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Cell Block Method and Conventional Smear Pathology in Pleural Fluid Cytology: A Comparative Study

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Abstract

Background: Cytological examinations of serous effusions have been well accepted and are often considered definitive diagnoses in malignancies, as the results help in staging, prognosis, and management. They also provide information about various inflammatory conditions. In conventional cytological smears, the exact identification of cells as either malignant or reactive mesothelial cells is a diagnostic problem

Materials and methods: The study is done for a period of 1 year (June 2019- May 2020). In this study, 120 patients are selected with unilateral or bilateral pleural effusion, irrespective of age and sex referred to the department of pathology for cytological examination.120 pleural fluid samples were analysed. Both conventional smears and cell blocks were prepared by using 10% alcohol-formalin as a fixative agent. Statistical analysis was done using Graphpad Instat3 version.

Results: Out of a total of 120 samples, the final diagnoses included 15(12.5%) malignancies and 105(87.5%) benign conditions which includes inflammatory and other infectious conditions. The additional yield for the malignancy was found to be 5.83% more by cell block as compared to that obtained by conventional smear method. Diagnostic yield for malignancy was significantly increased by using the cell block method.

Conclusion: The cell block methodology provides high cellularity, better morphological features, additional yield of malignant cells, better architectural patterns and increased sensitivity for cytodiagnosis of malignant lesions as compared to the Conventional Smear method

Keywords: Cell block; conventional smear; cytology; pleural effusion

Introduction

Diagnostic cytology is the logical illustration of understanding of cells from the human body that exfoliate or are expelled from their physiological environment. Inside most recent couple of decades, the cytological strategies for malignancy identification have changed the standpoint of ailment and its treatment. Cytopathology involves two types of specimen. In Exfoliative cytopathology (first type), spontaneous exfoliation of cells from surface of mucous membrane and serous cavity is studied. It also includes study of cells obtained by scraping tissue surface. In aspiration cytopathology (the second type), fine needle aspiration (FNA) biopsy is studied.[1]

The accumulation of fluid in body cavity is referred to as serous effusion and is classified into two types- **transudate** and **exudate.** Effusion fluids contain mesothelial cells and non-neoplastic cells like macrophages and other blood derived cells.

Accumulation of excess fluid in the pleural space is called as pleural effusion. **Transudate** effusion is caused by fluid leaking back into the chest due to disorders that cause a pressure imbalance in the blood vessels. Inflammatory disorders, such as cancers, infections and traumatic injuries cause **exudative** pleural effusion.

Cytological examination of serous fluids is one of the commonly performed investigations in India as it reveals information about inflammatory and malignant lesions of serous membranes. It helps the clinician to find the etiology of effusion and list of differential diagnoses. It also allows to follow the results of therapy and prognosis. In conventional cytological smears, the exact identification of cells as either malignant or reactive mesothelial cells is a diagnostic problem. Very meticulous screening of the smear is required for distinguishing benign from malignant cells. Lower diagnostic yield in CS method occurs due to cellular overlapping, delaying artifact, poor processing, preparatory cytotechnique and leaving behind useful material. This remaining material can be very helpful in increasing diagnostic yield by cell block method. The cell block (CB) technique is an old method to assess serous cavity fluids.[2].

If cell block is used the sensitivity for malignant cell identification is increased. A new technique of cell block preparation by using 10% alcohol-formalin as fixative was used to identify the sensitivity of diagnosis in comparison with the conventional smear study. This method is simple and cost effective and no extra material is used as compared to other methods. Cell block technique also causes a reduction in false positives. The principal benefits of the CB technique are preservation of tissue architecture and obtaining multiple sections for special stains and immunohistochemistry. [3] In this method there is direct transfer of centrifuged cellular material in lens paper or embedded in plasma or agar and then processed as a routine histological specimen. Cell block preparation may help to categorize neoplastic lesions.

Objectives

1. To study the cytomorphological features of different pleural fluids.
2. To compare the cytomorphological findings between conventional smear technique and cell block method

Materials And Methods

The study was conducted in the Department of Pathology, Silchar Medical College and Hospital in the study period of one year from June 2019 to May 2020. Detailed clinical history was taken and a complete physical examination done in all the patients. Pleural fluid was aspirated. Ten milliliters of fresh pleural fluid was divided into two parts. One part (5ml) was subjected to conventional smear technique and staining done with MGG stain and Papanicolaou stain. Another part (5ml) was subjected to cell block technique.

