Imaging of the Small Airway Diseases

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소기도 질환의 영상소견

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"소기도"라 일컬어지는 해부학적 부위는 말단부 막성 세기관지와 호흡성 세기관지로 구성된 직경 3 mm 이하의 기도부위이다. 방사선학적으로는 고해상 전산화단층촬영(CT)에서 흉막직하의 직경 약 1.0 cm으로 이루어진 2차 소엽내의 중심부에 위치하게 된다. 그러므로 이 부위의 질환때에는 중심소엽성 세기관지내의 가득찬 물질로 인해 나타나는 중심소엽성 결절들과 선상음영들이 보인다. 이외의 소견으로는 중심소엽성 폐기종, 모자이크 모양의 폐음영, 분절하 무기폐등이 있고, 호기시 CT 촬영에서 나타나는 공기포획이 있다. 최근에는 다검출기형식의 CT (multidetector CT)의 발전으로 인하여 이차원 재구성 (2 dimension reformat) 관상면, 시상면 CT 스캔을 매우 명확하고 빨리 얻을 수 있고, 기관지에 대한 삼차원 볼륨 영상 (3 dimentional volume rendering image) 등을 얻어서 가시적인 효과를 높이고 진단의 정확성에 보다 더 접근하게 되었다.

소기도를 침범하는 질환은 일차적인 것과 이차적인 것이 있는데, 병리조직학적으로는 원인별로 흡연으로 인한 소기도 질환, 세포성 세기관지염, 수축성 세기관지염, 증식성 세기관지염등으로 구분하며 여기에는 이와 같은 병리질환을 일으키는 다양한 원인들이 포함된다. 이외에도 드문 질환으로 미만성 범세기관지염, 광물질에 의한 소기도 질환등이 있다.
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Key words : Small airways, Computed Tomography

INTRODUCTION

The "small airways" of the lung are generally considered to consist of the membranous (terminal) bronchioles and respiratory bronchioles (Fig. 1), although the earliest use of this term defined small airways as all airways less than 3 mm in internal diameter, and thus included some cartilagenous airways[1]. The small airways contribute very little to resistance because, being so numerous, their overall cross sectional area is large. Consequently, there may be considerable destruction of the small airways before the patient becomes symptomatic and there is any detectable abnormality of the pulmonary function[2].

The small airways of the lung are now recognized to be primarily or secondarily affected in a variety of conditions including chronic obstructive pulmonary disease (COPD), asthma, bronchiectasis, rheumatoid arthritis, hypersensitivity pneumonitis, and sarcoidosis. Thurlbeck and Nagai[3,4] have suggested that pulmonary disease caused by cigarette smoking is multifaceted in nature, and that chronic bronchitis, emphysema, and small airway disease (SAD), or any

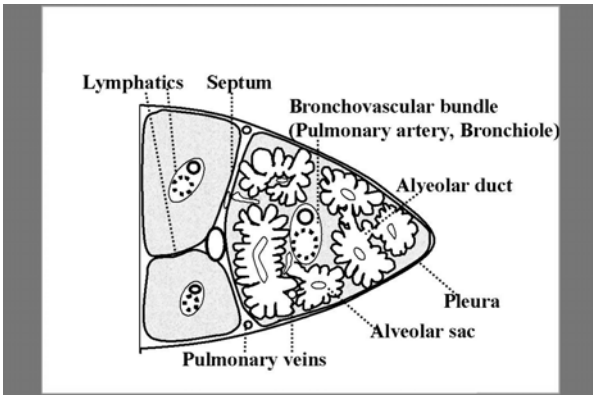

Figure 1. Anatomy of secondary pulmonary lobules. Small bronchovascular bundles consist of terminal bronchioles and pulmonary arteries in the center of secondary lobules (centrilobular region).

