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DIAGNOSTIC CONTRIBUTION OF CLOSED NEEDLE PLEURAL BIOPSY – A 10-YEAR RETROSPECTIVE ANALYSIS

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Abstract: Determining the etiology of a pleural effusion can present a major problem for the clinician. Diagnostic evaluation of pleural effusions should include relevant history, clinical course, radiographic abnormalities, and take into account the patient's desire and consent for further invasive investigations. The seventies were dominated by specific pleural effusions, but in the last three decades effusions of malignant etiology have dominated. Despite advances in diagnostics, about 20% of pleural effusions remain etiologically unexplained.

Objective: we present data on the diagnostic contribution and complications when using a Ramel's needle (Wolf's set) in investigating the nature of pleural effusions from an etiopathogenetic aspect.

Methods: This retrospective study included 284 transparietal closed pleural biopsies performed between January 2011 and December 2020.

Local anesthesia with 2% lidocaine was applied to the skin and subcutaneous tissue in all subjects (premedication with 1 mg of atropine or 10 mg of apaurin was sporadically applied); a chest radiograph was taken immediately before and within 4 to 12 hours after the procedure to rule out complications. The diagnostic positivity, accuracy and complication rate of the technique were evaluated.

Results: 175 men and 109 women (median age 60 years, range 19–88) underwent transparietal pleural biopsy with a Ramel's needle, 96% of pleural effusions were unilateral (53% in the right hemithorax). Pleural tissue was obtained in 98%.

The most common histological diagnosis included: malignancy (34.7%), nonspecific inflammation and mesothelial hyperplasia (32.3%), chronic inflammation with fibrosis (23.5%), granulomatous disease (4.3%), normal pleura and striated muscle (5.2%). Microbiological examination was performed in 24 samples (8.4%): Mycobacterium tuberculosis was present in 1 case, Escherichia Coli in one and Candida albicans in another patient. No pathogenic bacteria or fungi were identified in the rest of the examined.

The procedure was well tolerated. Complications occurred in 7 (2.4%): pneumothorax in 4 patients (1.4%), vasovagal reaction in 2 cases (0.7%), local hematoma (0.3%).

Conclusion: closed (percutaneous, blind) pleural biopsy with a Ramel's needle appears to be a simple technique, well tolerated, with a low complication rate and high diagnostic efficiency. Closed pleural biopsy has a relatively high sensitivity in the diagnosis of exudative pleural fluid, especially in tuberculous pleurisy and may provide an alternative technique in clinical practice. It can be applied to any unexplained pleural effusion, in cooperative patients with no coagulation abnormalities, in relation to standard biochemical, microbiological and cytological investigations, especially in hospital units without thoracoscopy. In our series, nonspecific inflammation was the most common histological diagnosis, and repeated biopsies significantly increased the diagnostic contribution.

Keywords: *closed pleural biopsy, blind pleural biopsy, tuberculous pleural effusion, malignant pleural effusion, diagnostic contribution*

Field: Medical Sciences and Health

INTRODUCTION

The first attempt to visualize the pleural space was made by Jakobeus in 1910 using a modified Nitze cystoscope (16). With find out the causal treatment to tuberculosis and simultaneously with the discovery and application of the Abram's and Cope's needle for percutaneous biopsy of the pleura, enviable efficiency in the diagnosis of malignant and tuberculous pleural effusions has been achieved (1,8). Closed pleural biopsy (CPB), first reported by De Francis in 1955 and later by Abram (1), Cope (8) and Raya (25) who introduced different types of needles named after the inventors, became common method of obtaining pleural tissue for the diagnosis of pleural diseases (11). Tru-cut have been used occasion-

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ally (23). Thoracoscopy and thoracotomy have been used as successful surgical methods to help obtain tissue from the visceral pleura and have shown a high yield in diagnosis (30), but require sophisticated instruments and expertise, associated with the risk of greater invasiveness (22, 36). Cope's and Abram's, then Ramel's were and still are the most popular CPB needles after practical modification (8, 1), as a simple and cheap technique for regular use in hospitals of different levels and also in outpatient settings. Complications of CPB are low (mainly minor pneumothorax, pain or vasovagal syncope and hemothorax) (6, 33). CPB has a lower diagnostic accuracy but with a lower rate of complications than thoracoscopy as shown by previous studies (14, 21). According to the results of numerous clinical studies in the area of clarifying the etiology of pleural effusions (3, 10, 24), the sensitivity of thoracoscopy is only approximately 90% to 95% (14, 21, 34). Therefore, CPB is still considered an essential method for diagnosing exudative pleural effusion due to its practicality and safety.

