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"Diagnostic role of bronchoscopy in nonresolving pneumonia"

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ABSTRACT: Introduction: Non-resolving pneumonia is often an area of concern and Fiberoptic bronchoscopy (FOB) may have a special role in etiologic evaluation of non-resolving pneumonia. **Aims and Objectives:** This study aimed to assess the efficacy of FOB in diagnosis of non resolving or slowly resolving pneumonia. **Materials and Methods**: After fulfilling the definition of non-resolving pneumonia by clinical and radiological parameters, patients were evaluated by FOB with relevant microbiological, cytological, histopathological investigations and CT scan of thorax. CT-guided FNAC was done in selected cases where FOB was inconclusive. **Observations:** Sixty patients were enrolled in the study, Range of Age: 19 years-74years with male to female ratio (2.33:1). Pulmonary tuberculosis was most commonly diagnosed disease found in 26(43.33%) patients, followed by bacterial pneumonia and bronchogenic carcinoma found in 9(15%) patients each. Nontubercular microbacteria was found in 2(3.33%) patients. Fungal pneumonia, carcinoid tumor and ruptured hydatid cyst was found in 1 patient each. 11(18.33%) patients remained undiagnosed by FOB. Out of these 4(36.36%) were diagnosed with squamous cell carcinoma from lymph node FNAC, 2(18.18%) were diagnosed with adenocarcinoma of lung (1 from CT FNAC of lung and the other from lymph node FNAC and PET scan), 3(27.27%) patients were lost to follow up and 2(18.18%) patients remain undiagnosed till date. **Conclusions:** Fiberoptic Bronchoscopic is very useful and safe diagnostic tool for evaluation of non-resolving pneumonia. (CT-guided FNAC also gives good yield when cases are properly selected.)

Key words: Fiberoptic Bronchoscopy, Brochogenic carcinoma, Non-resolving pneumonia, Tuberculosis

I. INTRODUCTION:

Unapparent resolution of pulmonary infiltrates is a common consultative problem for the pulmonologist. Nonresolving and slowly resolving pneumonias pose a diagnostic challenge. Operationally, nonresolving pneumonia may reflect inadequate antibiotic therapy, resistant or highly virulent organism, impaired host defense, nonbacterial causes, obstructing endobronchial lesions including neoplasms.

The term nonresolving pneumonia and slowly resolving pneumonia have been used interchangeably to refer to persistence of radiographic abnormalities beyond expected time course. In 1991 Kirtland and Winterbauer [1] defined delayed radiographic resolution as less than 50% clearance at 2 weeks or complete clearance at 4 weeks. More recently, Fein and colleagues [2] combined clinical and radiographic indices. It was described as a clinical syndrome in which focal infiltrates clearly begin with some acute pulmonary infection that is fever, expectorations, malaise and / or dyspnoea and do not resolve with "a minimum of 10 days of antibiotic therapy and or radiological infiltrate that has not resolved in an expected time" and defined nonresolving pneumonia as ''slow resolution of radiographic infiltrates or clinical symptoms despite adequate antibiotic therapy.'' The radiological features may present as a lobar pneumonia in which air bronchogram or aerated bronchi are surrounded by opacified lung involving a lobe or most part of a lobe. With modern antibiotics this features may not be present or the infiltrate may be multifocal or bilateral in distribution. Complete radiological clearance of community acquired pneumonia occurred in 50.6% patients at 2 weeks, 65.7% at 4 weeks, and 73.2% at 6 weeks. [3]

II. MATERIALS AND METHODS

It was a prospective longitudinal study done in NRS Medical College in the Dept. of Chest

Medicine for the period of 1 and ½ year from Jan' 17 to June'18. The patients with non-resolving pneumonia above 18 years attending chest OPD NRS Medical College were selected for the study. Total 60 cases were taken. Patient having respiratory symptoms with/without fever and radiological finding suggestive of non resolving pneumonia were included in our study. Diagnosed cases of Tuberculosis, malignancy, positive for HbsAg, anti HCV, HIV patient or having severe breathlessness were excluded from our study. Written consent from every patient and permission from ethical committee were also taken.

