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Original Article

Internal Medicine Section

Microbial Aetiology and Clinical Course of Pleural Space Infections in a Tertiary Care Hospital- A Cohort Study

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ABSTRACT

Introduction: Infection of pleural space that arises due to complicated parapneumonic effusion and empyema is a common worldwide problem that is known since very ancient times. The microbial aetiology of pleural space infections has changed since introduction of antibiotics. Gram positive organisms are slowly and steadily losing their foothold in the pleural space to the more resilient and resistance gram negative bacteria. Incidence of these infections are increasing and delayed treatment causes significant morbidity and mortality.

Aim: To study the age-sex profile, symptoms, microbiological findings, aetiology, management and treatment outcome of pleural space infections.

Materials and Methods: This cohort study was conducted at Veer Surendra Sai Institute of Medical Sciences and Research, Burla, Odisha, India, from November 2016 to October 2017 on 48 consecutive patients. Each patient was followed-up for a minimum period of two months. The demographic data, clinical presentation, microbiological findings, aetiology, clinical course and management information were collected in a predesigned proforma and analysed.

Results: The study population comprised of 33 (68.8%) male, 15 (31.2%) female patients. The mean age of the study population was 46±14 years. The most common presenting complaints were fever {43 (89.5%)}, shortness of breath {42 (87.5%)}, chest pain {38 (79.1%)} and cough {36 (75%)}. Pneumonia was diagnosed in 30 (62.5%) cases as the major cause of pleural space infection. Common organisms isolated were *Streptococcus pneumoniae* 11 (23%), *Streptococcus pyogenes* 9 (18.7%), *Staphylococcus aureus* 7 (14.5%) and *Escherichia coli* 7 (14.5%). The treatment was with Intravenous (i.v.) antibiotics followed by oral antibiotics. Most cases 46 (95.8%) required both thoracocentesis and Intercostal Tube Drainage (ICTD). Follow-up chest X-ray after two weeks showed complete lung expansion in 25 (52%) cases. Pleural thickening of <2 cm found in 22 (45.8%) cases and >2 cm found in 26 (54.2%) cases. At the end of one month of discharge 35 (73%) patient had complete resolution, 8 (16.7%) patients had persistent infection, 3 (6.2%) died and 2 (4.1%) patients were loss to follow-up. Out of the eight patients with persistent infection one patient had empyema necessitans and seven patients had bronchopleural fistula. On follow up after 2nd month out of the 8 (16.6%) persistence cases, 5 (10.4%) cases were cured and remaining 3 (6.2%) cases the infection persisted (pus) and ICTD was kept in-situ.

Conclusion: Pneumonia is the most common cause of pleural space infections. Most common pathogen isolated was gram positive organism *Streptococcus pneumoniae*. In significant number of cases gram negative organism *Escherichia coli* was isolated. Most cases required both thoracocentesis and ICTD for resolution. The key to successful management of pleural infection remains to be early diagnosis, initiation of empirical broad spectrum antibiotics, followed by specific antimicrobial therapy after microbial identification and drug sensitivity testing.

Keywords: Empyema, Lung abscess, Parapneumonic effusion

INTRODUCTION

Infection of pleural space is known since ancient times with the first recorded descriptions found in the medical text in the ancient Greece by Hippocrates in 500 BC [1]. Any effusion that occur secondary to an infectious process in the lung parenchyma such as pneumonia, lung abscess or bronchiectasis is defined as parapneumonic effusion [2]. A complicated parapneumonic effusion is one for which an invasive procedure such as tube thoracostomy, is necessary for its resolution or on which the bacterial cultures are positive. The most common cause of pleural space infection is pneumonia. In recent times, due to wide spread use of antibiotics, microbial aetiology of pleural space infections has changed. Dominant gram positive organisms are slowly being replaced by more resistant gram negative organisms [3]. There is wide geographic variation of organisms causing pleural space infections. The aetiology and bacteriology of healthcare associated empyema are quite different from those of community acquired empyema [3].

After starting treatment with broad spectrum antibiotics effective thoracentesis is performed and pleural fluid aspirated, is studied. Specific antibiotic therapy is started as per culture and sensitivity. If fluid cannot be removed with therapeutic thoracentesis, chest tube is to be inserted. If loculated pleural effusion persists, the patient is subjected to video assisted thoracoscopy surgery and if the lung cannot expand with this procedure, full thoracostomy with decortication is performed, the definitive procedure should be done in 14 days [4]. Fibrinolytic is applied to pleural space infections with extensive loculations [5].