MATERIALS AND METHODS

This was a retrospective study of patients with unidentified pleural effusion who underwent CPB in City General Hospital 8-mi septemvri Skopje during the past decade from January 2011 to December 2020.

Pleural biopsy

After taking anamnesis and performing a clinical and radiological examination, a diagnostic thoracocentesis was mandatory, then a biochemical examination and, in a small part, a bacteriological examination of the pleural fluid. Light's criteria and the calculated pleural fluid/blood score were used to distinguished exudative from transudative pleural effusion. Imaging examinations (ultrasonographic and computed tomography), as well as bronchological processing, were carried out.

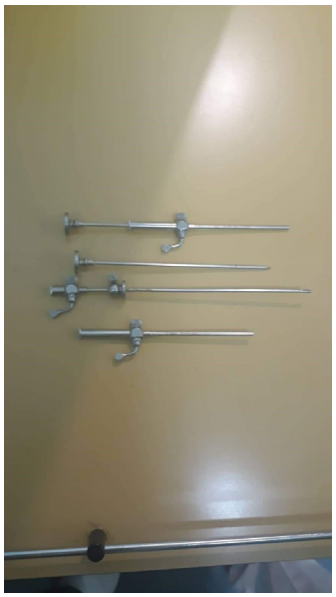


Figure 1 Ramel's pleural biopsy needle

Ramel's pleural biopsy was performed only in patients who cooperated and had no coagulation abnormalities. The technique is essentially the same as that of thoracentesis and no specific additional patient preparation is required.

The procedure was performed in the sitting position of the patients as described elsewhere (20). The physical examination determines the affected side of the chest and selects the site for biopsy. Before starting the thoracentesis, this area was thoroughly cleaned with antiseptics, and then the skin and subcutaneous tissue were infiltrated with the local anesthetic 2% lidocaine (premedication with 1 mg atropine or intramuscular 10 mg diazepam had been administered rarely, only in patients who gave symptoms of fear or pain). Confirmation of free fluid was obtained by aspiration with the same syringe. For free access, a small incision of 0.2 to 0.5 cm in size was made just above the upper border of the rib at the selected site. Ramel's needle was inserted through it. At least 3 specimens were taken from one skin location (with incision positioning at 3, 6, and 9 o'clock) required for histology and culture. The Ramel's needle was completely withdrawn after each specimen was obtained. The biopsy specimens were placed in two bottles:

one was fixed with 10 percentage formalin, for histopathological examination and one biopsy sample was minced with a scalper and placed as a coating in a tube with Lowenstein-Jensen medium for cultivation of the tubercle bacillus and in case of positive growth confirmed by Ziehl-Neelsen acid-fast staining. A posteroanterior and lateral chest X-ray film was taken in all patients immediately before and within 24 hours after the procedure to rule out complications. The diagnostic positivity, accuracy, and complication rate of the technique were evaluated, along with pleural fluid analyzes and other relevant investigations needed to obtain a specific diagnosis.

RESULTS

Overall, all 284 patients with pleural effusion determined clinically and by imaging studies underwent CPB. Adequate pleural tissue was obtained in 278 (98%), and striated muscle and inadequate tissue were histologically determined in 6 biopsies. The results are shown in Table 1, and the characteristic cases are presented in Figures 2-5. Of the biopsies where adequate pleural tissue was found, a histological diagnosis was found in 110 (39.5%), and in the remaining 168 a histological finding was obtained that cannot be highlighted as a final clinical diagnosis, but in more (especially in inflammatory diseases) the histological description assisted the clinician in making the final diagnosis.

Table 1	Number	Percentage
CPB with Ramel's needle	284	100
Adequate pleural tissue	278	98
Striated muscle and inadequate tissue	6	2
Histologically confirmed diagnoses	110	39
Other histological diagnoses and descriptions	159	56
Normal pleura	9	3
Muscle and inadequate tissue	6	2
Histological diagnoses and findings are classified into 4 groups - shown as in Table 2		

Table 2		Number		Percentage
Diseases confirmed by CPB		110		39
1.Pleural neoplasm		98		34.7
-primary(Mesotheliomamalignum)	34			
-secondary (metastatic	64			
- pulmonary	24			
- breast	17			
- gastrointestinum (stomach, colon, pancreas)	8			
- genitourinary	6			
- lymphoma and leukosis	3			
- undetected primary malignancy	6			
2. Granulomatosis		12		4.3
- tuberculosis	9			
- sarcoidosis	3			
3. Inflammatory, chronic and other conditions		159		55.8
- nonspecific inflammations and mesothelial hyperplasia	92		32.3	
- chronic inflammation, fibrin and fibrocollagenous tissue	67		23.5	
4. The rest		15		5.2
- normal pleura	9			
-muscle and inadequate tissue	6			

In 17 (6%) Ramel's CPB was repeated (one, two, or three times) because the first biopsy reported an indeterminate histologic diagnosis or inadequate tissue was obtained, predominantly from the intercostal muscle. Repeated histological reports increased the final diagnostic yield as shown: 9 (8%) for malignancy, 2 (1.8%) for tuberculous pleurisy, and 6 (5.5%) for inflammatory disease. Thus, a higher percentage of histologically confirmed diagnoses was obtained.

