

The Papanicolaou Society of Cytopathology Classification for Pulmonary Specimens: Application in Exfoliative Respiratory Cytology

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ABSTRACT

Background: Cytologic examination of specimens obtained from the respiratory tract is the primary and frequently used diagnostic technique in patients with respiratory symptoms or in those presenting with a pulmonary abnormality. Lung carcinoma is the leading cause of mortality in India. Hence, early diagnosis and effective treatment are keys to prolong the survival of lung cancer patients.

Methods: 100 consecutive samples were taken which included 66 samples of bronchial wash, 27 samples of brush and 7 samples of bronchoalveolar lavage. These were viewed independently by two pathologists to study the ease of applicability, reproducibility and role of Papanicolaou Society of Cytopathology classification for pulmonary specimens.

Result: The classification and terminology scheme recommend a six-tiered system comprising of non-diagnostic, negative, atypical, neoplastic (benign and neoplasms of low malignant potential), suspicious and positive for malignancy. In our study 43% were non-diagnostic, 33% were negative, 10% were atypical, 6% were suspicious for malignancy and 8% were malignant.

Conclusion: This classification system of respiratory cytology is easy to apply and interpret with minimal inter-observer variation. Standardized classification and terminology system provide a framework for consistent inter-intra departmental and inter institutional communication of diagnostic, prognostic and management information needed for consistent and optimal patient care.

Keywords: Papanicolaou, Bronchial Brush, Wash, Bronchoalveolar Lavage

Introduction

Lung carcinoma is the leading cause of mortality in India.^[1] In addition to primary tumour, lung is also a common site for metastatic tumours.^[2] Most lung cancer patients are diagnosed at an advanced stage of the disease, making curable surgery not an option. Hence, early diagnosis and effective treatment are keys to prolong the survival of lung cancer patients.^[3]

Cytologic examination of specimens obtained from the respiratory tract is a primary and frequently the initial diagnostic technique performed in patients with respiratory symptoms or in those presenting with a pulmonary abnormality. Both exfoliative cytology techniques and fine-needle aspiration (FNA) are used extensively for diagnosis of pulmonary lesions.^[4]

Currently, ancillary and molecular testing is also applied to these samples, further increasing their utility. However, lack of a standardized nomenclature and classification scheme has hampered communication between physicians managing patients.

1999, the PSC issued guidelines for the cytologic investigations of pulmonary lesions which included recommendations for a classification system^[5], but then it wasn't routinely used. The PSC revised these

guidelines in 2016 which proposed a six-category system for the diagnosis of cytologic samples obtained from the respiratory tract. These Categories includes non-diagnostic, negative (for malignancy), atypical, neoplastic, suspicious for malignancy, and positive for malignancy.^[4]

Materials and Methods

This prospective study was done in the Department of Pathology of a tertiary level centre for all respiratory diseases which receives a wide number of samples from respiratory tract. 100 consecutive samples were taken from the patients attending the pulmonary OPD and were independently viewed by two pathologists to study the ease of applicability, reproducibility and potential role of Papanicolaou Society of Cytopathology classification for pulmonary specimens, which includes bronchial washings, bronchial brush and bronchoalveolar lavage specimens. Ethical clearance was obtained from Institute's ethics committee. 66 samples of bronchial wash, 27 brush and 7 BAL were included in the study. Histological follow-up was obtained in 49 cases. For statistical analysis of diagnostic accuracy, the surgical pathology diagnosis was used as the "gold standard".

Samples were processed within 2 hours of receipt. The BAL/BW fluid were taken in a test tube and centrifuged

at 1500 revolutions per minute (rpm) for 10–15 minutes. The supernatant was discarded and three direct smears were prepared from the deposit. One smear was stained with Papanicolaou stain whereas the others were stained with H and E and May Grunwald Giemsa stain while Ziehl Neelsen staining was done in selected cases where indicated by morphological assessment.

Samples fulfilling the following criteria were included in the study i) samples from representative site, ii) no obstruction of cytomorphology by haemorrhage.