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combination of these lesions, can occur, or occur to a different degree, in a single patient. Mineral dusts can produce abnormalities in the small airways. Cellular bronchiolitis is seen in various infections including viral infections, mycoplasma pneumonia, and airway invasive aspergillosis, and in association with extrinsic allergic alveolitis, asthma, chronic bronchitis, and bronchiectasis. Constrictive bronchiolitis (bronchiolitis obliterans) is common manifestation in patients with rheumatoid arthritis, particularly those being treated with penicillamine, and is seen as a manifestation of chronic graft-versus-host disease following bone marrow transplantation, and chronic rejection after heart-lung and lung transplantation. It is rarely seen in association with inflammatory bowel disease and has recently been described in association with pulmonary neuroendocrine cell hyperplasia. Bronchiolitis obliterans with intraluminal polyps, which was previously termed proliferative bronchiolitis, is the pathologic term of "bronchiolitis obliterans with organizing pneumonia (BOOP). Idiopathic BOOP is not a new syndrome, and is used hereafter to refer to the interstitial lung disease. It may mimic an organizing pneumonia rather than an obstructive airway disease[1].

IMAGING MODALITIES

High-resolution Computed Tomographic findings

High resolution computed tomographic (HRCT) scan is currently the best imaging technique for assessment of diseases of the bronchioles. In HRCT scan, the bronchioles are centrilobular structures being clustered near the center of a secondary pulmonary lobule, which is defined as the smallest portion of lung surrounded by connective tissue septa[2]. This accounts for the characteristic centrilobular distribution of bronchiolar abnormalities on HRCT scan. The bronchioles within a secondary pulmonary lobule measures less than 1 mm in diameter[5].

1. Inspiratory CT scans

1) Centrilobular nodules

Direct sign of small airways disease refers to direct visualization of diseased bronchioles that are normally invisible at HRCT[6]. The appearance of a diseased small airway varies depending on the plane of section used for scanning and the nature of the disease process. When the airway walls are thickened and the airway dilated, ringlike, tubular, or branching tubular structures may be seen (Fig. 2). When wall thickening obliterates the airway or the airway becomes filled with mucus or debris, linear structures, or branching linear structures may be seen. In the lung periphery, abnormal small airways have a more distinctive appearances, whereas it can be difficult to differentiate these findings in the central portion of the lung, where architecture is more complicated and normal large airways are present. Any ringlike or tubular structure seen in this location is abnormal. When filled airways are imaged on cross sect-

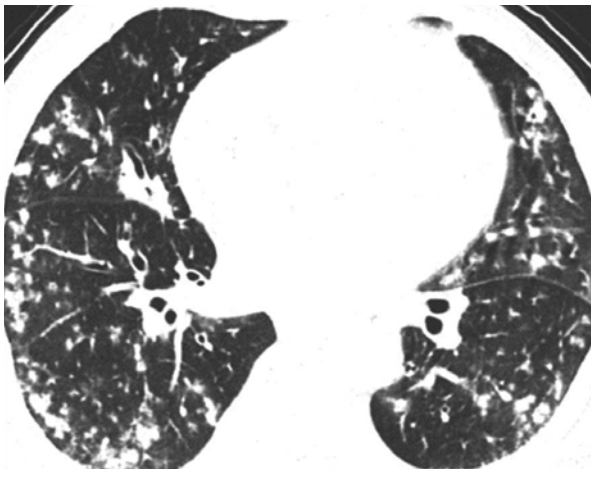

Figure 2. HRCT scan shows nodular, ringlike and branching structures of centrilobular distribution, suggesting bronchiolar nodules in bronchiolitis.

ion, however, subpleural nodules are seen, and these can be indistinguished from other causes of subpleural nodules, such as sarcoidosis or hematogenous metastases[7].

2) Centrilobular emphysema

Centrilobular emphysema occurs when small airways in the center of the pulmonary lobule and the parenchyma adjacent to them are completely destroyed. Areas of air attenuation without definable walls are seen adjacent to normal parenchyma. A central dot or line, representing the remaining artery, is often seen. Moderate, severe, and probably mild centrilobular emphysema can be reliably diagnosed and quantified at HRCT (Fig. 3).

3) Inhomogeneous attenuation (mosaic attenuation)

Mosaic pattern of attenuation, with patchy areas of increased and decreased attenuation, is nonspecific and may be seen on thin-section CT scans of the lungs (Fig. 4). Worthy et al.[8] suggested that airway disease may be differentiated reliably as the cause of mosaic attenuation on lung CT scans, whereas vascular disease is often misinterpreted as infiltrative lung disease or airway disease. Inhomogeneous attenuation depicted on thin section CT scans obtained at full inspiration can be a result of infiltrative lung disease (with ground glass opacity), air trapping (with mosaic attenuation), or vascular obstruction (with mosaic perfusion)[9]. In many cases, these three causes of inhomogeneous lung attenuation can be distinguished on the basis of CT findings (Fig. 5). In patients with ground glass opacity (infiltrative

