Original Article

Application of The International System for Reporting Serous Fluid Cytopathology (TIS) on Reporting Various Body Fluids: A Study from a Tertiary Care Hospital of Western India

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Abstract

Background: Serous effusion is the accumulation of fluid in body cavities due to various causes, with malignancies being one of the important contributors. The various sites from which fluid can be sent for analysis include the pleural, peritoneal, and pericardial cavities.

Materials and Methods: This was a retrospective observational study. A total of 114 fluids were studied. All received body fluid samples sent to the cytopathology section of the pathology department, including pleural and peritoneal fluids, were examined, excluding sputum and broncho-alveolar lavage fluid. Wherever available, histopathological samples from the same patient were used for correlation.

Results: A total of 114 fluids were studied. Histopathological correlation was available in 30 cases. Epithelial malignancy, including adenocarcinoma, was the most common malignancy involving pleural effusion and peritoneal fluid.

Conclusion: The international system of reporting is a user-friendly framework that can be easily applied to effusion fluid for better patient management and effective communication with clinicians. Due to the well-documented outcomes from adopting uniform cytology terminology for other organ systems, we recommend the use of this classification and believe its use will be paramount in improving diagnostic yield in effusion cytology.

Keywords:

Serous fluid, Classification, Effusion, Cytopathology, Malignancy

Introduction

Serous effusion is the accumulation of fluid in the body cavities due to various causes, with malignancies being one of the important contributors. Cytological examination of an effusion sample is a preliminary and minimally invasive method for diagnosing body fluids. The various sites from which fluid can be sent for analysis include the pleural, peritoneal, and pericardial cavities [1].

Serous effusions result from an imbalance between the production and reabsorption of fluid in the body cavities. Their etiology

ranges from infective and autoimmune disorders to neoplastic conditions [2].

Although the majority of effusions are due to reactive and non-neoplastic causes, cancer can also be a cause of effusion as a manifestation of advanced disease. Detecting neoplastic cells in effusion specimens in most clinical settings is often associated with advanced-stage cancer, which is usually incurable. In addition to malignancies, effusions may result from hemodynamic conditions such as heart failure, hypoalbuminemia, cirrhosis, or inflammatory processes, including parasitic infestations and bacterial, fungal, or viral infections. Other non-neoplastic causes include collagen diseases [3].

Among malignant effusions, adenocarcinomas are the most common cause of metastatic cancers, though almost any type of malignancy—including melanomas, hematopoietic neoplasms, sarcomas, and mesotheliomas—may involve serous cavities. The interpreter must be aware of the wide range of cytomorphologic appearances of reactive mesothelial cells in effusion fluids [3].

It is essential to understand these and other nuances related to effusion fluid cytology. Awareness of potential pitfalls during various stages—from processing to application of ancillary studies—would increase diagnostic accuracy and minimize atypical interpretations and false positives [3].

Serous effusions are easy to drain and can provide important diagnostic information. However, the reported diagnostic efficacy of these specimens has not been uniform across different laboratories [4]. To standardize practices, the International System for Reporting Serous Fluid Cytology (TIS) was developed in accordance with best international practices, the most up-to-date reported data, and expert consensus [4]. The classification provides an actionable framework for using immunohistochemical and molecular testing in effusion samples, particularly in cases deemed atypical or suspicious for malignancy.

For diagnostic purposes, these tests may be employed to distinguish between primary and secondary neoplasms, to confirm a diagnosis of malignant mesothelioma versus reactive mesothelial hyperplasia, and to accurately classify and determine the primary location of metastasis. Therapeutic and diagnostic molecular tests may also be used to evaluate potential therapeutic targets [5].

Cytology has shown high sensitivity for the diagnosis of malignancy in serous effusions. Nevertheless, a diagnostically gray area persists worldwide, including cases of atypia and those suspicious for malignancy, similar to other areas of cytology. The definition of inadequate and benign samples is also critical [6]. Cytological examination is a well-accepted method for evaluating the cellular components of serous effusions. It has gained increasing acceptance in clinical medicine to such an extent that a positive diagnosis is often considered definitive, preventing unnecessary exploratory surgery and aiding in the staging, prognosis, and management of patients with malignancies.

Materials and Methods

A retrospective study was conducted over one and a half years, from January 2022 to July 2023, at the Department of Pathology, GMERS Medical College and Hospital, Gotri, Vadodara. A total of 114 body fluids were studied. All received body fluid samples, including pleural and peritoneal fluids, excluding sputum and bronchoalveolar lavage fluid, were studied in the cytopathology section of the pathology department.

