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Differential Diagnosis of Non-Segmental Consolidations

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Abstract

Consolidation and Ground-Glass Opacities (GGO) are common findings on chest Computed Tomographic (CT) scans. Consolidation and GGO can be divided into segmental, non-segmental and interstitial pneumonia types based upon distribution pattern. The aim of this review is to highlight the importance of the non-segmental distribution pattern, and to explain its relevancy in various conditions. Non-segmental distribution pattern presents as lobar pneumonia histologically, whereas segmental distribution appears as bronchopneumonia. The different diagnoses that can be derived from non-segmental distribution consist of infectious pneumonias caused by *S. pneumoniae, K. pneumoniae* and *L. pneumophila, Chlamydophila psittaci, M. pneumoniae,* measles, viral pneumonia and tuberculosis, as well as non-infectious inflammatory diseases including Cryptogenic Organizing Pneumonia (COP), Chronic Eosinophilic Pneumonia (CEP) and Pulmonary Alveolar Proteinosis (PAP), and other conditions including Anti-Neutrophil Cytoplasmic Antibody (ANCA) related pulmonary hemorrhage and Bronchoalveolar Carcinoma (BAC). A detailed analysis and correlation of non-segmental distribution with other CT findings (e.g., ground-glass opacity, interlobular septal thickening, fibrosis, pleural effusion, air trapping, nodular lesions, and air bronchiologram and air bronchogram) can facilitate the accurate diagnosis of these respiratory diseases. Specifically of interest is *L. pneumophila* infection, which first presents as bronchopneumonia but later converts into lobar pneumonia. The mechanism behind this conversion involves inflammatory exudates that can pass through Kohn's pores and Lambert's channel during *L. pneumophila* infection. Therefore, *L. pneumophila* pneumonia pattern first presents as segmental at the start of infection and after 2 weeks or more converts into non-segmental type. Overall, this review demonstrates that the non-segmental distribution pattern can be very valuable in making respiratory disease diagnosis.

Keywords: Consolidation; Non-segmental pattern; Computed Tomographic scans (CT); *Legionella pneumophila;* Cryptogenic Organizing Pneumonia (COP); ANCA-related pulmonary hemorrhage

Introduction

There are various clinical, laboratory and radiological methods currently used to diagnose respiratory diseases. Chest Computed Tomography (CT) is a simple, rapid and reliable method in the field of the diagnostic imaging. Using this method, proper analysis of the distribution, pattern of consolidation and ground-glass opacification has been found to be very helpful in the diagnosis of various respiratory diseases [1-5].

On chest CT scans, consolidation appears as a homogenous increase in pulmonary parenchymal attenuation that obscures the margins of vessels and airway walls, with potential for air bronchogram presence [6]. This consolidation can be categorized into segmental (bronchopneumonia), non-segmental (lobar pneumonia) and interstitial pneumonia types based upon the distribution pattern of airspace opacifications [7]. Etiologically, airspace consolidation can be categorized into three groups: infectious disease, non-infectious inflammatory disease and other conditions [8]. Although segmental and non-segmental distributions are widely accepted in clinical settings, there are relatively few articles that discuss segmental and non-segmental distribution. The aim of this review is to discuss the importance of non-segmental distribution pattern in various respiratory diseases.

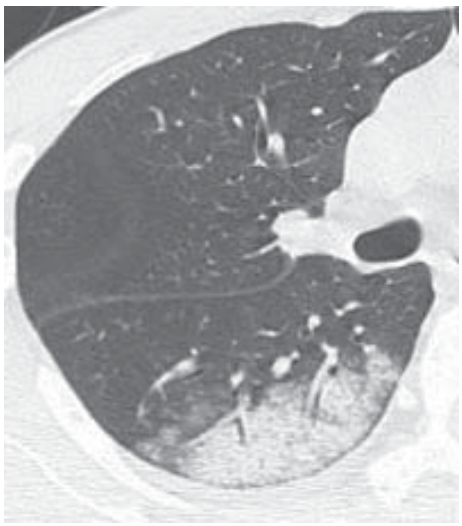

Figure 1: *Streptococcus pneumoniae* pneumonia. Computed tomography scan of right lobe showing airspace consolidation and ground glass opacities with a peripheral non-segmental distribution.

