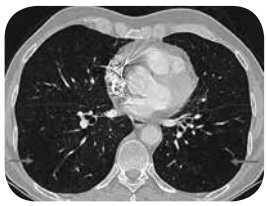

UPDATE IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE: CLINICAL AND RADIOLOGIC FINDINGS IN COMPUTED TOMOGRAPHY

Actualización de la enfermedad pulmonar obstructiva crónica: claves clínicas y hallazgos radiológicos en tomografía computarizada

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Palabras clave (DeCS)
Enfermedades pulmonares
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Summary
Chronic obstructive pulmonary disease (COPD) is a preventable and treatable disease characterized by the presence of persistent respiratory symptoms secondary to chronic exposure to particles. The main factors are airway disease and destruction of the lung parenchyma. Parenchymal abnormalities do not always occur simultaneously and progress at different speeds in each individual. Diagnostic imaging can be considered as part of the diagnosis and assessment in patients with COPD, taking into account that chest radiography is not useful for the diagnosis of COPD but is useful for the exclusion of differential diagnosis, while computed tomography is reserved for those patients in whom pulmonary parenchyma should be assessed for suspected bronchiectasis or those who are more likely to develop lung cancer due to expositional risk factors. Emphysema, chronic bronchitis and asthma are key to perform a radiological approach for diagnosis.

Resumen
La enfermedad pulmonar obstructiva crónica (EPOC) es una enfermedad prevenible y tratable, que se caracteriza por síntomas respiratorios persistentes secundarios a la exposición crónica a partículas. Los pilares fundamentales son la enfermedad de la vía aérea y la destrucción del parénquima pulmonar. Los cambios no siempre ocurren simultáneamente y progresan a diferentes velocidades en cada individuo. Las imágenes diagnósticas pueden ser consideradas como parte del diagnóstico y la valoración de los pacientes con EPOC, teniendo en cuenta que la radiografía de tórax no es útil para su diagnóstico, pero facilita la exclusión de los diagnósticos diferenciales, mientras que la tomografía computarizada se reserva para aquellos pacientes en quienes se debe valorar el parénquima pulmonar por sospecha de bronquiectasias o quienes por sus riesgos exposicionales tienen mayor probabilidad de desarrollar cáncer de pulmón. El enfisema, la bronquitis crónica y el asma son la clave para realizar un abordaje radiológico para el diagnóstico.

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Introduction

Chronic obstructive pulmonary disease (COPD) is a preventable and treatable disease characterised by persistent respiratory symptoms secondary to chronic exposure to harmful particles or gases (1). Its mainstays are airway disease and destruction of the lung parenchyma, whose contribution to the development of the disease varies between individuals (1). These changes do not always occur simultaneously and progress at different rates in each person (1). The term emphysema describes the destruction of the surface of the alveolus, which is a pathological (anatomical) alteration and therefore should not be used as a clinical term (1). Chronic bronchitis corresponds to the symptom of cough, productive or non-productive, for a period of three months in two consecutive years; however, many COPD patients do not meet this requirement, therefore, it is not part of the definition of the disease, although it is a clinical finding that predominates in patients with greater occupational exposures or greater exposure to cigarettes (1, 2).

The most common risk factor among COPD patients is smoking, although it is not the only one. Different types of tobacco such as pipes or marijuana, exposure to biomass fuels and occupational exposure are also risk factors for the development of COPD (1). Long-term exposure to harmful gases or particles together with genetic factors, bronchial hyperreactivity and impaired pulmonary development during childhood may contribute to the development of COPD in non-smoking patients (1, 3, 4).

Other factors that may influence the development of COPD include genetics, α-1 antitrypsin deficiency, age and sex: older age and female sex increase risk, delayed lung development and growth (low birth weight, respiratory infections), socioeconomic status inversely related, probably secondary to increased risk of exposure to pollutants and other risk factors, respiratory infections: severe childhood infections leading to impaired lung function and increased symptoms in adulthood, asthma and bronchial hyperreactivity and chronic bronchitis (1, 5-8).

