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Role of CT in diffuse pleural diseases: Detection, Characterization and Differential diagnosis.

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Abstract:
Background*: Various benign and malignant conditions can lead to widespread abnormalities in the pleura. Common culprits include asbestos-related pleural fibrosis, fibrothorax, empyema, mesothelioma, and metastatic disease. While the characteristic CT appearances of these diffuse pleural diseases have been documented, there is a notable gap in research analyzing the diagnostic utility of CT in distinguishing between them. Diffuse pleural abnormalities typically involve a mix of pleural thickening, calcification, and effusion, resulting in overlapping CT manifestations across different diseases.*
Our study aimed to identify the most informative CT features for distinguishing between various diffuse pleural diseases. By investigating the differential diagnosis of diffuse pleural disease, we sought to pinpoint specific CT characteristics that could aid in accurately identifying the underlying pathology.
Materials and Methods*: All patients with diffuse pleural disease seen in our institution between May 2023 and November 2023 who had a definitive diagnosis and in whom CTs scans had been obtained were included in this retrospective study. Thirty patients were selected by reviewing the medical records and CT reports.*
Results*: In the absence of clinical or pathologic data, we conducted a retrospective analysis of CT findings in a cohort of 38 consecutive patients with confirmed diffuse pleural disease. Based on the above mentioned four features, out of 38 patients, 19 were malignant and 19 were benign. The specificities of these findings were 100%, 94%, 94%, and 88%, respectively. The sensitivities were 41%, 51%, 36%, and 56%, respectively.*
Conclusion: *We conclude that CT is helpful in the differential diagnosis of diffuse pleural disease, particularly in differentiation of malignant from benign conditions. Features that were helpful in distinguishing malignant from benign pleural disease were (1) circumferential pleural thickening, (2) nodular pleural thickening, (3) parietal pleural thickening greater than 1 cm, and (4) mediastinal pleural involvement.*
Key Word: *Pleura, pleural thickening, Benign, malignant*

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I. Introduction

The pleura is a thin and delicate serous membrane that forms a closed sac around the lungs and lines the thoracic cavity. The pleural sac is comprised of of two layers: the visceral pleura, which adhere to the surface of the lungs, and the parietal pleura, which lines the inner surface of the chest wall and diaphragm.

This arrangement creates a potential space called the pleural cavity, which normally contains a small amount of fluid. The presence of this fluid allows the pleurae to slide smoothly against each other during breathing, facilitating the expansion and contraction of the lungs within the thoracic cavity. Pleural thickening is a term given to describe any form of thickening involving either the parietal or visceral pleura. It can occur with both benign and malignant pleural disease.(1,2,3)

II. Material And Methods

This is a retrospective study which was carried in patients of Department of Radio-diagnosis at Maharajah's Institute of medical sciences, Vizianagaram from May 2023 and November 2023. A total 30 adult subjects (both male and females) of aged ≥ 18, years were for in this study.

Study Design: Retrospective observational study

Study Location: This was a tertiary care teaching hospital based study done in Department of Radio-diagnosis at Maharajah's Institute of medical sciences, Vizianagaram.

Study Duration: May 2023 and November 2023

Sample size: 38 patients.

Sample size calculation: All patients with diffuse pleural disease seen in our institution between May 2023 and November 2023 who had a definitive diagnosis and in whom CT scans had been obtained were included in this retrospective study. Thirty patients were selected by reviewing the medical records and CT reports.

Subjects & selection method: The study population were a cohort of definitely diagnosed pleural disease patients who had done CT in Department of Radio-diagnosis at Maharajah's Institute of medical sciences, Vizianagaram and were later proven between May 2023 and November 2023.

Inclusion criteria:
1. Patients with proved diffuse pleural diseases.
2. Either sex
3. Aged ≥ 18 years

Exclusion criteria:
1. Sub diaphragmatic collections.
2. Focal pleural thickening.