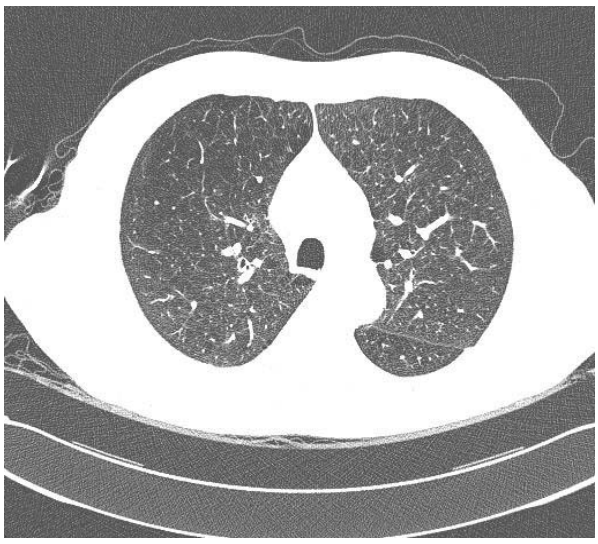

Figure 3. HRCT scan of the chronic obstructive lung disease demonstrates the decreased attenuation areas without definable walls in the right lung fields. Vascularity is also decreased in the affected lung fields.

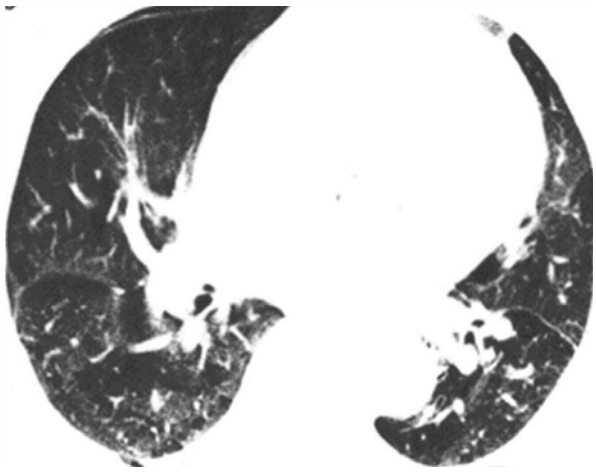

Figure 4. Mosaic pattern of attenuation, with patchy areas of increased and decreased attenuation is seen on thin-section CT scans of the lungs.

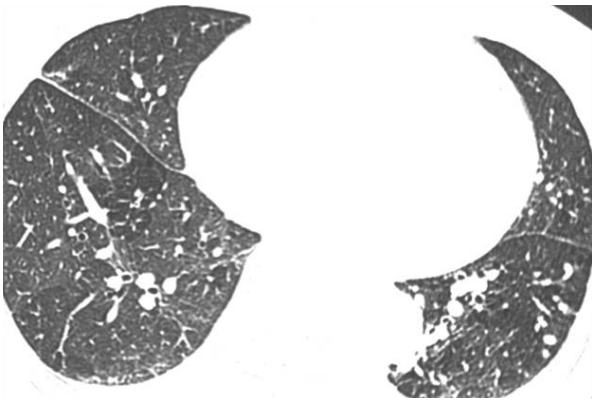

Figure 5. Inspiratory CT scan (usual HRCT scan) shows inhomogeneous parenchymal densities with relatively sharp border, but overall findings are indistinct. De-creased density areas were abnormal, being compa-tible with air trappings on expiratory CT scan (not seen here).

disease), pulmonary vessels appear uniform in size in areas of differing attenuation: in patients with mosaic perfusion, vessel size varies, appearing decreased in areas of decreased attenuation. In addition, the use of expiratory scans may allow mosaic perfusion due to airway disease to be distinguished from mosaic perfusion due to vascular obstruction: On expiratory scans, obtained in patients with mosaic perfusion secondary to airway disease, air trapping results in accentuation or the visible attenuation differences[10].

4) Subsegmental atelectasis

Subsegmental atelectasis occurs when the lung parenchyma distal to an obstructed small airway collapses. Wedge shaped areas of ground glass attenuation are typically seen at HRCT.