The smears obtained were examined for features such as background, cellularity, morphology and architecture and were given scores from 0 to 2+ scale according to Mair et al. [4] scoring system.(Table 1)

Final diagnosis was made considering detailed clinical history, radiological examinations, other laboratory tests and direct FNAC or biopsy of lesion if possible.

Methods of statistical analysis

The results of both smears and cell-blocks were analyzed to calculate their sensitivity, specificity, positive predictive value and negative predictive value in correlation with the final diagnosis. P value less than 0.05 is statistically significant. Data analysis were done using Graphpad Instat3 version.

Conventional Smear technique

The five milliliter sample was centrifuged at 2500 revolutions per minute for 15 minutes. The supernatant is disposed of. At least two thin smears were prepared from the sediment. One smear was prepared after air drying and it had been stained with the May-Grünwald-Giemsa stain. The other smear was instantly fixed in 95% alcohol and stained with the Papanicolaou stain.

Cell block preparation

There are various methods of cell block preparation. We followed the fixed sediment method of cell block preparation.

The 5 mL sample that remained was subjected to fixation for one hour by mixing with 5 mL of 10%

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alcohol-formalin (i.e., nine parts of 90% alcohol and one part of 7.5% formalin). Following 60 minutes, this 10 ml fluid was centrifuged at 2500 rpm for 15 minutes. The supernatant was disposed of and a further 3 mL of fresh 10% alcohol–formalin was once again added to the sediment and it was kept for one day. On the next day, the sediment containing the cell button of the pleural fluid sample was scooped out on to the filter paper and this cell button sediment sample was processed along with other routine histopathological specimens. The paraffin embedded cell button (cell block) sections of 4–6 μ thickness were prepared and stained with the haematoxylin and eosin stain. [5]

Ethics Statement: Permission from Institutional Ethical Committee was taken for this study. The purpose and objective of the study were clearly explained to the patients in the local language. The cases were taken after obtaining their written informed consent.

The patients were selected at random irrespective of age, sex and socioeconomic status. Thorough history and clinical examination was done. Relevant investigations were sent.

Results

Most of the patients were in the age above 60 years, followed by those in the age group between 51-60 years. The youngest patient was a 7 month old male and the oldest one was 90 years old. A male preponderance was seen. Males outnumbered female patients by 1.8:1 ratio.Amongst males, most common age group was patients in the age above 60 years, followed by patients in age group 51-60 years. Among the female cases also, most were in the age above 60 years, followed by 41-50 years. Cellularity was found more by the CB method when compared to the CS method.

Out of 120 cases of pleural effusion, 33 cases (27.5%) were transudates and 87 cases (72.5%) were exudates.Out of 87 cases of exudative effusion, 72 cases (82.75%) were inflammatory and 15 cases (17.24%) were neoplastic.

23 cases (19.16%) were of haemorrhagic fluid and 97 cases (80.83%) were of non haemorrhagic fluid out of the total 120 cases.

After analysis of the above samples, they were categorized as inconclusive, benign, suspicious for malignancy, or malignant samples.

Out of the total 120 cases, 87(72.5%) cases were diagnosed as benign/Inflammatory, 7 cases as suspicious for malignancy, and 5 cases as malignant by conventional smear technique. 21 cases were inconclusive.(Table 2)

Out of the total 120 cases, 94 cases were diagnosed as benign/Inflammatory, 2 cases as suspicious for malignancy, and 12 cases as malignant by cell block technique. 12 cases were inconclusive.(Table 3)

On the basis of cell block, clinical and radiological finding, 105 cases (87.5%) were found benign and 15 cases (12.5%) were found malignant.(Table 4)

All smears obtained by conventional method and cell block method were evaluated for parameters such as background, cellularity, cell morphology and cell distribution and were scored from 0 to 2+ scale according to the Mair et al., scoring system.(Table 1)

By conventional method, it was seen that maximum samples were in category 1 with respect to all parameters. Where as in cell block method, maximum samples were in category 2 with respect to all parameters except one parameter (cell morphology).(Table 5)

Significance of difference of each parameter for Conventional Smear and Cell Block was performed using Chi-Square statistical test. The difference between Conventional Smear and Cell Block for all the parameters was found statistically significant($p<0.05$)

By Conventional Smear technique, the Sensitivity was 78.57%, Specificity: was 98.82%, Positive predictive value was 91.67% and Negative predictive value was 96.55%.

