TUBERCULOUS PLEURAL EFFUSION: CYTOLOGIC REVIEW OF 52 PATIENTS WITH CORRESPONDING HISTOPATHOLOGICAL DIAGNOSIS

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ABSTRACT

Background: Microscopic appearance from cytological examination of pleural effusion due to tuberculous infection is not specific. The aim of this study was to investigate the role of cytology pleural effusion examination in an attempt to diagnose Tuberculous infection.
Methods: Fifty two pleural effusion cases from Hasan Sadikin General Hospital Bandung were reviewed in this study. All cases were sputum Acid Fast Bacilli positive and histopathologically showed typical Tuberculosis appearance on pleural biopsy.
Results: The mean age of the patient was 39.2 years and 35 cases (67%) were male. Almost all (92%) effusions were Rivalta positive, with mean level of Lactic dehydrogenase and Glucose were 1598.4 U/L and 84.7 mg/dL consecutively. The cytological findings showed moderate to high cellularity but 3 cases (5.8%) were hypocellular. Lymphocyte predominance was observed in 43 (82.7%) cases. Six (11.5%) cases were polymorphonuclear cells predominance. All cases showed scanty mesothelial cells. Proteinaceous background was found in 23 (44.2%) cases. There were no epitheloid cells observed in all cases.
Conclusions:Lymphocytes predominance and absence or scanty mesothelial cells were highly suggestive for Tuberculous pleural effusion. Cytology examination alone cannot confirm the diagnosis of Tuberculous infection.

Keyword: cytology; histopathology; pleural effusion; tuberculosis

INTRODUCTION

Tuberculosis (TB) is one of the main public health problems in Indonesia. Indonesia contributes the second largest TB burden in the world and one million new TB cases were reported annually.[1] Based on Global Tuberculosis Report WHO 2015, prevalences of all type-TB in Indonesia were 647 cases per 100,000 people and 41 TB deaths per 100,000 people.[2]

TB is a disease caused by *Mycobacterium tuberculosis* and rarely, by *M. bovis* and *M. africanum* infection. TB has two types based on the location: pulmonary TB and extrapulmonary TB. Extrapulmonary TB occurs due to hematogenous dissemination of *M. tuberculosis* that involves any organs. The most frequently extrapulmonary TB consists of lymph nodes (40%), pleura (16%), bone or joint (10%), peritoneal (6%), meningeal (6%), and genitourinary tract (5%).[3]

Pleural involvement caused by TB infection leads to inflammatory pleural disease or pleuritis. Pleuritis TB is the second most common extrapulmonary TB after lymphadenitis TB.[4, 5]Pleuritis is usually associated with pleural effusion, as a common manifestation that characterized by excessiveaccumulation of pleural fluid.[6]

It is a challenge to diagnose pleuritis TB, because standard criteria such as the presence of *M. tuberculosis* in sputum, pleural fluid, and/or tubercle in tissues, might be unrevealed.A few of diagnostic tools like Polymerase Chain Reaction (PCR), Adenosine deaminase and gamma interferon could be a help, although the results are still variative and not all health care have the tools.[7, 8]

Thoracocentesis with pleural fluid analysis is a simple technique that could narrowing the differential diagnoses of pleural effusion rapidly. For a complete diagnostic assessment, cytological examination of effusion should be performed.[9]Pleural fluid cytology of suggested TB pleural effusion shows lymphocyte-predominance, none or rare mesothelial cells, and presence of epitheliod cells.[7] Nevertheless, this concept of the cytological findings came from last decade-studies and the microscopic appearances are not specific. Therefore, research about cytopathological findings of pleural fluid in pleural effusion caused by *M.* tuberculosis should be conducted to increase the accuracy of diagnosis and therapy.