It is estimated that there is a prevalence of 11.7 % (95% CI 8.4-15 %) with approximately three million deaths annually caused by this disease and its complications (1, 10). Patients with COPD often have concomitant chronic (e.g. cardiovascular) diseases that increase the morbidity of these patients (1).

1. Clinical Keys to COPD Diagnosis

The diagnosis of COPD should be considered in patients with dyspnea, chronic cough and exposure to any of the risk factors mentioned for the disease (1). In this context, it is necessary to confirm the diagnosis by spirometry, the only reproducible and objective method for airflow measurement (1,9). The post-bronchodilator FEV1/FVC ratio < 0,70 confirms the persistent limitation and thus confirms the diagnosis (1). Despite its advantages, it is a technique that should not be used as the only diagnostic method given its low specificity (1,11).

In COPD patients dyspnea is progressive, worsens with exercise, and becomes persistent over time (1).

COPD, based on spirometry, is classified as: GOLD 1: mild, FEV1 > 80 % of the theoretical value; GOLD 2: moderate, 50 % < FEV1 < 80 % of the theoretical value; GOLD 3: severe, 30 % < FEV1 < 50 % of the theoretical value; and GOLD 4: very severe, FEV1 < 30 % of the theoretical value (1) (table 1).

Table 1. Classification of COPD by Spirometry

Grade	Definition
GOLD 1: slight	FEV1 > 80 % of theoretical value
GOLD 2: moderate	50 % < FEV1 < 80 % of theoretical value
GOLD 3: severe	30 % < FEV1 < 50 % of theoretical value
GOLD 4: very serious	FEV1 < 30 % of theoretical value

Source: Goldcopd (1).

Chronic respiratory symptoms usually begin before airflow limitation and are associated with the development of acute respiratory episodes (12). Patients may be respiratory symptoms without abnormalities in spirometry, and patients without alterations in airflow may demonstrate emphysema, thickening of airway walls and air entrapment (12, 13).

2. Radiological findings related to COPD

Diagnostic imaging can be considered as part of the diagnosis and assessment of COPD patients (1).

It should be noted that chest radiography is not useful for the diagnosis of COPD, but is useful for the exclusion of both pulmonary and cardiovascular differential diagnoses (1, 14).

High-resolution computed tomography (HR-CT) is reserved for those patients in whom the pulmonary parenchyma should be assessed due to suspicion of bronchiectasis or who, due to their exposure risks, are more likely to develop lung cancer (1). It may also be useful for excluding differential diagnoses in preoperative assessment for lung volume reduction or lung transplantation (1). The most important limitation of HR-CT is exposure to ionizing radiation, especially in those patients requiring control studies (15).

2.1 Radiological findings in COPD

The main components of COPD are emphysema, chronic bronchitis and small airway disease.

2.1.1 Emphysema

The destruction of the pulmonary parenchyma secondary to cigarette exposure is manifested as emphysema (16). It is defined in histopathology as the permanent and irreversible dilation of the distal airway to the terminal bronchiolus associated with destruction of the walls without clear signs of fibrosis, resulting in abnormally large airspaces within the pulmonary parenchyma (17). It is classified as centrilobular, panlobular, paraseptal or irregular, depending on the anatomical location (17). In order for emphysema to be identified in the HR-CT, it is necessary to destroy multiple alveolar septa that make this finding evident and that can be quantified (17).

In chest radiography, COPD findings (figure 1) may include signs of air entrapment with diaphragmatic flattening and increase of the retroesternal space, attenuation of the pulmonary vasculature with loss of the vascular branching pattern, thinning of the cardiac silhouette and

thickening of bronchial walls (16, 17). These findings are sensitive, but not very specific, for the diagnosis of COPD (16).

