|| Print ISSN: 2589-7837 || Online ISSN: 2581-3935 ||

International Journal of Medical Science and Diagnosis Research (IJMSDR)

Available Online at www.ijmsdr.com

Volume 3, Issue 1; January: 2019; Page No. 238-242

HISTOMORPHOLOGICAL PATTERN OF LUNG IN PULMONARY TUBERCULOSIS IN AUTOPSY AND RESECTED SPECIMEN

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Conflicts of Interest: Nil

ABSTRACT:

Tuberculosis (TB) continues to remain one of the most important health problems in India. India is the highest TB burden country in the world, accounting for one-fifth of the global incidence with an estimated 1.96 million cases per year. Without acid-fast bacteria (AFB) staining, smear-negative PTB is generally difficult to identify and may require mycobacterial culture and pathological or molecular diagnostics. Patient fails to take adequate treatment causing multidrug resistance to the anti-tubercular drugs. Some patients may require surgical intervention because of the associated complications. **MATERIAL AND METHODS**: Of the 15 surgically resected cases which include 8 lobectomy, 4 pneumonectomy, and 3 lung tissue for frozen section were taken. Patient demographic data and information was obtained from medical records and autopsy records. The specimens were stored in 10% formalin.

RESULTS: 24 cases from the autopsy and 15 cases from the surgically resected cases were diagnosed of tuberculosis which include 8 lobectomy, 4 pneumonectomy, and 3 lung tissue for frozen section. Age of the patients was ranging from 26 to 68 years with mean ± SD (standard deviation) was 34 ± 17.64. of the 39 cases 31 were male and 8 were female patients. In autopsy cases 21(87.50%) were male patients while 3(12.50%) were female. In surgical resection 10 (66.67%) were male cases and 5 (33.33%) were female. diagnosis of pulmonary tuberculosis was known in only 4 of 24 (16.67%) cases. All autopsies were done on patients who were suspected of tuberculosis and died within 24 hours of admission to hospital. On histopathology 7 cases were diagnosed as disseminated tuberculosis, 8 cases as fibrocavitary tuberculosis, and fibrocaseous tuberculosis (4 cases). A total of 19 cases were operated with suspicion of tuberculosis of which 2 were having associated malignancies hence were not included in the study and 2 were having Acquired immunodeficiency syndrome. So, finally 15 cases were included in this study. Histopathological evaluation of lung sections showed necrotizing granulomas in 32 (82.05%) patients, non-necrotizing granulomas in 3 (7.69%) of cases, caseous necrosis with Langhans giant cells in 2 cases (5.12%), and only caseous necrosis in 2 cases (5.12%). ZN stain for acid fast bacilli (AFB) was positive in 26 (66.67%) cases of which 12 (46.15%) were autopsy cases and 14(53.84%) surgically resected specimens.

CONCLUSION: Timely diagnosis of tuberculosis can significantly reduce the morbidity and mortality. Tor tuberculosis diagnosis immunohistochemistry or molecular techniques such as polymerase chain reaction to paraffin sections can be done. Histopathology remains one of the important methods for diagnosis of smear negative and suspected cases.

Keywords: PTB, AFB, ZN, DST, TDL, TB and HAFB.

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Introduction

Pulmonary tuberculosis (PTB) is one of the major public health problems worldwide. Of the 5.2 million patients with new or relapsed PTB diagnosed globally (2014), 3.0 million (58%) were bacteriologically confirmed, and the remaining 42% were diagnosed on the basis of clinical suspicion[i]. 95% of all tuberculosis-related deaths occurring in low- or middle-income countries[ii]. Tuberculosis (TB) continues to remain one of the most important health problems in India. India is the highest TB burden country in the world, accounting for one-fifth of the global incidence with an estimated 1.96 million cases per year[iii]. Pulmonary tuberculosis can be diagnosed on the basis of direct examination i.e. sputum smear microscopy, culture for *Mycobacterium tuberculosis*, and radiological findings suggestive of the disease can also be carried out[iv]. Without acid-fast bacteria (AFB) staining, smear-negative PTB is generally difficult to identify and may require mycobacterial culture and pathological or molecular diagnostics. Sputum culture is more sensitive than sputum AFB smears and can be considered as gold standard to identify the species of mycobacteria. Also, drug-susceptibility testing (DST) based on sputum is helpful for the treatment of drug-resistant mycobacteria infections. However, mycobacterial culture is time-consuming which require around requiring 2–6 weeks for results to come[v].