Demographic data, clinical history, and other relevant information were retrieved. The received fluid samples were centrifuged, and smears were prepared. Smears were stained using Hematoxylin & Eosin stain, Papanicolaou stain, and May-Grünwald Giemsa stain. Special stains were performed wherever applicable. Histopathological correlation was available for 30 fluids, and correlation was done.

These slides were then examined under a light microscope for cytological and histological diagnoses. Cytomorphological and histopathological evaluations of the smears were performed, and reporting was done. The smears were classified according to the International Classification of Serous Fluid Cytopathology (TIS) into the following categories: Category: Non-diagnostic (ND), Category: Negative for malignancy (NFM), Category: Atypia of undetermined significance (AUS), Category: Suspicious for malignancy (SFM) and Category: Malignant (MAL)

Ethics: This was a retrospective observational study with no intervention. The study was undertaken after receiving approval from the Institutional Ethics Committee.

Results

A total of 114 effusion samples were received over 1.5 years and included in the present study. Of the 114 effusions, 70 (61%) were from males and 44 (39%) from females. The majority were pleural fluids (62, 54%), followed by peritoneal fluids (52, 46%). The patients' ages ranged between 3 and 98 years, with a mean age of 50.5 years (Table 3). Epithelial malignancy, including adenocarcinoma, was the most common type of malignancy involving pleural effusion and peritoneal fluid.

The received fluids were classified based on the International Classification of Serous Fluid Cytology into five categories (Table 1). Out of the 114 fluids, 5 (4.4%) were non-diagnostic (Figure 1), 97 (86%) were negative for malignancy (Figure 2), 2 (1%) had atypia of undetermined significance (Figure 3), 3 (2.6%) were suspicious for malignancy (Figure 4), and 7 (6%) were malignant effusions (Figure 5). Histopathological correlation was performed whenever available.

Histopathological follow-up was available for 30 fluids, including 16 peritoneal and 14 pleural fluids. Risk of malignancy (ROM) calculation was performed based on the available histology records. A total of 84 cases were lost to follow-up, so the ROM was assessed for the remaining 30 cases. The ROM was 33%, 22%, 50%, 67%, and 100% for the ND, NFM, AUS, SFM, and MAL categories, respectively.

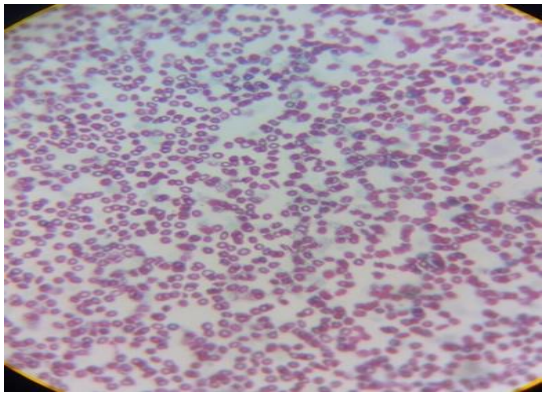

Figure 1: Non Diagnostic :Bloody smear (4x,PAP stain)

Discussion

Serous effusions result from an imbalance between the production and reabsorption of serous fluid. Their presence is always considered pathologic, as they indicate a wide range of diseases, from benign to malignant.

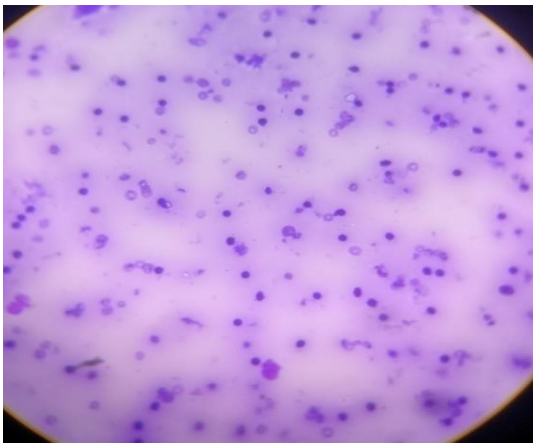

Figure 2: Negative for Malignancy :Lymphocytic effusion (10x, MGG stain)

