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Pulmonary Cystic Lesions in Multislice Computed Tomography: A Stepwise Diagnostic Approach Based on Radiological and Clinical Findings

TAKEYA A. TAYMOUR, M.D.*; ARWA E. ABD EL-GHANI, M.Sc.*; NAHLA NAEEM MOHAMED, M.D.**; HODA M. ABDEL-HAMID, M.D.*** and MOSTAFA A. KHAIRY, M.D.*

The Departments of Radiology, Rheumatology** and Pulmonology***, Faculty of Medicine, Cairo University*

Abstract

Background: Lung cysts are commonly seen on computed tomography (CT), and cystic lung diseases show a wide disease spectrum. Correct diagnosis of cystic lung diseases is a challenge for radiologists.

Aim of Study: To evaluate the role of multislice and high resolution CT in the diagnosis, differentiation and detection of causes of pulmonary cystic lesions.

Patients and Methods: This study involved 60 adult patients presented by different chest manifestations diagnosed as having pulmonary cystic lesions by multislice CT (MSCT) or high resolution CT (HRCT). Detailed history was taken, thorough clinical examination and different laboratory tests were considered. The cystswere evaluated for the following: Site, size, number and content.

Results: Females were slightly predominant compared to males accounting for 70%, smokers represented the majority of the included patients accounting for 65%. The distribution of the cysts was predominantly bilateral (97%). Most of the cases showed homogenous distribution of the cysts among all lobes (65%). Round shape was the commonest reported shape in 36 (60.0%) patients. Additional findings in the background of CT scan showed that 30 (50%) patients had nodules, 24 (40%) patients had ground glass opacities, 24 (40%) patients had interstitial/or septal thickening, 6 (10%) patients had fibrotic changes, 6 (10%) patients had a pneumothorax and 6 (10%) patients had associated honeycombing pattern. No associated CT findings other than cysts were seen in 9 cases. In the current study, the commonest diagnosis was LAM in 21 (35%) patients, followed by LCH in 18 (30%) patients, interstitial pneumonia in 13 (21.6%) patients, 6 (10%) cases with HP, two cases with genetic disease Birt-Hogg-Dubé syndrome.

Conclusions: Multislice computed tomography has an established role in assessment of pulmonary cystic lesions. Recommended step wise approach including exclusion of cyst mimickers first, then considering the clinical data and analyzing the radiographic characters of the cysts, all together can be used for differentiation and detection of causes of pulmonary cystic lesions.

Key Words: *Birt-Hogg-Dubé syndrome – Computed tomography – Langerhans cellhistiocytosis – Lymphangioleiomyomatosis.*

Correspondence to: Dr. Takeya A. Taymour,
The Department of Radiology, Faculty of Medicine,
Cairo University

Introduction

CYSTIC lung disease (CLD) is a group of lung disorders characterized by the presence of multiple cysts, defined as air-filled lucencies or low-attenuating areas, bordered by a thin wall (usually <2mm). The recognition of CLDs has increased with the widespread use of computed tomography **[1].**

Single or several cysts in a localized area are classified as solitary/localized cysts, while multiple

List of Abbreviations:
BHD : Birt-Hogg-Dubé.
CLD : Cystic lung disease.
CT : Computed tomography.
DIP : Desquamative Interstitial Pneumonia.
FOV : Field of view.
GGO : Ground glass opacity.
HP : Hypersensitivity pneumonitis.
HRCT : High resolution computed tomography.
ILD : Interstitial lung diseases.
LAM : Lymphangioleiomyomatosis.
LIP : Lymphocytic interstitial pneumonia.
MSCT : Multislice computed tomography.
PCP : Pneumocystis Jirovecii Pneumonia.
PFTs : Pulmonary function tests.
PLCH : Pulmonary Langerhans cell histiocytosis.

or numerous cysts distributed in both lungs are classified as multiple/diffuse cysts **[2].**

CT Chest is the imaging modality of choice to detect and differentiate among the various causes of diffuse cystic lung disease because it enables improved identification of cyst characteristics (including their size, number, location and distribution) and associated lesions, narrowing the differential diagnosis and often avoiding the need for diagnostic confirmation by lung biopsy **[3].**

Lung cysts are often confused with other air-filled lesions in the lung parenchyma (cyst mimickers). Therefore, single or several cysts in a localized area of the lung should be distinguished from a cavity, pneumatocele, or bullae. Moreover, multiple cysts diffusely distributed in both lungs should be distinguished from emphysema, honeycombing, and cystic bronchiectasis.

Multidisciplinary approach is necessary to make the correct diagnosis of lung cyst including clinical correlation and occasional tissue biopsy, however, a radiologic approach is particularly important in narrowing the differential diagnosis **[2].**

The purpose of this study is to evaluate the role of multislice and high resolution CT in the diagnosis, differentiation and detection of possible causes of pulmonary cystic lesions.

Patients and Methods

Study design:

This study involved 62 patients; 20 males and 42 females, age range 20-80 years (average of approximately 40 years). This study was done in the Radiology Department in Kasr Al Ainy Hospital After Institutional and Departmental Ethical Clearance over a period of 20-months (from November 2021 to June 2023).

Inclusion criteria:

Patients with different chest manifestations were referred to the Radiology Department in Kasr Al-Ainy from either chest or Rheumatology Department for NCECT or HRCT of the chest and only cases showing lung cysts as a main CT finding were included in our study.

Patients were subjected to the following:

- A written informed consent to be included in the study.
- Detailed history taking.
- Thorough clinical examination with general and chest examination
- Different laboratory tests were done.
- Histopathological assessment was done to 39 patients and PFTs were done in 18 cases according to the clinical and radiological findings.
- Genetic study for Birt-Hogg-Dubé Syndrome was done in two cases (2 siblings).

CT chest study technique:

Non contrast MSCT or HRCT chest was done to patients using Siemens Emotion MSCT 16 or Toshiba Aquilion MSCT 64 (Tables 1,2).

Table (1): MSCT technique.

	Siemens Emotion MSCT 16
Scout	Kv110 mA25 Holding breath
Detector Row	16
Slice Thickness	1.0 mm
FOV	351 mm
Kv	110
mA	25
Total exposure time	0.8 sec

Table (2): HRCT technique.

