CASE REPORT

Malignant Pleural Effusion: A Continued Relevance of Closed Needle Pleural Biopsy

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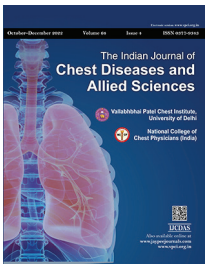

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Abstract

Introduction: Thoracocentesis and pleural biopsy are recommended for the evaluation of undiagnosed exudative pleural effusion. There are multiple etiologies associated with them, out of which malignancy is one of them. Hence, the diagnosis of malignant pleural effusion (MPE) has been proposed in recent perspectives. We aimed to find the profile of MPE, efficacy of percutaneous closed needle pleural biopsy (PCNPB) in diagnosing MPE, overall yield, and complication rate to evaluate the continued relevance of this traditional procedure.

Methods: This was a prospective study carried out on consecutive consenting patients at the Department of Pulmonary Medicine at a tertiary care hospital from July 2016 to May 2018. The diagnosis was based on cytobiochemical, microbiological, and histopathological results along with clinical history. Data were analyzed with respect to pleural fluid assessment in terms of cytobiochemical and microbiological evaluation; while pleural biopsy was studied histopathologically.

Results: Two hundred and fifty patients with exudative pleural effusion were enrolled. Tuberculosis (218, 87.2%) was the most common etiology followed by malignancy (22, 8.8%). The most common presenting complaint was chest pain (100%) followed by dyspnea (90.47%). Metastatic adenocarcinoma was found in 81.81% followed by mesothelioma in 18.18%. The sensitivity of pleural biopsy for malignancy was found to be 63.63% ($p < 0.003$, odds ratio [OR]: 2.01), and those fulfilling Leung's criteria, sensitivity was found to be 90.90% ($p < 0.001$, OR: 3.67). The sensitivity of pleural fluid for malignancy was 18.18% ($p < 0.05$, OR: 1.51). All cases of mesothelioma have asbestos exposure. The complication in the form of mild post-pleural biopsy pain was encountered in 10%, which required mild analgesics. Other complications in the form of self-resolving pneumothorax were seen in 6%, which increased hospital stay to 2–3 days and self-resolving hematoma (3%).

Conclusion: In this modern era, PCNPB still holds high sensitivity, efficacy rate, and relevance for diagnosing MPE with less complication rate, less hospital stay, and can be done on a daycare basis. Also, we have very less research and paperwork regarding this topic.

Keywords: Malignant pleural effusion, Mesothelioma, Metastatic adenocarcinoma, Percutaneous closed needle pleural biopsy.

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Abbreviations used in this Article

CECT = Contrast enhanced computed tomography; MPE = Malignant pleural effusion; OR = Odds ratio; PCNPB = Percutaneous closed needle pleural biopsy; PET = Positron emission tomography; WT = Wilms' tumor.

Introduction

A MPE[1] is the buildup of fluid and cancer cells that collects in pleural space. These cancer cells increase the production of pleural fluid and cause decreased absorption of the fluid. Pleural malignancies whether primary or metastatic harbor a grim prognosis.[2] These tumors can be highly symptomatic. An MPE can cause dyspnea, secondary to lung compression, or even tension physiology from a hydrothorax under pressure. Palliating these effusions is a seemingly straightforward clinical scenario, but with nuances, that can result in disastrous complications for the patient if not attended to appropriately. Solid pleural malignancies can cause great pain from chest wall invasion or can cause a myriad of morbid symptoms because of the invasion of thoracic structures, such as the heart, lungs, or esophagus.[3] People with lung cancer, breast cancer, and lymphoma are most likely to get an MPE. Mesothelioma (a rare cancer of the pleura itself) is another common cause of MPE. Other causes of MPE include cancer that has spread from the stomach, kidney, ovaries, and colon. Various imaging tests[4] are available in form of chest X-ray, ultrasound thorax, contrast-enhanced computed tomography (CECT), and positron emission tomography (PET). When a pleural effusion is suspected or confirmed via above the modalities, samples can be obtained from interventional procedures like thoracocentesis, PCNPB, imaging-guided biopsy, and thoracoscopic guided biopsy.[5] The goal of our current study was to find the profile of MPE referred to the tertiary care center and the efficacy of PCNPB in diagnosing MPE to understand the continued relevance of this procedure.

