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Original Research Article

ROLE OF BRONCHOSCOPY TO DETERMINE THE ETIOLOGY OF NON-RESOLVING PNEUMONIA IN A TERTIARY CARE INSTITUTE

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Abstract

Background: Pneumonia is a common clinical problem in day to day to practice for clinicians. Non-resolving pneumonia is a significant challenge for clinicians and pulmonologists. This study aimed to determine the aetiology of non-resolving pneumonia using bronchoscopy and evaluate the role of bronchoscopy in non-resolving pneumonia. **Materials and Methods:** Patients who fulfilled the criteria of nonresolving pneumonia included in this study .68 patients were admitted to the thoracic medicine ward of Tirunelveli Medical College Hospital between June 2015 and August 2016. Detailed clinical history, duration of symptoms, prior history of ATT, and associated co morbidities were recorded before bronchoscopy. **Result:** The majority of patients were older than 50 years, with males comprising 80% of the cohort. The overall diagnostic yield of FOB was 94%. Most common aetiology found in this study is infection, followed by malignancies. Among infections, Gram-negative pyogenic bacterial infections (klebisella) (41.1%) more common followed by Tuberculosis (25%). Squamous cell carcinoma was the most common type of malignancy. Diabetes and smoking were the most common comorbidities. **Conclusion:** The study concluded that Bronchoscopy plays an essential role in the management of non-resolving pneumonia and should be considered a diagnostic tool in patients with non-resolving pneumonia.

INTRODUCTION

Pneumonia is defined as inflammation of the pulmonary parenchyma caused by an infectious agent.1 Inappropriate or delayed treatment leads to mortality, morbidity, and drug resistance in a significant number of patients. Non-resolving pneumonia possess significant diagnostic challenge and defined as Patients who presented with pneumonia-like syndrome and the radiograph failed to resolve by 50% in 2 weeks, completely in 4 weeks, or did not show significant radiographic resolution after at least 10 days of antibiotic therapy.

Development of complications, infection with drug-resistant organisms, misdiagnosis of the pathogen, presence of comorbid conditions, and non-infectious aetiology are some reasons for non-resolution. The selection of patients and the appropriate timing for further evaluation can be challenging. Along with other routine investigations, fibreoptic bronchoscopy (FOB), computed tomography of the thorax, and CT-guided fine needle aspiration cytology (FNAC)/biopsy may help evaluate non-resolving or slowly resolving pneumonia. FOB is one of the most useful procedures for evaluating patients with non-resolving pneumonia.

Aim

This study aimed to determine the aetiology of non-resolving pneumonia using FOB, and the role of bronchoscopy in non-resolving pneumonia.

MATERIALS AND METHODS

This prospective observational study included 68 patients admitted to the thoracic medicine ward at Tirunelveli Medical College Hospital between June 2015 and August 2016. The study was approved by the institutional ethics committee before initiation, and informed consent was obtained from all patients.

Inclusion Criteria

Patients who fulfilled the criteria for non-resolving pneumonia and patients who presented with pneumonia-like syndrome and the radiograph failed to resolve by 50% in 2 weeks, completely in 4 weeks, or did not show significant radiographic resolution

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after at least 10 days of antibiotic therapy were included.

Exclusion Criteria

Unwilling patients, known cases of lung cancer in sputum-positive tuberculosis patients with poor general condition, haemodynamic instability, uncooperative patients, and recent myocardial infarction, were excluded.

Detailed clinical history, duration of symptoms, prior history of ATT, and associated comorbidities such as diabetes, hypertension, and coronary artery disease were recorded. A history of smoking and alcoholism was noted, and laboratory investigations such as complete blood count, random blood sugar, renal function tests, and liver function tests were performed in patients who were tested for HIV, hepatitis B, hepatitis C serology, and Sputum for AFB before the procedure. Sputum for Gram staining and culture, fungal staining and culture, and sputum cytology for malignant cells were sent. Chest radiography and chest CT were performed in all patients. Further investigations such as USG chest, USG-guided FNAC, cardiac evaluation, and serological tests were performed as needed. Before the procedure, all patients were treated with empirical antibiotics for at least 10 days, according to standard guidelines.

Patients undergoing bronchoscopy were provided with clear explanations of the procedure, its benefits, and potential complications in their local language, and their consent (both oral and written) was obtained. Vital signs including pulse rate, respiratory rate, blood pressure, and oxygen saturation were recorded before the procedure. The Olympus BF-TE 2 model conventional fibre-optic bronchoscope was utilised, featuring a 120-degree field of view for enhanced visibility.

