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Original Research Article

Pathological spectrum of lung lesions diagnosed by sputum cytology: A three years retrospective study in a tertiary health care centre of North India

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ABSTRACT

Introduction: Sputum Cytology is a cheap and noninvasive investigation contributing significantly to the workload of Cytopathology Laboratories. However, over the years, the use of Sputum Cytology has depreciated. It has been taken over by more advanced procedures like Broncho Alveolar Lavage and Trans Bronchial Needle Aspiration, which are comparatively invasive and expensive requiring a much higher learning curve. Hence, the usefulness of noninvasive samples like Sputum needs to be explored in resource limited settings.

Purpose: To study the spectrum of Lung lesions diagnosed using Sputum Cytology with Histopathological correlation wherever possible.

Materials and Methods: This was a three years retrospective study. Data of patients who had come with sputum sample was retrieved from the archives of the cytopathology lab between July 2019 and June 2022. Cytology findings were correlated with histopathological diagnosis, wherever possible.

Results: Out of the total sample size of 143, 67 showed inflammatory infiltrate, 1 out of which was confirmed to be malignant on biopsy. 17 cases were suspected to be malignant, out of which 15 were confirmed on biopsy. Other samples revealed the presence of fungal infection, dysplasia with no frank malignancy and reactive changes.

Conclusion: Our study shows that sputum testing can be quite an accurate method in the early diagnosis of many lung lesions including malignancies. The Sensitivity and Specificity for malignancy was 83.33% and 95% respectively. Therefore, it can be applied as a cheaper, noninvasive ideal screening test for the early detection of lung pathologies especially in resource poor settings.

1. Introduction

Exfoliative cytology has been the most easily accessible diagnostic modality world over since the advent of diagnostic sciences. Sputum examination, conventionally has been the most easily and cheaply available body fluid, providing insight into lung pathology. However with the advent of modern technology including Trans Bronchial Needle Aspiration and Broncho Alveolar Lavage, the utility of sputum is now mainly restricted to Cartridge Based Nucleic Acid Amplification Test (CBNAAT) for the diagnosis of Tuberculosis.

Sputum is the combination of mucus/phlegm and saliva. Mucus is the fluid secreted by airways which, in case of long standing comorbidities, is known as phelgm.[1] Sputum can be collected by two methods: -A) Early morning spontaneously produced sputum. B) Aerosol Induced.[2] There are two requirements for sputum sample to be considered adequate for cytopathological examination:- A) Presence/ Visibility of pulmonary/alveolar macrophages. B) Presence/ Visibility of bronchial epithelial cells. Statistical

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data from several studies show that sputum cytology can still be quite a reliable tool for the early workup of lung pathologies most importantly lung malignancies. According to 2020 data, Lung Cancer is the 2nd most incident malignancy worldwide (11.4%), the most incident in males (14.3%). It is the 4th most incident malignancy in India (5.5%).[3]

Since morphological changes of exfoliated bronchial epithelial cells from sputum are associated with incident lung cancer, sputum cytology can be used for detecting non-small cell carcinoma especially squamous cell carcinoma noninvasively, especially those arising in central airways.[4] In terms of radiological investigations, efficacy of Computed Tomography (CT) in reducing the mortality of lung cancer is not yet known, although it provides excellent anatomical information.[4] The increasing expenditure on medical imaging also needs to be considered. Although no recent study has been done on this, but a 2007 based study estimates that the annual enrollment cost of radiology imaging increased from $229/enrollment in 1997 to $463/enrollment in 2006.[5]

Apart from malignancies, the role of sputum cytology in other pathologies of the lung has also been documented, including pulmonary aspergillosis and bacterial infections of the lung. Recent studies have found nearly 3000000 prevalent cases of chronic pulmonary aspergillosis worldwide.[6] A study has found out that increased sputum purulence in patients of chronic bronchitis and bronchiectasis almost always means neutrophilic airway inflammation.[7]The aim of this study was to find out the pathological spectrum of diseases that can be diagnosed by sputum cytology with histological correlation wherever possible.

