

A STUDY ON NON-RESOLVING PNEUMONIA: ROLE OF FIBEROPTIC BRONCHOSCOPY AND CT-GUIDED BIOPSY

Surapaneni Vineela¹, Alla Bhagyaraj², Yelkoti Sushma Laxmi³, Rachakonda Ramakrishna⁴, Talatam Aruna⁵

¹Postgraduate, Department of Respiratory Medicine, NRI Medical College and General Hospital, Chinakakani, Guntur, Andhra Pradesh.

²Postgraduate, Department of Respiratory Medicine, NRI Medical College and General Hospital, Chinakakani, Guntur, Andhra Pradesh.

³Postgraduate, Department of Respiratory Medicine, NRI Medical College and General Hospital, Chinakakani, Guntur, Andhra Pradesh.

⁴Professor and HOD, Department of Respiratory Medicine, NRI Medical College and General Hospital, Chinakakani, Guntur, Andhra Pradesh.

⁵Professor, Department of Respiratory Medicine, NRI Medical College and General Hospital, Chinakakani, Guntur, Andhra Pradesh.

ABSTRACT

BACKGROUND

Slow resolution of pneumonia despite treatment is a common clinical problem. Delay in diagnosis results in increased morbidity. We wanted to establish the aetiology, assess the associated risk factors and study the role of fiberoptic bronchoscopy and CT-guided biopsy.

METHODS

This is a prospective observational study where in 50 patients presenting with an initial diagnosis of pneumonia, who had persistent symptoms and showed less than 50% clearance of chest radiograph at 2 weeks and less than complete clearance at four weeks despite appropriate antibiotic therapy for 10 days were included. All the patients were investigated thoroughly. CT-guided biopsy and fiberoptic bronchoscopy were done in selected cases. Obtained results were analyzed.

RESULTS

Mean age was 53.4 years. Male:female ratio= 1.8:1. Most common aetiology was due to infection seen in 31 (62%) patients. Common organisms isolated were Mycobacterium tuberculosis 18 (58%), fungi 5 (16%), organisms resistant to empirical antibiotic therapy 4 (13%), mixed pathogens 2 (6.5%), non-tuberculous mycobacteria (6.5%). The next common cause observed was malignancy, seen in 12 patients (24%). Adenocarcinoma (67%) was the most common histological type followed by squamous cell carcinoma (25%) and atypical adenomatous hyperplasia (8%). Other causes were cryptogenic organizing pneumonia, pulmonary sequestration and aspirated foreign body. Aetiology was unknown in 2 cases. Diabetes was the most common risk factor among the study group.

CONCLUSIONS

A thorough evaluation with timely utilization of the available investigations helps us in proper management of non-resolving pneumonias.

KEYWORDS

Non-Resolving Pneumonia, Bronchoscopy, CT-Guided Biopsy

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BACKGROUND

The term non resolving pneumonia (NRP) has been used to refer to "Persistence of radiological abnormalities beyond expected time of course".¹ Adequate knowledge regarding

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Corresponding Author:

Dr. Surapaneni Vineela,

#128, New P & T Colony-2, Ring Road,

Vijayawada, Andhra Pradesh- 520008.

E-mail: vineela.surapaneni228@gmail.com

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normal resolution in cases of community acquired or hospital acquired pneumonia is essential for selection of patients for further evaluation at appropriate time.² Delay in diagnosis and treatment may lead to a rise in mortality by 3-5% in both community-acquired pneumonia and nosocomial pneumonia.³⁻⁴ NRP is associated with significant morbidity and mortality and may require the use of invasive procedures like fiberoptic bronchoscopy (FOB) and image guided biopsies to obtain a definitive diagnosis.^{5,6} Approximately 20% of presumed non-responding community acquired pneumonias have a non-infectious aetiology.⁶ We wanted to establish the aetiology, assess the

associated risk factors and study the role of fiberoptic bronchoscopy and CT-guided biopsy.

METHODS

It is a prospective, observational study, conducted in the department of Respiratory medicine. 50 patients were included after taking their consent. Study was conducted between January 2019 and June 2019, over a period of six months. Institutional ethics committee clearance was obtained prior to the study.

