The Proportion of Bronchogenic Carcinoma among Patients Presenting As Slowly Resolving Pneumonia

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ABSTRACT

Introduction: Lung cancer is the most prevalent cause of cancer-related death worldwide. One of the presentations is slowly resolving pneumonia. Mistakenly treating these as pneumonia causes delay in diagnosis. Fibreoptic bronchoscopy (FOB) is considered a primary method for evaluating the patients with slowly resolving consolidation. This study is to assess the proportion of bronchogenic carcinoma in slowly resolving pneumonia patients.

Methods: A cross-sectional study in pulmonology wards in tertiary care setting of patients with slowly resolving pneumonia who underwent fibreoptic bronchoscopy over two years. Patients were evaluated with imaging, FOB, cytology, PTLB and any other means for a final diagnosis.

Results: Out of the 105 patients, presented as slowly resolving pneumonia, the number of bronchogenic carcinoma was 28 (26.7%). TB was present in 5.7% and 10.5% were in undiagnosed category. 51 patients were subjected to bronchial biopsy and 23 out of 51 patients (45.1%) were identified as malignant and 3 out of 51 patients (2.9%) were identified as other presentation.

Bronchial brushings was done for 62 patients (59%) out of which 4 patients were identified as malignant. The bronchial washing was done for all the patients. 6 patients were identified as malignant lesions from this method.

Conclusion: The proportion of bronchogenic carcinoma among patients presenting as slowly resolving pneumonia was 26.7%. Bronchoscopy was the major investigation of diagnosis. Bronchial biopsy yielded diagnosis in 45%, followed by bronchial washings and brushings. Commonest carcinoma identified among slowly resolving pneumonia patients was squamous cell carcinoma.

Keywords: Slowly resolving pneumonia; Bronchogenic carcinoma; Fibreoptic biopsy

INTRODUCTION

The term Non-Resolving Pneumonia (NRP) or Slowly Resolving Pneumonia (SRP) is not an uncommon clinical entity and has been used interchangeably to refer the persistence of radiographic abnormalities beyond the expected time limit. Inadequate knowledge regarding the expected clinical course and outcome of a community-acquired or nosocomial pneumonia is a common reason for...
pulmonary consultation; selection of patients and appropriate timing of further evaluation can be challenging. The term NRP has been used to refer to "Persistence of radiological abnormalities beyond expected time of course". The expected time course for resolution is controversial. During the year of 1975, Hendin defined slow-resolution pneumonia (PRS) as persistent pulmonary consolidation for more than 21 days. In 1991 Kirtland & Winterbauer defined SRP in immune competent patients based upon radiological criteria; Less than 50% clearings by 2 weeks or less than complete clearing 4 weeks.

It accounts for 10% - 15% of nosocomial pneumonias and is estimated to be responsible for approximately 15% of inpatient pulmonary consultation and 8% of bronchoscopies. Delay in diagnosis and treatment may lead to rise of mortality by 3-5%o in both community-acquired pneumonia and nosocomial pneumonia. Incorrect diagnosis, inadequate antibiotic therapy, defence of the altered host, atypical organisms, resistant pathogens, non-infectious causes, tuberculosis, endobronchial lesions, etc. They are the common causes of slowly resolving pneumonia or slowly resolving pneumonia.

Slow or incomplete resolution of pneumonia, despite treatment, needs a more aggressive evaluation. Bronchoscopy allows direct visualization of affected area and the direct obtaining of samples. Protected brush specimen (PBS), bronchoalveolar lavage (BAL) and trans bronchial biopsy (TBB) can be used to take the sample tissues. Microbiological studies of BAL and PBS may include staining in culture of usual bacteria, specific staining for AFB and culture, legionella, fungi, virus and direct immunofluorescence for legionella. Fibreoptic bronchoscopy (FOB), computed tomography (CT) scan of the thorax and CT-guided fine needle aspiration cytology (FNAC) may be helpful in the evaluation of slowly-resolving or slowly resolving pneumonia. Microbiological, cytological and histopathological tests of the specimens can be done for etiological diagnosis of underlying cause. Because the prognosis of lung cancer is unfavourable, early diagnosis plays an important role in increasing survival in lung cancer patients. The use of various methods can contribute to early diagnosis. Among the most commonly used methods are imaging tests (chest X-ray and CT), sputum cytology, and fibreoptic bronchoscopy. Fibreoptic bronchoscopy is currently considered the primary method for evaluating the tracheobronchial tree in patients with suspected lung cancer.