Due to the stigma and taboo associated with tuberculosis, there is a delay in diagnosis and treatment of tuberculosis which leads to unrestricted exposure of bacilli to environment. Secondly patient fails to take adequate treatment causing multidrug resistance to the anti-tubercular drugs. Some patients may require surgical intervention because of the associated complications. The prevalence of tuberculosis is high in the Indian subcontinent, and sometimes cases may not be diagnosed until after an autopsy is performed[vi],[vii],[viii].

Mycobacterium tuberculosis infected tissue contains necrotizing granulomatous inflammation which is composed of epithelioidhistiocytes which surrounds a central necrotic zone, and sometimes accompanied by a variable number of multinucleated giant cells and lymphocytes. Sometimes Non-necrotizing granulomas can be present. The major action of epithelioidhistiocytes is to contain the infection to a localized area, thus avoiding bacterial spread to surrounding healthy tissues and to other organs, and to concentrate the immune response to a limited infectious area[ix]. Pulmonary tuberculosis (PTB) can result in tuberculosis-destroyed lung (TDL), when parenchyma is destroyed, lymph nodes become obstructed, the bronchi undergo necrosis, and a secondary infection sets in[x]. Chronic granulomatous inflammation with central cessation is the characteristic histopathological finding in lung specimens from patients with TB and histological AFB (HAFB) staining of human tissue specimens is widely used to support the diagnosis of tuberculosis[xi],[xii]. The present study was carried out to evaluate the histopathological pattern of pulmonary tuberculosis in autopsy lung specimens and surgically resected specimens.

MATERIAL AND METHODS

A descriptive prospective histological study of tuberculosis was carried out in the Department of Pathology, at KM Medical College and Hospital Mathura, India, over a period of 2 years. A total of 24 autopsy lung specimen and 15 surgically resected specimens were collected for the present study.

Of the 15 surgically resected cases which contain 8 lobectomy, 4 pneumonectomy, and 3 lung tissue for frozen section were taken. Patient demographic data and information was obtained from medical records and autopsy records. The specimens were stored in 10% formalin. Gross examination was performed and sections were submitted. Slides were stained with Haematoxylin and Eosin (H&E) along with Ziehl-Neelsen (ZN) stain for identification of tuberculous bacilli.

Following criteria for diagnosis tuberculosis was taken into account

1. Demonstration of acid fast bacilli on ZN staining.

2. Presence of necrotizing granulomatous inflammation in the tissue.

3. Past history of tuberculosis and treatment with antituberculous therapy in absence of caseous

necrosis or failure to demonstrate acid fast bacilli in the smear.

4. Exclusion of other causes of granulomatous inflammation. Other non-infectious causes of granulomatosis diseases were excluded.

Other non-neoplastic findings in adjacent lung parenchyma were recorded. Fungal and other bacterial infections were excluded by microscopy and staining.

OBSERVATION AND RESULTS:

24 cases from the autopsy and 15 cases from the surgically resected cases were diagnosed of tuberculosis which includes 8 lobectomy, 4 pneumonectomy, and 3 lung tissues for frozen section. Age of the patients was ranging from 26 to 68 years with mean ± SD (standard deviation) was 34 ± 17.64. Of the 39 cases 31 were male and 8 were female patients.

Table 1: Age and Sex in Patients

Cases (n=39)	Male	Female	Total
Autopsy (n=24)	21 (87.5%)	3 (12.5%)	24
Surgical resection cases (n=15)	10 (66.67%)	5(33.33%)	15
Total	31 (79.49%)	8(20.51%)	39

In autopsy cases 21(87.50%) were male patients while 3(12.50%) were female. In surgical resection 10 (66.67%) were male cases and 5 (33.33%) were female. diagnosis of pulmonary tuberculosis was known in only 4 of 24 (16.67%) cases. All autopsies were done on patients who were suspected of tuberculosis and died within 24 hours of admission to hospital. On histopathology 7 cases were diagnosed as disseminated tuberculosis, 8 cases as fibro cavitary tuberculosis, and fibrocaseous tuberculosis (4 cases).

