Sevak Keshishyan[1], Viren Kaul[2], Anupam Gupta[2], Chul Ahn[3], Wilbert Aronow[4], Oleg Epelbaum[5]

[1]Division of Pulmonary, Critical Care and Sleep Medicine, Westchester Medical Center, Valhalla, NY, USA
[2]Division of Pulmonary and Critical Care Medicine, Elmhurst Hospital Center, Elmhurst, NY, USA
[3]Department of Clinical Sciences, University of Texas Southwestern Medical Center, Dallas, TX, USA
[4]Division of Cardiology, Westchester Medical Center, Valhalla, NY, USA
[5]Division of Pulmonary, Critical Care and Sleep Medicine, Westchester Medical Center, Valhalla, NY, USA

Sputum culture for the diagnosis of tuberculous pleural effusion: analysis of absolute and incremental yields

Abstract

Introduction: Pleural fluid culture yield in tuberculous pleural effusion (TPE) is disappointing in immunocompetent hosts. Herein, we attempt to define the role of serial sputum cultures in the diagnosis of TPE.

Material and methods: We identified cases diagnosed with TPE over a 16-year period in a high-prevalence US hospital. Absolute yields of one, two, and three sputa were calculated as well as the incremental yield of adding second and third sputa. These calculations were then performed separately for expectorated and induced sputum and for patients with and without infiltrates on chest X-ray.

Results: Sixty sputum collections were performed in 46 patients with TPE. The per-patient sensitivity of sputum culture was 45.6%. On a per-sputum collection basis, the overall yield of the first sputum was 30%, of two sputa 39%, and of three sputa 54%. The corresponding incremental yields were 9% and 15%, respectively. The three-sputum yields of expectorated and induced collections were similar. The three-sputum yield in patients with infiltrates on X-ray was 11% lower than that in those without infiltrates.

Conclusions: Serial sputum collection of three specimens can be expected to produce a yield of > 50% in cases of suspected TPE regardless of whether obtained by expectoration or induction, and the yield increases incrementally.

Key words: tuberculosis, mycobacteria, pleural effusion, infection

Adv Respir Med. 2019; 87: 281–288

Introduction

Although its incidence is slowly declining worldwide, tuberculosis (TB) remains a prevalent and morbid infection affecting predominantly the developing world [1]. The United States has experienced a sharp decline in TB incidence over the last two decades after an increase during the early years of the acquired immunodeficiency syndrome (AIDS) epidemic. Despite this trend, US urban centers such as New York City (NYC) continue to experience a heavy disease burden owing to their large immigrant populations from regions endemic for TB. Within NYC, the borough of Queens — in which the study institution is located — consistently reports the highest incidence of TB cases [2].

Tuberculous pleural effusion (TPE) is among the commonest manifestations of extrapulmonary TB and therefore an important clinical entity in areas of high TB prevalence. Although a lymphocyte-predominant exudative effusion with a high adenosine deaminase (ADA) level can be virtually diagnostic of TPE in such settings, microbiological confirmation may be desirable in uncertain cases and allows determination of antibiotic sensitivity. By itself, pleural fluid culture for acid-fast bacilli (AFB) has been associated with yields well below 30% in multiple studies among human immunodeficiency virus (HIV) negative

Address for correspondence: Oleg Epelbaum, Division of Pulmonary, Critical Care and Sleep Medicine, Westchester Medical Center, Valhalla, NY, USA; e-mail: oleg.epelbaum@wmchealth.org
DOI: 10.5603/ARM.2019.0050
Received: 07.05.2019

ISSN 2451–4934

cases [3]. Yields above 80% can be achieved by means of pleural biopsy specimens submitted for AFB culture and histological analysis, but this constitutes an invasive procedure with variable availability across centers. Sputum testing for AFB smear and culture has traditionally been considered a low-yield approach to the diagnosis of TPE, especially in HIV negative patients and those without overt parenchymal involvement on chest radiography (CR) [3]. Theoretically, sputum collection — by induction or expectoration — would be a highly efficient way of diagnosing TPE because of its low cost, broad availability, and well-established role in the diagnosis of pulmonary TB, for which a series of three sequential specimens is recommended as a means of potentially increasing sensitivity [4].