Procedure methodology

The CT scans were obtained on a 16 Slice CT General Electric Revolution act. Contiguous 1 -cm collimation scans were obtained from lung apices to the level of the adrenals. All scans were obtained at end-inspiratory lung volumes by using the standard algorithm and were photographed at windows appropriate for lung parenchyma and mediastinum. The CT scans were done as part of the initial assessment of these patients at our institution. The CT scans and accompanying chest radiographs were reviewed by two observers who were unaware of the pathologic diagnosis; a conclusion was reached by consensus. The scans were assessed for the presence of pleural effusion; presence, type, and extent of pleural thickening as suggested by previous studies presence or absence of extrapleural invasion; adenopathy; calcified nodes; loss of volume in the involved hemithorax; and coexisting pulmonary parenchymal abnormalities. Mediastinal nodes were considered enlarged if they were greater than 8 mm in short-axis diameter in the transverse plane. Pleural thickening was classified as either focal plaques or diffuse thickening. Pleural plaques were defined as areas of pleural thickening less than 5 cm in either transverse or craniocaudal extent. The location of the pleural thickening was classified as parietal, visceral, fissural, or mediastinal. Mediastinal involvement was defined as pleural thickening bordering the mediastinum, and no attempt was made to differentiate parietal from visceral mediastinal pleural involvement.

The distinction between visceral and parietal pleural thickening was made only in the presence of pleural effusion. The contour of the pleural thickening was characterized as smooth, irregular, or nodular. Parietal pleural involvement was further characterized by whether it was circumferential (defined as involvement of entire perimeter of hemithorax including mediastinum, or pleural rind), width of thickening, length of craniocaudal extension, and presence or absence of involvement of the lung bases (defined as pleural thickening in the lower third of the hemithorax). Pleural calcification was classified as involving plaques or diffuse thickening. In the cases for which high-resolution CT was available, these additional scans were judged to be of benefit when they enabled a classification change in any of the previously noted characteristics.

All pathologic specimens were reviewed by a pathologist. The histologic assessment of benign vs malignant was determined on the basis of standard architectural and cytologic features. The 4 mesotheliomas included one low-grade papillary epithelial mesothelioma, one desmoplastic mesothelioma, and two more usual epithelial and mixed patterns. In cases in which the differential diagnosis was between adenocarcinoma and epithelial mesothelioma, the diagnosis of adenocarcinoma was made if neutral mucin and/or carcinoembryonic antigen could be shown [11 , 12].

Statistical analysis

The clinical data were obtained from hospital and office charts. Statistical comparison between selected patient groups was performed by using the chi-square test.

III. Result

All patients with diffuse pleural disease seen in our institution between May 2023 and November 2023 who had a definitive diagnosis and in whom CT scans had been obtained were included in this retrospective study. Thirty eight patients were selected by reviewing the medical records and CT reports. 27 were men and 11 were women, with a mean age of 60 years (range, 18-78 years). The hemi thorax with the most involvement was the right in 23 cases and the left in 15. Definitive pathologic diagnosis based on the results of pleural biopsy was available in 16 of 19 cases of malignant pleural disease (6 mesothelioma, 9 metastatic pleural carcinoma, 2 non-Hodgkin lymphoma, 1 metastatic melanoma and one liposarcoma), one of three cases of fibrothorax, and two of three infectious processes. The diagnosis of metastatic adenocarcinoma in one patient was based on cytologic findings in a sample obtained by thoracentesis as well as the concomitant findings of multiple brain and lung

metastases. three patients with fibrothorax who did not have biopsy had known previous history of treated tuberculosis.

The seven patients with asbestos-related pleural disease had documented exposure to asbestos and had been referred either for evaluation of questionable radiographic findings with associated abnormal pulmonary function tests or pleural effusion of unknown cause. All seven patients had diffuse pleural thickening, defined as blunting of the costophrenic sulcus or localized areas of thickening extending for more than 5 cm in both craniocaudal and transverse diameters.

Infectious pleural disease was diagnosed on the basis of positive cultures of pleural fluid with biopsy confirmation performed in 4 of 6 tuberculous empyemas, two of three nontuberculous empyemas.

In patients with pleural thickening, the features most suggestive of a malignant cause were pleural rind (a finding seen only in patients with malignant pleural disease), with a specificity of 100% and a sensitivity of 41%; nodular pleural thickening, with a specificity of 94% and a sensitivity of 51%; parietal pleural thickening greater than 1 cm, with a of 94% and a sensitivity of 36%; and mediastinal pleural involvement, with a specificity of 88% and a sensitivity of 56% (Table 1). All these features were significantly more common in malignant than in benign pleural thickening ($p < .01$, chi-square test).