2. Expiratory CT scans

Air trappings

Air trapping is a prominent indirect finding in small airway disease. Air trapping is a pathophysiologic term indicating the retention of excess gas in all or part of the lung, at any stage of expiration [11]. Air trapping on CT is defined as "decreased attenuation of pulmonary parenchyma, especially manifest as less than normal increase in attenuation during expiration.". This phenomenon results from complete or partial airway obstruction or local abnormalities in pulmonary compliance, and it must be differentiated from the decreased attenuation of hypoperfusion associated with locally increased pulmonary artery resistance. In the healthy participants, lung attenuation averaged -829 H on inspiration (range, -858 to -770 H), and -685 H (range, -763 H to - 580 H) on expiration; differences in mean lung attenuation from inspiration to expiration averaged 144 H (range, 85 - 235 H)[12].

Various methods of performing expiratory thin-section CT have been employed by different investigators. These include a) scans obtained during forced expiration using an electron beam scanner (dynamic expiratory high-resolution CT); b) scans performed during exhalation at specific spirometrically controlled respiratory levels (spirometrically-triggered expiratory CT; c) scans obtained during suspended respiration after forced exhalation (postexpiratory thin section CT). Postexpiratory CT during suspended end expiration is the most widely used technique to visualize expiratory air-trapping. Low dose dynamic expiratory CT using a spiral CT scanner may prove usefulness in the evaluation of patients with lung diseases characterized by air flow obstruction with little increase in patients radiation dose[13]. Continuous-expiration CT technique, done by Lucidarme et al.[14] improved the conspicuity and apparent extent of air trapping. It consisted of a 15 mm-thick lung volume obtained above the bronchus intermedius that was acquired with 1.5 mm collimation and width a pitch of 1 in a caudocranial direction. A 180° linear interpolation reconstruction algorithm was used. Ten sections were obtained during a 10-second period as the patient performed an expiratory maneuver. Paired inspiratory-expiratory thin-section CT findings in patients with small airway diseases were differentiated from those with COPD[15]. But, visual assessment failed to differentiate between the SAD and normal groups. However, one measurement, an inspiratory-expiratory attenuation difference in the dependent lower lung, was different between SAD and normal group.

3. Multidetector (MD) CT scan

The MDCT has the ability to acquire contiguous HRCT images throughout the thorax during short period. The MDCT may contribute to improving the

visualization of the characteristic findings. One of the greatest advantages of this new technology is the improved quality of the two-dimensional (2D) multiplanar images (Fig. 6) and three-dimensional (3D) reconstruction images, including those developed specifically for airway imaging such as CT bronchography and virtual bronchoscopy. The use of MPVR-MIP technique has been proven to increase the number of bronchiolar changes compared with single-thin-section CT scans[16]. Increasing the thickness of the slab from 0.6 mm to 3.3 mm and 7.7 mm increases the profusion and visibility of multiple small ill-defined and hazy dense centrilobular nodules. Recently, volumetric expiratory high-resolution CT was investigated by Nishino and Hatabu[17]. This new volumetric expiratory HRCT protocol includes two volumetric HRCT scans: one on end-inspiration and one on end-expiration in the supine position using an 8- or 4-detector CT scanner. The parameter for the 4-detector CT scanner were: 2.5 mm collimation, 120 kVp, 240 mA, 0.5 s gantry rotation time and a table speed of 15 mm per rotation. A series of these images were reformated with 1.4 mm thickness and 10 mm intervals. The volumetric expiratory HR CT increased the detectability of the conducting airway to the areas of air trapping, and added significant information about extent and distribution of air trapping. In one report[18], MDCT with MPR image did not alter the confidence in bronchiectasis, bronchiolitis and emphysema, but some improvement in the accuracy of assessing bronchiectasis was observed, although it did not reach statistical significance.

