**The effectiveness of the cell block technique in the cytological diagnosis of** **pleural effusion at Ha Dong General Hospital from 2021 to 2024**

**SUMMARY**

***Aims****:*(1) Compare the results of cell block examination and cell smear cytology in diagnosing malignant pleural effusion at the Pathology Department of Ha Dong General Hospital from 2021 to 2024. (2) Identify factors associated with cytological diagnosis using the cell block technique for pleural effusion. ***Materials and Methods****:* A cross-sectional descriptive study was conducted on 176 pleural effusion samples at the Pathology Department of Ha Dong General Hospital from October 2021 to May 2024. ***Results*** The cell block technique detected malignancy in 22.1% of samples and suspected malignancy in 5.7%, whereas the cell smear technique identified malignancy in 7.4% and suspected malignancy in 2.3%. The cell block method detected more malignant and suspicious cases than the cell smear method (p<0.05). The concordance rate between the two techniques was 79.6%. The malignancy rate was higher in males than in females (p<0.05) and was significantly higher in cases with fluid volume >500mL (p<0.05). ***Conclusion****:* The cell block technique identified more malignant and suspicious cases than the cell smear technique in diagnosing malignant pleural effusion. A significant association was found between gender, fluid volume, and cytological diagnosis using the cell block technique.

***Keywords****: Pleural effusion, Cell block, Cell smear, Conventional smear cytology*

**I. INTRODUCTION**

Lung cancer remains the leading cause of cancer-related mortality worldwide, with 2.21 million new cases and 1.8 million deaths in 2020, projected to rise to 3.8 million cases by 2050 according to the GLOBOCAN project [1]. Histopathological diagnosis is the gold standard, but invasive biopsy is often not feasible in patients with respiratory failure or high bleeding risk. In this context, pleural effusion cytology plays a crucial role, primarily using two methods: cell smear and cell block. The cell block technique allows for the collection of entire cellular components in effusion and supports immunohistochemical and genetic mutation analyses, such as EGFR and ALK, enhancing malignant diagnosis efficiency. Although applied at Ha Dong General Hospital since October 2021, no study has evaluated its actual effectiveness in cancer diagnosis on pleural effusion samples at this hospital. Therefore, this study was conducted with two objectives: (1) Compare the results of cell block examination and cell smear cytology in diagnosing malignant pleural effusion at Ha Dong General Hospital. (2) Identify factors associated with cytological diagnosis using the cell block technique.

**II. STUDY SUBJECTS AND METHODS**

**2.1. Study subjects**

Pleural effusion samples sent to the Pathology Department from October 2021 to May 2024.Inclusion criteria: Pleural effusion samples indicated for both cell block and cell smear techniques at the Pathology Department with complete patient records.Exclusion criteria: Coagulated specimens.

**2.2. Study period and location**

The study was conducted from February 2024 to September 2024. Data were collected from October 2021 to May 2024 at the Pathology Department of Ha Dong General Hospital.

**2.3.** **Research Methods**

*2.3.1. Study design*

A cross-sectional descriptive study was conducted.

*2.3.2. Sample size and selection*

The study used a total sample approach. A total of 176 pleural effusion samples meeting inclusion and exclusion criteria were collected from October 2021 to May 2024.

## 2.4. Research variables

Cell block and cell smear diagnosis results were classified into three categories: 1) Benign: No abnormal or suspicious malignant cells. 2) Malignant: Presence of abnormal cells meeting malignant criteria. 3) Suspicious for malignancy: Presence of abnormal proliferative cells insufficient for malignancy diagnosis.

## 2.5. Research process

* Step 1: Collect patient information: age, gender, effusion aspiration site from medical records.
* Step 2: Record fluid volume and color through direct observation or medical records
* Step 3: Process specimens using cell block and cell smear techniques per Ministry of Health protocols. Cell blocks were embedded, sectioned, and stained with Hematoxylin-Eosin. Suspicious cases underwent immunohistochemical staining.
* Step 4: Record cytological diagnosis results. All diagnoses were performed by certified pathologists. Suspicious cases were reviewed by a pathology board for confirmation.
* Step 5. Data entry into Excel software.
* Step 6: Data analysis, report compilation, discussion, and conclusion formulation.

**2.6.** **Data Analysis and Processing**

Data were entered into Excel and analyzed using SPSS 26.0. Frequency and percentage statistics were used. Chi-square and Fisher’s exact tests assessed differences, with statistical significance at p<0.05.

**2.7. Ethical considerations**

The study was approved by the Ha Dong General Hospital Scientific Committee and hospital leadership. Data were collected honestly and objectively, solely for research purposes. Patient confidentiality was strictly maintained.