13 of 19 cases of malignant pleural disease had one or more of these features as compared with only 4 of 19 cases of benign pleural disease, representing a sensitivity of 72% and a specificity of 83% for malignancy (Table 1).

In concordance with study done by Leung AN. et. Al; the presence of pleural calcification was suggestive of benign cause, with a sensitivity of 46% and a specificity of 92% (Table 1)(7).

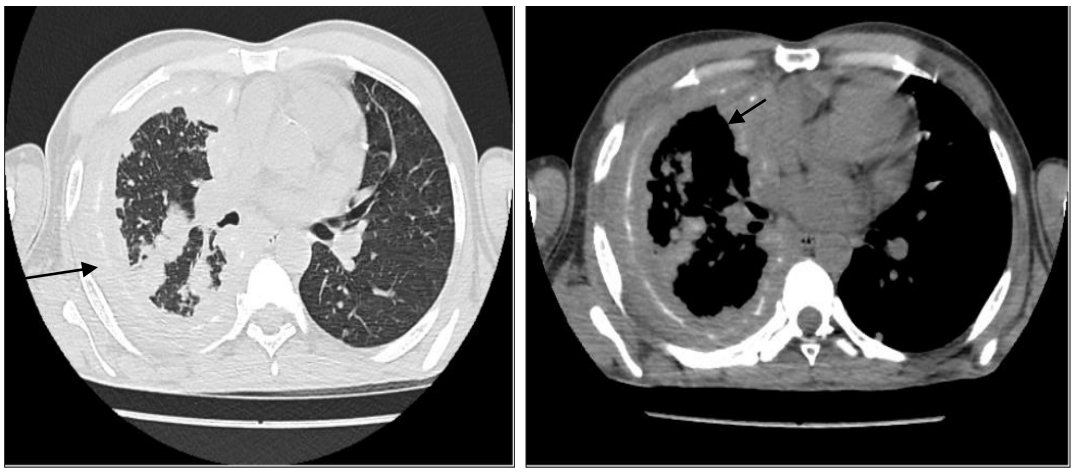
In most patients with mesothelioma, the CT findings were identical to those of metastatic pleural disease, including the presence of nodular pleural thickening, pleural rind, mediastinal or chest wall invasion, and loss of volume (Table 1). Pleural effusion as the only manifestation of pleural malignancy was a feature seen in pleural metastases and not in mesothelioma.

In this group, adenopathy (hilar and/ or mediastinal) was a more consistent finding ; circumferential pleural rind was not seen. The only case of pleural liposarcoma had a virtually pathognomonic appearance: an inhomogeneous pleurally based mass of tissue density intermixed with several areas of fat. Parietal pleural thickening was greater than 1 cm and irregular in contour; invasion into both mediastinum and chest wall was present. Features distinguishing mesothelioma from benign asbestos-related pleural thickening were essentially the same as those differentiating neoplastic from benign disease (Table 1).

The two most useful features in differentiating asbestos related pleural disease from other benign conditions were the presence of pleural plaques, with a specificity of 95% ($p < .01$) and bilateral pleural involvement, with a specificity of 74% ($p < .01$) for asbestos-related pleural disease (Fig. 5).All nine cases of empyema were seen on CT as a round or lenticular fluid collection separating slightly thickened visceral and parietal pleural surfaces (Fig. 6). The thickened pleura was usually smooth although sometimes irregular; neither nodularity nor thickening greater than 1 cm was seen (Table 1).

Table no 1: Characteristics of different pleural diseases

	Mesothelioma (6)	Metastases (9)	Lymphoma (2)	Asbestosis (7)	Empyema (9)	Fibrothorax (3)
Nodularity	4	6	1	0	0	1
Rind	5	5	1	0	0	0
Thickness>1cm	4	4	2	1	0	1
Mediastinal pleural involvement	5	7	1	2	1	1
Calcification	2	2	0	5	4	3
Lung base involvement	5	3	0	6	2	3
Visceral pleural involvement	2	4	0	3	2	2
Effusion	4	8	1	3	3	2
Plaques	3	0	0	4	0	2
Hilar or mediastinal adenopathy	2	7	1	2	1	2
Calcified nodes	0	2	0	1	0	1
Loss of volume	5	4	1	5	2	3