Only one contemporary study performed in Brazil was conducted specifically to address the utility of (induced) sputum collection in patients with suspected TPE, showing that the diagnosis can be made in this fashion in over 50% of cases, which held true even in the absence of parenchymal disease on CR [5]. The aim of the present study was to determine whether these findings can be replicated in a high-prevalence US hospital while also determining whether the collection of a second and third serial sputum sample in TPE results in a progressively increasing yield.

Material and methods

Case identification

The study was approved by the institutional review board of the Icahn School of Medicine at Mount Sinai [#15-2321(0001)]. Records of all patients evaluated at Elmhurst Hospital Center — a 545-bed municipal community teaching hospital — during the period of 01/01/1999 to 02/28/2015 and coded for both tuberculosis [International Classification of Diseases (ICD)-9 011.9] and pleural effusion (ICD-9 511.9). The 158 cases thus identified were then screened for the presence of TPE, which was diagnosed if one or both of the following two sets of criteria was met:

a) **Pathological/mycobacteriological criteria (one required):**
   — Granulomas on pleural biopsy with or without mycobacterial tissue smear/culture positivity;
   — Pleural fluid or tissue mycobacterial smear/culture positive for *M. tuberculosis*;
b) **Clinical criteria (all required):**
   — Exudative, lymphocyte-predominant pleural effusion;
   — Pleural fluid cytology negative for malignancy;
   — Pleural fluid ADA level >40 U/L.

An additional inclusion criterion was at least one sputum sample submitted for mycobacterial smear and culture by either the expectorated or induced route at the time of the index hospitalization or within the subsequent 30 days.

Mycobacteriological processing

Each patient could have undergone expectorated sputum collection, induced sputum collection, or both. In the study institution, sputum induction is performed using isotonic or hypertonic saline (NaCl) in accordance with recommended procedure [6]. Sputum for AFB is typically collected once per day on consecutive days. To evaluate a smear, sputum specimens submitted for AFB testing are concentrated by centrifugation, and 1–2 drops of the resulting pellet are used to prepare a slide, which is then air dried and heat fixed. The dried material undergoes fluorochrome (Auramine-O) staining and is examined using fluorescence microscopy. Smears deemed to contain fluorescent bacilli are subjected to confirmatory Kinyoun staining at room temperature. If the Kinyoun stain is likewise positive, a sample is sent for ribosomal ribonucleic acid (rRNA) amplification testing using the Amplified *Mycobacterium tuberculosis* Direct Test™ (Hologic, Inc., San Diego, CA, USA). For AFB culture, fluid preparations are incubated in the BD BACTEC™ MGIT™ automated mycobacterial detection system (Beckton, Dickinson & Co., Franklin Lakes, NJ, USA). Solid preparations for AFB culture are plated onto Löwenstein-Jensen medium. All cultures are monitored for at least 6 weeks. If positive, they are monitored for 10 weeks and sent for AccuProbe™ Mycobacterium Tuberculosis Complex Culture Identification Test (Hologic, Inc., San Diego, CA, USA).

Yield calculations

The unit of analysis was each sputum collection of up to three samples. The primary measurements of interest were the one-sputum, two-sputum, and three-sputum culture yields for *M. tuberculosis* along with the respective incremental yield of adding the second sputum to the first and then the third sputum to the first and second. These yields were calculated for all sputum collections irrespective of method as well as separately for expectorated and induced collections. Additionally, overall, expectorated, and induced yields were calculated separately

for those collections performed in patients with and without parenchymal abnormalities (e.g., consolidations, nodules, masses, reticular opacities) on the CR — regardless of the number of projections — that initially demonstrated the pleural effusion. The presence or absence of parenchymal chest radiograph abnormalities (and effusion size) was determined based on the official report by the radiologist as well as image review — when available — by several of the study authors experienced in chest radiography interpretation (SK, AG, VK, and OE). Chest computed tomography (CT) was not routinely performed in these patients and therefore was not used for adjudication. For the purposes of sputum culture yield determination of up to three samples, including the incremental yield, the following notation was used to designate each collection as originally proposed by Rieder *et al*. [7]:

— Pxx = first sputum positive, second and third sputa of no interest;
— NPx = first sputum negative, second sputum positive, third sputum of no interest;
— NNP = first and second sputa negative, third sputum positive;
— N99 = first sputum negative, second and third sputa not obtained;
— NN9 = first and second sputa negative, third sputum not obtained;
— NNN = all three sputa negative.