**III. RESULTS**

**3.1. General characteristics of study subjects**

Table 1. General characteristics of the study population

|  |  |  |
| --- | --- | --- |
| **Characteristics** | **Number (n)** | **Percentage (%)** |
| **Age group** |  |  |
| ≤50 | 28 | 15.9 |
| 51-60 | 16 | 9.1 |
| 61- 70 | 44 | 25.0 |
| >70 | 88 | **50.0** |
| **Gender** |  |  |
| Male | **111** | **63.1** |
| Female | 65 | 36.9 |
| **Fluid color** |  |  |
| Red | 43  | 24.4 |
| Serosanguinous | 48  | 27.3 |
| Yellow | **85**  | **48.3** |
| **Fluid volume** |  |  |
| <50 mL | 22  | 12.5 |
| 50 – 250 mL | 56  | 31.8 |
| >250 – 500 mL | **81**  | **46.0** |
| >500 mL | 17  | 9.7 |
| **Total** | **176** | **100** |

The study population mainly belonged to the >70 age group (50%). The proportion of males was higher than that of females. Yellow-colored fluid had the highest proportion (48.3%). The majority of submitted fluid samples fell within the >250-500 mL range (46%) (Table 1

**3.2. Comparison of cell block and cell smear results in pleural effusion diagnosis**

Table 2. Comparison of cytological diagnosis results between the cell block and cell smear techniques on pleural effusion samples

|  |  |  |
| --- | --- | --- |
| **Cell Smear** | **Cell Block** | **p** |
| Malignantn (%) | Suspiciousn (%) | Benignn (%) | Totaln (%) |
| Malignant | 13 (7.4) | 0 (0) | 0 (0) | 13 (7.4) | **<0.001\*\*** |
| Suspicious | 4 (2.3) | 0 (0) | 0 (0) | 4 (2.3) |
| Benign | 22 (12.4) | 10 (5.7) | 127 (72.2) | 159 (90.3) |
| **Total** | **39 (22.1)** | **10 (5.7)** | **127 (72.2)** | **176 (100)** |

*\*\*Fisher’s-exact test*

According to Table 2, the results of the cell block test on pleural effusion samples showed that 39 samples were malignant, accounting for 22.1%; 10 samples were suspicious for malignancy, accounting for 5.7%; and 127 samples were benign, accounting for 72.2%. Benign samples had the highest proportion.

The results of the cell smear test showed that 13 samples were malignant, accounting for 7.4%; 4 samples were suspicious for malignancy, accounting for 2.3%; and 159 samples were benign, accounting for 90.3%. Benign samples had the highest proportion.

A comparison of the cell block and cell smear test results on 176 pleural effusion samples showed that 140 cases had the same diagnostic results on both methods (accounting for 79.6%). Among them, 11 cases were malignant, 127 cases were benign, and there were no suspicious cases (with corresponding rates of 7.4%, 72.2%, and 0%, respectively).

There were 36 cases with differing results between cell smear and cell block (accounting for 20.4%). Among them, 4 suspicious cases and 22 benign cases on cell smear were diagnosed as malignant on cell block (accounting for 2.3% and 12.4%, respectively). Additionally, 10 benign cases on cell smear were diagnosed as suspicious on cell block (accounting for 5.7%).

Cell block identified more malignant and suspicious cases than cell smear. The results were statistically significant with p<0.05.

**3.3. Factors associated with cell block cytological diagnosis**

Table 3. Factors associated with cytological diagnosis results using the cell block technique for pleural effusion (n=176)

|  |  |  |
| --- | --- | --- |
| **Related Factors** | **Diagnosis Results** | **p** |
| Malignantn (%) | Suspiciousn (%) | Benignn (%) |
| **Age group** |
| ≤50 | 2 (7,1) | 2 (7,1) | 24 (85,8) | 0,308\*\* |
| 51-60 | 4 (25,0) | 1 (6,3) | 11 (68,7) |
| 61- 70 | 13 (29,6) | 1 (2,3) | 30 (68,2) |
| >70 | 20 (22,7) | 6 (6,8) | 62 (70,5) |
| **Gender** |
| Male | 19 (17,1) | 4 (3,6) | 88 (79,3) | **0.020\*** |
| Female | 20 (30,8) | 6 (9,2) | 39 (60,0) |
| **Fluid color** |
| Red | 8 (18,6) | 3 (7,0) | 32 (74,4) | 0,638\*\* |
| Serosanguinous | 8 (16,7) | 3 (6,2) | 37 (77,1) |
| Yellow | 23 (27,1) | 4 (4,7) | 58 (68,2) |
| **Fluid volume** |
| <50 mL | 5 (22,7) | 4 (18,2) | 13 (59,1) | **0,030\*\*** |
| 50 – 250 mL | 16 (28,6) | 2 (3,6) | 38 (67,8) |
| >250 – 500 mL | 13 (16,1) | 2 (2,5) | 66 (81,4) |
| >500 mL | 5 (29,4) | 2 (11,8) | 10 (58,8) |

\**Chi-square*

*\*\*Fisher’s-exact test*

Table 3 shows that:

There is a statistically significant association between gender and the cytological diagnosis results of the cell block technique for pleural effusion (p<0.05). The rates of malignancy and suspicious cases are higher in females than in males.