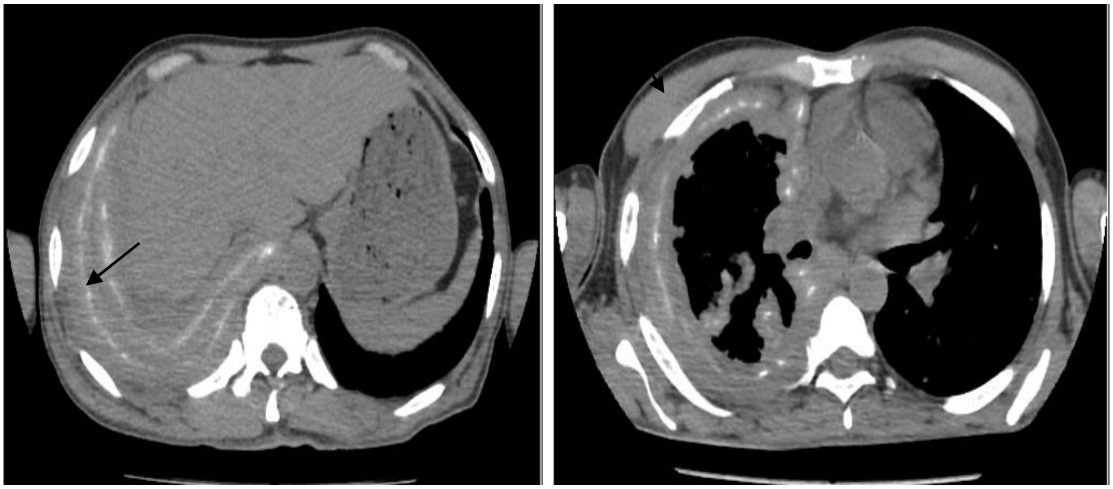
1 A) 1 B)

Fig.1 A - CT chest lung window of a 48 year old male showing diffuse right sided pleural thickening with nodular thickening of oblique and horizontal fissures.
Fig. 1 B – CT chest mediastinum window of the same patient showing internal calcifications with in the coastal and mediastinal pleural thickening (arrow).
Later proven with biopsy as Malignant mesothelioma.

IV. Discussion

The pleural response to a range of diseases is predominantly characterized by three radiologically detectable manifestations: effusion, thickening, and calcification. Pleural effusion often presents as a common manifestation of diffuse pleural disease. When evaluating unexplained pleural effusion using CT, a primary goal is to differentiate between benign and malignant causes(3). Malignant pleural effusions typically result from lymphatic obstruction, which can occur at any point between the stomata of the parietal pleura and the mediastinal lymph nodes. The effusion associated with malignancy is usually characterized as an exudate.

While attempts have been made to use fluid attenuation coefficients to distinguish fluid composition, such measurements have proven unreliable, with the exception of hemothorax. Studies, such as one by Maffessanti et al., (4) have suggested that the absence of pleural thickening does not rule out a neoplastic diagnosis. In their series, a significant number of patients with normal-appearing pleura had malignant effusions. Consistent with these findings, our results also show instances where pleural effusion was the sole manifestation of neoplastic pleural involvement, emphasizing the complexity and variability in the presentation of pleural diseases on CT scans.



2A) 2B)

Fig. 2A – CT Chest mediastinum window of a 65 year old male showing diaphragmatic pleural thickening with calcifications.
Fig. 2B - – CT Chest mediastinum window of the same patient showing mediastinal involvement along with bony chest wall infiltration in the form of anterior aspect of 4th rib(arrow) and lateral aspect of 5th rib.

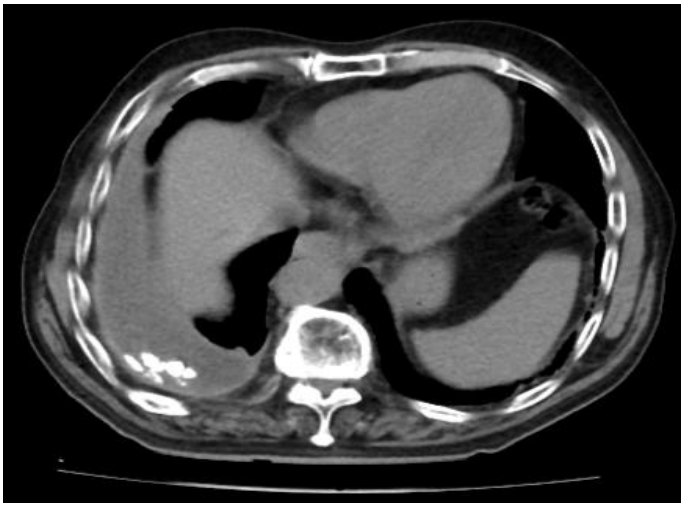


Fig. 4 – CT chest mediastinum window showing right loculated pleural effusion with pleural calcifications

