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Original research article

UTILITY OF IMMUNOHISTOCHEMISTRY ON CELL BLOCK FOR DETECTION OF PRIMARY MALIGNANCY IN MALIGNANT EFFUSION CYTOLOGY: IS IT ADJUNCT OR NECESSITY?

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Abstract

Background: In a parallel context, the utility of immunohistochemistry (IHC) on cell block specimens in detecting the primary site of malignancy in malignant effusions remains paramount. Much like in the primary discussion, it serves as both an adjunct and a necessity, contingent upon various factors. As an adjunct, IHC on cell block complements other diagnostic modalities, corroborating suspected diagnoses derived from clinical history, imaging, or initial cytological analysis. It enhances diagnostic precision, especially when distinguishing between closely related tumor types or confirming metastatic spread.

However, it assumes a critical role as a necessity when primary tumor identification proves elusive. In cases of poorly differentiated malignancies or when clinical presentation offers little guidance, IHC becomes indispensable for pinpointing the tissue origin. Its ability to discern specific molecular markers aids in tailoring treatment strategies and predicting therapeutic responses. Ultimately, the decision to employ IHC on cell block hinges on considerations such as diagnostic accuracy, treatment planning, and resource allocation.

While it may not always be feasible in resource-constrained settings, its judicious use significantly improves diagnostic outcomes and informs personalized patient care. In this study, we aim to assess the diagnostic accuracy and clinical utility of immunohistochemistry (IHC) on cell block specimens in identifying the primary site of malignancy in cases of malignant effusions. By evaluating the diagnostic accuracy of IHC compared to conventional cytology alone and investigating its impact on treatment

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planning and patient management, we seek to provide insights into the role of IHC as both a diagnostic adjunct and a necessity in enhancing diagnostic precision and guiding therapeutic decisions for patients with malignant effusions.

Aims & Objectives: To determine the utility of cellblock with IHC in diagnosis of primary in malignant effusion cytology.

Methodology: An institution based observational and analytical study was carried out over 3 year period. The residual amount of centrifuged deposit after preparation of conventional smear was mixed with 10% alcohol-formalin solution, and Cellblocks were prepared.

Calretinin, Wilms tumour1(WT1), Ck5/6 for reactive mesothelial cells, TTF1, Napsin for lung primary, Pax8,WT1 for ovary,Ck7,Ck20 for pancreaticobiliary and GI tract, GATA 3 for breast.

Results: A total of 250 were analysed comprising of pleural fluid (n=168), peritoneal fluid (n=67), pericardial fluid (n=13), and CSF (n=2). Of these n=181(72%) were malignant effusions, pleural (n=119), peritoneal (n=49), pericardial (n=11), and CSF (n=2) respectively.

Among peritoneal fluid (n=67) malignant effusions most common primary was from ovary (21,31%), 19(90.4%) cases are positive for PAX8 followed by malignant effusion >NEM (18,27%) >stomach (3,4.5%) =lung (3,4.5%) >pancreas (2,3%) >breast (1,1.5%). Among pleural fluid (n=168) malignant effusions most common primary was from lung (77,46%) of which shows 97.4% positive for TTF1 followed by NEM (49,29%) >malignant effusion (27,16%) >ovary (6,3.6%) >cervix (3,3.6%) > breast (2,1.2%) =multiple myeloma (2,1.2%).

>squamous cell carcinoma (1,0.6%), 1(0.6%) was T cell lymphoma. Among pericardial fluid (n=13) most common malignancy were lung (5,39%) and total number of CSF were 2 which show carcinomatous meningitis.

Discussion: Immunohistochemistry (IHC) stands as a pivotal tool in delineating the primary origin of malignancies, particularly in cases of ascitic and pleural effusions. Ovarian carcinomas often metastasize to ascitic fluid, while lung carcinomas commonly disseminate to pleural effusions, underscoring the significance of understanding metastatic patterns. By employing IHC on cell block material obtained from these effusions, clinicians can confidently confirm the primary tumor without necessitating invasive biopsies. This circumvents patient discomfort and mitigates the risks associated with invasive procedures. Furthermore, the availability of cell block material facilitates subsequent molecular testing, opening avenues for tailored therapeutic interventions and personalized treatment strategies for patients with metastatic effusions.

Conclusion: In conclusion, the integration of immunohistochemistry (IHC) analysis on cell block sections significantly enhances diagnostic capabilities compared to reliance solely on cytomorphology. By leveraging IHC, clinicians can confidently determine the primary origin of tumors in cases of ascitic and pleural effusions, particularly when faced with morphologically challenging presentations. This comprehensive approach not only improves diagnostic accuracy but also facilitates tailored treatment strategies based on the molecular characteristics of the tumor. Thus, the utilization of IHC on cell block material represents a pivotal advancement in the diagnostic armamentarium, offering invaluable insights into tumor origin and aiding in the management of patients

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with metastatic effusions.