Inclusion Criteria

Patients who were initially diagnosed to have pneumonia based on their symptoms and radiographic findings, presenting to respiratory medicine out-patient department with persistent symptoms with a chest radiograph showing less than 50% clearance at 2 weeks or less than complete clearance at 4 weeks, despite appropriate antimicrobial therapy were included in the study. Sputum smears for acid-fast bacilli for all the patients included in the study were negative on two separate occasions.

Exclusion Criteria

- a) Known case of tuberculosis, malignancy.
- b) Patients not willing to give consent.
- c) Seriously ill patients.
- d) HIV seropositive patients.

Study Protocol

A detailed clinical history and physical examination was carried out on all study subjects. Findings such as age, sex, occupation, symptoms and clinical signs (cough, expectoration, breathlessness, chest pain, haemoptysis, fever, chills and rigors, lymphadenopathy, clubbing, pallor, crepitations, bronchial breath sounds) were recorded. Comorbid conditions like diabetes, chronic kidney disease, hypertension, chronic obstructive pulmonary diseases were documented. Addictions like alcohol abuse, smoking history and others were noted. Routine investigations like complete blood picture, liver function tests, renal function tests, sputum examination (culture sensitivity, acid fast staining, Cartridge-based nucleic acid amplification tests, fungal culture) were done. Computed tomography of the chest was done and a CT-guided biopsy was done wherever necessary. Fiberoptic bronchoscopy was done in patients who gave consent and bronchial washings, brushings and biopsies were done wherever necessary. Obtained data was recorded in MS-Excel spread sheet and was analyzed using relevant statistical tests. Results are expressed using mean, percentages and ratios.

RESULTS

Mean age of the study population is 53.4 years. 60% of them i.e., 30 patients were above 40 years of age. Average duration of symptoms was 22.4 days. Fever was the most common presenting symptom seen in 24 patients (48%) followed by cough seen in 20 patients (40%) and haemoptysis seen in 16 patients (32%). Other presenting

symptoms include sputum production in 14 patients (28%), breathlessness in 10 patients (20%) and chest pain in 4 patients (8%). Infectious aetiology resulting in delayed resolution of pneumonia was seen in 31 (62%) patients. Tuberculosis was the most common cause in this group.

Sex	Number of Patients	Percentage
Male	32	64%
Female	18	36%

Table 1. Sex Distribution of the Study Population

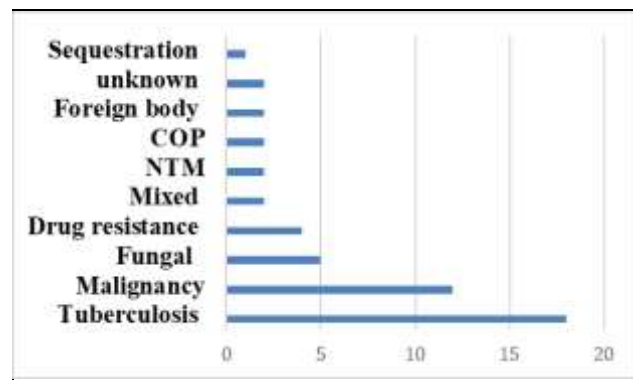


Figure 1. Etiological Causes of Non-Resolving Pneumonia

Fungal Pneumonia 5 patients (10%)		
Organism Isolated	Number of Patients	Percentage
Aspergillus species	3	60%
Candida species	1	20%
Fusarium species	1	20%
Drug Resistant Organisms 4 Patients (8%)		
Klebsiella species	2	50%
Pseudomonas aeruginosa	1	25%
Acinetobacter baumannii	1	25%
Infection with Mixed Pathogens 2 patients (4%) - Klebsiella species and Acinetobacter baumannii		