So, from the various literature it is clear the fibreoptic bronchoscopy is the most sensitive way to diagnose bronchogenic carcinoma in patients slow resolving pneumonia. Hence this study is undertaken to assess the proportion of bronchogenic carcinoma in patients that presents as slowly resolving pneumonia.

**MATERIALS AND METHODS**

**Study Design** - Observational Study

**Study Setting** - Department of Pulmonary Medicine, Government Medical College, Thrissur, Kerala, India.

**Study period** - two years

**Sample Size**

Sample size= $\frac{Z^2 \times (1-\alpha) / 2 \times (1-P)p}{\varepsilon^2 P}$

$P = \text{Proportion of diagnosis of bronchogenic carcinoma in patients that presents as slowly resolving pneumonia from literature.}$

$\varepsilon = \text{relative precision (it is recommended to fix the value e from a minimum of 10% to a maximum of 20%).}$

Expected Proportion - 0.8
Relative Precision (%) - 10

**Required sample size** - 96

Anticipating 10% dropout rate final sample size is 105.

**Sampling Method:**

All the patients who attended the Department of Pulmonary Medicine, Government Medical College, Thrissur with a provisional diagnosis of slowly resolving pneumonia during the two year study period who underwent fibreoptic bronchoscopy shall be included in this study based on the inclusion and exclusion criteria. Consecutive sampling will be done according to the sample size.
Inclusion Criteria
Slowly resolving pneumonia is defined in this study by the persistence of clinical symptoms and signs (cough, sputum production, with or without fever more than 100°F), failure of resolution of the radiographic features by 50% in 2 weeks or completely in 4 weeks on serial chest X-ray (examined with at least 2 consecutive chest X-rays) in spite of antibiotic therapy for a minimum period of 10 days.

Inclusion criteria include:
Consecutive patients who attended the Department of Pulmonary Medicine, Government Medical College, Thrissur, Kerala, India during the study period with a diagnosis of slowly resolving pneumonia who underwent fiberoptic bronchoscopy.

Exclusion Criteria
1. Patients with sputum smear positive for acid fast bacilli.
2. Patients with poor general condition like severe hypoxaemia, serious arrhythmia, unstable angina pectoris, recent myocardial infarction (in the past 6 weeks), haemodynamic instability, uncorrected bleeding diathesis.

RESULTS
BASELINE CHARACTERISTICS
Gender wise distribution
The gender distribution of showed that males were the majority 78.1% (82 nos.) and females were less than quarter of the total population 21.9% (23 nos.).

Age and Gender wise distribution
The mean age of the study population is 61.10 ± 11.34 years, in that male were having higher mean age of 62.54 ± 9.45 years when compared to 56±15.6 years for females. The age and gender wise distribution showed males were higher in age group 21 to 50 years. Whereas females were mostly higher in the age group 51 to 70 years Only one male was in the age group more than 80 years.

COMORBIDITIES, PERSONAL AND FAMILY HISTORY
The comorbidities seen among the patients showed that nearly quarter of the patients had Diabetes (24.8%), followed by Hypertension which is seen in 18.1% of the subjects. Renal disease was only present in a 6.7%, liver disease & Coronary artery disease in 3.8%. There were no patients presenting with prior malignancies. History of Tuberculosis, Interstitial lung disease (ILD) & COPD was detailed in 7.6, 2.9 and 22.9 % of the total study population.

