Case (65/F)

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호흡기내과
최하영

Chief complaint

- **Productive cough and blood-tinged sputum**
  - Onset: 2 years ago
  - Aggravated recently

Present illness

- 약 2년 전부터 타원에서 **기관지확장증** 및 **비결핵 항산균 폐 질환 의심** 진단하에 점액용해제 약물을 복용해오던 환자로, 최근 기침, 가래 및 객혈 증세가 악화하여 내원함
  - 타원 기록: 2년 전 폐포 세척액 검사에서 비결핵 항산균이 배양 되었으나 동정 검사 의뢰하지 않음

Review of System

- Fever/Chill (-/-)
- **Cough/Sputum** (+/+)
- Pleuritic chest pain (-)
- **Dyspnea** (+): **mMRC Grade 1**

Past Medical History

- **Chronic hepatitis B** on regular follow-up
- Operation Hx. : **subarachnoid hemorrhage**

- No known DM, HTN, Pulmonary TB

- Medication Hx. : **carvedilol** and **mucolytics** (N-acetylcysteine, erdosteine)

Physical examination

- General appearance – Chronic ill-looking appearance
- Chest
  - Bronchial breath sound with crackles in both lung fields
  - Regular heartbeat without murmur

Vital Sign

- HR – 80회/min
- RR – 20회/min
- BP – 130/80 mmHg
- Body temperature – 36.8^{o}C

Laboratory findings

- WBC 4,990/mm^3
- Hb 12.5 mg/dL