Table 2. Infection with Organisms other than Mycobacterium Tuberculosis

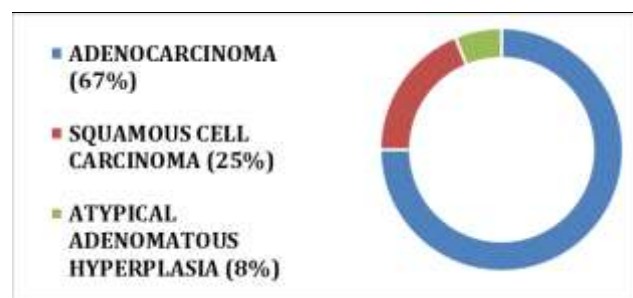


Figure 2. Histological Subtypes of Malignancy

Pattern	Number of Patients	Percentage
Unilateral consolidation	19	38%
Bilateral consolidation	14	28%
Cavitary lesions	12	24%
Reticular pattern	5	10%

Table 3. Radiographic Patterns

Consolidation 33 patients (66%)

Procedure Done	Yield
	Total Number of Cases= 50
Fiberoptic Bronchoscopy (n=45)	36 (80%)
CT-guided Biopsy and FOB Together	48 (96%)
Inconclusive Diagnosis	2 (4%)

Table 4. Investigation Procedures Used to Arrive at Final Diagnosis

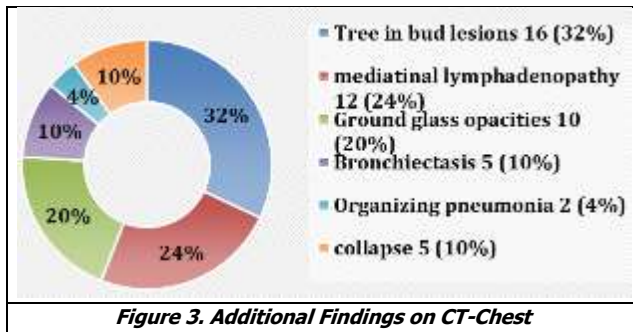


Figure 3. Additional Findings on CT-Chest

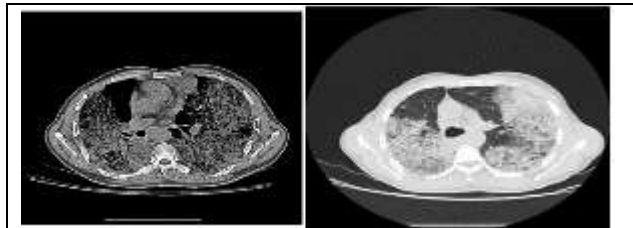


Figure 4

Figure 5

Figure 4 and 5. CT-Chest Showing Features Suggestive of Organizing Pneumonia- Histology of the Specimen Obtained After CT-Guided Biopsy Showed Bronchioloalveolar Cell Carcinoma



Figure 6. Chest Radiograph Showing Right Lower Zone Consolidation with Right Pneumothorax Following a CT-Guided Biopsy. Histopathology Showed Granulomatous Inflammation Suggestive of Tuberculosis



Figure 7. Chest Radiograph Showing Bilateral Multiple Cavities. Culture from Bronchial Washings Revealed Aspergillus Species



