FREQUENCY OF MALIGNANT CELLS IN SPUTUM CYTOLOGY OF TUBERCULOSIS SUSPECTED PATIENTS

Shazia Naz[1], Arshad Javaid[2], Walayat Shah[1]

[1] Department of Histopathology, Institute of Basic Medical Sciences, KMU, Peshawar

[2] Department of Pulmonology, Postgraduate Medical Institute, LRH, Peshawar

Address for correspondence:
Walayat Shah, PhD
Assistant Professor
Histopathology
Institute of Basic Medical Sciences,
Khyber Medical University,
Peshawar, Pakistan.
E-mail: walayats.ibms@kmu.edu.pk

ABSTRACT

Background: Prolonged pulmonary inflammation may cause tissue damage and genomic alterations. Furthermore, repair of tissue damage caused by tuberculosis can lead to pulmonary fibrosis and scarring. To find out the frequency of malignant cells on sputum cytology in suspected tuberculosis patients as it has been observed that all the chronic lung diseases along with tuberculosis raise the risk of lung cancer.

Methodology: From March 2013 to September 2013, 100 patients with suspected tuberculosis were included in the study .Samples were mainly collected from outdoor patients (OPD) laboratory at the Department of Pulmonology of Postgraduate Medical Institute, Lady Reading Hospital (PGMI-LRH) Peshawar. Both male and female of age 20 years or above with clinical and radiological suspicion were included in the study. Total of one hundred patients with age range 20 years to 70 years with mean age of 49 years were registered in this study. Out of these 100 patients, 59% were males and 41% females, and 47% belonged to urban area and 53% to rural area.

Results: The most common symptom was fever, observed in 98% of patients. Cough, hemoptysis and weight loss was observed in 96 %, 80% and 45% respectively. Only 2% were smokers for more than 5 years. However no malignant cells were observed in any of these patients. Out of total 100 patients 88 were diagnosed as having tuberculosis by different investigations and 12 were with other causes including pneumonia, COPD and lung infections.

Conclusion: Though chronic inflammation is one of the causative factors of lung cancer, and the major group of patients in our population pre-sented with tuberculosis but there were no malignant cells in their sputa on cytological examination to provide any clue of malignancy in these suspected patients of tuberculosis

Key words: Sputum cytology, malignant cells, pulmonary tuberculosis

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INTRODUCTION

Pulmonary tuberculosis primarily affects lungs and damage of the lungs is most frequent complication. Mycobacterium tuberculosis (MTB) is one of the major causes of deaths in developing countries[1,2]. It is spread from person to person by coughing[3]. While in most of these infected individuals TB remains clinically silent and latent for years[4].

Majority of the complications of tuberculosis are very serious and life threatening, especially in those cases where the disease is left untreated or not timely treated in a proper way. Other forms of tuberculosis spreading to the rest of body outside the respiratory system occur in about 15–20% of active cases[5]. It may spread to the other parts of body making the treat-ment more difficult. Tuberculosis itself is a major problem, but it adds further concern when it is learnt that it may have a connection to lung cancer. Smok-ing is the main cause and risk factor of lung cancer but it causes lung cancer in about 9 in 10 cases[6]. The relationship between tuberculosis and lung cancer be-comes more interesting when this parameter is taken into consideration where in many studies of the tissue biopsies tuberculosis inflammatory changes and malig-nant cells co-existed. TB infection may co-exist with malignancy in some cases or it may appear as the com-

plication of TB especially in chronic sclerotic scars[7]. It has been observed that other chronic lung diseases and tuberculosis increase the risk of lung cancer[8]. In-fants, elderly, and people with lower immunity are at risk of developing complication[9].

Nowadays research for carcinogenesis is expanding and the question is slowly arising about the possible correlation between chronic inflammation and devel-opment of cancer. TB has recently been associated with the development of lung malignancies at the site of scars created from old healed mycobacterial infec-tion[10,11] . Lung cancer is the utmost common cancer and causes the largest number of deaths with an estimated 1.35 million cases diagnosed and 1.18 million deaths occurring each year[12].

Prolonged pulmonary inflammation may cause tis-sue damage and genomic alterations. Furthermore, re-pair of tissue damage caused by tuberculosis can lead to pulmonary fibrosis and scarring[13]. This is also linked to increased lung cancer risk[8]. A few findings support this; lung cancer in those who have had TB tends to occur in the same lobe of a lung that was affected by TB[14]. Other studies in Taiwan and Korea have also found that TB appears to be an independent risk factor for lung cancer, though the relative increase in risk was not as high[8].