Figure 2 Pleural Tuberculosis, specific granulomatous inflammation with giant cells Langhans-type (staining H&E, x100)

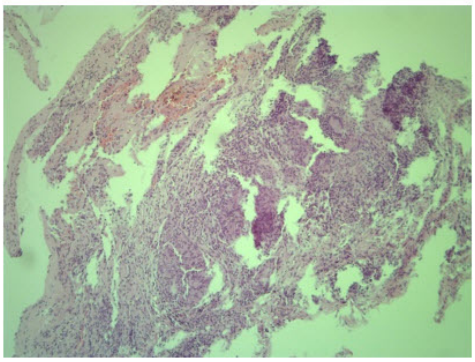


Figure 3 Pleural Mesothelioma (staining H&E, x100)

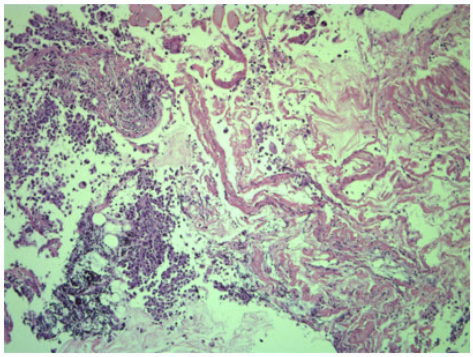


Figure 4 Pleural metastasis from Clear cell renal cell carcinoma (staining H&E, x100)

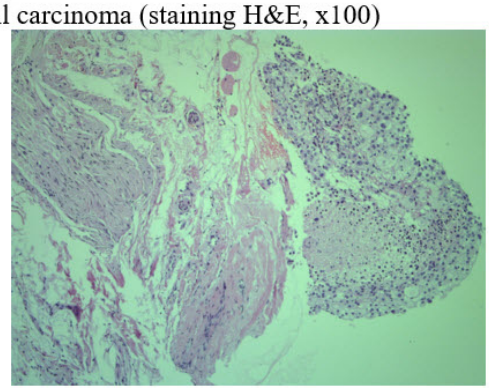
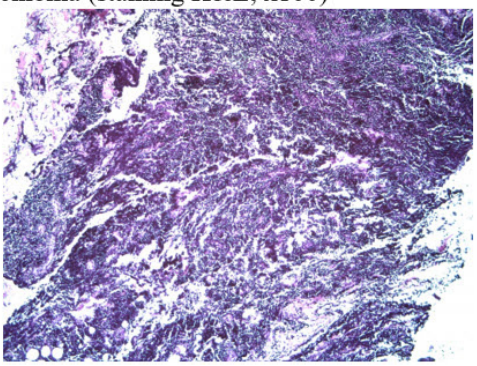


Figure 5 Pleural metastasis from Small cell lung carcinoma (staining H&E, x100)



A finding of normal parietal pleural tissue and findings described as: non-specific inflammation, mesothelial hyperplasia, serofibrinous inflammation, chronic inflammation with fibrosis, fibrocollagen structure, hyalinization, edematous tissue and striated musculature were commented as "negative".

A complication occurred in 7 cases, in 4 a partial pneumothorax in the form of "trapped air" that did not require special treatment. Subcutaneous emphysema or hematoma was observed less frequently, vasovagal reaction occurred in two patients. There were no immediate or life-threatening complications.

DISCUSSION

The diagnostic algorithm for pleural effusions of unclear etiology typically begins with thoracentesis, biochemical, microbiological and cytological examination. Bacteriological examination and culture of a sample of the parietal pleura confirm tuberculous pleural inflammation in only one to two percent (27). Cytological examination, even in large effusions, does not reveal metastatic involvement of the pleura in more than 60 percent and in about 20% of mesothelioma (26, 28). In this study, using a Ramel needle an adequate pleura was obtained in 98% of cases, which is somewhat higher than other reports (17). 110 (39.5% of 278 patients in whom an adequate pleura was obtained) were diagnosed based on histology. The reports on the diagnostic contribution of Cope's needle are similar (37, 4, 19).