Materials and Methods

This was a prospective study carried out in the Department of Pulmonary Medicine of a tertiary care hospital in Mumbai from July

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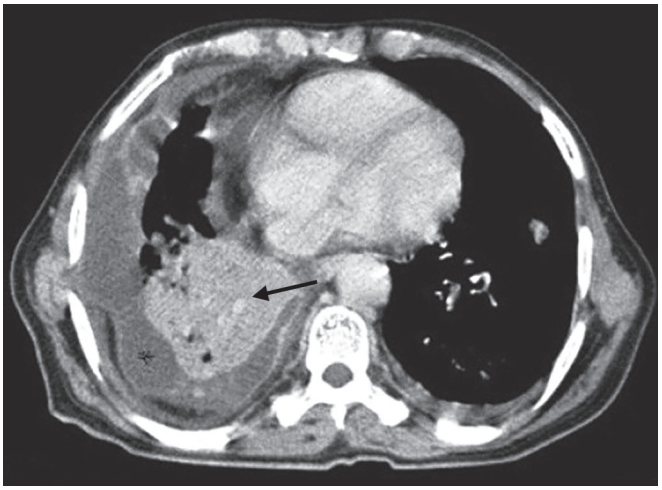

Fig. 1: Pie diagram showing the etiology of pleural effusion

Fig. 2: CECT thorax showing the right lung mass with pleural effusion with lymphadenopathy

2016 to June 2018 with IEC permission. Inclusion criteria consisted of patients above the age of 18 years, diagnosed with pleural effusion, and referred to our department during the study period. Exclusion criteria were age below 18 years, and patients were unwilling to give consent. Demographic data in the form of age and sex were collected. Clinical history, examination, radiological imaging, cytobiochemical, and microbiological evaluation of pleural fluid along with histopathological and microbiological investigations of pleural biopsy samples and final diagnosis were documented. Data collected were analyzed and presented as frequency, mean, and percentage. ANOVA and Chi-square tests were done to assess the difference in various etiology of MPE and efficacy of pleural fluid and PCNPB in diagnosing the above condition. Logistic regression was performed to assess whether asbestos exposure was associated with MPE after adjusting confounders (age, gender, smoking history, occupational exposure, and place of residency).

Results

Among 250 patients that were studied, tuberculosis (218, 87.2%) was the most common etiology followed by malignancy (22, 8.8%) as shown in Figure 1. Of these 134 (58.83%) were men and 104 (44.16%) were women. The right side pleural effusion was predominant over the left side in a ratio of 3:2. The most common age group affected with MPE was 50–60 years with a mean of 56.7 years. The most common presenting complaint was chest pain (100%), followed by dyspnea (90.47%). Out of 22 patients of MPE, 16 (72.72%) had hemorrhagic effusion while 6 (27.27%) had serous fluid and 2 (0.09%) had pus. All the patients had exudative effusion with lymphocyte predominant. Metastatic adenocarcinoma was found in 81.81% followed by mesothelioma in 18.18%. The sensitivity of pleural biopsy for malignancy was found to be 63.63% ($p < 0.003$, OR: 2.01), and those fulfilling Leung's criteria sensitivity was found to be 90.90% ($p < 0.001$, OR: 3.67). The sensitivity of pleural fluid for malignancy was 18.18% ($p < 0.05$, OR: 1.51). All cases of mesothelioma have asbestos exposure. Leung's criteria were fulfilled in 81.81% of cases. The most common radiological presentation was pleural effusion followed by lung mass, pleural nodules, lymphadenopathy, and pleural thickening, and the least was pleural plaque as shown in Figure 2. The most effective radiological imaging was PET scans effective in 100%. The most common IHC markers raised in mesothelioma were Wilms' tumor (WT)-1 gene and cytokeratin. For metastatic adenocarcinoma, the most common gene involved was thyroid transcription factor-1 and Napsin A. Complication in form of mild post-pleural biopsy pain was encountered in 10%, which required mild analgesics. Other complications in form of self-resolving pneumothorax were seen in 6%, which increased hospital stay to 2–3 days and self-resolving hematoma in 3%.

