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Original Research Paper

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BEYOND SIMPLE CYTOMORPHOLOGY: EVALUATING THE ARCHITECTURAL INTEGRITY AND DIAGNOSTIC SUPERIORITY OF CELL BLOCK IN PLEURAL FLUID CYTOANALYSIS

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ABSTRACT

Introduction: Pleural fluid cytology plays a crucial role in diagnosing various chest conditions, including infection, inflammatory disease or malignancy. Diagnostic problems arising in everyday practice to differentiate reactive atypical mesothelial cells and malignant cells by the routine conventional smear method, can be overcome by the cell block method. Cell block forms a bridge between cytology and histopathology. **Material and Methods:** The study was conducted in the cytology section of the Department of Pathology. 50 pleural fluid samples were subjected to diagnostic evaluation for over a period of 1 years. Along with conventional smears, cell blocks were prepared by using 10% neutral buffer formalin and absolute ethanol as fixative agents. After the cytological diagnosis, each case was objectively analyzed for cellularity, arrangement, cytoplasmic, and nuclear details. **Results:** On conventional smears, total of 6% cases were malignant, 22% suspicious and 72% benign. On cell block a total of 16% cases were malignant, 12% suspicious and 72% benign. By using the cell block method, 10% additional cases were detected as malignant, which meant more diagnostic yield for malignancy as compared to the conventional smear technique. **Conclusion:** In our study, we found that cell block method is better than conventional smear method, providing high cellularity, better architectural patterns, morphological features and an additional yield of malignant cells, and thereby, increasing the sensitivity of the cytodiagnosis. It plays a significant role in resolving the gray zone while determining the nature of cells on effusion whether reactive or suspicious. Also, it provides diagnostic advantage by making residual material available for special stains and IHC.

KEYWORDS : Cell block; Conventional smear; Pleural effusions, Cytopathology.

INTRODUCTION

Diagnostic cytology involves the study and analysis of cells that have shed naturally from epithelial linings or have been extracted from different bodily tissues. One of the most frequent responsibilities within the field of cytopathology is the clinical evaluation of fluids collected from serous compartments (1,2).

This procedure represents a comparatively straightforward and non-intrusive method that aids in distinguishing whether an effusion is inflammatory, benign, or malignant in origin. While a positive identification is considered definitive, a negative finding is insufficient to exclude the presence of malignancy. (1,3,4). Furthermore, the analysis of serous cavity fluids has evolved into a fundamental element of clinical management for both pediatric and adult populations (5,6,7). Securing a sufficient yield of exfoliated cells from serous fluids is a difficult undertaking, often leading to diagnostic uncertainty. This ambiguity not only jeopardizes patient results but also poses a significant challenge for the clinician. Consequently, the most demanding facet of a pathologist's role is the consistent differentiation between benign reactive changes and malignant cells within an effusion (5,6). Since Bahrenburg pioneered the cell block technique in 1896, the method has been utilized broadly for the analysis of bodily fluids. By 1928, Zemansky asserted that the cell block approach offered superior results compared to the conventional smear technique (2,5). The cell block (CB) method provides significant utility in identifying malignancies, determining disease stages, and establishing patient prognoses. Furthermore, this technique allows for the comprehensive evaluation of various non-infectious and infectious pathologies affecting the serous membranes, including those of bacterial, viral, fungal, and parasitic origin (1,7). As one of the most established methodologies for assessing tissue architecture, the cell block (CB) technique facilitates the acquisition of multiple sections for specialized staining and immunohistochemical analysis (1,3).