Figure 8 and 9

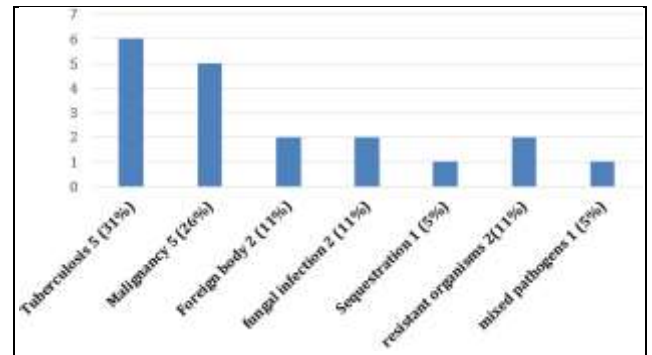


Figure 10. Causes for Unilateral Consolidation

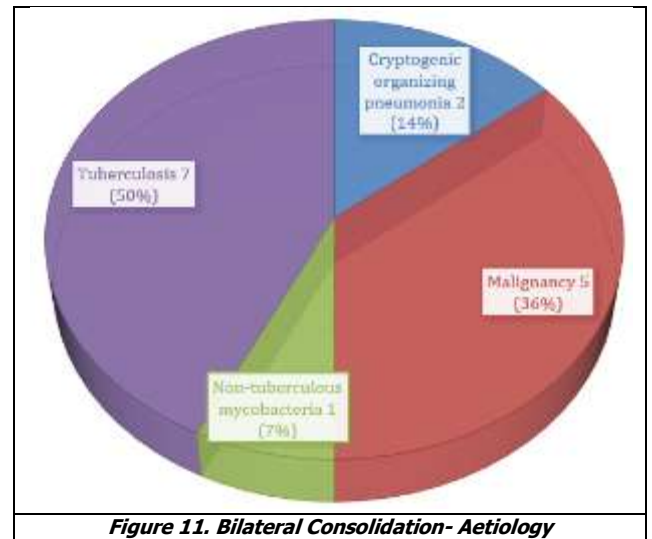


Figure 11. Bilateral Consolidation- Aetiology

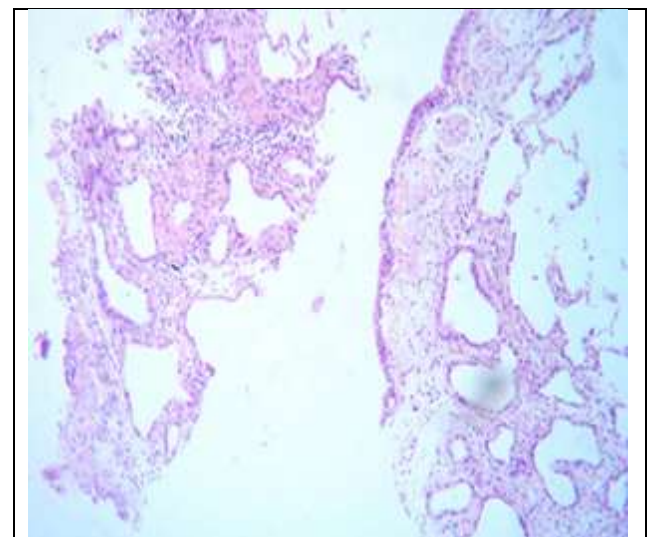


Figure 12. Histopathological Image Showing Atypical Adenomatous Hyperplasia

Bronchoscopic Findings	Number
Purulent secretions	20 (44.4%)
Foreign bodies	2 (4.4%)
Mucous plugs	3 (6.8%)
Inflamed mucosa	15 (33.3%)
Normal	5 (11.1%)

Table 5. Fiberoptic Bronchoscopy Findings (n=45)

Figures 8 and 9. Chest radiograph and CT-chest of a 13-year-old male patient showing left lower lobe pneumonia. CT-pulmonary angiogram was done for further evaluation

which revealed an intralobar sequestration on the left side. Left lower lobectomy was done and histopathology confirmed the diagnosis. Among cavitory lesions seen on chest radiograph, 6 patients (50%) were diagnosed to have tuberculosis, 2 patients (33%) showed infection with *Aspergillus* species, one patient was diagnosed to have pneumonia due to non-tuberculous mycobacteria and three patients were having squamous cell carcinoma. One patient out of fifty was diagnosed to have concurrent tuberculosis infection and adenocarcinoma of the lung. Out of 50 patients 30 (60%) were diabetic, 16 patients (32%) had hypertension, 12 patients (24%) were known to have chronic obstructive pulmonary disease and 5 patients (10%) had chronic kidney disease. 27 patients i.e., 54% of the study population were smokers while 24 patients (48%) consumed alcohol. Fiberoptic bronchoscopy was done in 45 patients and CT-guided biopsy was done in 15 patients.