By Cell Block method, the Sensitivity was 93.33 %, Specificity was 100 %, Positive predictive value was 100% and Negative predictive value was 98.93%. Therefore, in this study, utility of the Cell Block method in cytodiagnosis of malignant effusion was found highly significant as compared to Conventional Smear method.

Discussion

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The present study was done to study the cytomorphology of pleural fluid and the comparison between conventional technique and cell block method. 120 cases presenting with pleural effusion were included in the study. The cytological examination of body fluid effusions has more and more gained acceptance in clinical medicine, to such an extent that a positive diagnosis is frequently considered the definitive test and obviates explorative surgery. It is important not only in the diagnosis of malignant lesions, but also helps in staging and prognosis.[6]

Malignant pleural effusion is a common complication of cancers like pulmonary and gastric carcinomas.[7] In adult patients, examination of fluids from the serous cavities of the body is a vital part of management. Malignant neoplasms, especially lymphoid neoplasms, represent a major cause of death in children and in these cases cytological examination is very useful in their management.[4]

In CS cytology distinguishing reactive mesothelial cells from metastatic neoplasms is one of the most common problems. The problem is either secondary to marked atypia of mesothelial cells caused by the microbiological, chemical, physical, immunological, or metabolic insults to the bodily fluid membranes or to the subtle cytomorphological features of some malignant neoplasms, notably well-differentiated adenocarcinomas. The problem may become compounded by artefacts from poor fixation, preparation, or staining techniques.[8] Although the preparation of CS is a much simpler procedure than that of paraffin sections, it has limits, that is, lack of tissue architecture. In some cases, appreciation of tissue architecture make diagnosis easier.[9] Another limitation of the conventional cytological examination of effusions is that it has a sensitivity of only 40–70% for the presence of malignant disease due to overcrowding of cells, cell loss and completely different laboratory processing ways. Others like reactive mesothelial cells, abundance of inflammatory cells and paucity of representative cells contribute to significant difficulties in making definite diagnosis on conventional smears. [10]

Since the introduction of the CB technique by Bahrenburg nearly a century ago, it has been utilized for processing fluids. In 1928, Zemansky told that the CB method was superior to the CS technique and that examination of materials other than pleural and ascitic fluids was not reliable. Malignant cells in the pleural or ascitic fluid are almost always indicative of metastatic cancer, as tumors arising from mesothelial cells present in these spaces are rare. When present, the tumor cells are numerous and clusters may be found frequently. On CB glandular forms are more reliable. The demonstration of mucin in the tumor cells is evidence that they originate from a glandular epithelium.[11] Diagnostic problems arise whenever there is only marginal morphological distinction, for example, between reactive mesothelial cells and poorly differentiated malignant cells. [12]

The advantages of the CB procedure include:

1. Recognition of histological patterns of diseases that typically cannot be known reliably in conventional smears.
2. Multiple sections can be studied by routine staining, special staining and immunocytological techniques.
3. There is less difficulty in spite of background showing excess blood on microscopic observation.
4. There is possibility of storing slides for retrospective studies. But storage of the CS is a practical problem. [13]

Thus an attempt was made in this study to prepare and analyze both CS and CB from the same specimen. In this study, due thought was given to age, sex, site of effusion, clinical and radiological findings, to gain at a final diagnosis. Cell blocks could provide diagnostic information complementary or additional to that obtained from conventional cell smears. However, morphological preservation is often not satisfactory in cell blocks processed by routine procedures used for surgical specimens. In the study, 10% alcohol-formalin was used as a fixative for the CB preparation.

In the present study, most cases were in the age group of more than 60 years. This contrasts with findings by Bansode et al. [14] and Padmavathi et al., [15] who have reported most number of cases in the age group 41–60 years as 54% and 69.3%, respectively. Greater numbers of benign/inflammatory effusions and fewer malignant effusions were found in the present study

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as compared to those cited, [14,15] where more cases of malignant effusions were reported

In the present study, out of 120 cases, benign effusions were seen in 87.5% of cases, which were comparable with the results of studies done by Gandhi et al [16] in which benign cases were 82.14%, Pradhan et al [17] in which benign cases were 81.2% and Santwani and Vachhani [18] in which benign cases were 75.4%.