There is a statistically significant association between fluid volume and the cytological diagnosis results of the cell block technique for pleural effusion (p<0.05). The rates of malignancy and suspicious cases are higher in samples with a volume >500 mL compared to other samples.

The rates of malignancy and suspicious cases are higher in red-colored fluid samples than in other samples. However, this result is not statistically significant (p>0.05).

There is no statistically significant association between age group and the cytological diagnosis results of the cell block technique for pleural effusion (p>0.05).

**IV. DISCUSSION**

Our study, conducted on 176 pleural effusion samples, showed that the majority of samples were obtained from patients over 70 years old. Male patients outnumbered female patients, with corresponding rates of 63.1% and 36.9%. Yellow-colored fluid had the highest proportion (48.3%), while red-colored fluid had the lowest proportion (24.4%). Our results are similar to those of Nguyễn Quang Thi (2022), in which yellow-colored fluid accounted for the majority (61.3%) [2]. According to Ozcakar et al. (2010), a study on 390 cancer patients with pleural effusion concluded that in cases of pleural effusion with a history of cancer, bloody effusion is not significant in predicting the malignant nature of the effusion. The proportion of malignant cells found in bloody and non-bloody effusions was equivalent [3].

In our study, the majority of pleural effusion samples received from departments had a volume of >250–500 mL (46.0%), while 12.5% of the samples had a volume of <50 mL. There is still considerable debate regarding the optimal fluid volume required for the best diagnostic results. Determining whether a sample is benign or a false negative can be challenging in cases with low fluid volume. The Ministry of Health has recommended collecting 50–250 mL of fluid to obtain an adequate number of cells for diagnosis. [4]. In practice, we have received all pleural effusion samples indicated for the cell block test and observed that the larger the fluid volume, the more cellular sediment is obtained. With more cellular sediment, we have a stronger basis for diagnosis.

The cell smear technique was developed in the early 20th century, with the primary goal of facilitating the microscopic observation of cells. However, over time, researchers have recognized that the cell block technique can enhance the detection of malignant cells and provide more detailed information on cellular structures [5]. This method also facilitates more advanced analyses, such as immunohistochemistry, aiding in the early detection and accurate diagnosis of malignant diseases [6]. In our study, 72.2% of the samples were benign, 22.1% were malignant, and 5.7% were suspicious (Table 2). These proportions are consistent with previous studies, which indicate that the majority of cases are diagnosed as benign [2], [7], [8], [9]. According to Table 2, the concordance rate between cell smear and cell block results was 79.6%, while the discrepancy rate was 20.4%. The detection rates of malignancy and suspicious cases were higher with the cell block technique compared to the cell smear technique (22.1% and 5.7% vs. 7.4% and 2.3%, respectively). This difference was statistically significant with p<0.05. Our results are also consistent with other studies worldwide [7], [8], [9]. According to S.H. Kumar et al. (2020), the highest diagnostic concordance between the cell block and cell smear techniques was observed in synovial fluid (4/4, 100%) and pericardial fluid (1/1, 100%), followed by pleural fluid (38/40, 95%) and peritoneal fluid (33/39, 84.6%). The sensitivity and specificity of the cell smear technique compared to the cell block technique in effusion diagnosis were 86% and 100%, respectively [8]. According to S. S. Sabitha Rani et al. (2021), the lower malignancy detection rate of the cell smear technique compared to the cell block technique is due to the dispersed nature of cells in cell smears, with cellular morphology being obscured by a background of red blood cells, numerous inflammatory cells, necrotic debris, and reactive mesothelial cells. The cell block technique enhances the effectiveness of malignancy diagnosis by 6.66% compared to the cell smear technique [9].

Our study results showed a statistically significant association between gender and fluid volume with the cell block test results for pleural effusion (p<0.05). The study found that the malignancy diagnosis rate was higher in females than in males, and the malignancy rate was higher in the >500 mL group compared to other groups. There was no statistically significant association between age group and fluid color with the cell block test results (Table 3). According to several studies, malignant pleural effusion is commonly associated with lung cancer and breast cancer [8], [10]. Breast cancer occurs more frequently in females than in males because the ovaries in females produce higher levels of estrogen and progesterone. These hormones play a crucial role in the development of breast glandular tissue and cell division. Their continuous presence throughout the menstrual cycle can stimulate abnormal cell growth, increasing the risk of cancer [11].