During initial presentation, it is difficult to determine the prognosis of pleural space infections from clinical, radiological and pleural fluid characteristics. Long term complications of pleural space infections include residual pleural thickening (up to 13% of patients). Rarely extensive incapacitating pleural fibrosis may develop (fibrothorax). Pleural calcification, broncho pleural fistula formation and development of empyema necessitans are other rare complications [6]. Early diagnosis and proper treatment of the patients is required to prevent long term complications.

This study was conducted at a tertiary care hospital of Odisha, an eastern state in India. Regarding pleural space infections in this region, adequate information is not available regarding aetiology, clinical presentation, microorganisms, their drug susceptibility and complications. This study aims to find out the information about the age-sex profile, symptoms, microbiological findings, aetiology, management and treatment outcome of pleural space infections.

MATERIALS AND METHODS

This cohort study was conducted at Veer Surendra Sai Institute of Medical Sciences And Research (VSSIMSAR), Burla, Odisha, India from November 2016 to October 2017 with approval of Institutional Ethics Committee (Communication No-2016/P-I-RP/134). Written informed consent was obtained from patients or representatives before enrolling to this study. A 48 consecutive patients with pleural space infection admitted to Department of Medicine and Department of Pulmonary Medicine during the stated study period were selected as per inclusion criteria defined below.

Inclusion criteria: 1) Age more than 15 years; 2) Parapneumonic effusion or empyema with fluid thickness more than 10 mm on decubitus chest X-ray; 3) Parapneumonic effusion with pleural fluid pH <7.2, Lactate Dehydrogenase (LDH) >1000 IU/mL and Glucose <60 mg/dL. Case Definition: Parapneumonic effusion is defined as any effusion that occurs secondary to an infectious process in the lung parenchyma such as pneumonia, lung abscess or bronchiectasis. Empyema is defined as pus in pleural space [7].

Exclusion criteria: Pleural space infection associated with tubercular aetiology, traumatic and iatrogenic, congestive heart failure, chronic pancreatitis, metastasis, liver cirrhosis, nephrotic syndrome, pyoperitoneum and pelvic abscess were excluded from the study.

Study Procedure

After inclusion of patient in the study a detailed history was taken and thorough physical examination was done. Chest radiographs both Posteroanterior (PA) view and lateral view was done for all the patients. They were evaluated for routine blood examinations and diagnostic pleural aspiration was done. Pleural fluid aspirated was sent for cytological study (total cell count, differential count, malignant cell), Biochemical study {ADA (Adenosine Deaminase), Glucose, LDH}, Gram stain, culture sensitivity, AFB (Acid Fast Bacilli) staining, Cartridge Based Nucleic Acid Amplification Test (CBNAAT) was done. Ultrasonography of chest, abdomen and pelvis was done. Computed Tomography (CT) scan thorax was done in 12 selected patients where diagnosis was in doubt and to locate another associated lung pathology. The treatment was done primarily by empirical antibiotics followed by culture specific antibiotics. In addition to it, thoracocentesis was done in all cases of parapneumonic effusions and empyema. In culture positive patients and in case of empyema, ICTD was given. In general chest tube was left in place until the volume of the pleural drainage was less than 50 mL for 24 hours [8]. All patients were followed for 14 days of discharge and at the end of first month. If no improvement after one month they were next followed-up monthly for second and third month. In the follow-up visit, clinical examination, required blood and pleural fluid investigation were done. Patients were usually referred for surgical intervention like decortication or Video Assisted Thoracic Surgery (VATS) if not improved after three months [9].

STATISTICAL ANALYSIS

All the data was collected in predesigned format. These data were entered to Microsoft office excel which was used for various calculations. Statistical analysis were performed using the Statistical Package for the Social Sciences (SPSS) version 10.0 software for MS-Windows. Descriptive frequencies were expressed using mean±Standard Deviation (SD) and median (range).

RESULTS

The current study was conducted on 48 patients with pleural space infection. The male to female ratio was 2.2:1. The mean age of study population was 46±14 years. The most common age group was 46-60 years: 20 (41.7%) followed by 31-45 years: 16 (33.3%) [Table/Fig-1]. Alcohol was the most common risk factor followed by smoking [Table/Fig-2]. In 7 (14.5%) subjects more than one co-morbidity was present.

Age (years)	Males, n (%)	Females, n (%)	Total (48), n (%)
15-30	6 (12.5)	3 (6.25)	9 (18.8)
31-45	10 (20.8)	6 (12.5)	16 (33.3)
46-60	15 (31.2)	5 (10.4)	20 (41.7)
>61	2 (4.2)	1 (2)	3 (6.2)

[Table/Fig-1]: Age and sex distribution of patients enrolled in the study (N=48).