	Siemens Emotion MSCT 16	Toshiba Aquilion MSCT 64
Scout	Kv110 mA25 Holding breath	Kv120 mA50 Holding breath
Scan type	Helical	Helical
Detector Row	16	64
Slice thickness	1.0 mm	1.0mm
FOV	351 mm	Depends on patients' size
Kv	110	120-140
mA	25	120-160
	Holding breath in full inspiration Reconstruction type: STD (standard) Mediastinal window images are also taken	

Image analysis and interpretation:

- The cysts were evaluated for the following: site, size, number and content as well as associated parenchymal lung changes.
- All CT examinations were analyzed by three cardiothoracic radiologists having 11 to 25 years of expertise. After a debate between the two readers, their disagreement was settled by consensus decision after a discussion with a third radiologist having over 25 years of expertise.

Statistical analysis:

Statistical analysis was conducted using SPSS 22nd edition, qualitative variables were presented in frequency and percentages and compared using Chi^2, and quantitative variables were presented in mean and standard deviation and was compared using the student *t*-test.

Results

A total of 60 patients were eligible for inclusion in our final analysis afterexclusionof two cases diagnosed as incidental/idiopathic cysts based on radiological and clinical findindings and hence no further investigations or follow-up were needed. These two cases were two males; 50 and 54 years old showing few small mainly rounded cysts ; 4 in one of them seen localized in the right lower lobe and 7 cysts in the second one seen scattered in both lower lobes. They show no significant associated chest findings apart from scattered atelectatic bands and upper lobar cetrilobular emphysema in one of them. Clinically these two cases represented with mild cough and one of them gave history of previous chest infection.

The 60 cases included in our study had a mean age of 40 ± SD 17 years, females were slightly predominant compared to males accounting for 70%, smokers represented the majority of the included patients accounting for 65%, all of the included patients complained of dyspnea, cough, fatigue and only one reported weight loss.

Hypertension accounted for 30% of the included patients, while diabetes affected 10% and 8 patients reported a positive history of rheumatoid arthritis.

Pattern and distribution of cysts among the study population:

The distribution of the cysts was predominantly bilateral (97%). Most of the cases showed homogenous distribution of the cysts among all lobes (65%). Round shape was the commonest reported shape in 36 (60.0%) patients followed by bizarre shaped cysts in 18 (30.0%). Small sized cyst was the commonest reported size accounting for 50%.

Associated CT features with lung cysts:

Additional findings in the background of CT scan are demonstrated in (Fig. 1).

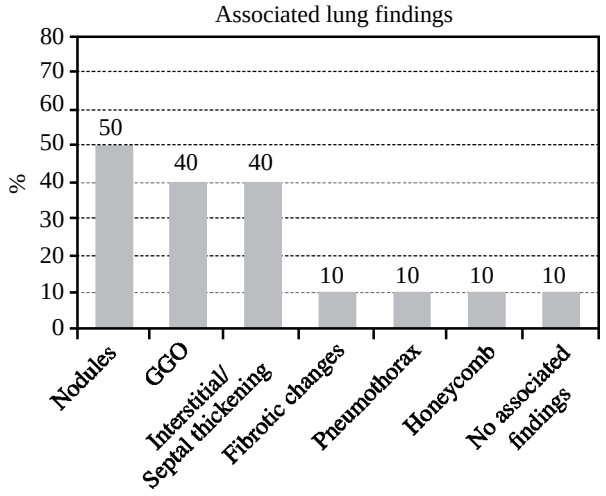

Fig. (1): Bar chart showing associated lung findings among study participants.

The number and percentage of the included cases of cystic lung diseases is shown in Table (3).

Table (3): Diagnosis of cystic lung diseases.

Final diagnosis	Number of patients (%) Total 40
LAM (Lymphangioleiomyomatosis)	21(35%)
PLCH (Pulmonary Langerhans cell Histiocytosis)	18(30%)
LIP (Lymphocytic interstitial pneumonia)	8(13.3%)
HP (Hypersensitivity pneumonitis)	6 (10%)
DIP (Desquamative interstitial pneumonia)	5(8.3%)
BHDS (Birt-Hogg-Dubé syndrome)	2 (3.3%)

The final diagnosis of the patients was made using lung biopsy in cases of LAM and LCH, Clinical diagnosis and pulmonary function tests were used in cases of interstitial pneumonia and HP, while genetic study was used in two cases of Birt-Hogg-Dubé syndrome.

Comparison of features according to diagnosis:

1- Cases of Lymphangioleiomyomatosis:

The comparison of the age and gender showed that Lymphangioleiomyomatosis patients were younger compared to other diagnoses with mean age of 30.1 ± SD 7.4 years and LAM was exclusively in females.

Regarding the distribution of lung cysts; it was bilateral and affected all lung lobes. The cysts are multiple and rounded with no associated nodules. The intervening parenchyma was found to be normal in 12 patients (57%), associated ground glass opacities in 9 patients (43%). Aassociated pneumothorax were noted in 3 patients (14.2%) (Figs. 2,3,4).

2- Cases of pulmonary langerhans cell histiocytosis:

Regarding Pulmonary Langerhans Cell Histiocytosis, males are predominant compared to females accounting for about 66.70% of cases. Most patients were young agedwith mean age of 32.7 ± SD 5.2 years. It significantly affects smokers and passive smokers.

Regarding cysts distribution; cysts showed bilateral predominantly upper lobar distribution. Cysts were all bizarre shaped and small to variable in size. Centrilobular nodules in the background were common association with this disease in 100% of cases (Figs. 5,6,7).

3- Cases of interstitial pneumonia:

Interstitial pneumonia cases were associated with small sized cysts, interstitial septal thickening, ground glass opacities and associated honeycomb-

ing. Cysts were predominantly bilateral (85%) affecting mainly lower lobes. 8 cases with interstitial pneumonia had history of collagen vascular disease which makes the diagnosis most likely to be LIP rather than DIP while the remaining cases had history of smoking which raises the possibility of being DIP (Figs. 8,9).

4- Cases of Hypersensitivity pneumonitis:

Hypersensitivity pneumonitis was mainly associated with few lung cysts, mosaic parenchymal pattern in the form of patchy ground glass opacities alternating with areas of air trapping and associated fibrotic changes. Cysts were predominantly affecting the lower lobes. Three cases with hypersensitivity pneumonitis had history of raising birdsand all cases were non-smokers (Fig. 10).

5- Cases of Birt-Hogg-Dubé syndrome:

The two cases of this disease showed the characteristic CT features of Birt-Hogg-Dubé syndrome which includes the multi-septated cyst appearance with variable predominantly lentiform shape seen abutting or surrounding the related portions of the pulmonary arteries or veins. Cysts were distributed along lower peripheral lungs and along the mediastinum, and the two cases showed pneumothorax as associated finding (Fig. 11).

