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Original Research Article

Ascitic Fluid Cytology with Biochemical Parameters and Clinical Correlation

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Abstract

Introduction: Ascites is the pathologic accumulation of fluid within the peritoneal cavity. Accumulation of fluid in the peritoneal cavity resulting in ascites has many different mechanisms.The proper evaluation of ascitic fluid helps in narrowing the diagnostic dilemma faced by the physicians and helps in better management of the patients.

Objectives: The present study aims to assess the value of ascitic fluid cytology in the differential diagnosis of ascites along with various biochemical parameters and its usefulness in the patient management.

Material and Methods: This prospective study was conducted in the Department of Pathology, at SNMC Bagalkot over a period of 6 months from November 2019 to april 2020. This study included 120 patients who presented with ascites.Detailed examination – physical, cytological, biochemical and microbiological (wherever indicated) was done.

Results: Most common cause of ascitis was cirrhosis followed by tuberculosis,Malignant ascitis was noted in 8.3% cases. Ascitic fluid cytology was useful not only in the diagnosis but also to assess the response to treatment in these cases. The total protein content of ascitic fluid was significantly lower in cirrhotic cases as compared to tubercular, acute infective cases and malignant cases.

Conclusion: The exudative ascites is seen with tubercular acute infective and malignant ascites, with protein content >3.0 gm/dl and lower glucose levels while the transudative ascites as seen commonly with cirrhotic ascites has protein content <3.0 gm/dl and a higher glucose levels.

The careful cytomorphological examination of ascitic fluid is a valuable, simple, rapid, inexpensive and reliable technique in the differential diagnosis of ascites.

Keywords: Ascitic fluid cytology; Transudate; Exudate; Cirrhosis.

Introduction

Ascites is the pathologic accumulation of fluid within the peritoneal cavity. The most frequent cause of ascites is cirrhosis-related portal hypertension in 85% of cases; 15% of cases are due to intra abdominal non cirrhotic conditions, including malignancies, infections, cardiac and renal failure. The proper evaluation of ascitic fluid helps in narrowing the diagnostic dilemma faced by the physicians and helps in better management of the patients.[4,5]

The present study aims to assess the value of ascitic fluid cytology in the differential diagnosis of

ascites along with various biochemical parameters and its usefulness in the patient management.

Materials and Methods

This prospective study was conducted in the Department of Pathology, at SNMC Bagalkot over a period of 6 months from November 2019 to april 2020. This study included 120 patients who presented with ascites. Relevant information regarding age, sex and clinical details were obtained.

The gross appearance of the fluid can provide useful diagnostic information. Ascitic fluid was categorized into serous, haemorrhagic, serosanguinous, purulent and seromucinous fluids.

All of the samples were processed immediately. The fluid was divided in two parts. One part was used for cell count by improved Neubauer counting chamber. The other part was poured in the centrifuge tubes and centrifuged at 2500 rpm for 10 minutes. The supernatant was discarded. Part of sediment was transferred to a clean glass slide and mixed with a drop of 1% Toluidine blue. After placing the coverslip, the slide was examined under the microscope for immediate identification of cell morphology. Remaining sediment was transferred with the help of pipette to three clean slides. One smear was air dried and stained with Geimsa. Other two smears were fixed in 95% alcohol and stained with papanicolaou stain and Hematoxylin and Eosin [H and E] stain. Smears were examined for cell type and cellular features. A repeat examination of fluid was done in those cases, in which malignancy was suspected, but was not conclusive on initial examination.

The biochemical examination of ascitic fluid included estimation of glucose level, proteins level and adenosine deaminase. Microbiological Analysis for gram stain, ZN stain and bacterial culture were done when indicated.

Results

Total of 120 patients were studied. The age of the patient ranged from minimum 10 years to maximum of 80 years. The maximum number of cases were in the age group of 30-55 years (82.5%). Male preponderance was noted with (85%) compared to that of females which was 15%. (Table 1)

Out of 120 cases, the leading aetiology of ascitis was cirrhosis which accounted for 52 cases (43.3%),Tubercular peritonitis constituted for 30 cases (25%), nephrotic syndrome constituted for 16 cases (13.3%) and malignancies accounted for 10 cases (8.3%).