Keywords: Cellblock, immunohistochemistry, malignant effusion, cytomorphology

Introduction

Indeed, fluid cytology remains the initial diagnostic modality for suspected malignant effusions due to its accessibility and non-invasive nature. However, the incorporation of cell block preparation and subsequent immunohistochemistry (IHC) testing has become routine practice in the evaluation of such effusions, offering invaluable insights into tumour characterization and origin. Firstly, IHC aids in definitively diagnosing cancer cells within effusion samples, providing crucial confirmation beyond morphological assessment alone. Additionally, IHC serves as a pivotal tool in cases where the primary tumor is unknown, facilitating not only identification of the primary site but also discernment of the specific tumor type. Moreover, the challenge of distinguishing rapidly proliferating cancer cells from mesothelial cells solely through cytology underscores the importance of IHC. In instances where morphological features alone may be insufficient for accurate diagnosis, IHC can elucidate tumor characteristics, guiding precise clinical management decisions. Thus, the incorporation of IHC in the assessment of malignant effusions represents a vital advancement in diagnostic practice, enhancing diagnostic accuracy and facilitating tailored therapeutic approaches for patients with suspected malignancies [1].

Aim and Objectives

Aim: The aim of this study is to investigate the utility of cell block preparation combined with immunohistochemistry (IHC) testing in fluid cytology, specifically focusing on its role in diagnosing the primary site of origin in malignant effusions.

Objectives

1) Evaluate the diagnostic accuracy of cell block preparation and immunohistochemistry (IHC) testing compared to conventional fluid cytology alone in identifying the primary site of origin in malignant effusions.
2) Characterize the contribution of IHC testing in delineating the tissue of origin in malignant effusions, including differentiation between various tumor types and identification of lineage-specific markers.
3) Investigate the clinical implications of integrating cell block preparation and IHC testing into routine diagnostic algorithms for malignant effusions, assessing its impact on treatment planning, patient management, and prognostication.

Materials and Methods

The study retrospectively analysed 250 effusion samples collected over a two-year period from January 2019 to December 2021 at the Department of Pathology, Nizam's Institute of Medical Sciences, Hyderabad. Data were extracted from cyto-pathology and clinical records. Each effusion sample underwent preparation of two cytology smears and one cell block. One smear was stained with May Grunwald Giemsa stain, while the other smear was stained with Papanicolaou stain, aiming to provide comprehensive cytological evaluation of the samples.

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Cell block preparation

The cell block preparation method involved centrifuging the residual fluid and mixing it with a 10% alcohol-formalin solution. Following fixation, histological sections were prepared and stained with Haematoxylin and Eosin (H&E) to enable microscopic examination of cellular morphology and architecture. This standardized technique ensured the preservation of cellular integrity and facilitated comprehensive evaluation of the effusion samples for diagnostic purposes.

Inclusion criteria

Only those cases with IHC on cell block are included.

Exclusion criteria

Cases on which IHC is not performed.

Immunohistochemistry

Immunohistochemistry were performed on I 6000 and Ventana Machine.

Table 1: Shows Immunohistochemistry in type of tissue

NImmunohistochemistry	Type of tissue
Calretinin, WT-1& Ck 5/6	Reactive mesothelial cells
TTF-1, Napsin, P40, P63	Lung
Pax8, WT1, ER	Ovary
Ck7, Ck20, Pan CK	Pancreaticobiliary, GI tract
GATA-3	Breast

Results

Total of 250 cases of cellblock with immunohistochemistry were done. The ages of the patients were in the range from 13 to 91 years with median of 57 years. Female to male ratio of 1.5:1. Out of 250 effusion samples taken for study, 168 were pleural fluid, 67 were ascitic fluids, 13 were pericardial fluid and 2 were CSF samples. Of these, 67 cases (27%) were negative for malignancy of which pleural (47), ascitic (18), pericardial (2), CSF (0). Table 2.

Total 181 cases (72%) turned out to be malignant, of which pleural fluid malignancies were (119), ascitic fluid (49), pericardial fluid (11) and CSF were (2). Table 2.

Table 2: Shows number of malignant and non-malignant cases in different effusion samples

Type of Effusion	Cellblock with IHC	Malignant effusion in CB	No evidence of malignancy (NEM)
Pleural	168(67.%)	119(71%)	49(29%)
ASCITIC	67(27%)	49(73%)	18(27%)
Pericardial	13(5.2%)	11(85%)	2(15%)
CSF	2(1%)	2(100%)	0
Total	250	181(72%)	69(28%)

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Pleural fluid

Out of 168 pleural fluid samples, 77(46%) showed primary pulmonary origin of which 97.4% cases are positive for TTF1.Chart 1.