The mean age of patients with tuberculous pleurisy was 32 years, slightly lower than previously reported (8). Adenosine deaminase (ADA) as a sensitive parameter for tuberculous effusion showed low specificity in this study. While in some ADA was highly sensitive (9), other studies reported lower results (37, 32). Alkaline phosphatase activity, a test previously shown to be useful in differentiating tuberculous from nontuberculous pleural effusions (20), was not used in this study. Histopathological reports of epithelioid granuloma with or without giant cells and the presence of caseous necrosis were found in 9 (18.2%) and this was the final diagnosis for them.

Almost the same results were reported previously (37). Only 1 subject in this study had acid-alcohol-resistant bacteria (AARB) observed in the histological preparation of the pleural biopsy specimen and confirmed by Ziehl-Neelsen staining, which is quite low compared to the others. While one series saw

no AARB on tissue smears (4), another reported a relatively higher percentage (37). The low positivity for AARB in the current series may be explained by the experience and bias of the investigator as well as the preparation of a small sample of tissue for culture by the crushing and maceration procedure, in addition other common causes should also be considered, such as the precision demonstrated by the microbiologist for culturing the specimen. However, AARB visualization or positive culture did not add further to the diagnosis as they were diagnosed on the basis of histopathology. Diagnostic yields of pleural biopsies in tuberculosis were 20% (7). Other factors such as the size of the pleural tissue obtained (20) and the number of times biopsied (7, 18,29) also determine the success rate. In 67 patients, the histopathological report was chronic inflammation; in 9 it was a normal pleural tissue. Nonspecific inflammation with varying degrees of fibrosis or normal pleura was found in 68% of patients in one study (18).

Viruses are thought to be one of the common causes of undiagnosed exudative pleural effusion, but is not always there a histological documentation; it is reported that the patients were immunocompromised (12, 29). There is an invaluable yield of Ramel's biopsy in exudative effusion. Published studies have compared the diagnostic contribution of Abram's and Cope's needle (24). No significant differences or advantages have been described in terms of access, safety, complications and diagnosis (38). A larger fragment, mesothelial cells, and fibrin were more often obtained with Abram's needle, while with the Cope's needle tussue of muscle was more often present. Both needle biopsies were very similar in terms of chronic inflammation, neoplastic tissue, granuloma, caseous necrosis, granulation, vessels, nerves, adipose tissue, neutrophils, hemorrhage,and epidermis. The advantages of using the Abram's needle did not translate into a better diagnostic yield in this series (25, 38). Of the 278 patients who underwent Ramel's biopsy and adequate pleural tissue was obtained, in 110 (39.5%) a definite diagnosis was made using the histopathology report alone. With repeated biopsies, the number of definitive diagnoses based on the histopathological report increased by 6%. In 60.5%, the histopathological report as chronic inflammation with fibrosis, collagen hyalinized and edematous tissue, as well as normal pleura with mesothelial hyperplasia, helped to exclude another clinical entity and confirm the final nonmalignant nature of the pleural effusion that could fit into the clinical diagnoses such as inflammation, heart and renal failure, protein and hematological abnormalities, pulmonary thromboembolism, viral pleuropneumonia, pleural effusion from an older date, other complex immunocompromising and multisystemic diseases as well as pleural effusion of insufficiently explained origin. Thus, a "negative" pathohistological report in relation with the clinical part and overall investigations could be to a large extent accepted as "positive" and help the clinician in establishing the final diagnosis. Nonspecific inflammation with varying degrees of fibrosis or normal pleura was found in 68% in one study (18). Several studies have highlighted the accuracy of needle biopsy in the diagnosis of malignant pleural effusion (2, 5, 26). The accuracy of needle biopsy in malignant pleural effusion was estimated to be high by this study because a large proportion were histological confirmed, and repeat biopsy is emphasized which increased the diagnostic contribution above all in malignant tumors. Overall, the contribution of closed pleural biopsy with a Ramel's needle in this study proved to be significant and useful in the explanation an effusion of unclear etiology. The contribution in establishing the final diagnosis was complete and maximal in 39.5%, and in the remaining 60.5% it was partial but helped the clinician a lot in establishing diagnosis.

CONCLUSION

The role of percutaneous closed pleural biopsy in cases of undiagnosed pleural effusion remains crucial as it has achieved a specific diagnosis in most cases. Despite improved laboratory technique, newer diagnostic tests for pleural fluid, and the wider availability of thoracoscopy, closed pleural biopsy has not been ignored or placed in an inferior position. It still remains an important and indispensable method due to its simplicity, cheapness and low complication rate, especially in elderly and high-risk patients, even more so because it can be performed at the bedside, no additional preparation is required and can be perform with little instrumental and labor support.

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