

 happinnovation 20\*20

삼성서울병원

# Case (74/F)

삼성서울병원  
호흡기내과  
전임의 이현

# Case (74/F)

- Chief complaint

- Cough

- Onset: 1 month ago

- Present illness

- 약 2개월 전 폐결핵 및 기관지 결핵으로 OO보건소에서 2HREZ/4HRE로 치료 후 완치 받은 환자로 약 1개월 전부터 다시 기침이 발생하여 본원 호흡기 내과 외래에 내원함.

# Case (74/F)

- Past history

- Pul TB, EBTB (초치료, S+/C+/PCR+/Cavity-, INH-R)

- 2004.8. 7. 도말 양성 폐결핵으로 초치료 시작

- 2004.8.10. 본원 호흡기 내과 내원

- Bronchial washing: S+/C+/PCR+

- DST (KIT): R to INH, S to other drugs

- 2004.8. ~ 2005.2. 치료 종료 (2HREZ/4HRE)

- DM/HTN/Hepatitis (-/-/-)

# Case (74/F)

- Systemic Review

- Fever/Chill (-/-)
- Cough/Sputum (+/+)
- Dyspnea (+)

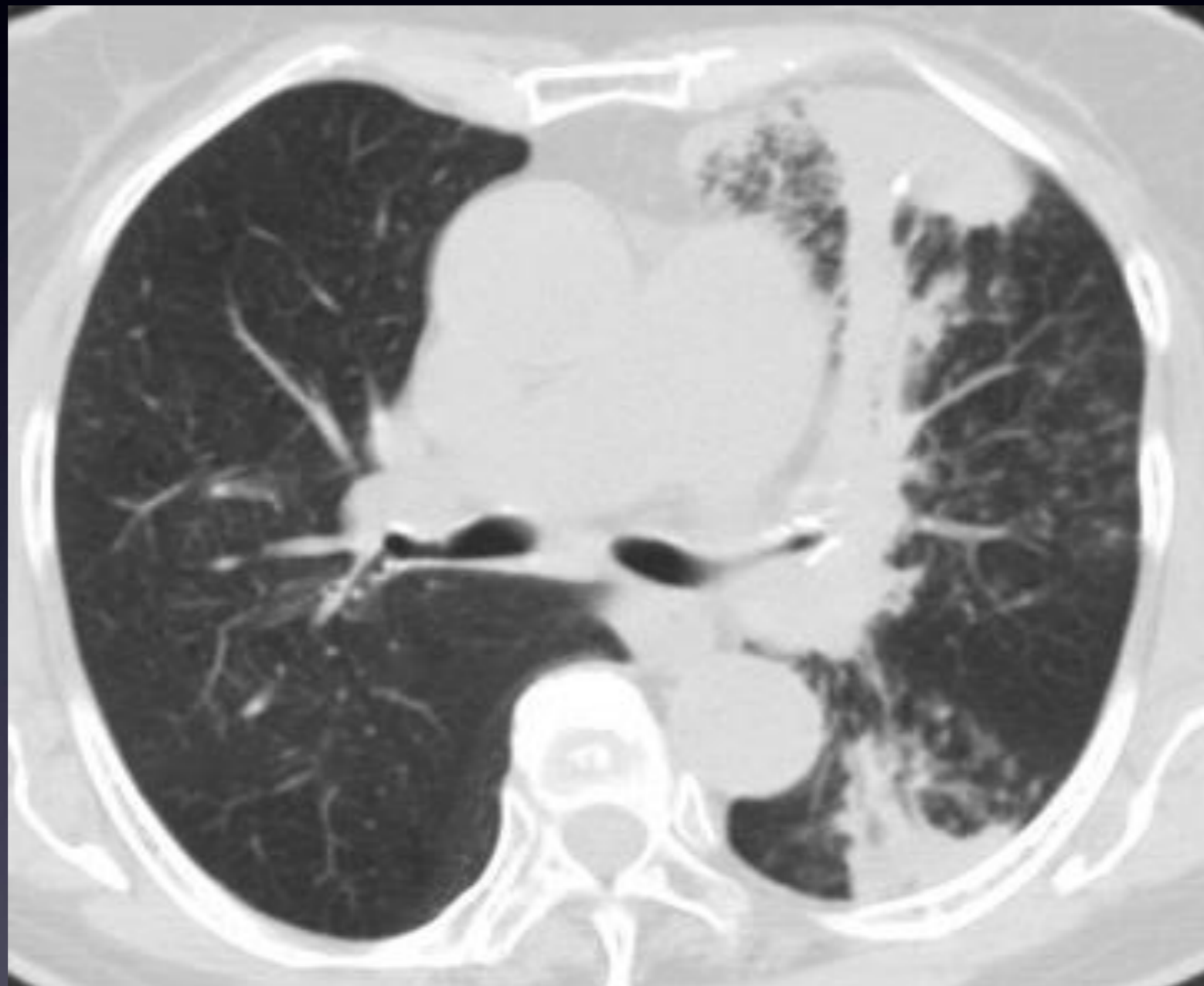
- Physical Exam

- Bronchial breathing sound with wheezing in left chest

# Chest X-ray



# Chest CT



# Progression

- 2005.04.04. REZ 재치료 시작
  - Bronchial washing: S 3+, PCR +, C+
  - DST (KIT): R to INH, S to other drugs
- 2005.08.04. 치료 4개월 S+/C+
- 2005.11.07. 치료 7개월 S+/C+
- 2005.12.05. 치료 실패 판정
  - REZ LFLX CS SM (750mg 주 3회) 변경

# Progression

- 2006.02.07
  - RE, LFLX CS SM (750mg 주 2회) 변경
  - DST (2010.11.07.객담): R to INH, PZA, S to other drugs
- 2006.03.14.
  - SM 중단, RE LFLX, CS
- 2006.12.05.
  - 치료종결 (완치, 06.02.07. 약제 변경 후 C-)

## Topic

# Treatment Regimen and Outcome of Isoniazid Resistant Pulmonary Tuberculosis

# Isoniazid mono-resistant TB

- Definition

