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Original Research Article

A Study on Identifying Risk of Malignancy by Cytopathology Reporting of Peritoneal Fluid Effusion Using Newly Proposed International System for Reporting Serous Fluid Cytology

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Abstract:

Introduction: Peritoneal fluid effusion are generally formed in many disease situations and it is quite easy to collect it. Exposing it to analysis will help recognize the etiology of the disease process and thereby help the clinicians to plan the treatment plan correctly. The appliance of The International System for Reporting Serous Fluid Cytology will further make it easy for the clinicians with its simpler terminologies and clear categorization of entities.

Materials and Method: All peritoneal effusion samples that were received for a period of past two years in our private laboratory were examined and categorized according to International System for reporting serous fluid cytology. Risk of malignancy (ROM) was also calculated.

Results: Among 240 cases, 12 (5%), 209 (87%), 8 (3.5%), 8 (3.5%), and 3 (1%) were reported as ND, NFM, AUS, SFM and MAL respectively. Risk Of Malignancy (ROM) was calculated for the cases collected in this study are 0% for ND, 0.96% for NFM, 37.5% for AUS, 75% for SFM and 100% for MAL

Conclusion: The International System (TIS) for Reporting Serous Fluid Cytopathology is very easy to employ and gives high accuracy with clear diagnostic criteria for each category, hence makes it easy to communicate with the clinicians by employing simple terminologies.

Keywords: serous fluid, peritoneal effusion, TIS.

Introduction

Serous fluids such as pleural and peritoneal effusions are generally produced in various non-neoplastic and neoplastic situations. To recognize the cause of effusion, these fluids are frequently evaluated with cytopathological analysis. The sensitivity and specificity of cytopathological examination of serous fluid in identifying malignancy ranges from 50% - 80% and 89% to 98% respectively.[1] The various sites from which fluid can be sent for analysis include a pleural, peritoneal, and pericardial cavity. It forms a large part of specimens received in the cytopathology laboratory of many hospitals and is a cost-effective, minimally invasive, and simple procedure that can help categorize fluids, a standardized cytological report can be of great help to inpatient treatment. Effusion is an unwavering important diagnostic sample and is an essential marker in the management plan, especially in diagnosing and staging malignancies.[2] Neoplasms are the cause of serious effusion in around 10–25% of pleural, pericardial, and peritoneal effusions.[3,4] In many cases, it may be the first manifestation of an unknown primary tumor. Peritoneal effusion is the initial presenting feature in more than 50% of gastrointestinal and gynecological malignancies with peritoneal metastasis.[5]

Peritoneal effusion is the initial presenting feature in more than 50% of gastrointestinal and gynecological malignancies with peritoneal metastasis.[5] Cytopathology reports consist of many descriptive terms which the clinicians find difficult to understand.[6] The International System (TIS) for Reporting Serous Fluid Cytopathology was developed and sponsored in 2020 by the International Academy of Cytology and American Society of Cytopathology.[7,8]

The International System (TIS) for Reporting Serous Fluid Cytopathology has five diagnostic

categories and they are as follows -Non – diagnostic (ND) , Negative For Malignancy (NFM) , Atypia of Undetermined Significance (AUS) , Suspicious for Malignancy (SFM) and Malignant (MAL).

This newly proposed diagnostic system has aimed at avoiding "uncertain" or "indeterminate" categories and has included AUS and SFM instead. Hence these categories will serve as a common language that bridges the gap between the clinician and the pathologist which ultimately improves better patient care based on Risk of Malignancy (ROM) for each diagnostic criteria. In addition, TIS also helps in calculating the ROM for each diagnostic category.

However, ROM varies from one laboratory to another and from one publisher to another based on availability of follow up tissue. Hence to overcome this overestimation of ROM due to selection bias, one can use the best ROM estimates in literature review. There are studies in the literature to calculate the ROM for each of these diagnostic categories.[9] We have done this study to evaluate the feasibility of these diagnostic categories in peritoneal fluid samples in assessing risk of malignancy.

Materials and Methods

This study was done as a observational study from the period of April 2021 to March 2023, 240 Cases of Peritoneal fluid samples obtained from patients of all age group and both sexes were included in the study from the samples received in our private pathology laboratory. While Fluids obtained other than peritoneal fluid were excluded, also fluids of patients not willing to take part in the study were also excluded. The standard handling of peritoneal fluid samples in our laboratory consists of adequacy criteria being minimal 50ml followed by centrifugation and preparation of conventional smears from the sediment that are ethanol fixed for Papanicolaou staining and Hematoxylin and Eosin (H & E) staining, whereas air dried smears were stained with Giemsa stain and the remaining sample present were refrigerated at 2–8°C.[10]

Immunocytochemistry (ICC) and cellblock preparations were reserved for cases that belonged to the AUS or SFM or MAL categories. Diagnostic routine in our department is carried out exclusively by all the pathologists posted in cytopathology division. The ISRSFC and IAC guidelines were applied and classified into five categories: ND, NFM, AUS, SFM, and MAL.[6,11,12,] The cellular component of each category was recorded. Each case was categorized into these five recommended diagnostic categories.