METHEDOLOGY

From 3rd March 2013 - 10th September 2013 about 100 patients all male and female of age 20-70 years with clinical and radiological suspicion of tuberculo-sis were included. One hundred patients with signs, symptoms and radiological findings highly suggestive of tuberculosis but yet to be diagnosed by sputum cul-ture and microscopy were included. They were select-ed for the trial in a progressive manner after making inquiries daily in the chest department to select the most appropriate cases. The patients were either ward patients or out patients, who had clinical evidence of pulmonary tuberculosis as reported by an accredited pulmonologist based on chest radiograph, symptoms, risk profile, or history suggestive of tuberculosis. Pa-tients were provided three sterile sputum containers. The sputum specimen collected by deep cough was an early morning sample, collected in a clean sterilize wide mouthed, bottle made of transparent glass or a disposable plastic bottle. The sample was well labeled and sealed with a tight fitting lid. For satisfactory spu-tum samples, patients were explained about the pro-cedure. The difference between sputum and spit was explained to them. They were advised to clean their mouth with water and after deep coughing the sputum were directly collected in the container, screwed the lid back on the container and checked for any leak. Consecutive three morning sputum samples were col-lected and the interruption was avoided as degener-ation takes place after 8-19 hours of collection. Each sample was labeled and transported immediately to the pathology laboratory of LRH.

These samples of sputum were utilized for the de-tection of abnormal cells. A small portion was selected and shifted on plain glass slide. Overlapping horizontal strokes were given with another clean glass slide to spread the sample evenly as to get a final preparation. The slides were air dried and examined under the mi-croscope after Hematoxylin and Eosin staining.

RESULTS

The age range of the patients was from 20 years to 70 years with mean age of 48.89 years (Table1). Most of the patients were of middle age exposed to day to day work load and working people. Out of total, 42% were in the age range of 41-60 years of age, followed by 29% were more than 60 years of age, and 29% in the age range 20-40 years. In our study 59% of patients were male and 41% were female Out of these only 2% were having the history of smoking for more than 5 years. Out of these 59%, 32.2% male (19) were in the age range of (20-40), 39% (23) males were from (41-60) and (17) 28.8% males were more than 60 years of age (Table1).

Now coming to the female ratio, out of total 41 fe-male 24.4%(10) were in the age range of (20-40),46.3% (19) were in the range of (41-60) and 29.3% (12) were more than 60 years of age .None of the female patients were smokers. Out of total 100 patients where 47% were from urban area 25.5% were in the age range of 20 to 40 years of age, 55.3% were from 41 to 60 years of age and 19% were above than 60 years. From rural areas which are far remote areas around the main city the ratio of the patients brought to hospital is high in people more than 60 years of age, that is, 37.7%. Depending on the symptoms of the disease most of the patients were suffering from cough (96%) and only few (4%) were not having productive cough. The frequency of cough was there in about 41 patients in age ranges from 40 to 60 years arising the suspicion of some infec-tive process rather than lung cancer which is common in the age above 70 years. Those who were not having cough were only 4 patients in whom 3 were in the age range of 20 to 40 years. Out of these 96 patients who were having productive cough 29 were more than age of 60 years.

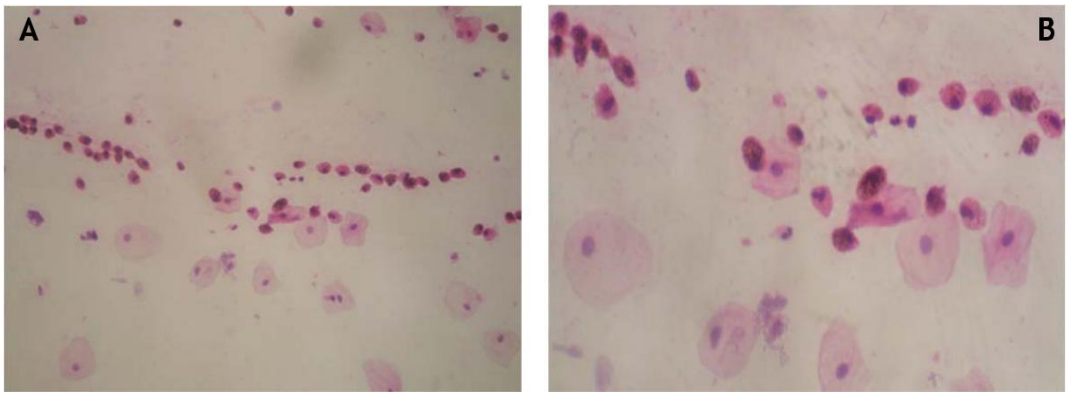

Figure 1: Representative photomicrographs of sputum smear of tuberculosis suspected patients showing squamous cells and pigment laden macrophages (H&E; A= X200, B= X400).

