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Closed Pleural Biopsy in Exudative Pleural Effusion in the era of Thoracoscopy– its Diagnostic yield and Safety

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Abstract:
Introduction: Before the era of thoracoscopy, closed pleural biopsy was considered to be the procedure of choice in cases of undiagnosed pleural effusion. With the descent of thoracoscopic era,thoracoscopic biopsyhas replaced closed pleural biopsy as the procedure of choice in these cases. However, it is still not readily available in resource-limited setups.
Objective: This study was done to analyse the diagnostic yield and establish the safety profile of the closed needle pleural biopsy by Abrams needle or Cope needlein exudative pleural effusion.
Methods:A cross-sectional study was done from July 2016 to June 2017.158 cases of pleural effusion were evaluated by complete pleural fluid examination - biochemical, microbiological and cytological examination. 52 of these patients were excluded from the study as the diagnosis was established on the initial pleural fluid examination in these cases. 6 of the patients were lost of follow up before closed pleural biopsy could be performed. The remaining (100) patients were considered for closed pleural biopsy with Abrams and Cope pleural biopsy needle. The main outcome measure was to analyse the diagnostic yield in the form of confirmed diagnosis.
Results: 100 patients with exudative lymphocytic pleural effusion were subjected to closed pleural biopsy, 59 (59%) of these cases were diagnosed on the first pleural biopsy. Among the remaining 41 patients, 24 patients consented for a repeat pleural biopsy. The diagnostic yield of second pleural biopsy was 70.83% (17). Therefore, the overall pleural biopsy diagnostic yield was 76% with the confirmation of diagnosis in 76 patients with exudative lymphocytic pleural effusion. The most common diagnosis on closed pleural biopsy was found to be tuberculosis followed by malignancy.
Conclusions: The diagnostic yield Closed pleural biopsy is comparative to that of thoracoscopic biopsy provided there is a proper selection of patients suffering with pleural effusions. In view of good diagnostic yield, easy availability, lower cost and low complication rates, it should be used routinely in all undiagnosed cases of exudative lymphocytic pleural effusion especially in resource limited set ups.

Key words:*Closed pleural biopsy, malignant pleural effusion, thoracoscopic pleural biopsy, tubercular pleural effusion*

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I. Introduction

One of the most commonly encountered clinical conditions in day-to-day pulmonary practice is Pleural Effusion. However, in spite of having a good clinical history, detailedclinico-radiological assessment and laboratoryinvestigations of aspirated fluid, it is difficult to establish the etiological diagnosis in several cases. As a result, several patients often receive empiricaltreatment in the absence of aconfirmatory diagnostic documentation.

Before the dawnof thoracoscopic era, closed pleural biopsies were considered to be the standard procedure in establishing the diagnosis in these cases. The diagnostic efficacy of closed pleural biopsy in such situations has been reported between 60% and 80%.[1-4] With the easy availability of thoracoscopy these days, the thoracoscopic biopsy is recommended as the procedure of choicein patients with undiagnosed pleural effusion, gradually replacing the closed pleural biopsy.[5] Though it has been repeatedly documented that thoracoscopy has better yield than pleural biopsy, such recommendations are not feasible in a resource-limited setting like India.

Previous studies have suggested that there may be an improvement in diagnostic yield of closed pleural biopsy if the procedure is repeated.[6,7] This study focuses on the combined yield of the first and, if required, a second pleural biopsy in the cases of undiagnosed exudative pleural effusion.

II. Methods

This study was conducted at Department of Pulmonary Medicine, Unique Multispecialty Hospital and Research Institute, Surat over the duration of 12 months from July 2016 to June 2017. The design of the study was tertiary hospital based cross-sectional study.One hundred and fifty-eight patients of pleural effusion were included in the study. The study and procedures were explained in detail following which a written informed consent was obtained from the patients. The study participants were evaluated with a thorough clinical history, detailed physical and radiological examinations and routine investigations. In cases where examinations and investigations indicated a clear cause of effusion, no further work-up was done. For example, patients presenting with bilateral effusion in a clinical setting strongly suggestive of transudative effusionwere excluded in our study, the exceptions being atypical features or failure to respond to therapy. In cases where no clear cause of pleural effusion could be established, a diagnostic thoracocentesis was performed and the aspirated fluid was evaluated for cell count, biochemistry, acid-fast bacilli smear and cytopathology for malignant cells. If the above investigations for pleural fluid analysisfailed to establish the diagnosis, such case were labelled as undiagnosed pleural effusionand subjected to pleural biopsy with Abrams or Cope pleural biopsy needle. Under all aseptic precautions, a small incision is made with a scalpel in the properly anesthetized skin and subcutaneous tissueand the pleural biopsyneedle is inserted. Once the tip of the needle is placed in the pleural space, the inner stylet is removed. The biopsy needle is slowly withdrawn while applyingconstant aspiration until the needle hooks onto the pleura. The outer trocar is then firmly held with one hand, the other hand is used to rotatethe inner cannula into the closed position thus cutting off a small piece of the parietal pleura. (Abrams needle)

