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Diagnostic Contribution of Gastric and Bronchial Lavage Examinations in Cases Suggestive of Pulmonary Tuberculosis

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We assessed whether acid fast bacilli (AFB) determination in gastric lavage (GL) and bronchial lavage (BL) contributes to diagnosis in cases radiologically suggestive of pulmonary tuberculosis but with either negative AFB in sputum or the inability to expectorate sputum.

Of 129 cases recruited for the study, 22 were excluded due to evaluation as inactive disease or non-tuberculosis disease. The remaining 107 cases were evaluated in 2 groups. Group A consisted of 49 patients that could not expectorate sputum and from whom GL was obtained. In group B, BL was performed in 58 patients that had negative sputum smear.

Smear positivity was 61.2% (30/49) and culture positivity was 30.6% (15/49) in group A, 51.7% (30/58) and 81% (47/58), respectively, in group B. Thirteen cases, in whom AFB could not be detected microbiologically but who were radiologically strongly suggestive of tuberculosis, were regarded as tuberculosis according to 'from treatment to diagnosis' criteria.

In conclusion, detection of AFB positivity in the diagnosis of tuberculosis is important in terms of early initiation of treatment and detection of resistant bacilli. Therefore, we suggest that it would be helpful to obtain GL in cases where the patient is unable to expectorate sputum, and perform BL in cases with negative sputum smear.

Key Words: Tuberculosis, gastric lavage, bronchial lavage

INTRODUCTION

Tuberculosis is one of the oldest diseases known. Although its agent has been known for 115 years and effective chemotherapeutic regimens for its treatment have existed for 53 years, tuberculosis is still a serious public health issue. Currently there are 1 billion infective individuals and 16 million tuberculosis cases in the world and each year 3 million people die of this disease. In addition, 8 million new cases are added each year.[1] Industrialized countries have partly solved the tuberculosis problem, but it is still a challenge for developing and undeveloped countries.

Although clinical and radiological evaluation plays a substantial contribution in the diagnostic process, the detection of the bacillus is of major importance. There are difficulties in diagnosing cases with negative acid fast bacilli (AFB) in sputum smear and cases where the patient cannot expectorate sputum. Growing the bacillus is also important in terms of determination of drug resistance, which is currently an important issue. Therefore demonstration of the bacillus with other methods is gaining importance in cases where the patient cannot expectorate sputum or in cases with negative sputum smear for the bacillus. Detection of the bacillus is necessary for differential diagnosis of the diseases that may be confused with tuberculosis and to ensure early initialization of tuberculosis treatment.

In our study we evaluated, among cases clinically and radiologically suggestive of tuberculosis, the contribution of gastric lavage (GL) assessment in cases where the patient cannot expectorate sputum and the contribution of bronchial lavage (BL) in cases with negative sputum smear to the determination of bacillus.

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MATERIALS AND METHODS

Patients

Included in the study were 129 cases that were

hospitalized in the Pulmonary Diseases Clinic of GATA Camlica Chest Diseases Hospital between January 2000 and January 2001 with an initial diagnosis of pulmonary tuberculosis.

Physical examination, routine hematological assessments and purified protein derivative (PPD) test were performed for all included cases. Cases were classified into three groups (minimal, moderately advanced and far advanced) according to the dissemination of the lesions on the chest X-ray.[2]

Twenty-two cases were excluded as they were regarded as inactive tuberculosis or non-tuberculosis disease. The remaining 107 cases are allocated into two main groups:

* Group A: Only one GL sample was obtained from 49 cases that had no sputum.
* Group B: Only BL via fiberoptic bronchoscopy was performed in 58 cases that had negative sputum smear during 3 consecutive mornings.

Sampling of gastric lavage

Informed consent about the procedures was obtained from the patients. Oral intake was stopped from the night before the procedure. Local anesthesia was applied to the nasal passage with 10% lidocaine via a pump spray just before patients get out of their bed in the morning. Following this, 20 ml of GL, obtained by using a nasogastric tube, was sent immediately to the laboratory for smear and culture tests.