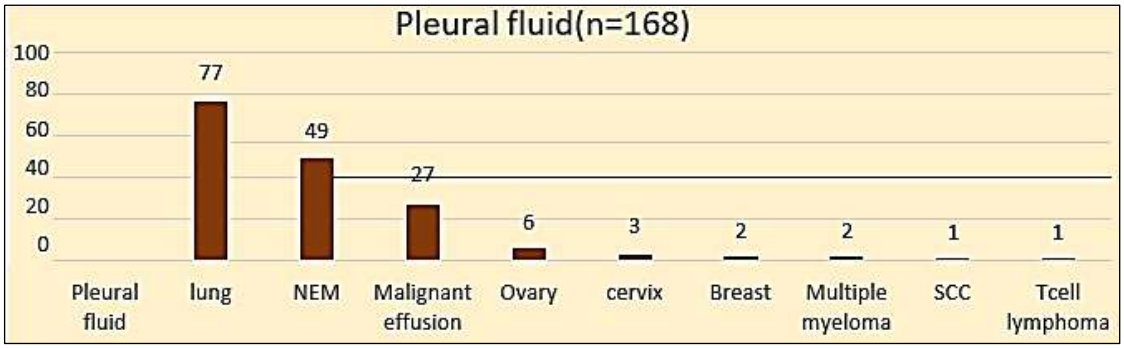

Chart 1: Distribution of cases in pleural fluid

Among 168 pleural effusions, 119(71%) were malignant and 49(29%) were negative for malignancy.

Among malignant pleural effusions (n=119), 77(65%) turned out to be of primary pulmonary origin, 27(23%) were from malignant effusion, 6(5%) were primary ovarian origin, 3(2.5%) were from cervix, 2(1.7%) were of primary breast origin, 2(1.7%) was given as involvement by multiple myeloma, 1(0.8%) was given as involvement by metastatic SCC, 1(0.8%) was T-cell lymphoma. Chart 1.

Most common tumour in pleural fluid is lung (77,46%) followed by NEM (49,29%). >malignant effusion (27,16%) >ovary (6,3.6%)>cervix (3,1.8%) >breast (2,1.2%) =multiple myeloma (2,1.2%)>squamous cell carcinoma (1,0.6%) =T cell lymphoma (1,0.6%). Chart 1.

Comparison between cytomorphology and cellblock with IHC in pleural fluid. (Table 3)

Out of 4 cases given as atypical cells on cytomorphology of which 1(25%) were from unknown primary, 2(50%) were of primary pulmonary origin and 1(25%) were from malignant effusion in k/c/o ovary in cellblock. 5 cases given as lymphocytic effusion on cytomorphology 1(20%) was given as NEM and 4(80%) were originally lymphocytic effusion in cellblock. Out of 91 cases reported as malignant effusion on cytomorphology of which 60(66%) were of primary pulmonary origin, 19(21%) were of unknown primary, 5(5.5%) were primary ovarian origin, 3(3.3%) was malignant effusion in k/c/o cervix, 2(2.2%) was malignant effusion in k/c/o multiple myeloma,1(1.1%) was T cell lymphoma and 1(1.1%) was malignant effusion in k/c/o breast in cellblock. 1 case which had only blood elements on cytomorphology. 19 cases given as suspicious of malignant effusion on cytomorphology but 14(74%) turned out to be of primary pulmonary origin,4(21%) turned out to be malignant effusion and 1(5.2%) turned out be SCC. Out of 48 fluids given as NEM on cytomorphology 1(2%) was from primary mammary origin, 2(4%) was lymphocytic effusion, 12(%) were primary pulmonary origin and 4(8.3%) were florid mesothelial proliferation, 1(2%) was from unknown primary but 39(81%) originally remained as NEM.

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Table 3: Comparison between cytomorphology and cellblock with IHC on pleural effusions

Cytology Opinion	Number of Cases	Cellblock with IHC Diagnosis
Atypical cells	4	2(50%) Primary pulmonary origin 1(25%) Malignant effusion 1(25%) Malignant effusion in k/c/o ovary
Lymphocytic effusion	5	4(80%) Lymphocytic effusion 1(20%) NEM
Malignant effusion	91	60(66%) Primary pulmonary origin 19(21%) Malignant effusion 5(5.5%) Primary ovarian origin 3(3.3%) Malignant effusion in a k/c/o carcinoma cervix 2(2.2%) Malignant effusion in k/c/o multiple myeloma 1(1.1%) Malignant effusion in a k/c/o carcinoma breast 1(1.1%) T cell lymphoma
Only blood elements	1	1(100%) Malignant effusion
Suspicious of malignant effusion	19	14(74%) Primary pulmonary origin 4(21%) Malignant effusion 1(5.2%) SCC
NEM	48	39(81%) NEM 4(8.3%) Florid mesothelial proliferation 2(4%) Lymphocytic effusion 1(2%) Primary mammary origin 2(4%) Lymphocytic effusion 1(2%) Primary pulmonary origin 1(2%) Malignant effusion

Ascitic fluid

Out of 67 ascitic fluid samples, 21 showed primary ovarian origin of which 19 (90.4%) cases are positive for PAX8.Chart 2. Among 67 ascitic fluid effusion samples 49(73%) were malignant and 18 (27%) were negative for malignancy. Table 2.