The PSC revised guidelines (2016) were used to obtain the result. These guidelines proposed a six-category system for the diagnosis of cytological samples obtained from the respiratory tract. These categories are non-diagnostic, negative (for malignancy), atypical, neoplastic, suspicious for malignancy and positive for malignancy (Table 1).^[4]

Results

1. **Non-Diagnostic:** Out of 43 cases, we received biopsy of 17 cases. Amongst these 17, 12 cases (71%) were inconclusive in HPE also, however rest 5 cases (30%) turned out to be malignant. This was probably due to improper sample collection. Risk of malignancy in our study (30%) was lower than that of literature review (40%). The high percentage for non-diagnostic reports especially for bronchial washings and BAL indicates the importance of sample collection. Proper sample collection can significantly increase the yield of these procedures, decreasing the need of invasive biopsy. There was no inter-observer variation.
2. **Benign:** There were 14 cases whose histopathology correlation were available, 11 cases (79%) were true

negative, 3 (27%) were malignant in HPE. This data is comparable to literature review (24-43%) for risk of malignancy. This may be due to sampling error. There was no inter-observer variation. Patient selection is important for cytology. Standardization of reporting will help as negative cases may not require follow up but non diagnostic requires follow up.

3. **Atypical:** Out of 10 cases, we received 7 (70%) cases for HPE. All turned out to be malignant. Our proportion of malignant cases reported as atypical is higher than that seen in literature (54%). This can be attributed to (a) background of inflammation and degeneration obscuring morphology (b) lack of clinical and investigation data (c) inter-observer variation. Two out of ten had inter-observer variation. Both cases were discussed by the two pathologists to achieve consensus. One was reported as atypical whereas other was upgraded to neoplasm and was confirmed on HPE.
4. **Neoplastic:** There was unusual categorization on this spectrum of samples. Early presentation is uncommon in patients with malignancy. We did not encounter any benign neoplasm in this study as most common lesion (carcinoid tumour) is usually confirmed on biopsy.
5. **Suspicious of Malignancy:** There were three cases out of six available for histopathological correlation. All of them were malignant. This was little higher than literature (82%) due to paucity of cells.
6. **Malignant:** Malignant cases were in concordance with the other data (100%). This highlights the role of cytology in diagnosing lung cancer.

Table 1: PSC Guidelines for Respiratory Cytology ^[4,8]

Diagnostic category and definition	Explanatory notes
I. Non diagnostic Insufficient and/or not representative cellular material for diagnosis.	This diagnostic category should be used when the specimen is acellular or when cells are not representative of the target being sampled. For example, bronchial cells and/or cartilage when the FNA target is a lymph node or lung mass. In addition, this category also applies to the FNA specimens of lymph node which show few lymphocytes, possibly from blood rather than a well sampled lymph node. It is recommended to process the entire specimen before designating a specimen “non diagnostic”
II. Benign The sample should be representative of the clinical lesion and benign. This category also includes reactive lymph nodes, granulomas, and other inflammatory reactive processes.	The lack of standardized adequacy criteria may explain the wide risk of malignancy range in this diagnostic category for both lung masses and lymph nodes.

Diagnostic category and definition	Explanatory notes
III. Atypical Can be used for both lung masses and lymph nodes	This diagnostic category should be used when atypical epithelial cells are seen. However, the quantity or quality of these cells is insufficient to determine whether they represent reactive bronchial cells or pneumocytes vs. malignant cells.
IV. Neoplasm A. Benign B. Undetermined malignant potential	A. This category includes neoplastic lesions in which the cytologic specimen is diagnostic of a specific benign neoplasm. B. This category should be used for cases where malignant neoplasm cannot be excluded. A majority of these cases will include neoplasms of low malignant potential.
V. Suspicious of malignancy (SM) This diagnostic category applies to sample showing feature most suggestive but not unequivocal for malignant neoplasm.	This diagnostic category should be used when the cellular atypia is favoured to be malignant but is not sufficient quantitatively or qualitatively for unequivocal malignancy.
VI. Malignant	Cytomorphology and/or immunohistochemistry (with antibodies validated in cytology samples) should be used to subclassify the tumour.

Table 2: Results of present study.

Categories	Bronchial wash	Bronchial wash	BAL	Total
Non Diagnostic	34	04	05	43
Benign	20	12	01	33
Atypical	06	03	01	10
Neoplastic	00	00	00	00
Suspicious of malignancy	06	00	00	06
Malignancy	00	08	00	08
Total	66	27	07	100

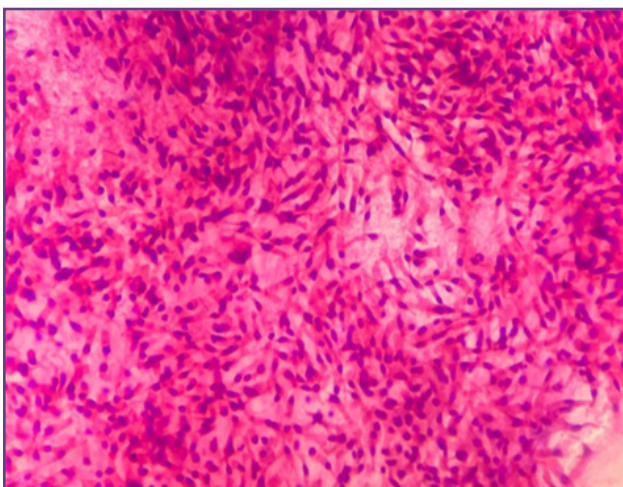


Fig. 1: Bronchial washing - showing respiratory cells (H and E, 400X).