HR-CT makes it possible to assess the extent and spatial distribution of emphysema in the pulmonary parenchyma (9,17). The sensitivity and specificity of the HR-CT for the detection of centrilobulillary emphysema is 88 and 90 %, respectively (17, 18). A window width (WW) of 1500 UH and a window level (WL) of -700 to -550 UH are ideal for the assessment of emphysema (17, 19). Emphysema is identified as areas of low pulmonary parenchymal attenuation that contrast with areas of normal attenuation (20). Areas of mild to moderate centrilobullar emphysema are identified as multiple rounded zones of low attenuation, predominating in the upper lobes (Figure 2) (20). It is characteristic that these areas do not have walls as they are surrounded by the pulmonary parenchyma (20). The degree of emphysema observed in the TACAR has a good correlation with the clinical classification of COPD, with predominance in the late stages of the disease (21).

2.1.2 Chronic bronchitis and small airway disease

Normally, the internal diameter of the small airway wall is less than 2 mm (20, 22, 23). In COPD, the site of obstruction is usually in the small airway with a diameter of less than 2 mm (16). In COPD patients there is a decrease in the number of small airways (diameters between 2 and 2.5 mm) at all stages of GOLD (20.24). Exposure to cigarettes or toxic particles leads to an immune response that develops rapidly in the airway generating the clinical symptoms of cough and expectoration with abnormal mucus production, mucociliary alterations, infiltration of the airway by inflammatory cells and disruption of the epithelium (20, 25). This finding precedes the emphysematous changes of the pulmonary parenchyma (20, 24). In addition, patients with COPD and symptoms of chronic bronchitis have increased airway thickness (20); however, the clinical definition of chronic bronchitis does not require abnormal findings in lung function tests or imaging abnormalities (17).

Chest x-ray is usually normal in patients with chronic bronchitis (17). Thickening of bronchial walls may occasionally be found in this imaging method, although it is not a specific finding (Figure 3).

Although HR-CT is best for demonstrating bronchial wall thickening, it is not a specific finding of this entity (Figure 4). In addition, centrilobulillary opacities can be found in "frosted glass" that reflect bronchial inflammation (26), although the dominant finding is centrilobulillary emphysema that coexists with chronic bronchitis (17, 26). Multiple measures have been proposed to determine bronchial thickness (16, 27); however, there is no consensus on these measures. Areas of air entrapment (less attenuation of the pulmonary parenchyma), especially in images during expiration, may be found in COPD patients as findings of small obstructive airway disease (26, 28).

2.2 Radiological findings associated with COPD

2.2.1 Pulmonary arterial hypertension

Pulmonary vascular disease is an independent predictor of mortality and morbidity in COPD (16). This remodelling of the pulmonary vasculature is even found in smokers with normal lung function (16, 29, 30). The pathophysiology is based on inflammation, hypoxic vasoconstriction, obliteration of the distal pulmonary vasculature or diseases of the left ventricle (16, 26). These changes are represented as pulmonary arterial hypertension (PAH) and even atherosclerosis. Patients with COPD and PAH are in group 3 of the Nice classification of 2013.

The diagnosis of pulmonary hypertension begins with the measurement of the pulmonary artery on computed tomography (31). The transverse diameter of the pulmonary artery greater than 29 mm or the diameter of the pulmonary artery greater than the transverse diameter of the aorta rising to the same level is indicative of pulmonary arterial hypertension (31, 32) (figure 5). Up to 66% of COPD patients develop PAH, usually mild (31, 33). Pulmonary hypertension is associated with severe episodes of exacerbation of COPD (34).

2.2.2 Trachea "in sabre"

The trachea "in sabre" is an acquired morphological anomaly of the trachea consisting of an increase in the anteroposterior diameter and a shortening of the transverse diameter (Figure 6) (35). It is an entity frequently found in COPD patients and usually predominates in the male gender (35). Airway obstruction in COPD patients is not related to altered tracheal morphology (35). The aetiology is not clear, but it should be noted that in post mortem studies there are no signs of tracheomalacia (35). Alterations in intrathoracic forces or remodelling of the tracheal wall may explain the acquired morphology (35).