Among malignant ascitic effusions (n=49), 21(43%) were of primary ovarian origin, 19(39%) were from malignant effusion, 3(6%) were primary stomach origin, 3(6%) were primary pulmonary origin, 2(4%) was primary pancreatic origin, 1(2%) was of primary breast origin. Chart 2. Most common tumor in ascitic fluid is ovary (21,31%) followed by malignant effusion (19,28%) >NEM (18,27%) >stomach (3,4.5%) =lung (3,4.5%) >pancreas (2,3%) >breast (1,1.5%). Chart 2.

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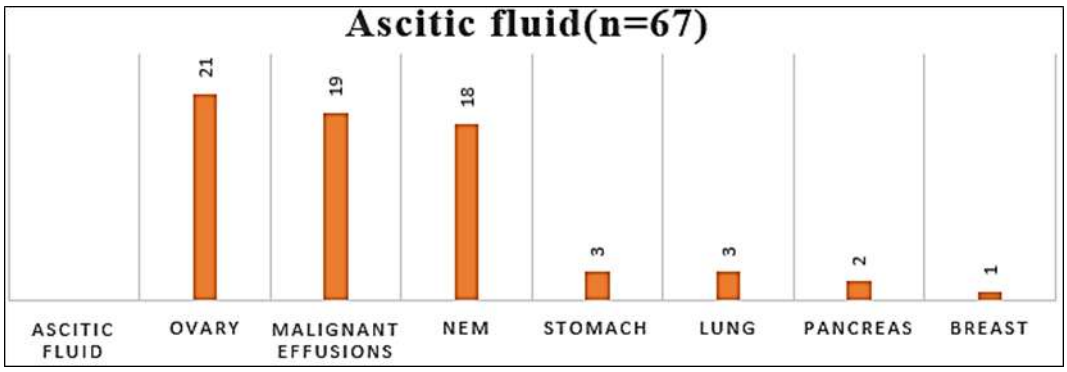

Chart 2: Distribution of cases in ascitic fluid

Comparison of cytomorphology and cellblock with IHC in ascitic fluid. (Table 4)

Out of 3 cases given as atypical cells on cytomorphology of which 1(33%) was given as NEM but 2(67%) turned to be malignant effusions on cellblock.

39 cases of malignant effusion on cytomorphology 17(43.5%) were primary ovarian origin, 12(31%) were from unknown primary, 3(7.7%) were primary pulmonary origin, 3(7.7%) was primary stomach origin, 2(5.1%) was primary pancreatic origin, 1(2.6%) was primary breast origin and 1(2.6%) was given as NEM. 7 cases given as suspicious of malignant effusion on cytomorphology 4(57%) were of primary ovarian origin and 3(43%) was from unknown primary. 18 cases reported as NEM on cytomorphology were originally NEM (16,89%) but two (11%) came out to be as malignant effusion to our surprise.

Table 4: Comparison between cytomorphology and cellblock with ihc on ascitic effusions

Cytology Opinion	Number of Cases	Cellblock with IHC Diagnosis
Suspicious of atypical Cells	3	2(67%) Malignant effusion 1(33%) NEM
Malignant Effusion	39	17(43.5%) Primary ovarian origin. 12(31%) Malignant effusion (Unknown). 3(7.7%) Primary in stomach 3(7.7%) Primary pulmonary Origin. 2(5.1%) Primary in pancreas. 1(2.6%) Primary in breast 1(2.6%) NEM
Suspicious of malignant effusion	7	4(57%) Primary ovarian origin. 3(43%) Malignant Effusion
NEM	18	16(89%) No evidence of malignancy. 2(11%) Malignant Effusion

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Pericardial fluid

Out of 13 pericardial samples, 5(39%) were from primary pulmonary origin, 4(31%) are from malignant effusion, 2(15%) are from primary mammary origin, 2(15%) were reported as NEM. Chart 3.