MATERIALS AND METHODS

Fifty two pleural effusion cases from Hasan Sadikin General Hospital Bandung, in January 2010 – Desember 2015, were reviewed. All cases were sputum Acid Fast Bacili positive and histopathologically showed typical Tuberculosis appearance on pleural biopsy.Pleural fluid analysis included differential cell count, especially lymphocytes, polimorphonuclear cells, and mesothelial cells. Medical records about clinical response to antituberculosis drugs also were reviewed.

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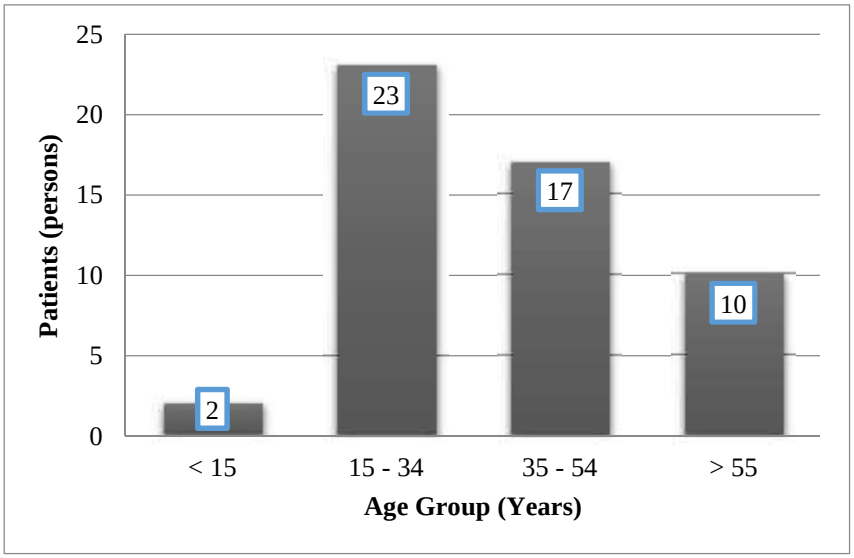
RESULTS

Based on medical records, fifty two patients who have been improved clinically after given antituberculous drugs, were reviewed. There was 35 men (67.3%) and 17 women (32.7%). Figure 1 represents the proportion based on age group, with the largest group was over 15 years old (96%). Themean age of the patient was 39.2 years old.

Fig 1. Proportion of patients based on age group



Almost all (92%) effusions were Rivalta positive, with mean level of Lactic dehidrogenase (LDH) and Glucose were 1598.4 U/L and 84.7 mg/dL, consecutively.All cases were determined as pleuritis TB histopatologically because of the findings of tubercles and caseous necrosis. All cases were positive acid-fast bacilli.

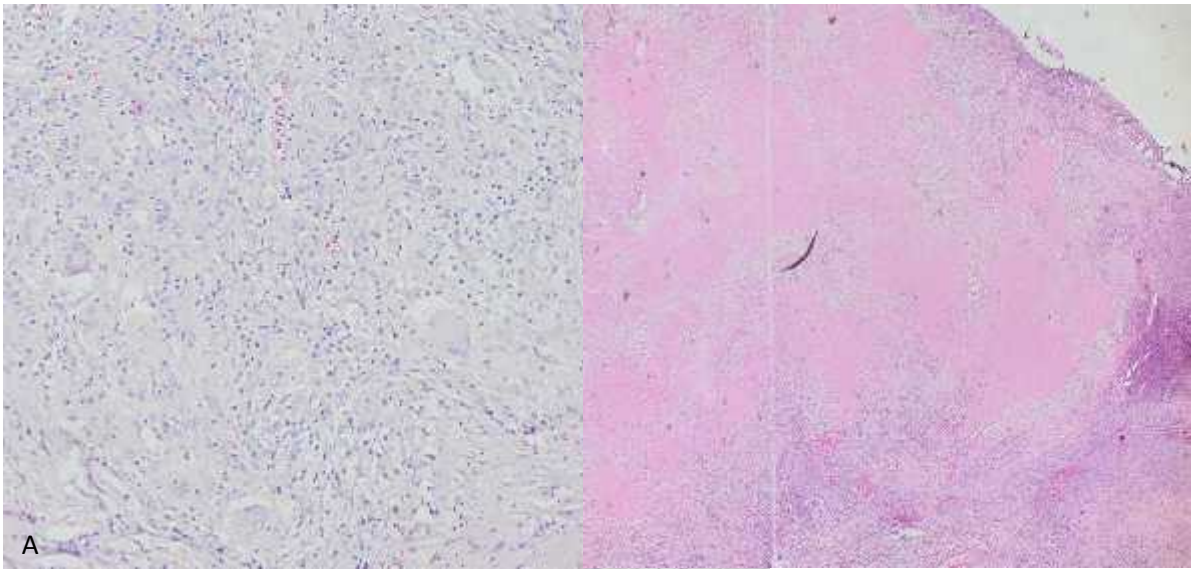
As stated in Table 1 and Figure 2–5, the cytological findings showed moderate to high cellularity but 3 cases (5.8%) were hypocellular. Lymphocyte predominance was observed in 43 (82.7%) cases. Six (11.5%) cases were polymorphonuclear cells