Likewise, findings related to trachea-bronchomalacia have been described as evidenced by excessive tracheal collapse during expiration that is not necessarily associated with disease severity or respiratory function tests (20)

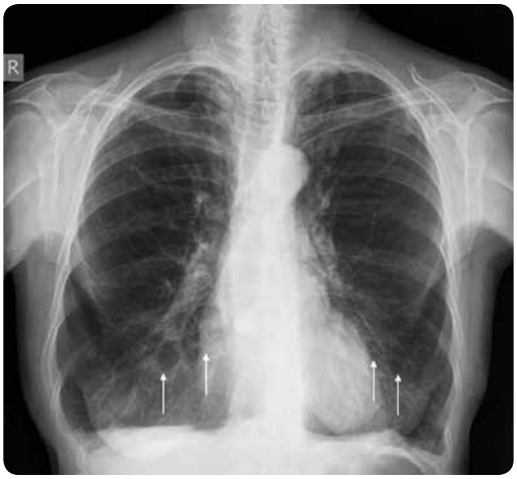

Figure 1. Posteroanterior chest x-ray. 78 year old patient with COPD: increased lung volumes and some radiolucent areas more evident in the lower lobes (white arrows). There are some interstitial opacities especially in the lower lobes with apparent thickening of the central bronchial walls. Obliteration of the costophrenic angles.