- Platelet 163K/mm^3

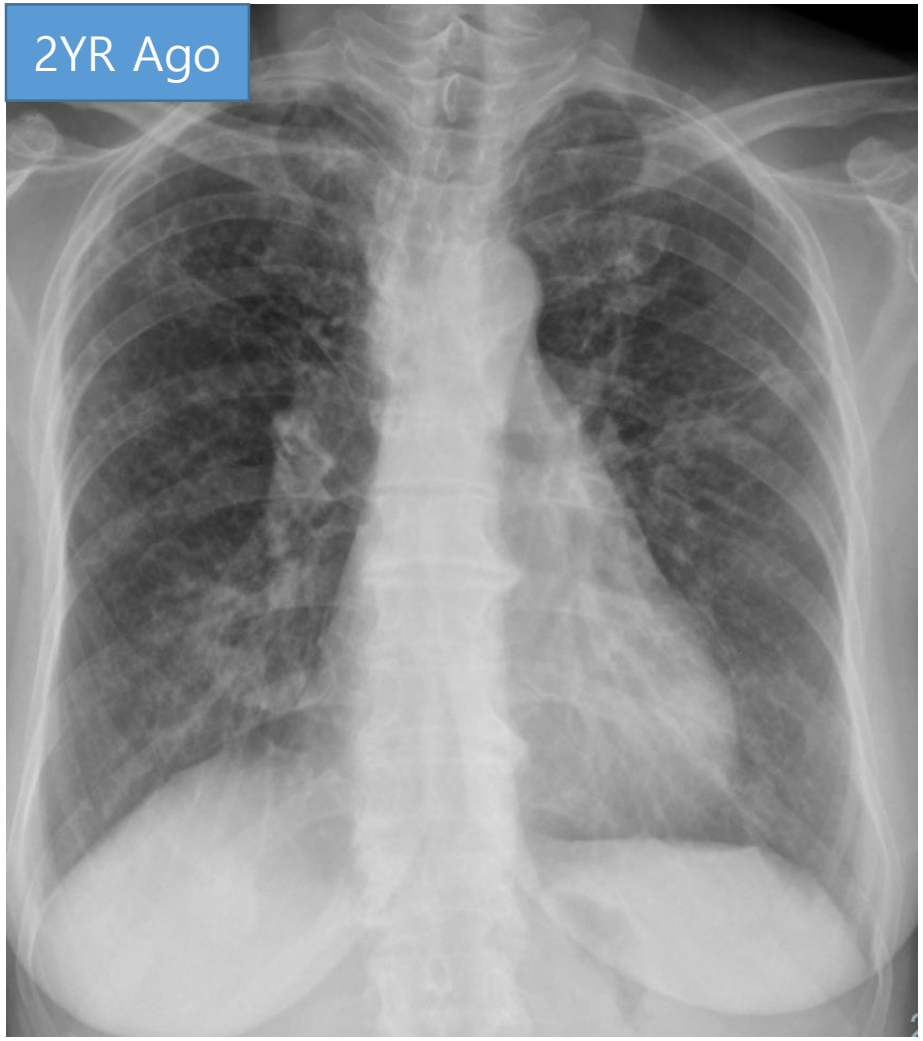
- **ESR 98 mm/hr**
- **CRP 5.8 mg/L**

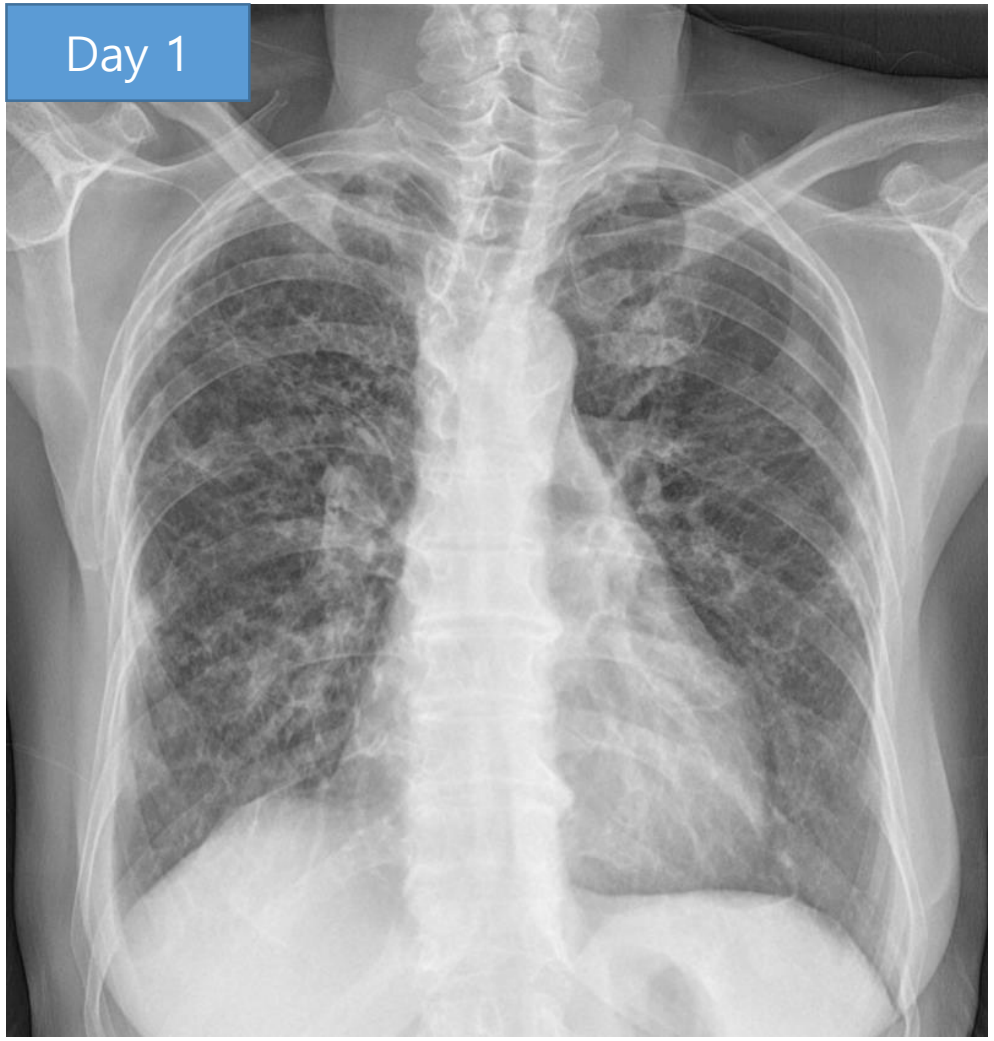
- **BUN 9.7 mg/dL**
- Cr 0.53 mg/dL

- **AST 46 IU/L**
- ALT 36 IU/L

- Bilirubin, total 0.7 mg/dL
- **Albumin 3.2 g/dL**

Chest X-ray

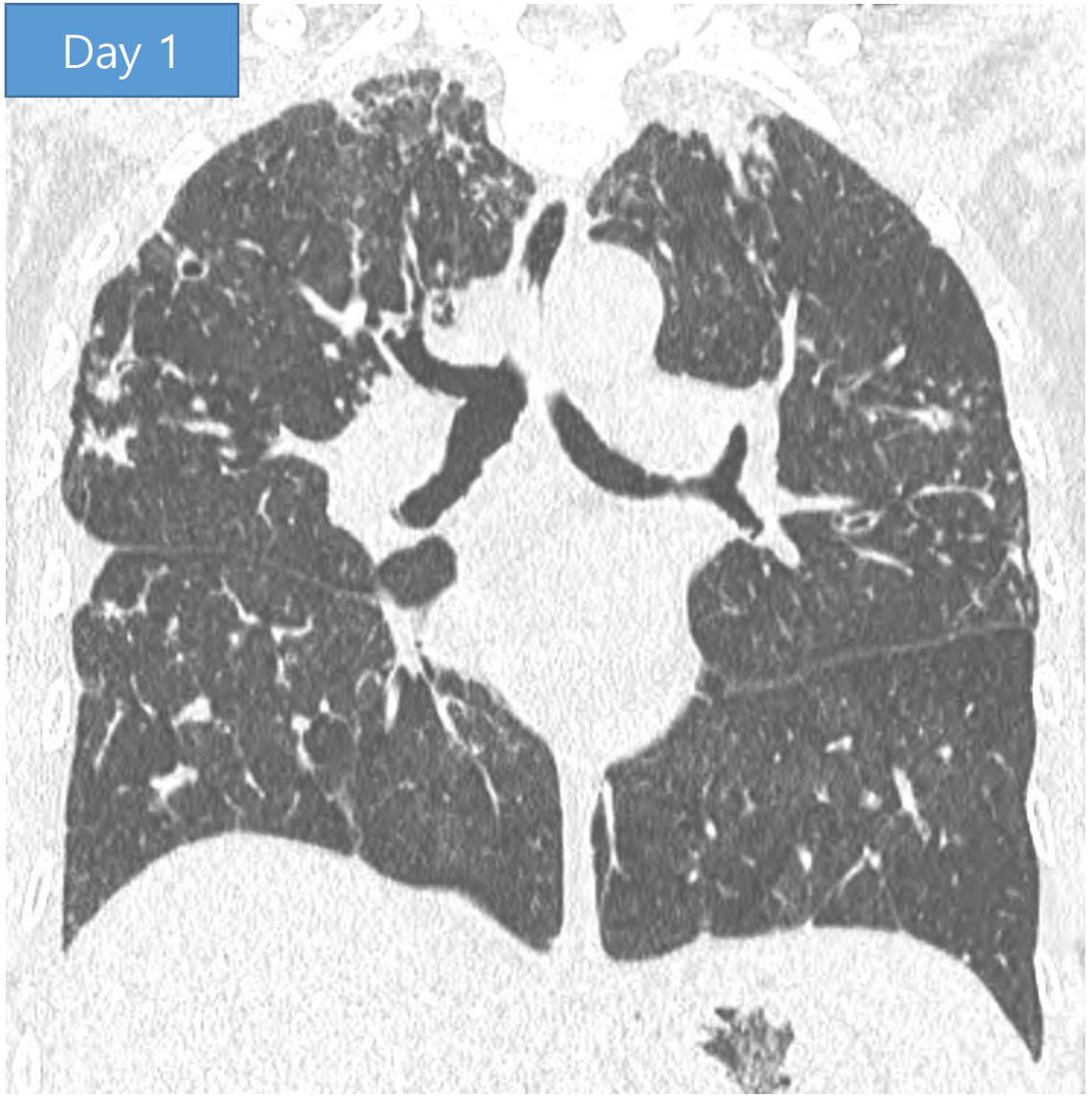




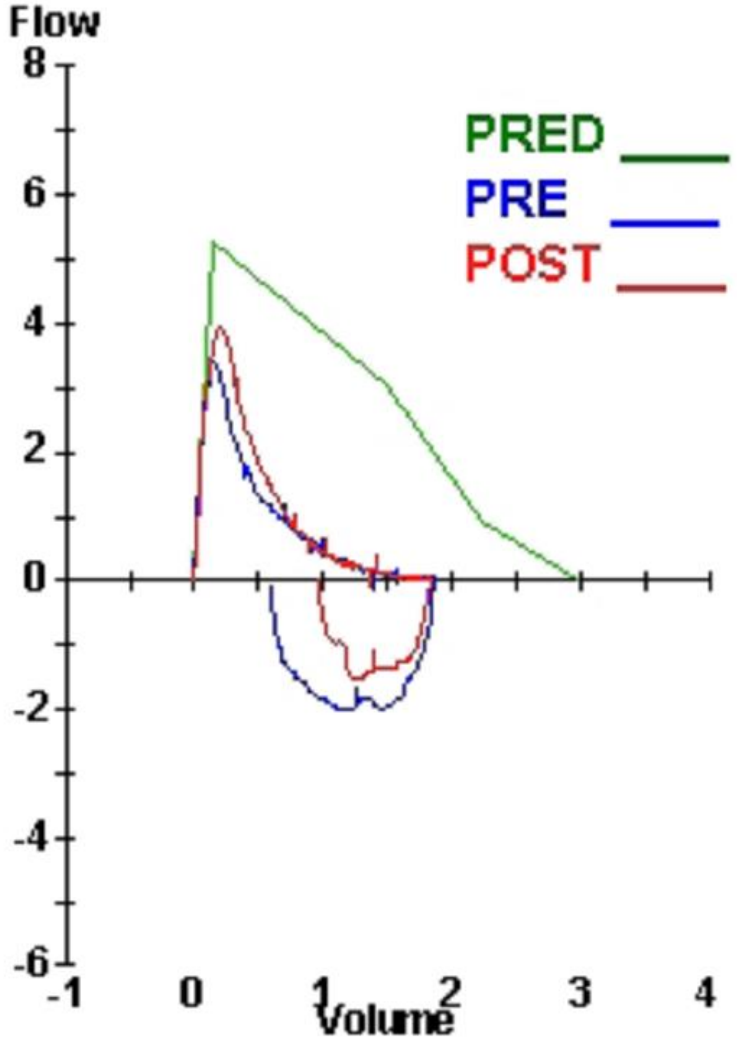
Chest CT

2YR Ago

Day 1



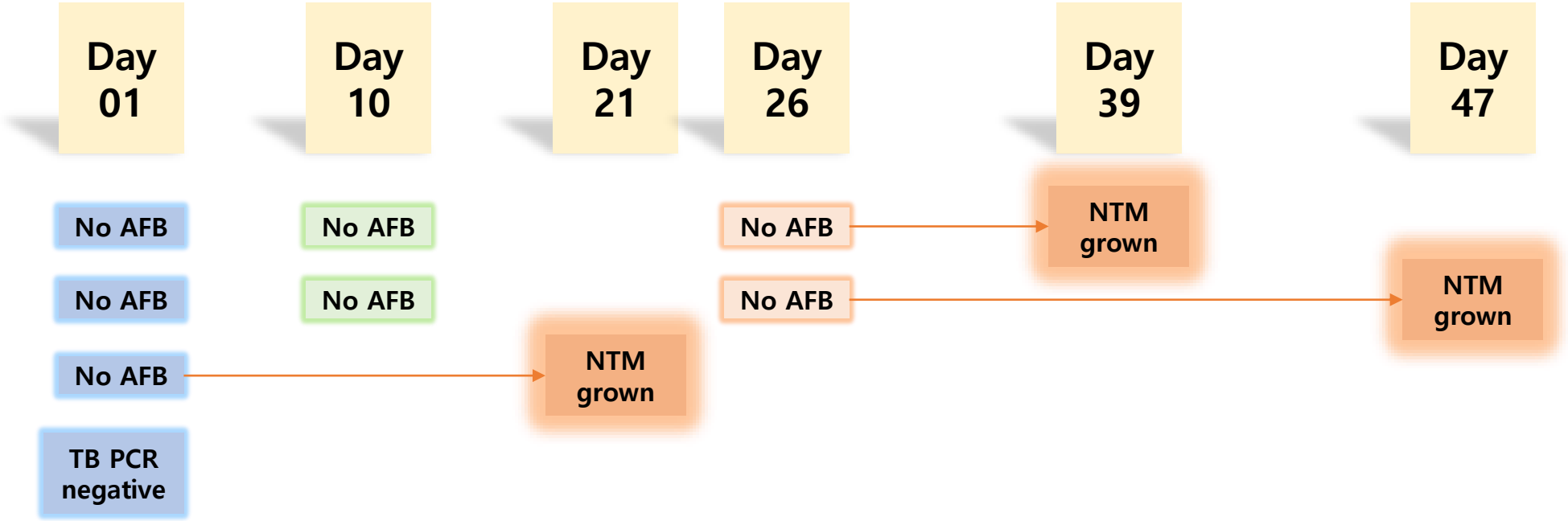
Pulmonary function test



- **FEV1/FVC 54%**

- **FEV1** 1.02L (**44%** pred)
- **FVC** 1.88L (**63%** pred)