Bronchial lavage with fiberoptic bronchoscopy

Informed consent about the procedures was obtained from the patients. Oral intake was stopped from the night before the procedure. The patients were premedicated with 1 mg atropine i.m. and 10 mg diazepam i.m., 30 minutes before bronchoscopy. Then local anesthesia was applied to the nasal passage and pharynx with 10% lidocaine via a pump spray. In addition, 5 ml of 10% lidocaine was applied via a nebulizer for anesthesia of the tracheobronchial tree. The bronchial system was entered with Pentax (FB-19TX, Tokyo, Japan) flexible fiberoptic bronchoscopy (FOB). Following examination of the tracheobronchial system, selective BL with 0.9% NaCl was performed at sites where a lesion was shown by chest X-ray or high resolution computed tomography (HRCT). During this procedure 50 ml of saline was administered and an average 20 ml of lavage fluid was taken back. No anesthetic agent was used after entry to the tracheobronchial system during the lavage procedure. The obtained material was sent to the laboratory immediately for smear and culture tests.

Preparation of the obtained material

Material sent to the tuberculosis laboratory underwent decontamination and neutralization procedures with 2% NaOH solution within two hours, then was centrifuged at 3000 rpm for 20 minutes, the sediment was stained by Ziehl-Neelsen method and the smear was examined. Sediment that remained for culture was incubated in BACTEC 460 TB culture media (BACTEC 460 Becton Dickinson, Sparks, Maryland, USA) and left growing. It was checked every two days during the first week and weekly thereafter. The final result of bacterial growth was determined at the end of the sixth week. BACTEC NAP (P-nitro-alpha-acetylamino-beta-hydroxypropiophenone) test was used for mycobacteria identification. The isolate was identified as Mycobacterium tuberculosis complex when the growth of mycobacteria was inhibited in the presence of NAP.

Criteria for the diagnosis of tuberculosis in study patients

Diagnosis of pulmonary tuberculosis was made either according to positive culture or smear test results for AFB with the obtained GL or BL, or according to clinical and radiological signs. Combined culture and clinical diagnosis was considered the gold standard.

Statistics

The obtained numerical data were analyzed as mean ± SD. Pearson's test was used to analyze the correlation between radiological classification and rate of bacillus positivity. The groups were compared using Chi-square test.

RESULTS

Mean age of the 107 patients was 26.8 ± 10.7 years (range, 19-71). Sixty-four patients were smokers (59.8%), and 13 (12.1%) had a family history of tuberculosis. Mean PPD measurement was 13.9 ± 7.4 (range, 0-32) mm; 15 cases were PPD negative. Radiological examinations revealed that 60.7% of cases were moderately or far advanced (Table 1).

Results of the study groups are as follows:

Group A (n=49): AFB was positive in 61.2% (30/49) of smears and 30.6% (15/49) of cultures.

Group B (n=58): AFB was positive in 51.7% (30/58) of smears and 81.0% (47/58) of cultures.

In 13 (12.1%) cases with clinical and radiological signs strongly suggestive of tuberculosis, but without microbiological evidence of AFB in GL or BL examination, diagnosis of tuberculosis was established by the criteria of 'from treatment to diagnosis'. Of the 9 cases with GL smear (+) and culture (-), 5 had cavities in the chest radiographs, and the other 4 had moderately advanced or far advanced radiologic findings. At the end of the therapy, all these cases were accepted as pulmonary tuberculosis.

When we compared bacillus positivity of our cases with radiological signs, radiological dissemination was positively and significantly correlated with GL smear, culture positivity and BL smear positivity. However, BL culture positivity for AFB was not correlated with radiological dissemination (Table 2). Furthermore, there was no relationship between PPD measurements and either GL, BL smear or culture positivity. When we compared methods of GL and BL in terms of demonstrating the bacillus, smear positivity did not differ between the two methods (χ^2=2.8, $p>0.05$), but there was significant difference for culture positivity (χ^2=67.7, $p<0.05$). Culture positivity was higher in BL than GL.

DISCUSSION

Problems of diagnosis and treatment are encountered in cases with negative sputum smear for AFB or cases where the patient cannot expectorate sputum. Diagnosis is particularly delayed in these patients and this leads to an increase in the number of infected individuals in the community.