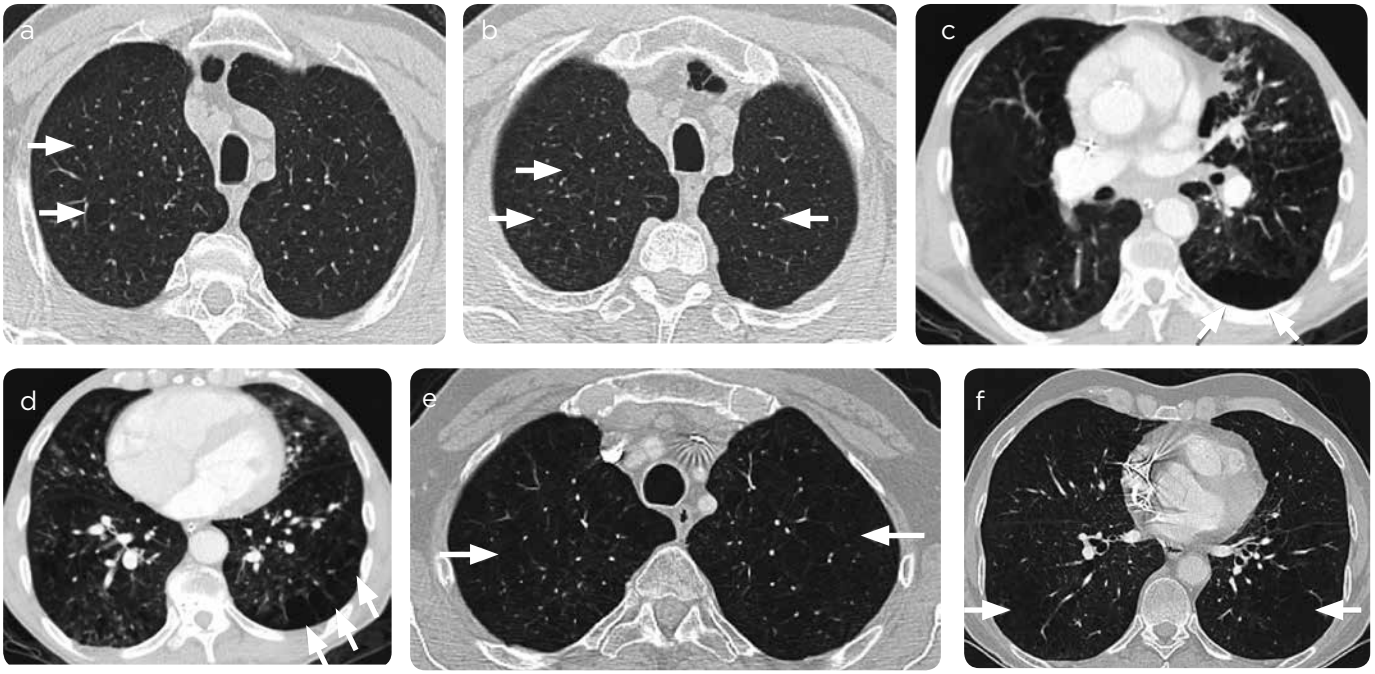

Figure 2. Chest tomography, lung window. a and b) Some areas of decreased attenuation of the centrilobulillar distributed pulmonary parenchyma that predominate in the upper lobes (arrows) corresponding to centrilobulillar emphysema in a 61-year-old patient with COPD. c and d) Lower lobes: some areas of decreased attenuation of the subpleurally located pulmonary parenchyma, configuring paraseptal emphysema (arrows) in the lower left lobe. e) Upper lobes and f) lower lobes: areas of decreased attenuation of the pulmonary parenchyma involving the centrilobullar and paraseptal regions in both the upper and lower lobes (arrows), corresponding to panlobulillar emphysema, in a 61-year-old patient with COPD.

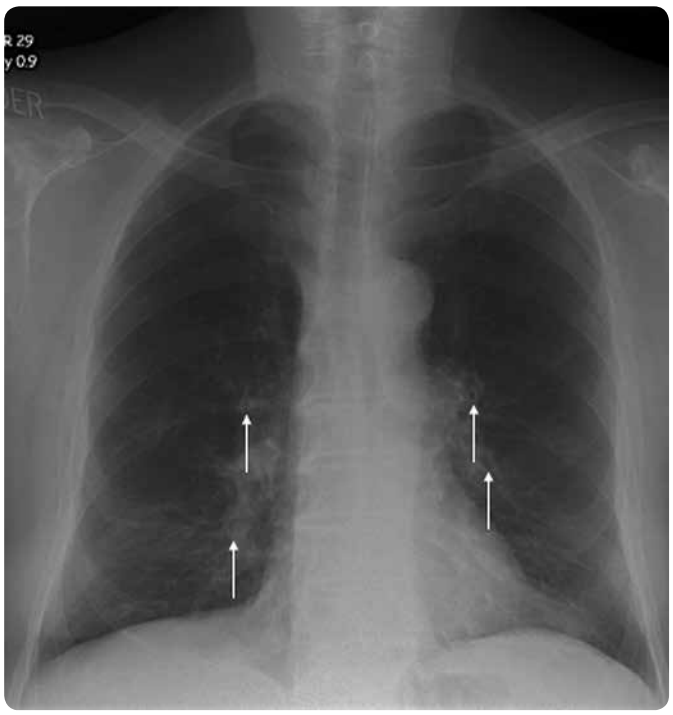

Figure 3. Posteroanterior chest X-ray. 71-year-old COPD patient: increased lung volumes and some radiolucent areas more evident in the lower lobes. There are some interstitial opacities especially in the lower lobes with apparent thickening of the central bronchial walls (arrows)