DISCUSSION

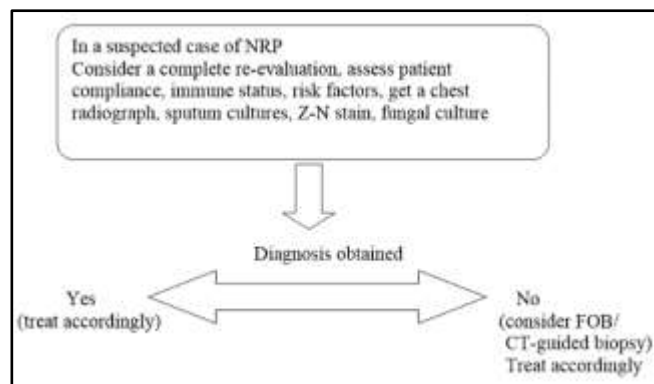
Non-resolving pneumonia presents a diagnostic challenge to the treating physician.⁵ Amberson was the first person to describe the term "unresolved organizing or protracted pneumonia."⁷ There are no definitive criteria available for defining non-resolving pneumonia.⁷ In 1975 Hendin defined slow resolving pneumonia (SRP) as pulmonary consolidation persisting for more than 21 days.⁸ During the course of evaluation of a case of NRP, it is important to keep in mind all the factors responsible for a delayed resolution.⁶ Majority of the reasons identified in the literature for non-resolving pneumonia are related to infection.⁶ Important considerations are pneumonia due to organisms not covered by initial empirical antibiotic therapy, such as multidrug resistant pathogens, atypical pathogens or tuberculosis, or severe infections with a recognized longer response time to treatment, like in *Staphylococcus aureus* pneumonia.^{9,10} In our study, most common cause for delayed resolution was identified to be due to an infectious aetiology, seen in 31 patients i.e., 62% of the study population. This was in accordance with the study conducted by Arancibia et al. in which infection was the most frequent aetiology.⁶ Among the infectious causes, tuberculosis was more common. Similar findings were seen in a study conducted by Chathamparamb et al.¹¹ Malignancy was the next common cause of non-resolution. CT-guided biopsy made it possible to diagnose these cases. 12 patients (24%) were diagnosed to have a neoplastic aetiology. Of them, 8 patients were identified as adenocarcinoma, while 3 patients showed squamous type on histology. Similar findings were noted in a study conducted by Chathamparamb et al.¹¹ One patient was diagnosed to have atypical adenomatous hyperplasia.

Many risk factors are associated with non-resolution. Most of them are related to impairment of the host immune defense.¹² Aging is one of the significant risk factors among them.¹³ In Chaudhuri et al study, 80% are above 40 years old.² In our study, 60% of the patients were above 40 years of age. In a study conducted by Chathamparamb et al 66.4% of the study population was of age >50 years and most of them were males (69.9%).¹¹ El Solh et al stated

that, age alone is an independent risk factor for NRP.¹⁴ Some studies showed that male patients are at greater risk of pneumonia.¹⁵ A male preponderance was observed in our study. Males: females ratio observed in our study was 1.8:1. This finding correlates well with a study conducted by Jayaprakash et al.¹⁶ Diabetes was the common risk factor found in our study. In another study, conducted by Sabale et al smoking was the most common risk factor noted among the study group.¹⁷ Smoking was the next common risk factor noted. Among 27 smokers, 9(33.3%) patients had malignancy and 2(7.4%) patients had pneumonia not responding to empirical antibiotics and 2 (7.4%) patients showed mixed pathogenic organisms and 14(51.9%) patients were diagnosed to have tuberculosis. Jayaprakash et al, stated that smoking was the most common comorbidity noted in his study.¹⁶ Other risk factors observed in our study are hypertension, chronic obstructive pulmonary disease and chronic kidney disease.

Invasive procedures like fiberoptic bronchoscopy and CT-guided biopsy are valuable in obtaining a final diagnosis. In our study 45 patients underwent FOB and a CT-guided biopsy was done in 15 patients. Yield observed in these procedures was 80% in cases of FOB alone and 96% when both the procedures were used together. These findings were similar to those observed by Chaudhuri et al.² A systematic approach is essential while evaluating a case of non-resolving pneumonia.

Algorithm for evaluating a case of non-resolving pneumonia-



CONCLUSIONS

Non-resolving pneumonia poses a challenge for the treating physician. It is always prudent to bear in mind the causes for delayed resolution. Relevant tests should be carried out at appropriate time to arrive at the final diagnosis, thereby reducing the morbidity and mortality.

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