Clinical Profile of Patients Presenting with Malignant Pleural Effusion to a Tertiary Health Care Centre

Nitin Gadewad¹, Kunal Deokar², Shivhari Ghorpade³

Abstract

Background: Malignant pleural effusions are one of the leading causes of exudative pleural effusions. We studied the clinical profile of patients presenting with malignant pleural effusion, their cytological and histopathological features and the efficacy of pleurodesis in preventing recurrence.

Materials and Methods: 100 patients who were positive for malignant cells in pleural fluid cytology or pleural biopsy were recruited. After history and clinical examination, Chest radiographs, Computed tomography of chest were performed. After diagnostic thoracocentesis and Pleural biopsy, Tube thoracostomy was done. Pleurodesis was performed in 40 patients.

Results: Most of the patients (65%) were in the age group of 61 to 70 years with a male to female ratio of 1.5:1. Most common presenting symptoms were breathlessness (86%) and cough (86%). All (100%) of the malignant pleural effusions were exudative. Pleural fluid cytology was positive in 86% while pleural biopsy was positive only in 44%. Pleural biopsy was positive only in 17% of patients with negative cytology. Adenocarcinoma (59%) was the most common type of cytological diagnosis. Pleurodesis was performed in 40 patients of which 30% had recurrence.

Conclusion: In our tertiary health care centre, malignant pleural effusions presented as large pleural effusions. Most common presenting symptoms were breathlessness and cough. They were exudative, lymphocytic predominant with low ADA levels. Thoracocentesis and cytologic study should be the initial diagnostic approach to malignant pleural effusions. Adenocarcinoma of the lung was the most common cause of malignant pleural effusion. Pleurodesis with oxytetracycline was successful in majority of cases.

Introduction

Malignant pleural effusions are one of the leading causes of exudative pleural effusions. They are a common medical problem associated with 50% of the cases of primary and metastatic pleural malignancies.¹,² They are commonly associated with carcinomas of the lung, breast, lymphoma and leukaemia.³,⁴ The diagnosis of malignant pleural effusions requires thorough history, complete clinical examination, radiographs of the chest, biochemical tests and cytological examination of the pleural fluid, needle biopsy of the pleura or thoracoscopy guided pleural biopsy. Accurate evaluation of the aetiology of pleural effusions in patients with known cancers is important as the prognosis and subsequent treatment of these patients may be different. Previous studies have shown that the accuracy of pleural fluid cytology in diagnosing malignant pleural effusions varies from centre to centre and has been reported to be between 40% and 87%.⁵ In approximately 6% of the patients, primary tumour is not identified.³,⁴ The treatment options for such patients include repeated therapeutic thoracocentesis, pleurodesis via tube thoracostomy or thoracoscopy, long term indwelling pleural

¹Senior Registrar, Fortis Hospital, Mumbai, Maharashtra; ²Consultant Pulmonologist, Sapphire Hospitals, Thane, Maharashtra; ³Professor and Head, Dept. of Pulmonary Medicine GMC, Nagpur, Maharashtra

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pleuroperitoneal shunt or pleurectomy.\(^6\) Pleurodesis is a treatment that aims to obliterate the pleural space by instillation of a sclerosing agent into the pleural space or by mechanically abrading the pleura. The aim of pleurodesis in patients with malignant pleural effusions is to prevent the re-accumulation of the effusion and thereby development of symptoms, and avoid the need for repeated hospitalization for thoracocentesis.

We studied the clinical profile of patients presenting with malignant pleural effusion, their cytological and histopathological features and the efficacy of pleurodesis in preventing recurrence of malignant pleural effusions.

**Materials and Methods**

It was a hospital based descriptive study which was carried out in the period from April 2012 to October 2013. The patients suspected of malignant pleural effusion were selected from outpatient departments of the Department of Medicine, Department of Pulmonary Medicine and Department of Oncology of the same institute. The study was carried out after approval from the institutional ethics committee and with fully informed written consent from the subjects. Patients included were those positive for malignant cells in pleural fluid cytology or those who were negative for malignant cells in pleural fluid cytology but positive on pleural biopsy. 100 consecutive patients were included in the study.