MATERIAL AND METHODS

This comparative cross-sectional study was conducted at the Chhattisgarh Institute of Medical Sciences (CIMS), Bilaspur, a tertiary referral centre, after obtaining institutional ethical approval. The study involved 50 pleural fluid samples collected from various hospital departments following written informed consent and the documentation of comprehensive medical histories, physical examinations, and relevant ancillary findings such as LDH, ADA, and radiological parameters. Upon receipt, each specimen underwent gross examination before being divided into two 5 ml aliquots for comparative analysis using the conventional smear and cell block techniques. For the conventional method, 5 ml of the sample was centrifuged at 3000 rpm for 10 minutes to obtain a sediment from which a minimum of three smears were prepared; one was air-dried for May-Grunwald-Giemsa staining, while two were fixed in 95% alcohol for Papanicolaou staining. Parallelly, the remaining 5 ml was processed via the Alcohol formalin method, where the fluid was fixed in an alcohol-formalin mixture at a 1:1 ratio for one hour, centrifuged at 3000 rpm for 10 minutes, and the resulting sediment was subjected to overnight fixation in additional alcohol-formalin. This fixed sediment was subsequently wrapped in filter paper, underwent routine histopathological processing, and was stained with Haematoxylin and Eosin. Finally, both the conventional smears and the paraffin-embedded cell block sections were analysed and compared based on cellularity, architectural arrangement, and cytomorphological details, with all findings subjected to statistical evaluation.

RESULTS

This study was conducted to compare the two techniques of

processing the pleural fluids collected from various departments, that is conventional method and cell block cytopreparatory technique. A total of 50 pleural fluids cases were subjected to cytological examination.

Age-Wise Distribution: The study cohort of 50 cases showed a peak incidence in middle-aged adults, with the 41–60 years group (17 cases) and 21–40 years group (16 cases) together comprising 66% of the total. Older adults in the 61–80 age bracket accounted for 10 cases, while younger populations (≤20 years) were the least represented with only 7 cases combined. [Table 1]

Gender-Wise Distribution: Demographic analysis revealed a clear male predominance in pleural fluid cases. Out of the 50 subjects studied, 58% (n=29) were male, while 42% (n=21) were female, indicating a higher frequency of pleural effusions among men in this study population. [Table 2]

Cellularity: The cell block technique demonstrated superior cellular yield over conventional smears. Specifically, cell blocks produced richly cellular results in 32 cases compared to 28 for smears and significantly reduced the occurrence of paucicellular samples from 10 cases down to 4. [Table 3]

Architectural Pattern: The architectural analysis demonstrated that while CS primarily featured singly/ scattered cells (31 cases), the CB method successfully preserved complex structures, identifying cell clusters and sheets in 15 cases each, and even revealing glandular formations (3 cases) that were entirely absent in conventional smears. [Table 4]

Diagnostic Categorisation: Analysis of the diagnostic stratification revealed that the CB method improved specimen adequacy by reducing unsatisfactory samples from 8% to 2% and increased benign findings to 70%. Furthermore, this diagnostic stratification showed that CB halved the "suspicious for malignancy" cases to 12% while more than doubling the definitive malignant detection rate to 16%. In cases definitively diagnosed as malignant, the cell block proved superior in identifying specific subtypes, detecting four cases of adenocarcinoma, one squamous cell carcinoma, and three instances of metastasis [one from Ovarian carcinoma-Mucinous cystadenocarcinoma and two from Gastrointestinal tract-Gastric adenocarcinoma and Ca rectum]. These results demonstrate the cell block's capacity to resolve inconclusive smears into actionable, definitive diagnoses. [Table 5,6]

Table 1: Age-Wise Distribution

Age Group (Years)	Number of Cases (n)	Percentage (%)
<14	3	6%
15 – 20	4	8%
21 – 40	16	32%
41 – 60	17	34%
61 - 80	10	20%
Total	50	100%

Table 2: Gender-Wise Distribution

Gender	Number of Cases (n)	Percentage (%)
Male	29	58%
Female	21	42%
Total	50	100%

Table 3: Cellularity

Cellularity	Conventional smear	Cell block
Pauci cellular	10	04
Moderately cellular	12	14
Richly cellular	28	32
Total	50	50

