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Original Research Article

Diagnostic Value of Serum-Effusion Albumin Gradient In The Differential Diagnosis of Pleural Effusion

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ABSTRACT

The aim of the study was to compare Serum-Effusion Albumin Gradient (Serum albumin level - Pleural fluid albumin level) with Light's traditional criteria for differentiating exudative and transudative pleural effusions. Pleural fluid samples collected from fifty patients with pleural effusion who were undergoing diagnostic or therapeutic thoracentesis **(**34 males and 16 females) were studied. The serum - effusion albumin gradient and Light's criteria were compared. Light's criteria correctly identified all the exudates but misdiagnosed 2 cases out of 6 transudates (cases of cardiac failure). By using albumin gradient of 1.2 g/dl or less to indicate exudate and values more than 1.2 g/dl to indicate transudate, all the patients (30 exudates and 20 transudates) were correctly diagnosed. Light's criteria are accurate for identifying exudates but not so much in the case of transudates. The serum-effusion albumin gradient is accurate equally for both exudates and transudates.

Key words: Exudate, Light's criteria, serum-effusion albumin gradient, transudate

INTRODUCTION

Pleural effusion is a common complication of many disease processes, either local or systemic where differentiation between transudates and exudates is necessary to assist in differential diagnosis.[1-8] Clinical diagnosis of pleural effusion depends much upon the nature of the pleural fluid, whether exudate or transudate. The criteria proposed by Light et al[9] in 1972 have been the standard method of differentiating exudates from transudates. Many pleural effusions, misclassified as transudates or as exudates have been reported using these criteria.[10,11] In cases of cardiac failure treated with diuretic therapy the transudates have high protein content.

The problem of high protein transudates is more common in the evaluation of ascites too, which has led to the development of serum-ascites albumin gradient.[12] A gradient of less than 1.1 g/dl is the best predictor of exudative ascites and is an accepted method for differentiating exudate from transudate.[13] In the present study, we have used the criteria of Roth et al,[14] that serum-fluid albumin gradient of 1.2 g/dl or less suggests exudate and a gradient above 1.2 g/dl suggests transudate.

MATERIALS AND METHODS

50 cases of pleural effusion admitted of diverse etiology were divided into 2 groups: Group I (exudates n=30): comprising of tuberculous (n=20), malignant (n=8) parapneumonic effusion (n=1) and rheumatoid arthritis (n=1) and Group II (transudates n=20): comprising patients of congestive cardiac failure (n=6) cirrhosis of liver (n=8) and nephrotic syndrome (n=6). Out of those, 34 were male and 16 were female. The diagnosis of patients was made according to the following predetermined criteria:

Tuberculous pleuritis was diagnosed if either the bacillus was isolated from the pleural fluid or biopsy specimen cultures or caseous granulomas were evident in pleural biopsy specimens. Malignant pleural effusion was diagnosed if malignant cells either at cytologic examination or in biopsy specimens were obtained.

Parapneumonic pleuritis was identified when there was an acute febrile illness with purulent sputum, pulmonary infiltrate and responsiveness to antibiotic treatment or identification of the organism in the pleural effusion in the absence of any other cause explaining the presence of the pleural effusions.

Rheumatoid arthritis was diagnosed by rheumatoid factor, radiological and laboratory investigations.

Congestive cardiac failure was diagnosed if the patient had cardiomegaly, radiological evidence of congested lungs, peripheral edema, and responded to treatment for congestive cardiac failure.

Cirrhosis of liver was diagnosed by laboratory investigations and ultrasound scan abdomen.

Nephrotic syndrome was diagnosed if the patient had proteinuria, edema and hypoalbuminemia.

The following tests were performed on pleural fluid samples - Total protein, albumin, glucose, lactate dehydrogenase (LDH), total cell count with differential count, Gram's stain, bacterial culture and acid fast bacilli (AFB) smear. A sample of serum was obtained for the measurement of glucose, total protein, albumin and LDH levels. Pleural biopsy and computed tomography (CT) scan of thorax were done in a few cases to arrive at diagnosis. Light's criteria for identifying exudate were as follows:

Pleural fluid/Serum total protein ratio > 0.5

Pleural fluid/Serum LDH ratio > 0.6

Pleural fluid LDH > 200 IU/L

Serum-effusion albumin gradient adopted from Roth et al, was used.

RESULTS

Out of the 50 effusions studied, 30 were exudates and 20 were transudates, shown in Table 1. The commonest cause of exudates was tuberculosis (40%); others were neoplasm (16%), parapneumonia (2%) and rheumatoid arthritis (2%). The transudative effusions were due to cardiac failure (12%), cirrhosis of liver (16%), and nephrotic syndrome (12%). The mean values of pleural fluid/serum protein and pleural fluid/serum LDH ratio are shown in Tables

2 and 3. Pleural fluid showed a high protein content in 2 cases out of 6 cases of cardiac failure. In this study, Light's criteria diagnosed all the 30 cases of exudates, but 2 cases of cardiac failure (transudate) were misclassified as exudate. Using serum-effusion albumin gradient, all cardiac failure patients were correctly classified as having transudate, shown in Table 4, including the 2 cases that had high protein content in pleural fluid. These 2 patients of cardiac failure had received diuretic therapy prior to the estimation of the protein content.