Microbiology



M. scrofulaceum

M. scrofulaceum + *M. chelonae*

M. scrofulaceum

Assessment

- *M. scrofulaceum* lung disease
- Bronchiectasis

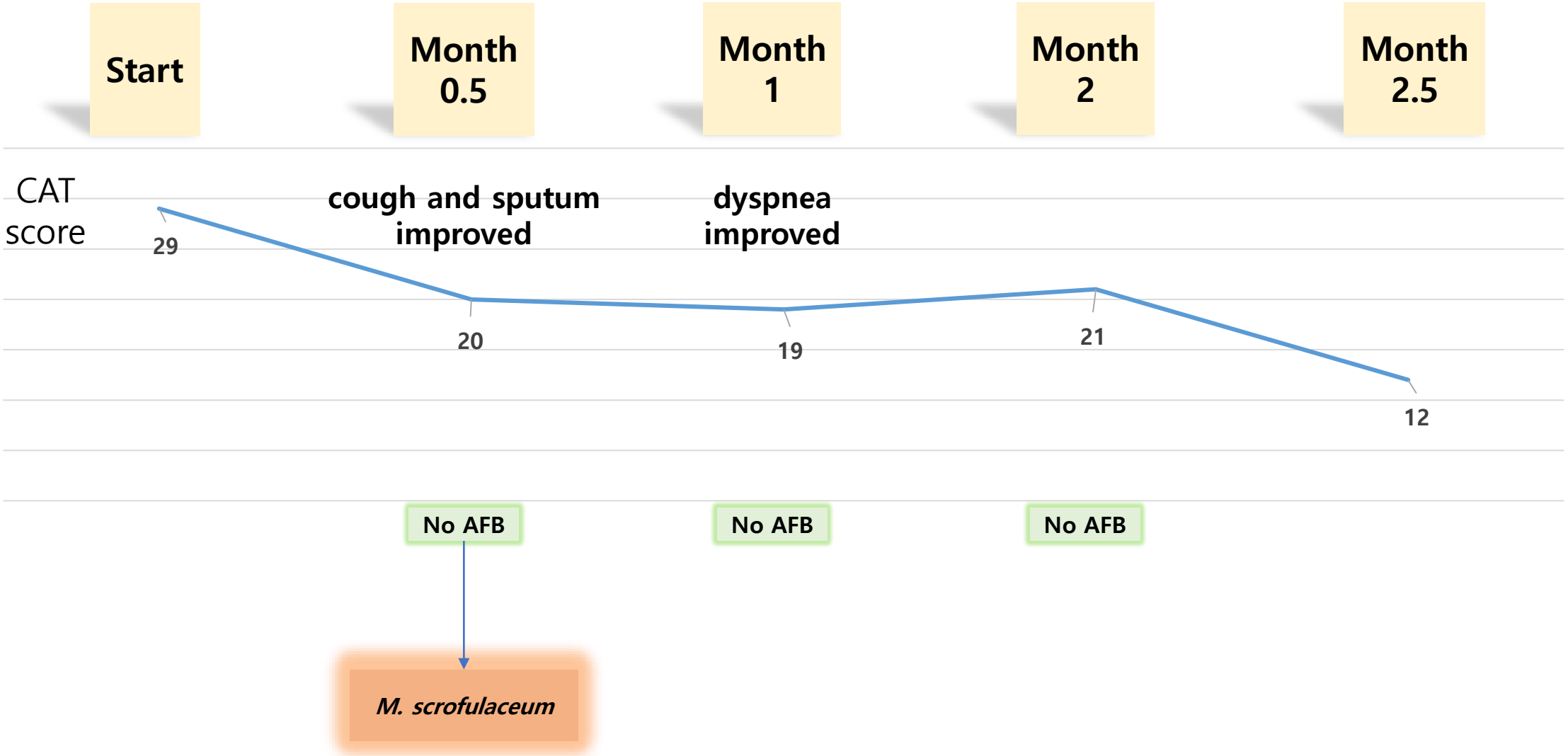
Treatment

