ORIGINAL RESEARCH PAPER

Pathology

CYTOLOGY OF DIFFERENT BODY FLUIDS : AN IMPORTANT AID TO DIAGNOSIS CANCER

KEY WORDS: Cerebrospinal fluid [CSF], cytology, peritoneal fluid, pleural fluid, urine

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ABSTRACT

Introduction: The cytological examination of exfoliated cells in various effusion fluids is very challenging and is of paramount importance for early diagnosis and management of various pathological processes. It is of utmost significance in identification of malignant cells and hence throws light on the cause, staging and prognosis of various cancers.

Materials and Methods: Analytical, observational study done over a period of six month from November 2020 to April 2021. A total of 210 cases including peritoneal fluid, pleural fluid, cerebrospinal fluid, urine and bronchoalveolar lavage fluid were analyzed. Samples were centrifuged for five minutes at 2000 rpm and smears prepared from deposit were stained by Papanicolaou (PAP) and May-Grunwald- Giemsa(MGG) stains.

Results: Out of 210, 97 were peritoneal effusions, 77 were pleural, 4 cerebrospinal fluids,21 urine and 11 bronchoalveolar lavage fluid. Out of 97 cases of peritoneal effusions, 84(86.59%) were non neoplastic and 11(11.34%) were malignant effusion. Out of total 77 pleural effusions, 69(89.61%) were non neoplastic and 6(7.79%) neoplastic.

Conclusions: Cytological evaluation of different body fluids is a simple, rapid, inexpensive and less invasive tool with high accuracy and thereby reducing the need for invasive investigations. It is especially helpful in evaluating and staging malignancies thereby guiding the clinician in further management of the patient.

INTRODUCTION

There are three major cavities present in our body: pleural, pericardial, and peritoneal. These cavities have parietal and visceral layers, both of which are lined by mesothelial cells overlying the submesothelial stromal matrix tissue [1]. The parietal and visceral layers are separated by thin layer of lubricating fluid which facilitates the movement of both membranes against each other in the absence of disease [2]. However in pathologic states, these cavities develop spontaneous effusions attributable to various patho-physiological processes. This fluid acts as a clinically useful specimen for cytological evaluation to diagnose the underlying pathologic process, such as infections, inflammation, neoplasia, etc [3]. Tapping and analyzing these fluids in terms of biochemical parameters and cytology not only serves in diagnosis and therapeutic intervention but also aids in staging, treatment outcome, disease monitoring and prognosis [4,5]. The diagnostic yield of effusion fluid is higher than needle biopsy since the cell population present in the sediment is representative of a much larger surface area [6,7]. Almost 20% of the effusions examined are directly or indirectly related to the presence of malignant disease [5, 8]. Many studies were performed previously on different fluids, few focusing on single fluid.

MATERIALS AND METHODS

Our study is a descriptive observational study, undertaken in the department of pathology in a tertiary care centre. The duration of the study was six month; from November 2020 to April 2021. Inclusion criteria were samples from pleural effusion, peritoneal effusion, cerebrospinal fluid (CSF),bronchoalveolar lavage fluid(BAL) and urine. Cases from either sex of any age group were included in the study. Complete clinical history including clinical examination along with all relevant blood, serum and radiological investigations of the patients were noted from the medical records of the patients. All the samples received were immediately processed. Sample volume ranged from 2 ml to 2000 ml. The gross appearance of the fluid was assessed. For hemorrhagic fluids, glacial acetic acid was used as a hemolysing agent and then it was processed routinely. The fluids were centrifuged at 2000 revolution per minute (rpm) for five minutes to produce uniform suspension of cells. Both wet fixed (methyl alcohol) and air dried smears were made and stained with Papanicolaou (PAP) and May-Grunwald Giemsa (MGG) stains respectively. PAP stain helped in the better interpretation of nuclear features and MGG stain for cytoplasmic features. The stained smears were studied on light microscopy and evaluated for cellularity, predominant cell type, size, architecture (acini / sheets/ 3-dimensionalballs/ papillae/ rosette, singly scattered), nuclear and cytoplasmic features, chromatin, degree of inflammation, reactive changes and other background features. All the data was analyzed and summarized.

