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Cytological Analysis of Pleural and Peritoneal Fluids: A Two Year Study in Tertiary Health Care Centre

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Abstract: Cytological examination of cavity effusions is extremely important as it highlight the cause, presence of metastatic cells, typing of unknown cases, prognosis and staging of cancer. To study and evaluate trends in cytological evaluation of cavity effusions for various pathological conditions in a tertiary health care centre. 2) To correlate their frequency in relation to diagnosis. Our Study was cross-sectional study performed in Department of Pathology, Sri Aurobindo Medical College and Post Graduate Institute from 1st January 2013 to 31st December 2014. Serous cavity effusions included in the study were pleural and peritoneal in origin. All other fluids (pericardial and synovial fluid) were excluded from the study. The history and relevant parameters were noted and correlated clinically. Cytospin and Conventional smear methods were performed on pleural and peritoneal fluids. Both air dried and wet fixed smears in methyl alcohol were used and stained with Papanicolaou (PAP) and May-Grunwald-Giemsa (MGG) stain. Out of 885 cases, 400 (45.19%) were pleural fluid, 485(54.8%) were peritoneal fluid .806 (91%) were of benign effusion and 79 (8.92%) were of malignant effusion. Total transudate cases in our study were 611 (69%) and exudates were 274 (30.9%). Male to female ratio was 1.5:1 with youngest patient 20 years old and eldest was 85years old. In younger age group benign effusions are common and malignant in older age group. Morphology and staining with May-Grunwald-Giemsa (MGG) and Papanicolaou (PAP) helped in better interpretation. Preliminary fluid analysis for cytology in resource limited settings, still remains the most convenient and cost effective method in arriving at the diagnosis, thereby reducing the need for invasive investigations and their related complications. Presence and absence of malignant cells at times can be the only clue to the presence of malignancy thereby affecting the prognosis and treatment outcome of the patient.

Keywords: Cavity Effusion, Transudate, Exudate, Adenocarcinoma.

INTRODUCTION

Body cavities (pleura, peritoneum) have a common embryologic origin in the mesenchymal embryonic layer and are lined by mesothelial cells. Their support system is appropriate connective tissue, vascular and nervous apparatus. Parietal and visceral layer are separated by thin layer of lubricating fluid that provides the movement of two membranes against each other in the absence of disease [1]. The serous cavities develop spontaneous effusions in pathologic states and hence provide useful sample for cytological evaluation. Cytomorphological examination of exfoliated cells in effusions may also provide information of various inflammatory conditions of serous membranes, infection with bacteria, fungus, viruses and parasitic infestations. It can also provide evidence of fistulous connection with a serous cavity [2]. Cytological examination of exfoliated cells in cavity effusions is challenging in clinical cytopathology. Twenty percentage of all effusions examined are directly or indirectly related to the presence of malignant disease, with carcinoma of lung as the most common underlying cause [3]. Cytological examination is better than biopsy of serous cavity and is important for the diagnosis of cancer, staging and the prognosis of the patient. Focal lesion on a serous surface may be missed by biopsy. This leads to false negative results. But in effusions malignant cells exfoliate and accumulate from all the surfaces lining that cavity which represent entire serous cavity. Hence, the diagnostic performance of the cytomorphological study of effusion 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 [4, 5]. If multiple effusion specimens are evaluated consecutively the rate of detection of malignant cells is increased. This study was conducted to evaluate the various trends of serous cavity effusions for pathological conditions diagnosed in a tertiary health care centre in Central India.