Based on our study results the recommended diagnostic approach for cystic lung diseaseis as follow:

- The first step is to identify true cyst and to be able to distinguish it from other mimics of lung cysts such as cavities, emphysema and cystic bronchiectasis.
- The second step is to identify cases of incidental/ idiopathic cysts which are solitary or few and localized mostly peripheral and lower lobar showing no related lung changes. It is seen most commonly above age of 40 due to aging process.
- Then cases of multiple diffuse lung cysts should be assessed for the cysts pattern and distribution as well as associated lung changes including nodules, ground glass patches and parenchymal fibrotic changes taking in consideration clinical background of the examined cases.

o Cases with multiple diffuse lung cysts involving all lobes and relatively normal intervening parenchyma apart from occasionally noticed few ground glass patches are usually encountered in cases of LAM. Cysts are usually rounded in shape and are exclusively found in young females.

o Cases with predominantly upper lobar cysts associated with centrilobular nodules are most commonly encountered in PLCH where cases are most commonly young adult smokers.

o Cases with few randomly distributed cysts associated with interstitial fibrotic changes are usually noted in cases of DIP (commonly found in smokers) and LIP (commonly seen in patients with collagen disease).

o Cases of BHD usually show multi-septated cyst appearance with variable predominantly lentiform shape seen abutting or surrounding the related portions of the pulmonary arteries or veins. They are usually associated with cutaneous and renal disease.

o In cases of hypersensitivity pneumonitis HP; if cysts are found they are usually fewer in number than other cystic lung disease and are seen associated with typical lung changes of HP which include mosaic lung attenuation showing alternating areas of air trapping and ground glass patches with occasionally detected fibrotic lung changes. Most of the cases give history for raising birds.

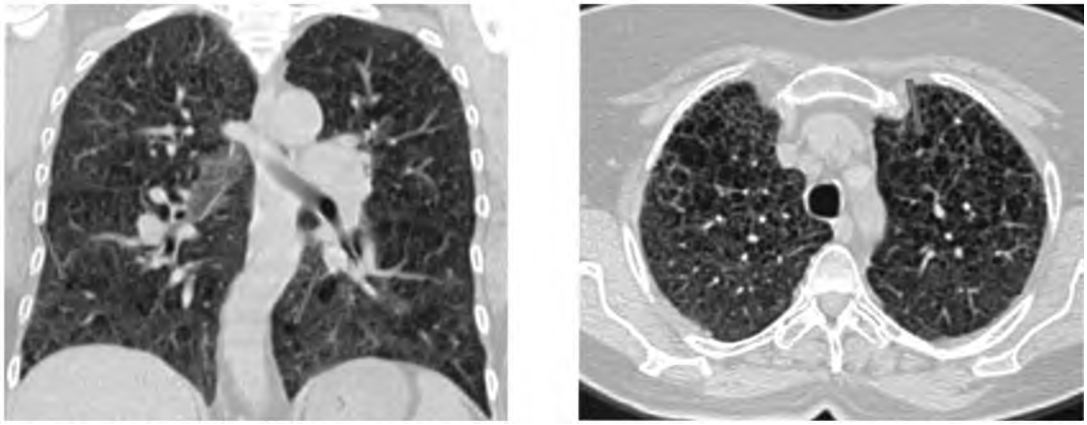

Fig. (2): Female patient non-smoker 27 years old presented by cough & dyspnea. HRCT coronal and axial images showing bilateral numerous diffuse small sized air-containing lung cysts (red arrow) with no associated CT findings other than cysts, suspecting the diagnosis of LAM & it was confirmed by histopathology.

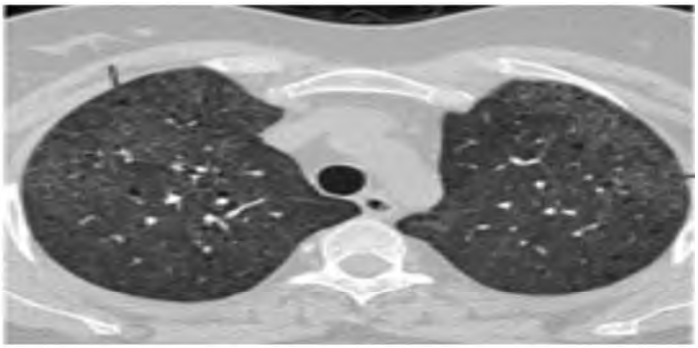

Fig. (3): Thirty nine years old female patient, diabetic & passive smoker presented by dyspnea, has old history of TB & interstitial lung fibrosis. HRCT axial image showing bilateral diffuse rounded small sized air containing lung cysts (red arrow) surrounded by parenchymal areas of ground glass veiling (blue arrow), suspecting the diagnosis of LAM & it was confirmed by histopathology.

