Study of Pleural Effusions in Patients Attending Katuri Medical College & Hospital, Chinakondrupadu, Guntur, Andhra Pradesh

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ABSTRACT

BACKGROUND

Pleural effusion is a common complication of many disease processes. Disorders causing distortion in body fluid mechanics will cause either transudative effusions or exudative effusions. Lights criteria are used to differentiate Exudative from Transudative Effusions. The present study is undertaken to study the aetiology and clinical features of pleural effusion in our institute. Tuberculosis is still one of the most important causes of exudative plural effusion. The levels of Adenosine De Aminase an enzyme found in most cases are increased and its determination has proven to be useful as diagnostic test in case of TPE. Elevated plural fluid ADA predicts TB plural effusion with a sensitivity of 90-100% and specificity of 89-100%.

METHODS

100 cases of pleural effusion admitted in Katuri Medical College were carefully studied, and investigated. Skiagram postero-anterior view of chest with both domes of diaphragm were done for all patients. Ultrasound chest-for estimating the quantity of fluid and site of aspiration was done in all cases and sent for pleural fluid ADA, counts, protein, sugar and LDH values. Pleural fluid cytology for malignant cells and gun biopsy of the malignant mass was done in 2 cases. Immunohistochemistry was done in both malignancies for TTF-1 and p40 for confirmation of squamous and adeno carcinomas respectively.

RESULTS

100 cases of pleural effusion were studied in a 2-year period in the Department of Pulmonology, Katuri Medical College, Chinakondrupadu. Among 100 cases, 97 are exudates and 3 cases are transudates. Tuberculosis is the most common cause of exudative pleural effusion (91 cases).

CONCLUSIONS

Out of 100 cases of pleural effusion 97 cases were exudates and 3 were transudates. Tuberculosis was the most common cause of exudative pleural effusion. Malignancy was the second most common cause. Congestive cardiac failure was the most common cause of transudative pleural effusions. The estimation of pleural fluid differential counts was important for ruling out other causes. ADA is a reliable tool for diagnosis of tuberculosis when applied along with Light's criteria.

KEY WORDS

TB (Tuberculosis), ADA (Adenosine De Aminase), LDH (Lactate Dehydrogenase), PET (Positron Emission Tomography), CT (Computerised Tomography)

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BACKGROUND

Excessive and abnormal accumulation of fluid in the pleural cavity is defined as pleural effusion. Pleural effusion is a common complication of many disease processes. Disorders causing distortion in body fluid mechanics will cause either transudative effusions or exudative effusions. Transudative effusions occurs in conditions like Heart failure or Nephrotic syndrome and exudative effusions occurs in Inflammatory or Malignant processes[1]. Lights criteria are used to differentiate Exudative from Transudative Effusions. The present study is undertaken to study the aetiology and clinical features of pleural effusion in our institute. Tuberculosis is still one of the most important causes of Exudative plural effusion.[1,2,3] The levels of Adenosine De Aminase an enzyme found in most cases are increased and its determination has proven to be useful as diagnosed test in case of TPE.[4,5] Elevated plural fluid ADA predicts TB plural effusion with a sensitivity of 90- 100% and specificity of 89-100%. Malignant pleural effusion (MPE) refers to the presence of neoplastic cells in pleural fluid.[6] The most common causes of MPE are Lung cancer, Breast cancer, Lymphoma, ovarian cancer and gastric cancer they all account for 80% of all MPE.

METHODS

A Prospective study was conducted at Katuri Medical College among 100 randomly selected OPD patients after satisfying inclusion and exclusion criteria. The study was conducted from to IEC clearance was taken and investigations done with proper consent.

Inclusion Criteria

All cases of pleural effusion that attend the Outpatient department of Katuri Medical College.

Exclusion Criteria

Patients below 18 years of age.

The following procedures were employed in investigating these cases-

1. Skiagram postero-anterior view of chest with both domes of diaphragm were done for all patients.
2. Ultrasound chest-for estimating the quantity of fluid and site of aspiration was done in all cases.
3. Aspiration of pleural fluid was done with full aseptic precautions and fluid was collected into 2 sterile bottles and sent for pleural fluid ADA, counts, and protein, sugar and LDH values.
4. Pleural fluid cytology for malignant cells and gun biopsy of the malignant mass was done in 2 cases.
5. Immunohistochemistry was done in both malignancies for ttf-1 and p40 for confirmation of squamous and adeno carcinomas respectively.