(PMN)predominance. All cases showed scanty mesothelial cells. Proteinaceous background was found in 23 (44.2%) cases. There were no epitheloid cells observed in all cases.

Table 1. Cell compositions

	Cell predominances, n (%)			Undetermined, n (%)
	PMN	Lymphocytes	Mesothel	
Total cases	6 (11,5)	43 (82,7)	-	3 (5,8)

Fig 2. The typical tubercles in biopsy



A. Epitheloid cells and Langhans giant cells B. Caseous necrosis

Fig 3. Lymphocyte predominances

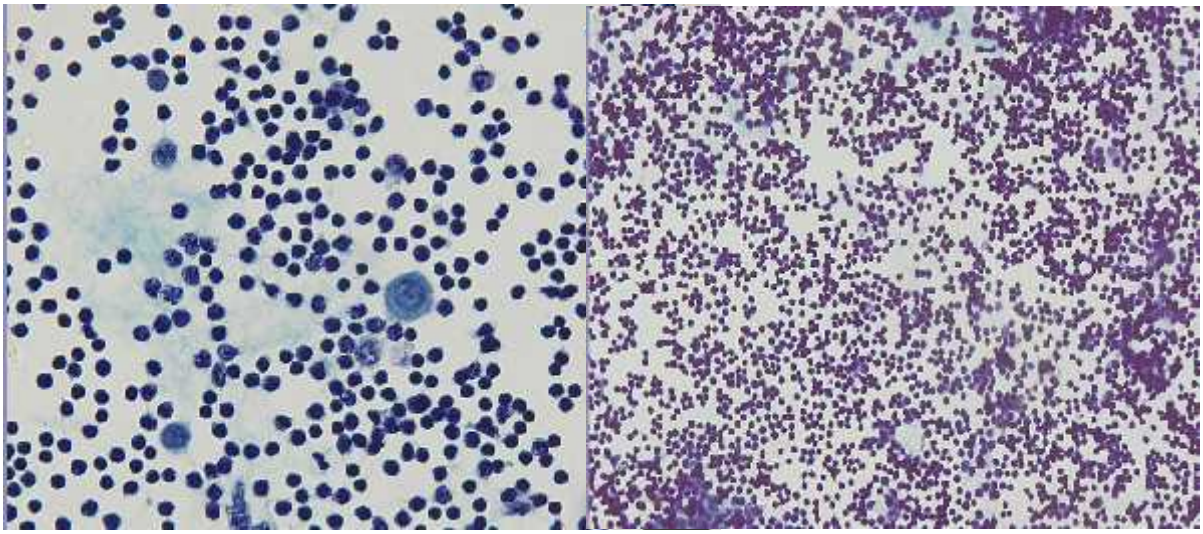


Fig 4. PMN predominances

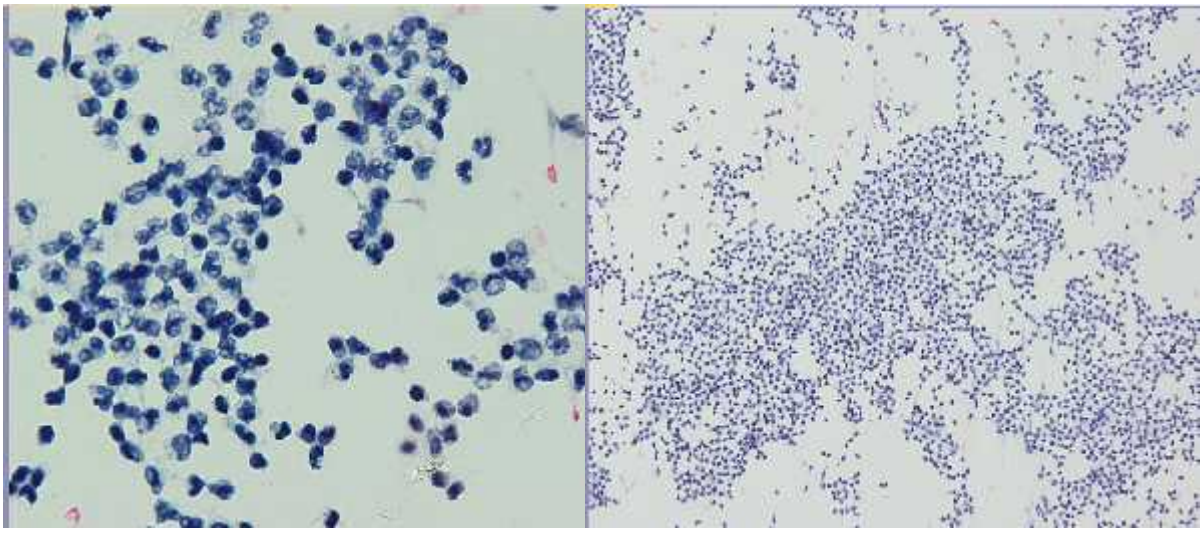
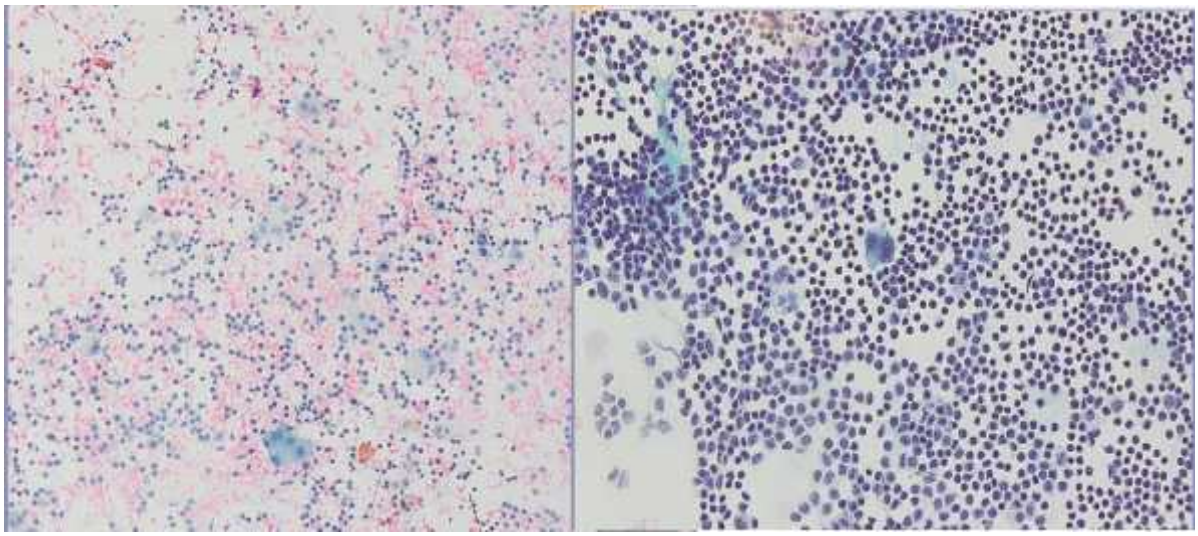