STUDY PROTOCOL: Sixty (60) consecutive patients of non-resolving pneumonia of both genders attending OPD of Dept. of Respiratory Medicine, Nil Ratan Sircar Medical College Hospital were selected by adhering to the inclusion and exclusion criteria.

After taking proper history and completing necessary investigation, patients with HbSAg, Anti HCV positive patients were excluded from the study. Detailed demographic and clinical parameters including age, sex, smoking history, clinical symptoms with duration (cough, fever more than 100°F, sputum production, hemoptysis, chest pain, breathlessness, hoarseness of voice) and clinical signs (pallor, cyanosis, clubbing, enlarged neck nodes, pulse, blood pressure, tachypnea, tachycardia ,raised temperature) were evaluated in all patients. Presences of any co-morbidity, especially diabetes mellitus, COPD were documented. Blood for complete hemogram, blood glucose, urea, creatinine, liver function test, and chest X-rays (posteroanterior and lateral view). All patients had undergone a contrast-enhanced CT scan of thorax for better anatomical delineation. Fiberoptic bronchoscopy (FOB) was planned next in all patients. Macroscopic appearance of bronchial tree during FOB (intra luminal growth, presence of secretions/pus, appearance of bronchial mucosa, etc.) was noted.

Bronchoalveolar lavage (BAL) fluid was sent for cytology, AFB smear, CBNAAT, BACTEC culture, gram stain and culture, fungal stain and culture, and malignant cells in all patients. Bronchial brushing and biopsy were also done in relevant patients and were sent for AFB smear and cytopathology, and histopathology respectively. Post-bronchoscopic sputum for AFB smear and malignant cells were also sent. Selective patients where results of FOB were inconclusive, were further evaluated by CT-guided FNAC, PET SCAN (in relevant cases). Blood for rheumatoid factor, anti-nuclear antibody (hep2 method), C-ANCA and p-ANCA, serum angiotensin converting enzyme (SACE), Serum for Echinococcal IgG, Immunocytochemistry and Immunohistochemistry of specimens were done additionally in selected patients wherever found relevant. After evaluation of all the relevant reports, determination of etiology of non-resolving or slowly resolving pneumonia was attempted.

III. RESULT AND ANALYSIS:

In our study, range of age was 19 to 74 years, mean being 45.5 years Male was 42 in number & 18 were female, male female ratio being 2.33:1. Mean age of male was 48 years, that of female was 39.7 years.

Out of 60 patients, 25 patients (i.e.41.6%) were in age of 40 years or below. Rest (i.e.35) were above 40 years. Most patients fall under age group of 31-40 and 41-50 (46.66% combined)followed by 61-70 years age group (i.e.18.33%). The 11-20 years group is least affected (Table - 1). Most patients were male (42 in number) and 18 were female.

Regarding smoking history, most male were smoker (35 out of 42 males) & only 2 female were smoker (Table – 2).

Only 5 patients (8.33%) had past history of ATT treatment (Table – 3)

Regarding symptoms, most (57) patients presented with cough 95% followed by fever (35) patients and weight loss in (29) patients (i.e. 51.67% and 48.33% respectively). Only 1 patients has hoarseness of voice (Table – 4).

Most common clinical sign was increased temperature (i.e. 32) patients (53.33%) followed by tachycardia in 26 patients (43.33%). Clubbing was present in (5) patients (8.33%) (Table – 5).

Co-morbidity was present in 21 patients. Out of them most (10) patients had COPD followed COPD and diabetes combined in 4 patients, 2 patients had only diabetes (Table – 6)

Depending on radiological findings, patient with non-resolving pneumonia were divided into three groups –

Gr. A – Non-resolving pneumonia shadow that includes hilar region (central).

