ORIGINAL ARTICLE

HISTOPATHOLOGICAL DIAGNOSIS OF PLEURAL BIOPSIES RECEIVED AT A TERTIARY CARE CENTRE

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Background: Pleural diseases are common, affecting a significant number of patients worldwide. Pleura are frequently involved secondary to diseases like pneumonia, cardiac failure and pulmonary tuberculosis, whereas primary pathological diseases of the pleura are exclusively uncommon. In majority of the cases diagnosis can be made by history, clinical examination, laboratory tests and imaging studies. Biopsy is however required for definitive diagnosis of certain infective conditions and all neoplastic lesions as in some cases, the management is prolonged and expensive as well. This study highlights the role of biopsies in diagnosis of uncommon pleural pathologies. **Methods:** All pleural biopsies received at the Pathology Department of Ayub Medical College, Abbottabad from Jan 2014 to Dec 2023 were included in the study. Haematoxylin and Eosin (H & E) stained slides were examined to determine the frequency of various pathological lesions affecting pleura. Special stains and immunohistochemistry were performed whenever required. **Results:** A total of 222 biopsies were included in this study. The most common pathology in pleural biopsies was chronic non-specific pleuritis constituting 86 (38.7%), followed by empyema in 85 (38.3%) cases. Chronic granulomatous inflammation due to tuberculosis was seen in 20 (9%) cases. Rare infections like actinomycosis and fungal infection were identified in 2 cases. **Conclusion:** In this study the most common pathology identified on pleural biopsy was chronic non-specific pleuritis, while one case each of actinomycosis and fungal infection were seen.

Keywords: Pleural biopsy, Empyema thoracis, Tuberculosis, Pleurisy
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INTRODUCTION

The pulmonologist is responsible for diagnosis and management of diseases affecting not only the lungs but also the pleura which consists of two layers composed of mesothelial cells enclosing a potential space which contains a small amount of fluid acting as a lubricant. The overall incidence of pleural diseases has increased with an annual incidence of 360 per 100,000 persons, which can be attributed to the increase in general population as well as increase in life span.[1] A wide spectrum of disease affects the pleura which commonly present clinically as pleurisy, pleural effusions and rarely as pleural mass or thickening.[2] It is extremely difficult to calculate the true incidence of diseases that affect the pleura as the most common lesion is pleurisy, which is self limited inflammation of the pleura occurring commonly after viral infections and treated conservatively.[3]

Primary diseases of the pleura are rare and consists mainly of neoplastic disorders like solitary fibrous tumour and malignant mesothelioma.[4] Most frequently the pleura is affected secondary to infections involving the lung parenchyma especially in the elderly population which if left untreated will be complicated by empyema.[5] Conversely, secondary involvement of the pleura in systemic diseases like cardiac failure, connective tissue disorders etc or by pathological lesions affecting the adjacent organs like lung, mediastinum or liver are much more common.[6]

Diagnosis is usually made on clinical examination, imaging and laboratory investigations including pleural fluid examination but sometimes these findings are inconclusive.[7] Cytological examination of the pleural fluid has its limitations, which include unclear cellular details, degenerate cells, haemorrhages, abundance of inflammatory cells and scanty neoplastic cells. Cell blocks can be used, but again provide limited information. Consequently, pleural biopsies continue to be the gold standard for diagnosing neoplastic lesions. They have been used for many years to diagnose pleural tuberculosis, and more recently, they have also been used to diagnose non-tuberculous pleural infections as well.[8] In short, the diagnostic challenging lesions are mostly tumours which require further investigations including biopsy to determine the exact histological type. Certain infections do not resolve with antibiotics, and pleural biopsy can be done to determine the type of infections so that appropriate treatment can be administered.