Despite the absence of pleural thickening evident on CT scans, the presence of nodules on the entire surface of the visceral pleura was identified during thoracotomy in one of the patients. This underscores a crucial point — that the lack of observable pleural thickening on CT does not necessarily exclude the possibility of pleural malignancy.(5)

In certain instances, the pathology may manifest as nodules rather than thickening, making it imperative for clinicians to recognize the diverse presentations of pleural diseases. This finding reinforces the need for a comprehensive diagnostic approach that considers various radiological manifestations and, when necessary, incorporates additional diagnostic modalities or interventions for a more accurate assessment of pleural conditions.

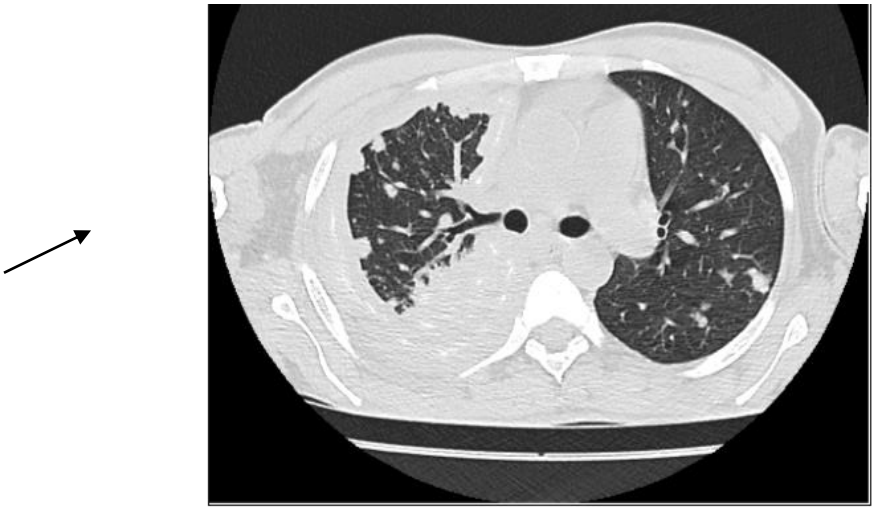


Fig. 3 – CT chest lung window of a 70 year old male patient showing pleural thickening >1cm (arrow) with nodularity.

The CT differentiation of benign and malignant pleural disease is important because the specific diagnosis is often difficult to make by clinical criteria, pleurocentesis, and percutaneous pleural biopsy.

Ryan et al. [6] reported 51 patients in whom no cause for a pleural effusion was found at thoracotomy. In 1 3 of these patients (25%), the diagnosis of malignancy (including lymphoma, carcinoma, and malignant mesothelioma) was established 1 2 days to 5 years after thoracotomy. The difficulty in pathologically differentiating benign reactive mesothelial cells from mesothelioma is a common and well-known probIem, and in many instances, the gross appearance assumes great importance in making this distinction [8].

The CT appearance plays a crucial role in assessing the gross distribution of disease, providing valuable insights into whether thoracotomy is warranted. It serves as a useful tool in guiding surgeons by directing their attention to specific sites that are more likely to yield a positive diagnosis. These targeted areas

typically encompass those exhibiting significant features such as greater than 1 cm pleural thickening, nodular pleural thickening, and thickening of the mediastinal pleura.

The presence of pleural calcification suggests a benign process. In this series, calcification was seen in 12 of 19 patients with benign pleural thickening and in only four of 19 patients with malignant pleural disease. Although calcified plaques may be seen in cases of mesothelioma, they are uncommon and were seen in 2 of our 6 mesothelioma patients. The relative absence of pleural calcification in mesothelioma may be due to absorption of calcification by the developing tumor [8] and the fact that a significant number of malignant mesotheliomas (range, 0-87%) are not asbestos-related [9].