Table 4: Architectural Pattern

Architectural pattern	Conventional smear	Cell block
Singly/scattered cells	31	8
Cell balls	5	9
Cell clusters	6	15
Papillae	-	00
Glands	-	03
Sheets	8	15
Total	50	50

Table 5: Diagnostic Categorisation

	Diagnostic categories	Method			
		Conventional Smear		Cell Block	
		No of all cases	%	No of all cases	%
1.	Unsatisfactory	04	04%	01	2%
2.	Benign	32	64%	35	70%
3.	Suspicious of malignancy	11	22%	06	12%
4.	Malignant	03	6%	08	16%
5.	Total	50	100%	50	100%

Table 6: Diagnostic Categorisation

	Conventional smear	Cell block
Adenocarcinoma	02	04
Squamous cell carcinoma	00	01
Metastasis	01	03
Total	03	08

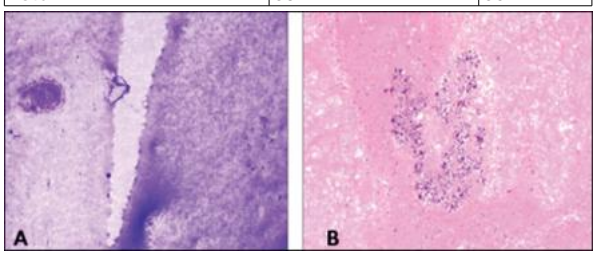

Figure A- CS [4x, MGG]-showing haemorrhagic smear, unsatisfactory for evaluation.

Figure B- CB [4x, H&E]-showing moderately cellular smears, cells in aggregates/clusters, comprising of dense inflammatory cells with some atypical cells in high power [40x], suggestive of suspicious for malignancy.

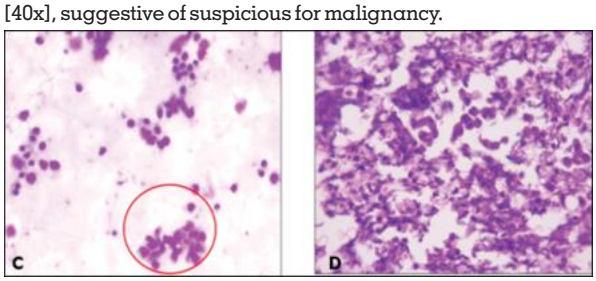

Figure C- CS [40x, H&E]- moderately cellular smears, showing atypical cells, with nuclear pleomorphism, high N:C ratio, irregular nuclear membrane and hyperchromasia, favouring diagnosis of Highly suspicious for malignant cells.

Figure D- CB [40x, H&E]- richly cellular, showing many malignant cells, signet ring cells arranged in sheets, abnormal mitotic figures, binucleation at some places also noted.

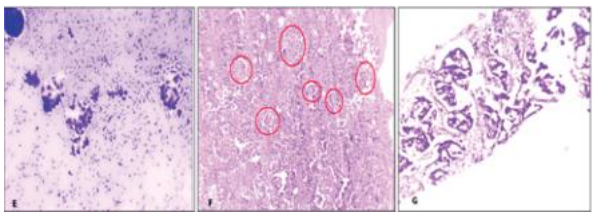

Figure E- CS [40x, H&E]-smears show cells arranged in 3D ball pattern, with malignant features.

Figure F- CB [40x, H&E]-showing Glandular pattern, suggesting Adenocarcinoma.

Figure G- CT guided Trucut Biopsy-[40x, H&E]- confirming adenocarcinoma arising from Left Lung.

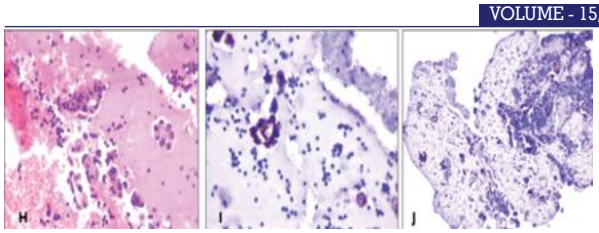

Figure H- CB [10x, H&E]-showing cells arranged in Acinar and Glandular pattern, with malignant mets features, suggestive of Metastatic Adenocarcinoma.
Figure I- Immunohistochemical marker CD7 showing positivity (+2, 25% of cells stained)
Figure J- Immunohistochemical marker CD20 done-displaying positivity (+3, 45% of cells stained).

