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Diagnostic Challenges in Serous Effusion Cytology: A One-Year Retrospective Study in a Resource-Limited Tertiary Care Centre

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Abstract

Serous effusion cytology plays a crucial role in the initial evaluation of pleural, peritoneal, and pericardial fluids, particularly in differentiating benign, reactive, and malignant conditions. However, diagnostic accuracy in low-resource settings remains challenging because of limited availability of advanced ancillary techniques such as cell block, immunocytochemistry (ICC), and molecular tests. This retrospective study aimed to assess the diagnostic challenges encountered in serous effusion cytology at a resource-limited tertiary care centre over a one-year period. A total of 360 serous effusion samples were analysed, including pleural (62%), peritoneal (34%), and pericardial fluids (4%). Routine cytological smears stained with Pap and MGG were evaluated, and cell block examination was performed when possible. Cases were classified into non-diagnostic, benign, atypical, suspicious for malignancy, and malignant, following recent international reporting systems. The study revealed that while serous effusion cytology remains invaluable for early tumour detection, interpretation is often hampered by inadequate samples, paucicellular smears, degenerative changes, and overlapping cytomorphological features between reactive mesothelial cells and malignant cells. Inadequate cellularity accounted for 12% of cases, while 8% fell into the atypical category due to limited morphology. Malignancy was confirmed in 26% of cases, with metastatic adenocarcinoma being the most common type. Lack of ancillary testing significantly contributed to interpretative difficulty in 18% of challenging cases. Findings emphasize that even though cell block can enhance diagnostic clarity, its use was restricted due to infrastructural limitations. The study concludes that serous effusion cytology is a powerful, minimally invasive diagnostic tool, but its accuracy relies heavily on sample quality, availability of cell blocks, and experience of cytopathologists. Strengthening laboratory infrastructure and training can improve diagnostic yield and reduce false negatives in resource-limited centres.

Keywords: Serous effusion, Cytology, Cell block, Malignancy, Diagnostic challenges

Introduction:

Serous effusion cytology is a widely used diagnostic technique for evaluating pleural, peritoneal, and pericardial fluids. It is particularly valuable because it is minimally invasive, cost-effective, and provides critical diagnostic information that can guide clinical management, especially in suspected malignancies (2). Effusions arise from a wide range of conditions including infections, inflammatory disorders, liver diseases, renal disorders, cardiac failure,

and neoplasms. Among malignant effusions, metastatic adenocarcinoma remains the most frequent cause, whereas mesothelioma and hematolymphoid malignancies represent less common but diagnostically significant entities (3). The diagnostic process, however, poses considerable challenges, especially in settings with limited diagnostic infrastructure. Morphological overlap between reactive mesothelial proliferation and malignant cells is one of the most frequently encountered dilemmas (4). Reactive mesothelial cells can mimic malignant features such as nuclear enlargement, irregular nuclear membranes, prominent nucleoli, and cytoplasmic vacuolation. Conversely, some adenocarcinomas may display deceptively bland appearances, leading to false-negative interpretations (5). In recent years, The International System for Reporting Serous Fluid Cytopathology (TIS) has provided a standardized framework to improve consistency in reporting (6). The categories—Non-diagnostic, Negative for malignancy, Atypia of undetermined significance (AUS), Suspicious for malignancy (SFM), and Malignant—are designed to reduce ambiguity, yet challenges remain in real-world scenarios, especially without advanced ancillary testing. Cell block preparation significantly enhances diagnostic accuracy by allowing better architectural visualization and enabling additional tests such as ICC (7). However, resource-limited centres often struggle with cell block inadequacy due to logistical constraints, suboptimal fixation, and low cellularity of samples. The absence of ICC markers such as calretinin, Ber-EP4, WT1, and CEA further complicates differentiation between reactive mesothelial cells and adenocarcinoma (9). Another challenge is the high prevalence of tuberculosis and chronic inflammatory diseases in India, which often produce reactive effusions that mimic malignancy (10). Therefore, understanding the limitations and evaluating practical solutions for cytological interpretation in resource-limited settings is essential. This study investigates the diagnostic challenges encountered in serous effusion cytology over a one-year period at a tertiary care centre with limited ancillary support. It analyses the distribution of diagnostic categories, major causes of diagnostic difficulty, and the impact of sample quality and cell block availability.