Exclusion criteria for pleural biopsy were age <12 years, non-cooperative patients and/or moribund patients, pleural fluid thickness <3 cm on ultrasonography at the infra-scapular border, patients with bleeding diathesis, transudative effusion, empyema[8]/neutrophilic effusion, and local skin infection. The patients who had negative pleural biopsy in the first attempt were asked to undergo a repeat pleural biopsy procedure. After taking consent, a repeat pleural biopsy was done by similar procedure.

Table 1: Demographic characteristics of patients

Patients and characteristics	Total	Male	Female
Number	100	71	29
Mean age±SD	52.65±17.42	51.24±16.82	56.10±18.76
Smoker Yes/no	54/46	48/23	6/23
Side of effusion Unilateral/bilateral	95/5	68/3	27/2
Colour of effusion Straw/hemorrhagic	63/37	46/25	17/12
Extent of effusion Mild/moderate/massive	5/73/22	4/54/13	1/19/9
Position of mediastinum Central/opposite/ipsilateral	66/27/7	50/16/5	16/11/2

III. Results

Out of the total 158 patients, 58 were excluded from the study. The diagnosis wasestablished before closed pleural biopsy in 52 of these patients and 6 patients were lost to follow up before the closed pleural biopsy could be performed. [Table 2]

Table 2: Etiology of effusion established on initial workup of pleural effusion (Excluded in the study)

Etiological diagnosis	Number of patients
Sputum positive for AFB smear	1
Pleural fluid positive for AFB smear	6
Cytology positive for malignant cells	8
Chylothorax	1
Transudative effusion	17
Parapneumonic effusion	12
Empyema	7
Total patients	52

The remaining 100 patients who were considered as having undiagnosed pleural effusion on initial evaluation were subject to closed pleural biopsy. In orderto obtain four satisfactory pleural biopsy samples, the average number of needle passes was 4.24 per patient. The first pleural biopsy analysis yielded

pleural tissue in 96% (96) of the patients. The diagnostic yield of the first pleural biopsy was 59%. In spite of pleural tissue being obtained during the biopsy procedure diagnosis could not be established in 37 of the patients on histo-pathological examination, while pleural biopsy failed to provide pleural tissue sample in 4%(4)of the patients. Thus, 41 patients had negative first pleural biopsy, out of which 24 patients could be subject for a repeat procedure of pleural biopsy (9 patients did not give consent, 6were lost to follow-up and 2 of the patients had partial resolution of pleural effusion). Out of the 24 patients who had repeat pleural biopsy, 17 had definitive histo-pathological diagnosis. The diagnostic yield of repeat pleural biopsy was 17/24 (70.83%). Hence, after a repeat pleural biopsy, combined yield of closed pleural biopsy increased to 76% (76/100). Out of the total 100 patients who underwent closed pleural biopsy, 39 patients were diagnosed as having tuberculosis (TB), 35 patients as metastatic carcinoma and 2 patients as Non-Hodgkin's lymphoma [Table 3]. In the 24 non-diagnostic pleural biopsy reports, 1 patient's report of the second and third microscopic examination of centrifuged sediments of pleural effusion showed microfilaria of Wucheriabancrofti in the absence of eosinophilia, both peripheral blood and pleural fluid. Hence the diagnosis of filarial pleural effusion was established (rare disease).

TB and metastatic carcinoma were the two most common etiological diagnoses on the first closed pleural biopsy, with the diagnosis of TB being significantly higher than metastatic carcinoma. However, a repeat closed pleural biopsy in the cases with negative first pleural biopsy showed proportionately more patients with metastatic carcinoma than TB.