Multiple studies have demonstrated a correlation between certain characteristics of pleural effusion and malignancy [12]. However, there is no evidence that pleural fluid volume directly determines the malignancy rate. Malignant pleural effusion often occurs in advanced or metastatic cancer stages, potentially due to angiogenesis leading to increased vascular permeability. This condition typically indicates that the patient may be in a severe disease stage with a poor prognosis [12]. On the other hand, a larger volume of pleural effusion results in a higher amount of cellular sediment, improving the ability to observe abnormal cells and increasing the likelihood of malignancy diagnosis.

Regarding color, pleural effusion can vary significantly in appearance depending on the underlying cause. For example, red or bloody fluid may suggest the presence of cancer or trauma, whereas clear or pale yellow fluid may indicate benign causes such as heart failure or cirrhosis. Although color alone is not a definitive indicator of malignancy, certain appearances, such as turbid or bloody fluid, may suggest a higher likelihood of cancer presence [12].

**V. CONCLUSION**

The cell block technique identified more malignant and suspicious cases than the cell smear technique in diagnosing malignant pleural effusion. A significant association was found between gender, fluid volume, and cytological diagnosis using the cell block technique.

**REFERENCES**

[1] R. Sharma, “Mapping of global, regional and national incidence, mortality and mortality-to-incidence ratio of lung cancer in 2020 and 2050,” *Int. J. Clin. Oncol.*, vol. 27, no. 4, pp. 665–675, Apr. 2022, doi: 10.1007/s10147-021-02108-2.

[2] Nguyen Quang Thi *et al.*, “Efficacy of cell block technique in the cytodiagnosis of some body cavityeffusions at the 108 Military Central Hospital,” *J. 108 - Clin. Med. Phamarcy*, vol. 17, no. 8, pp. 156–162, Aug. 2022, doi: 10.52389/ydls.v17iDB8.1316.

[3] Ozcakar, B *et al.*, “Does pleural fluid appearance really matter? The relationship between fluid appearance and cytology, cell counts, and chemical laboratory measurements in pleural effusions of patients with cancer,” *J. Cardiothorac. Surg.*, vol. 5, pp. 1–5, 2010.

[4] Ministry of Health, *Guidelines for Technical Procedures in Pathology and Cytology*. Hanoi: Medical Publishing House, 2016.

[5] L. G. Koss and M. R. Melamed, *Koss’ Diagnostic Cytology and Its Histopathologic Bases*, 5th ed. Lippincott Williams & Wilkins, 2006.

[6] M. Thapar, R. K. Mishra, A. Sharma, V. Goyal, and V. Goyal, “Critical analysis of cell block versus smear examination in effusions,” *J. Cytol.*, vol. 26, no. 2, pp. 60–64, Apr. 2009, doi: 10.4103/0970-9371.55223.

[7] S. S. S. Rani, I. S. Vamshidhar, N. A. John, and J. John, “Diagnosis of Pleural Fluid Effusions by Cell Block and Pleural Biopsy - A Comparative Study,” *J. Cytol.*, vol. 39, no. 4, pp. 169–173, 2022, doi: 10.4103/joc.joc\_91\_21.

[8] S. H. KUMAR, S. S, D. SHETTY, and R. RAO, “Clinicopathological Study of 117 Body Fluids: Comparison of Conventional Smear and Cell Block Technique,” *Curr. Health Sci. J.*, vol. 46, no. 4, pp. 336–343, 2020, doi: 10.12865/CHSJ.46.04.03.

[9] S. S. S. Rani and I. S. Vamshidhar, “Efficacy of Cell Block Technique in the Cytodiagnosis of Malignant Serous Effusions,” *Maedica*, vol. 16, no. 1, pp. 16–21, Mar. 2021, doi: 10.26574/maedica.2020.16.1.16.

[10] U. Shivakumarswamy, S. U. Arakeri, M. H. Karigowdar, and B. Yelikar, “Diagnostic utility of the cell block method versus the conventional smear study in pleural fluid cytology,” *J. Cytol. Indian Acad. Cytol.*, vol. 29, no. 1, pp. 11–15, 2012, doi: 10.4103/0970-9371.93210.

[11] V. Atashgaran, J. Wrin, S. C. Barry, P. Dasari, and W. V. Ingman, “Dissecting the Biology of Menstrual Cycle-Associated Breast Cancer Risk,” *Front. Oncol.*, vol. 6, Dec. 2016, doi: 10.3389/fonc.2016.00267.

[12] Ali Saeed Wahla, Mateen Uzbeck, Yaser Abu El Sameed, and Zaid Zoumot, “Managing malignant pleural effusion | Cleveland Clinic Journal of Medicine,” *Cleveland Clinic Journal of Medicine*, vol. 86, no. 2, pp. 95–99, 2019, doi: https://doi.org/10.3949/ccjm.86a.17095.