Diagnostic Approach to Pleural Effusion

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Abstract :

Aim : Normally the pleural cavities contain a capillary layer of fluid. Pleural effusion is the collection of abnormal quantity of fluid in pleural cavity. The aim of this study is to decide the diagnostic approach which is to be applied in different variety of patients with pleural effusion. **Material and Methods :** 100 patients of pleural effusion which were diagnosed on radiological investigations either through X-rays, ultrasonography or CT scan in a tertiary care hospital and in whom aspiration of pleural fluid was possible were selected for the present study. **Results :** The study shows CT scan was the most accurate in detecting the pleural effusion. Majority of the pleural effusion were found to be of exudative origin by Light's criteria, protein level and total cell count. The most common malignancy found in this study was adenocarcinoma of the lung in total 10 cases. **Conclusion :** In present study, we found that males were more affected than females and in both groups, the younger are more affected than the older ones with majority cases of infective origin. Other tests such as mycobacterial culture and pleural biopsy, if done routinely can aid the diagnostic information in many patients with undiagnosed effusion.

Introduction :

Pleural effusion is defined as accumulation of abnormal quantity of fluid in pleural cavity. Normally each pleural cavity contains 8.4 ± 4.3 ml fluid. [1] Fluid that enters the pleural space can originate in the pleural capillaries, the interstitial spaces of the lung, the intrathoracic lymphatics, the intrathoracic blood vessels, or the peritoneal cavity and it exits via pleural fluid lymphatics.[2]

Pleural effusions are classified into transudates and exudates. [3] A transudative pleural effusion occurs when the balance of hydrostatic forces influencing the formation and absorption of pleural fluid is altered to favor pleural fluid accumulation. The permeability of the capillaries to proteins is normal. In contrast, an exudative pleural effusion develops when the pleural surface and/or the local capillary permeability are altered. [4]The most commonly associated symptoms are progressive dyspnea, cough (mostly non-productive), and pleuritic chest pain. Night sweats, fever, hemoptysis, and weight loss should suggest tuberculosis. Hemoptysis also raises the possibility of malignancy, other endotracheal or endobronchial pathology, or pulmonary infarction. On physical examination, dullness to percussion, decreased tactile fremitus, and asymmetrical chest expansion, with diminished or delayed expansion on the side of the effusion, are the most reliable findings of pleural effusion.[5]

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The history and physical examination are critical in guiding the evaluation of pleural effusion. [6] Radiological diagnostic modalities include chest X-rays, utlrasonography and Computed Tomography (CT scan). After initial diagnosis of pleural effusion is made from radiography, thoracentesis should be performed for pleural fluid analysis in pleural effusions. Pleural fluid analysis would reveal either fluid is transudative or exudative according to Light's criteria. [7] Microscopic and biochemical analysis will further narrow down the diagnosis. Pleural biopsy can be performed when biochemical tests cannot establish the diagnosis. [8] Thoracoscopy and bronchoscopy like procedures can be performed as and when required. [8]

Material and method :

We analyzed 100 patients of pleural effusion diagnosed on radiological investigations either X-rays, ultrasonography or CT scan for 2 years in a tertiary care hospital.Patients of either sex, Patients of any age attending OPD or admitted as indoor patient, Diagnosed case of pleural effusion on basis of radiological investigations either X-rays,

ultrasonography or CT scan. Further, only those patients in whom thoracentesis can yield minimum amount of fluid required for diagnostic purposes were selected for the study. Amongst the 100 patients' included in the study75 were males, mean age of males was around 45.4 years and maximum number of patients (18) were from 31-40 years of age group. In the 25 female patients, mean agewas around 43.28 years and maximum number of patients (8) were from 21-30 years of age group.

Detailed clinical history, physical examination and all necessary serum investigations were done followed by thoracentesis, pleural fluid collection and investigations. Patients were divided according to age groups, gender, presenting symptoms, associated comorbid conditions, clinical examination findings, radiological findings, different pleural fluid reports like glucose, protein, cell count, and cytological examination. Light's criteria were applied in possible patients.