Statistical Analysis

Data was analysed using Microsoft Excel and results were expressed in terms of numbers and Percentages.

RESULTS

100 cases of pleural effusion were studied in 2-year period in the department of Pulmonology, Katuri Medical College, Chinakondrupadu.

	No. of Cases
Exudates	97
Transudates	3
Total	**100**

Table 1. Relative Distribution of Cases

According to table 1 Exudative effusions are more in our study than transudative effusions

	No. of Cases
Tuberculosis	91
Malignancies	4
Bronchogenic carcinoma	2
Carcinoma breast	1
Carcinoma stomach	1

Table 2. The Relative Distribution of Exudative Effusions

In our study out of 95 cases of exudative effusions tuberculosis was the most common cause constituting-93% of cases. Among Malignancies Bronchogenic carcinoma cases were more when compared to secondary deposits.

Age	Male	Female
21-30	5	3
31-40	6	9
41-50	11	13
51-60	6	10
61-70	9	9
71-80	6	9
81-90	3	1

Table 3. Shows the Age and Sex Distribution of Pleural Effusions

According to table 3 maximum number of cases of pleural effusion were seen between 41-50 years of age (4th Decade) and females outnumbered males.

Age	Male	Female
21-30	4	2
31-40	5	9
41-50	11	10
51-60	5	10
61-70	7	11
71-80	5	9
81-90	2	1

Table 4. Showing Age and Sex Distribution of Tuberculous Effusions

According to table 4 the commonest age for tuberculous effusion was 4th decade and females outnumbered males.

Symptoms	Percentage
Chest pain	90%
Breathlessness	90%
Cough	56%
Fever	32%
Loss of weight and loss of appetite	100%

Table 5. Patients with Presenting Symptoms of Tuberculous Effusion

According to table 5 loss of appetite and loss of weight were seen in all cases followed by chest pain and breathlessness.

31 – 40	11/out of 93
CD 4 count	150 – 200
Protein	3.5- 5 gm %
Sugar	85 - 90 mg/dl
ADA	60 – 70 IU/l

Table 6. Association with HIV

According to this table 6 Out of 93 cases of tuberculous pleural effusion 11 female patients in the age group of 31-40 were positive for HIV. CD4 count in both the cases ranged from 150-200.

Type	No. of Cases
Bronchogenic carcinoma	2
Ca stomach	1
Ca Breast	1

Table 7. Sites of Malignant Effusion

According to table 7 two cases of bronchogenic carcinoma and one case each of secondary pleural effusion with primary from carcinoma breast and carcinoma stomach were diagnosed.

Transudates	30 – 40	1 male
Congestive heart failure	41 – 50	1 female
Nephrotic syndrome	61 – 70	1 male

Table 8. Transudates

According to table 8, 2 cases were secondary to congestive heart failure and one was secondary to nephrotic syndrome.

DISCUSSION

Pleural effusion is one of the most common problems in developing countries and this study was done to demonstrate aetiology, clinical features and methods of diagnosis. According to Ramakrishna, Venkata Kalyan Kumar, out of 200 cases of pleural effusion studied they found that 182 cases were exudates and 18 were transudates. In our study 92 out of 100 cases were exudates and 8 were transudates which is in concordance with their study. A comparison of the results of our studies was made with those of other studies.[1,2,3,4,5] In the present study the mean age of presentation was in 4th decade which correlated well with the study of Sibert et al and Soez et al. there was female preponderance in our study which was not consistent with the available literature. In the literature available there was male preponderance.

Clinical Features

We compared the results of the incidence of various clinical features in our study with those of other studies[.3, 4, 5],. In our study of tuberculous effusions, the incidence of chest pain correlated with the study of Rashid et al[7] followed by breathlessness which was close to the study of Soe. z et. In our study protein and cell count did not correlate with available literature. ADA levels are coincident with the study Sol Z et.[8] The mean value of the pleural fluid lymphocyte % (88%) from our study was nearer to that obtained from I. J. C. R. Soe. Z et al. The mean value of pleural fluid protein (4.03 mg/dl) obtained from our study was nearer to that obtained in Anand Patel et al,[9] Soe. Z et al, the mean value of pleural fluid glucose obtained in our study did not match the values. The mean value of ADA from our study was nearer to that from Arch Int Med. Graph 8: Diagram showing laboratory parameters in the present study as compared with previous studies.