Table 3: Etiological diagnosis after pleural biopsy procedure

Etiological diagnosis	First pleural biopsy (n=100)	Repeat pleural biopsy (n=24)	Total patients n=100 (100%)
Tuberculosis	36	3	39 (39)
Metastatic carcinoma	22	13	35 (35)
Non-Hodgkinlymphoma	1	1	2 (2)
Total	59	17	76 (76)

IV. Discussion

Closed pleural biopsy isundeniably a valuable tool for the diagnosis of exudative pleural effusion. However, after the availability of thoracoscopy, the value of closed pleural biopsy has decreased. The BTS guidelines released in the year 2010 recommended that the thoracoscopic biopsy should be the next procedure following an initial inconclusive diagnostic pleural aspiration in the cases suspicious of being malignancy, and Abrams needle biopsies are only diagnostically useful in areas with a high incidence of TB.[5] However, in their earlier BTS guidelines published in 2003, they advised thoracoscopic pleural biopsy to be performed only after an initial negative closed pleural biopsy.[9]

In a country like India, a large number of patients present with similar clinical presentations of pleural effusion in both TB and malignancy. As per the BTS guidelines,[5] half of these patients should be subjected for thoracoscopic pleural biopsy without even considering a closed pleural biopsy. Taking into consideration the patient load and non-availability of infrastructure and expertise, there is a huge gap between what is recommended and what is actually available, not just in our country but also in majority of the developing countries. The diagnostic yield of the first pleural biopsy (59%) significantly improved on a repeat pleural biopsy to 76% in our study which is quite considerable. This figure would have been even higher if all patients with the first negative pleural biopsy would have been subjected to a repeat pleural biopsy. Our results of repeat pleural biopsy are higher in comparison to the studies by Chakrabarti et al.[6], Basu et al.[7] and comparable to Rajawatet al[11].

The etiology of effusion when correlated with the patients' demographic characteristics suggested that age above 50 years, smoking background, male gender and hemorrhagic effusion were significantly associated with malignant etiology. The more number of above-mentioned concomitant factors the more were the chances of a malignant etiology on pleural biopsy.

In our study, one patients developed a small pneumothorax and four had pain at biopsy site after closed pleural biopsy. Thus, five complications (4.03%) were occurred after 124 attempts of closed pleural biopsy (100 attempts for the first pleural biopsy and 24 attempts for repeat pleural biopsy) which was slightly higher than Rajawat et al (3.28%)[11]. Viskum and Enk[10] reported complication rate of 7%–8% in a series of 566 thoracoscopy examinations.

The results of our study clearly suggestgood diagnostic yields of closed pleural biopsies (nearly comparable to the thoracoscopic pleural biopsies) in a selected population. Again, considering the increase in the diagnostic yield on performing repeat pleural biopsies in our study, a closed pleural biopsy shouldalways be considered before thoracoscopic pleural biopsy. The relative ease in performing the procedure, obvious advantage over open biopsy and lack of any significant complications should prompt more frequent use of closed pleural biopsies in the resource limited set ups. In the presence of adequate training, blind pleural

biopsy is well tolerated by the population who often have a poor performance status, short life expectancy and comorbidities. Therefore, the BTS guidelines [5,9] are not perfectly applicable in our setup, and one should not forget the usefulness of the simple procedure which can be performed even in a sick patient on bedside. [11] The limitation of our study was no comparison with a similar group undergoing thoracoscopic pleural biopsy.

V. Conclusions

In the diagnostic work-up of pleural effusion, closed pleural biopsy has shown to provide a high diagnostic yield in the diagnosis of pleural TB and malignancy. Low cost, easy availability and low complication rates makeclosed pleural biopsy a good diagnostic tool. Hence it should always be considered as an initial diagnostic tool in the workup of exudative pleural effusion especially in resource limited settings like India.Considering the high diagnostic yields of a repeat pleural biopsy in our study and by Rajawat et al[11], a closed pleural biopsy may also be considered before thoracoscopic pleural biopsy. A higher diagnostic yield of thoracoscopic pleural biopsy should always be weighted in the context of available resources, expertise and morbidity of patients.

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