Discussion

Malignant pleural effusion usually presents in the disseminated and advanced stage of malignancy. Dyspnea and chest pain are the debilitating symptoms, which need palliation in these patients. They present either synchronously or as recurrence after the completion of treatment of the primary malignancy. The pathogenesis[6] of MPE is by hematogenous or lymphatic implantation of tumor cells or by direct extension of tumor cells from adjacent organs such as the lung, breast, chest wall, or pleura.[7] Neoplasms of the lung, breast, ovary, and lymphomas constitute more than 75% of cases of MPE. Metastatic adenocarcinoma is the most common cause.[8] In male patients, lung cancer is the most common cause and in female patients, breast cancer is the most common cause. The presence of MPE implies disseminated or advanced disease and reduced survival. The median survival following a diagnosis of MPE depends on the organ of origin of the primary tumor, histological type and stage, and usually ranges from 3 to 12 months.[9] Lung cancer has the shortest, ovarian cancer has the longest, and cancer of unknown primary has an intermediate survival.

The main symptom of MPE is chronic shortness of breath, although cough and pain can also be debilitating. All these greatly diminish the quality of the final phase of life for patients living with cancer. The management[10] of dyspnea is the main complaint, which needs palliation in MPE. Treatment goals for these patients should focus on the relief or elimination of dyspnea, restoration of normal activity and function, minimization or elimination of hospitalization, and efficient use of medical care resources.

Malignant pleural effusion is an exudative effusion with lymphocytic predominance and is often hemorrhagic.[11] It is defined by the presence of malignant cells in the pleural space; for which fluid needs to be sent for cytology (200 units of heparin in 20 mL of fluid).[12]