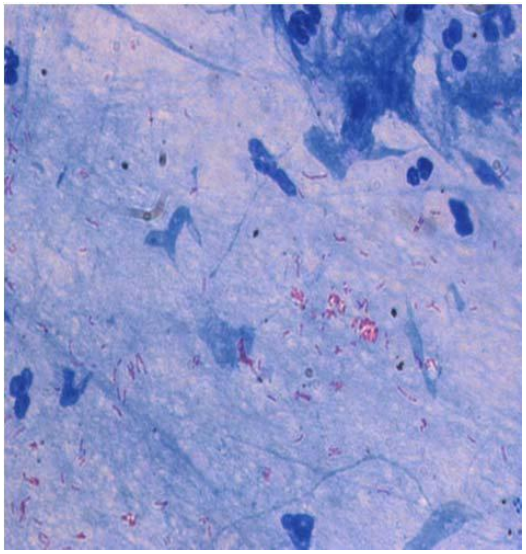

Figure 2: Representative Photomicrographs of sputum smear of tuberculosis suspected patients showing squamous cells, macrophages and acid fast bacilli (ZN stain; X1000)

Table 1: Association of Gender and response

Age group	Frequency	Percent
20-40	29	29.0
41-60	42	42.0
> 60	29	29.0
Male	59	59.0
Female	41	41.0
Rural	53	53.0
Urban	47	47.0
Total	100	100.0

Regarding fever 98 patients had the history of fever mostly in the evening. Out of these 2 patients were afebrile. Total 40 patients were in the age between 40 and 60 years. Out of these patients 45 % were present-ed with hemoptysis, 22 patients (48.9%) were between the age of 40 and 60 years followed by 16 patients (35.6%) more than 60 years of age. Total 100 patients brought to the pulmonology unit, 80% were having the history of weight loss in the previous two months of the disease more common in the age group of 40 to 60 years of age about 31 patients (38.8%) followed by 27 (33.8%) in the age of 20 to 40 years.

SPUTUM CYTOLOGY

None of the sputum smear of these suspected pa-tients of tuberculosis was positive for the presence of malignant cells. Our results were; Normal/negative for malignant cell, Enough number of alveolar mac-rophages, pigmented macrophages and neutrophils, little ciliated columnar cells and mucous spirals. Epi-theloid cells, giant cells and predominant lymphocytes suggestive of tuberculosis. Neutrophils were observed suggestive of inflammation of the lung.

DISCUSSION

This study was conducted on local population of Pe-shawar with the hypothesis that there can be a link in chronic infections like tuberculosis and lung malig-nancy. To our knowledge such study in our population has not been conducted before. The results suggest that this was negative study and we did not detect any cases of malignancy in the study population.

There are a few factors that we believe are the rea-son for this negative finding. First of all we know that sputum cytology for detecting lung malignancy has a very low yield compared to other standard investiga-tions[15]. The second reason will be the lower number of smokers in our study population and this is not unex-pected to find the lung cancer detection low in non- or light-smokers compare to heavy smokers. Smoking is a common etiological factor for the lung cancer. In our study only 2% male patients were smokers while none of females were smokers. The third possible factor could be the age of our study population as most of our subjects were younger age group (<70 years old) and therefore at low risk of developing lung cancer and hence positive cytology. Considering the results of our study, the study patients were between 20-70 years which is not an elder age and lung cancer is pre-dominantly a disease of elder age group. Nevertheless this negative results in this small study inform us that the detection of malignant cytology sputum specimens are very low and therefore it should not be consid-ered in future work up for suspecting lung cancer. This will also need a larger more robust study to clarify the situation in our population. The fourth reason could be that this is a single center study in a tertiary care hospital with small number of patients.

Sputum cytology is a definite diagnostic test for lung cancer. A review of 22 articles revealed that ma-lignant cells had been found in 28.6% to 88.9% of pa-tients with histologically proven cancer. The diagno-sis is difficult when these two conditions are present in the same patient. In such cases bronchoscopy, CT and transthoracic lung biopsy should be done. Myco-bacterium is found in sputum of patients with history of tuberculosis. The association of two condition was firstly described twenty years ago by Bayle who con-sidered 'cavitation cancerous' as one of the various types of TB[16]. It would have been interesting to have a long term follow up of these patients for a real ef-fect and any link but we did not have the facility for long term follow up of our patients due to logistic and socioeconomic factors. We could also have employed more advance investigations like CT scans for any de-tection of occult malignant lesion if we had the budget and facilities available to us. Further studies should be incorporated to find out the possible mechanisms by which TB influences lung cancer.

CONCLUSION

In conclusion we in this small prospective and well conducted study did not find any evidence of malignant cytology in patients with suspected Tuberculosis cases based on clinical and radiological suspicion. There are some factors responsible for the negative outcome of the result but on the whole our sound methodology and rigor suggest that in our population the incidence of malignancy in suspected tuberculosis cases is proba-bly very low and as such patients should be worked up more for tuberculosis diagnosis rather than malignan-cy except in high risk groups like heavy smokers, older age and previous history of any malignancy.

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