Cytohistological Correlation and ROM calculation:

Histopathology of tissue sample for the peritoneal fluid effusions received were analyzed and the corresponding blocks were subjected to immunohistochemical analysis wherever required. Risk of malignancy (ROM) assessment was calculated based on a combination of histology whenever available. All the statistical analysis were done using statistical package for social services (SPSS - version 24).

Results

This study included 240 peritoneal fluid effusion cases among which 12 (5%), 209 (87%), 8 (3.5%), 8 (3.5%), and 3 (1%) were reported as ND, NFM, AUS, SFM and MAL respectively. The age group of patients ranged between 18 to 88 years, with a mean age of 58.69 years.

The gender distribution was 107 (44.5%) females and 133 (55.5%) males, with a male to female ratio of 1.25:1. The age range among the pleural effusion and peritoneal effusion patients are listed in Tables 1 which show that there is some risk of malignancy if the average age range is above 50 years.

Table 1: Age range among various categories of peritoneal fluid

TIS category	Age range in Years
ND	26 – 88
NFM	18 – 88
AUS	44 – 86
SFM	45 – 70
MAL	56 - 75

Cytohistological Correlation: Among the 240 peritoneal effusion cases, tissue biopsy was available for all 240. Total number of cytology diagnosis availability and their histopathological diagnosis correlation are listed in Table 2.

Table 2: Histological correlation for peritoneal fluid

Cyto-Diagnostic Category	Total Number Diagnosed by Cytology	Histological Correlation
Non-Diagnostic	12	06 – 50%
Negative For Malignancy	209	129– 61.7%
Atypia of undetermined significance	8	5 – 62.5%

Suspicious For Malignancy	8	6 – 75%
Malignancy	3	3 – 100%
Total	240	158– 65.8%

ROM calculation: Risk Of Malignancy (ROM) was calculated for the cases collected in this study are 0% for ND, 0.96% for NFM, 45.45% for AUS, 71.42% for SFM and 100% for MAL. The ROM is given in the Table 3.

Table 3: ROM for s pericardial effusion cases

Cyto-Diagnostic Category	Malignant	Total samples	ROM
Non-Diagnostic	0	12	0%
Negative For Malignancy	2	209	0.96%
Atypia of undetermined significance	3	8	37.5%
Suspicious For Malignancy	6	8	75%
Malignancy	3	3	100%

1a

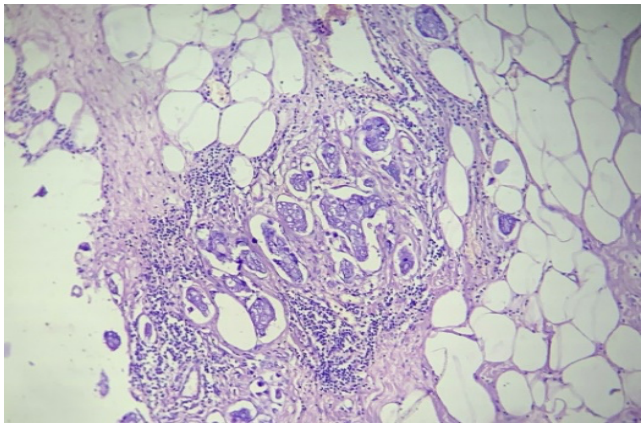

Figure 1a: Metastatic adenocarcinoma deposit in peritoneum

1b

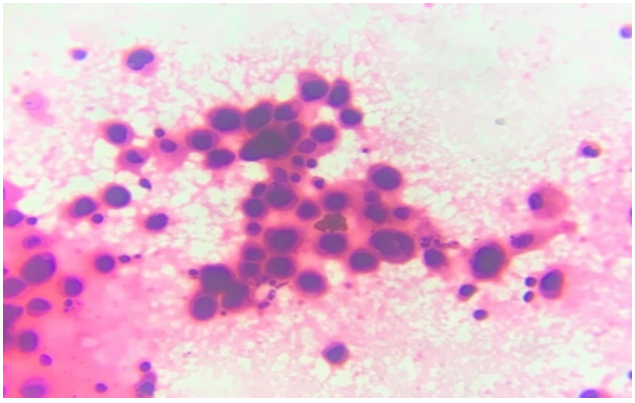

Figure 1b: Cluster of pleomorphic tumor cells with moderate to scant eosinophilic cytoplasm and hyper chromatic round to oval nuclei

Discussion

Periotoneal fluids are commonly formed in various pathological conditions and they are comparatively easy to be collected.

