

The Value of Routinely Culturing for Tuberculosis During Bronchoscopies in an Intermediate Tuberculosis-Burden Country

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Purpose: Many medical centers routinely culture bronchoscopy samples for *Mycobacterium tuberculosis*, even when tuberculosis is not strongly suspected. The value of this practice, however, is controversial. We evaluated the role of that procedure in the diagnosis of pulmonary tuberculosis in an intermediate tuberculosis-burden country. **Patients and Methods:** A prospective, observational study was conducted in a tertiary referral center and included 733 consecutive patients who underwent bronchoscopy examination. **Results:** *M. tuberculosis* was isolated in 47 patients (6.4%). According to radiographic features, the rate of positive culture for *M. tuberculosis* was relatively high in patients with atelectasis (5/33, 15.2%) and those with pulmonary infiltrations of suspicious infections (26/183, 14.2%). *M. tuberculosis* was isolated even in patients with pulmonary masses (9/266, 3.4%) and those with pulmonary nodules (5/175, 2.9%). In 16/47 (34.0%) patients with positive cultures for *M. tuberculosis*, active pulmonary tuberculosis was not suspected at the time of bronchoscopy. **Conclusion:** These results suggest that routinely culturing for *M. tuberculosis* during bronchoscopy is still useful in the diagnosis of pulmonary tuberculosis in an intermediate tuberculosis-burden country.

Key Words: Bronchoscopy, diagnosis, pulmonary tuberculosis

INTRODUCTION

Routinely culturing for *Mycobacterium tuberculosis* during bronchoscopy is valuable in diagnosing

pulmonary tuberculosis according to prevalence. In areas with a low prevalence of tuberculosis, such as the United States and Israel, some reports have recommended not routinely performing cultures to diagnose tuberculosis for all patients undergoing bronchoscopy and to avoid such testing in patients with a low clinical suspicion of active pulmonary tuberculosis.¹⁻⁴ In areas with a high prevalence of tuberculosis, such as Hong Kong and India, however, previous reports have suggested that routine cultures of bronchial aspirate are useful for the diagnosis of pulmonary tuberculosis.^{5,6} These studies were conducted about 15 years ago, and there have been no recent reports from areas with a relatively high prevalence of tuberculosis.

The aim of the present study was to evaluate the role of routinely culturing bronchoscopy samples for the diagnosis of tuberculosis in an intermediate tuberculosis-burden country. This six-month, prospective study was conducted in a major, tertiary referral hospital in Korea, where the incidence of active tuberculosis is intermediate (90/100,000 per year).⁷

PATIENTS AND METHODS

Patients

This prospective, observational study was conducted at the Samsung Medical Center (a 1250-bed referral hospital in Seoul, Korea) between 1 January and 30 June 2006. A total of 970 patients who underwent bronchoscopy were enrolled. The

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115 patients on whom bronchoscopy was performed only for inspection of the airways before surgery for esophageal cancer or after sleeve lobectomy were excluded from the study. In addition, 122 patients who underwent therapeutic, rigid bronchoscopy for ballooning or stenting were also excluded. The final study group consisted of 733 patients who underwent bronchoscopy and routine culture for tuberculosis. Informed consent was obtained from all patients before inclusion into the study, and the study protocol was approved by the institutional review board.

Before bronchoscopy, patients were classified by pneumonologists according to the radiographic features seen on chest X-rays and CT scans. These features included: (1) pulmonary mass (diameter \geq 3 cm), (2) pulmonary nodule (diameter $<$ 3 cm), (3) atelectasis, (4) pulmonary infiltration of a suspicious infection, 5) pulmonary infiltration of a suspicious interstitial lung disease, and (6) hemoptysis without specific lesions on chest X-ray.

Bronchoscopic procedures

Bronchoscopy was performed transnasally or transorally under conscious sedation (intravenous midazolam 2 - 8 mg), by an experienced pneumonologist using a flexible fiberoptic video bronchoscope (Olympus, Tokyo, Japan). Patients were usually premedicated with intramuscular atropine and pethidine HCl. As a local anesthetic, 4% lidocaine aerosol (3 mL) was applied to the pharynx for about 10 minutes before the bronchoscopy. After advancing the bronchoscope through the vocal cords, 5 mL of 2% lidocaine solution was infused through the scope and

additional volumes of 2% lidocaine solution were infused, if needed, during the procedure.

After the bronchial tree was inspected, bronchial washing fluid was obtained in the trap bottle by immediate suction after instillation of 10 mL of normal saline to the affected bronchus. The procedure was repeated until 5 - 10 mL of material was collected for Ziehl-Neelsen staining to perform acid-fast bacillus (AFB) and culture. If another sample was needed for cytological examination, another series of washings was performed and the aspirate was collected in a separate trap bottle. The specimens were decontaminated with the N-acetyl-L-cystein 2% NaOH method. The processed specimens were plated onto 3% Ogawa medium and liquid culture medium (BacT/ALERT 3D MP vial, bioMerieux; Durham, NC., U.S.A.). All AFB isolates were assessed to distinguish between *M. tuberculosis* and NTM, according to growth rates, colony morphology, and pigmentation, with a commercial DNA probe (Gen-Probe Amplified *Mycobacterium Tuberculosis* Direct Test; Gen-Probe Inc, San Diego, CA, USA).