ADA Levels

The table below shows the cut off values of in various studies on ADA levels in tuberculous pleural effusions. In our study the lowest value of ADA obtained was 40 IU/L. This was nearer to the cut offs in the studies Raj et al, Gilhotra et al, Subhakar et al, Maldhure et al and Ghelani et al. Based on these studies we found out that ADA level of 40 and above was sensitive and specific enough for diagnosis of Tuberculous pleural effusion when the clinical and biochemical parameters were also taken into account. From our study of the analysis of cases of tuberculous pleural effusion we are of the opinion that basis biochemical and cytology of tuberculous pleural effusion including ADA level, when combined with clinical scenario was adequate for the diagnosis of tuberculous pleural effusion and ruling out other causes.

HIV and Tuberculosis

According to Sunitha H et al TB is the most common opportunistic infection in HIV positive individuals. Pleural effusion is commonly reported in HIV associated pulmonary tuberculosis constituting 2.9% of cases. According to the age and sex distribution in pleural effusion in HIV – associated tuberculosis patients 56.7% were between 20-30 years and 43.3% between 31-40 years In the present study out of 93 cases of TB plural effusion 11 cases were found to be positive for HIV all the cases were females and seen between 31-40 years of age.[10,11] The CD4 count in all the cases range from 150 to 200. According to our study HIV positive plural effusions constituted 0.11% of cases.

Transudative Effusions

According to Ramakrishna, Venkata Kalyan Kumar the analysis of 18 Cases of Pleural Transudates were as follows- COPD with cor-pulmonale 8 cases, congestive heart failure 4 cases, hypoproteinaemia 2 cases, Chronic renal impairment and generalised anasarca 2 cases each Congestive heart failure is the most common cause of pleural effusion and when the fluid was analysed it was usually transudate. The clinical features were breathlessness on exertion, swelling of feet, orthopnea or paroxysmal nocturnal dyspnoea. In our case all the clinical features were present. Ratio of pleural fluid protein to serum protein were less than 0.5, LDH- less than 0.6 and absolute pleural fluid LDH was below two thirds of upper limit of normal. Our features were in concordance with the study of Richard. W. Light.[12]

Nephrotic Syndrome

Is one of the common causes of pleural effusion. 21% of patients with nephrotic syndrome have pleural effusion. However, in our study there was a single case which was referred to nephrology and fluid showed features consistent with transudate.

Malignant Pleural Effusion (MPE)[13,14,15,16]

In our study 4 cases of malignant pleural effusions were diagnosed. According to Neeraj R. Desai and Hans J.nee Malignant pleural effusion is a common complication of primary and secondary Malignancies of the lung with an incidence of over 1,50,000 cases out of which lung cancer, breast cancer and lymphomas were the most common causes. According to A.M. Egan, D.M.C. Phillips et al the etiological factors are lung cancer, breast cancer, lymphoma, ovarian cancer and gastric cancer in the descending order of frequency. In our study 2 cases were primary lung carcinomas 1 was metastatic from stomach and 1 from metastasis from carcinoma breast accounting for 4 percent of total pleural effusions.

Clinical Presentation

Age Incidence

In the current study the youngest patient with lung malignancy was 39 years and the oldest 81 years with a mean age of 59 years. The incidence was highest for 5th and 6th decade of life, constituting 54% of all cases. Comparative analysis with other studies showed that mean age was slightly higher in the current study and highest incidence was among 5th and 6th decades Noronho et al, 2012[13], Krishna Murthy et al, 201210

Gender Incidence

In our current study females accounted for 54% of all cases with a female to male ratio of 1.17:1. The gender difference and male to female ratio of the current study correlated well with Noronho et al, 20129 and Krishna Murthy et al, 201210