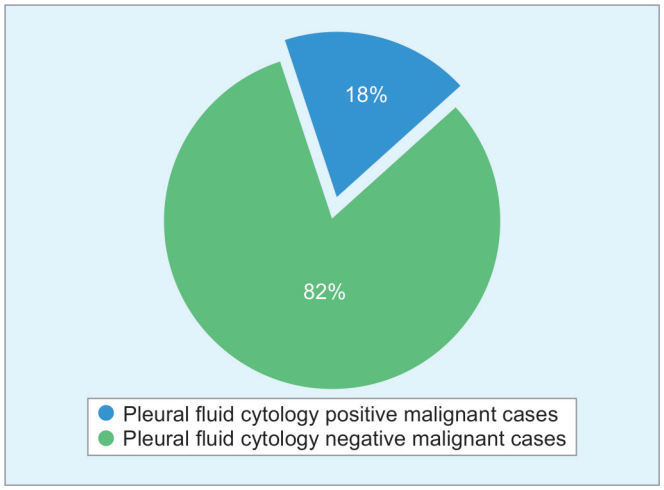

Fig. 3: Pie diagram showing the yield of pleural fluid cytology

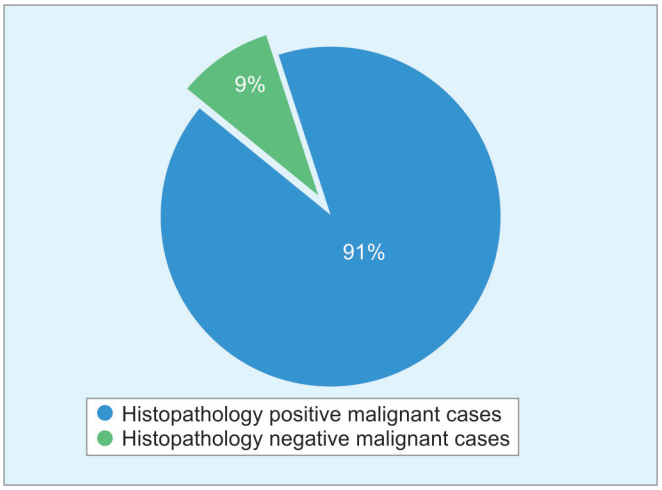

Fig. 4: Pie diagram showing the yield of pleural biopsy in diagnosing malignancy

Standard pleural fluid cytology can provide confirmation of an MPE but has a diagnostic yield of only 60%. Patients with cancer can develop pleural effusion as an indirect effect of cancer, even when cancer cells are absent from the pleural space. These effusions are known as paraneoplastic or paramalignant pleural effusions. They can result from mediastinal lymph node tumor infiltration, bronchial obstruction, radiochemotherapy, pulmonary embolism, superior vena cava syndrome,[13] or decreased oncotic pressure. Leung's criteria used for the diagnosis of malignant effusion include contrast-enhanced CT scan finding, i.e., circumferential, nodular pleural, and parietal pleural thickening greater than 1 cm, and mediastinal pleural involvement or evidence of a primary tumor. Each of these findings reported a specificity of 22–56% and a sensitivity of 88–100%. The sensitivity of closed needle biopsy for adenocarcinoma has been reported to be 69% when adequate tissue is obtained. In a randomized study, Maskell et al.[14] observed higher diagnostic yields with CT-guided biopsy compared with closed pleural biopsy, with sensitivities of 87% and 47% and specificities of 100% for both. The negative predicted values for both were 80% and 44%, respectively. Thoracoscopy has a 90–100% sensitivity for MPE.

Pleural effusions are a common problem in pulmonary practice and those secondary to malignancy require thorough workup. This study was done to determine the efficacy of pleural fluid and pleural biopsy (PCNPB by cope's needle)[15] in diagnosing MPE. One of the traditional modalities to workup such cases is the PCNPB. Very little literature is available showing closed pleural biopsy for diagnosing MPE.

Pleural fluid cytology for malignant cells is the easiest way to diagnose MPE. However, it lacks good sensitivity and specificity. The use of percutaneous closed pleural biopsy for the diagnosis of cytology negative MPE can improve diagnostic ability.[16] In a study by Bhattacharya et al.[17] closed pleural biopsy showed malignant histology in 48% of cases and was negative in 52% of cases. Metastatic adenocarcinoma was also the most common type of pleural malignancy followed by mesothelioma. In this study, there were 22 cases where either one or both pleural fluid cytology and pleural biopsy were positive. Cytological–pathological concordance of these cases are as follows: (1) cytology and histology giving diagnosis 2 (9.09%) cases, (2) cytology inconclusive but histology diagnostic in 18 (81.81%) cases, (3) cytology diagnostic but histology inconclusive in 2 (9.09%) cases, and (4) cytology and histology giving different diagnosis in 0 (0%) cases. Out of 22 cases of malignancy, 20 cases were histopathologically proven while 2 (9.09%) did not show malignant features on histopathology. Similarly, pleural fluid malignant cytology was positive in 4 out of 22 cases. Thus, for pleural biopsy samples, the sensitivity was 90.90%, specificity was 100%, positive predicted value (PPV) was 100%, and negative predicted value (NPV) was 99.13%. For pleural fluid cytology, the sensitivity was 18.18%, specificity was 100%, PPV was 100%, and NPV was 92.68% in this study as shown in Figures 3 to 5.

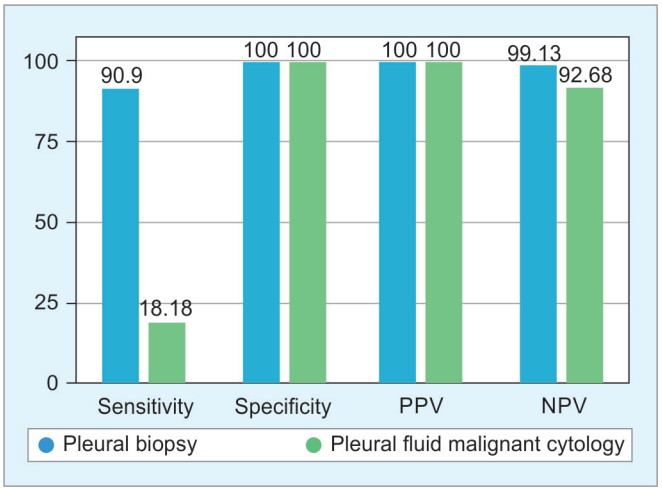

Fig. 5: Bar diagram showing the comparison of pleural fluid cytology and pleural biopsy for diagnosing malignancy

Thus, PCNPB still holds high sensitivity and efficacy rate for diagnosing MPE with less complication rate, less hospital stay, and can be done on a daycare basis especially in the group that has remote access to thoracoscopy and satisfy Leung's criteria on CT. Hence this traditional procedure still holds relevance even in the current era of advanced therapeutics.

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