Section: Pathology

Original Research Article

APPLICATION OF THE INTERNATIONAL SYSTEM FOR REPORTING SEROUS FLUID CYTOPATHOLOGY AND ASSESSMENT OF THE RISK OF MALIGNANCY - AN OBSERVATIONAL STUDY

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ABSTRACT

Background: The International system for reporting serous fluid cytopathology is a very effective weapon in the hands of pathologists and clinicians to become more comprehensive and approachable in cases of serous fluid related diseases. The International System classifies serous fluid cytopathology in five groups: 1. Non –Diagnostic, 2. Negative for malignancy, 3. Atypia of unknown significance, 4. Suspicious for malignancy, 5. Malignant.

Materials and Methods: In Pathology department of Santosh medical college, Ghaziabad we took total 200 cases of pleural and ascitic fluid from 2022. Cell blocks were prepared wherever needed and immunohistochemistry was also applied as per need.

Results: Out 200 cases, 77 were pleural fluids and 123 were ascitic fluids. Out of which 0.5% cases were in non-diagnostic, 85.5% cases were in Negative for malignancy, 6% cases were in Atypia of unknown significance, 5% cases were in Suspicious for malignancy, and 3% cases were in Malignant category. ROM was also calculated which turned out to be 0% in Non –Diagnostic, 0% in Negative for malignancy, 0% in Atypia of unknown significance, 20% in Suspicious for malignancy, and 100% in Malignant category. For calculation of risk of malignancy (ROM), histopathology and radiological tools clinical follow up were used. Our results justify the use of TIS classification for reporting serous fluid cytopathology as a connecting platform for clinicians and pathologists for benefit of patients.

Conclusion: The TIS system proposed a tiered scheme which places the effusion cytology into well-defined categories, and therefore has lesser chances of false-positive and false-negative cases. Despite there being heterogenicity and morphological overlap between different categories, TIS caters to the need of cytopathologists because beside being a simple, easy, and user-friendly system, it has the benefit of risk stratification and ROM for each category and it provides a standardized terminology for better communication among pathologists and clinicians.

Keywords: Serous fluid, pleural fluid, ascitic fluid, TIS, cancer, cytology, cancer.

INTRODUCTION

Serous effusions, both in the pleural and the peritoneal cavities, result from an imbalance between the production and reabsorption of serous fluid. Their presence is always considered a pathologic condition, and they reflect a wide range of diseases from benign to malignant.[1] When handled and analyzed properly, effusion specimens can facilitate a prompt and accurate diagnosis that has a significant effect on clinical care.[2] Patient care is guided by the accurate identification and type of tumor cells in effusion samples. However, in the event of non-malignant effusions, exclusion of malignancy permits appropriate therapy.[3]

In cytology samples serous fluids are very common that can predict a wide range of diseases and lend themselves to broad spectrum of investigations which can be microscopy, chemical analysis, cell count, cultures, and analysis for biomarkers and immunomarkers.[4]

Many times, diagnostic uncertainty rises because of poor sampling or quantitatively less samples obtained in labs. Before ISRFC atypia and uncertain for malignancy, these two words used quite oftenly.[5]

The international system for serous fluid cytopathology was introduced to give common platform to pathologists for categorization of serous fluid cytopathology.[6]

The International Academy of Cytology (IAC) and American Society of Cytopathology (ASC) sponsored a team of experts to develop a standardized system for serous effusion cytology reporting called the International System for Reporting Serous Fluid Cytology (TIS), following in the footsteps of other nomenclature systems for reporting cytology. TIS seeks to provide a framework for reducing reporting variability based on the most recent research and professional consensus.[2] The International System for Reporting Serous Fluid Cytopathology (TIS) classifies serous effusions into five categories: non-diagnostic (ND), negative for malignancy (NFM), atypia of unknown significance (AUS), suspicious for malignancy (SFM) and malignant (MAL).[3] The cytology of effusions is not restricted to morphology. Microscopic examination is followed by special stains, immunohistochemical stains or flowcytometry, according to the initial morphologic findings. Furthermore, the site of origin of the metastatic malignant effusion in patients without or even, occasionally, with a history of malignancy has to be clarified.[3]

Cytological examination of serous fluid is very important in diagnosing malignant cases, but negative result does not rule out malignancy7.

Aims and objectives: Present study was done with the following aims and objectives-

1. To study cytological findings of serous fluid and classify them into the international system for reporting serous fluid cytopathology.
2. Provide an estimate of the risk of malignancy (ROM) for each category.
3. To categories malignant effusion on the basis of special stain and immunocytochemistry.

MATERIALS AND METHODS

The study was conducted in a tertiary care centre on fluids received in the pathology department for cytological examination. Patient details including relevant clinical and radiological data was also collected.