- Resistance to INH alone or INH plus SM and S to other first-line drugs
  - First line drugs - INH, RFP, EMB, PRZ, SM

- Incidence

- **Most common** drug resistance
  - 13% Including new and retreatment cases worldwide
  - 5% in new cases and 7% in retreatment cases in Korea

# Treatment of INH-R TB

- Treatment outcomes
  - **Poor** compared to those of drug sensitive TB
    - INH resistance is associated with **higher treatment failure, relapse, and acquired drug resistance**
- Obstacles for the successful treatment

**No optimal regimen  
and  
duration of treatment**

**Probably insufficient  
numbers of effective  
drugs**

Espinal et al, JAMA, 2000  
Seung, CID, 2004  
Menzies, Plos Med, 2009

# Current treatment regimen

Current guidelines	Recommended regimen	Fluoroquinolone
WHO	6-9REZ	<p><b>May be used to strengthen treatment regimens for INH-resistant TB, especially in those with extensive disease</b></p>
ATS/CDC/IDSA	6REZ	
UK	2REZ + 10RE	-

WHO guideline, 2014  
 ATS/CDC/IDSA guideline, 2007  
 NICE guideline, 2011

# Current guideline

- 권고요약

- INH를 중단하고 REZ를 유지하여 6-9개월간 치료 (IIIA)
- 병변의 범위가 넓고 심한 경우 Quinolone계 약제 추가를 고려(IIIB)
- 초치료 표준요법(HREZ)으로 치료를 시작한 후 PZA를 중단한 시점에서 INH 단독 내성으로 확인되면 INH를 중단하고 RE를 사용하여 총 12개월간 치료하는 것을 고려(IIIB).

