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Clinical Manifestations of Persistent Smear Positive and Culture Negative Sputum Tests 5 Months after First-line Anti-Tuberculous Chemotherapy

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Background: It is not known with certainty whether patients with persistently positive sputum smear results who have also had negative sputum culture results require prolongation of treatment for tuberculosis in order to avoid an increased risk of eventual relapse. The purpose of the present study was to retrospectively describe the treatment characteristics and evaluate the appropriate duration of treatment in these patients.

Methods: Sixty of 69 patients with sputum smear positive and culture negative tests at 5 months after first line anti-tuberculous chemotherapy from 2002 to 2003 were retrospectively analyzed. Exclusion criteria included incomplete treatment or resistance to rifampicin or two additional antibiotics, as determined by a drug susceptibility test (DST).

Results: Smear conversion of the study subjects was observed after 8.3 ± 2.3 months treatment, and the patients were culture negative after 2.0 ± 0.8 months. The relapse rates of the study subjects were 3.8, 10.0, and 25.8% after 1, 2, and 5 years of anti-tuberculosis chemotherapy, respectively. The relapse rates were not significantly affected by a series of risk factors such as age, sex, presence of diabetes, a sputum culture examination after 2 months treatment, previous treatment history, chest radiograph, and duration of the treatment ($p > 0.05$).

Conclusion: Regimen change is not required for patients with persistent smear positive but culture negative tests in the fifth month for first line antituberculous treatment. However, a further study will be needed to clarify the high relapse rate in this specific group of patients. *(Tuberc Respir Dis 2007;63:417-422)*

Key Words: Pulmonary tuberculosis, Acid-fast bacilli, Relapse

서   론

5~6   3~4

1.

2007

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2.

3,   5

2~5%   46

5~6

.   . Kaplan-Mer

log rank test

대상 및 방법   .

2002 1 1   2003 12 31   ### 결   과

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1,717   5

. 2   111   , 1   69

.   ,   60   .

,   ,   ,   3

,   ,   ,   ,

.   .

2   ,   3   2   9   2

,   , 1   12

,   ,   3   (Table 1).

.   8   19   11.6±2.0

(National   −3

Tuberculosis Association)[7].   7   3.3±2.1   (Table 1).

2   isoniazid (INH), rifampi-   INH   3   2   12

cin (RFP), ethambutol (EMB), pyrazinamide (PZA),   1   9   PZA

INH, RFP, EMB   ,   INH, RMP, EMB   .

, 2   .   48±16   ,   50

PZA   (83%)   .   14 (23%)   ,

[8].   46 (77%)   ,   12

±   SPSS   9   40   25.8±8.7   ,

(version 15.0, SPSS Inc, Chicago, Illinois, USA)   48   38.9±

.   20.7   (Table 2).

8.3±2.3   ,

,

Table 1. Treatment characteristics of the study subjects

Table 2. Demographic characteristics of the study subjects

	Non-relapse (n=48)(%)	Relapse (n=12)(%)
Age (years)	49.0±16.4	48.5±12.9
Male	39 (81)	11 (92)
DM	11 (23)	3 (25)
Patient category		
New	37 (77)	9 (75)
Relapse	4 (8)	3 (25)
Return after default	7 (15)	0 (0)
Treatment duration (month)	11.6±2.3	11.5±1.2
Follow-up duration (month)	38.9±20.7	25.8±8.7*

*means relapse time.

TD after SC*	Treatment duration (months)					
	8	9	10	11	12	≥13
<0	0	2	0	0	1	0
0~2	1	5	0	1	6	3
3~5	0	6	3	0	18	4
≥6	0	0	0	0	8	2

*TD after SC means treatment duration after smear conversion (months).

2.0±0.8   ,   2

    17 (28%)   ,

                37 (62%)   .

            2+   20 (33%)   (Table 3).

                    49 (81%)

    (Table 4).

          1   3.8%, 2   10%, 3   23.2%,

4   25.8%   40   .   ,

   ,   ,   2   ,   ,

                    (p＞0.05)(Table 5).