Table 1. Distribution of cases according to etiology and sex

Group	Etiology	Cases			Percentage
		Number	Male	Female	
Exudates					
	Tuberculosis	20	14	6	40
	Neoplasm	8	6	2	16
	Parapneumonia	1	1	-	2
	Rheumatoid arthritis	1	-	1	2
	Subtotal = 30				
Transudates					
	Cardiac failure	6	5	1	12
	Cirrhosis of liver	8	4	4	16
	Nephrotic syndrome	6	4	2	12
	Subtotal = 20				
	Total	50	34	16	100

Table 2. Distribution of cases according to etiology and mean serum protein, pleural fluid protein and fluid-serum protein ratio

Group	Etiology	Serum protein g/dl	Fluid protein g/dl	Fluid-serum protein ratio
Exudates				
	Tuberculosis	6.3	4.29	0.68
	Neoplasm	5.7	4.55	0.79
	Parapneumonia	6.9	4.7	0.69
	Rheumatoid arthritis	5	3.5	0.7
Transudates				
	Cardiac failure	6.2	2.68	0.43
	Cirrhosis of liver	5.1	2.42	0.47
	Nephrotic syndrome	4.8	2	0.41

Table 3. Distribution of cases according to etiology and mean serum LDH, pleural fluid LDH and fluid-serum LDH ratio

Group	Etiology	Serum LDH U/L	Fluid LDH U/L	Fluid-serum LDH ratio
Exudates				
	Tuberculosis	330	400	1.21
	Neoplasm	850	630	0.74
	Parapneumonia	680	650	0.95
	Rheumatoid arthritis	700	690	0.99
Transudates				
	Cardiac failure	295	125	0.42
	Cirrhosis of liver	200	90	0.45
	Nephrotic syndrome	150	70	0.47

Table 4. Distribution of cases according to etiology and mean serum albumin, pleural fluid albumin and serum-fluid albumin gradient

Group	Etiology	Serum albumin gm/dl	Fluid albumin gm/dl	Serum fluid albumin gradient
Exudates				
	Tuberculosis	4.2	3.35	0.85
	Neoplasm	4	3.24	0.76
	Parapneumonia	4	3.25	0.95
	Rheumatoid arthritis	4.2	3.40	0.6
Transudates				
	Cardiac failure	4.1	1.82	2.3
	Cirrhosis of liver	2.9	1.35	1.56
	Nephrotic syndrome	2.55	1.15	1.40

DISCUSSION

The initial step in determining the cause of a pleural effusion is to categorize effusion as transudate or exudate. The classic criteria given for differentiation of exudates from transudate was provided by Light, et al. However, several reports have shown that these criteria misclassified a large number of effusions, especially transudates. Both albumin and globulin fractions in the pleural fluid are believed to originate from the serum via diffusion,[15-17] However, some protein can form within the pleural space, such as LDH from pleural fluid leukocytes.[18]

In abnormal states, pleural fluid can be collected for a number of reasons which leads to either increased fluid formation or decreased fluid absorption or both. Causes

for production of a transudative effusion usually occur in association with an intact microvascular endothelium and thus, the gradient between serum and fluid protein is maintained. Etiologies for production of an exudative effusion, on the other hand, usually involve some type of inflammation that results in a compromised pulmonary or pleural micro-vasculture, which in turn leads to an increased fluid leakage, a higher protein concentration and hence a lower albumin gradient. The collection of pleural fluid may be due to a number of reasons including increased fluid formation, decreased fluid reabsorption or both. The cases of transudative effusion usually occur with intact microvascular endothelium and therefore, the gradient is maintained. On the other hand, causes of exudative effusion usually involve some type of inflammation, which leads to increased leakage of fluid that has a higher concentration of protein. Therefore, the gradient between serum and fluid proteins will be low. The occurrence of pleural effusion in cardiac failure could probably be attributed to increased leakage of fluid into the pulmonary interstitium and in the pleural space. Chakko et al[(19)] showed that diuretic therapy in cases of heart failure with pleural effusion leads to a concentration of pleural fluid protein, which can fall in the exudative range. Two out of six cases of cardiac failure in this series had received diuretic therapy prior to thoracentesis. The criterion of albumin gradient > 1.2 g/dl indicates transudate and all the cases of heart failure were transudative by this method.

In our study, sensitivity for identifying exudates was 100% with Light's criteria but for transudates it was 90%. The corresponding sensitivity for identifying exudates and transudates with albumin gradient was 100%. In the study of Roth et al,[(14)] the serum-effusion albumin gradient had a sensitivity and specificity of 87%, and 92%, respectively. However, another study obtained a sensitivity of only 63% and a specificity of 81%.[(20)]

CONCLUSION

Regarding the good results obtained, the use of albumin gradient as an effective means of discriminating exudative from transudative pleural effusions is suggested. Since this method only relies on measurements of effusion and serum albumin concentrations, it can be very helpful when other measurements are not available.

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