The personal history showed that Silica exposure was seen among 10.5% of the subjects, whereas asbestos exposure was only in 6.7%. Smoking habits showed nearly a quarter of the patients had never smoked before (23.8%), almost half were current smokers (44.8%), around 31.4% had stopped smoking and 8.6% had Environmental tobacco smoke exposure. Alcohol use showed more than a quarter (27.6%) had never used alcohol, half of the subjects only used alcohol occasionally (54.3%), 3.8% had abused alcohol consumption and 14.3% were regular users of it. Other history showed 17.1% having family history of cancer. Travel history, high risk behaviour and other addictions were seen in 1%, 1.9% and 1.9% respectively.

Bronchoscopy Findings
The bronchoscopy finding was normal in 22.9% patients. Extra luminal compression alone was seen in 5.7% of the patients. Intraluminal mass was present in 18.1%. A quarter of the patients (25.7%) had secretions only, and less than a quarter had other findings (23.8%) like congestion, erythema. (Table-1)

Bronchial biopsy findings & Bronchial Brushing
Out of the 105 patients, 51 patients were subjected to bronchial biopsy, from its findings 23 out of 51 patients (45.1%) were identified as malignant and 3 out of 51 patients (2.9%) were identified as other presentations.

The bronchial brushing was done for 62 patients (59%) only. 4 patients were identified as malignant lesions from this method. (Table-2)

Final Diagnosis among slowly resolving pneumonia patients
The proportion of Bronchogenic carcinoma patients among slowly resolving was identified as 28 patients (26.7%). TB was present in 5.7% and 10.5% were in undiagnosed category. (Table-3)

Method of Diagnosis among Bronchogenic
carcinoma patients

The proportion of patients with bronchogenic carcinoma who were diagnosed by bronchoscopy was very high (89%). USG guided FNAC lung was used in 10.7% (Figure-1)

DISCUSSION

A hospital-based study was done in patients presenting to the pulmonary medicine department in tertiary care centre. Subjects who are diagnosed to have slowly resolving pneumonia are included in the study. A total of 105 patients were included in the study, who satisfy the inclusion and exclusion criteria.

Age and Gender wise distribution

In our study the gender distribution showed that males were the majority 78.1% (82 nos.) and females were less than quarter of the total population 21.9% (23 nos.). The mean age of the study population is 61.10 ± 11.34 years, in that males were having higher mean age of 62.54 ± 9.45 years when compared to 56±15.6 years for females. The age and gender wise distribution showed males were higher in age groups 21 to 50 years, whereas females were mostly higher in the age group 51 to 70 years. Only one male was in the age group more than 80 years.

Other reviewed studies showed that, 80% patients were over the age of 40 years and nearly 50% were over the age of 50 years by Chaudari et al.9 El Solh et al. stated that age alone has the most striking influence on resolution of pneumonia, and in their study, rate of resolution on chest X-ray was found to be 35.1% by 3 weeks and 60% by 6 weeks in patients above 70 years of age.10 Fein has also shown in his study that only 30% of patients above 50 years of age show complete radiologic resolution by 4 weeks.11

Comorbidities

In our study the comorbidities seen among the patients showed that nearly quarter of the patients had diabetes (24.8%), followed by hypertension which is seen in 18.1% of the subjects. Renal disease was only present in a 6.7 %, liver disease & Coronary artery disease in 3.8%

Pneumonic Consolidation

In our study the pneumonic consolidation involvement of the patients showed that majority of the patients had consolidation on the right lung (47.6%), followed by 32.4 % on the left lung. Only 21 patients had consolidation bilaterally (20%). Similar to our study Chaudari et al. demonstrated consolidation was the predominant radiological finding (100%) and associated cavity lesions were present in 6 (60%) cases. On chest X-ray, consolidation was present in 53 patients, consolidation along with cavity was present in 5 patients, and only cavity was present in 2 patients.9 In the present study, CT thorax was done in 45 patients. There was no malignancy identified by CT guided FNAC in this study. Chaudari et al.9 showed that among CT scan patients, malignancy was found in 8 cases (66.7%). In a study conducted by Ferretti et al. in 23 patients of non-resolving pneumonia with negative FOB results, CT-guided core needle biopsy was done. Diagnostic yield of biopsy was 78%, 15 patients were diagnosed as malignancy, and 8 patients were diagnosed to have benign disease. The sensitivity and specificity for malignancy were 87% and 100%, respectively.12