Non-segmental Consolidation (Lobar Pneumonia)

Non-segmental distribution represents consolidation distributed in several segments of the lung (greater than two) [9] (Figure 1). However, in clinical settings, non-segmental distribution pattern has been observed within one segment. For example, Figure 2 demonstrates that although consolidation was limited to one segment, distribution pattern of consolidation resembled that of non-segmental distribution. Figure 3A is a diagrammatic illustration of different patterns observed in various clinical cases of parenchymal abnormalities involving

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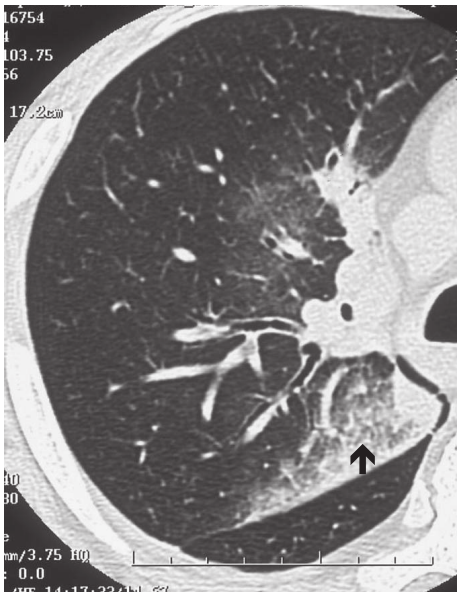

Figure 2: *Legionella pneumophila* pneumonia. Computed tomography scan of right lobe showing ground glass opacities with a peripheral distribution (arrow) located in one segment of an upper lobe.

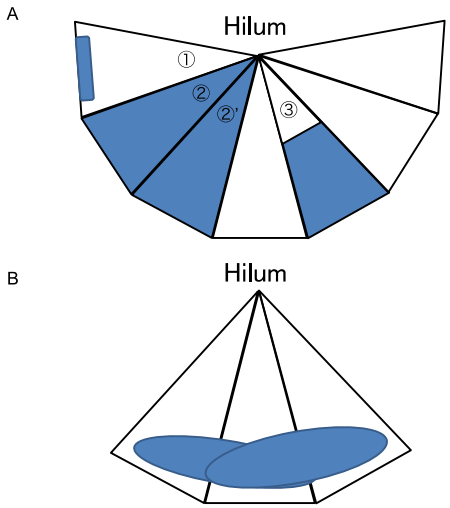

Figure 3: Diagrammatic illustration of non-segmental distribution of parenchymal abnormalities. (A) Types of non-segmental pattern of consolidation seen in chest CT scans of patients with infectious pneumonia. Figure 1 is an example of type 1, Figure 2 is also an example of type 1, and Figure 4 is an Example of 2 + 2'. (B) Anothertype of non-segmental pattern of consolidation found in chest CT. Figure 7 is an example of this type.

non-segmental distribution. Another pattern of non-segmental consolidation involves bilateral peripheral GGO and consolidation. This type is illustrated in Figure 3B.

In the case of non-segmental distribution, air bronchograms as well as air-bronchiolograms are frequently observed. Air-bronchograms present as a pattern of air-filled (low attenuation) bronchi on a background of an opaque (high attenuation) air- less lung [6]. An air-bronchiologram is defined as an air containing branching or linear structure less than 1mm in diameter within consolidation. Air-bronchiologram represents dilated small bronchioles within a consolidated area (Figure 4). These are rarely observed in infectious pneumonia with a segmental consolidation. CT scans display non-segmental distribution as homogenous consolidation involving adjacent segments of a lobe. This consolidation usually begins in the periphery of the lung, and spreads along the pleura or the inter lobar fissure [10,11].

Differential Diagnosis of non-Segmental Consolidation

The differential diagnoses derived from non-segmental distribution (Table 1) on Chest CT due to infectious diseases include lobar pneumonias caused by *Streptococcus pneumoniae*, *Klebsiellapneumonia,*or *Legionella pneumophila*. Other differential diagnoses include *Mycoplasma pneumoniae* pneumonia, tuberculosis, measles, *Chlamydophila psittaci* pneumoniaand viral pneumonia. Lobar pneumonia is characterized histologically by alveolar airspaces filled with exudates of edema fluid and neutrophils [11]. Non-infectious inflammatory diseases that can result in non-segmental consolidation pattern include Cryptogenic Organizing Pneumonia (COP), Pulmonary Alveolar Proteinosis (PAP) and eosinophilic lung disease, particularly chronic eosinophilic pneumonia (CEP). Other conditions that may lead to non-segmental distribution pattern include anti-neutrophil cytoplasmic antibody (ANCA)-related pulmonary hemorrhage and broncho-alveolar carcinoma (BAC) [12-14]. The identification of non-segmental distribution in combination with other