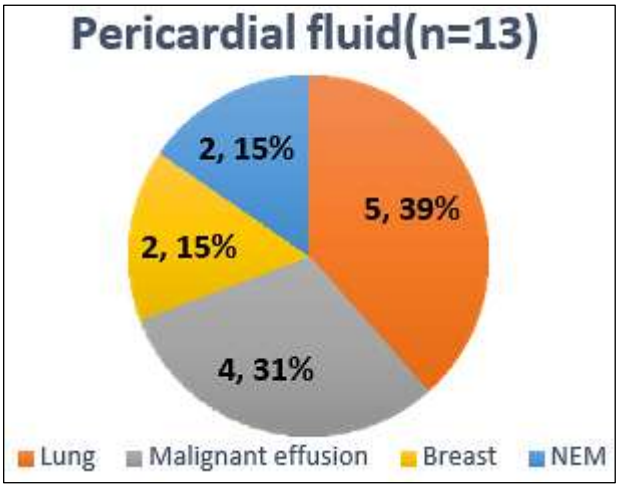

Chart 3: Distribution of cases in pericardial fluid

Comparison between cytomorphology and cellblock with IHC on pericardial effusions (Table 5)

7 cases given as malignant effusion in cytomorphology 3(43%) cases was from primary pulmonary origin, 2(29%) cases are from primary mammary origin, 2(29%) cases were from unknown primary.2 cases given as NEM in cytomorphology were originally turned out to be NEM (2,100%) in cellblock.4 cases given as suspicious of malignancy in cytomorphology 2 (2,50%) cases was from primary pulmonary origin, 2(50%) were from unknown primary.

Table 5: Comparison between cytomorphology and cellblock with IHC on pericardial effusions

Cytology Opinion	Number of Cases	Cellblock with IHC Diagnosis
Malignant effusion	7	2(29%) Breast 3(43%) Lung 2(29%) Malignant effusion
NEM	2	2(100%) NEM
Suspicious of malignancy	4	2(50%) Malignant effusion 2(50%) Lung

CSF fluid

Out of 2 CSF samples analysed one was from ovary and one was from stomach primary. 1(50%) carcinomatous meningitis in a known case of carcinoma ovary.
1(50%) metastatic carcinoma in known case of carcinoma stomach.

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Illustrations

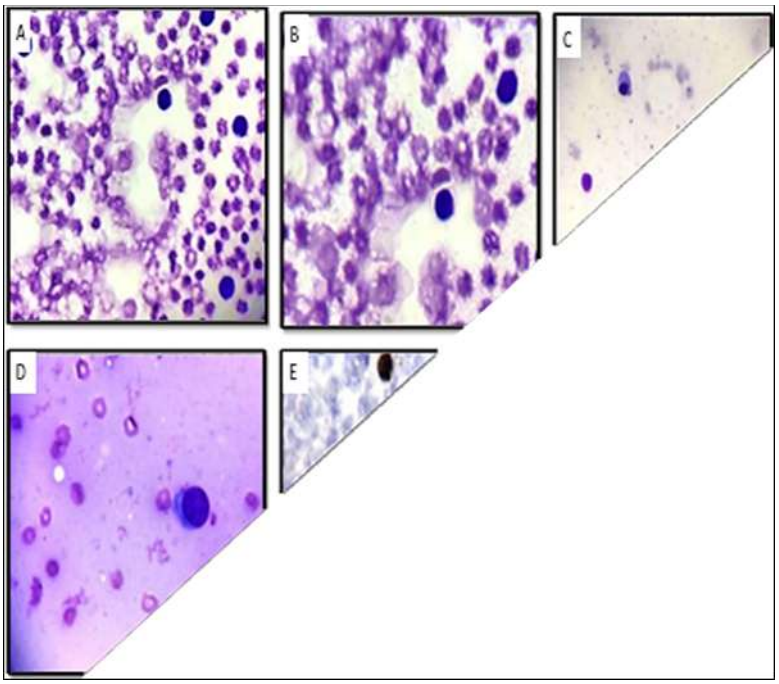

Image 1: Pericardial fluid involvement by pulmonary adenocarcinoma
A & B: Cytospin showing cells arranged in clusters in MGG and PAP stain (400 x). C: Cellblock showing cells arranged in clusters (400 x). D: IHC with TTF1 positive (1000x). E: IHC with Napsin positive (100x). F,G & H:IHC with P40, WT1 and Calretinin are negative (100x)