Bronchoscopy findings

In our present study the bronchoscopy findings revealed, 22.9% of the patients to be normal. Extra luminal compression alone was seen in 4 patients and with intraluminal mass was identified in 5.7% of the patients. Intraluminal mass was present in 18.1 %. A quarter of the patients (25.7%) had secretions only, less than a quarter had other squamous cell carcinoma. Endobronchial biopsy was done in 12 patients. Out of these, malignancy was diagnosed in 6 patients (squamous cell carcinoma in 3 patients, adenocarcinoma in 2 patients and small cell carcinoma in 1 patient). Endobronchial biopsy of 4 patients showed features suggestive of tuberculosis. Central malignancies producing obstruction of bronchus and distal consolidation are a well known causes of nonresolving consolidation and hence FOB is a preliminary choice of investigation in non resolving consolidation.17

Final Diagnosis among slowly resolving pneumonia patients

In our study the number of bronchogenic carcinoma among patients presenting as slowly resolving pneumonia was 28 (26.7%). TB was present in 5.7% and 10.5% were in undiagnosed category. In a study
by Chaudari et al., bronchogenic carcinoma was found in 16 patients (26.6%), of which squamous cell carcinoma was the commonest variety followed by adenocarcinoma and ten patients (62.5%) were smokers among the patients with malignancy within 53% of patients with pneumonia. Silver et al. found malignancy as a specific cause for non-resolving pneumonia in 11.4% cases in their series of 35 patients. Tuberculosis was diagnosed in 16.7% cases in the present study. Silver et al. found tuberculosis in 5.7% cases from culture of bronchial lavage fluid as a cause of non-resolving pneumonia. Silver et al. also found malignancy as a specific cause for non-resolving pneumonia in 11.4% cases in their series of 35 patients.

**Yield of Bronchoscopy diagnosis**

In our present study the bronchoscopy was used to diagnose bronchogenic carcinoma in 25 patients. Out of the 105 patients, 51 patients were subjected to bronchial biopsy, from its findings 23 out of 51 patients (45.1%) were identified as malignant and 3 out of 51 patients (2.9%) were identified as other presentations. The bronchial brushing was done for 62 patients (59%) out of which 4 patients were identified as malignant. The bronchial washing was done for all the patients and 6 patients were identified as malignant. The proportion of patients with bronchogenic carcinoma who were diagnosed by bronchoscopy was very high (89%). In a study conducted by Ferretti et al. in 23 patients of non-resolving pneumonia with negative Fibreoptic bronchoscopy results, Diagnostic yield of biopsy was 78%, 15 patients were diagnosed as malignancy, and 8 patients were diagnosed to have benign disease. The sensitivity and specificity for malignancy were 87% and 100%, respectively. Other reviewed studies showed biopsy and washing as the most common method of diagnosis. USG guided FNAC lung was used to identify 3 patients with bronchogenic carcinoma. However, in the reviewed study by Chaudari et al., CT-guided FNAC was done in 12 patients, and etiological diagnosis was established in 11 cases (diagnostic yield being 93.7%). Among these patients, malignancy was found in 8 cases (66.7%). CT-guided core needle biopsy was done.