RESULTS

Mycobacterium tuberculosis was isolated from 47 of the 733 patients (6.4%). In these 47 patients, a positive AFB smear of the bronchial washing fluid was documented in 12 patients. These patients consisted of 23 men and 24 women with a median age of 51 years (range 21-78 years).

According to the radiographic features, the rate of positive culture for *M. tuberculosis* was relatively high in patients with atelectasis (5/33, 15.2%)

Table 1. Indications for Bronchoscopy and the Rate of Positive Culture for *M. tuberculosis*

Indication for bronchoscopy	n	Positive culture for <i>M. tuberculosis</i> (%)
Pulmonary mass	266	9 (3.4)
Pulmonary nodule	175	5 (2.9)
Atelectasis	33	5 (15.2)
Infiltration suspicious of infection	183	26 (14.2)
Infiltration suspicious of interstitial lung disease	50	0
Hemoptysis without specific lesion on chest X-ray	11	1 (9.0)
Others	15	1 (6.7)
Total	733	47 (6.4)

Table 2. Presumptive Diagnosis at the Time of Bronchoscopy in 47 Patients with Positive Cultures for *M. tuberculosis*

Presumptive diagnosis	No. of patients (%)
Pulmonary tuberculosis	31 (66.0)
Lung cancer*	14 (29.8)
Sequelae of pulmonary tuberculosis	1 (2.1)
Radiation pneumonitis	1 (2.1)

* Two patients had coexisting lung cancer and pulmonary tuberculosis.

and in those with pulmonary infiltration of suspicious infections (26/183, 14.2%). *M. tuberculosis* was isolated even in patients with pulmonary masses (9/266, 3.4%) and in those with pulmonary nodules (5/175, 2.9%) (Table 1).

A presumptive diagnosis of active pulmonary tuberculosis had been made before bronchoscopy in only 31 (66.0%) of the 47 patients with positive cultures for *M. tuberculosis*. All these patients had negative sputum acid-fast bacilli smear results (n = 17) or could not expectorate sputum before the bronchoscopy (n = 14).

In 16 (34.0%) of the 47 patients with positive cultures for *M. tuberculosis*, the presumptive diagnosis before bronchoscopy was not active tuberculosis but included lung cancer (n = 14), sequelae of previous pulmonary tuberculosis (n = 1), and radiation pneumonitis (n = 1) (Table 2). Two patients with pathologically confirmed lung cancer had coexisting active pulmonary tuberculosis.

DISCUSSION

Many centers routinely culture bronchoscopy samples for *M. tuberculosis*, even when tuberculosis is not strongly suspected. The contribution of a bronchoscopy sample culture to the diagnosis of pulmonary tuberculosis is controversial, however, and the value of sending bronchoscopy specimens for routine culture has been questioned. In Korea, it has been customary to send bronchial aspirates to culture for *M. tuberculosis* from all patients undergoing bronchoscopy, regardless of the presumptive diagnosis before bronchoscopy.

This study evaluated the role of the routine culture of bronchoscopy samples for tuberculosis

in an intermediate tuberculosis-burden country, and we made some interesting observations. First, the rate of positive culture for *M. tuberculosis* was 6.4% (47/733). Second, *M. tuberculosis* was isolated even in patients with pulmonary masses (3.4%, 9/266) and pulmonary nodules (2.9%, 5/175). Third, active pulmonary tuberculosis was not suspected at the time of bronchoscopy in 16 (34.0%) of the 47 patients with positive cultures for *M. tuberculosis*.

The practice of routinely sending bronchial aspirates for *M. tuberculosis* culture is controversial. Kavale et al. examined 859 patients in Detroit, MI, USA, who underwent bronchoscopy with a routine culture for tuberculosis from bronchial washings over a five-year period and found only three patients (0.35%) with a positive culture for *M. tuberculosis*.⁸ Of the 4120 bronchoscopic specimens from the Mayo Clinic reviewed by Jett et al., only 32 (0.77%) grew *M. tuberculosis*.⁴ It has been suggested that the culture of bronchoscopic aspirates for *M. tuberculosis* should not be obtained routinely.