RESULTS

The cytological examination of 210 fluids was done which included pleural fluid, peritoneal fluid, cerebrospinal fluid), bronchoalveolar lavage fluid and urine. The age ranged from 11 years to 85 years. Male preponderance was observed with male samples percentage 57.61 %.The most common fluid was peritoneal fluid 97 (46.19%) cases ,followed by pleural fluid 77 (36.66%) cases, urine 21(10%) cases ,BAL 11 (5.23%) cases and least common was CSF 4 (1.9%) cases (Table 1). The most common age group affected was 6th decade followed by 5th decade. (Table 2) All individual cases were categorized into 3 major categories; (88.57%) benign/negative for malignancy, (2.38%) suspicious for malignancy and (9.04%) positive for malignancy (Table-3). Out of 210 cases of cytological specimens, 186 (88.57%) were negative for malignancy. In peritoneal fluid 86.59 % (84/97), pleural fluid 89.61% (69/77), CSF 100% (4/4) ,BAL 90.9% (10/11)and in urine 90.47% (19/21) were present in this category. These cases included smears which were predominantly inflammatory (acute, chronic as well as mixed) or reactive, having mesothelial cells and macrophages in abundance. 5 out of 210 cases (2.38%) were kept in the category of suspicious of malignancy .These cases did not show definitive features of malignancy .However showed presence of atypical looking cells, either obscured by too

much of hemorrhage , inflammation ,necrosis, etc. or had low cellularity with changes depicting only a doubt of malignancy. Presence of reactive mesothelial cells, close mimickers of malignancy also raised suspicion of malignancy in few cases. Few of these cases lost follow-up and few underwent repeat cytological or histopathological test rendering a definite diagnosis. Malignant cells were detected definitely in 19 (9.04%)cases. Maximum number of malignant effusions were peritoneal (11.34%) followed by pleural (7.79%) and bronchoalveolar fluid (9.09%). 4.76 % cases of urine specimen show malignancy.

Table 1: Distribution of cases according to the type of specimen and their gender wise incidence.

Type of Specimen	Number of Cases	Male		Female	
		(NO.)	(%)	(NO.)	(%)
Peritoneal Fluid	97	51	52.57	46	47.42
Pleural Fluid	77	46	59.74	31	40.25
Urine	21	14	66.66	7	33.33
BAL	11	8	72.72	3	27.27
CSF	4	2	50	2	50
Total	210	121	57.61	89	42.38

Table 2: Age wise distribution of cases in peritoneal and pleural effusion, urine, BAL and CSF.

Age in years	Peritoneal Fluid	Pleural fluid	Urine	BAL	CSF	Total	(%)
11-20	4	-	-	-	1	5	2.38
21-30	9	14	2	1	-	26	12.38
31-40	15	8	1	1	-	25	11.9
41-50	22	15	2	1	1	41	19.52
51-60	19	21	4	3	1	48	22.85
61-70	26	10	10	3	1	50	23.9
71-80	1	9	2	2	-	14	6.67
>80	1	-	-	-	-	1	0.48
Total	97	77	21	11	4	210	100

Table 3: Distribution of cases on the base of diagnosis.

Site	Benign/Negative for Malignancy		Suspicious for Malignancy		Malignant		Total
	(No.)	(%)	(No.)	(%)	(No.)	(%)	(No.)
Peritoneal Fluid	84	86.59	2	2.06	11	11.34	97
Pleural Fluid	69	89.61	2	2.59	6	7.79	77
Urine	19	90.47	1	4.76	1	4.76	21
BAL	10	90.9	-	-	1	9.09	11
CSF	4	100	-	-	-	-	4
Total	186	88.57	5	2.38	19	9.04	210

