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Application Of International System For Serous Fluid Cytopathology: A Retrospective Study.

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ABSTRACT

The most frequently encountered clinical manifestation in medical practice is serous effusion. Collection of most serous fluids from various effusions is relatively simple and one of the most common specimens for cytological evaluation. Thus, interpretation of cytopathology as positive for malignant cells is highly critical in staging and management of patients. However, cytopathologic evaluation of serous fluid is complex. The international system for reporting serous fluid cytopathology (ISRSFC) is recently developed in 2019 to standardize practices reporting effusion fluid cytology. This study aimed to assess the utility of application of ISRSFC reporting categories and to assess risk of Malignancy (ROM) for each category and increase the diagnostic yield of serous fluids. A retrospective cohort study included 1335 effusion cases, which were retrieved and reclassified based on the newly proposed ISRSFC System into five categories during January 2022-December 2022 in Karnataka institute of medical sciences (KIMS), Hubballi. Cellblock and clinico radiological information was obtained, correlation was done and risk of Malignancy (ROM) was assessed whenever available. In our study 920 (69.2%) were men and 409(30.8%) were women. There were 757(56.8%) cases of ascitic fluid, followed by 563(42.1%) cases of pleural fluid, 15(1.1%) of peritoneal fluid in the analysis. Of all the cases 363(27.2%) were non diagnostic, 943(70.6%) were negative for malignancy, 2(0,1%) were atypia of uncertain significance, 6(0.5%) were suspicious of malignancy and 21(1.6%) were malignant. ROM for each diagnostic category was 10% for ND, 16.6% for NFM, 50% for the atypical category and 66.6% in suspicious, 100% were for positive for malignancy category. The ISRFC and IAC guidelines are feasible and convenient for standardized reporting of effusion samples, thus avoiding subjective variations and false positive reporting. The standardization and reporting terminologies ensure an accurate cytological diagnosis, which helps in clinical management of patients.

Keywords: Serous effusion, international system for reporting serous fluid cytopathology, Risk of malignancy.

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INTRODUCTION

Serous effusion is the accumulation of fluid in the body cavities due to various causes and malignancies being an of the important cause of effusion [1]. The common sites from which fluid can be sent for analysis include pleural, peritoneal and pericardial cavity. Fluid cytology is cost effective, minimally invasive, simple and safe procedure that helps in determining the initial diagnosis, staging , prognosis and recurrence status of the patients [2]. Due to cytomorphologic overlap of reactive mesothelial cells with malignant cells, general cytologic criteria for diagnosis of malignancy in single cells cannot be applied in most of effusions. Thus, cytomorphological features of cancer cells may not be same as seen in routine cytopathology of FNAC, and exfoliative, brushing specimens. It essential to understand potential pitfalls during various stages from processing to application of ancillary studies would increase the diagnostic accuracy and minimize atypical interpretation and false positivity [3].

Neoplasm's are cause of serous effusions in approximately 10-25% of all fluids [3-5]. Amongst malignant effusions, adenocarcinomas are most common cause of metastatic cancer, but almost any type of malignancy may involve serous cavities [3]. As there are no uniform guidelines for reporting fluid samples, so many centres are following their own reporting system, thus creating discrepancy in the diagnosis and causing difficulty in reaching definite management plan. Recently proposed international system for reporting serous fluid cytopathology (ISFRSC)standardizes the reporting of serous fluid cytology in the 5 categories: Category 1: Non diagnostic(ND), Negative for malignancy(NFM), Atypia of uncertain significance(AUS), Suspicious for malignancy(SFM) and Malignancy(M) [6].

The ISRFC is an internationally accepted system and provides the risk of malignancy (ROM) for each category, which improves the clinical management and enhances professional communication [7]. The present study was therefore conducted to assess the ROM for each of the diagnostic categories and the diagnostic performance of this system based on our institutional experience.

MATERIALS AND METHODS

The present retrospective cohort study was conducted at KIMS, Hubballi from January 2022-December 2022. Since the study is retrospective in design and did not involve any intervention, an exemption from Ethical Committee was taken. A broad consent was taken for patient's clinical details and Procedures. Two sediment smears were prepared using the cytocentrifugation method. One smear was fixed with alcohol spray for pap stain and air dried for Giemsa stain. The left over samples were stored in the refrigerator at 2-8 C until the case was reported by the pathologist. Cell block was prepared on the next day from remaining sample using Agar gel method were ever needed. The ISRSFC guidelines were applied and classified into five categories: ND, NFM, AUS, SM, and MAL. The cellular components of each category were recorded. Each case was categorized into these five recommended diagnostic categories.