- *M. scrofulaceum* lung disease treatment
  - No drug susceptibility test

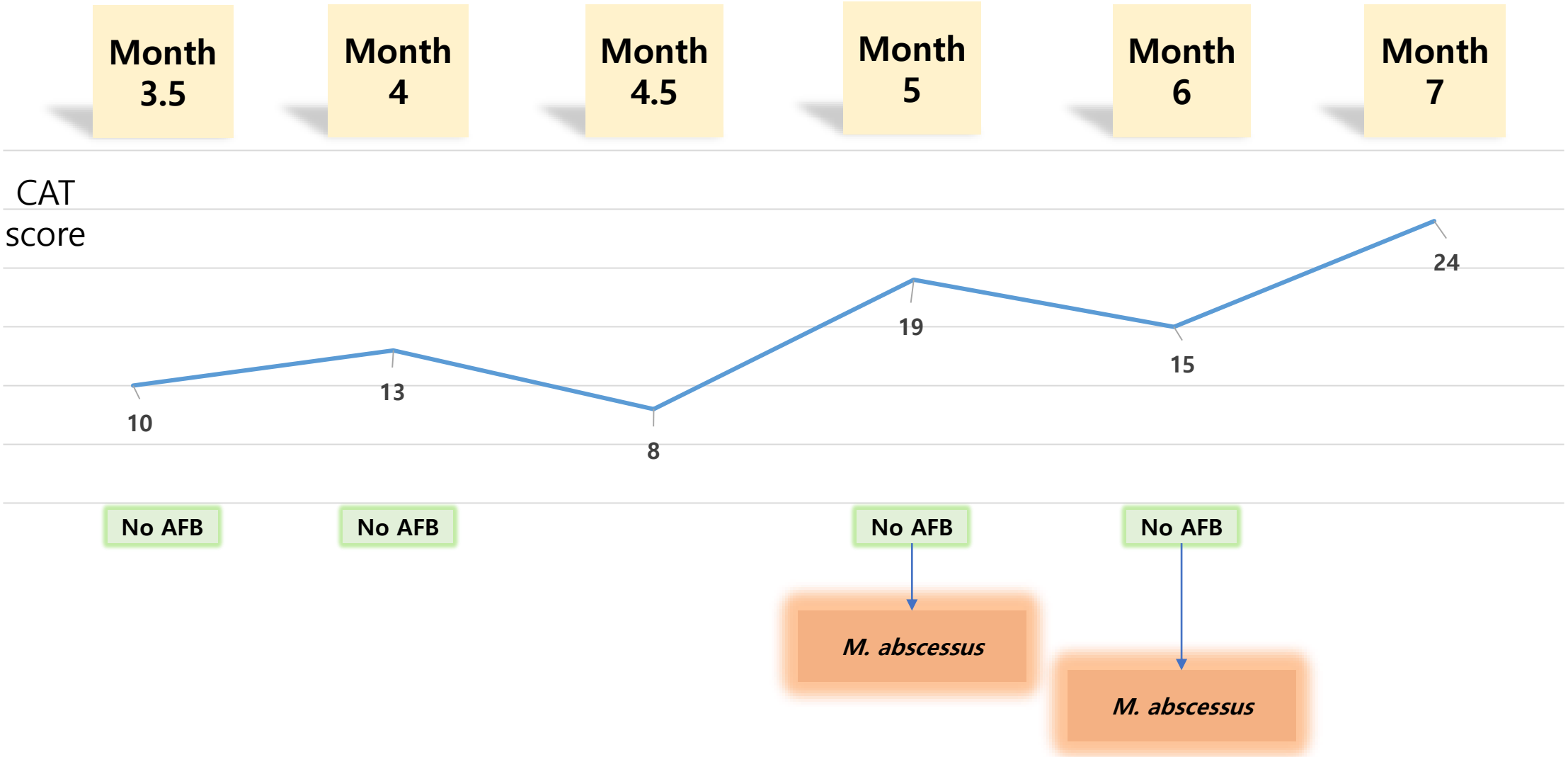
  - Azithromycin 500mg
  - Rifampicin 600mg
  - Ethambutol 1200mg
    - three times a week