In the present study, out of 120 cases, 12.5% of cases were diagnosed as malignant. Gandhi et al [16] found malignant cases to be 17.85%. Santwani and Vachhani [18] found malignant cases to be 24.6%.

Out of 150 cases studied by Archana et al, 39(26%) were positive for malignancy by cell block method, while by routine method only 29 samples were reported as positive for malignant cells. Thus it was found that there was significant difference between the results obtained by direct smear method and cell block method. 34 cell blocks had no cellularity. [19]

In the present study, out of total 120 cases, 5 cases were found positive for malignancy by conventional smear method. 12 cases were found positive for malignancy by cell block method. Thus in this study also there was significant difference between the results obtained by direct smear method and cell block method. Thus it is seen that cell block method is superior to conventional smear method.

In the present study, Sensitivity, Specificity, Negative Predictive Value (NPV) and Positive Predictive Value (PPV) of Conventional Cytological smear for diagnosing malignancy were 78.57%, 98.82%, 96.55% and 91.67%, respectively. Bansode et al. [14] have reported Sensitivity, Specificity, NPV and PPV of Conventional Cytological smear for diagnosing malignancy as 79%, 100%, 100% and 93%, respectively. Padmavathi et al. [15] have reported Sensitivity, Specificity, NPV and PPV of Conventional Cytological smear for diagnosing malignancy as 91.3%, 100%, 100% and 98.3%, respectively. Nair and Manjula have reported Sensitivity, Specificity, NPV and PPV of cytological smear for diagnosing malignancy as 32.3%, 100%, 14.48% and 85.5%, respectively. [20]

In a study done by Khan et al, additional findings were diagnostic in 16% of malignant cases. [21] Additional 18 cases for malignant lesions were diagnosed by cellblock method in study done by Takagi. [22]

According to various studies additional diagnostic yield for malignancy was noted if conventional smear technique is supplemented by cellblock method. [23,24] In present study, the additional yield for the malignancy was found to be 5.83% more by CB as compared to that obtained by CS method.

In the present study diagnostic yield for malignancy was significantly increased by using the cell block method.

Conclusion

In the present study, the cytomorphological features of different pleural fluids were studied. It was seen that morphologic features was found to be better if both MGG and Pap staining methods were used.

The cell block methodology provides high cellularity, better morphological features, additional yield of malignant cells, better architectural patterns and increased sensitivity for cytodiagnosis of malignant lesions as compared to the Conventional Smear method.

Multiple sections of the same material can be processed in cell block technique for immunohistochemistry.

Additional yield for the malignancy was found to be 5.83% more by CB as compared to that obtained by CS method.

References

1. Chitale D, Kini SR. Overview. In: KIni SR. Color Atlas of Differential diagnosis in exfoliative and aspiration cytopathology. 2nd ed. USA: Williams & Wilkins;2011.p 05.
2. Wojcik EM, Selvagi SM. Comparison of smears and cell blocks in the fine needle aspiration diagnosis of recurrent gynecologic malignancies. Acta Cytol. 1991;35:773-6.
3. Nathan NA, Narayan E, Smith MM, Horn MJ. Cytology-improved preparation and its efficacy in diagnostic cytology. Am J Clin Pathol. 2000;114:599-606.
4. Mair S, Dunbar F, Becker PJ, Du Plessis W. Fine Needle Cytology: Is aspiration suction

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necessary? A study of 100 masses in various sites. Acta Cytol 1989;33(6):809-13.