Received samples were processed within 2 hrs of receipt. The specimens were centrifused at 1500 rpm for 10 min, the supernatant was decanted and smears were prepared from the sediment pellet. In a subset of cases where sample quantity was sufficient cell blocks were also prepared. Cell blocks were prepared by formalin cell block technique by fixing the cell pellet with 10% formalin. The cell pellet was wrapped in a filter paper and was processed and further embedded in paraffin wax. A panel of selected immunohistochemical markers was analysed as per the need of the case. All cases were reclassified according to the TIS system into 5 categories.

Statistical analysis was conducted using Microsoft excel software 2016. To calculate ROM, malignancy was confirmed by cytology, radiology, cell block, immunohistochemistry.

Inclusion Criteria: All pleural and peritoneal fluid samples received for cytological examination at pathology laboratory of tertiary care center in Ghaziabad.

Exclusion Criteria: All fluids other than pleural and peritoneal fluids and patients under follow up of known diseased cases.

RESULTS

Total number of males participated in this study was 107 and number of female participants was 93. Average age involved in the study was 58 yrs. Average age was higher in malignant category while lowest in negative for malignancy.

Out of 200 cases 77 cases were from pleural fluid. Two cases from pleural fluid turned out to be malignant.

Out of total 200 cases 123 cases were from ascitic fluid. Out of these 4 ascitic fluid cases were found to be malignant.

171 cases (85.5%) were negative for malignancy. All cases were in follow-up clinically.

Ancillary techniques used

12 cases (06%) were found in atypia of unknown significance category. Immunocytochemistry was applied on this case; all cases were turned out to be benign.

10 cases (5%) were in suspicious for malignancy category. For all these cases Immunocytochemistry was applied. In two ascitic fluid cell blocks Cytokeratin and Calretinin were applied. Out of these two in 1 case Immunocytochemistry came insufficient for reporting. In other case Immunocytochemistry turned out to be inflammatory.

Out of these 10 cases of suspicious for malignancy, 2 pleural fluid case turned out to be TTF1 positive which was suspected to be adenocarcinoma of lung. On H&E it was shown as Adenocarcinoma of lung. These two patients were male and they were cigarette smokers.

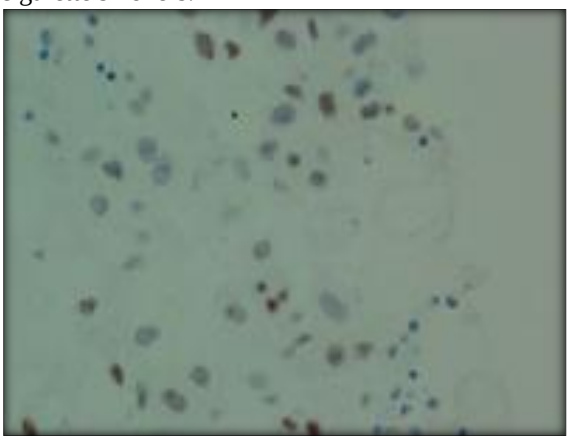

Figure 1: Pleural fluid positive for TTF1(lung adenocarcinoma) in cell block

Risk of Malignancy

ROM was calculated on the basis of clinical findings, radiological findings, and histological findings wherever applicable.

So, in our Non-diagnostic category ROM turned out to be 0%, In Negative for malignancy category risk of malignancy came to be 0%, in atypia of unknown significance ROM was 0%, in suspicious for malignancy category ROM turned out to be 20%. In malignant category ROM turned out to be 100%. Out of 171 cases of negative for malignancy category ,24 cases (14%) were turned out to be tubercular. CBNAT and other ancillary techniques were definitive in these cases.

Table 1: Category wise distribution of cases

DIAGNOSTIC CATEGORY	ND	NFM	AUS	SFM	MAL	TOTAL
NUMBER OF PATIENTS/PERCENTAGE	1/ 0.5%	171/85.5%	12/ 6%	10/ 5%	6/ 3%	200
OPD/IPD	1/0	60/111	4/8	3/7	2/4	70/130
NUMBER OF MEN/WOMEN	1/0	92/79	6/6	6/4	2/4	107/93
AVERAGE AGE	52	58	63	58	59	58
CELL BLOCK SLIDES	0	0	12	10	06	28
SEROUS EFFUSION SOURCE						
PLEURAL	01	60	7	7	2	77
ASCITIC	0	111	5	3	4	123
VOLUME (median range)	49.5	61	72	58.5	65.5	61.3

ND-Non-diagnostic, NFM- Negative for malignancy, AUS-Atypia of unknown significance, SFM- Suspicious for malignancy, MAL- Malignant