RESULTS

In the study 1335 cases from 1329 patients were included during 1yr. Out of these, 920(69.2%) were men and 409(30.8%) were women. Patient's ages ranged between 3days to 79 yrs with a mean age of 45.4yrs. There were 757(56.8%) cases of ascitic fluid, followed by 563(42.1%) cases of pleural fluid, 15(1.1%) of peritoneal fluid in the analysis. Of all the cases 363(27.2%) were non diagnostic in which there were no diagnostic cells with presence of a few RBCs, occasional lymphocytes and cells showing degenerative changes, 943(70.6%) were negative for malignancy in which there was the presence of either lymphoid or neutrophilic predominance in the effusion sample along with the presence of few benign and reactive mesothelial cells in these category, 2(0,1%) were atypia of uncertain significance in which cells showed reactive atypia of mesothelial cells or lymphoid cells that did not favour malignancy, but were showing atypical changes to categorize into benign reactive category, 6(0.5%) were suspicious of malignancy in which groups and clusters of epithelial cells with features of malignancy but were falling short of quantitatively or qualitatively for the definitive diagnosis of malignancy and 21(1.6%) were malignant in which there were definitive features of malignancy beyond doubt were noticed.

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Table 1: Categorisation of fluids using ISRSFC system

Category (ISRSFC)	Peritoneal n (%)	Pleural n (%)	Pericardial n (%)	Percentage- n= 1335 n (%)
Category1 (ND)	119(21.1%)	243(32.1%)	1 (6.6%)	1363(27.2%)
Category 2 (NFM)	431 (76.5%)	498 (65.7%)	14 (93.4%)	943 (70.6%)
Category 3 (AUS)	-	2 (0. 2%)	-	2(0.1%)
Category 4 (SFM)	3 (0.5%)	3 (0.3%)	-	6 (0.5%)
Category 5 (M)	10 (1.9%)	11 (1.8%)	-	21 (1.6%)
Total	563	757	15	1335

A retrospective study was performed and 4684 samples of pleural effusions were reviewed they observed that out of a total of 364(7.8%) positive for cancer cells, 295(81%) were classified as adenocarcinomas or carcinoma not otherwise specified. There were 32(8.8%) cases of malignant mesotheliomas, 14(3.8%) cases of small cell lymphomas, 13(3.5%) cases of hematolymphoid malignancies, 10(2.7%) of squamous cell carcinomas [13, 14]. They conclude that although adenocarcinomas is the most common malignancy seen in pleural effusions, other hematologic and non-haematological malignant cases can also be found should be kept in mind [15].