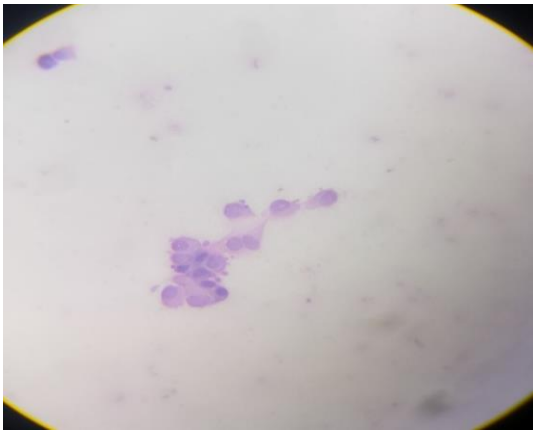

Figure 3: Atypia of undetermined significance(10x, H & E stain)

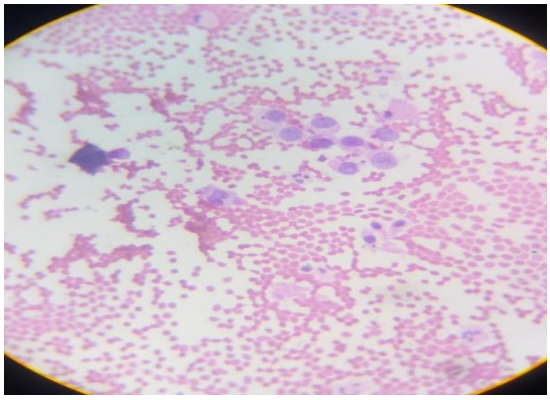

Figure 4: Suspicious for Malignancy (40x, H&E stain)

In this study, received fluids were categorized based on The International System for Reporting Serous Effusion Cytology (TIS). The study shows a large number of serous effusions were received, contributing significantly to the annual workload of the cytopathology lab. Clinicians use cytology to diagnose or exclude malignancy, and it also plays an important role in further clinical workup and therapeutic management. During the 1.5-year study, 62 pleural and 52 peritoneal effusions were processed, and

reevaluation with TIS categories was done. Pleural effusions were classified as 3.2% ND, 81% NFM, 1.6% AUS, 3.2% SFM, and 9.6% MAL. Peritoneal effusions were classified as 5.7% ND, 90% NFM, 2% AUS, 2% SFM, and 2% MAL.

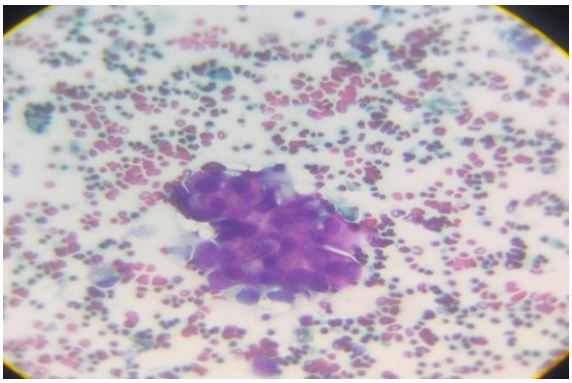

Figure 5: Malignant– Adenocarcinoma (40x, H&E, PAP stain)

Table 1: Classification category wise distribution

	ND	NFM	AUS	SFM	MAL	TOTAL
PLEURAL	02 (3.2%)	50 (81%)	01 (1.6%)	02 (3.2%)	06 (9.6%)	62 (100%)
PERITONEAL	03 (5.7%)	47 (90%)	01 (2%)	01 (2%)	01 (2%)	52 (100%)
TOTAL	05	97	02	03	07	114

Table 2: Risk of malignancy (ROM%)

Category and No of cases	Follow-up available	malignant	benign	Risk of malignancy (ROM)
ND - 05	03	01	02	33%
NFM -97	18	04	14	22%
AUS- 02	02	01	01	50%
SFM - 03	03	02	01	67%
MAL - 07	04	04	00	100%
TOTAL: 114	30	12	18	-

Table 3: Age wise distribution

Age Group	ND	NFM	AUS	SOM	MAL	TOTAL
0-10	-	01	-	-	-	01
11-20	01	07	-	-	-	08
21-30	02	25	-	-	-	27
31-40	01	25	-	-	01	27
41-50	01	15	-	01	-	17
51-60	-	12	01	-	01	14
61-70	-	11	01	02	03	17
71-80	-	01	-	-	01	02
81-90	-	-	-	-	-	00
91-100	-	-	-	-	01	01
TOTAL	05	97	02	03	07	114

Our results are compatible with other studies, which also include pleural and peritoneal effusions [9][10][11][12]. The most common malignancy includes metastatic epithelial malignancy, most commonly adenocarcinoma, involving both pleural and peritoneal effusions. In our hospital, pleural and peritoneal biopsies are confined to cases with strong radiological evidence and strong clinical suspicion of malignancy or indeterminate effusion cytology. These biopsies are used for histological correlation and evaluation of the risk of malignancy (ROM). ROM was 33%, 22%, 50%, 67%, and 100% for ND, NFM, AUS, SFM, and MAL categories, respectively.