Gr. B – Non-resolving peripheral parenchymal shadow.

Gr. C – Non-resolving parenchymal cavitary lesion.

X-ray abnormalities persisting for 4 weeks or longer inspite of minimum 10 days of antibiotics were considered non-resolving in the study.

Out of 60 patients 33 (55%) patients, had left lung involvement and 29 (48.33%) patients had

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right lung involvement, 7 patients (11.67%) had chest x-ray involvement in more that one zone out of which only 2 (3.33%) patients had bilateral lung involvement and the rest had unilateral lung involvement.

In our study, most patients (29 i.e. 48.33%) had group B involvement followed by group A. Group C involvement was found in 11 patients (i.e. 18.33%) (Table – 7).

Regarding FOB finding, most patients had normal bronchial tree (group I FOB finding) (i.e. 41.7%) followed by edematous mucosa in (15) patients (i.e. 25%). (Table 8)

In our study commonest underlying disease was pulmonary TB found in 26 patient (43.33%) followed by bacterial pneumonia and bronchogenic carcinoma in (9) patients each (i.e. 15% in each group).

11 patients were undiagnosed by FOB (i.e. 81.33%) (Table – 9)

26 patients presenting as non-resolving pulmonary infiltrate were diagnosed as pulmonary Tuberculosis, out of which BAL was positive for AFB staining, CBNAAT and BACTEC in (19.23%) patients (Table – 10)

In bacterial pneumonia commonest organism was S. Pneumonia found in 3 out of 9 patients (i.e. 33.33) case.

Klebsiella and S. aureus were least commonest, one in (i.e. 11.11%) each. (Table – 11)

Among 9 cases of bronchogenic carcinoma SCC was mostly found (i.e.4 out of 9 patients) followed by adenocarcinoma i.e. in 3 patients.

Small cell ca was found only in 2 patients (i.e.22.22%) (Table – 12).

The undiagnosed cases in FOB method, 4 were diagnosed as SCC by lymph node FNAC and PET Scan, 2 were diagnosed as adeno ca lung (one from CT FNAC lung,other from lymph node FNAC and PET Scan, 3 (27.27%) were lost to follow up and 2 (18.18%) patients remain undiagnosed till date. (Table – 13).

IV. DISCUSSION:

In the study, out of 60 patients age of 25 (41.6%) patients were 40 years or below and the rest 35 (58.3%) patients were above 40 years. Fein has shown in his study that only 30% of patients above 50 years of age show complete radiological resolution by 4 weeks. [2] Non-resolving or slowly resolving pneumonia is common in elderly patients due to age related impairment of several components of host defences.

COPD was the most commonly associated co-morbid condition found in 14 (23.33%) patients Jaiprakash et al. in their study also found that COPD (35.7%) and diabetes (45.7%) were the major co-morbidities in patients of non-resolving consolidation.[4]

In this study patients were considered smokers if they smoked at least one packet of cigarette per day and ten pack year during their lifetime and had been smoking within the previous two years. Out of the 60 patients 37 (61.67%) were smokers and the rest (23) were non smokers. Jayaprakash et al, stated that smoking was one of the common co-morbidity noted in his study. [4]]

The most frequently recorded symptom was cough, found in 57 (95%) patients, followed by fever, found in 35 (58.33%) patients. Weight loss was recorded in 29 (48.33%) patients, shortness of breath was recorded in 27 (45%) patients, haemoptysis was recorded in 26 (43.33%) patients, chest pain was recorded in 17 (28.33%) patients, and hoarseness of voice was recorded in 1 (1.67%) patient. Kirtland et al. studied 39 patients of slowly resolving pneumonia and found cough as commonest symptoms (92%) followed by chest pain (38%), breathlessness (38%), fever (36%), and haemoptysis (28%).[82] Chaudhuri et al study showed cough was 100%, followed by fever 96.6%, haemoptysis 53.5%, chest pain 38.5% and shortness of breath in 33.3%.[1]]