A patient with pulmonary tuberculosis infects 2-3 individuals in developed countries and 3-5 individuals in developing countries before being diagnosed.[3] According to a survey conducted in our clinic, the total delay in the diagnosis of pulmonary tuberculosis was 26.3 ± 18.4 (range: 2-78) days.[4] Delayed initiation of treatment in tuberculosis cases also leads to the progression of

Table 1. General Case Features by Group

Features	Group A (n=49)	Group B (n=58)	Total (n=107)
Age (± SD)	24.6 ± 8.1	28.7 ± 12.3	26.8 ± 10.7
Sex (M/F)	46/3	57/1	103/4
Smoking Habit	29 (59.2)	35 (60.3)	64 (59.8)
Tb in the family	5 (10.2)	8 (13.8)	13 (12.1)
PPD negativity	3 (6.1)	12 (20.6)	15 (14)
Radiological Classification			
Minimal	17 (34.7)	25 (43.1)	42 (39.2)
Moderately Advanced	24 (49.0)	25 (43.1)	49 (45.7)
Far Advanced	8 (16)	8 (13.8)	16 (14.9)

Table data are numbers of cases; numbers within parenthesis are percentages.

Table 2. Correlations of between Radiological Dissemination and Acid-fast Bacilli Examination

AFB Examination	Correlations of Radiological Dissemination	
	r	*p*
GL smear	0.38	0.0001
GL culture	0.287	0.007
BL smear	0.262	0.009
BL culture	-0.034	0.7

AFB, Acid-fast bacillus; GL, Gastric lavage; BL, bronchial lavage.

Table 3. Gastric Lavage Results in the Literature

Authors	Gastric Lavage Smear Positivity	Gastric Lavage Culture Positivity
Norrman[11]	n/a†	11.60%
Abadco[12]*	0%	50%
Rizvi[13]	80%	30%
Somu[14]*	n/a†	32%
Singh[15]*	n/a†	17.20%
Kohno[16]	n/a†	29.40%
Saka[17]	36%	37.50%
Our study	61.20%	30.60%

*Child cases.
†data not available.

the disease. In a study of 100 cases, 95.4% had moderately or far advanced radiological signs when they were diagnosed.[5] We observed a significant correlation between radiological dissemination and obtaining bacillus. Therefore, in cases with lesions in chest X-ray, all methods should be utilized until demonstration of the bacillus.

In countries like Turkey where tuberculosis prevalence is high and drug resistance is frequent, detection of tuberculosis bacillus is important not only in terms of proper diagnosis, but also for the evaluation of drug resistance.[6]

Smear negative, pulmonary tuberculosis leads to various difficulties for the clinician in terms of diagnosis and treatment plan. The empirical treatment used for these cases may result in unnecessary treatment, because these cases may not be active or even have tuberculosis. Failure to isolate the causative agent also leads to an inability to detect new resistance patterns that are increasing rapidly.

Many studies have investigated the contribution of GL and BL examinations to diagnosis in sputum negative cases for AFB and in cases where the patient is unable to expectorate sputum. Lavage performed by FOB, brushing and biopsy are said to accelerate the diagnostic process.[7-9] GL examination is particularly recommended for children who swallow the sputum.[10] However, we think that GL examination should be performed in adult patients unable to expectorate sputum before bronchoscopic investigations.

Previous studies with GL have produced different results[11-17] (Table 3). Generally, the positivity rate of GL cultures is less than smears. The GL obtained should undergo laboratory examina-

Table 4. Bronchial Lavage or Bronchoalveolar Lavage Results in the Literature

Authors	Bronchial Lavage Smear Positivity	Bronchial Lavage Culture Positivity
Fujii[9]	34%	88%
Norrman[11]	n/a†	20.90%
Abadco[12]*	0%	10%
Rizvi[13]	90%	70%
Somu[14]*	n/a†	12%
Kohno[16]	23.90%	84.80%
Russel[18]	12%	96%
Baughman[20]	68%	92%
Chawla[21]	24%	40%
Mohan[22]	26%	44%
Danek[23]	24%	63%
Our Study	51.70%	81%

*Child cases.
†data not available.

tion within 4 hours, or be stored in a refrigerator after a neutralization procedure to maintain pH at 7.0. Procedural errors during these stages may have unfavorable effects on growing bacillus in culture. In our study, the low rate of bacillus positivity in culture may have been caused by laboratory problems. On the other hand, high positivity of GL smear is reported to be affected by atypical mycobacterium.[7]

According to Norrman et al.,[11] bronchoalveolar lavage (BAL) is better than GL. However, Abadco and Steiner[12] found higher culture positivity for GL than BAL, so they support GL examinations. In our study culture positivity for BL was higher than for GL. We think that the biochemical characteristics of GL play a role in this finding.