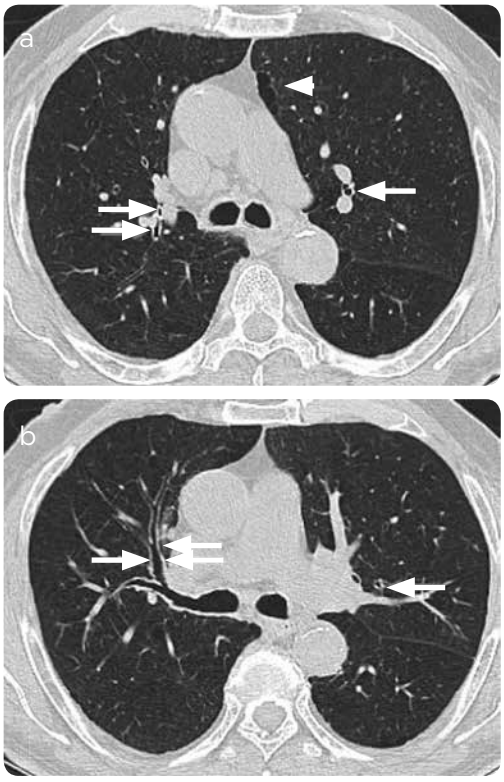

Figure 4. Chest CT scan, window of lung a) in carina and b) in source bronchi: some areas of thickening of bronchial walls related to chronic bronchitis (arrows) in patient with a history of heavy smoking and COPD. Discrete areas of paraseptal emphysema in upper left lobe (arrowhead).

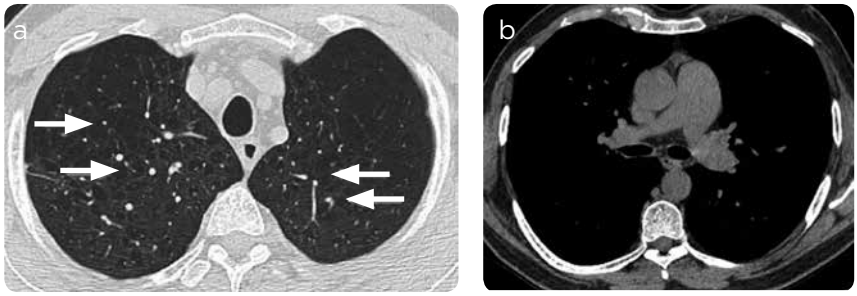

Figure 5. Chest tomography, a) mediastinum window at the height of the pulmonary artery and b) lung window in upper lobes. a) There are areas of decreased attenuation of the pulmonary parenchyma that predominate in the upper lobes (arrows) corresponding to centrilobullar emphysema. b) Dilatation of the trunk of the pulmonary artery due to pulmonary arterial hypertension secondary to pulmonary disease (Group 3).

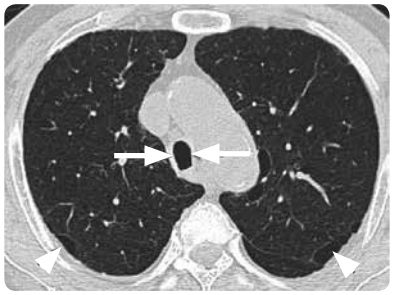

Figure 6. Chest tomography, lung window in upper lobes. Deformity of the trachea with increased anteroposterior diameter of the chest and decreased transverse diameter by "sabre" trachea (arrows) in COPD patient. Some areas of paraseptal emphysema can be seen in upper lobes (arrowheads).

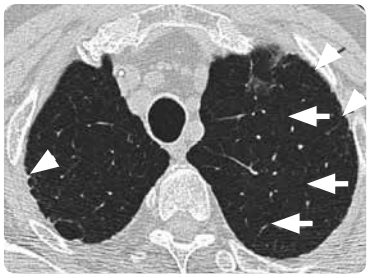

Figure 8. Chest tomography, lung window in upper lobes. Irregular thickening of interlobular septa in the subpleural region of the upper lobes (arrow heads) associated with some areas of decreased attenuation of the centrilobular disposition pulmonary parenchyma (arrows).