Using this notation, the yield of obtaining one sputum was calculated as follows:

a) One sputum yield = Pxx/total number of sputum collections

The yield of obtaining two sputa was defined as collections positive on first sputum plus collections positive on second sputum divided by all collections minus those that did not contain a second sputum despite a negative first sputum:

b) (Pxx + NPx) / (total number of sputum collections — N99)

Correspondingly, the yield when three sputa are obtained was defined as collections positive on first sputum plus collections positive on second sputum plus collections positive on third sputum divided by all collections minus those that did not contain a second sputum despite a negative first sputum and minus those that did not contain a third sputum despite a negative first and second sputum:

c) (Pxx + NPx + NNP) / (total number of sputum collections — N99–NN9)

The incremental yield of obtaining two sputa as opposed to one was therefore designated as b–a, and similarly the incremental yield of obtaining three sputa instead of two was designated as c–b.

Statistical Methods

Chi-square or Fisher's exact test was used to examine for significant differences in categorical baseline variables between patients with and without lung disease on CR. Student's T-test or Wilcoxon rank-sum test was used to investigate for significant differences in continuous baseline variables between patients with and without lung disease on CR.

Results

Of the 158 potential cases of TPE identified, 46 met the study criteria for TPE. These 46 patients underwent a total of 60 sputum collections: 27 expectorated collections and 33 induced collections; 14 patients underwent both. Of the latter 14 cases, only 3 had non-diagnostic expectorated collections but diagnostic induced collections. All of the 46 patients had at least one sputum specimen collected. Of the 27 expectorated collections, 23 (85%) were complete collections (i.e., Pxx, NPx, NNP, and NNN); of the 33 induced collections, 27 (82%) were complete All but two patients had sputum collected during the index hospital admission; the two who did not underwent collection within one month following their admission, and both had positive AFB culture results (Pxx).

The characteristics of the 46 patients with TPE eligible for analysis are summarized in Table 1. All of the patients with a known country of origin were born outside the United States, predominantly in Hispanic and Asian countries. The overwhelming majority of those with a known status were HIV negative. The majority (76%) of effusions were moderate to large. Most cases (33/46 or 72%) fulfilled the pathological/ /mycobacteriological criteria for diagnosis of TPE as outlined above. The remaining 28% met only the clinical criteria. No patient had a positive pleural fluid AFB smear, but of the 45 patients whose pleural fluid underwent mycobacteriological analysis, 16 (35%) had a positive AFB culture.

On a per-patient basis (N = 46), the sensitivity of sputum culture was 45.6%. On a per -sputum collection basis (N = 60), the overall sensitivity was 45.0%. The yields of one, two, and three sputa for the diagnosis of TPE irrespective of collection method were 30.0%, 38.9%, and 54.0%, respectively. The incremental yield of adding the second sputum to the first was 8.9%, and the incremental yield of adding the third sputum to the initial two was 15.1%.