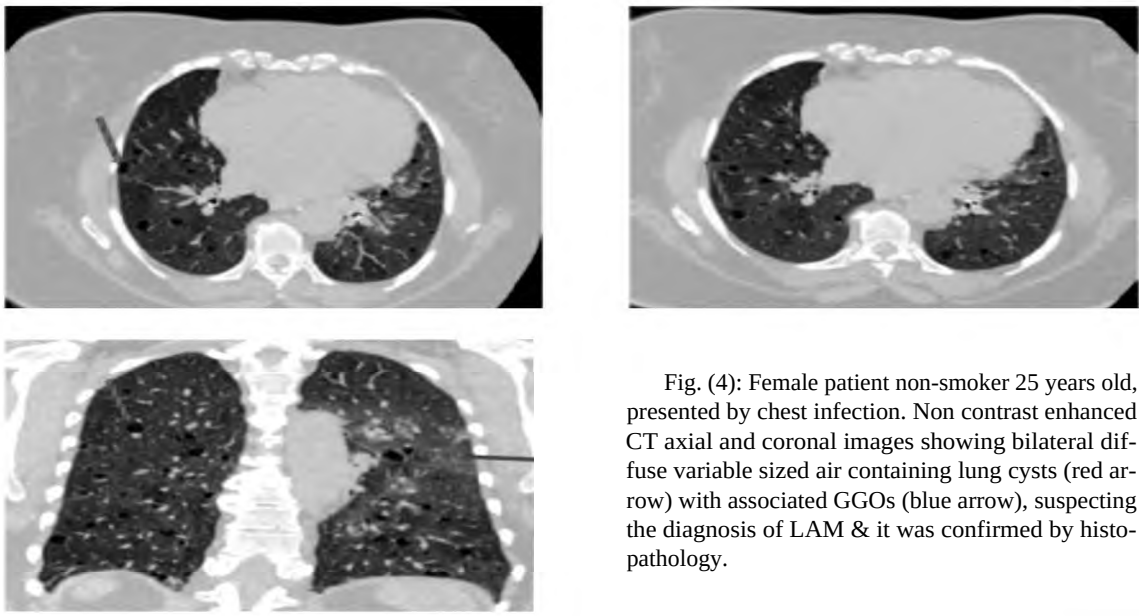

Fig. (4): Female patient non-smoker 25 years old, presented by chest infection. Non contrast enhanced CT axial and coronal images showing bilateral diffuse variable sized air containing lung cysts (red arrow) with associated GGOs (blue arrow), suspecting the diagnosis of LAM & it was confirmed by histopathology.

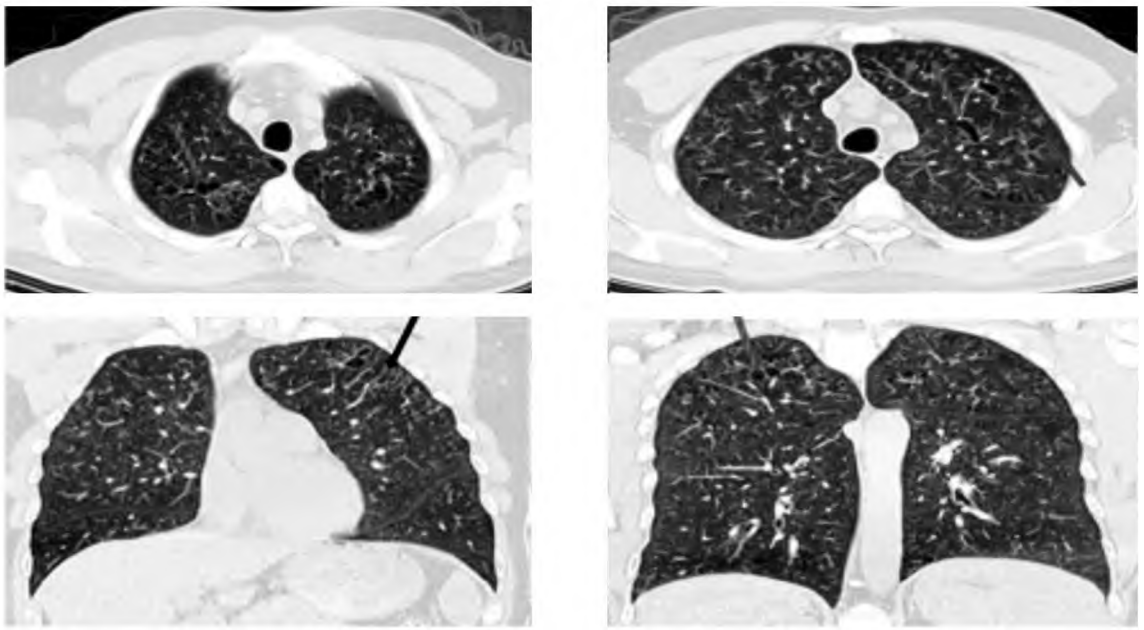

Fig. (5): Male patient 25 years old known smoker presented by cough & dyspnea. Non contrast enhanced CT axial and coronal images showing bilateral predominantly upper lobar bizarre-shaped air containing lung cysts (red arrow) with associated nodular densities(blue arrow) & mild interstitial thickening (black arrow), suspecting the diagnosis of PLCH & it was confirmed by histopathology.