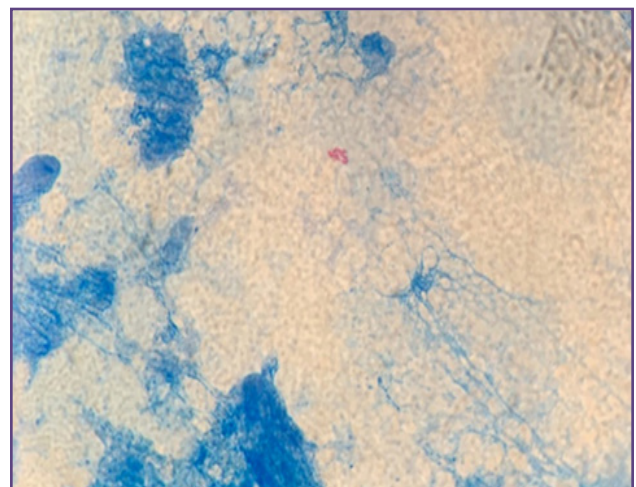


Fig. 2: Bronchial washing - showing acid fast bacilli (ZN stain, 1000X oil immersion).

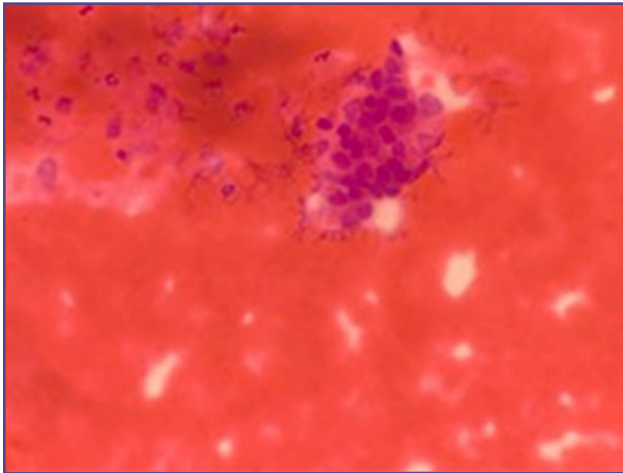


Fig. 3: Bronchial brush – showing atypical cells (H and E, 400X).

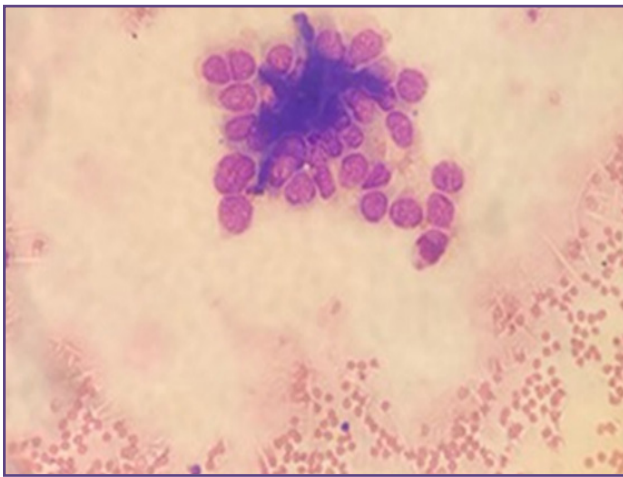


Fig. 4: Bronchoalveolar lavage – showing malignant cells (May Grunwald Giemsa stain, 400X).