DISCUSSION

Analyzing serous cavity fluids is a routine cytopathology task (1,2,3). This simple, non-invasive method distinguishes between inflammatory, benign, and malignant effusions (4,5). Although a positive result confirms a diagnosis, a negative one does not exclude malignancy (6,7). "Cytological assessment is conducted across various preparation formats, encompassing traditional smears, cytospins, and liquid-based methods—such as ThinPrep or SurePath—as well as cell blocks [8,9]. Routine conventional smears (CS) face recognized constraints that make it difficult to tell the difference between reactive mesothelial cells and cancer. Because of these issues, additional tools like cell block (CB) techniques are required to ensure a more reliable diagnosis. [9,10,11] The cell block (CB) method involves harvesting sediment, coagulated blood, or visible tissue fragments from cytological samples. These materials are embedded into paraffin blocks and typically processed with hematoxylin-eosin (H&E)—a staining technique universally recognized by pathologists [12,13]. Cell block (CB) has emerged as an invaluable tool for diagnosing effusions, overcoming problems with conventional smears that can arise due to improper smearing, staining causing cell overlapping, cell loss, repeat sample in case of turbid or hemorrhagic fluid (2,14). "Cell blocks also provide multiple serial sections, allowing for various ancillary studies such as special stains, immunohistochemistry, and molecular testing." [9,15].

Unlike the standardized tissue processing seen in surgical pathology, no universal method exists for preparing cell blocks. Instead, laboratories utilize a diverse range of 'in-house' techniques alongside various commercial kits currently on the market."[9].

This study was conducted to compare the two techniques of processing the pleural fluids collected from various departments, that is conventional method and cell block cytopreparatory technique.

A total of 50 pleural fluids cases were subjected to cytological examination.

The highest incidence of effusion was found in age group of 41-60 years which is 34% and least cases in the age group of 0-14yrs [paediatric population] and in between 15-20 years, which are 6% and 8% respectively. Male to female ratio was 1:3.1, showing male predominance.

Sri ESK et al. (2020) found that most patients were between 40 and 60 years old and that there were more males than females, which matches our findings. However, they reported more cancerous effusions than benign ones, a result that differs from our study, where benign cases were more common.

Mandloi P et al. (June 2024) evaluated the diagnostic utility of fluid cytology and concluded that the cell block method yields better cellularity than conventional smears, aligning with established standards.

Suri J et al. (September 2015) observed that the cell block technique allows for a better appreciation of architectural patterns than conventional smears.

Mulkalwar M et al. (2016) found that cell block and cytospin methods performed identically for benign cases, aligning with our data. Their reported rates for suspicious (5.9% CS, 2.9% CB) and malignant (20% CS, 22.9% CB) findings highlight specific diagnostic variations, though these percentages differ from those observed in our study.

CONCLUSION

The cell block (CB) technique has emerged as a vital pillar of modern cytopathology, offering superior cellular yield and morphological detail compared to conventional smears. By preserving tissue architecture, it effectively bridges the gap between cytology and histology, allowing for the identification of malignant patterns in otherwise inconclusive cases. This structural clarity is essential for resolving the "gray zone" between reactive and suspicious cells, particularly in clinically or radiologically suspected malignancies. Furthermore, CB specimens serve as an enduring resource for ancillary testing, such as immunohistochemistry and molecular profiling, which are critical for identifying primary malignancy sites. Ultimately, incorporating the cell block into routine fluid diagnosis maximizes diagnostic accuracy while remaining a simple and economical procedure.

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