Table 2: Calculation of risk of malignancy in each category

AUS/SFM	No.(%)	Surgical pathology /clinical diagnosis Benign Malignant	Risk of malignancy (ROM)
NON- DIAGNOSTIC	1	1	0%
NFM	171	171	0%
AUS	12	12	0%
SFM	10	08 02(after ICC) transferred to malignant category	20%
MAL	06	00 06+02	100%
TOTAL	28	06+02	

DISCUSSION

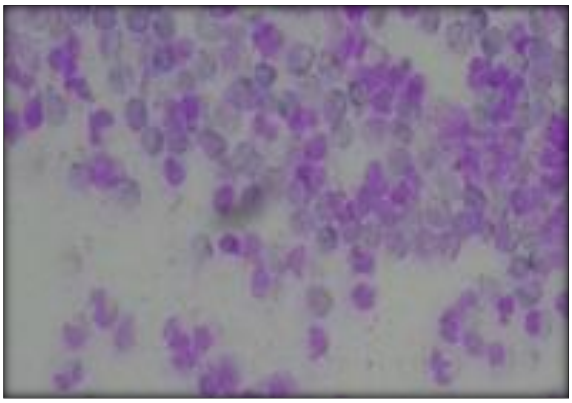

Figure 2: Malignant ascitic fluid

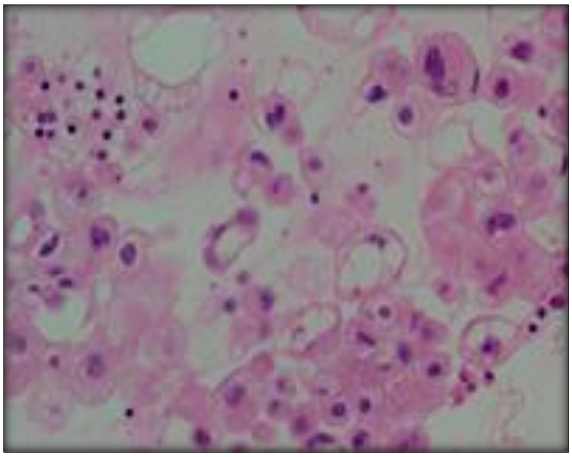

Figure 3: Malignant ascitic fluid

Tis Classification

Non-Diagnostic

Current study showed 0.5% cases in non-diagnostic category which was in concordance with studies done by Alexandros Pergaris et al,[8] (0.57%), Yan Li Zhu et al,[9] (0.5%), Ahuja et al,[10] (0.4%). Yang H. et al,[11] (0.4%), H.Yang et al (0.4%). Mostly in all the studies, the material was insufficient or the technique was poorly performed.

Negative For Malignancy

Our study showed 85.5% cases in negative for malignancy category and this correlated with several other studies done by Daniel et al,[1] (72.29%), Alexandros et al,[8] (81.44%), Ahuja et al 10(76.4%), Ritu kundu et al,[12] (71.2%).

Atypia of Unknown significance

These serous fluids showed cellular smear with clusters of cells showing mild atypia in the form of non-significant nuclear pleomorphism, overlapping of nucleus, with prominent nucleoli occasionally. In our study 6% cases were found in this category which was similar to studies done by H. Yang et al,[11] (4.5%), Ahuja S. et al,[10] (7.5%).

Suspicious for Malignancy

In current study 10 cases were found to be suspicious for malignancy in which 2 cases were pleural fluid with haemorrhagic background. In these 2 cases Immunocytochemistry was applied and TTF1 came positive, these 2 cases were diagnosed as lung adenocarcinoma and they shifted to malignant category after applying immunocytochemistry. In 1 other case from ascitic fluid PAN Cytokeratin and Calretinin was applied and these came out to be inflammatory, this case was shifted to atypia of unknown significance category after applying immunocytochemistry. One more case from pleural fluid was applied with PAN Cytokeratin and Calretinin and this turned out to be negative.

In current study 5% cases were in suspicious for malignancy category which was in concordance with studies done by Daniel et al,[1] (4%), and Ritu kundu et al,[12] (4.4%).

Malignant

This category included 6 cases (3%). The findings on serous fluid cytology were hypercellular, canon ball like appearance with loss of window. These were enlarged cells with hyperchromatic nucleus, increased N:C ratio, moderate to marked nuclear pleomorphism, prominent nucleoli, and irregular nuclear membranes. Two cases were of lung adenocarcinoma, and four cases were from adenocarcinoma of peritoneal origin.