5. Shivakumarswamy U, Arakeri SU, Karigowdar MH, Yelikar B. Diagnostic utility of the cell block versus the conventional smear study in pleural fluid cytology. Journal of cytology.2012;29(1):11-5.
6. Dekker A, Bupp PA. Cytology of serous effusions: a comparative study of two slightly preparative methods. Acta cytologica.1976;20(4):394-9.
7. Sears D, Hajdu SI. The cytologic diagnosis of malignant neoplasms in pleural and peritoneal effusions. Acta cytologica. 1987;31(2):85-97.
8. Price BA, Ehya H, Lee JH. Significance of pericellular lacunae in cell blocks of effusions. Acta Cytol. 1992;36:333-7.
9. Kung IT, Yuen RW, Chan JK. Technical notes. Optimal formalin fixation and processing schedule of cell blocks from the fine needle aspirates. Pathology. 1989;2:143-5.
10. Mezger J, Stotzer O, Schilli G, Bauer S, Wilmanns W. Identification of carcinoma cells in ascitic and pleural fluid. Comparison of four panepithelial antigens with carcinoembryonic antigen. Acta Cytol. 1992;36:75-81.
11. Velios F, Griffin J. Examination of body fluids for tumour cells. Am J Clin Pathol. 1954;24:676-81.
12. Bousfield LR, Greenberg ML, Pacey F. Cytogenetic diagnosis of cancer from body fluids. Acta Cytol. 1985;29:768-73.
13. Zito FA, Gadaleta CD, Salvatore C, Filotico R, Labriola A, Marzulla A, Prete F, Marzullo F. A modified cell block technique for fine needle aspiration cytology. Acta cytologica. 1995;39(1):93-9.
14. Bansode S, Kumbalkar D, Nayak S. Evaluation of cell block technique in the cytodiagnosis of body fluids. Int J Sci Res 2015;4:87-94.
15. Padmavathi A, Prasad BV, Anuradha B. A comparative study of fluis cytology with smear and cell block preparation. J Evid Based Med Healthc 2016;3:3532-5
16. Gandhi B, Shanthi V, Mohan RN, Reddy C. The diagnostic utility of cell block as an adjunct to cytological smears. International Journal of Medical Research and Health Sciences. 2014. Jan 1;3(2):278-84.
17. Pradhan SB, Pradhan B, Dali S.Cytology of body fluids from different sites: an approach for early diagnosis of malignancy. JNMA; Journal of Nepal Medical Association. 2006;45(164):353-6.
18. Viral MB, Santwani PM, Vachhani JH. Analysis of diagnostic Value of Cytological Smear Method Versus Cell Block Method in Body fluid cytology: Study of 150 cases. Ethiopian Journal of health Sciences. 2014 Apr;24(2):125.
19. Joshi A, Mahajan N, Karmakar PJ, Mahore SD. Diagnostic utility of various techniques used in body fluid cytology. IOSR. Journal of Dental and Medical Sciences(IOSR-JDMS).2014;13(1):13-8.
20. Nair GG, Manjula AA. Comparative study of cell blocks & routine smears of pleural & peritoneal fluids in suspected cases of malignancy. Indian J Pathol Oncol 2015;2;61-8.
21. Khan N, Sherwani KR, Afroz N, Kapoor S. Usefulness of cell blocks versus smears in malignant effusion cases. Journal of Cytology 2006;23(3):129-132.
22. Takagi F. Studies on tumour cells in serous effusion. Am J Clin Patholgy 1954;24:663-675.
23. DekkerA,BuppPA.Cytologyofserouseffusions: An investigation into the usefulness of cell blocks versus smears. American journal of clinical pathology. 1978 Dec 1;70(6):855-60.
24. Bodele AK, Parate SN, Wadadekar AA, Bobhate SK, Munshi MM. Diagnostic utility of cell block preparation in reporting of fluid cytology. Journal of Cytology 2003;20(3):133-135