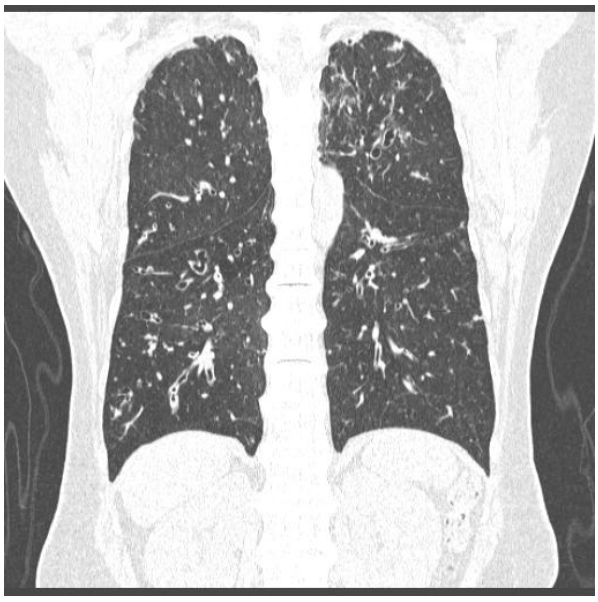

Figure 6. Multidetector CT of diffuse panbronchiolitis patient: Peripherally distributed centrilobular branching structures and nodules are more conspicuous and easily detected on two dimensional, coronal reconstruction view.

DISEASE CLASSIFICATION AND RADIOLOGIC FINDINGS

1. Diseases of the small airways caused by cigarette smoke

Airway can be deformed in several ways: 1) Thickening of the airways as a result of inflammatory edema and cellular infiltrates, 2) Airway wall distortion because of fibrous tissue scarring in both the submucosa and the adventitial compartments, and 3) early airway collapse on expiration secondary to des-

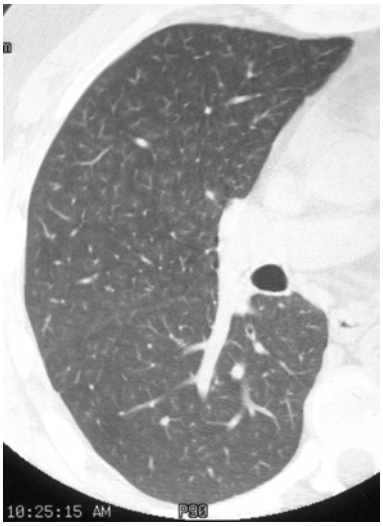

Figure 7. Respiratory bronchiolitis-interstitial lung disease (RB-ILD) in smoker: HRCT scan shows diffuse, ill-defined,centrilobular ground glass opacities.

truction of the peribronchiolar alveolar attachments and loss of airways parenchymal interdependence[1].

Respiratory bronchiolitis occurs in the vast majority of smokers, but it is usually mild, the majority of patients being asymptomatic[19]. Rarely, particularly in heavy smokers, the condition may be severe enough to lead to abnormalities on HRCT scan. In this case, it is referred to as *respiratory bronchiolitis-interstitial lung disease* (RB-ILD) (Fig. 7). The HRCT findings consist of ill-defined centrilobular opacities, and patchy areas of ground glass attenuation, attributed to smokers' alveolitis. The lesion tend to have a predominantly upper lobe distribution. Other HRCT findings in smoker or exsmoker are segmental and lobar air trapping on expiratory CT scans[20].

2. Cellular bronchiolitis

Cellular bronchiolitis is characterized by inflammatory cellular infiltrates that involve the lumen, the wall of the bronchioles, or both. It is seen in various infections, and in association with extrinsic allergic alveolitis, asthma, chronic bronchitis, and bronciectasis (Fig. 8). The HRCT findings reflect the inflammation of the bronchiolar walls and consist predominantly of centrilobular branching lines and nodules. In infections, focal areas of consolidation may also be seen reflecting the bronchopneumonia. In hypersensitivity pneumonitis, centrilobular nodules are characteristics with ground glass attenuations, suggesting alveolitis, and mosaic attenuation due to partial bronchiolar obstruction[21] (Fig. 9). Patients with as-

