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DIVERSE CONNOTATIONS - GUISE OF CELLS IN PLEURAL FLUID CYTOLOGY INTERPRETATION FOR PERSONIFICATION PERSE OF ACCURATE DIAGNOSIS

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ABSTRACT

Background: Non-malignant and malignant causes of effusion can be ascertained comparatively by non-invasive technique of interpretation of pleural fluid cytology. With this basis the present study on cytology of pleural fluids was chosen to be studied. The diagnostic efficacy and accuracy of the cytologic study of the fluid is ascertained to the fact that the cell population present in the sediment is a bigger picture of a much larger surface area than that obtained by needle biopsy. **Materials and Methods**: One hundred and twenty (120) samples of pleural fluid were examined for total cell count, cell type and cellular features along with fluid biochemistry from Oct 2014 to Oct 2016. **Results**: A total of 80% samples were exudative and 20% were transudative. Total leukocyte count (TLC) was less than1000 cells/cu.mm in most (85.89%) of transudative effusions. Overall 50.44% of exudative effusions had TLC greater than 1000 cells/cu.mm. It was noted that 99.88% of tuberculous effusions had more than 50% lymphocytes, 77.25% had protein greater than 5 gm/dl and 89.63% had glucose greater than 60 mg/dl. Approximately 18% of pleural effusions were positive for malignant cells. The primary site could be assessed by pleural fluid cytology in many case scenarios. **Conclusions:** The most useful test in establishing the diagnosis of pleural effusion is pleural fluid cytology and pleural fluid cell count. Cytologic study of pleural fluid is a complete diagnostic modality which aims at pointing out the etiology of effusion as well as, in certain cases, a means of prognostication of disease process.

KEYWORDS: Effusion; pleural fluid, exudate, malignant effusion.

INTRODUCTION

Aspiration cytology of serous cavities is a simple, cost effective and relatively non-invasive technique to achieve a prerogative diagnosis. The information.

Provided by body fluid analysis serves several functions, it helps the clinician in formulating, in order of priority, a list of differential diagnoses, allows one to follow the result of therapy.[1] Hence, the study of body effusions cytology is an important diagnostic modality which leads to the genesis ciphering of effusion as well as in certain cases the diagnostic performance of the cryptologic study of the fluid may be attributable to the fact that the cell constitution present in sediment is representative of a bigger surface are than that obtained by needle biopsy alone.[2,3]

MATERIALS AND METHODS

The pleural fluid cytology study was done in the Department of Pathology, KIMS, Mangalore, Karnataka over a period of two years from, clinical information regarding age, sex, symptoms and accompanying signs were obtained from the patients. The fluid was studied on emergency basis as soon as it came with a lag time of two hours, if the investigation was delayed the fluid was stored at 4-6 degrees Celsius. The fluid was kept in two components, one part was used for cell count and the other part was poured into the centrifuge tubes and centrifuged for 15 minutes at 2500-3000 rpm. The supernatant was poured off and part of the sediment was transferred to a clean glass slide and mixed with a part of 1% toluidine blue and examined. The remaining part of sediment was transferred with the help of a Pasteur pipette to three slides coated with albumin. One was air dried and stained with Giemsa, the other two were fixed in 95% alcohol for 15 minutes and stained with Haematoxylin and Eosin, Papanicolaou stains. For haemorrhagic fluids, glacial acetic acid or 0.1 N HCl was used as haemolysing agent and then they were processed. For cell count one drop of fluid was mixed with a drop of toluidine blue and the cells were counted in Neubauer's counting chamber. For all cases biochemical analysis of protein, sugar, chloride, lights criterion was applied, and bacteriological culture of pleural fluid was done.