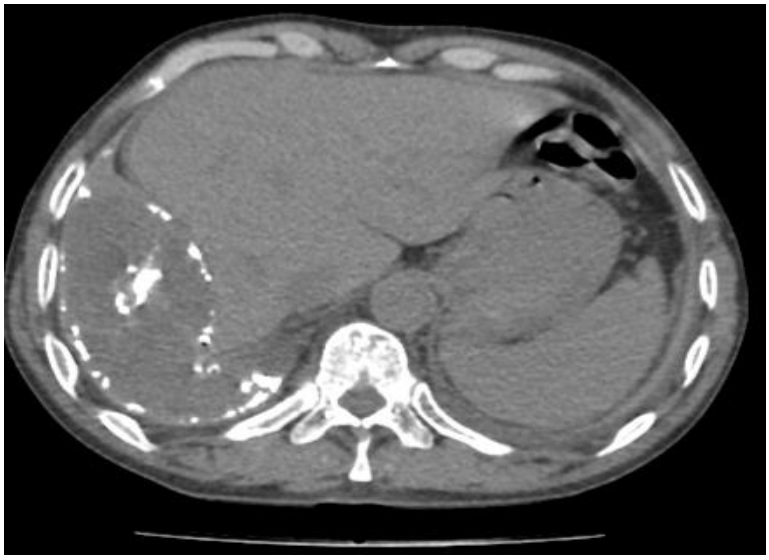


Fig. 5 – CT chest mediastinum window showing a well-defined crescent shaped, lobulated, intra pleural area with internal and peripheral wall calcifications in right lower pleural cavity – Consistent with chronic empyema.

In concordance to the study done by June Young Bae et. al;the invasion of the chest wall or mediastinum, when observed on CT scans, serves as a specific marker for malignancy. It was seen in 70% of our patients.(8)

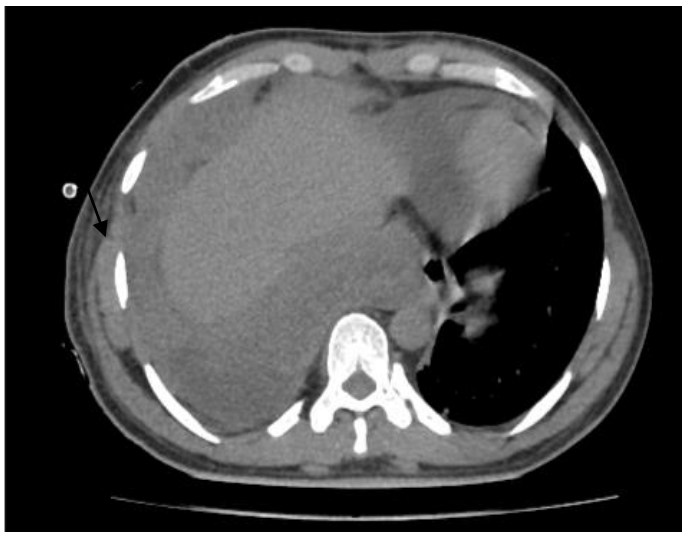


Fig. 7 – CT chest mediastinum window shows loss of fat planes of the lesion with thoracic oesophagus and right hemi diaphragm.

Adams et al. [10] have suggested that the presence of hilar adenopathy may be helpful in differentiating metastases from mesothelioma. However, true hilar involvement with no mediastinal involvement is rare in metastatic pleural disease except for bronchogenic carcinoma, lymphoma, and renal cell carcinoma. In our study, hilar adenopathy was identified in 13 patients with malignancy. Out of 13, 9 were seen in metastases.

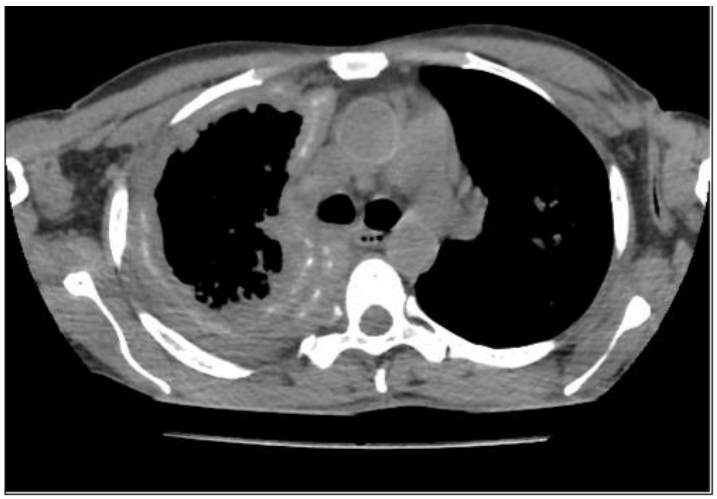


Fig. 8 – CT chest mediastinal window showing precarinal lymphadenopathy (arrow)along with prevascular and pretracheal lymphadenopathy.