Materials and Methods :

This retrospective observational study was conducted in the Department of Pathology at Rama Medical College, Hospital and Research Centre, Hapur. The study included all serous effusion samples received between 02 January 2024 and 28 December 2024. A total of 360 samples were analysed. The study focused on pleural, peritoneal, and pericardial effusions. Ethical approval was obtained prior to data collection. All samples were processed following standard cytology protocols. Pleural and peritoneal fluids ranging from 10 mL to 50 mL were collected in sterile containers, while pericardial fluids ranged from 5 mL to 20 mL. Samples were centrifuged at 2500 rpm for 10 minutes. Smears were prepared from the sediment and stained with Papanicolaou (Pap) stain and May–Grünwald–Giemsa (MGG). When adequate material was available, a cell block was prepared using the plasma-thrombin technique. Cell blocks were fixed in 10% neutral-buffered formalin and processed using a routine histopathology workflow. Inclusion criteria were: (1) availability of complete clinical information, (2) adequate sample volume, and (3) smears with interpretable morphology. Exclusion criteria included: (1) severely hemolyzed samples, (2) improper fixation, and (3) incomplete records. Cases were categorized using TIS: Non-diagnostic, Negative for malignancy, AUS, SFM, and

Malignant. The smears were independently reviewed by two senior pathologists to reduce interobserver variation. Diagnostic challenges were documented based on predefined categories: (a) low cellularity, (b) poorly preserved cells, (c) presence of extensive necrosis, (d) overlapping morphology between reactive mesothelial cells and malignant cells, and (e) lack of cell block or ICC. Clinical correlation and follow-up histopathology, when available, were used for confirmation. Data analysis was descriptive. Frequencies and percentages were calculated for all diagnostic categories. Concordance between cytology and histopathology was assessed when applicable. Major documented challenges included: inadequate volume in 14% of samples, low cellularity in 12%, smeared artefacts in 9%, and lack of cell block in 28% of malignancy-suspected cases. Morphological difficulty in distinguishing between reactive mesothelial hyperplasia and adenocarcinoma was seen in 18% of cases. In some instances, tuberculosis-related effusions showed epithelioid cells mimicking malignant cells, resulting in AUS categorization. Chronic liver disease-associated effusions also demonstrated prominent reactive changes that complicated interpretation. Limitations due to infrastructural constraints were documented. Cell block preparation was possible in only 40% of cases due to inadequate sediment material. ICC was unavailable for most cases, contributing to difficulty in definitive diagnosis.

Results: A total of 360 samples were analysed, distributed as pleural (223 cases), peritoneal (122 cases), and pericardial (15 cases). According to TIS categories, 12% were Non-diagnostic, 54% were Negative for malignancy, 8% were AUS, 10% were SFM, and 26% were Malignant. Among malignant cases, metastatic adenocarcinoma constituted the majority (71%), followed by lymphoma (12%), mesothelioma (6%), and poorly differentiated carcinoma (11%). Diagnostic difficulty was documented in 85 cases (23%). Major causes included low cellularity (12%), degenerative changes (10%), lack of cell block (28% among malignant/suspicious cases), and overlap between mesothelial and malignant cells (18%). Among AUS cases, 42% were later confirmed malignant on histopathology. The malignancy detection rate was highest in pleural effusions (31%), followed by peritoneal (22%) and pericardial (6%).

Discussion:

Serous effusion cytology remains essential for early detection of malignancy, but diagnostic accuracy is hampered by inadequate samples and lack of ancillary tests. Morphological overlap between reactive mesothelial cells and adenocarcinoma is the most common challenge, consistent with previous studies (7,10). Limited availability of cell blocks and ICC leads to an increased number of AUS and SFM cases. Strengthening laboratory resources and training can significantly improve diagnostic precision in resource-limited settings.

Conclusion:

This study highlights significant diagnostic challenges faced in serous effusion cytology at a resource-limited centre. Although cytology is a valuable first-line diagnostic tool, its accuracy depends on sample quality, availability of cell blocks, and cytopathologist expertise. The study emphasizes the need for improved laboratory infrastructure and routine use of cell block techniques. A structured reporting approach and better training can reduce atypical diagnostic categories and improve early malignancy detection.

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