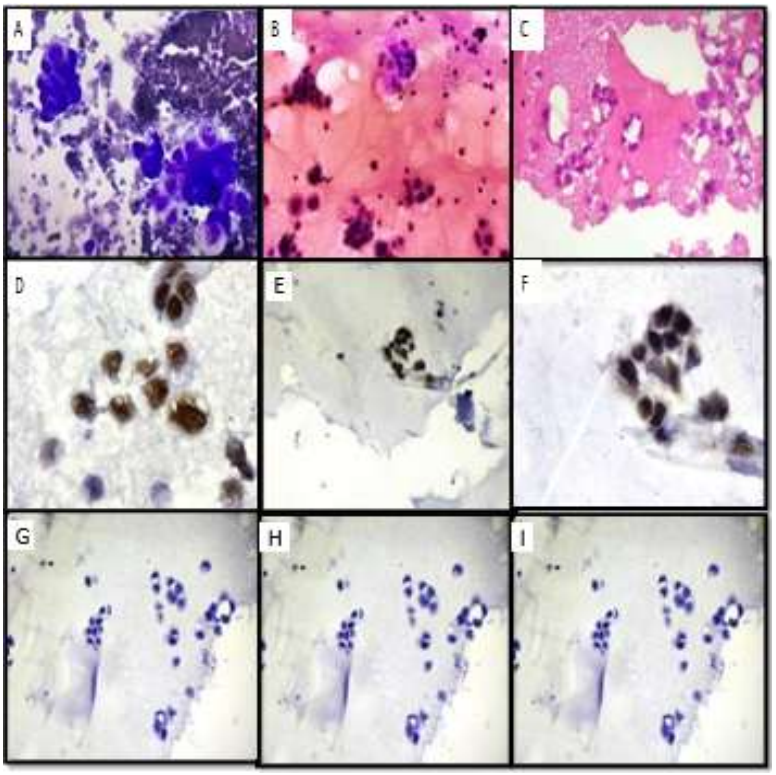

Image 2: Pleural fluid involvement by Multiple Myeloma

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A &B: Cytospin showing lymphocytes in hemorrhagic background (400 x). C: Cytospin showing plasma cells (400 x). D: Cytospin showing plasma (1000x). E: IHC with CD138 highlighting plasma cells (1000x) in cytospin

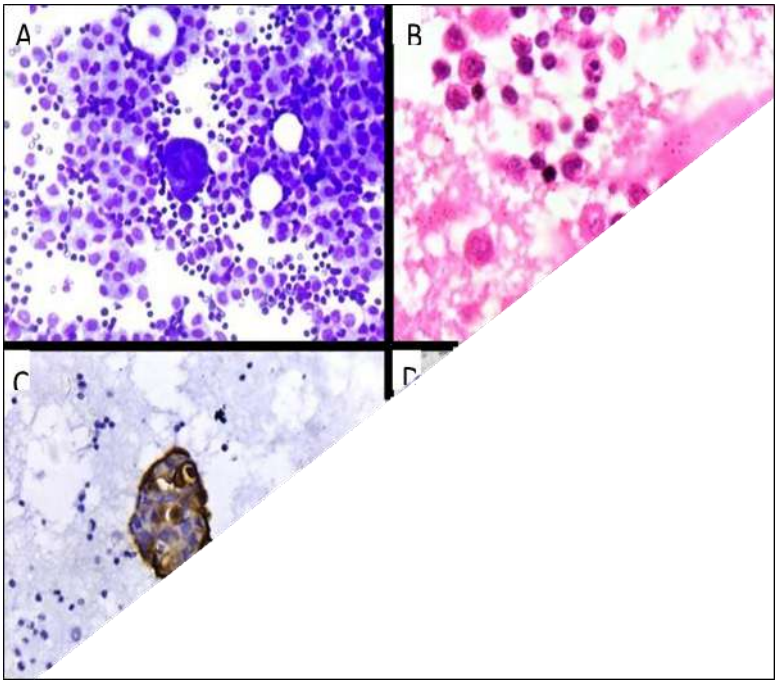

Image 3: Pleural fluid involvement by Primary ovarian origin
A & B: Cytospin showing lesion cells in clusters and 3D balls in MGG and PAP stain (400 x). C: Cellblock showing lesion cells in clusters (400 x). D & E: IHC with WT1 (1000X) &PAX8 is positive in lesion cells (400x). F: IHC with ER is positive (1000x). F, G & H: IHC with TTF1, Napsin & P40 are negative (400x)

Image 4: Ascitic fluid involvement by Primary pancreatic origin
A: Cytospin showing cells arranged in 3D Balls admixed with reactive mesothelial cells (400 x).
B: Cellblock showing individual scattered cells (1000x) C & D: IHC with CEA and CA19-9 are positive (1000x)

Discussion

Serous effusions represent a broad spectrum of fluid accumulations within body cavities, including the pleural, pericardial, and peritoneal spaces. They can arise from various underlying causes, ranging from benign inflammatory processes to more ominous neoplastic conditions. Infections, such as pneumonia or tuberculosis, can lead to serous effusions, as can inflammatory conditions like rheumatoid arthritis or systemic lupus erythematosus.