Table 1. Characteristics of the study patients

Variable	CXR with lung disease (n = 29)	CXR without lung disease (n = 17)	All patients (n = 46)	P-value
Age mean ± SD	35.7 ± 20.0	34.8 ± 12.8	35.4 ± 17.5	0.8602*
Gender (%)				
Male	17 (59)	12 (71)	29 (63)	0.4170
Female	12 (41)	5 (29)	17 (37)	
Ethnicity (%)[a]				
Hispanic	13 (45)	10 (59)	23 (50)	0.5144**
Asian	13 (45)	4 (34)	17 (37)	
African	2 (7.0)	2 (12)	4 (9.0)	
Unknown	1 (3.0)	1 (6.0)	2 (4.0)	
HIV status (%)[a]				
Positive	1 (3.0)	2 (12)	3 (7.0)	0.1518**
Negative	23 (79)	9 (53)	32 (70)	
Unknown	5 (17)	6 (35)	11 (24)	
PPD/IGRA status (%)[a]				
Positive	11 (38)	5 (29)	16 (35)	0.6557**
Negative	3 (10)	1 (6.0)	4 (9.0)	
Unknown/indeterminate	15 (52)	11 (65)	26 (57)	
Effusion size (%)[a]				
Small	6 (21)	1 (6.0)	7 (15)	0.2441**
Moderate	11 (38)	5 (29)	16 (35)	
Large	11 (38)	8 (47)	19 (41)	
Unknown	1 (3.0)	3 (18)	4 (9.0)	
Pleural fluid chemistry median (IQR)				
LDH (U/L)	518 (262–683)	646 (399–766)	535 (325–704)	0.1302***
Lymphocyte fraction	73 (65–92)	80 (69–93)	80 (65–92)	0.5765***
Adenosine deaminase (U/L)	49.5 (32.9–60.2)[b]	52.5 (43.9–58.1)[c]	52.0 (38.3–60.3)[d]	0.4948***
Pleural fluid mycobacteriology (%)				
AFB smear positive	0 (0)	0 (0)	0 (0)	0.3696**
AFB smear negative	29 (100)	16 (94)	45 (98)	
AFB smear unavailable	0 (0)	1 (6.0)	1 (2.0)	
Pleural fluid mycobacteriology (%)				
AFB culture positive	10 (34)	6 (35)	16 (35)	0.5811**
AFB culture negative	19 (66)	10 (59)	29 (63)	
AFB culture unavailable	0 (0)	1 (6.0)	1 (2.0)	
Pleural tissue (%)				
Granulomas present	17 (59)	13 (76)	30 (65)	0.5257**
Granulomas absent	4 (14)	1 (6.0)	5 (11)	
Not biopsied	8 (28)	3 (18)	11 (24)	
Pleural tissue (%)				
AFB culture positive	3 (10)	2 (12)	5 (11)	0.8970**
AFB culture negative/unavailable	18 (62)	12 (71)	30 (65)	
Not biopsied	8 (28)	3 (18)	11 (24)	

→

Table 1 cont. Characteristics of the study patients

Variable	CXR with lung disease (n = 29)	CXR without lung disease (n = 17)	All patients (n = 46)	P-value
Biopsy type (%)				
Needle	20 (69)	12 (71)	32 (70)	0.5332**
Surgical	1 (3.0)	2 (12)	3 (7.0)	
Not done	8 (28)	3 (18)	11 (24)	
Basis for TPE diagnosis (%)				
Histology/mycobacteriology	19 (66)	14 (82)	33 (72)	0.3150**
Pleural fluid clinical criteria only	10 (34)	3 (18)	13 (28)	
Sputum for AFB[e] (%)				
Expectorated (E) collection	14 (48)	13 (76)	27 (59)	N/A
Induced (I) collection	23 (79)	10 (59)	33 (72)	
At least 1 complete collection (E or I)	27 (93)	16 (94)	43 (93)	

[a]Percentages may not add up to 100% due to rounding; [b]Based on data from 14 patients; [c]Based on data from 8 patients; [d]Based on data from 22 patients; [e]Totals add up to more than the number of patients because some patients had both types of collections; *By T-test; **By Fisher's Exact Test, otherwise by Chi-Square Test; ***By Wilcoxon rank-sum Test.

IGRA — interferon gamma release assay; LDH — lactate dehydrogenase; N/A — not applicable; PPD — purified protein derivative; IQR — interquartile range

The three-sputum yields of expectorated and induced collections were similar: 52.2% versus 55.6%, respectively. Table 2 summarizes these results and separately displays the corresponding absolute and incremental yields of expectorated and induced collections.

When analyzed according to the presence or absence of parenchymal abnormalities on CR, the three-sputum yield was higher in the latter group: 46.9% versus 57.9%, a difference of 11%. Table 3 presents the full absolute and incremental yield breakdown based on separation by this parameter as well as after further subdivision by sputum collection method.

Of the 27 diagnostic sputum collections, two-thirds (18) were positive on the first sputum, and the remaining one-third became positive only on the second or third sputum. The second sputum was the first diagnostic specimen in 3/27 collections (11.1%), whereas the third sputum was the first diagnostic specimen in 6/27 collections (22.2%).