Lidocaine used in BL or BAL procedures has an antibacterial effect.[18,19] Therefore, there are differences between studies of BAL and BL in the detection of tuberculosis bacillus (Table 4).[9,11-14,16,18,20-23]

One of the other methods for the detection of Mycobacterium tuberculosis in GL or BL specimens is Polymerase Chain Reaction (PCR) assay. PCR assay is useful for rapid diagnosis of tuberculosis and its use to detect the presence of Mycobacterium tuberculosis in clinical specimens has been widely reported.[24-26] In these studies, it was suggested that PCR assay was more sensitive than smear and culture tests for the detection of Mycobacterium tuberculosis in BAL specimens of patients with sputum smear negative pulmonary tuberculosis or no sputum.[27-31] Although PCR can be specific and sensitive, it may be limited by contamination or the presence of amplification inhibitors.[32,33]

As a result, in cases suggestive of tuberculosis, evaluations of GL and BL can assist in the detection of bacillus. Therefore, in order to obtain culture samples for definitive diagnosis, GL should be performed in cases where the patient is unable to expectorate sputum, whereas BL should be performed in cases with negative sputum assessments. If possible, PCR assay should be used to detect Mycobacterium tuberculosis in GL or BL specimens.

REFERENCES

1. Sudre P, Ten Dam G, Kochi A. Tuberculosis: A global overview of the situation today. Bull WHO 1992;70: 149-59.
2. Seaton A, Seaton D, Leitch AG. Crofton & Douglas's Respiratory Diseases. 4th ed. London: Oxford Blackwell Scientific Publications; 1989. p.409-10.
3. Grange JM. Mycobacterial diseases in the world: Yes-