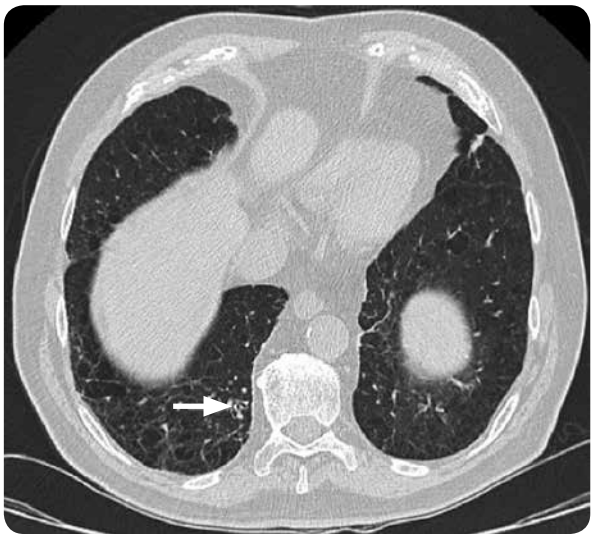

Figure 7. Chest tomography, lung window: some areas of decreased attenuation of the pulmonary parenchyma that compromise the centrilobulillar region associated with some discrete bronchioloectasis in the right lower lobe (arrow).

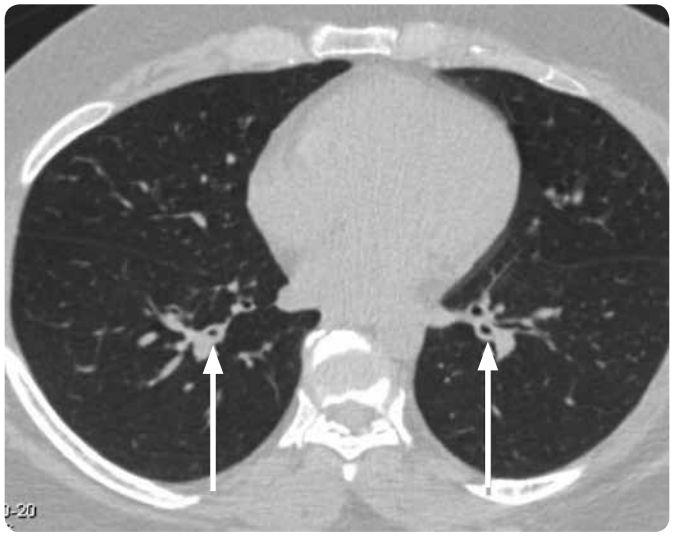

Figure 9. Chest tomography, lung window in lower lobes. Concentric thickening of bronchial walls in the bronchi for the basal segments of the lower lobes (arrows) in patients with a history of asthma.

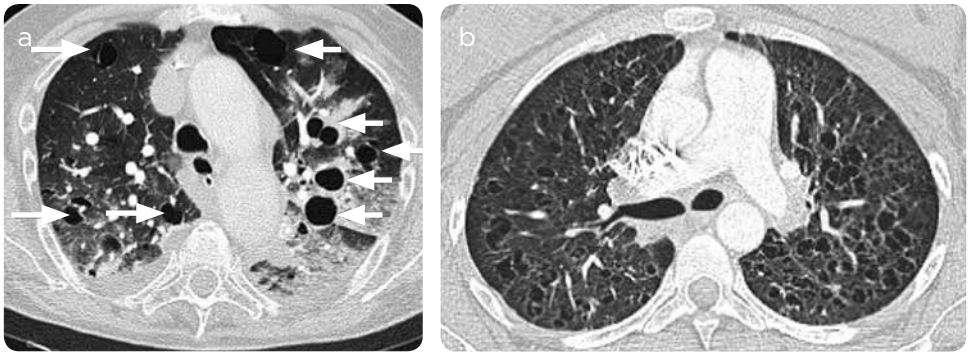

Figure 10. Chest CT scan, lung window. a) 78-year-old female patient with Sjögren syndrome and suspected lymphocytic pneumonia. Some thin-walled cystic areas in the upper lobes (arrows) are seen in relation to pulmonary cystic disease. There are areas of consolidation of the pulmonary parenchyma and areas of "frosted glass" by superinfection. b). Female patient of 45 years: cystic areas of thin walls and some thickened in upper lobes in relation to lymphangioleiomyomatosis.