Table 1: Age and Sex Distribution of Ascitic Fluid Cases.

Diagnosis	Gender		Age(years)					Total
	Female	Male	10-20	20-30	30-40	40-50	>50	
Cirrhosis	0	52	0	6	12	20	14	52
Tuberculosis	10	20	1	4	15	7	3	30
Nephrotic Syndrome	5	11	0	2	6	5	3	16
Malignancy	0	10	0	0	5	2	1	10
Bacterial peritonitis	1	5	0	1	3	1	0	6
Hypoproteinemia	2	2	1	0	0	1	0	4
CCF	0	2	0	0	1	0	0	2
Total	18 (15%)	102 (85%)	2	13	42	36	21	120

Table 2: Gross Appearance of Ascitic Fluid.

Nature of the fluid	No of cases	Percentage (%)
Serous	65	54.1
Haemorrhagic	28	23.3
Serosanguinous	12	10.0
Purulent	08	6.8
Seromucinous	07	5.8
Total	120	100

Gross examination of Ascitic fluid showed that maximum specimens (65 cases) were serous effusions seen in cirrhosis followed by hemorrhagic effusions (28 cases) which was mostly seen in malignant ascitis. (Table 2)

Total cell count less than 100 cells/cumm were seen in cases of cirrhosis in which majority of them showed lymphocytic predominance along with few mesothelial cell proliferation [Figure 3]. High total cell count (> 500 cells/cumm) were seen in all cases of sub acute bacterial peritonitis, malignant effusions and few cases of tuberculosis. Lymphocytic predominance and in few cases mesothelial predominance was seen in tuberculosis. (Table 3)

Biochemical investigations revealed that majority of the cases of cirrhotic ascitis had glucose concentrations between 80 -120 mg/dl. Cases of tubercular ascitis, nephrotic syndrome, Subacute bacterial peritonitis and malignant ascitis had glucose concentration less than < 80 mg/dl/. ADA levels were increased (> 60 IU/L) in tubercular peritonitis. SAAG was found to be low (<1.1 gm/dl) in tuberculosis, infective ascitis and malignant effusion. High SAAG (> 1.1 gm/dl) was seen in cases cirrhosis and congestive cardiac failure. LDH levels (>300 U/L) were found to be increased in malignant effusion and in few cases of Subacute bacterial peritonitis and tubercular effusions, low levels of LDH (< 300 U/L) were seen in cases of cirrhosis. (Table 4)

On the basis of protein content of ascitic fluid using a discriminative value of 3 mg/dl, the categorisation into Transudative and Exudative fluid was done. Patients with cirrhotic ascites, nephrotic syndrome, hypoproteinemia and CCF had protein concentration of < 3.0 gm/dl, while all cases of tubercular ascites, malignant ascites and subacute bacterial peritonitis had protein content of > 3 gm/dl. (Table 5)

Table 3: Distribution of Total Cell Count in Ascitis Cases.

	Total cell count			No of cases
	< 100 / mm3	100-500/ mm3	>500/ mm3	
Cirrhosis	50	02	–	52
Tuberculosis	–	05	25	30
Nephrotic syndrome	–	10	06	16
Malignancy	–	02	08	10
SBP	–	-	06	06
Hypoproteinemia	–	04	–	04
CCF	–	02	–	02
Total	50	25	45	120

Table 4: Biochemical Parameters of Ascitic Fluid Compared with Different Diseases.

Test	Cirrhosis	Tuberculosis	Nephrotic syndrome	Malignancy	SBP	CCF
Gross appearance	Clear straw or milky	Milky	Turbid	Milky/bloody	Cloudy or turbid	Clear or pale yellow
Total protein (Normal range : 6- 8 g/dL)	<25 g/1	≥25 g/1	≥25 g/1	≥25 g/1	≥25 g/1	<25 g/1
Glucose (normal range: 80-120 mg/dL	Normal	Reduced	Reduced	Reduced	Reduced	Normal
ADA (Normal range: <39 u/L)	Reduced or normal	Increased	–	Reduced or normal	–	–
SAAG (serum ascites albumin gradient)	≥1.1 g/dl	<1.1 g/dl	<1.1 g/dl	<1.1 g/dl	<1.1 g/dl	≥1.1 g/dl
LDH (Normal range: < 300 U/L)	Reduced	Increased or normal	Increased or normal	Increased	Increased or normal	Reduced or normal

Table 5: Transudative and Exudative Fluids on the Basis of Protein Content.