MATERIALS AND METHODS

The study was performed to evaluate serous effusions for various pathological conditions in the Department of Pathology, Sri Aurobindo Medical College and Post Graduate Institute, Indore, Madhya Pradesh from 1st January 2013 to 31st December 2014. All the cases of benign and malignant diseases with serous effusion from pleura, and peritoneal cavity were included. All other fluids were excluded. Clinical data and history were noted and correlated accordingly. The samples of serous effusions were received in the rubber stopper labelled glass bottles, sterile containers as well as in properly closed large jars in case of large volumes with properly filled requisition forms. Sample was stored at temperature of 2-60 C whenever delay was anticipated in processing. Smears were prepared using the sediment obtained by routine centrifugation at 2000-3000 rpm for 5 minutes and by cytospin method. Both wet fixed (methyl alcohol) and air dried smears were used. They were stained with Papanicolaou (PAP) and May-Grunwald-Giemsa (MGG). Papanicolaou (PAP) stain helped in better interpretation of nuclear features and May-Grunwald- Giemsa (MGG) stain for cytoplasmic features.

RESULTS

In the present study, total 885 serous fluid samples were studied. Out of 885 fluids, 400 were pleural fluids, 485 were peritoneal fluids. The maximum number of cases (25.6%) was observed in the 4th decade and minimum number (3.10%) was observed in 2nd decade with none in 1st decade of life. Age range of the patients in the present study was from 20 to 70 years. Male preponderance was noted with the ratio of male to female being 1.5:1 [Table 1].

Out of total 485 cases of peritoneal effusion, maximum number of cases (139) was observed in the age group of 31-40 years with female preponderance; male to female ratio was 1:1.4. Total 349 cases were transudate in nature and 136 were exudate in nature. Cytological examination revealed, out of 136 cases of exudate in nature, 46 cases were of malignant effusion and 90 cases were nonmalignant causes of exudative effusion [Table 3]. Of all the 46 cases of malignant effusion, female preponderance was observed; male to female ratio was 1:5 and ovarian carcinoma being the commonest primary site. Of all the peritoneal effusions, 300 cases were of straw coloured, 70 cases were turbid, 66 cases were haemorrhagic and 49 were clear in nature [Table 2].

Out of 400 cases of pleural effusion, maximum number of cases (108) was observed in the age group of 21-30 years with male preponderance; male to female ratio being 1.8:1. Total 262 cases were transudate in nature and 138 were exudate in nature. Transudate effusions had protein level less than 3 gm% and exudate effusions had more than 3 gm%. Out of 138 cases of exudate in nature, cytological examination revealed, 33 cases were of malignant effusion and 105 cases were of nonmalignant causes of exudative effusion [Table 3] Of all the 33 cases malignant effusion, male predominance was observed with male to female ratio 1.2:1 and lung carcinoma being the most common primary site. Of all the pleural effusion 240 cases were straw coloured, 103 cases were turbid, 45 were hemorrhagic and 12 were clear in nature [Table2].

Cytological examination of non-neoplastic effusions showed sheets and singly scattered reactive mesothelial cells with windows and clear spaces in between them scattered among macrophages and inflammatory cells [Figure 1]. In neoplastic effusions, three dimension balls, aggregates forming gland like structures with lumen, and papillary structures were commonly observed [figure 2]. Adenocarcinoma was the most common morphological pattern observed in our study.

RESULTS & OBSERVATIONS

Table-1: Age wise and Sex distribution of all the serous effusions

Age in(years)	Pleural	Peritoneal
0-10	00	00
11-20	19	09
21-30	108	110
31-40	90	139
41-50	52	74
51-60	45	63
>60	86	90
Total cases	400	485
Male:Female ratio	1.8:1	1:1.4

Table-2: Distribution on the basis of appearance of various effusions in the study

Type Of Fluid	Straw	Turbid/Purulent	Haemorrhagic	Clear
Pleural	240	103	45	12
Peritoneal	300	70	66	49

Table 3: Distribution of transudate and exudate on the cytological examination

Type of fluid	Transduate	Exudate Non malignant	Malignant
Pleural fluid	262	105	33
Peritoneal fluid	349	90	46