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FIGURES

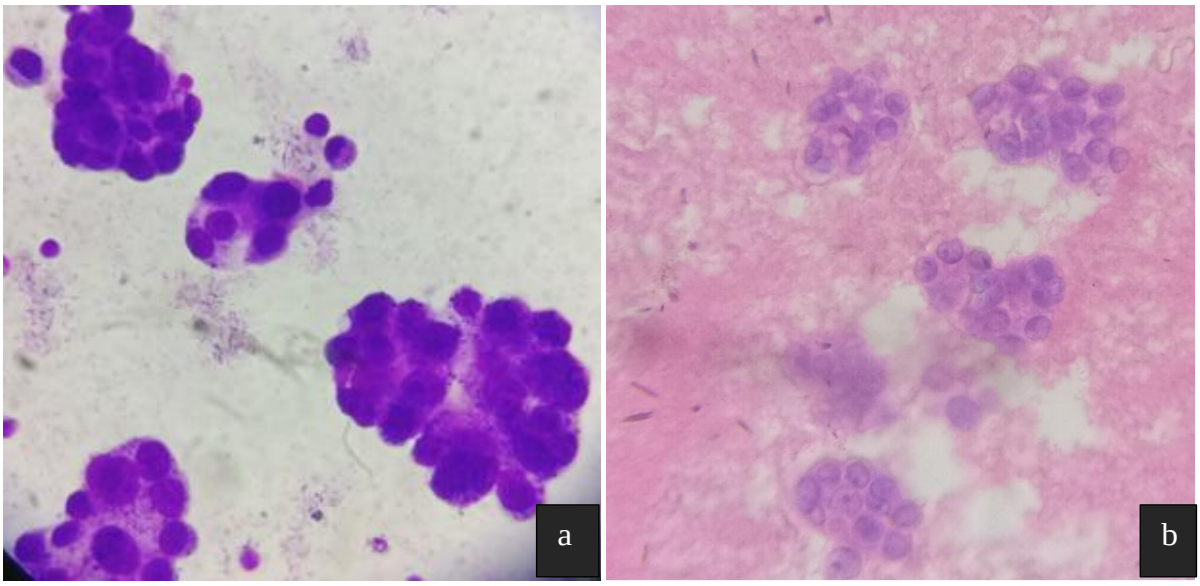

FIGURE 1: (a) Photomicrograph showing adenocarcinoma in conventional smear (Giemsa) (b) Photomicrograph showing adenocarcinoma in cell block (H and E)

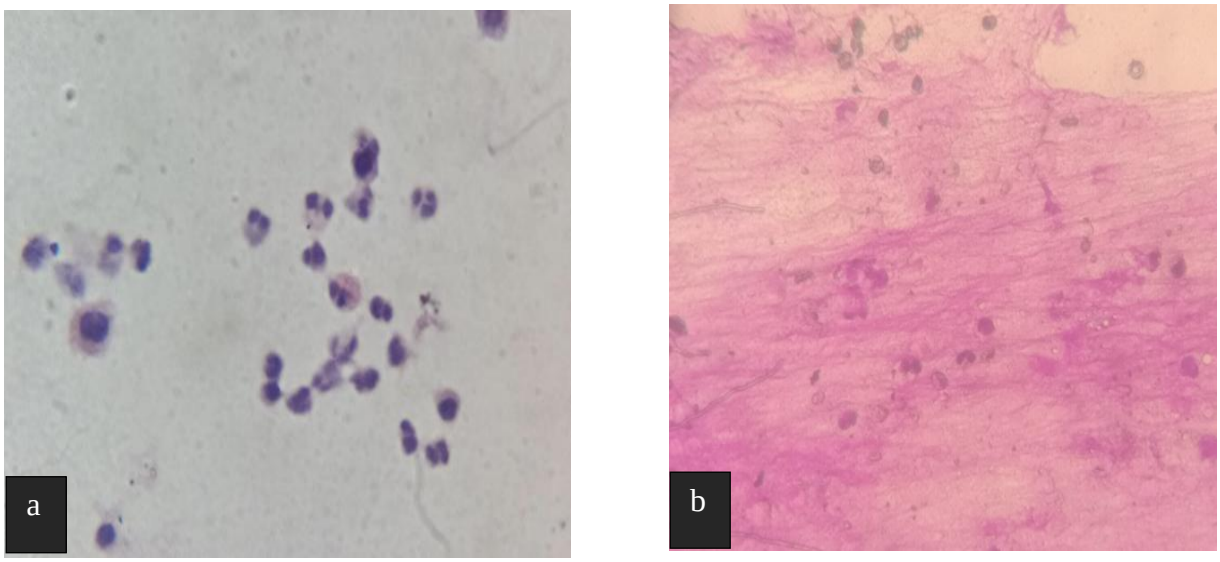

FIGURE 2 : (a) Photomicrograph showing acute inflammation in conventional smear (Giemsa), (b) Photomicrograph showing acute inflammation in cell block (H and E)