2. Materials and Methods

This was a 3 years retrospective study (January 2019-January 2022) where the provisional diagnosis of all sputum samples recorded in the archives of the cytopathology laboratory of our hospital were retrieved. In each case, complete sputum series was obtained over a period of 5 days. Patients had been asked to make a deep cough from the diaphragm upon awakening. For each day, the sputum was submitted within 24 hours of expectoration. Stain used was papanicoleau stain

The provisional diagnosis of each of the cases was carefully studied to find out the range/ spectrum of lung pathologies that could be deciphered from sputum cytology. Histopathological correlation was done, wherever possible, to confirm the diagnosis obtained by sputum cytology. The sensitivity, specificity, positive and negative predictive value of sputum to diagnose lung malignancy was found out.

3. Results

A total of 143 sputum samples were received at the cytopathology lab of Jawaharlal Nehru Medical College and Hospital, Aligarh Muslim University between, January 2019 to January 2022. Out of these, 29 samples were found out to be inadequate for opinion. 3 samples showed bacterial colonies, suspicious of contamination of sample. 67 samples showed inflammatory infiltrate, out of which 6 showed mixed inflammatory infiltrate, 2 showed histiocytes. The remainder showed predominantly neutrophils. 2 samples showed predominantly eosinophilic infiltrate.

A total of 10 samples revealed fungal infection (or contamination of the sample). 2 samples received during the study period were suggestive of Mucormycosis.

10 cases were found to be having few atypical/ dysplastic cells with no frank malignancy, out of which 1 showed metaplastic squamous cells, 1 showed a single cell with moderate dysplasia, 1 slide showed cells in groups, inflammatory cells and 2 to 3 highly atypical cells and the remainder showed only a few dysplastic cells.

A total of 17 cases were diagnosed as suspicious of malignancy. 3 cases showed only reactive changes.

The spectrum of lung lesions diagnosable by sputum cytology as per our study has been illustrated in Tables 1 and 2 .

Table 1: Spectrum of lung lesions diagnosed by sputum cytology

Provisional diagnosis	Percentage
Inflammatory infiltrate	60.36
Suspicious of malignancy	15.32
Dysplasia with no frank malignancy	9.01
Fungal infection	9.01
Reactive changes	2.7
Mucormycosis	1.80
Eosinophilic Infiltration	1.80

Table 2: Nature of inflammatory infiltrate found in sputum

Type of infiltrate	Percentage
Predominantly neutrophilic	88.06
Mixed	8.96
Histiocytic	2.98

Histopathological correlation was mostly available for the cases suspected of malignancy. Out of the 17 cases suspicious of malignancy, 15 were confirmed on biopsy (2-small cell carcinoma,-13- non small cell carcinoma)(Figure 1).1 case suspected to be malignant turned out to be benign**.** In 1 case, the sputum smear had revealed scattered benign squamous cells. Previous histopathological examination had revealed the patient to be having squamous cell carcinoma of skin. 1 case with numerous polymorphs, lymphocytes, and histocytes on cytopathological examination turned out to be malignant on

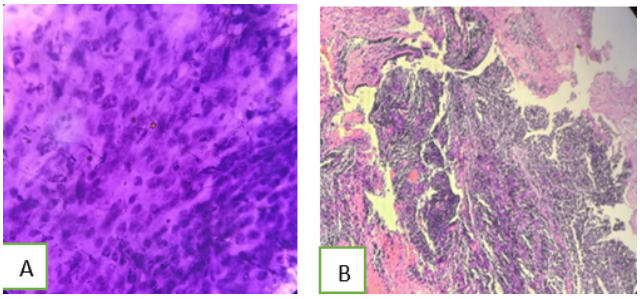

Fig. 1: Cytopathogical analysis of sputum diagnosed as highly suspicious of malignancy (**A**) was confirmed as squamous cell carcinoma of lung in (**B**) in the same patient.