Discussion

This retrospective analysis of 60 sputum collections in 46 patients with TPE is one of the few studies on the diagnosis of this condition ever conducted in the United States, a non-endemic country for TB. Given the persistently high incidence of TB in the part of NYC in which the study institution is located, it is not surprising that one of the earliest US series of TPE patients was published in 1973 by the same institution [8]. Our results are in agreement with prior reports indicating that the yield of sputum culture for the diagnosis of TPE can exceed 50%, making it likely the second most sensitive diagnostic modality for TPE after pleural biopsy, which is much more uncomfortable and invasive. Importantly, our study is the first to examine the question of whether serial sputum collection of up to three distinct specimens for mycobacterial culture results in progressive increase in diagnostic yield in cases of TPE like it does in cases of parenchymal TB. Analysis of our entire sample shows that, in fact, three sputum specimens may be required to achieve a greater than 50% yield for TPE, a finding that is mirrored by a separate analysis of expectorated and induced collections. An 8.9% incremental yield was observed with the addition of sputum #2 and a further 15.1% increase was seen with the addition of sputum #3, for an overall incremental yield of obtaining three sputa as opposed to one of 24.0%. One-third of the diagnostic sputum collections in our study would have been non-diagnostic had they been limited to only a single sputum. One quarter of the diagnoses would have been missed without the third sputum.

It would be reasonable to speculate that sputum cultures obtained from TPE patients with concurrent parenchymal abnormalities on CR will have higher diagnostic yield. The opposite

Table 2. Overall and separate expectorated and induced yields of one, two, and three sputa

Number of sputa	Overall yield	Incremental yield	Expectorated yield	Incremental yield	Induced yield	Incremental yield
One	18/60 (30.0%)	N/A	8/27 (29.6%)	N/A	10/33 (30.3%)	N/A
Two	21/54 (38.9%)	+8.9%	8/25 (32.0%)	+2.4%	13/29 (44.8%)	+14.5%
Three	27/50 (54.0%)	+15.1%	12/23 (52.2%)	+20.2%	15/27 (55.6%)	+10.8%

N/A — not applicable

Table 3. Sputum yields of patients with and without parenchymal disease on CXR, including further subdivision by collection method

Number of sputa	Overall yield	Incremental yield	Expectorated yield	Incremental yield	Induced yield	Incremental yield
CXR with lung disease						
One	10/37 (27.0%)	N/A	4/14 (28.6%)	N/A	7/23 (30.4%)	N/A
Two	13/35 (37.1%)	+10.1%	4/14 (28.6%)	0%	10/21 (47.6%)	+17.2%
Three	15/32 (46.9%)	+9.8%	5/13 (38.5%)	+9.9%	11/19 (57.9%)	+10.3%
CXR without lung disease						
One	7/23 (30.4%)	N/A	4/13 (30.8%)	N/A	3/10 (33.3%)	N/A
Two	7/20 (35.0%)	+4.6%	4/11 (36.4%)	+5.6%	3/8 (37.5%)	+4.2%
Three	11/19 (57.9%)	+22.9%	7/10 (70.0%)	+33.6%	4/8 (50.0%)	+12.5%

N/A — not applicable

Table 4. Comparison of sputum AFB culture yields among five contemporary studies

Parameter	Seibert 1991 [7]	Valdés 1998 [8]	Conde 2003 [5]	Ruan 2012 [9]	Present study*
Country	USA (AL)	Spain	Brazil	Taiwan	USA (NY)
Design	Retrospective	Retrospective	Prospective	Retrospective	Retrospective
Number of patients	70	254	84	382	46
Collection method	Unspecified	Unspecified	Induction	Unspecified	Induction
Sputum AFB smear yield	Not reported	62.5%	11.9%	Not reported	0%
Sputum AFB culture yield	50.0%	100%	52.4%	48.2%	55.6%

*Listed culture yield is based on collection of three sputa by induction.