Pleural diseases can never be diagnosed with a single test. Customising the investigations required for each patient and carrying out tests with the highest diagnostic yield at an early stage are essential for effectively managing the patient. This commonly includes pleural biopsy especially in infections and malignancies. Several different techniques can be used to obtain the biopsy, e.g., blind/ultrasound-guided biopsy, video-assisted thoracoscopic biopsy, etc.[9]

The spectrum of pathological lesions occurring in the underdeveloped countries is quite different with increase number of cases of tuberculosis.[10] Some rare infections like actinomycosis and fungal infections may mimic tuberculosis clinically, and unfortunately some of these patients get labelled as multidrug resistant tuberculosis without further workup. Hence proper workup of the patient is essential for effective management of these infections. In our study the frequency of various pathological lesions affecting the pleura were studied and the results were compared with other national and international studies, highlighting the importance of pleural biopsies in diagnostically challenging cases, where other non-invasive investigations are inconclusive. The objective of this study was to determine the frequency of various pathological lesions affecting the pleura.

MATERIAL AND METHODS

This retrospective study started in March 2024 after approval of Institutional Medical and Ethics Review Committee vide RC-EA-2024/112. The pleural biopsy of patients of all ages and both genders, needle or open were included. Biopsy specimens which were autolysed or inadequate were excluded from the study.

Informed consent was taken, and the clinical and histopathological record of 234 pleural biopsies recovered from the Pathology Department of Ayub Teaching Hospital were analysed, out of which 222 were included in the study as the rest were inconclusive. These biopsies were received over a period of ten years from 1st Jan 2014 to 31st Dec 2023. The pleural biopsies were received in 10% formalin along with proforma containing relevant clinical, imaging and laboratory investigations. The volume of sample received depended on the type of biopsy, provisional diagnosis and whether the lesion was diffuse or patchy. Histopathological examination using Haematoxylin and Eosin stain was performed. In some cases, special stains (PAS and AFB) were used while in case of malignancy immuno-histochemistry was performed for definite diagnosis. Data was recorded and analysed using SPSS-23.

RESULTS

A total of 234 biopsy were received during a 10-year period from 2014 to 2023 out of which 12 cases were not included in the study as the biopsies were inadequate. Among the 222 cases, 129 (58.1%) were male and 93 (41.9%) were female. The youngest patient was 6 months old while the oldest was 85 years of age. The frequency of patients in various age groups is given in Table-1 while frequency of various pleural pathologies is given in Table-2.

The most common lesions identified was chronic non-specific pleuritis and empyema which constituted 86 (38.7%) and 85 (38.3%) cases respectively. Granulomatous inflammation was seen in a total of 22 cases, out of which 20 (9%) had tuberculosis, and one case each of fungal infection and actinomycosis was identified. Malignancy was seen in 17 (7.7%) cases.

Table-1: Frequency of patients in various age groups (n=222)

Age Groups	Frequency	Percentage
<10 Years	45	20.3
11–20 Years	31	14.0
21–30 Years	32	14.4
31–40 Years	33	14.9
41–50 Years	32	14.4
>51 Years	49	22.0

Table-2: Frequency of various pathological lesions (n=222)

Pleural Pathologies	Frequency	Percentage
Chronic non-specific inflammation	86	38.7
Empyema	85	38.3
Tuberculosis	20	9.0
Metastasis	17	7.7
Pleural fibrosis	12	5.4
Actinomycosis	1	0.45
Fungal infection	1	0.45

DISCUSSION

Advances in the management of pleural disease require accurate diagnosis. Before moving onto invasive procedures various other diagnostic modalities including routine blood tests, imaging studies, biochemical and cytological examination of pleural fluid are done.[11] If the results of these test are inconclusive then pleural biopsy can be done to assist in the diagnosis and management. Special stains and immunohistochemistry are helpful in further categorizing these lesions so that appropriate management can be started. Common indications of pleural biopsy include recurrent pleural effusions of unknown aetiology and pleural mass or thickening.

The pleura are involved in a wide variety of pathological processes. However pleurisy secondary to viral infection is the most common condition, but it rarely requires medical attention and resolves on its own. On the other hand, pleural effusions, pleural thickening and tumours constitute most of the cases requiring admission and further workup. The most common clinical presentation of pleura disease hence is pleural effusion. Every year pleural effusion is diagnosed in 1.5 million people in the USA and 200,000–250,000 in the UK.[12] Most of the times the underlying causes of pleural effusion can be readily diagnosed without invasive procedures. Other pleural pathologies pose a diagnostic challenge and sometimes pleural disease present due to pathologies of the associated adjacent organs, e.g., pneumonia, oesophageal and lung tumours etc.