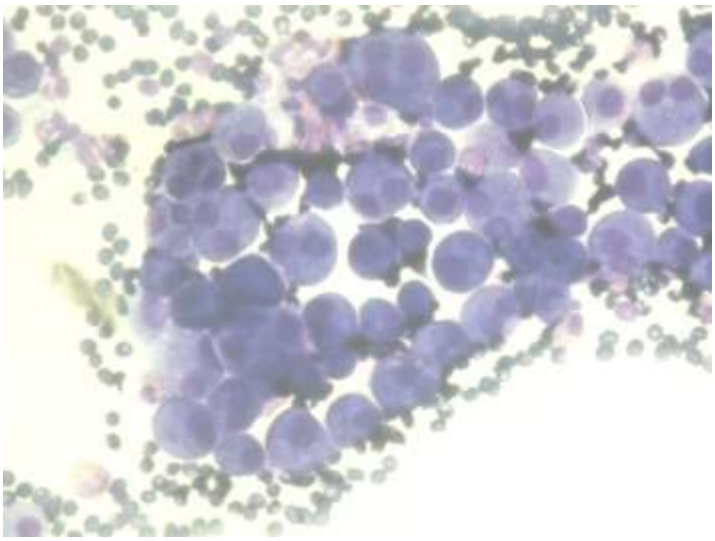

Fig-1: Photomicrograph showing sheets of reactive mesothelial cells with windows in case of pleural effusion (Giemsa, x400)

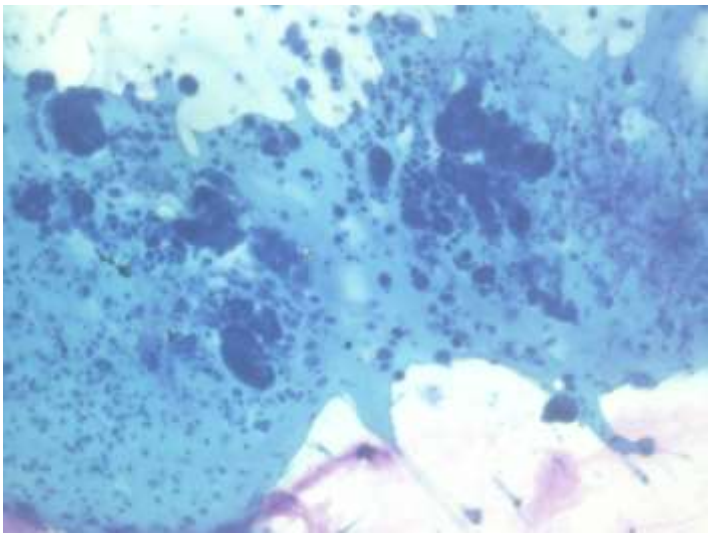

Fig-2: Photomicrograph of metastatic adenocarcinoma in pleural effusion showing acini of pleomorphic tumor cells (Giemsa 10x)