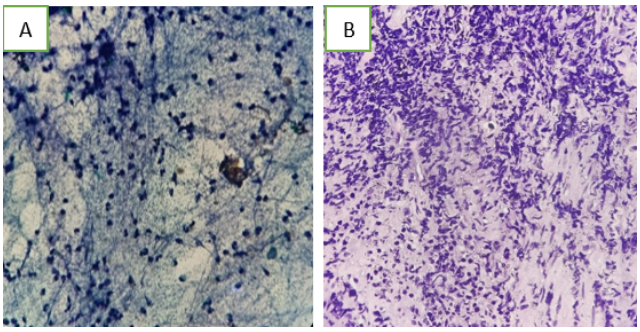

Fig. 2: Sputum Cytology revealing mixed inflammatory infiltrate consisting of polymorphs, lymphocytes and histiocytes (**A**) Turned out to be Small Cell Carcinoma of Lung in the same patient in (**B**)

biopsy favouring small cell carcinoma (Figure 2)

1 case with dense neutrophilic infiltrate turned out to be chronic fungal infection of lung (Aspergillosis) with necrotising lymphadenitis (Figure 3)

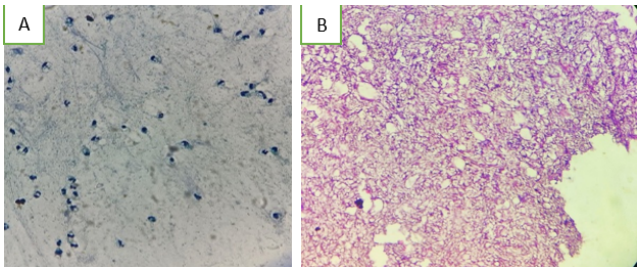

Fig. 3: Predominantly neutrophilic infiltrate was seen in sputum cytology as in (**A**). however it turned out to be Pulmonary Aspergillosis on histological examination as in (**B**)

Out of the total 114 adequate samples of sputum which were received at the cytopathology lab, histopathological confirmatory diagnosis was available for 38. Out of the 38 biopsy results, 18 were malignant and 20 were non - malignant.

On statistical analysis, the sensitivity of sputum cytology for detecting malignancy was found to be 83.33 %, specificity was 95%. The Positive Predictive Value (PPV) was 93.75%, while the Negative Predictive Value(NPV) was 86.36%. (Table 3).

Table 3: 2 X 2 table showing thehistocytological correlation of the lesions

	Malignant	Non malignant
Positive on cytology	15	1
Negative on cytology	3	19
Total	18	20

4. Discussion

Our study clearly demonstrates that Sputum Cytology can detect a wide spectrum of lung lesions, and can also serve as an effective screening test for malignancies. This has been well elucidated by a few studies in the past including one by Bechtell et al, in which 14% of the patients screened to be suspicious of malignancy by sputum cytology had Carcinoma in Situ, 74% had Stage 1 disease, 86% of the patients had Squamous Cell Carcinoma, 6% had Adenocarcinoma, 4 % were Small Cell Carcinomas, while the remaining 4% were undifferentiated.[8]

The Specificity for detecting malignancy (95%) was found to be greater than the Sensitivity(83.33%). This trend matches the results of an extensive study that was carried out on sputum cytology by using different preparations by Erkilic et al. which found out the Sensitivity to be 69.4%, 84.4% and 87.5% for smear, cell block and smear cell block combined group respectively. The corresponding specificity was 99.5%, 100% and 99.5% for the three groups respectively.[9]

The decreased Sensitivity to pick up malignancies can be attributed to the lack of robust processing methods to retrieve all the diagnostic materials clogged in mucus, inflammatory exudates and blood.[10]

5. Conclusion

The cost-effectiveness of using sputum over other more sophisticated methods makes it a pertinent approach to the early detection and screening of lung pathologies in resource limited settings including those of South East Asia. A study has estimated that the annual savings of adopting sputum cytology as the first test for diagnosing lung cancer in the United States is at least $30 million.[11] Sputum cytology can be a sensitive as well specific tool for picking up lung malignancies early. Apart from malignancies, it can also be an early screening tool for picking up fungal pulmonary infections. The role of sputum in diagnosing fungal infections was well established by a dissertation by Mustafa et al, in which 14% of the 110 sputum samples were positive for the presence of fungal elements. Most common species present in the positive cases was found to be Candida (8%), followed by Aspergillus (5%) and

Actinomyces (0.9%).[12]

6. Conflicts of interest

There are no conflicts of interest.

7. Source of Funding

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