At first meticulous history with detailed clinical examination was done by filling a written questionnaire. Chest radiographs PA and lateral views in erect position were obtained. On chest radiograph, the pleural effusion was quantified as follows:\(^7\)

- a. Minimal, free-flowing effusion (<10 mm on lateral decubitus).
- b. Moderate free-flowing effusion (>10 mm and <½ hemithorax).
- c. Large, free-flowing effusion (>½ hemithorax), loculated effusion, or effusion with thickened parietal pleura.

Computed tomography of thorax was performed to look for presence of pleural nodularity, lung masses, nodules, infiltrates, mediastinal adenopathy, chest wall involvement, lymphangitis carcinomatosa.

Diagnostic thoracocentesis used to be undertaken as outlined in Pleural procedures and thoracic ultrasound: British Thoracic Society pleural disease guideline 2010.\(^8\) The pleural fluid was immediately sent for following investigations:

i. pH – 1 ml of pleural fluid drawn in a heparinized syringe immediately after aspiration and immediately capped to avoid exposure to air.

ii. Protein and LDH – 5 ml of pleural fluid in a plain container.

iii. Sugar – 3 ml in a bulb containing fluoride oxalate.

iv. Cytological examination and differential cell count – 40 ml of pleural fluid in a plain container.

Pleural biopsy was carried out under strict aseptic conditions and after fully informed written consent from the patient. Using Abrams pleural biopsy needle, four to six biopsy specimens were taken and sent for histopathological examination.

Tube thoracostomy used to be undertaken as outlined in Pleural procedures and thoracic ultrasound: British Thoracic Society pleural disease guideline 2010.\(^8\)

**Pleurodesis**

**Selection of patients for pleurodesis**

1. Those willing for pleurodesis
2. Lung fully expanded on chest radiograph
3. No bubbling in the drainage bag

Pleurodesis was done using 35 ml/kg of oxytetracycline. The patients in whom pleurodesis was done were followed up at 1 month, 3 months and 6 months post procedure. Chest radiograph PA view was done at each visit to look for recurrence of effusion.

Data was entered in Microsoft excel 2007 and analyzed using Epi Info 2000. The proportions of study variables were calculated and expressed in terms of percentages.

**Results**

Most of the cases 65(65%) were in age group of 61 to 70 years with a mean age of 61.48 ± 9.5 years. Most of the cases were male 60(60 %) and 40(40%) were female with a male to female ratio of 1.5:1.

It was observed that most common presenting symptoms were breathlessness 86(86%), cough 86(86%) followed by loss of appetite 78 (78%) chest pain 75 (75%), hemoptysis 19 (19%), fever 35 (35%). Common physical signs on admission were Lymphadenopathy 38(38%) followed by finger clubbing 30(30%) and SVC obstruction 13(13%).

92 patients (92%) had large pleural effusion and 8 patients (8%) had moderate effusion. The abnormalities which were noted on computed tomography of thorax were lung masses, nodules or infiltrates (57%), mediastinal adenopathy (51%), pleural nodularity (43%), lymphangitic carcinomatosa (11%), chest wall involvement (6%).

52 % subjects had blood stained fluid while 48 % had straw coloured fluid. All (100%) of the malignant pleural effusions were exudative. 82(82%) patients were exudative by protein criteria and 18 (18%) of the patients were exudative by LDH criteria. Mean pleural fluid pH was 7.39(± 0.17). Mean pleural fluid protein level was 4.71(± 0.72) g/dl, mean serum protein level was 6.42 (± 0.62) g/dl and pleural fluid to serum protein ratio was 0.73 (±0.12), mean pleural fluid LDH level was 623.98 (± 81.14) U/L, mean serum LDH level were 630.85
Table 1: Biochemical data of serum and pleural fluid of patients with malignant pleural effusion