RESULTS

The medical records of all 120 patients with pleural effusion were available for review. The ages of the patients ranged from 5 to75 years, with maximum cases (39.36%) in the sixth decade. To differentiate transudate from exudate, the ratio of pleural fluid and serum protein; the ratio of pleural fluid and serum LDH were calculated. Light's criteria were applied in which, in Exudative pleural fluid, total protein level was > 3gm/dl, level of LDH was > 200 IU/L While in Transudative pleural fluid, total protein level was < 3 gm/dl, level of LDH was < 200 IU/L. Male preponderance of effusion was noted. Our results show that, mean value of Protein in pleural fluid of tuberculosis pleural effusion patients, is 5.3 ±1.4 and mean value of LDH is 1007.2 ± 167.6 this result, when compared with Light's criteria, in tuberculosis pleural effusion, pleural fluid appears to be exudative type. And its mean glucose level is 39 ± 4.8. The ratio of male to female being 2:1. Of all the effusions, 31.19% were haemorrhagic; 26.61% turbid, 23.85% clear, 11.93% purulent, 3.67% viscous and 2.75% opalescent. Transudates comprised 18% of cases. Most of them were secondary to Cirrhosis and congestive cardiac failure (Table 1). Overall 82% of pleural effusions were exudative in nature. The most frequent cause of exudative effusion was tuberculosis (39.02%) followed by malignancy (30.49%), premalignancy (8.54%), pneumonia (7.32%), and empyema (4.89%). In 53.57% of malignant effusions there were predominantly lymphocytes. All samples of parapneumonic effusions had polymorphonuclear cells as the predominant cell type. Approximately 82% of effusions had protein level greater than 3 gm%, hence were exudative (Table 2). Maximum number of the transudative effusions were clear in appearance and most of the exudative effusions were haemorrhagic. Clinically 43 cases were diagnosed to be tuberculous but with cytological and biochemical study only 32 cases were confirmed to be of tuberculosis. Approximately 96.88% Approximately 96.88% of samples of tuberculous effusion had lymphocyte count greater than 50%, 81.25% had protein level greater than 5 gm% and 90.63% had pleural fluid glucose greater than 60 mg/dl (Table 3). Malignant cells were present in pleural fluid of 28 patients. Out of them 89.29% samples were exudative and 10.71% were transudative. 71.43% of malignant effusions were haemorrhagic. Diagnosis of metastatic adenocarcinoma was made in pleural fluid cytological examination of nine cases in which all the fluids showed sheets, clusters and acini of large tumour cells having large dense hyperchromatic nuclei and pale cytoplasm. Around 55% of patients were in the sixth decade. It was noted that 88.89 were exudative effusions and all samples were haemorrhagic. Diagnosis of metastatic papillary carcinoma was made in four samples. Smears showed clusters and papillary groups of large abnormal epithelial cells having large dense nuclei and conspicuous nucleoli. Nuclear chromatin was coarse. A few psammoma bodies were seen. 50% of patients were in the sixth decade. All samples were exudative and haemorrhagic. Mesothelioma was diagnosed in six samples. Mesothelial cells were arranged singly or in three dimensional groups forming spherical, morule-like configuration with knobby borders. Single atypical cells were also present. Atypical nuclear features like variation in nuclear size, shape, multinucleation, hyperchromasia and enlarged nucleoli were seen. All samples were exudative and 66.66% samples were viscous in appearance. Metastatic mucin secreting carcinoma was seen in a pleural fluid sample from an elderly 65 year female patient who clinically diagnosed to have malignant ovarian tumour.(fig1) The fluid was exudative in nature. Smears showed clusters of abnormal epithelial cells having mucin filled cytoplasm and eccentric large nuclei with conspicuous nucleoli. Metastatic small cell carcinoma was seen in the pleural fluid sample of elderly male patient who was clinically diagnosed to have tuberculosis. The fluid was exudative innature. Smears showed scattered and loose cohesive clusters of small abnormal epithelial cells two to two-and-a-half timesthe size of lymphocytes. Anaplastic large cell lymphoma was seen in the pleural fluid sample of a 12-year-oldfemale patient. The fluid was transudative in nature and hemorrhagic. Smears showed lymphocytes, neutrophils and macrophages. There were scattered and loose aggregates of large pleomorphic densely staining cells with cleaved nuclei and pale cytoplasm. Non-Hodgkins lymphoma was diagnosed in the pleural fluid sample of a 49–year-old male patient with clinical diagnosis of tuberculosis. The fluid was exudative in nature. Smears showed predominantly large lymphoid cells with cleaved nuclei, speckled chromatin and scanty pale vacuolated cytoplasm. Out of 24 samples of malignant pleural effusions, six (21.43%) had the primary site in the pleura, two (7.14%) each in breastand ovary, two (7.14%) had effusion positive for lymphoma/ Leukaemia, one (3.57%) had effusion due to small cell lung carcinoma and the same number of patients had the primary site in the cervix. Out of 24 clinically suspected malignant effusions 18 were diagnosed to be malignant after cytological examination. The remaining seven samples turned out to be premalignant. 100% samples of clinically diagnosed pneumonia were confirmed to be ofpneumonia on cytological examination. Clinically 43 samples were diagnosed to be tuberculous in origin but tuberculosis was cytologically confirmed in 32 cases. Among the remaining seven cases of clinically suspected tuberculous effusion, two were of metastatic adenocarcinoma, one each of mesothelioma, metastatic papillary carcinoma, metastatic small cell carcinoma, non-Hodgkin's lymphomaand metastatic carcinoma undifferentiated.