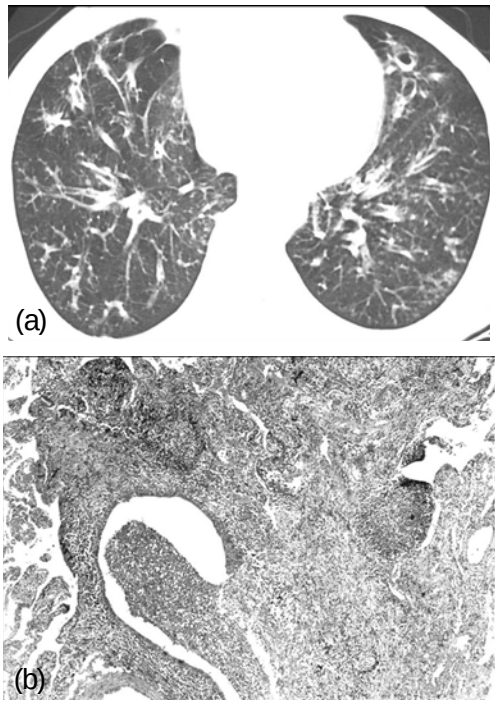

Figure 8. CT scan (**a**) shows irregular, dilated and thickened bronchi with centrilobular nodules in patient with chronic inhalation exposure or organic solvent. Histopathologic specimen (**b**) reflects the bronchiectasis and bronchiolitis.

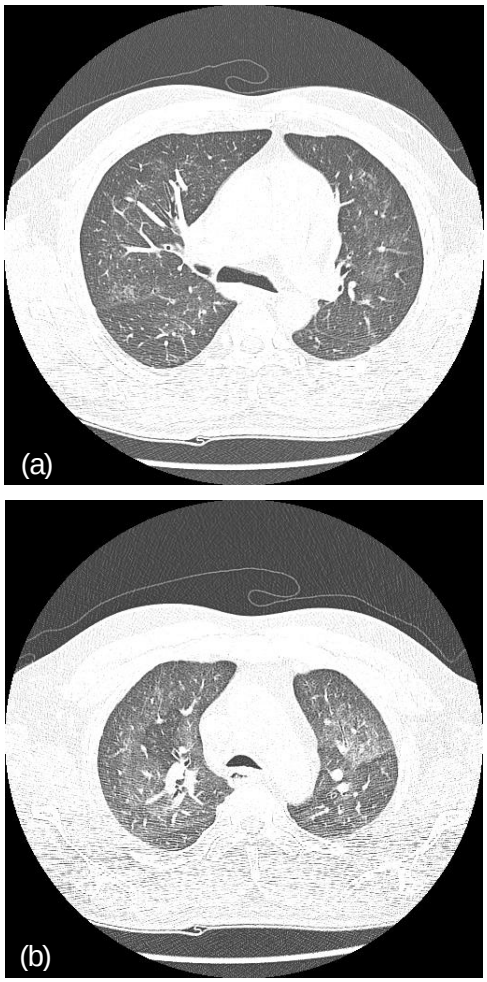

Figure 9. HRCT scan (**a**) shows multifocal, ill-defined, ground glass opacities, and expiratory CT scan (**b**) shows associated air trappings (low density areas) in hypersensitivity pneumonitis.

thma may have changes in both the large and small airways. CT scan in asthmatic patients reveals the bronchial wall thickening. The severity of air trapping also correlates with the severity of the asthma.

3. Constrictive bronchiolitis

Constrictive bronchiolitis is characterized by bronchiolar inflammation, peribronchiolar and submucosal scarring, and progressive bronchiolar luminal narrowing. The terms *obliterative bronchiolitis* and *bronchiolitis obliterans* are synonymous with constrictive bronchiolitis. The clinical criteria used for the diagnosis of contstrictive bronchiolitis are irreversible airflow obstruction with a forced expiratory volume in 1 second less than 60% of predicted value in the absence of emphysema, chronic bronchitis, asthma or other cause of airflow obstruction[22]. It may be seen as the result of childhood viral infection, mycoplasma pneumonia, or toxic fume inhalation, connective tissue disorder (Fig. 10), and transplantation. HRCT findings include mosaic attenuation, bronchial dilatation, and air-trapping. In most cases, the major findings are mosaic perfusion and air trapping[23]. They might be lobular, segmental, or larger areas of reduced lung attenuation in conjuction with reduced vessel size and adjacent areas of normally ventilated lung. Occasionally, these findings may be seen predominantly affecting one lung as Swyer-James syndrome. This entity is a postinfectious constrictive bronchiolitis, usually viral in infancy or early childhood.