Additionally, neoplastic etiologies, such as metastatic carcinomas or lymphomas, may also manifest as serous effusions.

Malignant effusions, characterized by the presence of cancer cells within the fluid, often represent an early sign of an underlying malignancy. They can occur as a result of direct tumor infiltration into the serous membranes or as a consequence of metastatic spread from primary tumors elsewhere in the body. Given their potential as a harbinger

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of malignancy, diagnosing the exact cause of malignant effusions is paramount for initiating timely and appropriate treatment. One of the challenges in diagnosing serous effusions lies in distinguishing between benign and malignant cells. Reactive mesothelial cells, which are commonly encountered in response to inflammation or injury, can morphologically resemble malignant cells, leading to diagnostic uncertainty. In such cases, ancillary techniques like immunohistochemistry become invaluable, enabling the identification of specific protein markers that can differentiate between benign and malignant cells with greater precision.

Cytologic examination of effusions is a minimally invasive procedure that can yield vital diagnostic information. Not only does it provide insights into the underlying pathology, but it can also guide therapeutic interventions, such as drainage procedures or the administration of chemotherapy agents directly into the affected cavity. However, in instances where the cytologic findings are equivocal or inconclusive, immunohistochemistry serves as a valuable adjunct, enhancing diagnostic accuracy and facilitating appropriate patient management.

Overall, while cytology alone is often sufficient for diagnosing serous effusions, the judicious use of ancillary techniques like immunohistochemistry can further refine diagnostic certainty, particularly in challenging cases characterized by scanty tumor cells or an abundance of reactive mesothelial cells. [3]Immunohistochemistry (IHC) plays a pivotal role in determining the primary origin of malignancies, particularly in cases of malignant effusions [6]. These effusions are commonly associated with malignancies originating from various primary sites, including the lung, breast, gastrointestinal tract, and ovary [2]. Notably, ascitic effusions frequently represent metastases from ovarian malignancies, while pleural effusions often originate from lung tumors.

In our present study, among peritoneal fluid malignant effusions, ovarian malignancy emerged as the most common primary origin. Notably, a high proportion of these cases (90.4%) tested positive for the immunohistochemical marker PAX8, providing additional support for their ovarian origin. Similarly, in pleural fluid malignant effusions, lung malignancy predominated as the primary source. The overwhelming majority of these cases (97.4%) exhibited positivity for the immunohistochemical marker TTF1, further confirming their lung origin. It's noteworthy that immunohistochemistry was not performed for pericardial fluid and cerebrospinal fluid (CSF) samples in our study, as the primary origin was already known for these cases. This highlights the selective application of IHC based on clinical context and the availability of relevant diagnostic information.

Overall, our findings underscore the indispensable role of immunohistochemistry in elucidating the primary origin of malignant effusions, guiding diagnostic and therapeutic decisions, and improving patient care outcomes.

Comparison of malignancies between cytomorphology and cellblock with IHC. (Table 6)

Out of 250 cases, 139 (55.6%) were diagnosed as malignancy on cytomorphology alone and with the use of Immunocytochemistry, malignant cases are increased to 181(72.4%).

Out of 181(72%) cases of malignancy, primary pulmonary origin were (85), Malignant effusion of unknown primary were (50), primary ovarian origin were (27), primary

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mammary origin were (5), primary stomach origin were (3), primary cervix origin were (3), primary pancreatic origin was (2), metastatic SCC was (1), Metastatic adenocarcinoma was (1), multiple myeloma was (2) and carcinomatous meningitis was (1) and T cell Lymphoma was (1). As the primary was confirmed on Cellblock material, there is no requirement for biopsy by invasive procedures in these cases and cellblock material can be submitted for further molecular testing.

Table 6: Comparison of malignancies between cytomorphology and cellblock with IHC

	Cytomor Phology	Cellblock	IHC
Malignancy	139(55.6%)	181(72.4%)	50-Malignant Effusion (unknown primary) 27-Primary Ovarian origin 85-Primary Pulmonary origin 5-Primary mammary origin 3-Primary stomach origin 3-Primary cervix origin 1-Tcell lymphoma 2-Primary pancreatic origin 1-Metastatic SCC 2-Multiple myeloma 1-Metastatic carcinoma 1-carcinomatous meningitis

In our study, the comprehensive evaluation of malignant effusions utilizing cytology, cell block preparation, and immunohistochemistry (IHC) revealed valuable insights into the diagnosis and characterization of these fluid samples. Initially, cytological examination identified malignancy in 55.6% of cases, highlighting its primary role in the diagnostic process. However, the diagnostic yield significantly increased to 72.4% with the implementation of cell block preparation, emphasizing its enhanced sensitivity compared to cytology alone. Furthermore, IHC played a crucial role in further refining the diagnosis, particularly in cases where the primary origin of the malignancy was unknown. Through IHC analysis, specific primary sites of origin were identified, including ovarian, pulmonary, mammary, gastric, cervical, and pancreatic origins, among others. This comprehensive approach underscores the importance of integrating cell block preparation and IHC into routine diagnostic algorithms for malignant effusions, as it facilitates more accurate diagnosis and subsequent patient management decisions. Overall, our findings emphasize the utility of cell block preparation and IHC in enhancing the diagnostic accuracy and characterization of malignant effusions, ultimately contributing to improved patient care outcomes.