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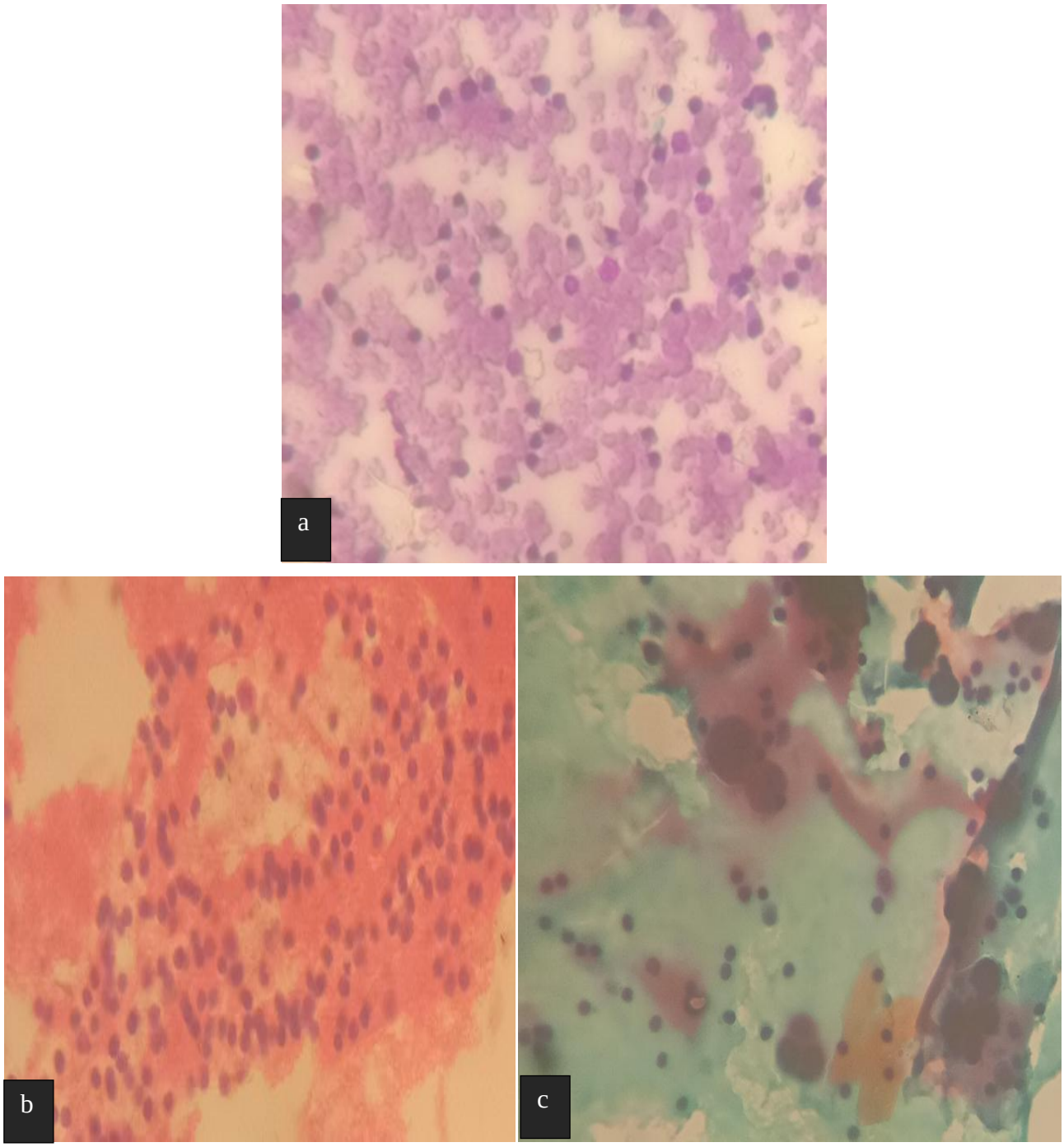

FIGURE 3:(a) Photomicrograph showing chronic inflammation in conventional smear (Giemsa), (b)Photomicrograph showing chronic inflammation in cell block (H & E) (c) Photomicrograph showing chronic inflammation in conventional smear (PAP)