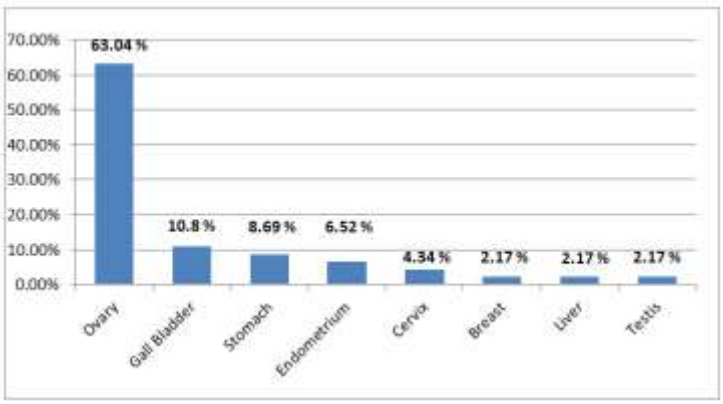

Fig-3: Distribution of various primary sites for metastatic peritoneal effusion

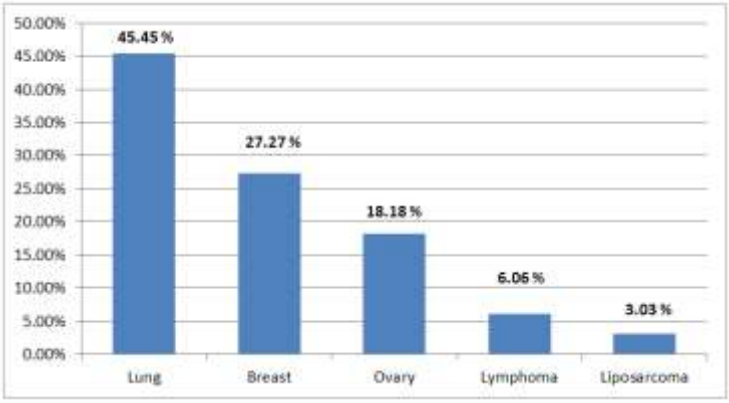

Fig-4: Distribution of various primary sites for metastatic pleural effusion

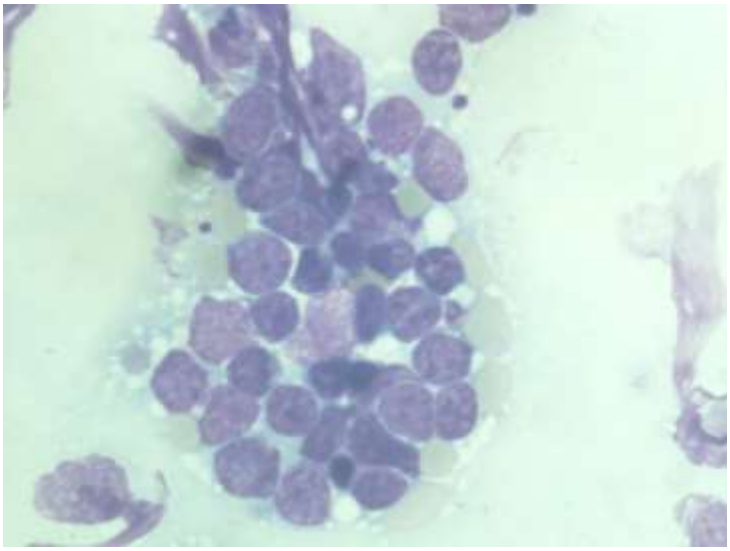

Fig-5: Photomicrograph of Metastatic Lymphoma showing monomorphic tumor cells with irregular nuclear membrane (Giemsa 100x)

DISCUSSION

The cytological examination of body fluid is a complete diagnostic modality which points out its etiology. The diagnostic performance of the cytologic study of effusion may be attribute to the fact that the cell population present in representative of a much larger surface area than that obtained by needle biopsy [4,5]. Examination of fluid cytology is sometimes difficult as morphology of reactive mesothelial cells may mimic malignant cells. Hence, distinction between these two on cytological examination of effusion cytology is a diagnostic challenge. The present study was undertaken to analyse the trends of various serous effusions in Central India and to study the importance of fluid cytology in the diagnosis of various benign and malignant conditions.

In our study, the most common effusion was peritoneal followed by pleural effusion. Our study correlated with finding of Sherwani R *et al*. [5]. In pleural fluid examination, male preponderance was seen with male to female ratio 1.8:1. Our study show concordance with study by Romero *et al*. [6] and Rasik Hathila *et al*. [7] However, maximum number of patients with pleural effusion were seen in the 4th decade in the present study. Out of 400 cases of pleural effusions of which maximum number of cases (262) were transudate in nature. Differentiation from transudate on routine examination of fluid is mainly based on levels of protein (Transudate less than 3 gm% and exudate more than 3gm %), Rasik Hathila *et al*. [7] had similar finding. On the cytological examination, transudative effusions are usually characterised by a majority of lymphocytes or other mononuclear cells. In present study, all the transudate effusions had more than 50% lymphocytes which were comparable with study of Kushwaha *et al*. [8] which showed 83.33% of samples of transudate effusion had more than 50 % of lymphocytes. The pattern of predominantly polymorph nuclear cells were observed in most cases of exudative effusion and clinically suspected cases of pneumonia and emphysema. Of all the 138 cases of exudative pleural effusion, 33 cases were malignant effusion with male preponderance and lung carcinoma was the most common primary site which is in agreement with study of Lim *et al*.[9] Breast carcinoma followed by ovarian carcinoma was the next most commonest primary site in the pleural effusion group [Figure 3]. On the basis of