2.2.3 Bronchiectasis

It is the irreversible dilation of the bronchi (27, 36). It is usually found between 27 and 58 % (36-39), findings that vary depending on the population (36). In patients with COPD they are usually cylindrical and are associated with increased airway obstruction and an increased number of exacerbation episodes (26, 39) (Figure 7).

2.2.4 Combination of pulmonary fibrosis and emphysema

A link has been established between cigarette exposure and pulmonary fibrosis (40). An odds ratio of 1.6 is considered for smoking and the development of pulmonary fibrosis (41). This entity is characterized by emphysema in the upper lobes and fibrosis of the lower lobes, which predominate in the 6th to 7th decades of life (40, 42). Generally, lung volumes are normal, resulting in virtually normal spirometry (42), and a high prevalence of PAH, higher than in patients with these two conditions independently. It is associated with higher morbidity and mortality (40, 43).

The findings in HR-CT are similar to those of idiopathic pulmonary fibrosis, the usual interstitial pneumonia (UIP) pattern predominates, with areas of reticulation in the lower lobes, predominantly peripheral distribution, bronchiectasis and/or "honeycomb", but also with areas of opacity in "frosted glass" simulating a pattern of non-specific interstitial pneumonia (NSIP) (43, 44). In these patients emphysema is predominantly paraseptal (43).

In some cases, the areas of emphysema and fibrosis may coexist in the same location which, as a consequence, has areas of low attenuation corresponding to emphysema with thick walls, which represent thickening of the interlobular septa (Figure 8) (40).

2.3 Differential diagnoses of radiological findings in COPD

2.3.1 Asthma

Asthma is characterised by reversible airway obstruction secondary to bronchoconstriction (36). It is one of the main differential diagnoses and a possible risk factor for the development of COPD (1). Compared to COPD, asthma is characterised by earlier onset symptomatology (usually in childhood), varying symptoms during the day, worsening during lower temperature hours, and usually a family history of allergies; however, asthma may develop in adults and older adults (1).

In patients with asthma, radiologic abnormalities can be divided into parenchymal and bronchial. HR-CT parenchymata include hyperinflation, rarely emphysema, or cysts (45). Up to 19% of patients with asthma develop changes from emphysema; however, in this study the majority of patients had had cigarette exposure (45, 46). In non-smoking asthmatic patients, emphysema changes are related to pericicatricial peribronchial fibrosis (45). Cysts found in asthma patients are usually secondary to distal hyperinflation secondary to chronic inflammatory bronchiolitis (45) (Figure 9).

2.3.2 Cystic lung diseases

Cystic lung disease is a group of entities characterized by the replacement of the lung parenchyma by cysts containing air (47). Discrete cysts may be found in patients who are exposed to smoking or age changes (47,48); however, multiple cysts are indicative of an underlying disease (47). Lymphangioleiomyomatosis (LM) and Langerhans cell histiocytosis (LCH) are the two main examples. LM predominates in women of reproductive age, characterized by tests of lung function showing an obstructive pattern with increased lung volumes (47). The cysts are thin-walled, on average not exceeding 5 mm, although sometimes reaching 25 to 30 mm, respecting the pulmonary apexes (Figure 10) (47, 49, 50). LCH predominates in young patients with a history of cigarette exposure (95 %) (47). LCH cysts have lobed and irregular contours, described as "star" (47, 51).

3. Conclusions

COPD is a clinical diagnosis with morphological abnormalities that can be seen on CT scan. Emphysema, chronic bronchitis and small airway disease are the keys to radiological diagnosis. Computed tomography is the mainstay for the imaging assessment of the disease's own findings and possible complications in COPD patients and, in some cases, allows other differential diagnoses to be excluded. The radiologist should be clear on these points.

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