Out of 60 patients in this study, pulmonary tuberculosis was most commonly diagnosed disease found in 26 (43.33%) patients, followed by bacterial pneumonia and bronchogenic carcinoma found in 9 (15%) patients each. Non tuberculous mycobacterium was found in 2 (3.33%) patients. Fungal pneumonia, carcinoid tumor and ruptured hydatid cyst was found in 1 patient each. 11 (18.33%) patients remained undiagnosed by FOB. In the study by Silver et al., FOB was diagnostic in 86% cases, and infections were the most common etiology obtained at FOB.[5] Balamugesh et al. have also found FOB a very useful tool in evaluating nonresolving pneumonia.[6]]

In this study tuberculosis was diagnosed in 26 (43.33%) cases. 26 patients presenting as non resolving pulmonary infiltrates were diagnosed with pulmonary tuberculosis, out of which Bronchoalveolar lavage (BAL) was positive for AFB staining, CBNAAT and BACTEC in 5 (19.23%) patients. 13 (50%) patients were positive for BAL CBNAAT and BACTEC but negative for BAL AFB staining. 8 (30.77%) patients were positive for BAL BACTEC only. Studies by Chaudhuri et al and Feinsilver contributed to 16.7% cases 5.7% of tuberculosis cases respectively. [7, 8]

Out of the 9 patients diagnosed from BAL culture to be suffering from non resolving bacterial pneumonia, 3 (33.33%) were infected with Streptococcuspneumoniae, 2 (22.22%) were infected with MRSA and Streptococcusviridans each, and 1 (11.11%) from Staphylococcusaureus and Klebsiellapneumoniae each. Goodman and Rogers [9] isolated S pneumoniae in 32% (41 out of 127 patients) in a study of nonresolving pneumonia. Israel and Co-workers [10]found that streptococcus pneumoniae was the pathogen in 78 of 139 patients (56%) with slowly resolving pneumonia. Ake Ortqvist, Mat Kalin et al[11] isolated S pneumoniae in 47% cases from BAL.

9 (15%) patients presenting with non resolving pulmonary infiltrates were diagnosed with bronchogenic carcinoma, out of which 3 (33.33%) were diagnosed with adenocarcinoma, 2 (22.22%) were diagnosed with small cell lung carcinoma and 4 (44.44%) were diagnosed with squamous cell carcinoma. Gleichman TK et al[12] and Israel HE et al [10] found endobronchial carcinoma as an infrequent cause for nonresolving pneumonia, only found in 0-8 % cases. Steven H Feinsilver et al [13] found malignancy as a specific cause for nonresolution in 4 of 35 (11.4%) patients.

So, overall our findings are more or less similar to several other studies concluded in different parts of the world and in India. However in this study Tuberculosis is found to be more frequent than studies conducted in western countries.

V. CONCLUSION:

Nonresolving pneumonia is often an area of clinical dilemma to the treating physician because establishing the cause for the non-resolution of pneumonia takes time and requires invasive investigations. Apart from bacterial pneumonia not responding to empirical antibiotics, tuberculosis and malignancy contributed as major cause for non-resolution.

Age itself is an important risk factor apart from smoking, diabetes and alcoholism. It is very much needed to observe every patient for the adequate response to treatment and to utilize other modalities of investigations like FOB, CT guided FNAC (in peripheral lesions), PET SCAN whenever required .Fiberoptic Bronchoscopy, including BAL fluid PAP Stain, bronchoscopic biopsy ,BAL fluid AFB, CBNAAT, BACTEC culture and BAL culture was helpful to get a confirmed diagnosis. There was no major complication with Fiberoptic Bronchoscopy with local anesthesia in patients.

So the role of fiberoptic bronchoscopy is indispensable in the diagnosis of patients presenting with nonresolving pneumonia.