cytomorphology, metastatic adenocarcinoma was the most common finding in malignant pleural effusion. Di Bonito *et al.* [10] studied on cytomorphological diagnosis in pleural effusion with autopsy confirmation and found most cases were of adenocarcinoma. Hallman *et al*. [11] also did a comprehensive study on cytology of fluid from different cavities in children and found lymphoreticular neoplasm to be the cause of almost all malignant effusion in children. Here we found two cases of Non Hodgkins Lymphoma, both were seen in children.

In peritoneal fluid examination, female predominance was observed with male to female ratio 1:1.4 and ovarian malignancy was the most common primary site. Jha R *et al*. [12] reported gastric malignancy as the commonest primary in their study, however in female patients ovarian malignancy was the commonest which correlated with our study. Parson *et al.* [13] Wilailak *et al*. [14] Monte SA *et al*. [15] and Karoo *et al*. [16] also found ovarian malignancy as commonest primary site, shedding malignant cells in peritoneal fluid. In peritoneal effusion, out of 485 cases, maximum number of cases (349) was transudate in nature. Rasik Hathila *et al*. [7] had similar findings. Of all the 136 cases of exudative effusion, 46 were malignant in nature. Of all the malignant peritoneal effusions, ovarian carcinoma was commonest followed by gall bladder carcinoma and other gynecological cancers. [Figure 4]

The diagnosis of different types of malignancy was made On the basis of tumor cell morphology and its arrangement. Most common morphological pattern observed in our study was Adenocarcinoma. Breast carcinomas of the medium or large cell type are easily recognized as malignant in effusion since cells have classical features of metastatic adenocarcinoma which includes presence of large, three-dimensional clusters of round, oval or irregular configuration and the cells are superimposed on each other. Nuclear features comprise of nuclear enlargement, granularity of chromatin, prominent nucleoli and abnormal mitosis and are classic of malignant cell. Similar cytomorphological features were shown by Lung adenocarcinoma. Papillary configuration was also seen in some cases. However, there are group of poorly differentiated adenocarcinoma which can be easily recognized as malignant but fail to display any of the features to call it as a tumor. Adenocarcinoma as Commonest cytomorhological pattern was also shown by metastatic ovarian carcinomas. The exact identification of tumor type may be possible in some cases. The cancer cells never form cohesive clusters, instead lie singly irrespective of the type of malignant lymphoma,. Tumor cells have spherical to oval nuclei with irregular contour, nuclear indentation with prominent nucleoli and scant cytoplasm [Figure 5]. Cytological evaluation of serous effusions helps in evaluating presence or absence of cancer cells and hence affecting prognosis staging and treatment plan for the patients.

CONCLUSION

Non neoplastic effusions are common in younger age group and malignant in older age group. In benign effusions reactive mesothelial cells with window effect were commonly observed. In malignant effusions papillary structures and three dimensional balls were observed. Combined approach to morphology with May-Grunwald- Giemsa (MGG) and Papinicolaou (PAP) helped in better interpretation than either methods used individually. Preliminary fluid analysis for cytology in resource limited setting still remains the most convenient and cost effective method in arriving at the diagnosis, thereby reducing the need for invasive investigations and their related complications. Cytological analysis of serious cavity effusions have a better diagnostic performance vis-a-vis needle biopsy as the population of cells obtained in sediment is representative of a larger surface area than the latter. Serous effusions may be present in a case of malignancy either as a manifestation of progression of disease or maybe attributable to any other cause except malignancy. This results in the upstaging or downstaging of tumour and thereby affects prognosis and treatment plan for the patient. Therefore cytological analysis of pleural and peritoneal effusions should be requested along with its clinicopathological correlation.

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