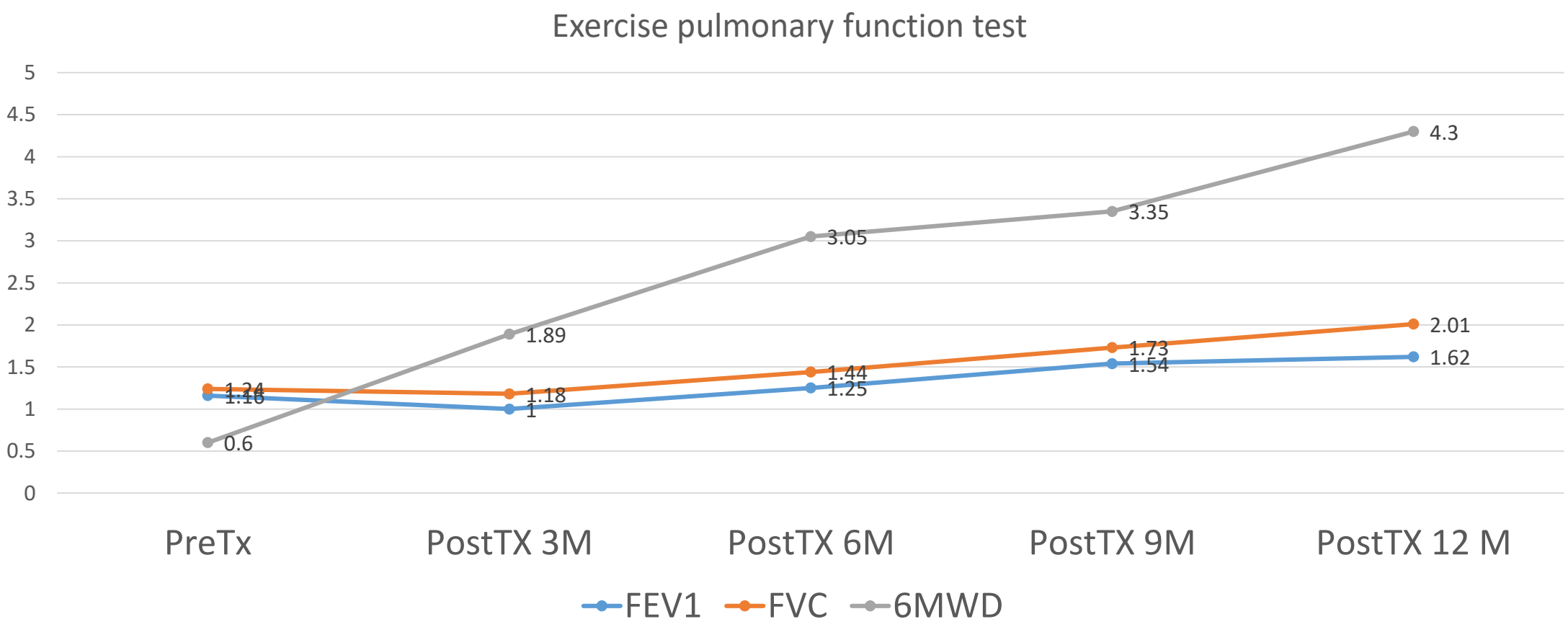


Post-transplant 90 days , Influenza A, H1N1





Post-transplant 1 year and 3 months



Clinical presentation of De novo TMA following lung transplantation

Hallmark	Clinic	Biochemy
Non-immune hemolytic anemia	Fatigue, pallor, icterus	Low hemoglobin and hepatoglobin High reticulocytosis, LDH and indirect Bilirubin Schistocytes Negative coombs test
Thrombocytopenia	Mucosal bleeding, purpura	Thrombocytopenia
Microvascular thrombosis Renal Cerebral Coronary Pulmonary Mesenteric	 Oliguria, hypertension Focal neurological deficit, confusion Visual disturbances Chest pain, conduction defects Diffuse alveolar hemorrhage Abdominal pain	High creatinine

Transplantation associated TMA

	Liver	Lung	Visceral	Heart	Kidney	HSCT
Incidence	4%	2.3%	?	Rare	0.8~14%	8.2%
Onset	2 weeks	37 weeks	8 weeks	2 years	<3 months	7 weeks
Survival	73.6%	71.4%	66.7%	40.0%	80% graft recovery	25–39%
Risk factors	Stop PI < 1 week post transplantation HLA-sensitization ABO-incompatibility HCV Splenectomy Transplantation for FHF Longer anhepatic phase	History of TMA Female gender CNI + mTORi Concurrent disease	Acute rejection		CMV, parvovirus 19 Deceased donor Anti-phospholipid antibodies	Female gender Older age Unrelated or HLA-mismatched donor GVHD Systemic infection Advanced or refractory disease for which the transplant was done PI:

Conclusion

- TMA is a rare but serious complication of organ transplantation
- Diagnosis: thrombocytopenia + Coombs negative hemolysis without a more likely explanation
- Plasma exchange has no proven value in TA-TMA
- Solid organ transplantation(including lung transplantation) require a multidisciplinary team to provide comprehensive post-transplant care.