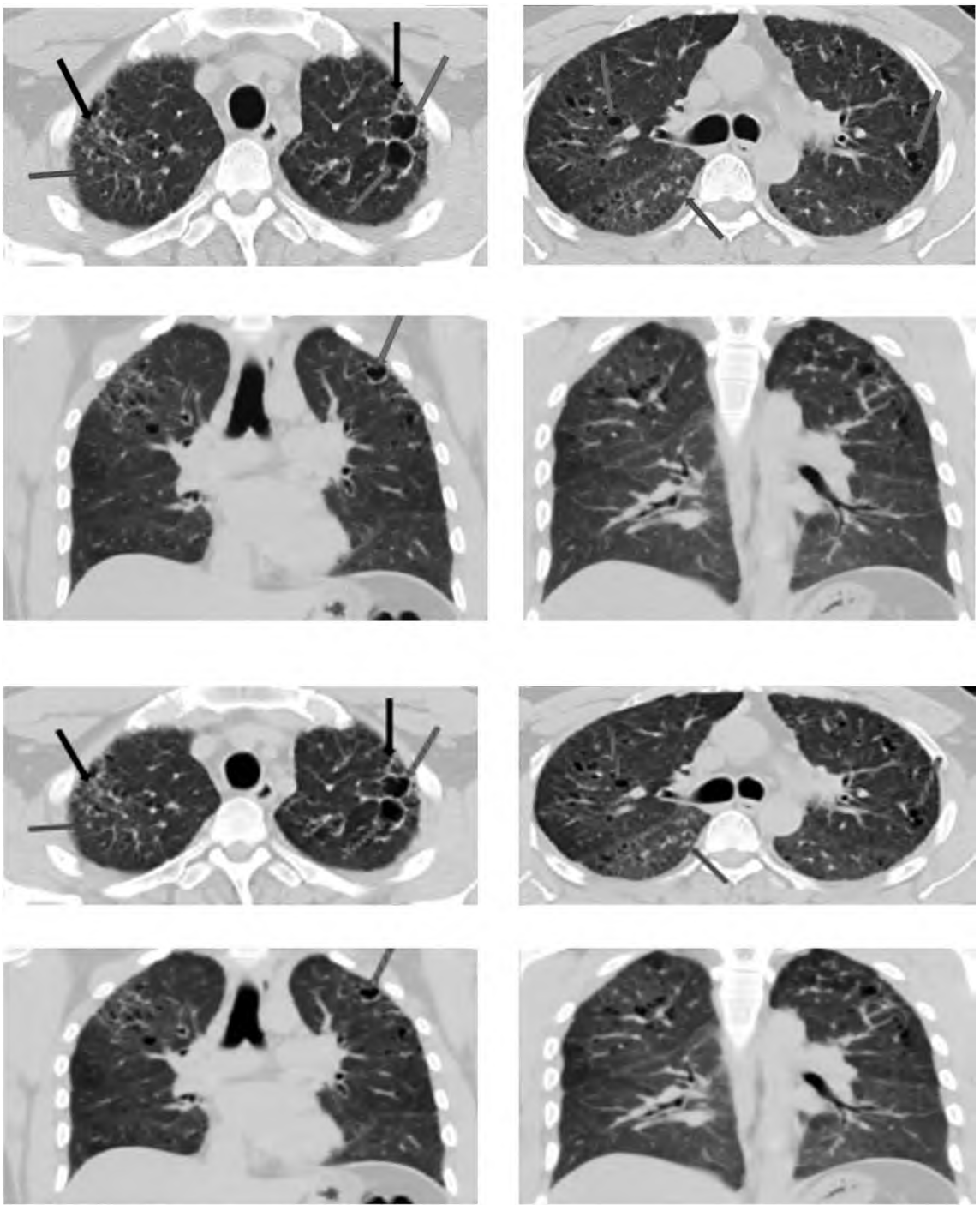

Fig. (6): Male patient 28 years old known smoker presented by dyspnea. HRCT axial and coronal images showing bilateral predominantly upper lobar bizarre-shaped air containing lung cysts (red arrow) with associated scattered small centrilobular nodules (blue arrow) & reticulations (black arrow), suspecting the diagnosis of PLCH & it was confirmed by histopathology.

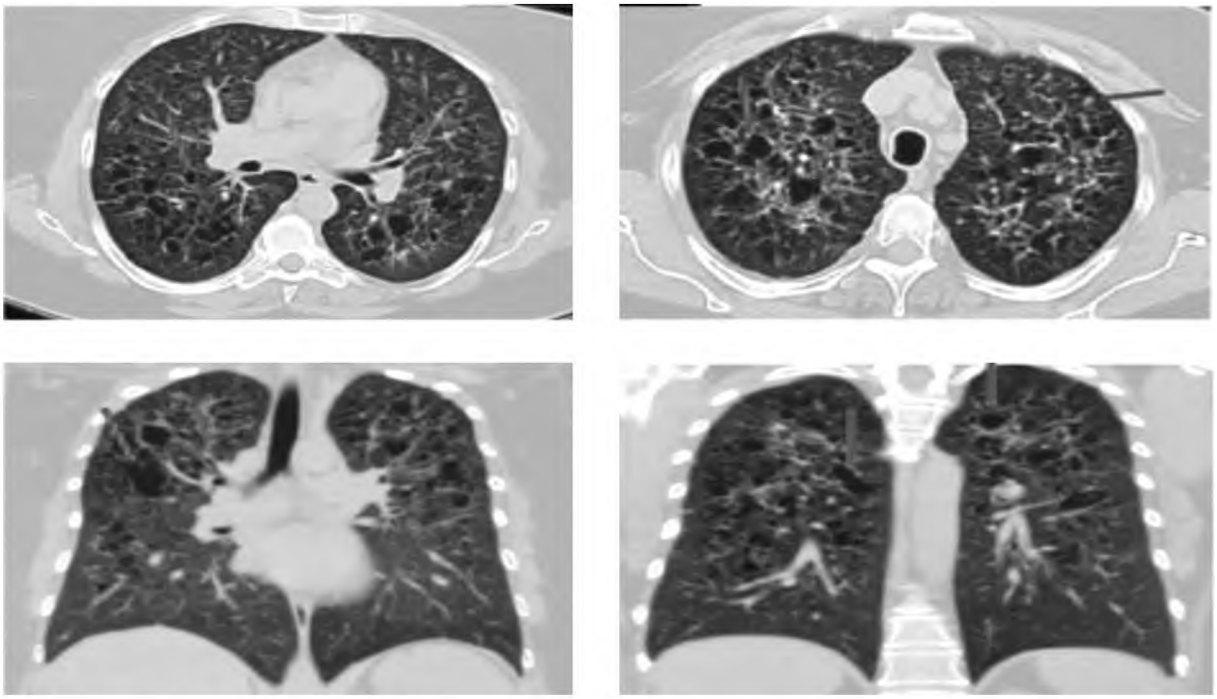

Fig. (7): Female patient 39 years old known smoker presented by dyspnea & cough. Non contrast enhanced CT axial and coronal images showing bilateral predominantly upper lobar variable sized bizarre-shaped air containing lung cysts (red arrow) with associated tiny centrilobular nodular densities (blue arrow) as well as fine reticulations, suspecting the diagnosis of PLCH & it was confirmed by histopathology.