Table 2: Histopathological diagnosis on autopsy

Histopathological diagnosis	Cases N=24	%
Disseminated tuberculosis	9	37.50%
Fibrocavitary tuberculosis	8	33.33%
Fibrocaseous tuberculosis	7	25.00%
Tubercular bronchopneumonia	2	4.16%

A total of 19 cases were operated with suspicion of tuberculosis of which 2 were having associated malignancies hence were not included in the study and 2 were having Acquired immunodeficiency syndrome. So, finally 15 cases were included in this study.

Table 3: Surgical resection

Surgical diagnosis	**Cases (n=15)**	**%**
Lobectomy	8	53.33%
Pneumonectomy	4	26.67%
Lung tissue from frozen section	3	20.00%

Of the 15 cases operated, 10 cases were known cases of pulmonary tuberculosis with history of anti-tubercular treatment (ATT) and also having associated complications, like, hemoptysis, emphysema and bronchiectasis.

Histopathological evaluation of lung sections showed necrotizing granulomas in 32 (82.05%) patients, nonnecrotizing granulomas in 3 (7.69%) of cases, caseous necrosis with Langhans giant cells in 2 cases (5.12%), and only caseous necrosis in 2 cases (5.12%). ZN stain for acid fast bacilli (AFB) was positive in 26 (66.67%) cases of which 12 (46.15%) were autopsy cases and 14(53.84%) surgically resected specimens.

Primary case of tuberculosis was seen in 8 cases with hilar lymph node involvement. Fibrocavitary and fibrocaseating tuberculosis was observed in 15 cases. Miliary tuberculosis and empyema were seen in 16 cases.

DISCUSSION

Pulmonary tuberculosis (PTB) is a major public health problem worldwide. In China around 4.99 million patients with active PTB were diagnosed

(2010), of whom only 0.72 million were smear-positive this means, approximately 85.6% of patients with PTB were smear-negative).[xiii] Early laboratory diagnosis of TB can lead to earlier treatment initiation, improved patient outcomes, decrease morbidity, increased opportunities to interrupt transmission, and more effective public health interventions[xiv]. Mycobacterium tuberculosis typically affects the lungs hence pulmonary TB, but can affect other sites as well which is called as extra pulmonary TB. In our study most of the patients were young, in 3rd decade of life with male predominance. Similar to our study Aziz et al. observed a distribution with a younger age group of less than 30 years and an older age group of more than 50 years[xv]. Revised National Tuberculosis Programme shown that nearly three times more male than female TB patients are reported and diagnosed, also Ganapathy et al. observed male predominance[xvi].

The undetected cases of TB at autopsy vary from 44% to 70% in various studies[xvii,xviii] . In our study 24 cases were diagnosed at autopsy. Miliary TB is a fatal form of TB which results from massive lymphohematogenous dissemination. Diagnosis can be difficult because of nonspecific symptoms and chest radiographs do not always reveal classical miliary changes[xix]. In our study 1n 16 cases military tuberculosis was observed. Many infectious granulomatous lesions may also resemble tuberculosis. Fungal infections like histoplasma capsulatum show necrosis similar to tuberculosis. But the diagnosis can be done by careful interpretation of surrounding tissue reaction and special stains[xx].

In our study Acid fast bacilli were seen in 26 (66.67%) cases. Park et al. observed microbiologically confirmed pulmonary tuberculosis in 50% of patients which was further confirmed by nested PCR[xxi]. Tissues containing necrotizing granulomas are more likely to give positive results than specimens showing only nonnecrotizing granulomas or acute inflammation. Failure to demonstrate acid fast bacilli does not exclude a diagnosis of tuberculosis and for making a definitive diagnosis application of immunohistochemistry or molecular techniques such as polymerase chain reaction to paraffin sections can be done

CONCLUSION

Incidence of pulmonary tuberculosis is still not under control. Histopathology remains one of the important methods for diagnosis of smear negative and suspected cases. As timely diagnosis can be significantly reduce the morbidity and mortality. For tuberculosis diagnosis immunohistochemistry or molecular techniques such as polymerase chain reaction to paraffin sections can be done

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