Smoking

Smoking is an established etiological factor for lung cancer and is implicated in all the subtypes. Tobacco smoking plays a pivotal role in lung cancer carcinogenesis and also affects prognosis of lung cancer patients In this current study 11 out of 37 subjects were non-smokers accounting for 29.72% and 26 have smoking habit, constituting 70.72% of all cases. A significant number of non-smokers with lung cancer were females (87.5%), when compared to males (13.7%) in the present study. The median age at presentation for non-smokers was 53.5 years which was less than that of smokers (61 years). These observations well correlated with other studies Krishna Murthy et al, 2012 [14] and Noronho et al, 2012[13] The fraction of lung carcinoma in never-smokers has increased in recent times. The percentage of lung carcinoma in never smokers worldwide is 10 to 25%. Studies from Asian countries including China, Japan and Northern India demonstrated that 65%, 70% and 94% of non-smokers with lung cancer were females. In United States, only 9.13% of female lung cancer patients are never smokers.[14] Differences in epidemiological characteristics and histological subtypes between smokers and never- smokers have been demonstrated, especially among Asian patients. Lung cancer is symptomatic at presentation in about 85% of cases. The most common symptoms of lung cancer are cough, dyspnoea, haemoptysis caused by the tumour proper and chest pain due to pleural involvement. Paraneoplastic syndrome is more common in Small cell carcinoma lung. In the current study chest pain was the most common symptom constituting 40.5% of all other features. This was well correlated with other studies. The second common presenting feature was by dyspnoea. But Krishna et al, Chin lin et al [15] and Hamilton et al[11] documented dyspnoea as the next frequent complaint followed by chest pain.

Site and Localization

Mass lesions were more common constituting 81% in the present study. These findings correlated well with the literature. CP Sharma et al[17] also mentioned mass lesion was more common(50%). Peripheral lesions constitute 83% with the rest being central lesions in the current study. But CP Sharma et al recorded 70% central lesions. This increased number of peripheral lesions can be attributed to the greater number of Adenocarcinomas in the present study and also 56 % of Squamous cell carcinomas were located peripherally. This increase in peripheral squamous cell carcinoma was also observed by Quinn et al.[18] According to Neeraj R. Desai and Hans J. Nee the clinical features of MPE can vary from no symptoms to acute respiratory distress. breathlessness was the most common presenting symptom due to alteration in chest wall/ diaphragmatic mechanics. Most common additional symptom was chest pain. In our study common symptoms were dyspnoea followed by chest pain which was in concordance with above author.

Chest Radiograph

Chest x-ray was abnormal if there is presence of more than 200 ml of pleural fluid on PA view and 50 ml on lateral view. In our study all the cases presented with moderate effusions.

Ultrasound Chest

In cases of pleural effusion ultrasonography has higher sensitivity than chest radiography as screening tool. It helps in identification of pleural metastasis and thickness of the pleural lining. Pleural metastasis appears as small hypoechoic masses having obtuse margins with chest wall or as complex echogenic large masses. In our study all the 4 cases presented as hypoechoic masses.

Thoracocentesis

According to lights pleura all the malignant effusions show features of exudates. In our study pleural fluid protein, LDH, ADA the values were consistent with exudative effusions. With the advent of targeted therapy for advanced lung carcinomas and significant differential response to them, it is recommended to further classify NSCLC into Adenocarcinoma and Squamous cell carcinoma based on morphology and ancillary techniques like IHC [immunohistochemistry] for the eligibility to Targeted therapy.[19,20] When the morphological criteria of Squamous cell carcinoma and Adenocarcinoma were present, diagnosis can be easily established. When the tumour does not show the classical morphological criteria, immunohistochemical work up is necessary for further typing. Immunohistochemistry was given importance in the new classification. TTF 1 is sensitive marker for Adenocarcinoma lung.[19,20,21] p40 is highly sensitive marker for squamous cell carcinoma. Minimal panel of two antibodies was recommended for cytology and small biopsies. NSCLC positive for TTF 1 and negative for p40 were termed as NSCLC favour adenocarcinoma. Tumours positive for p40 and negative for TTF 1 were termed NSCLC favor squamous cell carcinoma. Tumours negative for both markers are diagnosed as NSCLC, NOS.

In our study Transbronchial biopsy was done for one case of primary carcinoma of lung. It showed features in favour of Non-small cell carcinoma of lung. Immunohistochemistry (IHC) showed positivity for p40 favouring the diagnosis of squamous cell carcinoma. In the second case Gun biopsy was done which showed features of adenocarcinoma. IHC done for this case showed positivity for TTF1 which confirmed the diagnosis of Adenocarcinoma.

CONCLUSIONS

Out of 100 cases of pleural effusion, 97 cases were exudates and 3 were transudates. Tuberculosis was the most common cause of exudative pleural effusion. Malignancy was the second most common cause. Congestive cardiac failure was the most common cause of transudative pleural effusions. The estimation of pleural fluid differential counts was important for ruling out other causes. ADA is a reliable tool for diagnosis of tuberculosis when applied along with Light's criteria.

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