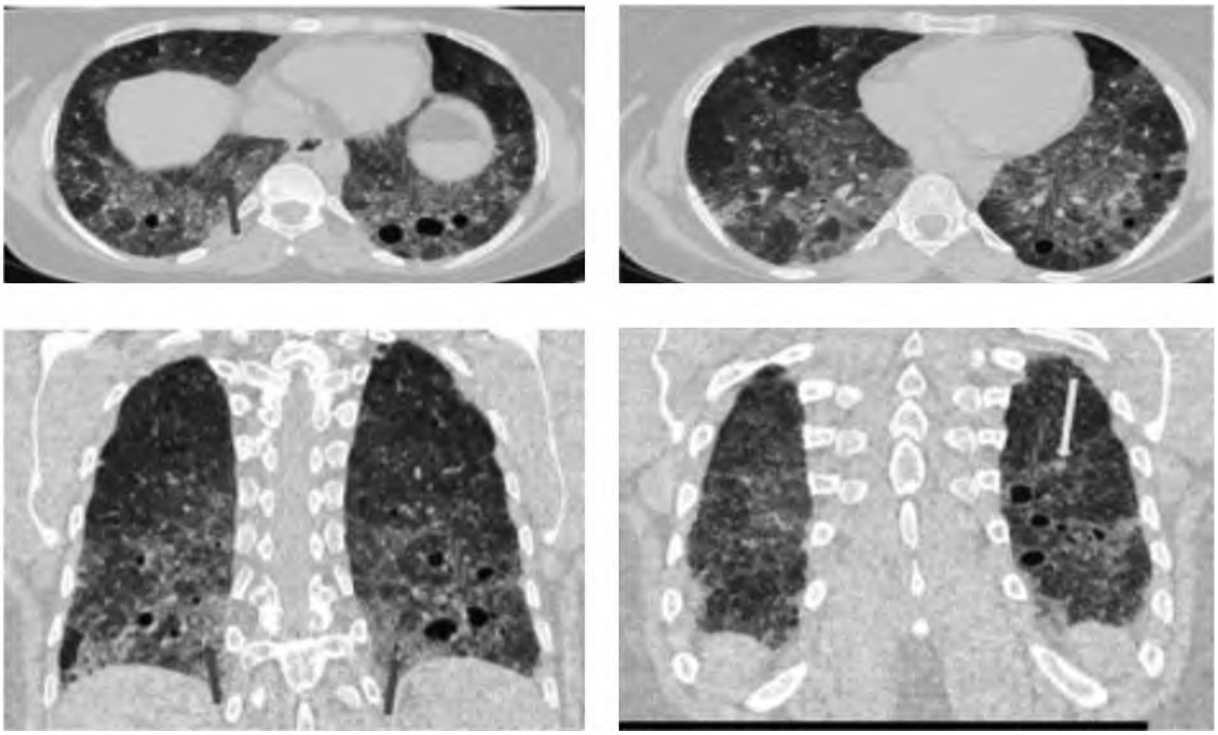

Fig. (8): Female patient 40 years old with history of rheumatoid arthritis presented by severe dyspnea and cough. HRCT axial and coronal images showing bilateral diffuse few rounded variable sized air containing lung cysts (red arrow) with associated GGOs (blue arrow), septal thickening & few scattered nodular densities (yellow arrow), suspecting the diagnosis of interstitial Pneumonia (LIP), Pulmonary function tests were done showing restrictive pattern.

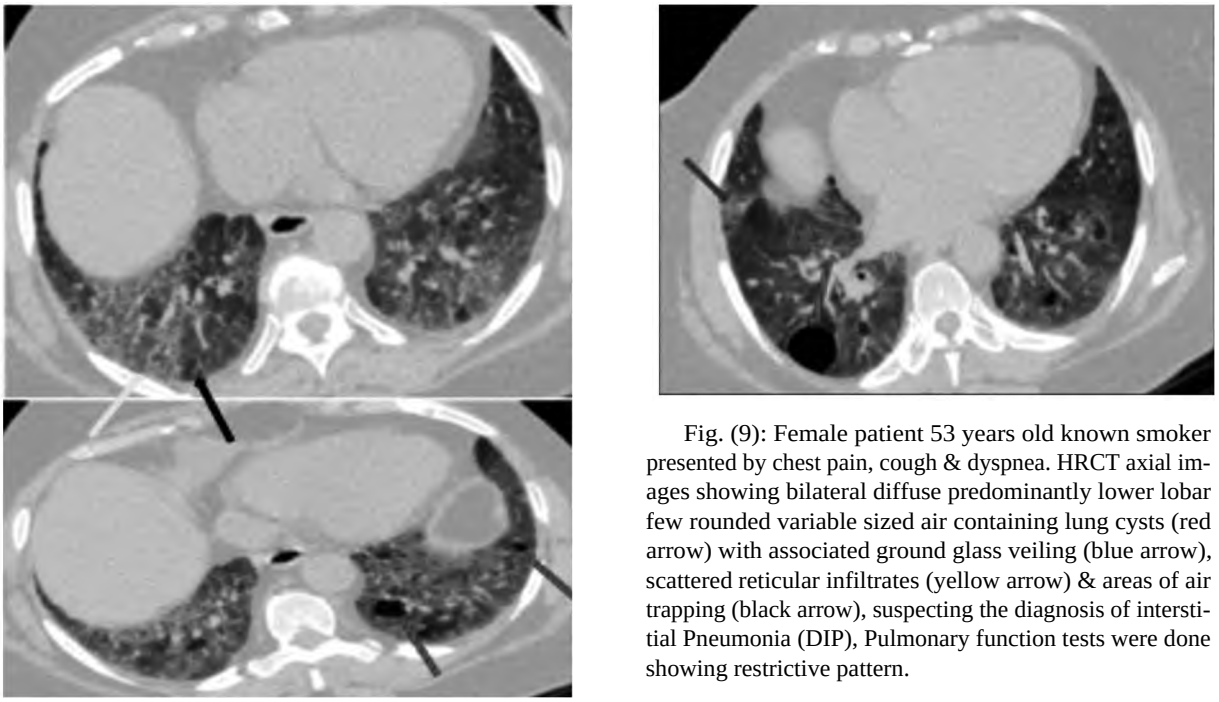

Fig. (9): Female patient 53 years old known smoker presented by chest pain, cough & dyspnea. HRCT axial images showing bilateral diffuse predominantly lower lobar few rounded variable sized air containing lung cysts (red arrow) with associated ground glass veiling (blue arrow), scattered reticular infiltrates (yellow arrow) & areas of air trapping (black arrow), suspecting the diagnosis of interstitial Pneumonia (DIP), Pulmonary function tests were done showing restrictive pattern.