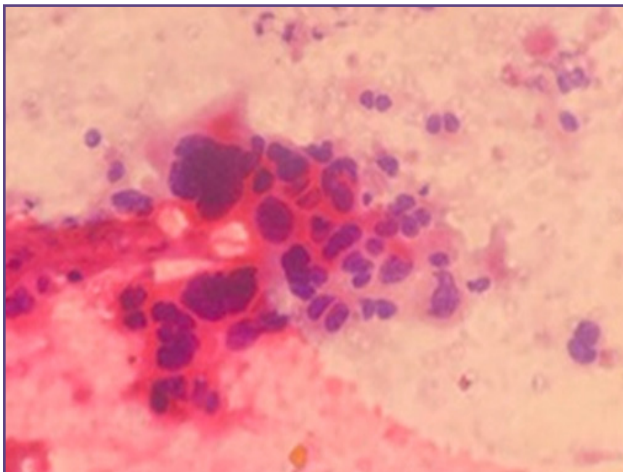


Fig. 5: Bronchial brush – showing malignant cells consistent with non small cell carcinoma (Pap stain , 400X).

Discussion

Lung carcinoma is not only the leading cause of mortality in India, but lung is also a common site for metastatic tumours.^[1,5] Cytological examination of specimens obtained from the respiratory tract is the primary and frequently used diagnostic technique in patients with respiratory symptoms or in those presenting with a pulmonary abnormality. While occasional cytological specimens are obtained from the upper respiratory tract, the majority of pulmonary diagnostic cytology involves the study of the lower respiratory tract. Due to the complexity of the respiratory tract and the location of various target lesions, a variety of cytological techniques have been developed for the study of diseases of respiratory system. Both exfoliative cytology techniques and fine-needle aspiration (FNA) are used extensively for diagnosis of pulmonary lesions. While respiratory cytology is used predominantly for the study of neoplastic or potentially neoplastic diseases, it is also variably useful in the investigation of a variety of benign diseases including opportunistic infections, tuberculosis, sarcoidosis, industrial disease (e.g. asbestosis) and lung transplant rejection.^[3]

BW/lavage cytology is a widely accepted, safe, simple and minimally invasive technique to evaluate lung pathologies. Moreover, bronchial wash technique samples out peripheral areas of lung that are beyond the reach of bronchial brush.^[3] Currently, ancillary and molecular testing are also applied to these samples, further increasing their utility.

The Papanicolaou Society of Cytopathology (PSC) has been involved in diagnostic nomenclature for cytological material derived from other sites including thyroid, cervix and pancreaticobiliary system.^[6-8] In addition to proposing diagnostic criteria and categories, these classification systems have provided estimates of malignancy risk for each of the proposed categories.^[4,6,8] In 1999, the PSC issued guidelines for the cytological investigations of pulmonary lesions which included recommendations for a classification system,^[3] but then it wasn't routinely used. However, the need for standardization remained until PSC 2016. Though the classification was released in 2016, on literature search we did not find any studies addressing to its applicability and use. Layfield et al tried to apply this classification to FNA samples from pulmonary nodules with inconsistent results.^[9] We did not find any studies using Papanicolaou classification on exfoliative cytology samples, therefore undertook this study.

While the collection and processing techniques for different respiratory cytology samples are now well established, same has not been done yet for reporting the samples. A major objective for these reporting systems was to increase

agreement among cytopathologist and to provide a uniform diagnostic terminology. These systems have been variably successful at improving intra-inter departmental and inter institutional communication of diagnostic, prognostic and management information needed for consistent and optimal patient care.

The PSC for respiratory cytology reinforces sample collection and patient selection. It is easy to apply without any modifications in routine practice and we found it to be easily reproducible. Regular use of this will also enable the clinicians to be aware of different categories.

Using PSC for respiratory cytology may be the first step in developing a systematic algorithm for diagnosis and planning management of patients suspicious of carcinoma lung as well as other pulmonary lesions. Also, while conducting this study we found not much work has been done in this field which encouraged us to study it more. The PSC for respiratory samples will contribute significantly to patient care like it has done for cervical, thyroid and pancreaticobiliary samples.

In our opinion, use of this classification will further help in standardizing the diagnosis of patients with presumed and proven lung cancer as well as in correct interpretation of reports and will also help in reviewing the cases reported at different institutes leading to more effective treatment management.

We recommend that it should be routinely utilized by all the pathologists even in centres with low respiratory cytology workload.

Cytology of pulmonary lesions is a reasonably accurate diagnostic tool with a sensitivity of 81.48% and specificity of 93.33% for both neoplastic and non-neoplastic lesions, if the sample obtained is appropriate, adequate and representative. Cytological evaluation must be assessed in conjunction with clinico-radiological findings. Cytology becomes more significant where biopsy is contraindicated.^[10]

Conclusion

The Papanicolaou 2016 classification is easy to use, and we found it to be easily reproducible. In our opinion use of this classification will further help in standardising

the diagnosis of patients with presumed and proven lung cancer, leading to more effective treatment.

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None

Competing Interests

None declared

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