

## The International System for Reporting Serous Fluid Cytopathology along with Diagnostic Pitfalls of Serous Effusion Cytology

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### Description

Serous effusions result from an imbalance between production and reabsorption of fluid in the peritoneal and pleural cavities. Their etiology ranges from infective, autoimmune to neoplastic disorders. Ascites may be the first presentation of malignancy especially in ovarian and gastrointestinal malignancies [1-4].

Serous effusion cytology is a minimally invasive, cost effective and rapid test for evaluation of malignancy and further patient management. In addition to microscopic examination and special stains, ancillary techniques like immunocytochemistry, flowcytometric immunophenotyping and molecular analysis can also be performed for further typing of malignant effusions [5]. The International System for Reporting Serous Fluid Cytopathology (ISRSFC) was developed to provide a uniform reporting format for interpretation of serous effusions [6].

### Pitfalls of serous effusion cytology

Majority of false positives in effusion cytology are due to reactive mesothelial proliferations which may show morules/mulberry like clusters with multi nucleation, degenerative cytoplasmic vacuoles and signet ring morphology thus mimicking the three dimensional clusters of adenocarcinoma. However, the intercellular windows seen in the mesothelial cells are absent in clusters of adenocarcinoma. Moreover, metastatic adenocarcinoma cells display eccentric nuclei while mesothelial cells demonstrate blebs with central nuclei. The demonstration of a second foreign population apart from inflammatory and mesothelial cells in effusion fluids is consistent with a metastatic neoplasm [6-8]. However, confirmation and further typing is needed using ancillary techniques.

### The International System for Reporting Serous Fluid Cytopathology (ISRSFC)

The ISRSFC was developed by International Academy of Cytology and American Society of Cytopathology. This standardized reporting format was evolved to develop evidence based diagnostic system, provide diagnostic categories with well-defined Risk of Malignancy enabling better clinical management and enhanced professional communication. It also aims to improve diagnostic yield of serous effusion cytology and increase inter observer agreement [6].

The diagnostic categories of ISRSFC are as follows: i. Non Diagnostic- Although no well-defined adequacy criteria are defined, a minimum of 50-75 ml fluid volume with well preserved, well spread, adequately stained cells are needed for interpretation. Any specimen

which is acellular, degenerated, and haemorrhagic and provides no diagnostic information in appropriate clinical context is deemed to be non-diagnostic in absence of any atypical cell. A repeat sample is suggested in the above scenario.

ii. Negative for Malignancy- Any specimen comprising of only benign elements like mesothelial cells, inflammatory cells, histiocytes with minimal atypia are classified under this category. An adequate follows up and clinical correlation is advised with this diagnosis.

iii. Atypia of Undetermined Significance- It represents a gray zone where specimens lack qualitative or quantitative cytological features to be accurately diagnosed as benign or malignant. This includes low cellularity effusions with atypical cells demonstrating mild to moderate nuclear pleomorphism, slightly increased nucleocytoplasmic ratio and prominent nucleoli. It needs to be followed up by ancillary testing and histopathological correlation.

iv. Suspicious for Malignancy- It is defined as specimens with cytological features of malignancy but insufficient qualitatively or quantitatively to make a definite diagnosis of malignancy. The accurate diagnosis in the above scenario is usually limited by obscuring artefact, low cellularity or abundant mucinous material. It needs to be followed by ancillary testing and biopsy.

v. Malignant- Specimen with cytomorphological features which are diagnostic of a primary (malignant mesothelioma) or secondary neoplasm (metastasis) are classified in this category. The subtyping is done based on immunocytochemistry in Figure 1, flow cytometry or molecular analysis to guide further treatment protocols.

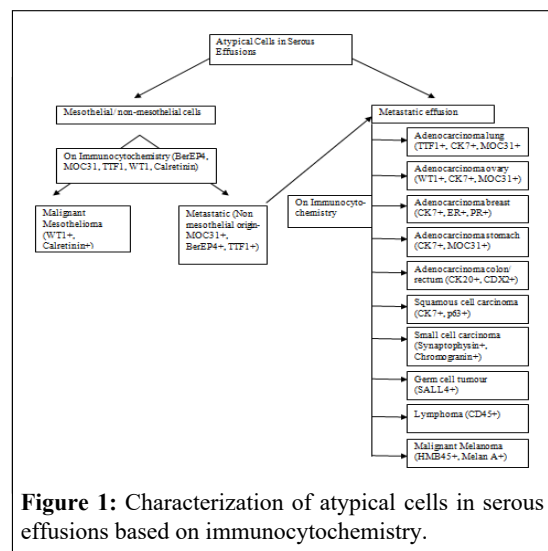


Figure 1: Characterization of atypical cells in serous effusions based on immunocytochemistry.

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## Conclusion

In this group of diseases, immune complexes circulate in the blood as soluble form. They cross through the vascular wall and locally trigger an inflammatory reaction by binding the complement, particularly the C3 fraction. The complement attracts polymorphous leukocytes and trigger lesions of vasculitis. The newly proposed ISRSFC provides a standardized reporting platform with better reproducibility of reports and better communication between clinician and pathologist, similar to the Milan System for Reporting Salivary Gland Cytopathology and Bethesda system for reporting thyroid Cytopathology.

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