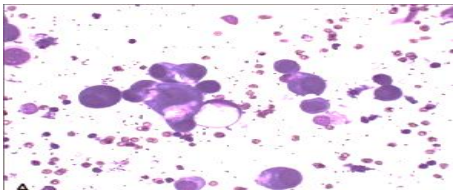

Fig. 1: Mucin seceting ca mets in pleural fluid.

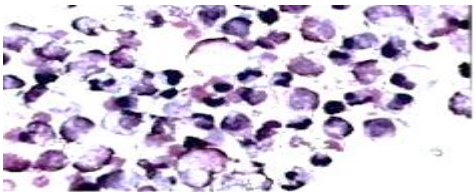

Fig. 2: Empyematous pleurisy.

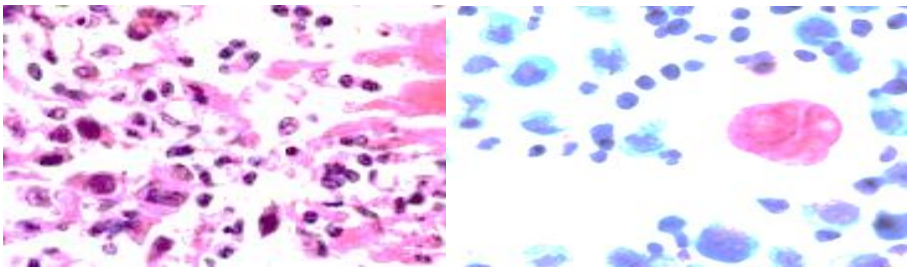

Fig. 3,4: Chronic pleurisy with viral cytopathic effects, squamous cell carcinoma in laryngeal carcinoma.

Table 1: Clinical causes of transudative pleural effusion, total and differential cell count, biochemical features.

Etiology	No of patient	Tlc 0-500	Tlc 500-1000	Tlc>1000	poly	Lymph	Other Eoino, meso, atypical cell	Protein	Protein >3
Cirrhosis	7	2	4	-	1	6	-	6	
CCF	6	5	1	-	1	5	-	6	
Rheumatoid arthritis	1	0	1	-	-	1	-	1	
Trauma	1	-	1	-	-	1	-	1	
Meig's syndrome	1	1	-	-	-	1	-	1	
malignancy	2	1	1	1	1	1	-	3	
Total	18	9	8	1	3	15	-	18	

Table 2: Clinical causes of exudative pleural effusion, total and differential cell count, biochemical features.

Etiology/pathology mentioned in clinical case sheets	No of patient	Tlc0 -500	Tlc50 0-1000	Tlc> 1000	Predomcel-Polymorphs	Predomcel-Lymphocytes	Eosinophils	Mesothelial	Malignant cells	Protein <3	(gm%) >3
Tuberculosis	43	02	22	19	02	41				43	
Pneumonia	26	-	10	16	26	-				26	
Empyema	04	-	03	01	04	-				04	
Trauma	11	-	-	11	11	-				11	
Liver disease	01	-	-	01	-	01				01	
Hepatic abscess	01	-	-	01	01	-				01	
Pelvic abscess	01	-	-	01	01	-				01	
Acute cholecystitis	01	-	01	-	-	01				01	
Connective tissue disorder	01	-	01	-	-	01				01	
Myocardial infarction	01	-	01	-	01	-	-	-	-	01	
Premalignant/borderline	07		04	03	02	05	-	-	-	06	
Malignant	24	02	15	07	03	13	-	03	06	24	
Total	120									120	

Table 3: Tuberculous effusion lymphocyte count, biochemical parameter and light scoring.

No. of samples	Lymphocyte count		Protein count(gm%)		Glucose count(mg%)		Ldh count	
	<50	>50	3-5	>5	<60	>60	>0.6	<0.6
43	2	41	17	26	11	32	30	13