Progression

Treatment course



Treatment course



What is your next plan?

1. Continue ***M. scrofulaceum*** treatment
2. Start **mixed NTM infection** treatment (*M. scrofulaceum* + *M. abscessus*)
3. Stop *M. scrofulaceum* treatment and start ***M. abscessus*** treatment
4. Stop *M. scrofulaceum* treatment; **wait and see** when it comes to *M. abscessus* treatment

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Clinical Characteristics and Treatment Outcomes of Patients with Acquired Macrolide-Resistant *Mycobacterium abscessus* Lung Disease

Hayoung Choi,[a] Su-Young Kim,[a] Dae Hun Kim,[a] Hee Jae Huh,[b] Chang-Seok Ki,[b] Nam Yong Lee,[b] Seung-Heon Lee,[c] Soyoun Shin,[c] Sung Jae Shin,[d] Charles L. Daley,[e] Won-Jung Koh[a]

약제명	시험농도	결과 MIC	판정
Clarithromycin	0.5-64	<=0.5, >64	IR

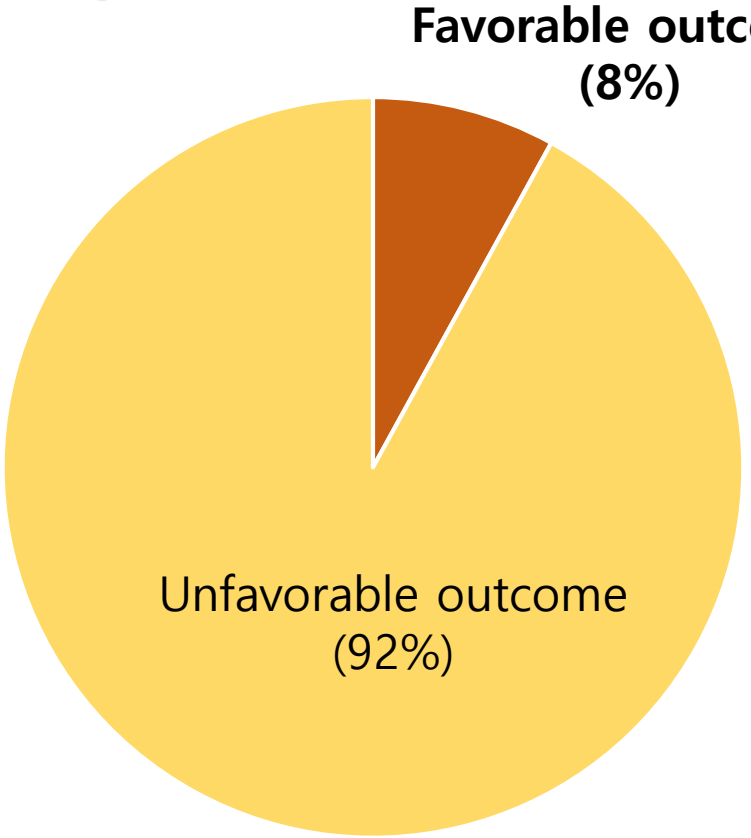
Inducible resistance

- *erm*(41) gene mutation

Clarithromycin	0.5-64	>64	R

Acquired resistance

- *rrl* gene mutation



Treatment duration, months
: 24.0 (16.0-43.0)