**Type of Bronchogenic carcinoma**

Squamous cell carcinoma was seen in exactly half of the patients 14 nos. (50%), followed by adenocarcinoma 10 nos. (35.7%), small cell carcinoma 3 nos. (10.7%) and 1 no. undifferentiated carcinoma in 3.6%. Other reviewed studies by Rajesh Kumar Balakrishnan et al. showed that 6 patients had carcinoma and among them 3 had adenocarcinoma, 2 had squamous cell carcinoma and 1 patient had small cell carcinoma among slowly resolving pneumonia patients. Similarly Chaudari et al. showed Bronchogenic carcinoma accounted for 16 cases (26.67%) of non-resolving pneumonia in this study. Squamous cell cancer was the predominant variety (n = 10) followed by adenocarcinoma (n = 5); small cell variety was diagnosed in 1 case. Seven out of 10 patients (70%) of squamous cell carcinoma were diagnosed by bronchoscopy procedures with bronchoscopy biopsy, showing positive histopathology in all the 7 cases and in addition bronchial lavage fluid and bronchial brushings also showed positive result in 3 of these 7 cases.

**CONCLUSION**

The number of bronchogenic carcinoma among patients presenting as slowly resolving pneumonia was 28 (26.7%).

Out of the total malignancy detected, squamous cell carcinoma was seen in half of the patients, followed by adenocarcinoma, small cell carcinoma and undifferentiated carcinoma in small fraction.

**REFERENCES**


17. Postobstructive Pneumonia: An Underdescribed Syndrome.


<table>
<thead>
<tr>
<th>Table 1 Bronchoscopy findings (N=105) in slowly resolving consolidation</th>
</tr>
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<tbody>
<tr>
<td><strong>Bronchoscopy</strong></td>
</tr>
<tr>
<td>------------------------</td>
</tr>
<tr>
<td>Normal</td>
</tr>
<tr>
<td>Extra-luminal compression</td>
</tr>
<tr>
<td>Intraluminal mass</td>
</tr>
<tr>
<td>Extra luminal compression with intraluminal mass</td>
</tr>
<tr>
<td>Secretions Only</td>
</tr>
<tr>
<td>Others (25 nos.)</td>
</tr>
<tr>
<td>a. Tracheal wall showing nodular lesion</td>
</tr>
<tr>
<td>b. Tracheal wall shows brownish macule</td>
</tr>
<tr>
<td>c. Vocal cord palsy</td>
</tr>
<tr>
<td>d. Oropharyngeal candidiasis</td>
</tr>
<tr>
<td>e. Unhealthy Mucosa</td>
</tr>
<tr>
<td>f. Accessory lobe present</td>
</tr>
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Table 2: Bronchial Biopsy & Bronchial Brushing (N=105) results

<table>
<thead>
<tr>
<th>Bronchial Biopsy</th>
<th>Present n (%)</th>
</tr>
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<tbody>
<tr>
<td>Done</td>
<td>51 (48.6)</td>
</tr>
<tr>
<td>Not done</td>
<td>54 (51.4)</td>
</tr>
<tr>
<td>Malignancy</td>
<td>23 (45.1)</td>
</tr>
<tr>
<td>TB</td>
<td>0.0 (0.0)</td>
</tr>
<tr>
<td>Others</td>
<td>03 (2.9)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Bronchial Brushing</th>
<th>Present n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Done</td>
<td>62 (59.0)</td>
</tr>
<tr>
<td>Not done</td>
<td>43 (41.0)</td>
</tr>
<tr>
<td>Malignancy</td>
<td>4 (6.5)</td>
</tr>
<tr>
<td>TB</td>
<td>0.0 (0.0)</td>
</tr>
<tr>
<td>Others</td>
<td>0.0 (0.0)</td>
</tr>
</tbody>
</table>

Table 3: Final Diagnosis (N=105)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Present N(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bronchogenic Carcinoma</td>
<td>28 (26.7)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>59 (56.2)</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>6 (5.7)</td>
</tr>
<tr>
<td>Other Granulomatous diseases</td>
<td>1 (1.0)</td>
</tr>
<tr>
<td>Undiagnosed</td>
<td>11 (10.5)</td>
</tr>
</tbody>
</table>

Figure 1: Method of diagnosis of bronchogenic carcinoma in slowly resolving consolidation