DISCUSSION

The feasibility of pleural fluid aspiration, analysis and cytological examination has kept alive the search for a testto inexplicably differentiate the various causes of effusion. The cytological examination of body effusion is a complete diagnostic modality which aims at pointing out the etiology of effusions. The diagnostic performance of the cytologic study of the fluid may be attributable to the fact that the cell population present is representative of a much larger surface area than that obtained by needle biopsy. The present study deals with the accuracy he clinical presentation of malignant tumor is an indispensable, effective aid to a cytopathologist and may increase the yield by several times. So we tried to to study the relationship between clinical and cytological diagnosis.[3] One study showed that the incidence of dull chest pain is higher in malignant disease, while pleuritic chest pain is higher in patients with benign disease.[4] Symptoms of less than seven days occur mostly in benign diseases. Mare The present study showed slight male preponderance with female to male ratio of 1:1.3. Our study is in concordance with the study done by Romero *et al*. In our study most of the effusions (82%) were exudative in nature. Transudates comprised 18% of cases. Most of malignant effusions were exudative except three cases which were transudates which could be explained on the basis of concomitant anemia and hypoproteinemia. In a study done by Sherwani*et al.*[5] two cases of malignancy had transudates due to similar reason. he presence of predominantly polymorphonuclear cells in pleural fluid indicates that the fluid is the result of acute pleural inflammation, hence raising the probability of pneumonia with effusion. In the present study we got a case of a 50 year old male patient with a history of trauma, where 15% eosinophils were found in the pleural fluid. Hence diagnosis of eosinophilic pleural effusion was made. Fluid was hemorrhagic in nature. This can be attributed to the fact that the blood in the pleural space acts as an eosinophilic substance. There are other factors involved since a significant number of eosinophilic effusions are non-hemorrhagic and not all hemorrhagic effusions are eosinophilic.[7] Air in pleural space has been shown to be t is possible to diagnose the type and source of malignant tumor cells in serous effusions with an overall accuracy of 50%. In the present study, out of 24 samples with malignancy, the primary site could be confirmed on cytology in 16 (57.14%) of cases. In our study the most common primary site was the pleura (21.43%) followed by the breast, ovary and lymphoma / leukaemia, each comprising 7.14%. Prostate, gall bladder, female genital tract and lung made up 3.57%. In the present study pleural fluid cytology was not helpful in ascertaining the cause of pleural effusion in 12 (42.86%) of patients, thereby indicating its limitations. Malignant pleural effusion was found to affect females more than males (2.1:1), which is in agreement with the study done by Sears *et al.*[11] Another cause of eosinophilic inflammatory response. In our study 68.97% of hemorrhagic effusions were positive for malignancy. But all hemorrhagic fluids need not be due to malignancy and non-hemorrhagic fluids can have malignant cells.[6] In the present study mesothelioma was the second most common malignancy accounting for six samples (21.43%). Mesothelial cells were arranged singly or in three dimensional groups. These cell clusters had spherical morule like configuration. Single atypical mesothelial cells were also present. Atypical nuclear features, such as variation in nuclear size, shape, multinucleation, hyperchromasia and enlarged nucleoli were seen. The cells had dense perinuclear cytoplasm, centrally placed nuclei and slit like spaces between some cells. There was also focal vacuolisation of the cytoplasm and a prominent lymphocytic infiltrate. Grandos *et al.* showed similar findings in cytologic analysis of fluid from malignant mesothelioma.[12] In the present study there was only one case of metastatic small cell carcinoma of the lung in an elderly male patient. Grossly, the fluid was hemorrhagic. Smears showed neoplastic cells arranged singly or in small clusters. Individual cells were about two to two-and-half times the size of small lymphocytes, with scant cytoplasm and hyperchromatic nuclei. Nucleoli were inconspicuous. Nuclear molding was noted and best appreciated within cohesive groups. Chhieng*et al.* and Khan *et al.*[14] observed similar features in their study.[13] We had two cases of pleural effusion due to metastasis from breast carcinoma. Pleural fluid was hemorrhagic in both cases. The cells were cytologically innocuous[15] confirmed similar findings in Spieler et al study. We found two cases of metastatic pleural effusion due to primary foci in the ovary. One was diagnosed as metastatic mucin secreting adenocarcinoma and it showed clusters of abnormal epithelial cells with mucin filled cytoplasm and eccentric large nuclei with conspicuous nucleoli. The other case was of metastatic papillary carcinoma. It showed papillary clusters of abnormal epithelial cells with large densely staining nuclei and pale cytoplasm. Psammoma bodies were present.

CONCLUSION

The present study demonstrates that the most useful test in establishing the diagnosis of pleural effusion is pleural fluid cytology and pleural fluid cell count. Cytologic study of pleural fluid is a complete diagnostic modality which aims at pointing out the etiology of effusion as well as, in certain cases, a means of prognostication of disease process. The diagnostic performance may be attributable to the fact that the cell population present in the sediment is representative of a much larger surface area than that obtained by needle biopsy. Thus patients with an undiagnosed pleural effusion should be evaluated in an individualised stepwise manner.

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