Diagnosis	Transudate fluid protein <3gm/dl		Exudate fluid protein >3 gm/dl	
	Number	%	Number	%
Cirrhosis	52	43.3	0	0
Tuberculosis	0	0	30	25
Nephrotic syndrome	16	13.3	0	0
Malignancy	0	0	10	8.3
Bacterial Peritonitis	0	0	6	5
Hypoproteinemia	4	3.3	0	0
CCF	2	1.8	0	0
Total	74	61.7	46	38.3

Table 6: Frequency of Different Etiologies of Ascites Among Patients Described in Various Studies.

	Cirrhosis		Tuberculosis		SBP		Malignancies		Others		Total	
	n	%	n	%	n	%	n	%	n	%	n	%
Bhargava et al (1990)	31	35.6	17	19.5	7	8	22	25.3	10	11.4	87	100
Vijay kumar bodal et al (2013)	109	43.6	61	24.5	26	10.4	12	4.8	42	16.8	250	100
S P Tathe et al (2018)	1292	80.6	60	3.7	82	5.2	72	4.5	94	5.9	1600	100
Selvaraju K et al (2020)	53	53	08	08	05	05	07	07	27	27	100	100
Present study (2020)	52	43.3	30	25	6	5	10	8.3	22	18.3	120	100
Total	1537		176		126		123		195		2209	100

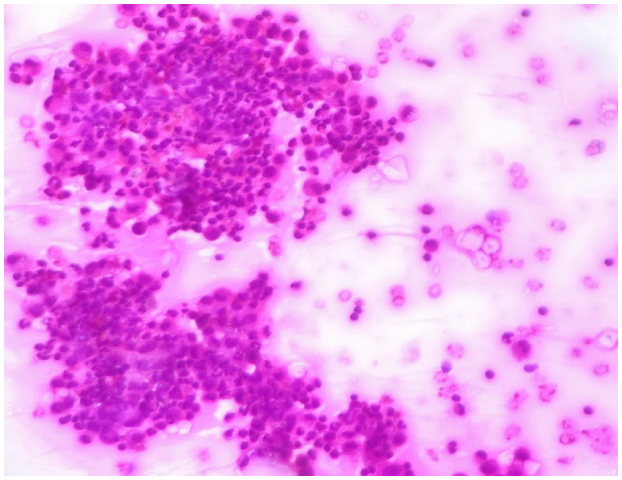

Fig. 1: Smears Showing Predominantly Neutrophils in Sbp, HandE, 40X.

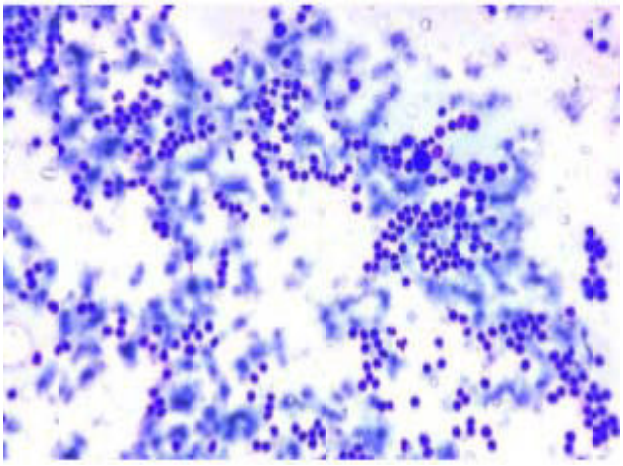

Fig. 2: Smears Showing Predominantly Lymphocytes in Tuberculosis, HandE, 40X.