AFB — acid-fast bacilli

was true, however, in the study by Conde *et al.*: 45.0% with parenchymal lesions versus 54.7% without. When we separated all of our sputum collections by whether the corresponding patient did or did not have parenchymal CR abnormalities, as in the Conde study, the three-sputum yield was numerically higher in the group with no parenchymal lesions than in the group with such lesions: 57.9% versus 46.9%, respectively. It should be borne in mind that these numbers, which are very similar between the two studies, were achieved in the present study only with the collection of three sputum samples. For comparison, single-sputum yields with and without parenchymal disease were 27.0% and 30.4%, respectively, while the corresponding two-sputum yields were 37.1% and 35.1%. For clinical purposes, the patient type of greater interest is the one with suspected TPE but without parenchymal CR abnormalities in whom sputum collection may not be automatically triggered by concern for pulmonary TB. TPE is believed to

result from a pleural hypersensitivity reaction to a sub-pleural focus of pulmonary TB, which explains the disappointing mycobacterial yield of pleural fluid culture in immunocompetent hosts, so it is not surprising that sputum culture would have substantial yield in this condition. Why TPE patients without visible parenchymal infiltrates on CR might have even higher sputum yield than those with radiographic parenchymal disease — as in the current study and the one by Conde *et al.* — remains unexplained. Effusion size, which could affect the ability to discern lung involvement on CR, was equally distributed by category between those with and without parenchymal disease in our sample (Table 1). It is possible that the ability to review chest CT images would have increased the detection rate of lung abnormalities as has been shown previously [9]. Of note, none of the sputum samples included in our study was positive for AFB on examination of the smear.

In the last 30 years, our study is among four others to report on the yield of sputum culture in TPE: Seibert *et al.* [10] in 1991 (a US registry review from Alabama), Valdés *et al.* [11] in 1998 (Spain), the aforementioned Conde study from Brazil in 2003, and a Taiwanese study by Ruan *et al.* [12] in 2012. Seibert *et al.* included 70 TPE patients in their analysis and reported an overall sputum yield of 50% without providing any details about sputum collection method or number of specimens per collection. The sputum yield was markedly higher in those with an infiltrate on CR (88.6%) than in those without (11.4%). It is noteworthy that in 67.7% of patients with an infiltrate, sputum was the sole diagnostic specimen. Valdés *et al.* reviewed 254 patients with TPE, of which the 48 with parenchymal disease on imaging underwent sputum collection. The smear was positive in 62.5% and culture in 100% of such cases. As in the Seibert study, no details are available about sputum collection methodology or quantity. The Conde study, results of which have been quoted earlier, was unique in that its 84 subjects with TPE were evaluated prospectively. All sputum was collected by induction, but the number of sputum samples submitted per patient is not specified. This study is the only one of the three to provide data on the HIV status of its subjects. Similar to our study, the population was predominantly HIV negative: 84.5%. In patients with abnormal parenchyma, our overall three-sputum culture yield (46.9%) as well as the yield of induced sputum only (57.9%) are much more closely aligned with that in the Conde study (54.7%) than with that of Seibert *et al.* (88.6%) and Valdés *et al.* (100%). Table 4 compares the sputum results obtained in these four studies to those of the present study. The retrospective Ruan study is the largest of the group with 382 cases of TPE who also underwent sputum AFB culture testing, the yield of which was 48% by itself and 79% in combination with pleural fluid AFB culture. Again, information about the number of sputum samples collected and the collection method is not provided. Notably, in our study, of the 19 patients with negative sputum who had pleural fluid analyzed for AFB, 12 had positive pleural fluid for a combined sensitivity of sputum and pleural fluid of 71.7%. Our per-patient diagnostic yields of sputum alone (45.6%) and of sputum plus pleural fluid (71.7%) are in close alignment with Ruan *et al.*, which is the largest study of TPE diagnostics. According to these numbers, sputum and pleural fluid together can approach the yield of pleural biopsy.

Our study has several important limitations aside from its retrospective design and reliance on the accuracy of ICD coding. Not all of the sputum collections were complete sets of three specimens, so one-sputum, two-sputum, and three-sputum yield calculations were based on different numbers of samples. In two cases, sputum collection was not performed during the index hospitalization. CR interpretation for the presence or absence of parenchymal infiltrates was based on the impression of a group of study authors along with the official radiologist interpretation as opposed to a group of independent observers. Many of the subjects in our study were diagnosed with TPE presumptively based not on pleural histology or mycobacteriology but on the combination of suggestive pleural fluid characteristics. For logistical reasons, we were unable to corroborate the diagnosis of TPE in these presumptive cases by assessing for resolution of the pleural effusion following anti-tuberculous therapy. Additionally, our already relatively small sample size became even smaller once the results were separated based on sputum collection method and then further parsed according to the presence or absence of parenchymal involvement.