Risk factors/Co-morbidity	Number of cases {n (%)}
Smoking	25 (52)
Alcohol	28 (58.3)
Chronic obstructive pulmonary disease	10 (20.8)
Diabetes	10 (20.8)
Malignancy	3 (6.25)
Tuberculosis	3 (6.25)
No risk factor	12 (25)

[Table/Fig-2]: Risk factors and co-morbid illness in the study subjects (N=48).

Fever 43 (89.5%), cough 36 (75%), chest pain 38 (79.2%) and shortness of breath 42 (87.5%) were major presenting complaints in patients with pleural space infection [Table/Fig-3].

Symptoms and signs	Number of cases {n (%)}
Fever	43 (89.5)
Cough	36 (75)
Chest pain	38 (79.2)
Shortness of breath	42 (87.5)
Constitutional	28 (58.3)
Pallor	7 (14.6)
Clubbing	3 (6.2)
Lymphadenopathy	2 (4.2)
Tachycardia	30 (62.5)
Tachypnoea	43 (89.6)
Hypoxia	12 (25)
Temperature >99°F	45 (93.7)
Hypotension	8 (16.6)

[Table/Fig-3]: Symptoms and signs of patients with pleural space infections (N=48).

Average duration of illness at the time of presentation was 12±2.5 days. A 26 patients presented between 1-2 weeks [Table/Fig-4].

Most of the cases had pneumonia that was cause of pleural space infection. It was found in 30 (62.5%) of cases [Table/Fig-5].

Duration of illness (week)	Number of cases {n (%)}
<1	4 (8.3)
1-2	26 (54.2)
>2	18 (37.5)

[Table/Fig-4]: Duration of symptoms at the time of presentation (N=48).

Pathology	Number of cases {n (%)}
Pneumonia	30 (62.5)
Lung abscess	3 (6.2)
Encysted pleural effusion	4 (8.3)
Malignancy	3 (6.2)
Iatrogenic	4 (8.3)
Idiopathic	4 (8.3)

[Table/Fig-5]: Aetiopathology found in patients with pleural space infections in the study (N=48).

In pleural fluid analysis, 41 (85.4%) cases had neutrophil predominance in cytology. Pleural fluid glucose was less than 60 mg/dL in 46 (95.8%) of cases and ADA less than 40 IU/L in pleural fluid analysis was present in 46 (95.8%) of cases [Table/Fig-6]. All cases were having

pleural fluid LDH level more than 1000 IU/L. Total cell count was raised in all samples of pleural fluid collected. Average total cell count was 2800±660 cells/mm^3. Malignant cells were found in three samples of aspirated pleural fluid.

Pleural fluid analysis		No of cases {n (%)}
Cytology	Lymphocyte predominance	7 (14.6)
	Neutrophil predominance	41 (85.4)
Glucose	>60 mg/dL	2 (4.2)
	<60 mg/dL	46 (95.8)
ADA	>40 IU/L	2 (4.2)
	<40 IU/L	46 (95.8)

[Table/Fig-6]: Cytological and biochemical analysis of pleural fluid aspirated from patients of pleural fluid infections (N=48).
ADA: Adenosine deaminase

The AFB staining and CBNAAT (for *Mycobacterium tuberculosis*) of aspirated pleural fluid from all cases were negative. Culture results of aspirated pleural fluid showed predominantly gram positive organism i.e., in 39 (81.25%) cases. In 9 (18.75%) cases fluid was sterile [Table/Fig-7].

Gram stain		Organism identified	Percentage of cases n (%)
Organisms isolated 39 cases (81.25%)	Gram (+) organism	*S. pyogenes*	9 (18.75)
		S. pneumoniae	11 (23)
		S. aureus	7 (14.5)
	Gram (-) organism	*E. coli*	7 (14.5)
		P. aeruginosa	4 (8.5)
		Citrobacter spp.	1 (2)
9 (18.75%) cases: No growth.			

[Table/Fig-7]: Gram stain and culture results of aspirated pleural fluid from patients (N=48).

Mean duration of hospital stay in study subjects was 13±4 days. Duration of antibiotics therapy and duration of ICTD is presented in [Table/Fig-8].

Duration	Mean±SD (days)
Duration of i.v. antibiotics	12±5
Duration of oral antibiotics	21±5
Duration of intercostal tube drainage	25±5
Duration of hospital stay	13±4

[Table/Fig-8]: Duration of treatment in patients with pleural space infections (N=48).

Out of 48 patients with pleural space infection, 46 (96%) cases required thoracocentesis followed by ICTD and only two cases (4%) resolved with thoracocentesis only.

Radiological outcome parameters like chest expansion and pleural thickening were measured on follow-up. Complete expansion after two weeks was found in 52% of cases [Table/Fig-9]. Clinical outcome on follow-up after one month is shown in [Table/Fig-10].