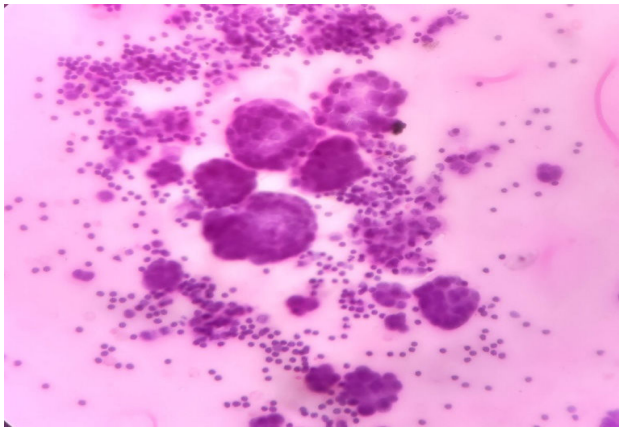

Fig. 3: Mesothelial Cell Proliferation Seen in Cirrhosis, HandE, 40X.

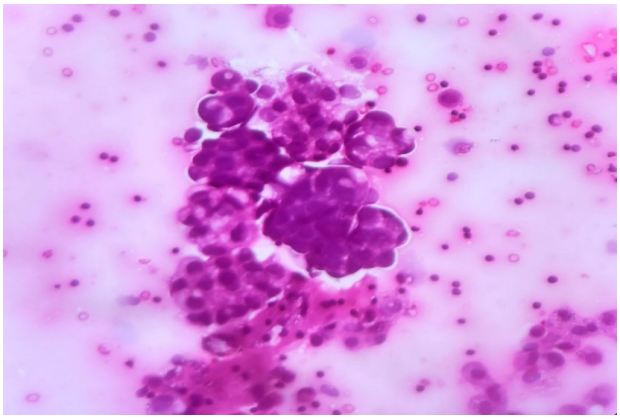

Fig. 4: Metastatic Adenocarcinoma Showing 3D Clusters and Acinar Arrangement of Tumour Cells, HandE, 40X.

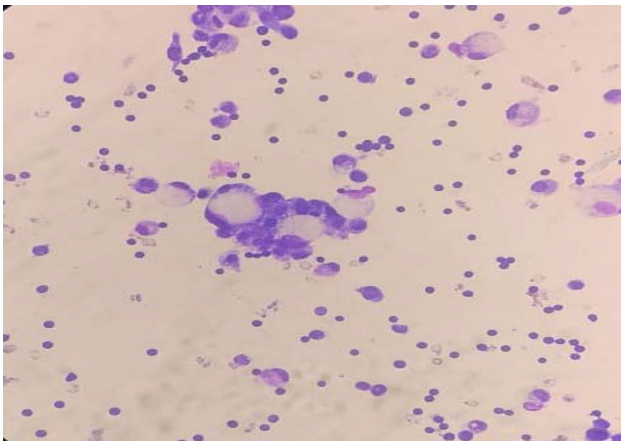

Fig 5: Signet Ring Cells in Mucinous Adenocarcinoma, HandE, 40 X

Discussion

The cytological examination of effusion is a complete diagnostic modality which aims at pointing out the etiology of effusion.[1,2] The most useful test in establishing the differential diagnosis of ascites is ascitic fluid cytology and ascitic fluid cell count.[13]

In this present study, total 120 cases of ascites were included. Males outnumbered females with M:F ratio of 3:1.This is in concordance with most of the studies.[1,8,9] Maximum number of cases (65.5%) was in the age group of 40-60 years as observed by other authors.[1,3,10]

Out of 120 cases, 110 cases were of non neoplastic effusion and 10 cases were of malignant effusion. Common cause for non neoplastic effusion was Cirrhosis (43.3%) which corresponds with similar studies conducted by Huang LL et al and Mahmmod et at.[1,3,6]

(Table 6) Comparison with various studies. In our study, the most common cause of ascitis observed was cirrohis which was seen in 52 cases. This was similar to the study done by vijay kumar bodal et. al.[1] Contrasting results were observed by the studies done by S P Tathe et al[24], Selvaraju K et al, Bhargava et. al.[23]

