DIFFERENTIAL DIAGNOSIS OF HUMAN ASCITES

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SUMMARY : *Various analyses were performed in the serum and ascites fluid samples for the differential diagnosis of ascites in 39 patients with cirrhosis, 13 patients with malignancy without liver involvment and 5 patients with tuberculous peritonitis.*

Diagnostic accuracies of the parameters which separate the cirrhotic ascites from non - cirrhotic ascites are 91.2 % for S-A albumin difference being > 1.1; 93.0 % for the ascitic / serum total protein level ratio being < 0.5; 80.7 % for ascitic / serum LDH level ratio being < 0.6; and 77.2 % for the ascites fluid LDH level being < 400 u/L. Diagnostic accuracies of these same parameters in distinguishing cirrhotic ascites from the malignant group are 90.4 % for S-A albumin difference being > 1.1; 92.3 % for the A/S total protein level ratio being < 0.5, 84.6 % for ascitic fluid LDH level being < 400 U/L and 80.8 % for A/S LDH level ratio being < 0.6. Thus, the most valuable parameter to distinguish the cirrhotic ascites from the non - cirrhotic ascites and the malignant group is S-A Alb difference (Having a 88.9 % specificity, 92.3 % sensitivity, 91.2 % diagnostic accuracy and 84.6 % specificity, 92.3 % sensitivity, 90.4 % diagnostic accuracy respectively). The second most valuable parameter is the A/S total protein level ratio (100 % specificity, 89.7 % sensitivity, 93.0 % diagnostic accuracy and 100 % spesificity, 89.7 % sensitivity, 92.3 % diagnostic accuracy respectively). Tumor cytology had a diagnostic specificity of 100 %, but could be identified in only 53.8 % of the malignant ascites in our series.

Key Words : *Ascites, Differential Diagnosis.*

INTRODUCTION

No laboratory test is completely able to seperate the malignant ascites from ascites associated with cirrhosis. Cytology is highly specific for diagnosis of malignancy but has a diagnostic sensitivity of only 40-60 % (2). Traditionally, ascites has been classified as being either transudative or exudative, based upon the ascitic fluid (AF) total protein concentration (4) or upon the AF fluid to serum ratio of total protein or Lactic dehydrogenase (LDH) or upon the AF level of LDH (1, 10). Several investigators have demonstrated the superiority of serum ascites albumin (S-A Alb.) difference in separating transudative (S-A Alb. > 1.1 g/dl) from exudative (SA Alb. < 1.1 g/dl) ascites (9, 12). Some others didn't find it diagnostic for abdominal malignancy (3, 6). Moreover, several investigators considered the ascitic fluid cholesterol determination as an excellent parameter which discriminates ascites due to cirrhosis from ascites due to malignancies (2, 5). Despite the emergence of such many parameters,

the differential diagnosis is not always clear.

The aim of the present study was to evaluate the diagnostic value of some parameters in serum and ascitic fluids of cirrhotic and non cirrhotic patients.

MATERIALS AND METHODS

Patients : Adult patients with advanced chronic liver disease, malignancy without liver involvement and tuberculosis were included in this study. Fifty - seven patients with ascites were studied prospectively. In addition to diagnostic paracentesis, all patients underwent nonivasive radiographic studies such as ultrasound, CT scan, or radionuclide scintigraphy to evaluate the liver and peritoneal cavity. Clinical diagnosis of chronic liver disease was established in 39 (4 alcoholic, 5 cardiac originated, 30 posthepatic) patients. The diagnosis was confirmed also by biopsy in 20 patients.

Thirteen patients had malignancy and ascites, and of these; four had adenocarcinoma of unknown origin, two had adenocarcinoma of the stomach, two had ovarian carcinoma and one had malign epithelial tumor. Four had carcinoma of kidney, colon, prostat, and peritoneal mesothelioma, respectively. Patients with ascites classified as malignant had primary or metastatic malignancy in the abdomen or pelvis. Five patients with proven tuberculous ascites (bacteriological, pathological or laparotomical diagnosis) were also evaluated.

Methods : Serum and ascites samples were collected 24 h before any therapeutic intervention such as intravenous fluids administration or a new diuretic therapy. Total protein was measured by biuret reaction and albumin with bromocresol green dye binding assay. LDH concentration was determined using a Lactate to pyruvate spectrophotometric method (DMA, Technicon RA, XT TEXAS). Triglycerides and cholesterol were quantitated enzymatically with commercial test kits (SCIAVO, USA). Cytological examination was performed within 2 h of aspiration of the AF on Giemsa stained smears of the sediment which was obtained by centrifugation of 20 ml samples at 300 rpm for 10 min. Statistical analysis was evaluated by the Mann Whitney-U test. A p value of $p < 0.05$ was considered to be statistically significant.

RESULTS

The results are summarized in table 1. As a whole the cirrhotic group fit into the criteria for "transudate" ascites, 15 patients (38.5 %) having a high AF total protein (TP). 3 patients (7 %) with cirrhosis had a S-A Alb. difference less than 1.1. Cytology was negative in all the patients.

The group with malignant ascites-tradionally classified as an "exudate" had significantly higher AF TP ($p < 0001$), TP_R ($p < 0.0001$), AF LDH ($p < 0.00005$), LDH_R ($p < 0.0002$) levels compared to the cirrhotic group. Mean of the AF cholesterol level was significantly higher ($p < 0.001$) in the malignant group as compared to the cirrhotic group. Mean of the AF Triglyseride level was not significantly ($p>0.25$) different from the cirrhotic group. S-A Alb difference was significantly lower ($p < 0.00001$) in the malignant group compared to the cirrhotic group. In the malignant group, only seven patients had an AF positive cytology (% 53.84). Malignant ascite parameters and their results are illustrated in table 1, 2.