결핵진료지침 (개정판) 2014

# Standard treatment in INH-R TB

- New cases
  - The risk of **treatment failure was greater** among cases with **any INH resistance** (RR, 3.06; 95% CI, 1.85–5.05;  $P < .001$ ) other than multidrug-resistant TB.
- Retreatment cases
  - Retreatment cases with **any INH resistance** other than multidrug resistance were **more likely to fail** (RR, 2.08; 95% CI, 1.30–3.35;  $P = .004$ ) than susceptible cases.

# Composition of drugs and Treatment outcomes

**Table 6.** Adjusted incidence rate ratios of failure, relapse, and acquired drug resistance in INH resistant strains.

Factor	Failure	Relapse	Acquired Drug Resistance <sup>a</sup>
<b>Duration of rifampin therapy</b>			
1–2 mo	<b>4.1 (1.2–13.4)</b>	<b>3.8 (1.6–9.0)</b>	0.7 (0.4–1.3)
3–4 mo	0.8 (0.2–5.0)	1.9 (0.7–5.2)	1.0 (0.3–3.0)
5–7 mo	1.0 (reference)	1.0 (reference)	1.0 (reference)
≥8 mo	1.6 (0.8–2.8)	1.0 (0.5–2.0)	2.1 (0.9–4.9)
Overall significance ( <i>p</i> -value) <sup>b</sup>	(0.004)	(0.02)	(0.20)
<b>Number of drugs in regimen to which strains sensitive</b>			
<i>Initial intensive phase</i>			
0 or 1 drug	<b>6.9 (1.4–33)</b>	<b>5.9 (1.0–33)</b>	No obs.
2 drugs	2.7 (0.7–10.0)	1.9 (0.6–6.7)	<b>18 (1.4–99)</b>
3 drugs	1.6 (0.4–6.0)	3.1 (0.9–9.9)	9.6 (0.8–99)
4 or more drugs	1.0 (reference)	1.0 (reference)	1.0 (reference)
Overall significance ( <i>p</i> -value) <sup>b</sup>	(0.06)	(0.12)	(0.25)
<i>Continuation phase</i>			
0 or 1 drug	2.5 (0.7–9.0)	1.0 (0.5–2.3)	1.8 (0.5–6.5)
2 drugs	2.2 (0.6–8.5)	1.2 (0.7–2.5)	1.2 (0.3–5.0)
3 or more drugs	1.0 (reference)	1.0 (reference)	1.0 (reference)
Overall significance ( <i>p</i> -value) <sup>b</sup>	(0.36)	(0.80)	(0.25)

# Factors associated with poor outcomes

	No	Countries	Unfavorable outcomes	Acquired drug resistance	Factors associated with poor outcome
1994-2001 <sup>a</sup>	60	Korea	13 (22%)	4 (7%)	<b>Cavitary</b> lesion Regimen without <b>RFP</b>
2001-2005 <sup>b</sup>	39	Korea	3 (8%)	2 (5%)	<b>Cavitary</b> & extensive lesions
1999-2010 <sup>c</sup>	89	UK	6 (7%)	6 (7%)	Poor adherence
2006-2007 <sup>d</sup>	134	Taiwan	20 (15%)	-	<b>Prior TB treatment</b>
2004-2011 <sup>e</sup>	395	Taiwan	67 (17%)	10 (3%)	<b>Cavitary</b> lesion <b>RFP</b> interruption Cancer

<sup>a</sup> Koh et al., TRD 2004; 56:248-260

<sup>b</sup> Kim et al., BMC infectious diseases 2008;8:6

<sup>c</sup> Munang ML et al., QJM. 2015; 108:19-25

<sup>d</sup> Wang et al., Plos One; 2014;9:e86316

<sup>e</sup> Chien et al., Clin Microbiol Infect 2015; 21:59-68

# Suggestion

- 초치료로 표준치료(2HREZ/4HRE)를 시행할 경우 재발 가능성이 높다.
- 재치료, 공동 양성이거나 병변이 넓은 환자는 quinolone을 추가하여 6-9개월 치료를 고려.