During bronchoscopy, various procedures, including gross inspection of the upper respiratory tract, visualisation of vocal cord movements, tracheobronchial tree inspection, and FOB-guided interventions, were conducted. The vital signs and oxygen saturation levels were continuously monitored throughout the procedure. All interventions adhered to standard guidelines and universal precautions.

The collected samples were immediately sent to the laboratory. BAL fluid was centrifuged at 1500 rpm for five minutes. The smear was stained with haematoxylin and eosin, and cell count and cytology analysis were performed. BAL fluid was also sent for AFB, Gene Xpert, Gram stain and culture, Fungal stain, and culture. Samples obtained from the bronchial brushings were sent for cytological examination. The transbronchial lung biopsy specimens were preserved in formalin and sent for histopathological examination. USG-guided FNAC was performed in patients with inconclusive results of the FOB procedure. After the procedure, the patients were observed for at least one hour for any complications, such as massive haemoptysis or hypoxia. Post-procedure chest radiography was performed to rule out a pneumothorax.

RESULTS

Among the 68 patients, most patients were above 50 years of age, and in the gender distribution, most of the patients were males 54(80%) and females 14 (20%). [Table 1]

Most of the patients with non-resolving pneumonia had lesions affecting the right lower lobe (33%, n=23), followed by lesions distributed in the right upper lobe (26%, n=18). Non-resolving consolidation was observed in the left lower lobe in 14% (n=10) and the left upper lobe in 11% (n=8) of patients. The lingular segment was affected in two patients (3%, n=2) of patients. A multilobar distribution of consolidation was observed in 4% of the patients (n=3) [Table 2].

The FOB showed various findings during gross inspection of the tracheobronchial tree. The FOB study was normal in 25%(n=17) of the patients. Inflamed mucosa along with mucopurulent secretions was noted in 32%(n=22) of patients. Visible endobronchial mass lesions or nodular lesions were observed in 19% (n=13) of the patients. In 8%(n=) of the patients' mucoid secretions, mucoid impaction was noticed in a few patients, and bronchial segments were irregular, inflamed, and narrowed in the remaining 8%.

The overall diagnostic yield for FOB was 94%(n=64). In 3 of 4 patients, USG-guided FNAC was performed, which revealed the diagnosis. In the remaining 1 patient diagnosis could not be made.Most cases were diagnosed as infectious diseases, followed by malignancies. Infections were the cause of non-resolution in 60.29% (n=1) of patients. In 26.47% (n=18) of the patients, malignancy was the aetiology. A combined aetiology was noted in 5.88%(n=4), and interstitial pneumonitis was diagnosed in 1%(n=1) [Table 3].

Gram-negative pyogenic bacterial infections were diagnosed in 41.1% (n = 28) of the cases. Tuberculosis was diagnosed in 25% (n=17), and fungal infection-mucormycosis was diagnosed in 1%(n=1). Klebsiella species is the predominant bacterial infection identified followed by pseudomonas infection. Squamous cell carcinoma was the predominant malignancy, followed by adenocarcinoma and small-cell carcinoma. Dual aetiology was diagnosed in four patients. Squamous cell carcinoma along with tuberculosis was diagnosed in two patients. Another patient was diagnosed with squamous cell carcinoma combined with secondary bacterial (Klebsiella species) infection. Another patient was diagnosed with tuberculosis and coagulase-negative Staphylococcus aureus [Table 4].

Of the 68 patients, TBLB was performed in 36. Of these, TBLB was diagnosed as the aetiology of NRP in 24 patients, malignancy in 17 patients, and

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granulomatous pathology in five patients. One case of HPE revealed mucormycosis infection, and another was diagnosed with interstitial pneumonitis [Table 5].

Table 1: Demographic data of the study

		Number of patients (%)
Age	15-20	2 (3%)
	21-30	2 (3%)
	31-40	10 (15%)
	41-50	12 (18%)
	51-60	17 (25%)
	61-70	21 (30%)
	71-80	4 (6%)
Gender	Male	54 (80%)
	Female	14 (20%)

Table 2: CT chest pattern of the study

	Number of patients (%)
Right upper lobe	18 (26.4%)
Right middle lobe	4 (5.88%)
Right lower lobe	23 (33.8%)
Left upper lobe	8 (11.7%)
Lingular lobe	2 (2.94%)
Left lower lobe	10 (14.7%)
Multi lobar	3 (4.41%)