In the group with tuberculous peritonitis-classified as an "exudate" the AF consantrations of ascites, TP, TP_R, S-A Alb difference, Ascitic LDH, LDH_R, mean of cholesterol and TG weren't significantly different from that of the malignant group. However, these patients were too few in number to comment on.

The tubeculous peritoritis group and their results are illustrated in table 1. Diagnostic values of the ascitic parameters are illustrated in table 2, 3.

DISCUSSION

A relatively high ascites protein concentration maybe seen in patients with transudative ascites when the blood oncotic pressure-determined chiefly by the albumin concentration - is relatively well summing preserved; as occurs in patients with cirrhosis up to 25 % (11). Conversly, a relatively low ascites protein concentration may be found in patients with exudative ascites if there is a severe reduction of the serum albumin concentration. In our study we found high AF TP (> 2.5 gm/dl) in 38 % of patients with cirrhosis. TP_R was significantly ($p<0.001$) lower in cirrhotic patients. TP_R was the second most valuble parameter which separate the cirrhotic ascites from the non cirrhotic or malignant ascites (Table 2, 3).

The serum ascites albumin difference - as an index of oncotic pressure difference-is on the other hand, independent of the serum albumin concentra-

Parameters	C (39)	Non - cirrhotic group MO (13)	tb (5)
Density	1012.18 ± 18	1015.38 ± 4.31	1013.8 ±
TP (gm/dl)	2.22 ± 1.50	5.49 ± 1.09	5.74 ± 0.75
TP_R	0.31 ± 0.19	0.74 ± 0.10	0.76 ± 0.048
LDH unites / liters	101.64 ± 62.2	489.15 ± 452	219.2 ± 98
LDH_R	0.51 ± 0.55	1.20 ± 1	0.85 ± 0.15
S-A Alb.	1.94 ± 0.78	0.50 ± 41	0.02 ± 1
Cholesterol (mg/dl)	65.26 ± 44.4	118.15 ± 38.32	138.4 ± 46
Triglycerides (mg/dl)	84.16 ± 63.4	50.82 ± 10.39	78.25 ± 30
proportion of patients with "transudative" parameters and positive cytology			
TP > 2.5	15 / 39	13 / 13	5 / 5
TP_R>0.5	4 / 39	13 / 13	5 / 5
LDH > 400	0 / 39	5 / 13	0 / 5
LDH_R>0.6	7 / 39	10 / 13	4 / 5
S-A<1.1	3 / 39	11 / 13	5 / 5
Positive cytology	0 / 39	7 / 13	0 / 5
Density > 1015	5 / 38	5 / 13	2 / 5

* C : Cirrhotic group; malignancy without liver involvment; TP : total protein, TP_R : total protein ratio; LDH : Lactic dehyrogenase units / liter; LDH_R : LDH ratio; S-A Alb : Serum ascites albumin difference. Number in parantheses indicates total numoer of patients in each group.

Table 1 : Summary of results of diagnostic parameters*

	Sensitivity (%)	Specificity (%)	Diagnostic accuracy (%)
TP < 2.5	61.5	100	71.2
TP_R<0.5	89.7	100	92.3
LDH < 400	100	38.5	84.6
LDH_R<0.6	82.1	76.9	80.8
S-A Alb.>1.1	92.3	84.6	90.4
Positive cytology	53.8	100	88.5
Density < 1015	86.8	38.5	74.5

Table 2 : Diagnostic value of ascitis parameters for separating ascites of the cirrhotic group (n=39) from ascites due to malignant origin (n=13).

tion and therefore should be more effective than the serum ascites protein concentration in separating transudative and exadative origin of the ascites (4). Our study has confirmed and extended the observation reported in prior studies (7, 12) that the serum ascites albumin difference is a better parameter in distinguishing patients with malignant ascites without liver involvment from non malignant ascites (table 2). Serum ascites albumin difference was also the most valuable diagnostic parameter in distinguishing cirrhotic ascites from non cirrhotic ascites (Table 3).

	Sensitivity (%)	Specificity (%)	Diagnostic accuracy (%)
TP < 2.5	61.5	100	73.7
TP_R<0.5	89.7	100	93.0
LDH < 400	100	27.8	77.2
LDH_R<0.6	82.1	77.8	80.7
S-A Alb.>1.1	92.3	88.9	91.2
Density < 1015	86.8	38.9	71.4

Table 3 : Diagnostic value of ascitis parameters for separating ascites of the cirrhotic (n=39) from the non cirrhotic group (n=18).

In 1958, Rovelstad et al (10) reported elevated total lipid concentrations in the ascites of patients with malignant neoplasms. Polak et al. (8) demonstrated a marked elevation of total cholesterol in malignant and inflamatory AF compared to the cirrhotic ascitic fluid with regard to the discrimination between malignant and non malignant ascites. Castaldo et al. reported in a study of 58 patients, ascitic cholesterol and LDH levels as highly sensitive and specific parametres in distinguishing ascites due to a malignancy from cirrhotic ascites (2). Jungst et al. also reported the significance of AF cholesterol in discriminating ascites caused by malignancies (5). In the present study, we found the mean of cholesterol in the malignant patients and in the non-cirrhotic group significantly higher ($p < 0.001$) than that of the cirrhotic group.

In the malignant group, cytologic investigation of the ascitic fluid is specific but not very sensitive (40-70 %) and may thus give rise to a large percentage of false negative results (2). In our study cytology had a diagnostic specificity of 100 %, but identified onhy 53.8 % of the malignant ascites (Table 2).

We conclude that the S-A albumin difference and TP_R are both reliable and better indicators in discriminating cirrhotic ascites from malignant ascites or non cirrhotic ascites.

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