

Progression of Tuberculous Pleurisy: From a Lymphocyte-Predominant Free-Flowing Effusion to a Neutrophil-Predominant Loculated Effusion

Won-Jung Koh, M.D.

Division of Pulmonary and Critical Care Medicine, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea

Tuberculous pleurisy is the most common form of extrapulmonary tuberculosis (TB) and is the main cause of pleural effusion in Korea^{1,2}. In Korea, 3,089 new tuberculous pleurisy

cases were reported in 2015, which accounted for 9.6% of the 32,181 new TB cases and 46.6% of the 6,631 extrapulmonary TB cases (Table 1)³.

Table 1. Tuberculous pleurisy in Korea (2005–2015)

Year	Total	Pulmonary TB	Extrapulmonary TB	Tuberculous pleurisy*
2005	35,269	30,098 (85.3)	5,171 (14.7)	1,568 (30.3)
2006	35,361	30,317 (85.7)	5,044 (14.3)	1,409 (27.9)
2007	34,710	29,705 (85.6)	5,005 (14.4)	1,409 (28.2)
2008	34,157	28,344 (83.0)	5,813 (17.0)	1,545 (26.6)
2009	35,845	28,922 (80.7)	6,923 (19.3)	1,979 (28.6)
2010	36,305	28,176 (77.6)	8,129 (22.4)	2,569 (31.6)
2011	39,557	30,100 (76.1)	9,457 (23.9)	3,167 (33.5)
2012	39,545	31,075 (78.6)	8,470 (21.4)	2,884 (34.0)
2013	36,089	28,720 (79.6)	7,369 (20.4)	2,565 (34.8)
2014	34,869	27,906 (80.0)	6,963 (20.0)	2,857 (41.0)
2015	32,181	25,550 (79.4)	6,631 (20.6)	3,089 (46.6)

Values are presented as number of patients (%).

*Number of patients with tuberculous pleurisy/Number of patients with extrapulmonary TB.

TB: tuberculosis.

Address for correspondence: Won-Jung Koh, M.D.

Division of Pulmonary and Critical Care Medicine, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, 81 Irwon-ro, Gangnam-gu, Seoul 06351, Korea

Phone: 82-2-3410-3429, **Fax:** 82-2-3410-3849, **E-mail:** wjkoh@skku.edu

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Traditionally, tuberculous pleurisy is indicated by predominant lymphocytosis in the pleural fluid and a low yield of effusion culture due to the paucibacillary nature of TB¹. However, several recent studies have reported that the lymphocyte counts in pleural fluid were decreased in patients who were diagnosed with tuberculous pleurisy, and 10%–17% of the patients with tuberculous pleurisy had neutrophil-predominant pleural fluid^{5–8}. In addition, the yield of effusion culture is reported to be higher (15%–63%) than previously thought, with the introduction of a liquid culture method, and the lymphocyte percentage in pleural fluid was negatively associated with the probability of a positive effusion culture^{6–9}.

The radiographic appearances of tuberculous pleurisy can be subdivided into two types, based on the chest X-ray, chest computed tomography, or chest ultrasonography findings: free-flowing and loculated effusions^{10,11}. Residual pleural thickening is a common complication of tuberculous pleurisy, and a loculated effusion at the initial presentation was associated with significant residual pleural thickening^{12,13}. Intrapleural fibrinolytic therapy can reduce this residual pleural thickening in patients with loculated tuberculous pleurisy^{10,14}. In comparison, the characteristics of the effusion in loculated tuberculous pleurisy have not been well studied.

In this issue of *Tuberculosis and Respiratory Diseases*, Ko et al.¹⁵ described the pleural fluid characteristics in patients with tuberculous pleurisy to examine the association between loculation and positive mycobacterial cultures of pleural fluid. Among 219 patients with tuberculous pleurisy, loculation was identified in 86 patients (39%), and 69 patients (32%) had effusion cultures positive for *Mycobacterium tuberculosis*. The proportion of loculation was much higher in the patients with positive effusion cultures (86%, 59/69) than in the patients with negative effusion cultures (18%, 27/150). In other words, the majority of patients (69%, 59/86) with loculated tuber-

culous pleurisy had positive effusion cultures, whereas positive effusion cultures were found only in 7.5% of the patients (10/133) without loculation. In their study, nine patients had neutrophil-predominant pleural effusions. All of them were culture positive for *M. tuberculosis* in pleural fluid, and six of them had loculated tuberculous pleurisy. Compared to the patients with negative effusion cultures, those with positive effusion cultures had a lower lymphocyte percentage, pH, and glucose level and a higher neutrophil percentage and higher protein and lactate dehydrogenase (LDH) levels in the pleural effusion, and higher serum C-reactive protein levels. Multiple logistic regression analysis found that loculation of the pleural fluid (adjusted odds ratio [OR], 40.06; 95% confidence interval [CI], 9.36–171.56; $p < 0.001$) was associated, and lymphocyte percentage was inversely associated (adjusted OR, 0.93; 95% CI, 0.90–0.97; $p = 0.001$) with a positive effusion culture.

The traditional concept of the pathogenesis of tuberculous pleurisy is rupture of a subpleural caseous focus followed by a delayed hypersensitivity reaction to *M. tuberculosis* antigens¹. These occurrences result in lymphocyte-predominance and a low yield of effusion culture in tuberculous pleurisy⁶. However, tuberculous pleurisy may involve a continuous spectrum of disease processes (Figure 1). In the early phase of tuberculous pleurisy, the pleural effusion could have lymphocyte-predominance, a high pH, and high glucose levels. As the tuberculous pleurisy progresses, the pleural effusion could develop neutrophil-predominance, and high protein and LDH levels, as well as loculation and positive effusion cultures, as found in Ko et al.¹⁵.

From a clinical perspective, Ko et al.¹⁵ indicated that suspicion and the differentiation of tuberculous pleurisy from a parapneumonic effusion are very important in patients with loculated pleural effusions. Loculated pleural effusions, especially neutrophil-predominant effusions, are typically considered to be parapneumonic effusions in clinical practice. The inclusion of tuberculous pleurisy in the differential diagnosis and prompt sputum and pleural fluid examination for possible tuberculous pleurisy are needed, especially in TB-endemic areas.

Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

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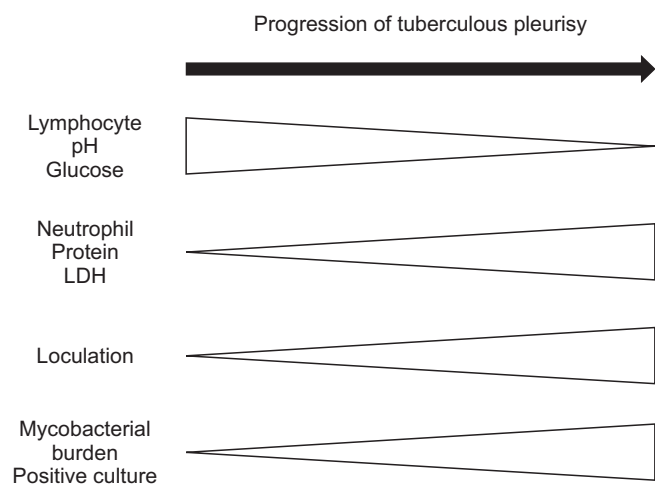


Figure 1. Continuous spectrum of tuberculous pleurisy. LDH: lactate dehydrogenase.

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