In this study a total of 234 pleural biopsies were examined out of which 222 cases were included. The non-neoplastic lesions of the pleura including chronic

non-specific pleuritis, empyema, chronic granulomatous inflammation secondary to tuberculosis, constituted majority of the cases. Pleural fibrosis occurred secondary to viral or bacterial infections especially in the younger age group. Two cases, one of fungal infection and other of actinomycetes were also identified.

Chronic non-specific inflammation or pleuritis is commonly used to describe a biopsy characterized by chronic inflammation and fibrosis and in which granulomatous inflammation and malignancy has been ruled out.[13] The diagnosis lacks specificity and in general does not point to a specific aetiology. Causes include lung tumours, post pneumonic complication, subphrenic abscess, congestive heart failure etc.[14] Hence biopsy should be interpreted in light of complete clinical data including imaging studies. Out of 222 cases in our study, 86 (38.7%) cases of chronic non-specific inflammation were identified and this group constituted the most common pathology in our population. Kapp *et al*[15] mentioned that <30% of pleural biopsy consists of non-specific inflammation however in our study the percentage is slightly higher and can be attributed to lower socioeconomic status and poor living conditions.

Empyema thoracis was the second most common diagnosis occurring in 85 cases out of which 26 were in children less than ten years of age. This is comparable to studies carried out by Saleem *et al*.[16] In our setup empyema thoracis occurred commonly in children admitted for pneumonia complications. Most of them belonged to lower socioeconomic group and delayed seeking medical treatment resulting in the development of empyema.

Granulomatous inflammation was seen in a total of 22 cases, out of which 20 (90%) had tuberculosis and one case each of fungal infection and actinomycosis was identified. Mycobacterium tuberculosis is the causative organism of tuberculosis, a disease that primarily affects the lungs, especially in Pakistan. Despite significant medical and social interventions, in Pakistan, the prevalence of pulmonary tuberculosis is high, with approximately, 1.5 million patients affected by the disease thus placing Pakistan's TB case count at 6th in the world.[17] In a study by Ruan *et al*[18], 74% of the pleural biopsies in cases of suspected tuberculous pleurisy showed granulomas histologically, hence supporting the use of pleural biopsies in cases of suspected tuberculous pleurisy.

Pulmonary actinomycosis is a rare disease especially in developed countries, presenting with non-specific clinical features. In a study conducted by Kim *et al*[19], a total of 94 cases of pulmonary actinomycosis were diagnosed over a period of 10 years in Korea. In our study only one case was diagnosed and that was due to involvement of the adjacent pleura.

In an review article by Panou *et al*[20], recent updates in the diagnosis of pleural lesions were discussed, including imaging techniques in which thoracic ultrasound and computed tomography were considered pivotal in the diagnosis of pleural lesions, while the role of magnetic resonance imaging was reserved for a few diagnostically challenging cases. The use of pleural fluid biomarkers in diagnosis of pleural effusions secondary to heart failure, pneumonia and tuberculosis was reviewed by Chan and another[21], and can be used to support the diagnosis. However, further research to identify biomarkers in malignant pleural fluid is required. For neoplastic lesions, the sensitivity of pleural fluid cytology was only 50% hence making pleural biopsies the gold standard.[20]

CONCLUSION

The most common pleural pathology identified in this study was chronic non-specific inflammation followed by empyema thoracis, tuberculosis, metastatic adenocarcinoma and fibrosis. However, two rare cases, one each of actinomycosis and fungal infection were also identified.

RECOMMENDATIONS

Before labelling a patient as having MDR-TB, a complete workup which may include pleural biopsy should be done to rule out rare causes of infections other than tuberculosis. Any pleural pathology requires a comprehensive workup to establish a definitive diagnosis so that an effective management plan can be implemented.

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FJ: Data collection and analysis
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