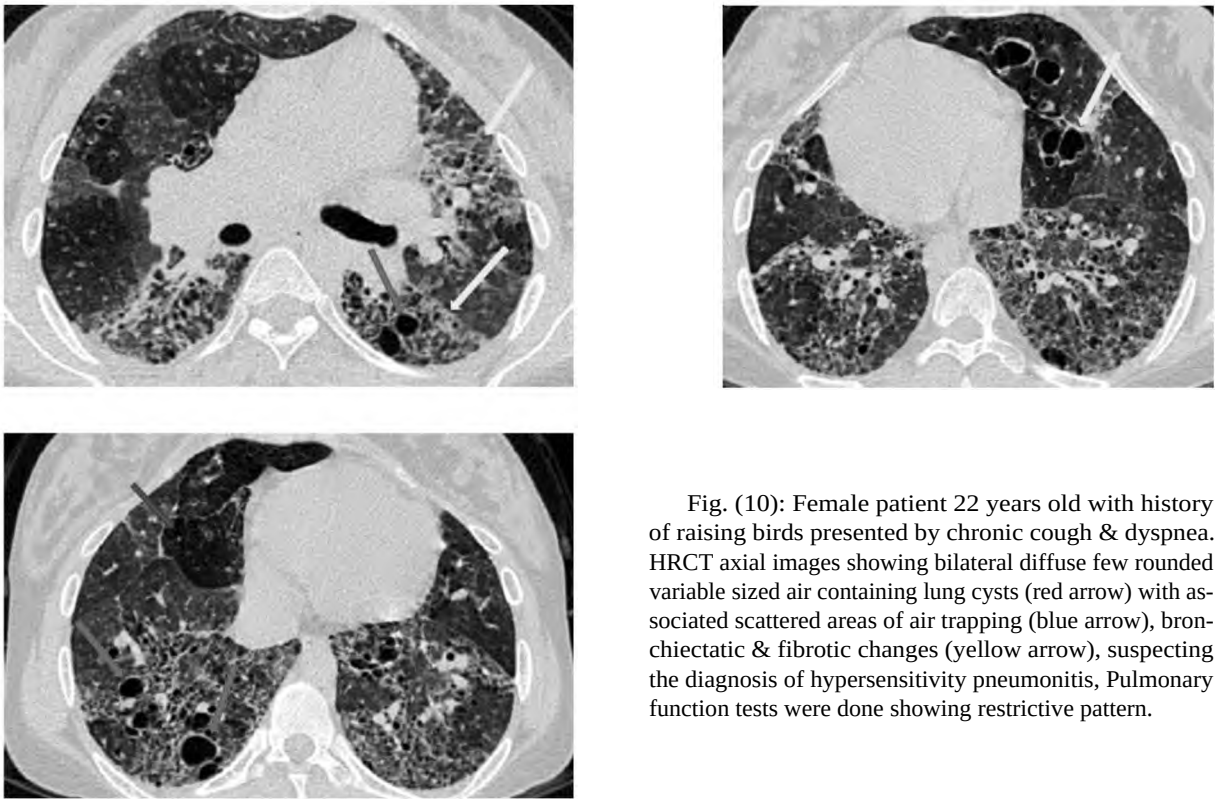

Fig. (10): Female patient 22 years old with history of raising birds presented by chronic cough & dyspnea. HRCT axial images showing bilateral diffuse few rounded variable sized air containing lung cysts (red arrow) with associated scattered areas of air trapping (blue arrow), bronchiectatic & fibrotic changes (yellow arrow), suspecting the diagnosis of hypersensitivity pneumonitis, Pulmonary function tests were done showing restrictive pattern.

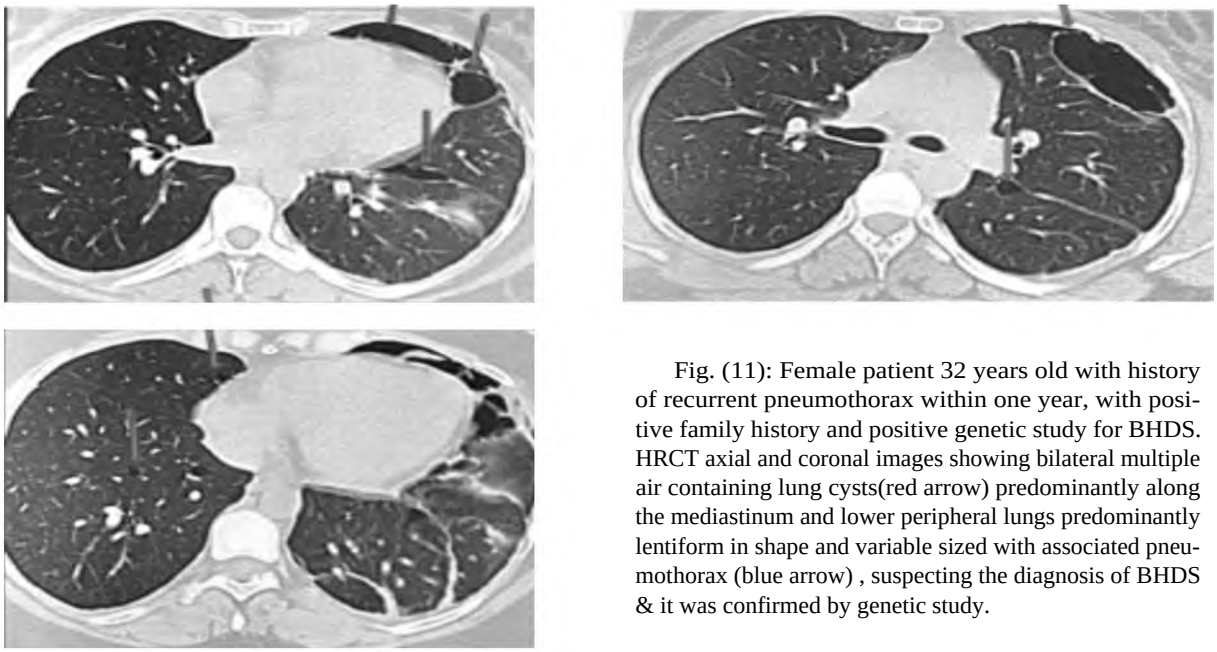

Fig. (11): Female patient 32 years old with history of recurrent pneumothorax within one year, with positive family history and positive genetic study for BHDS. HRCT axial and coronal images showing bilateral multiple air containing lung cysts(red arrow) predominantly along the mediastinum and lower peripheral lungs predominantly lentiform in shape and variable sized with associated pneumothorax (blue arrow) , suspecting the diagnosis of BHDS & it was confirmed by genetic study.

Discussion

Cystic lung diseases show a wide disease spectrum. Thus, correct diagnosis of cystic lung diseases is a challenge for radiologists.

In our study, the commonest diagnosis was LAM in 21 (35%) patients, followed by LCH in 18 (30%) patients, interstitial pneumonia in 13 (21.6%) patients, six cases with HP, two cases with genetic disease Birt-Hogg-Dubé syndrome.

A comparable study was done in 2016 by Sabri et al., the study results showed that diffuse infiltrative lung disease (ILD) represented (50%) of multiple cystic lung diseases including LAM, PLCH, DIP, LIP & UIP while cystic pulmonary metastases represented (11%) of multiple cystic lung diseases **[4]**.

In our study, in patients diagnosed as LAM, patients were significantly younger compared to other diagnoses and LAM was exclusively in females.

Regarding the distribution of lung cysts, it was significantly bilateral and affected all lung lobes, while nodules were never reported in LAM patients. The intervening parenchyma was found to be normal in 12 (57%) patients.

In the study conducted by Sabri et al., the predominant high-resolution computed tomographic (HRCT) finding in patients with LAM were multiple thin-walled regular cysts distributed diffusely throughout the lungs with relatively normal lung parenchyma among the cysts **[4]**.