In this study the total WBC count of <100 cells/cumm were seen in 41.6% in majority of cirrhotic cases compared to study conducted by Jain S C et al(36%),[15,16] cell count between 100-500 cells/cumm were seen in 20.83% and cell > 500 cells/cumm were seen in 37.5% cases. In cases of spontaneous bacterial peritonitis, polymorphs were predominant. (Fig. 1) In liver cirrhosis lymphocytic predominance was found as compared to Nath et al where it was 59%.[16] In cases of nephrotic syndrome, CCF and anaemia-hypoproteinemia, lymphocytic predominance was observed. In tuberculous peritonitis, lymphocytic predominance was seen in all cases. (Fig. 2) In malignant ascitis lymphocytic predominance and exfoliative cytology for malignant cells was positive. (Fig. 4)

A positive effusion for malignant cells is an important prognostic indicator in cancer patients. In the present study, 10 (8.3%) cases had malignant ascites. The most common primary site was ovary followed by GIT.[1,10] One cases showed features of mucinous carcinoma. (Fig. 5) Similar studies conducted by Khan et al and Sherwani et al also observed that ovaries and GIT were among the most frequent causes of malignant ascites.[14]

The measurement of ADA level in ascitic fluid is a fast and accurate test for diagnosis of tuberculosis.In this present study total of 120 ascitic fluid were examined, 10 cases were found to be of tubercular origin. All of them had high ADA

levels. The beginning of empirical treatment when a patient has high ADA value in ascitic fluid seems to be good approach while waiting for the results of mycobacterial cultures or biopsies.[7,17]

Transudative ascitic fluid contains glucose in same concentration as that of blood. Exudative ascitic fluid has glucose level lower than transudatives, due to destruction or glycolysis of glucose by the action of bacteria and cells. Low glucose can also be found in malignant ascites. In neoplastic effusion and secondary bacterial peritonitis, glucose level is <60 mg/dl.[11] Presents study reported with significantly lower ascitic fluid glucose levels as in concordance with study done by Attanasio.[18] Runyon et al reported lower ascitic fluid glucose in patients with malignant ascites as compared to cirrhotic ascites which is comparable to the results of the present study.[19]

The estimation of ascitic fluid total proteins was the important criterion used to classify ascites. In this study out of 120 ascitic fluid which were studied , 73 were found to be transudates and 47 were exudates. Jungst D et al found that ascitic fluid protein levels had discriminative value of differentiating cirrhotic from non –cirrhotic ascites but not malignant from tubercular ascites, with lower protein concentrations in cirrhotic as compared to malignant and tubercular cases.[20] This is in accordance with the present study.

The most common cause of ascites development is associated with portal hypertension which is related to liver cirrhosis. While defining ascitic fluid, high albumin gradient (≥1.1 g /dl) and low albumin gradient (<1.1 g/dl) replace the terms transudate and exudate respectively.[12,21] According to the etiological investigation of ascites in patients with SAAG ≥ 1.1 g/dl, the most common causes are associated with diseases such as liver cirrhosis with a rate of 97%, Budd-Chiari syndrome, veno-occlusive disease, alcoholic hepatitis and congestive heart failure that cause portal hypertension. In case of SAAG <1.1 g/dl, diseases like malignancy, infectious diseases, nephrotic syndrome and pancreatitis should be considered.[22] This is in concordance with present study in which SAAG >1.1 g/dl in cirrhosis and congestive cardiac failure and SAAG < 1.1 g/dl in malignant ascitis, nephrotic syndrome and SBP.

Conclusion

Ascites can be a consequence or complication of many primary diseases and carries an unfavorable prognosis that largely depends on the underlying causes.The exudative ascites is seen with tubercular acute infective and malignant ascites, with protein content >3.0 gm/dl and lower glucose levels while the transudative ascites as seen commonly with cirrhotic ascites has protein content <3.0 gm/dl and a higher glucose levels.

The careful cytomorphological examination of ascitic fluid is a valuable, simple, rapid, inexpensive and reliable technique in the differential diagnosis of ascites, particularly in resource limited settings.

Conflict of Interest: The authors declare that they have no conflict of interest.

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