Hence, they are frequently used for cytopathological assessment to recognize the origin of the effusion. This study here focuses on relating the TIS reporting system which has already recognized as a solid method to correctly classify the category of peritoneal effusion, thereby finding the source. [13,14]In our setup, peritoneal biopsies are limited to cases with solid radiologic proof and clinical suspicion of malignancy and negative or indeterminate effusion cytology. In these cases, repeat paracentesis samples may lead to diagnosis, evading more interventional analysis. Particularly in cases with no previous history, morphologic assessment in concurrence with radiologic evidence and other clinical details helps in selection of IHC markers, which further assists in knowing where the origin of the tumors from and also whether there is need of subsequent biopsy or when to plan surgery.

In a study conducted by Alexandro Pergaris, the age range in peritoneal fluid cases were 16 to 93 years.[15] Overall age range among all the 240 cases was 18 to 88 years with a Mean age of 58.69 years. In Yan Li Zhu's study the overall age range in the peritoneal effusion patients were 9 years to 93 years with a mean age of 58.7 years.[16] The age range in both the studies are almost comparable to our study.

The sex distribution in our study among the 240 peritoneal fluid effusion cases presented a male preponderance. In Yan Li Zhu's and Neha Sharma's studies, there was a slight female preponderance with an M:F ratio of 1:1.04 and 1:1.6.[17] this was not in concordance with our study. The reason for male preponderance in our study may be attributed to the cases which we included during our time period of study and also comparatively less number of cases assesed.

Among the 240 peritoneal effusion cases included in this study 12 (5%), 209 (87%), 8 (3.5%), 8 (3.5%), and 3 (1%) were reported as ND, NFM, AUS, SFM and MAL respectively, on comparing our data with previous works done by Garima Rakheja and Patrizia Straccia, malignancy cases were high in their studies relatively.[18,19] Most common malignancies seen in peritoneal fluid were metastatic deposit of ovarian carcinoma in women and adenocarcinoma colon in men in our study. The same was seen in a study conducted by Alexandros Pergaris with ovaries, stomach and breast being the first three frequent malignancies commonly seen.

Risk Of Malignancy (ROM) calculated for the cases collected in this study are 0% for ND, 0.96 % for NFM, 37.5 % for AUS, 75 % for SFM and 100% for MAL, when compared to a study conducted by Farahani SJ, Chandra A and Garima Rakheja the ROM was 17%, 22%, 66%, 82% and 99% for the TIS categories ND, NFM, AUS, SFM and MAL respectively.[20,21] The main difference was seen among the ND, NFM and AUS categories, which may be due to absence of radiological details. Nevertheless, the other groups such as SFM and MAL were almost similar to the previous work done by Claudia Lobo and Alexandros Pergaris.[22]

Our results in relation to SFM and MAL is more harmonious with the ROM reported by Kundu et al. and Xu et al., namely 77.8% for SFM and 100% for MAL [23,24]. It seems that the absence of false positives with ROM of 100% in the malignant (TIS5) category is a common finding. The high PPV (100%) of serous effusion cytology is undeniable when it comes to malignancy. Inconsistencies in the reports of various studies are expected, as the study method and clinical management all over different institutions are different. Nevertheless, we consider ROM calculation more valued as it gives substantial evidence to the clinicians.

The presence of false negatives in may be due to either extremely small or large sample capacity or tumors with spread to the serosal membranes without shedding tumor cells in the fluids extracted particularly. Large sample volume can render a diagnostic challenge in cases where malignant cells are present in lesser numbers, as they can be hard to detect. In such cases, in the setting of strong clinical suspicion for malignancy, the process of centrifugation and slide preparation is repeated many times over, and multiple slides are prepared.

Conclusion

The International System (TIS) for Reporting Serous Fluid Cytopathology is very easy to employ and gives high accuracy with clear diagnostic criteria for each category. This system also makes it easy to communicate with the clinicians by employing simple terminologies. Classification of the "uncertain" category into AUS and SFM has further made it easy to diagnose and plan the treatment strategy.

References:

1. Hou T, Landon G, Stewart J, Roy-Chowdhuri S. The value of a tiered cytology diagnostic reporting system in assessing the risk of malignancy in indeterminate serous effusions. Cancer Cytopathol 2021; 129:75-82.
2. Pleural, Peritoneal and Pericardial Fluids in Comprehensive Cytopathology (3rd ed). Philadelphia, PA: WB Saunders Co; 2008. p. :515-77.
3. Gecmen C, Gecmen GG, Ece D, Kahyaoglu M, Kalayci A, Karabay CY, et al. Cytopathology of pericardial effusions: experience from a tertiary centre of cardiology. Herz. 2018; 43:543-7.
4. Lee YM, Hwang JY, Son SM, Choi SY, Lee HC, Kim EJ, et al. Comparison of diagnostic accuracy between Cell prep Plus and Thin Prep® liquid-based preparations in effusion cytology. Diagn Cytopathol. 2014; 42:384-90.
5. DeBiasi EM, Pisani MA, Murphy TE, Araujo K, Kookoolis A, Argento AC, et al. Mortality among patients with pleural effusion undergoing thoracentesis. Eur Respir J. 2015; 46:495-502.
6. Pinto D, Chandra A, Crothers BA, Kurtycz DFI, Schmitt F. The international system for reporting serous fluid cytopathology-diagnostic categories and clinical management. J Am Soc Cytopathol 2020; 9:469-77.
7. Pinto D, Chandra A, Schmitt F. The International System for Reporting Serous Fluid Cytopathology: How to Incorporate