Table 3: Correlation of ROM with other similar studies

Author	Specimen type	year	Total cases	ROM				
				ND	NFM	AUS	SFM	MAL
Current Study	PF+AF		200	0%	0%	0%	20%	100%
Yan Li et al	PF+AF+ Peri cardF	2021	3588	38.5%	28.6%	52.1%	99.4%	100%
Daniel Pinto et al	PF	2021	350	40%	20.16%	42.86%	78.57%	100%
Exandros Pergaris et Al	PF AF	2020	528 500	0% 16.6%	5.3% 9%	33.33% 38.46%	93.33% 83.33%	100% 100%
H.Yang et Al	PF+AF+PeriF	2022	2103	50%	24.9%	36.8%	89%	100%
Yang H.et Al	All Serous Fluid	2022	2103	50%	24.9%	36.8%	89%	100%
Yan Li Zhu et al	All Serous Fluid	2021	3633	38.5%	28.6%	52.1%	99.4%	100%
Ahuja S.et al	PF AF	2020	831 457	0% 50%	2.1% 4.8%	33.3% 22.2%	94.1% 83.3%	100% 100%

Ritu kundu et al	All Serous Fluid		1340	20%	16.7%	50%	94.4%	100%

Abbreviations: ND- non diagnostic, FM negative for malignancy, AUS atypia of undetermined significance, FM suspicious of malignancy, AL malignancy pleural fluidal ascitic fluid, Peri F pericardial fluid.

CONCLUSION

The TIS system proposed a tiered scheme which places the effusion cytology into well-defined categories, and therefore has lesser chances of false-positive and false-negative cases. Despite there being heterogenicity and morphological overlap between different categories, TIS caters to the need of cytopathologists because beside being a simple, easy, and user-friendly system, it has the benefit of risk stratification and ROM for each category and it provides a standardized terminology for better communication among pathologists and clinicians.

REFERENCES

1. Pinto D, Cruz E, Branco D, Linares C, Carvalho C, Silva A, Chorão M, Schmitt F. Cytohistological correlation in pleural effusions based on the international system for reporting serous fluid cytopathology. Diagnostics. 2021 Jun 20;11(6):1126.
2. Ali, S.Z.; Cibas, E.S. The Bethesda System for Reporting Thyroid Cytopathology: Definitions, Criteria, and Explanatory Notes; Springer: Berlin/Heidelberg, Germany, 2017. [Google Scholar]
3. Chandra, A.; Crothers, B.; Kurtycz, D.; Schmitt, F. Announcement: The International System for Reporting Serous Fluid Cytopathology. Acta Cytol. 2019, 63, 349–351. [Google Scholar] [CrossRef][Green Version],,,,,,,
4. Michael CW. Serous fluid cytopathology: Past, present, and future. Diagn Cytopathol. 2021 May;49(5):577-581. doi: 10.1002/dc.24663. Epub 2021 Feb 26. PMID: 33634959 (4)
5. Chandra A, Schmitt F. Cytologic diagnosis of "atypical" in serous fluid cytopathology. Approach of the international system for reporting serous fluid cytopathology. Diagn Cytopathol. 2022 Apr;50(4):208-211. doi: 10.1002/dc.24864. Epub 2021 Sep 9. PMID: 34499418.
6. Crothers BA, Chandra A. Proceedings of the American Society of Cytopathology Companion Session at the 2019 United States and Canadian Academy of Pathology Meeting Part 1: towards an International System for Reporting Serous Fluid Cytopathology. J Am Soc Cytopathol. 2019 Nov-Dec;8(6):362-368. doi: 10.1016/j.jasc.2019.08.006. Epub 2019 Sep 28. PMID: 31672335.
7. Ehya H. Effusion cytology. Clin Lab Med. 1991 Jun;11(2):443-67. PMID: 1873966.
8. Pergaris A, Stefanou D, Keramari P, Sousouris S, Kavantzas N, Gogas H, Mikou P. Application of the International System for Reporting Serous Fluid Cytopathology with cytohistological correlation and risk of malignancy assessment. Diagnostics. 2021 Nov 28;11(12):2223.
9. 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. Diagnostic Pathology. 2022 Dec;17(1):1-1.
10. Ahuja S, Malviya A. Categorisation of serous effusions using the International System for Reporting Serous Fluid Cytopathology and assessment of risk of malignancy with diagnostic accuracy. Cytopathology. 2022 Mar;33(2):176-184. doi: 10.1111/cyt.13089. Epub 2021 Dec 28. PMID: 34913541
11. Yang H, Zhu J, Wang P. Application of the International System for Reporting Serous Fluid Cytopathology (ISRSFC) in reporting serous effusion: A retrospective study. Medicine (Baltimore). 2023 Oct 27;102(43):e35707. doi: 10.1097/MD.0000000000035707. PMID: 37904355; PMCID: PMC10615507.
12. 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 Jan-Mar;38(1):1-7. doi: 10.4103/JOC.JOC_224_20. Epub 2021 Feb 17. PMID: 33935385; PMCID: PMC8078616.