Another studies showed that lung parenchyma interposed between the cysts of LAM is typically normal; although thickened interlobular septa have been described at high-resolution CT in rare cases **[5]** revealed that Patchy areas of ground-glass attenuation were reported in some cases with LAM and are thought to represent foci of pulmonary hemorrhage. And this is similar to our study as (42.8%) of LAM cases had associated ground-glass opacities.

In our study, regarding Pulmonary Langerhans Cell Histiocytosis, most patients were young aged. It significantly affects smokers and passive smokers. Regarding cysts distribution, Cysts were all bizarre and variable in size. Cysts were predominantly affecting upper lobe, sparing lung bases & costophrenic recesses. Centrilobular nodules in the background were common association with this disease. Sabri et al., in 2016 revealed that HRCT findings in PLCH were irregular (bizarre) cysts predominantly upper lobar with nodule and abnormal intervening lung Parenchyma and this is similar to our results **[4]**.

Suri et al., revealed that the distribution of lung cysts in PLCH has relative sparing of the lower lung fields and costo-phrenic angle and this is similar to our results **[6]**.

In our study, patients with interstitial pneumonia (DIP & LIP) were mainly associated with small sized cysts, & honey combing and GGOs. Interstitial septal thickening was reported all casesof ILD patients. Cysts were predominantly bilateral (85%) and affecting lower lobe (75%).

Another study done by Koyama et al., showed that the HRCT finding in twenty-two LIP patients were ground glass attenuation and poorly defined centrilobular nodules, and cystic changes were noted in 68% of patients. Cysts were bilateral in ten patients and unilateral in five patients and had a random distribution involving less than 10% of the lung parenchyma **[7]** and this agrees with our results.

In 2015, Gupta et al., reported that ground glass attenuation was the most common radiographic abnormality in DIP and cystic changes have been reported in 32–75% of patients. The cysts in DIP were typically lower lung zone predominant involve less than 10% of the parenchyma and often appeared within areas of ground glass attenuation in smoker patients and this is similar to our study **[8].**

In our study, two siblings (1st degree relatives) were diagnosed as Birt-Hogg-Dubé syndrome, Cysts had multiseptated appearance with variable shape predominantly lentiform and they were abutting or including the proximal portions of the lower pulmonary arteries or veins. Cysts were distributed alonglower peripheral lungs & along the mediastinum with associated pneumothorax.

Earlier studies showed that the cysts of Birt-Hogg-Dubé syndrome usually vary in size and shape, multiseptated and are lower lung predominant in distribution and this is similar to our results **[9].**

Zbar et al., reported that the frequency of pneumothorax occurrence in Birt-Hogg-Dubé increases with the patient's age and this is in concordance with our study where our patients had pneumothorax **[10].**

In our study, six cases with hypersensitivity pneumonitis were mainly associated with few cysts (100%) and all cases showed mosaic attenuation with associated fibrotic changes. Cysts were predominantly affecting lower lobe.

Franquet et al., reported that cysts can be found in a minority of patients with hypersensitivity pneumonitis, they are usually few in number, range from 3mm to 25mm in diameter, and have a random distribution **[11].**

The relatively limited number of cases is considered a limitation in our study, so we recommend further research on a larger population to confirm our results.

Conclusions:

Multislice computed tomography has an established role in assessment of pulmonary cystic lesions. Recommended step wise approach including exclusion of cyst mimickers first, then considering the radiographic characters, distribution of the cysts and clinical background, all together can be used for differentiation and detection of causes of pulmonary cystic lesions.

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الآفات الكيسية الرئوية فى التصوير المقطعى المحوسب متعدد الشرائح : نهج تشخيص تدريجى يعتمد على النتائج الاشعاعية والسريرية

يُعرّف الكيس بأنه منطقة دائرية مقيدة محاطة بجدار طلائى أو ليفى بسمك متغير. فى التصوير المقطعى المحوسب للصدر، يُنظر إلى الكيس على أنه منطقة ذات معامل توهين منخفض فى حمة الرئة، ولها واجهة محددة جيدًا مع الرئة الطبيعية المجاورة وعادة ما تحتوى على الهواء، على الرغم من أنها قد تحتوى أحيانًا على محتوى سائل أو صلب.

شملت هذه الدراسة ٤٠ مريضاً ١٢ ذكراً و ٢٨ أنثى تتراوح أعمارهم بين (٨٠-٢٠سنة) المتوسط حوالى ٤٠ سنة. هدفت الدراسة إلى تقييم دور التصوير المقطعى متعدد الشرائح وعالى الدقة فى التشخيص والتمايز والكشف عن الأسباب المحتملة للآفات الكيسية الرئوية.

تم إخضاع جميع المرضى لأخذ التاريخ التفصيلى، والفحص السريري الشامل، وإجراء الاختبارات المعملية المختلفة، وتم إجراء التقييم المرضى للنسيج على ٢٦ مريضًا ، وتم إجراء اختبارات وظائف الرئة (PFT) فى ١٢حالة وفقًا للنتائج السريرية والإشعاعية. تم إجراء دراسة وراثية لمتلازمة بيرت هوغ دوبى فى حالتين (شقيقان).

كان المرضى الذين تم تشخيصهم على أنهم LAM أصغر سناً بشكل ملحوظ مقارنة بالتشخيصات الأخرى وكانوا من الإناث فقط. كان ثنائيًا بشكل كبير وأثر على جميع فصوص الرئة، بينما لم يتم الإبلاغ عن العقيدات مطلقًا فى مرضى LAM. وجد أن الحمة المتداخلة طبيعية فى (٨٥٧٪) مرضى.

فيما يتعلق بكثرة المنسجات لخلايا لانجرهانز الرئوية ، كان معظم المرضى من الشباب. يؤثر بشكل كبير على المدخنين والمدخنين السلبيين ، تم الإبلاغ عن فقدان الوزن فى العروض السريرية. فيما يتعلق بتوزيع الأكياس، كانت جميع الأكياس غريبة ومن صغيرة إلى متغيرة الحجم. أثرت الأكياس فى الغالب على الفص العلوى، وقواعد الرئة المستثارة، وفترات الاستراحة الضلعية.

ارتبطت أربع حالات مصابة بالتهاب رئوى فرط الحساسية بشكل أساسى بعدد قليل من الأكياس (١٠٠٪) والتغيرات الليفية المرتبطة بها. كانت الخراجات تؤثر فى الغالب على الفص السفلى.