Molecular Data in Cytopathology Reports. Journal of Molecular Pathology 2021; 2:66-76.
8. Muhammad Ahmed, He Wang. Cytopathology in Focus: Serous Fluid Cytopathology – Recent Progress and Yale's Experience. CAP Today, January 2023 issue.
9. Farahani SJ, Baloch Z. Are we ready to develop a tiered scheme for the effusion cytology? A comprehensive review and analysis of the literature. Diagn Cytopathol. 2019;47:1145–59
10. Srinivasan R, Rekhi B, Rajwanshi A, Pathuthara S, Mathur S, Jain D, et al. Indian Academy of Cytologists Guidelines for Collection, Preparation, Interpretation, and Reporting of Serous Effusion Fluid Samples. J Cytol 2020; 37:1-11.
11. Faquin WC, Rossi ED, Baloch Z, Barkan GA, Foschini MP, Kurtycz DFI, editors. Vol. 2018. Berlin: Springer Press; 2018. The Milan System for Reporting Salivary Gland Cytopathology.
12. Mezei T. Current classification systems and standardized terminology in cytopathology. Rom J Morphol Embryol. 2020; 61:655–63.
13. Shidham VB, Layfield LJ. Approach to Diagnostic Cytopathology of Serous Effusions. Cytojournal 2021; 18:32.
14. Vanden Bussche CJ, Crothers B, Chandra A, Schmitt F, Kurtycz DFI. The international system for reporting serous fluid cytopathology: The initial project survey. Cytopathology 2023; 34:191-97.
15. Pergaris A, Stefanou D, Keramari P, Sousouris S, Kavantzas N, Gogas H, et al. Application of the International System for Reporting Serous Fluid Cytopathology with Cytohistological Correlation and Risk of Malignancy Assessment. Diagnostics (Basel) 2021; 11:2223.
16. Zhu YL, Ren WH, Wang Q, Jin HZ, Guo YY, Lin DM. A retrospective analysis of serous effusions based on the newly proposed international system for reporting serous fluid cytopathology: a report of 3633 cases in an oncological center. Diagn Pathol 2022; 17:56.
17. Neha Sharma, Krishna Dubey, H. Gurubasavaraj, S.S. Hiremath. Peritoneal fluid analysis clinicopathological study. International Journal of Contemporary Medical Research 2019; 6:112-16.
18. Rakheja G, Singh M, Priyadarshnee B, Marimuthu B, Dhar L, Jain S, et al. Categorisation of peritoneal serous effusions using the International System for Reporting Serous Fluid Cytopathology-A study on gynaecological samples. Cytopathology 2023; 34:138-45.
19. Straccia P, Chiappetta M, Magnini D, Cancellieri A. Application of the International System for Reporting Serous Fluid Cytopathology (TIS): A retrospective institutional study. Cytopathology 2022; 33:305-11.
20. Farahani SJ, Baloch Z. Are we ready to develop a tiered scheme for the effusion cytology? A comprehensive review and analysis of the literature. Diagn Cytopathol 2019; 47:1145-59.
21. Chandra A, Crothers B, Kurtycz D, Schmitt F. Announcement: The International System for Reporting Serous Fluid Cytopathology. Acta Cytol 2019; 63:349-51.
22. Lobo C, Costa J, Petronilho S, Monteiro P, Leça L, Schmitt F. Cytohistological correlation in serous effusions using the newly proposed International System for Reporting Serous Fluid Cytopathology: Experience of an oncological center. Diagn Cytopathol 2021; 49:596-605.
23. Xu Y., Hu A., Wang S., Wang Q., Pan Y., Zhang S. A retrospective analysis of pleural effusion specimens based on the newly proposed International System for Reporting Serous Fluid Cytopathology. Diagn. Cytopathol. 2021; 49:997–1007.
24. Kundu R., Srinivasan R., Dey P., Gupta N., Gupta P., Rohilla M., Gupta S., Bal A., Rajwanshi A. Application of Indian Academy of Cytologists Guidelines for Reporting Serous Effusions: An Institutional Experience. J. Cytol. 2021; 38:1.