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AGE INTERVAL	**FREQUENCY**	**PERCENTAGE**
11-20	**1**	**1.67**
21-30	**10**	**16.67**
31-40	**14**	**23.33**
41-50	**14**	**23.33**
51-60	**8**	**13.33**
61-70	**11**	**18.33**
71-80	**2**	**3.33**
TOTAL	**60**	**100**

Table 1
Distribution of Age

TABLE 2

DISTRIBUTION OF SMOKING HABIT:

Patients were considered smokers if they smoked at least one packet of cigarette per day and ten pack year during their lifetime and had been smoking within the previous two years.

	MALE	**FEMALE**	**TOTAL**
SMOKER	**35**	**2**	**37**
NON SMOKER	**7**	**16**	**23**
TOTAL	**42**	**18**	**60**

TABLE 3

DISTRIBUTION OF PAST HISTORY OF ATT:

	FREQUENCY	**PERCENTAGE**
H/O ATT PRESENT	**5**	**8.33**
H/O ATT ABSENT	**55**	**91.67**
TOTAL	**60**	**100**

TABLE 4

DISTRIBUTION OF CLINICAL SYMPTOMS:

SYMPTOMS	**FREQUENCY**	**PERCENTAGE**
COUGH	**57**	**95**
CHEST PAIN	**17**	**28.33**
HEMOPTYSIS	**26**	**43.33**
WEIGHT LOSS	**29**	**48.33**
FEVER	**35**	**51.67**
SHORTNESS OF BREATH	**27**	**45**
HOARSENESS OF VOICE	**1**	**1.67**

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TABLE 5

DISTRIBUTION OF CLINICAL SIGNS:

SIGNS	FREQUENCY	PERCENTAGE
RAISED TEMP	32	53.33
TACHYCARDIA	26	43.33
TACHYPNOEA	20	33.33
PALLOR	14	23.33
LYMPHADENOPATHY	10	16.67
CLUBBING	5	8.33

Most common clinical sign was increased temperature in 32 patients i.e. 53.33% followed by tachycardia in 26 patients i.e. 43.33%. Clubbing was present in 5 patients (8.33%). Regarding co morbidities illness, 21 patients had co morbidity, out of them, most (10 patients) had COPD followed by COPD and diabetes in 4 patients and diabetes was present only in 2 patients.

DISTRIBUTION OF DURATION OF ILLNESS:

Range of duration of illness: 1-6 months
Mean duration of illness: 2.8 months

DISTRIBUTION OF LEUCOCYTOSIS: Out of the 26 patients diagnosed with pulmonary tuberculosis 7 (26.92%) had leukocytosis. Out of 9 paatients diagnosed with bronchogenic carcinoma 5 (55.55%) had leucocytosis. Out of the 9 patients diagnosed with bacterial pneumonia 6 (66.67%) patients had leucocytosis.

TABLE 6

DISTRIBUTION OF COMORBID ILLNESS

COMORBID CONDITIONS	FREQUENCY
COPD (ONLY)	10
DIABETES (ONLY)	2
COPD+DIABETES	4
ALCOHOLISM	1
ASTHMA	1
BRONCHIECTASIS	1
KYPHOSCOLIOSIS	1
EPILEPSY	1

TABLE 7

DISTRIBUTION OF RADIOLOGIC FINDINGS: Patients with nonresolving pneumonia were distributed into three groups [93] according to Chest X Ray abnormality into the following three types:

- Group A: non resolving pneumonic shadow that includes hilar region (central)
- Group B: non resolving peripheral parenchymal shadow
- Group C: non resolving parenchymal cavitary lesion

Chest X Ray abnormalities persisting for 4 weeks or longer despite minimum 10 days of antibiotics were considered nonresolving in the study.