Results :

A total of 100 patients were selected for this study with variety of complains and symptoms (Table 1). Many of these patients also had other clinical conditions such as diabetes, hypertension etc. (Table 1)

Table 1 : Presenting symptoms and comorbid conditions in patients*

Symptom	No. of Patients	Comorbidities	No. of Patients
Cough	82	DM	11
Expectoration	45	Hypertension	11
Dyspnea	78	IHD	4
Fever	61	Hypothyroidism	4
Chest pain	58	COPD	5
Anorexia/weight loss	38	Malignancy	18
Hemoptysis	2	GIperforation	2
Abdominal pain	5	Others	5
Backache	2		
Others	6		

*Multiple Responses

Table 2 : Comparison between diagnostic methods of detecting pleural effusion

Variable	Comparing physical examination and chest X-ray		Comparing Chest X-ray and USG		Comparing chest X-ray & CT scan	
	As per Physical Examination	As per Chest X-Ray	As per Chest X-ray	As per USG	As per Chest X-ray	As per CT scan
Total patients	100	100	39	39	16	16
Unilateral effusion	90	90	32	29	14	15
Bilateral Effusion	9	9	7	10	1	1
Undetected	1	1	-----	-----	1	0

Table 2 shows that, out of the total 100 patients 90 patients had a unilateral pleural effusion on chest X-ray, which was clinically detected as unilateral pleural effusion only. Only 9 patients had bilateral pleural effusion on chest X-ray which was clinically detected as bilateral effusion as well. Only 1 patient out of 100 had no clinically detectable signs of pleural effusion neither showed any evidence of pleural effusion on chest X-ray. In this study, 39 patients underwent ultrasonography of chest as well as routine chest X-ray. Out of 39, chest X-ray of 32 patients showed a unilateral pleural effusion while only 7 patients'chest X-ray had bilateral pleural effusion, while during ultrasonography of same patients, 29 patients had unilateral effusion and 10 patients showed a bilateral pleural effusion. 16 patients included in the study were investigated with CT scan of thorax, out of which 15 patients showed unilateral effusion and 1 patient showed bilateral effusion on CT scan. In those same patients, 14 patients had unilateral pleural effusion on chest X-ray and 1 patient had a bilateral pleural effusion, while 1 patient did not have any detectable pleural effusion on chest X-ray.

Table 3: Distribution of Glucose level in pleural fluid

Glucose level	No. of samples	Malignant effusions
<60 mg/dl	29	8
≥60 mg/dl	67	10
Total	96	18

In this study, 96 pleural fluid samples were tested for glucose levels, out of which 29 samples had glucose levels below 60 amongst which 8 were malignant effusions, while 67 samples had glucose levels above 60 amongst which 10 were malignant effusions (Table 3).

Table 4 : Distribution into exudative and transudative effusions by different methods

variable	Transudative	Exudative	Total
Light's criteria	5	30	35
Pleural fluid protein levels	13	83	96
Total counts < 1000/mm^3	9	27	36
Total counts > 1000/mm^3	2	57	59

In this study Light'scriteria were applicable on 35 pleural fluid samples, out of which 30 turned out to be exudative effusions and 5 were transudative pleural effusions. If we consider pleural fluid protein alone to differentiate between transudative andexudative effusions (where pleural fluid protein >3.0g/dl is considered to be an exudative effusion), [9, 10] 83 out of 96 samples were exudative pleural effusion and 13 were transudative pleural effusion. Out of 95 samples that were tested for cellcounts, 36 samples had total cellcounts less than 1000/ mm^3, amongst them 27 samples were exudative according to pleural fluid protein content of >3.0g/dl and 9 samples were transudative having pleural fluid protein of ≤ 3.0g/dl. The other 59 samples had total counts >1000/ mm^3, out of which 57 samples had pleural fluid protein of>3.0g/dl while only 2 samples were transudative having pleural fluid protein of ≤3.0g/dl. 73 of those 95 samples had more than 50% mononuclear cells, and 22 samples had more than 50% polymorphonuclear cells (Table 4). Out of total 100 patients, samples of pleural fluid from 94 patients were also tested for ADA (adenosine deaminase) levels, 44 samples had ADA level of >40 U/l, favoring more of tuberculous origin of fluid. In those 44 samples 3 samples were of malignant pleural effusion. While from the rest of the 50 samples, 14 samples were of malignant pleural effusion.

Out of total 62 samples which were sent for pleural fluid cytological examination, 19 turned out to be positive for some malignancy. Out of these, in two ofthe patient second samplesent for cytology showed positive result for malignancy while for one patient the fifth pleural fluid sample of the patient came to be positive for malignancy. For the rest of the patients the first sample itself sent for histopathological examination turned out to be positive for malignancy. Various types of malignancies were found to cause pleural effusion in this study (Table 5).

Table 5: Various types of malignancies diagnosed in malignant pleural effusions cases

Type of malignancy	No of patients
Adenocarcinoma of lung	10
Squamous cellcarcinoma of lung	1
Mesothelioma	1
Squamous cellcarcinoma of tongue	1
Infiltrating ductal carcinoma breast	1
Leukemic infiltration ofpleura	1
Urinary bladder carcinoma	1
Ovarian carcinoma	1
Non-typified malignant effusion	2
Total	**19**

Table 6 : Results of microbiological tests done on pleural fluid samples

Microbiological Test	Positive	Negative/ non-significant	Total
Gram stain	0	29	29
AFBstain	0	28	28
Culture and sensitivity	5	26	31

In this study, 29 pleural fluid samples were sent for gram stain which did not yield any significant result. 28 samples were tested for acid fast bacilli (AFB) staining which did not show any acid fast bacilli in the pleural

fluid. 31 samples were sent for aerobic culture and sensitivity, amongst them 5 samples yield positive growth of bacteria, which were: Escherichia Coli, Pseudomonas Aeruginosa, Entrococci, Acinetobacter Wolfii and Staphylococcus Aureus (Table 6).