Variables	Parameters	No. of cases {n (%)}
Chest expansion on repeat imaging	Complete expansion	25 (52.0)
	Partial expansion	23 (47.9)
Pleural thickening	<2 cm	22 (45.8)
	>2 cm	26 (54.2)

[Table/Fig-9]: Radiological outcome after two weeks of follow-up (N=48).

Follow-up	Loss to follow-up	2 (4.1)
	Death	3 (6.2)
	Persistence	8 (16.7)
	Cured	35 (73.0)

[Table/Fig-10]: Outcomes (clinical) after one month of follow-up (N=48).

After second month 8 (16.7%) cases in which pleural space infection persisted were followed-up. Out of them five cases were cured and ICTD was removed. After third month of follow-up of rest 3 (37.5%) persistence cases infection persisted. They were referred to higher center with ICDT in-situ for surgical intervention.

DISCUSSION

This is the first cohort study in this region describing epidemiology, microbiology and clinical outcomes of patients with pleural space infections. In this study, mean age of the study population was 46±14 years. Recent studies from Europe, US and Canada reported the average age of patients diagnosed with pleural infection was 58-63 years [10-14]. However, a recent systematic review pointed out that age bracket of adult patients with pleural infection from lower income and Asian countries tended to be 15 years younger on average than western countries [15]. In the present study, males outnumbered females in ratio 2.2:1 which was similar to results of the study by Gupta I et al., [11].

In the current study group, tobbaco smoking 25 (52%), alcohol 28 (58.3%), chronic obstructive pulmonary disease 10 (20.8%) and diabetes 10 (20.8%) were major risk factors associated with pleural space infections. These results were similar with recent population based studies [13,16].

The most common symptoms at presentation were fever 43 (89.5%), followed by shortness of breath 42 (87.5%), chest pain 38 (79.2%) and cough in 36 (75%) of cases. One study by Kamat A, reported cough (94%) to be the most common symptom followed by fever (76%), chest pain (75%) and dyspnea (53%) [17].

Pneumonia is found to be the most common aetiology 30 (62.5%) of pleural space infection in the current study which was in consistence with results of recent studies [12,13]. Pleural fluid analysis of the subjects of this study showed neutrophilic predominance in 41 (85.4%) cases, low glucose (less than 60 mg/dL) in 46 (95.8%) cases and LDH level more than 1000 IU/L in all cases. Pleural fluid glucose <60 mg/dL alongside pleural LDH >1,000 IU/L (i.e., more than three times the upper normal limit for serum LDH) is suggestive of pleural infection [18].

In the current study, 39 (81.25%) subjects were culture positive and in 9 (18.75%) cases fluid was sterile. Out of culture positive cases gram positive organisms were major isolates in 27 (69.2%)subjects than gram negative organisms in 12 (30.8%) subjects. Common organisms isolated were *Streptococcus pneumoniae* 11 (23%), *Streptococcus pyogenes* 9 (18.75%), *Staphylococcus aureus* 7 (14.5%) and *E. coli* 7 (14.5%) (most common gram-negative organism isolated). A recent systematic review on the microbiology of pleural infection in adults reported that gram positive cocci (namely *Staphylococcus aureus*, Viridans-Group Streptococci (VGS), and *Streptococcus pneumoniae*, in descending order of frequency) were the most common organisms implicated in causing pleural infection [19]. These results are different as trend of organisms in a community is region specific.

This study showed average duration of antibiotics therapy was 35 (±6) days which included 12 (±5) days of i.v. antibiotics and rest period of oral antibiotics. In the present study, ICTD was used in higher number of cases i.e., in 46 (96%) subjects. In a recent study by Meyer CN et al., average duration of antibiotic therapy was 35 days and ICTD was used in 86% of cases [10]. Long duration antibiotic treatment and ICTD were first line of management of patients with pleural space infection. Average duration of hospital stay and duration of ICTD use were found to be 13 (±4) days and 25 (±5) days respectively. Similar results were reported in recent studies [10,15,16]. The mortality in the present study was 6.2% which was similar to that seen in other studies [20,21].

Limitation(s)

The present study has been carried out in a single tertiary care hospital which can result into a selection bias. Symptoms of the

patients were not quantified. Higher treatment modalities like use of fibrinolytic and surgical intervention like decortication, video assisted thoracotomy were not performed in study institution.

CONCLUSION(S)

This study confirms pneumonia being the most common cause of pleural space infection. Male sex, smoking, alcoholism and diabetes are important risk factors. Gram positive organisms are predominantly isolated among which *Streptococcus pneumoniae* was the most common. Long duration antibiotic therapy and ICTD remains the mainstay of management of pleural space infections.

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