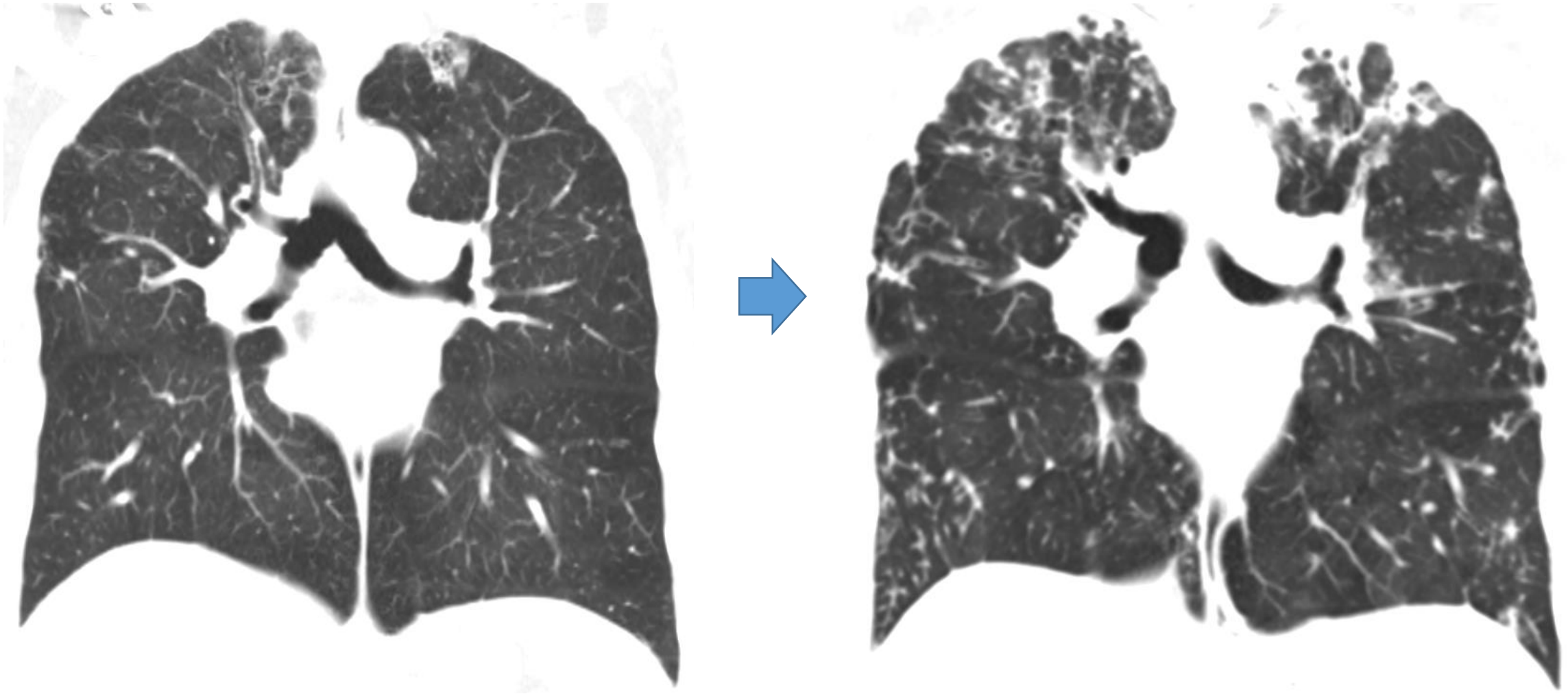
What is your next plan?

1. ✖ Continue ***M. scrofulaceum*** treatment
2. ✖ Start **mixed NTM infection** treatment (*M. scrofulaceum* + *M. abscessus*)
3. Stop *M. scrofulaceum* treatment and start ***M. abscessus*** treatment
4. Stop *M. scrofulaceum* treatment; **wait and see** when it comes to *M. abscessus* treatment

Assessment

- *M. abscessus* lung disease
- s/p *M. scrofulaceum* lung disease
- Bronchiectasis

Chest CT



Microbiology

Date	AFB smear	AFB culture
2018-06-08	negative	*M. scrofulaceum*
2018-07-04	negative	*M. scrofulaceum*
2018-08-27	negative	negative
2018-09-17	negative	negative
2018-10-29	negative	negative
2018-12-10	negative	***M. abscessus***
2019-01-21	negative	***M. abscessus***
2019-04-05	negative	***M. abscessus***
2019-07-29	negative	***M. abscessus***
	1+	***M. abscessus***
	1+	***M. abscessus***

➳ Start treatment for *M. abscessus* lung disease

Brief Review – *M. scrofulaceum* Lung Disease

M. scrofulaceum

- slow-growing mycobacterial species
- wide range of environments
  - house dust, tap water, and soil
- Origin: **scrofula**-like infections in children

Latin
scrofa (breeding sow)

Late Latin
scrofula
(swellings of neck LN)

Can J Microbiol 1957;3:91-100
Infect Dis 2019;51:602-609

Epidemiology

- Well-known cause of **pediatric cervical lymphadenitis**?
  - report since 1950s
  - abrupt change of predominant etiology from ***M. scrofulaceum*** **to MAC in 1970s**
  - taxonomic similarity: *M. avium-intracellulare-scrofulaceum* (MAIS)
  - difficulty in sub-species identification