<table>
<thead>
<tr>
<th>Biochemical levels</th>
<th>No. of patients 'n'</th>
<th>Mean</th>
<th>SD</th>
<th>Maximum</th>
<th>Minimum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pleural fluid ADA (U/L)</td>
<td>100</td>
<td>23.50</td>
<td>3.93</td>
<td>30.54</td>
<td>11.10</td>
</tr>
<tr>
<td>Pleural fluid (PF) Protein (g/dl)</td>
<td>100</td>
<td>4.71</td>
<td>0.72</td>
<td>5.40</td>
<td>2.30</td>
</tr>
<tr>
<td>Serum (S) Protein(g/dl)</td>
<td>100</td>
<td>6.42</td>
<td>0.62</td>
<td>6.84</td>
<td>5.00</td>
</tr>
<tr>
<td>(PF:S) Protein</td>
<td>100</td>
<td>0.73</td>
<td>0.12</td>
<td>0.64</td>
<td>0.35</td>
</tr>
<tr>
<td>Pleural fluid(PF) LDH (U/L)</td>
<td>100</td>
<td>623.98</td>
<td>81.14</td>
<td>1100</td>
<td>518</td>
</tr>
<tr>
<td>Serum (S) LDH (U/L)</td>
<td>100</td>
<td>630.85</td>
<td>90.08</td>
<td>876</td>
<td>626</td>
</tr>
<tr>
<td>(PF:S) LDH</td>
<td>100</td>
<td>0.98</td>
<td>0.07</td>
<td>1.29</td>
<td>0.37</td>
</tr>
<tr>
<td>Pleural fluid Glucose (mg/dl)</td>
<td>100</td>
<td>64.98</td>
<td>10.86</td>
<td>91</td>
<td>39</td>
</tr>
<tr>
<td>Pleural fluid PH</td>
<td>100</td>
<td>7.39</td>
<td>0.17</td>
<td>7.7</td>
<td>7.1</td>
</tr>
<tr>
<td>Pleural fluid leucocyte subsets (%Total WBC)</td>
<td>100</td>
<td>1307</td>
<td>478.89</td>
<td>3000</td>
<td>500</td>
</tr>
</tbody>
</table>

In the present study out of total 66 patients pleural fluid for malignant cells was positive in 46 (69%) cases. It has been reported that the diagnostic yield of pleural fluid cytology for malignant cells ranges from 62%-90%. Several factors influence the yield of pleural fluid cytology including mechanism of effusion, type of primary tumour, nature of specimens, number of specimens and the skill of the cytopathologists.

In our study, closed needle biopsy of the pleura was positive only in 44(44%) of the patients. The sensitivity of closed pleural biopsy is less than pleural fluid cytology in malignant effusions. The diagnostic yield of closed pleural biopsy ranges between 40 to 75%. Factors which influence the yield of closed pleural biopsy include metastatic tumor areas not reached during blind biopsy, minimal pleural involvement and the skill of the person performing the procedure.

We observed that closed needle pleural biopsy was positive in 17(17%) of the patients with negative cytology. Studies have shown that closed needle pleural biopsy is positive in 7 to 12% of the patients with negative cytology.

In present study we observed that adenocarcinoma (59 (59%)) was the most common type of cytological diagnosis in malignant pleural effusion, followed by small cell carcinoma (08 (08%)), lymphoma (66%), squamous cell carcinoma (4 (4%)), large cell carcinoma (4 (4%)). In 19 (19%) patients exact histological type could not be determined. Bhattacharya et al11 observed similar findings, with adenocarcinoma being the most common type of malignancy (65%) on the basis of analysis of histopathological examination of pleural biopsy sample while other histological types were squamous cell carcinoma (3%), small cell carcinoma (6%), large cell...
carcinoma (3%), and indeterminate (23%).

We observed that the most common primary site in patients with malignant pleural effusion was lung (59(59%)) followed by breast (25(25%)), lymphoma 6(6%) female genital tract 1(1%) and in 09 (09%) patients primary site could not be determined. Similar findings were observed by Spriggs and Boddington et al15 who found that most common primary site was lung (43%), followed by breast (25%), lymphoma (08%), female genital tract (06%), malignant melanoma (02%) and primary could not be determined in 10%.

We performed pleurodesis in 40 patients and followed them at 1, 3 and 6 months after pleurodesis. It was observed that 12(30%) patients had recurrence of pleural effusion. In a review of 11 reports16 involving 359 patients, the success rate with tetracycline was 67% which is consistent with present study.

Conclusions
In our tertiary health care centre, malignant pleural effusions presented as large pleural effusions. Most common presenting symptoms were breathlessness and cough. They were exudative, lymphocytic predominant with low ADA levels. Pleural fluid cytology plays an important role in diagnosis. Thoracentesis and cytologic study should be the initial diagnostic approach to malignant pleural effusions. Adenocarcinoma of the lung was the most common cause of malignant pleural effusion. Pleurodesis with oxytetracycline was successful in majority of cases.

References