Discussion :

There are various etiologies of pleural effusion and we need to reach to the etiologic clue in order to treat various types of effusions. The diagnosis of pleural effusion starts from the history and clinical examination of the patient, followed by radiology in form of a chest X-ray and thoracic ultrasonography as and when required. Various studies have been done to study the cause of pleural effusion on the basis of laboratory investigations done on pleural fluid. One of such studies is discussed here which was published in Thorax 1979 with title of "pleural effusion: laboratory tests in 300 cases."[11]

According to the distribution of total counts, in our study 59 samples had total counts of >1000/mm3 and 36 samples were having total counts <1000/mm3. The mentioned study had 88 samples with cell counts of >1000/mm3 and 71 samples were having total counts <1000/mm3. In our study 73 of 95 samples had more than 50% mononuclear cells, while in the given study 209 samples had more than 50% mononuclear cells either lymphocytic or mesothelial cells.

Bacteriological culture of the pleural fluid was performed on 31 samples of pleural fluid in our study, out of which 5 turned out to be positive for the growth of bacteria, which were: Escherichia Coli, Pseudomonas Aeruginosa, Entrococci, Acinetobacter Wolfii and Staphylococcus Aureus. In the reference study, all the 270 samples were investigated for bacteriological culture and yield bacterial growth in 17 patients, which were: Streptococcus, Pneumococcus, Staphylococcus Aureus, Proteus, Pyocyaneus and anerobes.

In our study, 28 samples were tested for acid fast bacilli (AFB) staining which did not show any acid fast bacilli in the pleural fluid. In the reference study 270 samples were tested for AFB staining, out of which only 10 were positive for acid fast bacilli. Cytological examination on pleural fluid was done in 62 samples in our study out of which 19 turned out to be positive for malignancy. In the given study, cytology was done on all 270 samples and 63 samples were positive for malignancy. In our study, ADA levels of pleural fluid were also tested in 96 samples and 44 samples had ADA level of >40 U/L, favoring more of tuberculous origin of fluid. In those 44 samples 3 samples were of malignant pleural effusion. While from the rest of the 50 samples, 14 samples were of malignant pleural effusion. In our study, we have also conducted detailed clinical examination and it was consistent with the X-ray findings of pleural effusion. Out of the total 100 patients that were included in the study, 90 patients had a unilateral pleural effusion on chest X-ray, which was clinically detected as unilateral pleural effusion only. Only 9 patients had bilateral pleural effusion on chest X-ray which was clinically detected as bilateral effusion as well.

Pleural biopsy and mycobacterial cultures give more space and opportunity to diagnose pleural effusions when diagnostic dilemma is there. Such further investigations can be useful in diagnosis of pleural effusion.

Conclusion :

In the study that we carried out males were more affected than females and in both groups, the younger ages are more affected than the older ones. The cause of pleural effusion in younger adults tends to be more of an infective etiology like tuberculous pleural effusion than malignancy in country like India. In our study we have not used more advanced tests like pleural biopsy (thoracoscopic or closed) or mycobacterial culture to prove a tuberculous effusion as tuberculous. A nonmalignant exudative effusion with clinical findings and history compatible with a natural course of tuberculous effusion is directly treated by antituberculous drugs. In a resource limited setup where these costly tests are not done routinely it is better to start antituberculous therapy in clinically suspected individuals who have simple pleural fluid reports like high protein content, ADA levels more than 40U/L and more of lymphocytes in pleural fluid cell counts suggestive of tuberculous effusion. If the effusion responds with the therapy only serial monitoring is required during the course of treatment. If it does not respond to therapy than other investigations like pleural biopsy can be performed to look for alternate diagnosis or mycobacterial culture can be

done in suspected drug resistant cases.

In cases of malignant pleural effusions seen during this study, it was noted that in most of the patients, the first sample that was sent for cytological examination turned out to be positive for malignancy owing to good histopathological reporting. Adenocarcinoma was most common primary malignancy associated with malignant pleural effusion in our study.

Other tests that are not widely used in this study like mycobacterial culture and pleural biopsy, if done routinely can aid the diagnostic information in many patients with undiagnosed effusion. Still further research is useful in this direction to evaluate the usefulness of these tests in diagnosis of pleural effusion.

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