4. Bronchiolitis obliterans with intraluminal polyp (BOOP)

This condition was previously termed proliferative bronchiolitis and is characterized histologically by the presence of granulation tissue polyps within the lumina of the bronchioles and alveolar ducts. In the vast majority of cases this is seen in conjuction with patchy areas of organizing airspace pneumonia. Cryptogenic organizing pneumonia may be the best single term for this condition since it emphasizes that the clinical and morphologic features mimic an organizing pneumonia rather than an obstructive airway

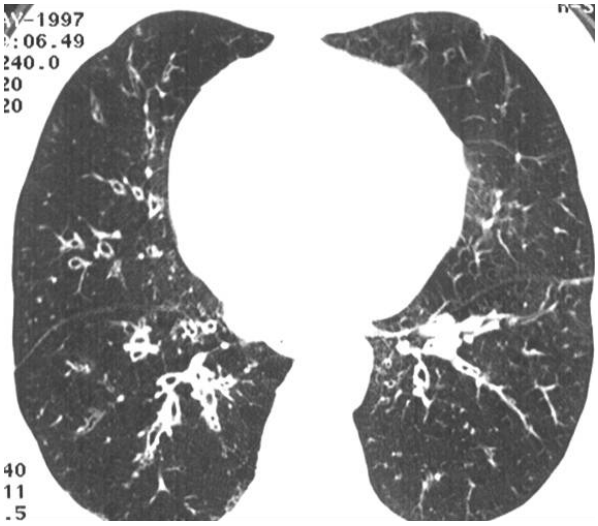

Figure 10. Bronchiolitis obliterans in rheumatoid arthritis patient: The whole lung density of enlarged lung is diffusely decreased with central bronchial wall thickenings and dilatations.

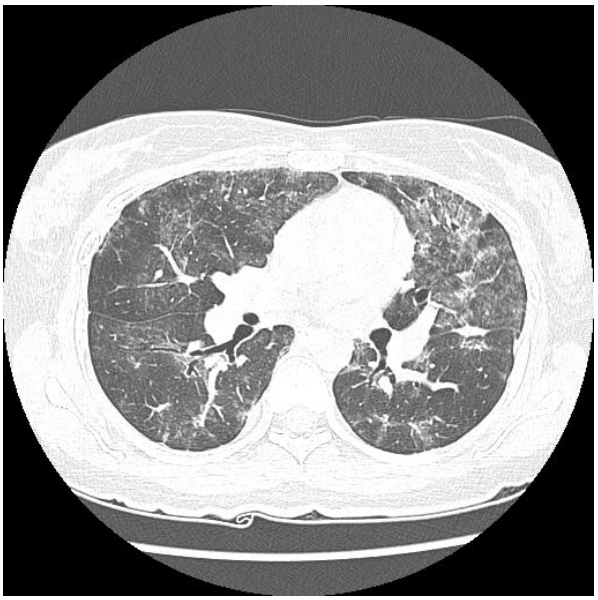

Figure 11. HRCT scan of idiopathic BOOP demonstrates the peribronchial distribution of multifocal, ill-defined ground glass opacities.

disease. Idiopathic BOOP comprises a distinct clinicopatholic syndrome that often appears to follow an upper respiratory infection and is associated with progressive cough and dyspnea. The duration of symptoms is generally less than 2 months. BOOP is not always idiopathic and in those that are a reaction to the organizing phase of any viral, bacterial, or fungal pneumonia, chronic eosinophilic pneumonia; collagen vascular disease; drug reactions; or following bone marrow and lung transplantation and irradiation.

The predominant HRCT findings are those of an organizing pneumonia with areas of consolidation, frequently bilateral. Sometimes, there is a peribronchial (Fig. 11) or subpleural distribution. Nodules related to focal pneumonia surrounding bronchioles may be seen occasionally.

5. Miscellaneous

1) Diffuse panbronchiolitis

This is an inflammatory lung disease of unknown etiology that is seen commonly in Japan and Korea but is rare in North America. The clinical presentation is of an chronic progressive cough and dyspnea. It affects principally the respiratory bronchioles. Histologically, it is characterized by mononuclear cell inflammation of the respiratory bronchioles and the presence of foamy macrophages in the bronchiolar lumina and adjacent alveoli. The HRCT findings are diffuse peripheral centrilobular nodules, suggesting bronchiolitis (Fig. 6). Branching linear opacities, progressive bronchiectasis, and air trappings are visualized. Treatment with erythromycin at an early stage of the disease is associated with a reduction in the size and number of nodules.

2) Diseases of the small airway due to mineral dusts

Bronchiolitis may be seen in several pneumoconiosis including asbestosis and silicosis. Constrictive bronchiolitis is seen in severe cases.

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