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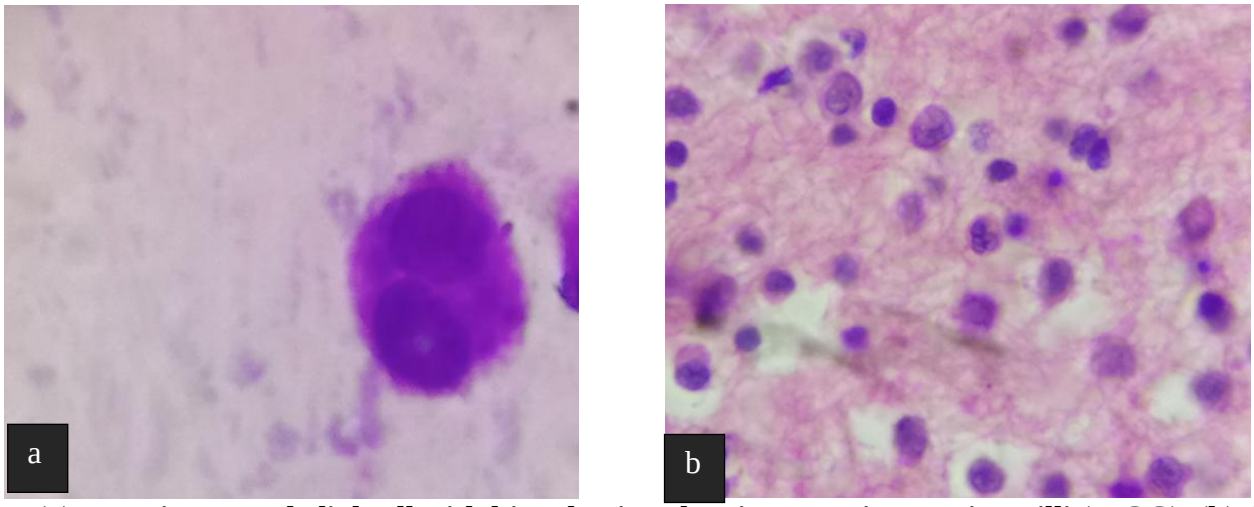

FIGURE 4:(a) Reactive mesothelial cell,with binucleation showing prominent microvilli (MGG), (b) Cell block preparation showing reactive mesothelial cells, some with multiple nuclei showing prominent nucleoli in a proteinaceous background with lymphocytes(H & E stain)

TABLE 1: **Scoring system**.

Parameter	Quantitative Description	Score
1.Background or proteinaceous material	Large amount, great compromise in diagnosis Moderate amount, diagnosis possible Minimal , diagnosis easy	0 1 2
2.Amount of Cellular material	Minimal to absent, diagnosis not possible Sufficient for cytodiagnosis Abundant , diagnosis simple	0 1 2
3. Cell Morphology, Cellular degeneration and trauma	Marked cellular degeneration, diagnosis not possible Moderate cellular degeneration, diagnosis possible Minimal cellular degeneration, diagnosis easy	0 1 2
4. Retention of appropriate architecture and cellular arrangement	Minimal to absent: non diagnostic Moderate : some preservation e.g., follicles, papillae, acini, syncytia or single cell pattern Excellent architectural display closely reflecting histology: diagnosis obvious	0 1 2

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TABLE 2: Distribution of cases on the basis of cytological analysis by conventional smear

Diagnosis	No. of cases	Percentage
Inconclusive	21	17.5%
Benign/Inflammatory	87	72.5%
Suspicious	7	5.8%
Malignant	5	4.1%
Total	120	100%

TABLE 3: Distribution of cases on the basis of cytological analysis by Cell Block

Diagnosis	No. of cases	Percentage
Inconclusive	12	10%
Benign/Inflammatory	94	78.33%
Suspicious	2	1.66%
Malignant	12	10%
Total	120	100%

TABLE 4: Distribution of cases as benign and malignant on the basis of cell block, clinical and radiological finding

Diagnosis	No. of cases	Percentage
Benign	105	87.5%
Malignant	15	12.5%
Total	120	100%

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TABLE 5: Descriptive statistics for each of the four parameters by conventional smear method and cell block method.

Method	Parameter	Frequency	Percentage
Conventional	Background		
	0	22	18.33%
	1	74	61.67%
	2	24	20%
	Cellularity		
	0	27	22.5%
	1	70	58.34%
	2	23	19.16%
	Cell Morphology		
	0	32	26.67%
	1	62	51.67%
	2	26	21.67%
	Architecture		
	0	33	27.5%
	1	72	60%
	2	15	12.5%
Cell block	Background		
	0	14	11.67%

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	1 2	52 54	43.33% 45%
	Cellularity 0 1 2	 14 38 68	 11.67% 31.67% 56.67%
	Cell Morphology 0 1 2	 13 57 50	 10.83% 47.5% 41.67%
	Architecture 0 1 2	 26 35 59	 21.67% 29.17% 49.16%

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