By contrast, Ip et al. have reported positive cultures for *M. tuberculosis* in 119 (6.9%) of 1734 patients who underwent routine bronchoscopic examination in Hong Kong.⁵ Sarkar et al. revealed positive cultures for *M. tuberculosis* in 23 (14.0%) of 164 patients with non-tuberculous lung disease who underwent routine bronchoscopic examination in India.⁶ They have suggested that bronchial washings should be examined routinely for tuberculosis because of the high diagnostic yield. We found positive cultures for *M. tuberculosis* in 47 (6.4%) of 733 patients, and this finding is consistent with those of Ip et al.⁵ and Sarkar et al.⁶ In a recent study in Taiwan, Yang et al. reported that 38 (3.7%) of 1024 patients grew *M. tuberculosis*

in routine cultures from bronchial washing fluid.⁹ The discrepancy between our percentages and those in developed countries may be attributable to differences in the incidence and prevalence of tuberculosis in each country's overall population.

In the present study, *M. tuberculosis* was isolated even in patients with pulmonary masses and those with pulmonary nodules, as well as in patients with atelectasis or with pulmonary infiltration with suspicious infections. Recently, Rubins and Bofenkamp examined the role of routine culture for tuberculosis during bronchoscopy, specifically in 436 patients with suspected lung cancer in the USA, and found none to have active tuberculosis.³ Shitrit et al. have reported that only 1 (0.6%) of 168 patients with pulmonary masses in Israel was positive for *M. tuberculosis* following bronchial aspirate culture.²

Interestingly, in our study, active pulmonary tuberculosis was not suspected at the time of bronchoscopy in 16 (34.0%) of the 47 patients with positive cultures for *M. tuberculosis*. In 14 patients who were initially suspected to have lung cancer, two concurrently had both lung cancer and active pulmonary tuberculosis. The relationship between pulmonary tuberculosis and lung cancer has been reviewed.¹⁰⁻¹² In fact, the coexistence of lung cancer and pulmonary tuberculosis, even in the same lobe, is relatively common in Korea.¹³ Therefore, we should not exclude the possibility of coexisting pulmonary tuberculosis during a diagnostic workup of lung cancer, and routine bronchoscopic culture may play a role in the diagnosis of unexpected pulmonary tuberculosis.

In conclusion, routinely culturing for *M. tuberculosis* during bronchoscopy may still be useful for the diagnosis of active pulmonary tuberculosis in an intermediate tuberculosis-burden country such as Korea. These procedures may detect clinically unsuspected tuberculosis in an appreciable proportion of cases.

REFERENCES

1. Shitrit D, Vertenshtein T, Shitrit AB, Shlomi D, Kramer MR. The role of routine culture for tuberculosis during bronchoscopy in a nonendemic area: analysis of 300 cases and review of the literature. *Am J Infect Control* 2005;33:602-5.
2. Shitrit D, Dekel S, Bar-Gil Shitrit A, Kramer MR. The role of routine culture for tuberculosis during bronchoscopy examination of lung masses. *Respiration* 2005;72:402-5.
3. Rubins JB, Bofenkamp C. Routine culture for tuberculosis during bronchoscopy for lung cancer is not warranted. *J Bronchol* 1999;6:236-40.
4. Jett JR, Cortese DA, Dines DE. The value of bronchoscopy in the diagnosis of mycobacterial disease. A five-year experience. *Chest* 1981;80:575-8.
5. Ip M, Chau PY, So SY, Lam WK. The value of routine bronchial aspirate culture at fiberoptic bronchoscopy for the diagnosis of tuberculosis. *Tubercle* 1989;70:281-5.
6. Sarkar SK, Sharma TN, Purohit SD, Gupta ML, Gupta PR. The diagnostic value of routine culture of bronchial washings in tuberculosis. *Br J Dis Chest* 1982;76:358-60.
7. World Health Organization. Tuberculosis. 2007 May 15. Available from: URL: <http://who.int/tb>.
8. Kvale PA, Johnson MC, Wroblewski DA. Diagnosis of tuberculosis: routine cultures of bronchial washings are not indicated. *Chest* 1979;76:140-2.
9. Yang CJ, Chen TC, Hung JY, Lu PL, Sheu CC, Tsai JR, et al. Routine culture for Mycobacterium tuberculosis from bronchoscopy in Taiwan. *Respirology* 2007;12:412-5.
10. Ripstein CB, Spain DM, Bluth I. Scar cancer of the lung. *J Thorac Cardiovasc Surg* 1968;56:362-70.
11. Fontenelle LJ, Campbell D. Coexisting bronchogenic carcinoma and pulmonary tuberculosis. *Ann Thorac Surg* 1970;9:431-5.
12. Gopalakrishnan P, Miller JE, McLaughlin JS. Pulmonary tuberculosis and coexisting carcinoma: a 10-year experience and review of the literature. *Am Surg* 1975;41:405-8.
13. Kim YI, Goo JM, Kim HY, Song JW, Im JG. Coexisting bronchogenic carcinoma and pulmonary tuberculosis in the same lobe: radiologic findings and clinical significance. *Korean J Radiol* 2001;2:138-44.