Table 7: Comparison with other studies in ascitic fluid

Ascitic fluid	Shiva Kumaraswamy *et al.* [4]	Jyotsna Shri *et al.*	Present Study
Cytology	70%	8.3%	54.2%
Cellblock	84%	19.4%	73%

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The comparison of diagnostic yield between cytology and cell block preparation for ascitic fluid, as reported by Shiva Kumaraswamy *et al*., Jyotsna Shri *et al*., and the present study, is as follows:

Cytology: Shiva Kumaraswamy *et al*. reported a diagnostic yield of 70%, Jyotsna Shri *et al*. reported 8.3%, and the present study reported 54.2%.

Cell Block: Shiva Kumaraswamy *et al*. reported a diagnostic yield of 84%, Jyotsna Shri *et al*. reported 19.4%, and the present study reported 73%.

Table 8: Comparison with other studies in pleural fluid

Pleural Fluid	Patil Shital *et al.*	Assawasaksakul T *et al.* [6]	Present study
Cytology	42%	61.2	58.2%
Cellblock	96%	61.9	71%

The comparison of diagnostic yield between cytology and cell block preparation for pleural fluid, as reported by Patil Shital *et al*., Assawasaksakul T *et al*., and the present study, is as follows:

- **Cytology:** Patil Shital *et al*. reported a diagnostic yield of 42%, Assawasaksakul T *et al*. reported 61.2%, and the present study reported 58.2%.
- **Cell Block:** Patil Shital *et al*. reported a diagnostic yield of 96%, Assawasaksakul T *et al*. reported 61.9%, and the present study reported 71%.

These findings suggest that cell block preparation generally yields higher diagnostic rates compared to conventional cytology for the evaluation of pleural fluid across the studies referenced.

Table 9: Comparison with other studies in pericardial fluid

Pericardial Fluid	Thapar *et al.* [7]	Present study
Cytology	71.4%	59%
Cellblock	85.7%	85%

The comparison of diagnostic yield between cytology and cell block preparation for pericardial fluid, as reported by Thapar *et al*. and the present study, is as follows:

- **Cytology:** Thapar *et al*. reported a diagnostic yield of 71.4%, while the present study reported 59%.
- **Cell Block:** Thapar *et al*. reported a diagnostic yield of 85.7%, while the present study reported 85%.

These findings suggest that cell block preparation maintains a consistently higher diagnostic yield compared to cytology for the evaluation of pericardial fluid across the studies referenced.

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Table 10: Comparison with other studies in serous effusions

Serous Effusions	Celen *et al.*	Richardson *et al.*	Present study
Cytology	71.4%	12%	55.6%
Cellblock	85.7%	13%	72.4%

The comparison of diagnostic yield between cytology and cell block preparation for serous effusions, as reported by Celen *et al*., Richardson *et al*., and the present study, is as follows:

- **Cytology:** Celen *et al*. reported a diagnostic yield of 71.4%, Richardson *et al*. reported 12%, and the present study reported 55.6%.
- **Cell Block:** Celen *et al*. reported a diagnostic yield of 85.7%, Richardson *et al*. reported 13%, and the present study reported 72.4%.

These findings suggest that cell block preparation generally yields higher diagnostic rates compared to conventional cytology for the evaluation of serous effusions across the studies referenced. However, there may be variations in diagnostic yield based on different methodologies, sample sizes, and population characteristics.

Conclusion

In conclusion, the incorporation of cell block sections with immunohistochemistry (IHC) into the diagnostic evaluation of serous effusions significantly enhances diagnostic accuracy, yielding approximately 16.8% more accurate results compared to cytomorphology alone.

This comprehensive approach not only improves diagnostic precision but also facilitates the determination of the primary origin of tumors, particularly in morphologically challenging cases. By leveraging IHC, clinicians can confidently identify the tissue of origin and differentiate between benign and malignant cells, thereby guiding appropriate treatment strategies and ultimately improving patient care outcomes. Hence, the integration of cell block preparation with IHC emerges as a valuable adjunct in the diagnostic algorithm for serous effusions, offering enhanced diagnostic capabilities and ensuring more accurate patient management.

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