RADIOLOGIC CHANGE	FREQUENCY	PERCENTAGE
Group A	20	33.33
Group B	29	48.33
Group C	11	18.33

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TOTAL	**60**	**100**

Table 8

DISTRIBUTION OF FIBRE OPTIC BRONCHOSCOPY FINDINGS: Bronchoscopic findings were classified into the following 5 types:

- Group I: Normal bronchial tree
- Group II: Edematous mucosa with purulent secretion coming out

from the bronchial lumen

- Group III: Narrowing and / or distortion of bronchi with normal overlying mucosa (external compression)
- Group IV: Narrowing and / or distortion of bronchi with mucosal ulceration or hypertrophy.

Group V: Intraluminal growth

Out of 60 patients, most patients had normal bronchial free (group 1FOB finding) 41.67% followed by edematous mucosa in 15 patients 25%.

FOB FINDINGS	FREQUENCY	PERCENTAGE
GROUP I	**25**	**41.67**
GROUP II	**15**	**25**
GROUP III	**5**	**8.33**
GROUP IV	**8**	**13.33**
GROUP V	**7**	**11.67**
TOTAL	**60**	**100**

Table 9

DISTRIBUTION OF DISEASES:

DISEASE	FREQUENCY	PERCENTAGE
PULMONARY TUBERCULOSIS	**26**	**43.33**
BACTERIAL PNEUMONIA	**9**	**15**
BRONCHOGENIC CARCINOMA	**9**	**15**
NON TUBERCULOUS MYCOBACTERIUM	**2**	**3.33**
FUNGAL PNEUMONIA	**1**	**1.67**
CARCINOID TUMOR	**1**	**1.67**
RUPTURED HYDATID CYST	**1**	**1.67**
UNDIAGONED BY FOB	**11**	**81.33**
TOTAL	**60**	**100**

Table 10

DISTRIBUTION OF MODE OF DIAGNOSIS IN PULMONARY TUBERCULOSIS:

26 patients presenting as nonresolving pulmonary infiltrates were diagnosed as pulmonary tuberculosis, out of which Bronchoalveolar lavage (BAL) was positive for AFB staining, CBNAAT and BACTEC in 5 (19.23%) patients. 13 (50%) patients were positive for BAL CBNAAT and BACTEC but negative for BAL AFB staining. 8 (30.77%) patients were positive for BAL BACTEC only.

MODE OF DIAGNOSIS	FREQUENCY	PERCENTAGE
BAL AFB+CBNAAT+BACTEC	**5**	**19.23**
BAL CBNAAT+BACTEC	**13**	**50**
BAL BACTEC	**8**	**30.77**
TOTAL	**26**	**100**

TABLE 11

DISTRIBUTION OF ORGANISMS IN BACTERIAL PNEUMONIA:

ORGANISMS	FREQUENCY	PERCENTAGE
S PNEUMONIAE	3	33.33
MRSA	2	22.22
S VIRIDANS	2	22.22
S AUREUS	1	11.11
KLEBSIELLA	1	11.11
TOTAL	9	100

TABLE 12-explanation

DISTRIBUTION OF BRONCHOGENIC CARCINOMA.

BRONCHOGENIC CARCINOMA	FREQUENCY	PERCENTAGE
ADENO CARCINOMA	3	33.33
SMALL CELL CARCINOMA	2	22.22
SQUAMOUS CELL CARCINOMA	4	44.44
TOTAL	9	100

TABLE 13

Out of the 11 cases not diagnosed by FOB 4 (36.36%) patients were diagnosed with squamous cell carcinoma from lymph node FNAC and PET SCAN, 2 (18.18%) patients were diagnosed with adenocarcinoma of lung (1 patient from CT FNAC of lung and the other from lymph node FNAC and PET scan), 3 (27.27%) patients were lost to followup and 2 (18.18%) patients remain undiagnosed till date.

	FREQUENCY	PERCENTAGE
SQUAMOUS CELL CARCINOMA	4	36.36
ADENOCARCINOMA	2	18.18
LOST TO FOLLOWUP	3	27.27
UNDIAGNOSED TILL DATE	2	18.18
TOTAL	11	100