Table 3: Yield of FOB IN NRP

		Number of Patients (%)
Infectious aetiology	Pyogenic bacterial infection	26 (60.29%)
	Tuberculosis	14 (60.29%)
	Mucormycosis	1 (60.29%)
Malignancy		18 (26.47%)
Combined aetiology		4 (5.88%)
Interstitial Pneumonitis		1 (1.47%)
Undiagnosed		4 (5.88%)

Table 4: Diagnosis of NRP in the study

	Number of patients (%)
Klebsiella Species	17 (25%)
Pseudomonas Species	9 (13%)
Tuberculosis	14 (20%)
Squamous Cell Carcinoma	13 (19%)
Adeno Carcinoma	4 (6%)
Small Cell Carcinoma	1 (1%)
Squamous Cell Carcinoma & PTB	2 (3%)
Squamous Cell Carcinoma & Klebsiella	1 (1%)
PTB & CONS	1 (1%)
Mucormycosis	1 (1%)
Interstitial Pneumonitis	1 (1%)
Un diagnosed	4 (6%)

Table 5: Transbronchial lung biopsy of the study

	Number of patients (%)
Squamous cell carcinoma	12 (50%)
Adeno carcinoma	4 (17%)
Small cell carcinoma	1 (4%)
Caseating granuloma	5 (21%)
Mucormycosis	1 (4%)
Interstitial pneumonitis	1 (4%)

BAL fluid cytology revealed malignancy in 9%(n=6) of patients. Nonspecific inflammatory changes were observed in the remaining 91% of the patients. Of the 68 patients, BAL culture revealed bacterial infection in 28. Klebsiella pneumoniae was the predominant organism 17%(n=12) followed by Pseudomonas aeruginosa (13%) (n=9). Klebsiella oxytoca was identified in 9%(n=6) and coagulase-negative Staphylococcus aureus was identified in 1%(n=1) of patients. Pyogenic bacterial infections were the most common aetiology, with Klebsiella spp. (26%) being the predominant pathogen. Tuberculosis was the aetiology of non-resolving pneumonia in 17 patients (25%). The AFB smear cytology was positive in 12 patients. BAL fluid CBNAAT analysis detected Mycobacterium tuberculosis in 5 patients. TBLB revealed caseating granulomas in five patients.

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FOB-guided brush cytology revealed malignancy in 10% (n=7) of patients. Squamous cell carcinoma was diagnosed in four patients, and brush cytology in the remaining patients showed probable malignancy which was later confirmed as squamous cell carcinoma by TBLB HPE reports. Of the 68 patients,41.1%(n=28) were diabetic, and 51.47% were smokers. Diabetes is predominantly associated with infectious aetiology. Other comorbidities included CKD (n=8), postrenal transplant (n=1), and CA oesophagus(n=1). COPD, CAD, OLD CVA, and hypertension were other comorbidities.

DISCUSSION

All the patients underwent bronchoscopy. Of the 68 patients, 64 were diagnosed with an aetiological diagnosis. USG-guided FNAC was performed in the remaining four patients, and diagnosis was made in three patients. However, the aetiology could not be determined in one patient. The diagnostic yield of FOB to determine the aetiology of NRP in our study was 96%(n=64) which is comparable to that in other studies. In a study conducted by Chaudhri et al., the yield of FOB in NRP was 85.7%, whereas in a study by Jain et al., the diagnostic yield of FOB was 81%.[2,3] Bhadke et al. concluded that FOB was diagnostic in 75% of NRP cases.[4] In a study by Asari et al., the diagnostic yield of FOB for NRP was 87%.[5] Khara et al., studied the diagnostic yield of FOB in 3 common lung conditions (pneumonia, TB, and lung cancer) and concluded overall yield of FOB was 55.7%.[6]

In our study, the majority of the patients were males (80%). Among females, infections (71%) were the most common aetiology of NRP when compared to malignancy (28%). Among males, the major cause of NRP was infections, but the incidence of malignancy was higher in males than in females probably because of the high incidence of smoking habits. Depressed mucociliary function in smokers is a risk factor for the development of infectious pneumonia.