        12   18 (30%), 12   42

(70%)   ,   2 , 10

Table 3. Laboratory findings of the study subjects

	Non-relapse (n=48)(%)	Relapse (n=12)(%)
Smear conversion time (month)	8.2±2.1	8.9±2.8
Culture conversion time (month)	2.1±0.8	2.0±0.6
Positive sputum culture at 2 months of treatment	15 (31)	2 (17)
Drug susceptibility test		
Pansensitive	29 (61)	8 (67)
INH resistant	1 (2)	2 (17)
EMB resistant	2 (4)	0 (0)
Unknown	16 (33)	2 (17)
Negative sputum smear at completion of treatment	47 (98)	10 (83)
TD after SC*		
≥2	42 (88)	8 (67)
<2	6 (12)	4 (33)
Initial AFB smear		
1+	7 (15)	4 (33)
2+	16 (33)	4 (33)
3+	10 (21)	2 (17)
Unknown	15 (31)	2 (17)

*TD after SC means treatment duration after smear conversion (months).

Table 4. Radiologic findings of the study subjects

	Non-relapse (n=48)(%)	Relapse (n=12)(%)
Classification*		
Minimal	0 (0)	1 (8)
Moderate advanced	8 (17)	2 (17)
Far advanced	40 (83)	9 (75)
Bilaterality of lesion	38 (79)	11 (92)
Involvement of greater than one lung zone	34 (71)	7 (58)
Cavity	11 (23)	3 (25)
Residual Cavity	22 (46)	6 (50)

*classification according to National Tuberculosis Association.

Table 5. Analysis of risk factors for relapse

	Cumulative relapse-free proportion (%) at			p-value[+]
	1 year	2 years	5 years	
Overall	96.2	90.0	74.2	
(cases)	(50)	(42)	(6)	
Age				
≥40 years	97.1	87.2	69.2	0.32
<40 years	94.7	94.7	82.5	
Sex				
Male	95.6	88.4	72.1	0.45
Female	100	100	85.7	
DM				
Yes	100	87.5	62.5	0.41
No	95.2	90.3	76.5	
Culture status at 2 months of treatment				
Negative	94.6	89.5	71.7	0.52
Positive	100	91.7	83.3	
Previous tuberculosis history				
New	97.5	89.5	75.2	0.92
Retreatment	92.3	92.3	71.2	
Disease extent				
Far advanced	100	90.0	68.6	0.58
Moderate advance or minimal	97.7	90.1	75.6	
Cavity				
Yes	100	100	75.2	0.75
No	97.5	86.5	74.1	
Residual cavity				
Yes	91.7	82.5	72.2	0.52
No	100	96.3	76.5	
Drug susceptibility test				
INH resistant	50.0	50.0	100	0.01
Pansensitive	100	90.3	73.4	
TD after SC*				
≥2	95.5	93.1	79.2	0.06
<2	100	75.0	50.0	
Treatment duration				
≥12 months	94.5	85.6	68.0	0.18
<12 months	100	100	86.7	

*TD after SC means treatment duration after smear conversion (months). [+]p value by log rank test.

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(p=0.18).   77%   1

18 (30%)

42 (70%)   .

INH   5   ,   ,

26.6%, 100%   ,   HIV

(p=0.01) INH   3   2   ,   HIV

(Table 3).   [9], Tam [14]

2   50 (83%)   2   5   2%

5   79.2%, 50%   11%   .

(p=0.06)(Table 4).

고　찰   .

INH   PZA

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[15], Koh [16]

.   1   2.1%

.   ,   . INH   3

,   ,   ,   18 (30%)

,   2+   (selection bias)   .

.   ,   ,   ,

2   ,   ,

,   , 12   ,

,

.   [4][17]. Vidal [5]

2

, INH   ,

.   Al-Moamary [4]   13

,   6~48

,   ,   ,   .   11   1

[9].   2

.

,   ,   .   ,

3+   .

1%

PZA   6   .   ,

4.3%   [10].   2

1   3.8%   2   95%   .   ,

4   25.8%   .   , HIV   .

1   [11]   ,

[12], Verver [13]

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요 약

연구배경: 5

방 법: 2002 1 1   2003 12 31 .

결 과: 60
    8.3±2.3   ,
    2.0±0.8   .
14 (23%),   46 (77%),
    37 (62%),
    49 (81%)   .
1   3.8%, 2   10%, 5   25.8%   ,
, , 2   , ,
    ,
    .

결 론: 5

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