The tendency of mesothelioma to involve the inferior hemithorax has been suggested as a specific sign. However, in our study, it was observed that basal involvement was not exclusive to patients with mesothelioma; rather, it was also prevalent in the majority of patients with metastatic pleural disease. This finding underscores the challenge in relying on a single characteristic, as certain features may be shared among different pleural pathologies.

The overlap in imaging characteristics between mesothelioma and metastatic pleural disease emphasizes the need for a nuanced and comprehensive evaluation. A multidimensional approach that considers various radiological features, clinical information, and, when necessary, additional diagnostic procedures is essential for accurately differentiating between these entities and guiding appropriate management decisions.

Nodularity of the pleura has been recognized as a helpful discriminating feature, and in your study, nodular pleural thickening was observed in a majority of cases of mesothelioma, while none of the cases of benign asbestos-related diffuse pleural disease displayed this characteristic. However, it's essential to note that extensive nodular thickening of pleural plaques, which can mimic mesothelioma, has also been reported. In such instances, where the radiological appearance may lead to diagnostic ambiguity, open pleural biopsy is considered the only reliable method to definitively establish the diagnosis of benign disease.

While loss of volume is a common manifestation in mesothelioma, it is acknowledged as a relatively nonspecific finding, as it can also be observed in various other malignant and benign conditions. In our series, it was noted that volume loss was present in approximately 50% of patients, irrespective of the underlying cause of diffuse pleural disease. This highlights the limitation of relying solely on volume loss as a distinguishing feature, as its occurrence is not exclusive to mesothelioma and can be encountered in a diverse range of pleural pathologies.

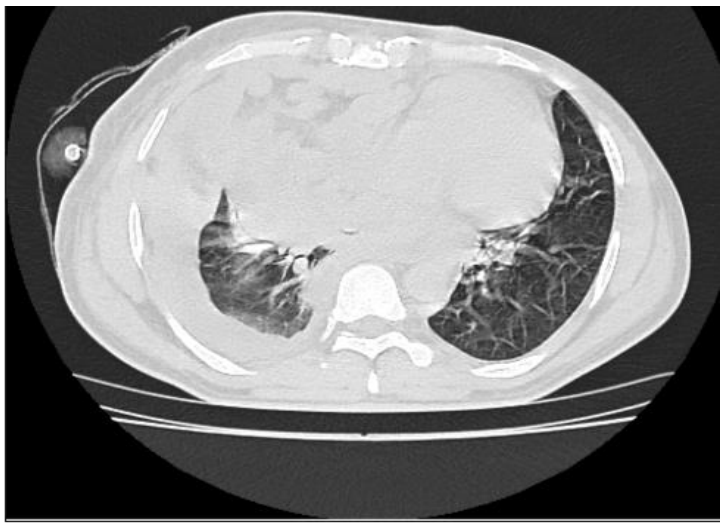


Fig.6 – CT chest lung window showing volume loss of right hemithorax.

Our study was limited by the relatively small number of cases of some diseases and by the relatively small number of diseases included by which the overall sensitivity and specificity may be effected.

V. Conclusion

Our study suggests that certain CT features are particularly useful in distinguishing malignant from benign pleural diseases. Key indicators include the presence of a pleural rind, nodular pleural thickening, pleural thickening exceeding 1 cm, and mediastinal pleural involvement. Pleural calcification typically is present in benign pathologies. Loss of volume does not emerge as a reliable distinguishing feature.

Notably, our findings underscore the difficulty in differentiating mesothelioma from metastatic pleural disease solely based on CT scans. The majority of patients with these conditions exhibit overlapping features on CT, emphasizing the need for additional diagnostic methods for a more accurate assessment.

This insight reinforces the importance of utilizing advanced imaging techniques to enhance diagnostic precision, especially in cases where subtle distinctions can significantly impact clinical management.

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