DISCUSSION

The history of serous effusion cytology can be traced back to the 19th century. Lucke and Klebs were apparently the first investigators who recognized the presence of malignant cells in an ascitic fluid in 1867. In 1882 Quincke was credited for detailed descriptions of ovarian and lung cancer cells in serous effusions. Since that time reports on effusion cytology have started to appear in the medical literature, and serous effusion cytology is now a routine diagnostic procedure worldwide Further with the advent of lumbar puncture in the year 1891, in Germany CSF cytological examination was introduced in the field of cytopathology [7].In the current scenario the cytological examination of effusion has become a complete diagnostic modality which aims at pointing out the etiology of effusions [9] 'Starlings Law governs the mechanism of formation of abnormal fluidin the body cavity. It states that fluid is accumulated when there is decrease in the plasma colloidal pressure and increased capillary hydrostatic pressure [9-11]. However; it is not always possible to characterize a fluid into an exudate or transudate. This provides only a general guideline for possible underlying etiology. Hence, fluid protein is used as a basis to distinguish between exudates and transudates [9].

In the present study of 210 cases of fluids, the age ranged from 11-85 years. The age range in study was from first to ninth decade which was in concordance too our study [4-7, 9, 10, 12-15]. Male preponderance was found in most of the studies [4, 5, 7-10, 12-14] which is similar to the present study. The most common fluid received was peritoneal fluid (46.19%), followed by pleural fluid (36.66%), urine (10%) ,BAL (5.23%) and least common was CSF (1.9%). The present study correlated with the findings of Chakrabarti etal. [8] Shulbha et al. [10] Bhagat et al. [13] Bhade et al. [14] and Gupta et al. [15]. Other authors found pleural fluid as the commonest fluid [4-7, 9, 12]. This could be attributed to the various epidemiological factors. In our study the difference may be due to more number of cases of abdominal malignancies.

In 97 cases of peritoneal fluid, most common age group involved was 61-70 years with a female preponderance. These findings were in concordance with Ayyagari et al. and Chakrabarti et al. Who also observed female preponderance. However age group affected was different in their studies [6, 8].

Pleural fluid was found as the second most common effusion fluid having 77 cases similar to the observation by various authors (8, 10, 13-15) .Most common age group involved was 51-60 years. There was a slight male preponderance ,this was in concordance with Hathila et al. and Chakrbarti et al. [5,8].

Identifying blast cells and their percentage in the CSF is an important prognostic factor in pediatric ALL and determines the incidence of relapse and need for the change in treatment protocol. 20 It is important to identify infectious causes of exudative CSF effusion for early diagnosis, improvement in prognosis and reduce spread of disease and complication [10,14].

Urine cytology for screening of transitional cell carcinoma (TCC) has been used for long time. Despite the advent of several newer techniques for screening and diagnosis of urothelial malignancies, cytomorphology still remains an important tool. "Atypical cells" in urine have been recognized and studied time and again. The accurate interpretation of the character of "Atypical cell" in urine is a major challenge for cytopathologists [16].

Almost all the studies came across difficulty in interpretation of malignancy due to the presence of reactive mesothelial cells which are a very close mimicker of malignancy as they also have the tendency of rosette formation, pseudoacini or acini, with or without prominent nucleoli [4-6]. In our study, we also found 5 out of 210 cases (2.38%) of various fluids being reported as suspicious of malignancy. There is an increased role of cytocentrifuge and cell block study which not only increases the cellularity, but cellular morphology, nuclear and cytoplasmic details, are better appreciated. We can reduce false negative results and increase diagnostic sensitivity and specificity. Also, cell block carries advantage of performing immunohistochemistry which helps in the diagnosis and can be used for typing of tumor without invasive tissue biopsy [4,17,18].

CONCLUSION

Preliminary cytological analysis of various fluids remains the simple, relatively painless, convenient, less time consuming, cost effective, first line method in arriving at the diagnosis and to understand the disease progression. This thereby reduces the need for invasive investigations and their related complications. Cytological analysis of serous effusions have a better diagnostic performance visa-vis needle biopsy as the population of cells acquired in a sediment is representative of

a larger surface area than the latter. It is especially helpful in evaluating and staging malignancies thereby guiding the clinician in further management.

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