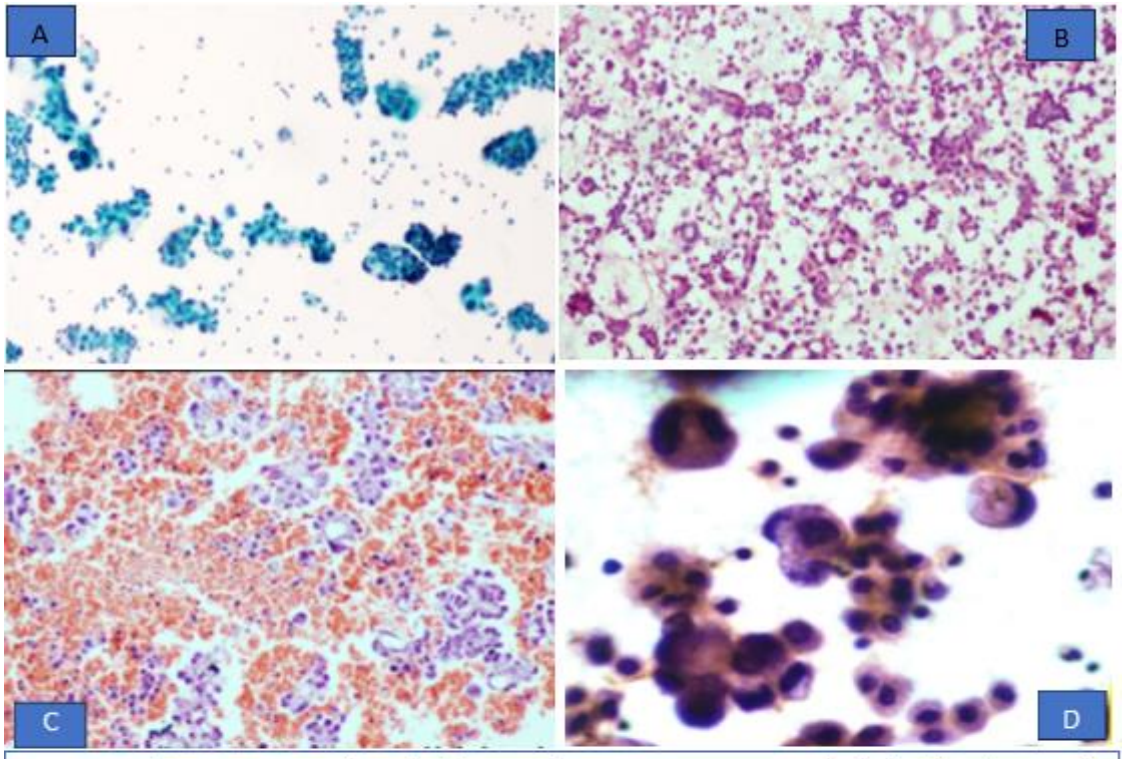

Figure 1: A) Category 2, pleural effusion showing reactive mesothelial cells along with chronic inflammatory cells and macrophages, Giemsa stain (10x). B) Category 4, Cytomorphology showing aggregates of atypical cells with vesicular chromatin, prominent nucleoli, Papanicolaou stain (10X). C) Category 5, Ascitic fluid shows clusters and 3D balls consistent with adenocarcinoma ovary, Papanicolaou stain(40x) .D) Cell clock section showing neoplastic cells arranged in acinar pattern, H&E stain (10x).

Cell block was available in 41 cases. Ovarian cancer, followed by lung cancers was the most common malignancies involving the pleural effusion and ovarian cancer was the most common cause of peritoneal effusion.

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Table 2: ROM for each category

Category (ISRSFC)	No. of cases	Follow up samples	Malignant	Benign	Risk of Malignancy (ROM)
Category 1 (ND)	363	10	1	9	10%
Category 2 (NFM)	943	12	2	10	16.6%
Category 3 (AUS)	2	2	1	1	50%
Category 4 (SFM)	6	3	2	1	66.6%
Category 5 (M)	21	14	14	-	100%

DISCUSSION

Cytological diagnosis is one of the first step in the evaluation of the effusion samples. It is minimally invasive, simple and cost effective. Tumor cells can be diagnosed only on cytomorphology or ancillary studies may be needed including immunohistochemistry and molecular analysis [8]. There is a cytomorphological overlap of reactive mesothelial cells and malignant cells. It is due to the surface tension related phenomenon that round up cells after exfoliating into serous fluid and the tumor cells may continue to proliferate in the nutrient rich effusion sample and may form proliferation spheres. Interpretation of cytopathology as positive for malignancy is highly critical which is manifestation of advanced stage and is critical in planning clinical management. Thus, its important to keep this factor in mind while reporting effusion sample [9]. Kundu et al where a total of 1340 samples were analysed from 1085 patients over a period of 1 year. They categorized them into 35(20.6%) as ND, 954(71.2%) as NFM, 17(1.3%) as AUS, 59(4.4%) as SFM and 275(20.5%) as malignant categories [6].

Farahani SJ et al analyzed eighty studies in their systematic review on 34941 samples. They categorized them into 52(0.2%) as ND, 22202 (72.7%) as NFM, 194(0.6%) as AUS, 711 (2.35) as SFM and 6507 (21.3%) as malignant category [7]. In our study in all 1330 cases 363 (27.2%) were non diagnostic, 943 (70.6%) were negative for malignancy, 2(0, 1%) were atypia of uncertain significance, 6(0.5%) were suspicious of malignancy and 21(1.6%) were malignant.

Table 3: ROM comparison with other studies.

Category (ISRSFC)	ROM Farahani SJ, Baloch Z [5] 2019	ROM Kundu R et.al.[6] 2021	Risk of Malignancy (present study)
Category 1 (ND)	17.4%	20%	10%
Category 2 (NFM)	20.7%	16.7%	9.1%
Category 3 (AUS)	65.9%	50%	50%
Category 4 (SFM)	81.8%	94.4%	66.6%
Category 5 (M)	98.9%	100%	100%

In Kundu et al ROM for each diagnostic category was 20% for category (ND), 16.7% category 2 for (NFM), 50% for category 3 (atypical) and 94.4% for category 4 (suspicious), 100% were for category 5 (malignancy)[6] In Farahani et al ROM for each diagnostic category was 17.4% for category (ND), 20.7% category 2 for (NFM), 65.9% for category 3 (atypical) and 81,8% for category 4 (suspicious), 98.9% were for category 5 (malignancy) [7]. Compared with the present study, ROM for category 1 was high in their study when compared to present study [Table 3]. This is because we had less follow up cases available for this category.

These results support the role of cytological analysis in serous effusion in confirming the existence of malignancy. AUS and SFM in effusion cytology are currently not available [10]. Although, it is annoying for the pathologist and the clinician to use categories as atypical or suspicious. These categories are essential and need to be used cautiously, to provide meaningful clinical information [11]. International system for reporting serous fluid cytology developed a tiered classification system to provide better categorization for reporting [12].

CONCLUSION

Effusion cytology is an important diagnostic tool in the evaluation of benign and malignant fluids. The international system for reporting serous fluid cytopathology is feasible. The standardization and reporting terminologies ensure an accurate cytological diagnosis, which helps in clinical management of patients.

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