terday, today and tomorrow. In: Radladge C, Stanford J, Grange JM, editors. The Biology of the Mycobacteria. Volume: 3. London: Academic Press; 1989. p.3-36.
4. Okutan O, Kartaloglu Z, Cerrahoglu K, Ilvan A, Tozkoparan E, Aydilek R. Time to beginning therapy and affecting factors in Turkish Soldiers with pulmonary tuberculosis: An analysis of a Turkish Military Chest Diseases Hospital. The Internet Journal of Pulmonary Medicine 2001 Vol 2 N1. http://www.ispub.com/journals/IJPM/Vol2N1/tbc.html
5. Hooi LN. Case finding for pulmonary tuberculosis in Penang. Med J Malaysia 1994;49:223-30.
6. Tahaoglu K, Kizgin O, Karagoz T, Tor M, Partal M, Sadoglu T. High initial and acquired drug resistance in pulmonary tuberculosis in Turkey. Tuber Lung Dis 1994;75:324-8.
7. Lloyd NF. Mycobacterium Tuberculosis. In: Bone RC, editor. Pulmonary and Critical Care Medicine. St. Louis: Mosby-Year Book Inc.; 1993. part K5, p.21-2.
8. Willox PA, Benator SR, Patgier PD. Use of bronchoscope in diagnosis of sputum-negative pulmonary tuberculosis. Thorax 1982;37:598-601.
9. Fujii H, Ishihara J, Fukara A, Kashima N, Tazawa H, Nakajima H, et al. Early diagnosis of tuberculosis by fiberoptic bronchoscopy. Tuber Lung Dis 1992;73:167-9.
10. Rossman MD, Oner-Eyuboglu AF. Clinical presentation and treatment of tuberculosis. In: Fishman AP, editor. Fishman's Pulmonary Disease and Disorders. 3rd ed. New York: Mc Graw-Hill; 1998. p.2486-7.
11. Norrman E, Keistinen T, Uddenfeldt M, Rydstrom PO, Lundgren R. Bronchoalveolar lavage is better than gastric lavage in the diagnosis of pulmonary tuberculosis. Scand J Infect Dis 1988;20:77-80.
12. Abadco DL, Steiner P. Gastric lavage is better than bronchoalveolar lavage for isolation of Mycobacterium tuberculosis in childhood pulmonary tuberculosis. Pediatr Infect Dis J 1992;11:735-8.
13. Rizvi N, Rao NA, Husssain M. Yield of gastric lavage and bronchial wash in pulmonary tuberculosis. Int J Tuberc Lung Dis 2000;4:147-51.
14. Somu N, Swaminathan S, Paramasivan CN, Vijayasekaran D, Chandrabhooshanam A, Vijayan VK, et al. Value of bronchoalveolar lavage and gastric lavage in the diagnosis of pulmonary tuberculosis in children. Tuber Lung Dis 1995;76:295-9.
15. Singh M, Moosa NV, Kumar L, Sharma M. Role of gastric lavage and broncho-alveolar lavage in the bacteriological diagnosis of childhood pulmonary tuberculosis. Indian Pediatr 2000;37:947-51.
16. Kohno S. Diagnostic value of bronchoscopy in diagnosis of pulmonary tuberculosis: bronchial aspirate, bronchial washing and transbronchial pulmonary biopsy.[abstract] Kekkaku 1990;65:33-6.
17. Saka D, Calisir HC, Ogretensoy M. The place of gastric lavage in diagnosis of pulmonary tuberculosis. Geneva, Sweden: ERS Annual Congress; 1998. p.1489.
18. Russel MD, Torrington KG, Tenholder MF. A ten-year experience with fiberoptic bronchoscopy for mycobacterial isolation. Am Rev Respir Dis 1986;133:1069-71.
19. Schmidt RM, Rosenkranz HS. Antimicrobial activity of local anesthetics: lidocaine and procaine. J Infect Dis 1970;121:597-607.
20. Baughnam RP, Dohn MN, Loudon RG, Frame PT. Bronchoscopy with bronchoalveolar lavage in tuberculosis and fungal infections. Chest 1991;99:92-7.
21. Chawla R, Pant K, Jaggi OP, Chandrashekhar S, Thukral SS. Fiberoptic bronchoscopy in smear-negative pulmonary tuberculosis. Eur Respir J 1988;1:804-6.
22. Mohan A, Pande JN, Sharma SK, Rattan A, Guleria R, Khilnani GC. Bronchoalveolar lavage in pulmonary tuberculosis: a decision analysis approach. QJM 1995; 88:269-76.
23. Danek SJ, Bower JS. Diagnosis of pulmonary tuberculosis by flexible fiberoptic bronchoscopy. Am Rev Respir Dis 1979;119:677-9.
24. Forbes BA, Hicks KE. Direct detection of Mycobacterium tuberculosis in respiratory specimens in a clinical laboratory by polymerase chain reaction. J Clin Microbiol 1993;31:1688-94.
25. Kocagoz T, Yilmaz E, Ozkara S, Kocagoz S, Hayran M, Sachedeva M, et al. Detection of Mycobacterium tuberculosis in sputum samples by polymerase chain reaction using a simple procedure. J Clin Microbiol 1993;31:1435-8.
26. Okutan O, Kartaloglu Z, Ilvan A, Cerrahoglu K, Kunter E, Aydilek R. Polymerase chain reaction in pulmonary tuberculosis. East J Med 2000;5:7-9.
27. Shibuya Y, Shiozaki T, Hayashi M, Sugiyama Y. Efficacy of Amplicor PCR for the diagnosis of tuberculosis in respiratory specimens other than sputum. Tuber Lung Dis 2000;80:209-15.
28. Bahrmand AR, Bakayev VV, Babaei MH. Use of polymerase chain reaction for primary diagnosis of pulmonary tuberculosis in the clinical laboratory. Scand J Infect Dis 1996;28:469-72.
29. Liam CK, Chen YC, Yap SF, Srivinas P, Poi PJ. Detection of Mycobacterium tuberculosis in bronchoalveolar lavage from patients with sputum smear-negative pulmonary tuberculosis using a polymerase chain reaction assay. Respirology 1998;3:125-9.
30. Salajka F, Mezensky L, Pokorny A. Commercial polymerase chain reaction test (Amplicor set) in the diagnosis of smear-negative pulmonary tuberculosis from sputum and bronchoalveolar lavage. Monaldi Arch Chest Dis 2000;55:9-12.
31. Brugiere O, Vokurka M, Lecossier D, Mangiapan G, Amrane A, Milleron B, et al. Diagnosis of smear-negative pulmonary tuberculosis using sequence capture polymerase chain reaction. Am J Respir Crit Care Med 1997;155:1478-81.

32. Kox LF, Rhienthong D, Miranda AM, Udomsantisuk N, Ellis K, van Leeuven J, et al. A more reliable PCR for detection of Mycobacterium tuberculosis in clinical samples. J Clin Microbiol 1994;32:672-8.
33. Clarridge JE, Shawar RM, Shinnick TM, Plikaytis BB. Large-scale use of polymerase chain reaction for detection of Mycobacterium tuberculosis in a routine mycobacteriology laboratory. J Clin Microbiol 1993;31: 2049-56.