In our study, the majority of the patients were aged > 50 years. The reason for this was depressed immunity and associated comorbidities among them compared to the young population. In chest CT findings, right lung involvement was more common than on the left side. The right lower lobe (33%) was predominantly involved followed by the right upper lobe (26%) and left lower lobe whereas, in studies done by Chaudhri et al., Jain et al., El-Shabrawy et al., right upper lobe involvement was more common.[2,3,7]

Purulent muco secretions (32%) were noted in most patients during gross inspection of the tracheobronchial tree. Approximately 25% of patients showed no significant findings during gross inspection, but various FOB-guided procedures revealed specific diagnoses. The most common aetiology of NRP in our study was pyogenic bacterial infection (38%), followed by malignancy (26%), and tuberculosis (21%), which is comparable to other studies. Studies conducted by Chaudhri et al., Bhadke et al., Asari et al., and El-Shabrawy et al. concluded that pyogenic bacterial infection was the most common aetiology of NRP, followed by malignancy and tuberculosis.[2,4,5,7] A study by Jayaprakash et al. concluded that TB was the most common aetiology, followed by malignancy. In Visakhapatnam, Kumari et al. also concluded similar results.[8,9]

Among the bacterial infections, Klebsiella spp. was the most common cause, followed by Pseudomonas and CONS which is comparable to other studies. A study done by El-Shabrawy et al. revealed Klebsiella pneumoniae was the most common organism isolated in 29 (24.8%) patients followed by Pseudomonas (19.65%) and Streptococcus pneumoniae (19.65%).[7] Kumari et al., concluded in their study, the most common pathogen identified was Klebsiella (57.14%) followed by Pseudomonas (28.5%) and E. coli (14.2%) Chaudhri et al., reported Klebsiella species were isolated in 13 cases followed by Pseudomonas.[2,9]

All the above-quoted studies showed that gram-negative organisms were the predominant cause of non-resolving pneumonia compared to gram-positive organisms. But a study conducted by Asari et al., found, the most frequent organism isolated was streptococcus pneumoniae (42.1%) and Bhadke et al., also found in his study that Streptococcus pneumoniae was the most bacterial aetiology found in 16 (50%) patients followed by Staphylococcus in 10 (31.25%) and Klebsiella in 6 (18.75%) patients.5,4Jain et al., concluded in their study, that Streptococcus pneumoniae (50%) was the most common bacteria isolated.[3] When compared to the present study, all these studies showed gram-positive organisms were responsible for the aetiology of non-resolving pneumonia. This might be due to the variation in organisms according to their local epidemiological pattern.

In a study by Brownback et al., in immunocompromised individuals, viral infections were the most common aetiology found in 38(48.1%) patients, followed by bacteria in 9(11%), invasive aspergillosis in 14 (17.7%), and Pneumocystis jirovecii in 6 (7.6%) patients.[10] In immunocompromised individuals, the infectious causes were different from the general population as they acquired more atypical organisms and invasive fungal infections due to decreased immunity. In the study done by Jain et al., Squamous cell variety was the predominant carcinoma which is comparable to our study.[3] Chaudhri et al., also concluded in their study that the most common cause of Squamous cell carcinoma followed by adenocarcinoma.[2]

In contrast, Jayaprakash et al. found Adenocarcinoma (42.1%) was the most common among malignancies.[8] Asari et al., reported adenocarcinoma 4 (50%) was more common, followed by squamous cell carcinoma 25%, small cell 12.5% and large cell carcinoma.[5] In both studies, CT-guided FNAC was used as one of the diagnostic procedures which is better in diagnosing

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peripheral tumours like Adenocarcinoma. Squamous cell carcinoma is the predominant central tumour that is best diagnosed using FOB.

In all patients, before the procedure, three sputum samples were sent for AFB smear to rule out smear-positive tuberculosis. Using FOB-related procedures, TB was diagnosed in 17 patients with NRP. We utilised the AFB smear, rapid diagnostic method CBNAAT, and TBLB to detect Mycobacterium tuberculosis in a few patients. The use of FOB in the diagnosis of sputum smear-negative pulmonary TB by Nikbakshi et al. found tuberculosis in 63% of the cases. Therefore, FOB is a very useful procedure to diagnose TB in smear-negative pulmonary tuberculosis patients.[11] A combined aetiology was found in four patients. Squamous cell carcinoma associated with secondary bacterial (Klebsiella) infection was found in one patient. In two patients, squamous cell carcinoma was associated with tuberculosis.

CONCLUSION

This study found that the most common cause of non-resolving pneumonia was infection, and bronchoscopy was an effective tool for determining the aetiology of non-resolving pneumonia.

The study concluded that bronchoscopy plays an essential role in the management of non-resolving pneumonia and should be considered a diagnostic tool in patients with non-resolving pneumonia.

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