- **2–3%** of all mycobacterial isolates in the USA (1980)
  - *M. scrofulaceum* disease in adults is rare
  - unclear clinical manifestation and management strategies

Can J Microbiol 1957;3:91-100
Infect Dis 2019;51:602-609
Clin Infect Dis 1995;20:954-963
J Infect Dis 1982;146:829-833

INT J TUBERC LUNG DIS 3(6):501–507

Mycobacterium kansasii and *M. scrofulaceum* isolates from HIV-negative South African gold miners: incidence, clinical significance and radiology

- 1993–1996
- Single center in South Africa (n = 41)
- Sole tertiary center for miners working for a large mining company

Characteristics	N = 41
Age ± SD	44.1 ± 7.4
Sex, male	41/41 (100)
Smear positive	35/41 (85)
History of TB treatment	21/41 (55)
Cavitation at diagnosis	31/35 (89)
Underlying silicosis	24/35 (69)

- Combination of 3–4 drugs
  - Rifampicin
  - Isoniazid
  - Ethambutol
  - Streptomycin
  - Terizodone

    ➠ Treatment failure: 12%

✓Risk factors: chronic structural lung disease or environmental exposure

✓Limitation: gold miners with lung destruction

Int J Tuberc Lung Dis 1999;3:501-507

J Infect Chemother 22 (2016) 611–616

Clinical characteristics of pulmonary *Mycobacterium scrofulaceum* disease in 2001–2011: A case series and literature review

- 2001–2011
- Two hospitals in Japan (n = 8) and Literature review (n = 23)

Characteristics	N = 31	N = 41
Age ± SD	**63.8 ± 13.6**	44.1 ± 7.4
Sex, male	**19/31 (61)**	41/41 (100)
Smear positive	**20/31 (65)**	35/41 (85)
History of TB treatment	**7/31 (23)**	21/41 (55)
Underlying pulmonary MAC disease	**5/31 (16)**	Unknown
Underlying COPD	**5/31 (16)**	Unknown
Cavitation at diagnosis	**19/31 (61)**	31/35 (89)
Underlying silicosis	**0/31 (0)**	24/35 (69)

- Treatment – 3/8 from Japan cohort

Case	Age (yr)	Sex	Drug (mg)	Duration (mo)	Outcome
1	74	Male	RFP (600) + EMB (500) + CLR (800)	49	Continue Tx
2	70	Male	RFP (450) + EMB (750) + CLR (600)	2	FU loss
3	48	Male	RFP + EMB + ethionamide	18	Improved
			(5-year interval)		
			INH (300) + EMB (750) + AZM (500 EOD)	34	Improved

J Infect Chemother 2016;22:611-616

- Treatment – 20/23 from literature review

Case	Age (yr)	Sex	Drug (mg)	Outcome
1	46	M	RFP + EMB + CLR	Improved
2	47	M	INH + RFP + EMB + CLR	Improved
3	68	M	INH + RFP + EMB + CLR + SM	Improved
4	56	M	INH + RFP + EMB + CLR	No change
5	59	M	INH + RFP + EMB + CLR	Improved
15	46	M	INH + RFP + PZA + CLR	No change
16	70	M	INH + RFP + EMB + SM	Advanced
17	51	F	INH + RFP + EMB	No change
18	74	F	INH + RFP + KM	No change
19	77	F	INH + RFP + EMB + PZA + AMK	No change
20	82	F	INH + RFP + SM	Improved

J Infect Chemother 2016;22:611-616

Mycobacterium scrofulaceum disease: experience from a tertiary medical centre and review of the literature

- 2000–2015
- Single center in the USA (n = 10)
  - **Pulmonary and pleural infection (n = 4)**
  - Bone and joint infection with a foreign body (n = 2)
  - Skin and soft tissue infection (n = 2)
  - Brain abscess (n = 1)
  - Pediatric cervical adenitis (n = 1)

Infect Dis 2019;51:602-609

- Six patients extrapulmonary disease
  - all resolved with treatment for 0.5–12 months
- Four patients with pulmonary disease

Age/sex	AFB smear	Treatment	Duration (mo)	Outcome
91/F	Positive	AZM + LVF → AZM + MXF + Rifabutin → AZM + Linezolid + Rifabutin	16	Progression/ deceased
77/F	Negative	CLR + EMB + RFP	18 mo (12 mo after conversion)	Improved
63/M	Positive	AZM + RFP + EMB + INH	23 mo	Improved
75/M	Negative	Not started	-	Deceased – pulmonary hemorrhage

Infect Dis 2019;51:602-609

Summary

- ***M. scrofulaceum* pulmonary disease**
  - Rare NTM infection
  - Previous study – case series mostly
  - Risk factors: chronic structural lung disease or environmental exposure
  - Macrolide-based antibiotics combination treatment
    - MAC treatment regimen?
    - CLSI 2018
  - Generally favorable treatment outcomes

경청해주셔서 감사합니다.