Summary

In conclusion, despite its relatively small sample size, our study corroborates prior published literature reporting sputum culture yield of approximately 50% in cases of TPE, which would place this approach behind only pleural biopsy and ahead of pleural fluid culture in the

typical hierarchy of diagnostic yields for TPE. For unclear reasons, our study is one of two to report a higher sputum culture yield in TPE cases not accompanied by lung parenchymal findings. Our data also suggest that in clinical practice, a yield of > 50% may be reached only upon collection of three serial sputum samples akin to the common practice in pulmonary TB. The difference in yield between obtaining one sputum versus three sputa could be in the range of 20–25% according to our data, so in aggregate these results support obtaining a set of three sputum samples in all patients presenting with a pleural effusion for which pleural TB is an etiological consideration.

Acknowledgments

Dr. Oleg Epelbaum is the guarantor of this paper. He takes responsibility for the content of the manuscript which also includes data and analysis.

SK, AG, and OE had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. SK, VK, AG, CA, WSA and OE contributed substantially to the study design, data analysis and interpretation and the writing of this manuscript.

None of the authors has any financial or non-financial disclosures.

Conflict of interest

None declared.

References:

1. World Health Organization. Global Tuberculosis Report 2014. Available at: www.who.int/tb/publications/global_report/en/ [access: 28.10.2015].
2. New York State Department of Health. Data & Reports 2014. Available at: http://www.health.ny.gov/statistics/chac/general/pdf/g36.pdf [access: 30.12.2015].
3. Gopi A, Madhavan SM, Sharma SK, et al. Diagnosis and treatment of tuberculous pleural effusion in 2006. Chest. 2007; 131(3): 880–889, doi: 10.1378/chest.06-2063, indexed in Pubmed: 17356108.
4. Lewinsohn DM, Leonard MK, LoBue PA, et al. Official American Thoracic Society/Infectious Diseases Society of America/Centers for Disease Control and Prevention Clinical Practice Guidelines: Diagnosis of Tuberculosis in Adults and Children. Clin Infect Dis. 2017; 64(2): 111–115, doi: 10.1093/cid/ciw778, indexed in Pubmed: 28052967.
5. Conde MB, Loivos AC, Rezende VM, et al. Yield of sputum induction in the diagnosis of pleural tuberculosis. Am J Respir Crit Care Med. 2003; 167(5): 723–725, doi: 10.1164/rccm.2111019, indexed in Pubmed: 12598215.
6. Weiszhar Z, Hovarth I. Implementing p-M Analysis Step-by-Step. Breath. 2013; 9: 300–306, doi: 10.1183/20734735.042912.
7. Rieder HL, Chiang CY, Rusen ID. A method to determine the utility of the third diagnostic and the second follow-up sputum smear examinations to diagnose tuberculosis cases and failures. Int J Tuberc Lung Dis. 2005; 9(4): 384–391, indexed in Pubmed: 15830743.
8. Berger HW, Mejia E. Tuberculous pleurisy. Chest. 1973; 63(1): 88–92, doi: 10.1378/chest.63.1.88, indexed in Pubmed: 4630686.
9. Kim HJ, Lee HJu, Kwon SY, et al. The prevalence of pulmonary parenchymal tuberculosis in patients with tuberculous pleuritis. Chest. 2006; 129(5): 1253–1258, doi: 10.1378/chest.129.5.1253, indexed in Pubmed: 16685016.
10. Seibert A, Haynes J, Middleton R, et al. Tuberculous pleural effusion. Chest. 1991; 99(4): 883–886, doi: 10.1378/chest.99.4.883.
11. Valdés L, Alvarez D, San José E, et al. Tuberculous pleurisy: a study of 254 patients. Arch Intern Med. 1998; 158(18): 2017–2021, doi: 10.1001/archinte.158.18.2017, indexed in Pubmed: 9778201.
12. Ruan SY, Chuang YC, Wang JY, et al. Revisiting tuberculous pleurisy: pleural fluid characteristics and diagnostic yield of mycobacterial culture in an endemic area. Thorax. 2012; 67(9): 822–827, doi: 10.1136/thoraxjnl-2011-201363, indexed in Pubmed: 22436167.