In a recent meta-analysis on serous effusion cytology, the mean ROM for cytological diagnoses of ND, NFM, AUS, SFM, and MAL was 17.4%, 20.7%, 65.9%, 81.8%, and 98.9%, respectively [9]. A comprehensive review by Farahani and Baloch [9] reported a mean ROM for all types of serous effusions of 17.4%, 20.7%, 65.9%, 81.8%, and 98.9% for TIS categories.

Our results are compatible with these studies. It is concluded that the absence of false positives with a ROM of 100% for MAL is a universal finding. There are chances of discrepancies in the reports of different studies, which are inevitable due to the variable study and clinical material used across different studies. However, we believe that the assessment of ROM will provide more valuable information for clinicians for further therapeutic management.

Conclusion

From our study, we conclude that the international system provides basic principles for the laboratory handling of serous effusion specimens and offers adequacy criteria. It also establishes standardized reporting terminology with well-defined criteria for each diagnostic category. Careful morphological diagnosis, along with ancillary tests, can provide an accurate diagnosis of effusion. The international system of reporting is a user-friendly approach that can be easily applied to effusion fluid for better patient management and more effective communication with clinicians. Given the well-documented outcomes of adopting uniform cytology terminology for other organ systems, we recommend the use of this classification and believe its adoption will be paramount to improving diagnostic yield in this area of cytology.

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Competing Interests: There are no conflicts of interest in this study.

References

1. Kolte S, Zaheer S, Aden D, Ranga S. Application of the international system for reporting serous fluid cytopathology on reporting various body fluids; experience of a tertiary care hospital. Cytojournal. 2022;19:52.
2. Ahuja S. The international system for reporting serous fluid cytopathology along with diagnostic pitfalls of serous effusion cytology. 2022.
3. Shidham VB, Layfield LJ. Approach to diagnostic cytopathology of serous effusions. Cytojournal. 2021 Dec 6;18:32.
4. 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 Nov-Dec;9(6):469-77.
5. Pinto D, Chandra A, Schmitt F. The International System for Reporting Serous Fluid Cytopathology: How to Incorporate Molecular Data in Cytopathology Reports. J Mol Pathol. 2021;2(2):66-76.
6. 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 Nov 28;11(12):2223.
7. Sachan R, Gupta A, Awasthi P. Application of international system for reporting serous fluid cytology in effusion samples—a prospective study in an oncology setting. 2023 Sep-Oct;351-61.

8. Lee YM, Hwang JY, Son SM, Choi SY, Lee HC, Kim EJ, et al. Comparison of diagnostic accuracy between CellPrepPlus and ThinPrep liquid-based preparations in effusion cytology. Diagn Cytopathol. 2014;42:384-90.
9. Farahani SJ, Baloch Z. Are we ready to develop a tiered scheme for effusion cytology? A comprehensive review and analysis of the literature. Diagn Cytopathol. 2019;47:1145-59.
10. 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.
11. Lobo C, Costa J, Petronilho S, Monteiro P, Leca L, Schmitt F. Cytohistological correlation in serous effusions using the newly proposed International System for Reporting Serous Fluid Cytopathology: experience of an oncologic center. Diagn Cytopathol. 2021;49:596-605.
12. Kundu R, Srinivasan R, Dey P, Gupta N, Gupta P, Rohilla M, et al. Application of Indian Academy of Cytologists Guidelines for Reporting Serous Effusions: An Institutional Experience. J Cytol. 2021;38:1.
13. Ebata T, Okuma Y, Nakahara Y, Yomota M, Takagi Y, Hosomi Y, et al. Retrospective analysis of unknown primary cancers with malignant pleural effusion at initial diagnosis. Thorac Cancer. 2016;7(1):39-43.
14. Sears D, Hajdu SI. The cytologic diagnosis of malignant neoplasms in pleural and peritoneal effusions. Acta Cytol. 2017;31:85-97.
15. Gecman 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.