Fig 5. *Giant cells*



DISCUSSION

Pleural effusion TB could be a manifestation of primary or progressive post-primary (reactivated) TB.[5]This study showed that most of cases were male (67%). It could be predicted, because the pulmonary infection patients in Indonesia were male, statistically.[2]

There are three pathological types of pleural effusion TB. Pleural effusion TB could be a manifestation of primary TB thatoccurs very often in children; as a result of TB reactivation; or empyema TB.[3-4, 10]In this study, mostly patients were over fifteen years old; only two cases were children. The results were consistent with study by Moudgil H (1994) in which pleural effusion usually occured due to reactivation of TB infection in industrial countries.[8]

Pleural involvement occurs from direct contact to pulmonary lesion that induces the immunologic reaction (delayed hypersentivity) toward TB antigens. Pathogenesis of pleuritis is associated with rupture of subpleural caseous focus to pleural cavity. Delayed hypersentivity reaction begins when *M. tuberculosis* antigens invade pleural cavity and interact with sensitized-T lymphocytes. Exudation happens because of increased capillary permeability and the impairment of lymphatic drainage.[5, 8]

The effusion is generally exudate and contains scanty bacilli.[4] The fluid could be turbid or serosanguinous, but almost never be red because of blood.[5] There were three cases (5.8%) whose hemorrhagic fluid. Almost all cases were Rivalta positive in this study, and most of them were exudate. Mean level of LDH was 1598.4 U/L, consistent with study by Soe and Shwe (2010) which found LDH level in pleural fluid of TB patients was over 500 U/L.[11]Pleural effusion TB could have low glucose level in pleural fluid, but usually near to serum level. Spriggs (1960) stated that glucose level in pleural fluid of TB patients was under 80 mg/dl, generally.[8, 12]In this study, only eighteen cases (42.9%) had glucose level under 80 mg/dL.

Salazar *et al*. (1997) reported that it was difficult to diagnose TB pleural effusion because of scanty amount of *M. tuberculosis* in the fluid and leading to false negative.[7]Direct examination of pleural fluid by Zeihl-Neelsen stain requires bacterial density 10,000/mL; therefore, it could only detect under 10% cases. Culture requires minimum 10 – 100 live bacteria, so the sentivitiy is variable from 12 to 70%.[5]

Pleural fluid cytology of suggested TB pleural effusion showed lymphocyte-predominance(lymphocytic effusion*)*, none or rare mesothelial cells, and presence of epitheloid cells.[7]This study revealed six cases (11.5%) with PMN predominances. These occurred because of secondary infection, such as rupture of pulmonary TB focus into pleural cavity that led to empyema with cytological appearance consist of mostly neutrophils. Chronic empyema could cause pleural fibrosis with fluid localization and then encysted. In this condition, effusion showed hypocellularity and contained cholesterol crystals associated with cell membrane disruption.[13] PMN-predominance may also occur because of acute stage of illness.[14]From six PMN predominance-cases, total of mesothelial cells was under 30 per 100 cells (<3%).

Cytological examination of lymphocyte composition and particularly mesothelial cells in pleural fluid could support diagnostic assessment of etiologies of pleural effusion. The none or scanty mesothelial cells lead TB pleural effusion. It is consistent with study by Spriggs (1959) and Koegelenberg (2007).[12, 15]

In conclusion, lymphocytes predominance and absence or scanty mesothelial cells were highly suggestive for Tuberculous pleural effusion. Cytology examination alone cannot confirm the diagnosis of Tuberculous infection.

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