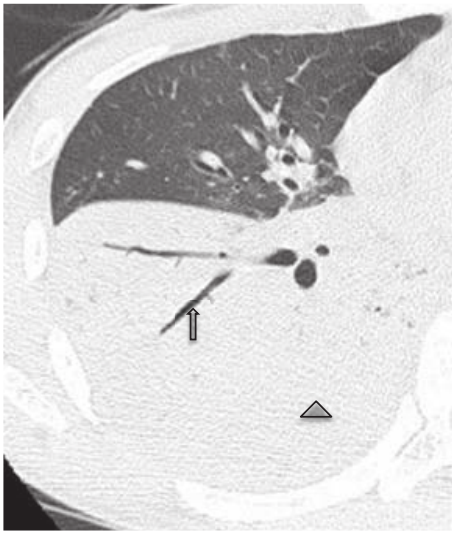

Figure 4: *Streptococcus pneumonaie* pneumonia. Computed tomography scan demonstrates homogenous airspace consolidation (arrow head) with a peripheral distribution in right lobe. Air bronchiologram (arrow) is also seen.

Disease Types		References
1. Infectious	*S. pneumoniae*	[11,16]
	K. pneumoniae	[11,17]
	L. pneumophila	[10,11,19,20]
	M. pneumoniae	[23]
2. Non-infectious inflammatory	Crytogenic organizing pneumonia	[8,27]
	Chronic eosinphilic pneumonia	[8,28]
3. Others	Pulmonary alveolar proteinosis	[30]
	Bronchioloalveolar carcinoma	[33]
	ANCA-related pulmonary hemorrhage	[12]

Table 1: Differential diagnoses from the literature with a non-segmental consolidation pattern.

clinical data is helpful in narrowing the range of diagnostic possibilities, or even in suggesting a specific diagnosis.

Non-segmental Consolidation in Infectious Pneumonia

Among respiratory diseases, pneumonia is the 6th leading cause of death, and is the number one cause of death due to infection worldwide [15]. Among community-acquired pneumonia, *S. pneumoniae* is the most frequently detected pathogen (48% of all cases).The common CT findings in pneumonia caused by *S. pneumoniae* are non-segmental consolidation, reticular opacities and centrilobular nodules [11,16] (Figures 1 and 4).

K. pneumoniae accounts for 0.5 to 5%of all pneumonias [17]. The most common CT findings of *K. pneumonia* pneumonia are ground-glass opacifications followed by consolidation and interalobular reticular opacity. These findings are predominantly seen in the periphery of both sides of lung accompanied with unilateral or bilateral effusion. In a study by Okada et al. involving 198 patients with *K. pneumonia* infection [17], it was reported that 96% of the patients displayed peripheral non-segmental airspace consolidation or ground-glass opacification.

L. pneumophila is an important cause of severe pneumonia [18]. According to previously reported data, the common CT findings in pneumonia caused by *L. pneumophila* include airspace consolidation, ground-glass opacification, cavitations and pleural effusion [19,20]. In a recent study involving 23 cases of *L. pneumophila* infection, Yu et al. reported that consolidation with a non-segmental distribution accompanied with pleural effusion were the most common CT findings [10]. Interestingly, it was noted that *L. pneumophila* infection which begins as a segmental distribution or bronchopneumonia has the ability to convert to a non-segmental distribution or lobar pneumonia after two or more weeks. This conversion is due to the pathogenesis of *L. pneumophila*. Infection of bronchioles by this pathogen results in the initial accumulation of neutrophils in airspaces. *L. pneumophila* is then phagocytized by macrophages in which these bacteria are able to multiply, thereby producing proteases to deplete the host defenses. These neutrophils can then travel through pores of the Kohn and Lambert's channel from one alveolus to another, thereby resulting in consolidation in the peripheral lung [10,21]. Therefore, it is presumed that *L. pneumophila* starts as bronchopneumonia, but after an interval of bacterial proliferation in pulmonary macrophages as well as diffusion and migration, the development of non-segmental airspace opacification takes place (Figure 2). This situation is rarely observed in pneumonia caused by other pathogens [10]. Another important finding is non-segmental distribution is almost always associated with pleural effusion in cases of infectious pneumonia, whereas pleural effusion is rarely seen with segmental distribution [8,10].

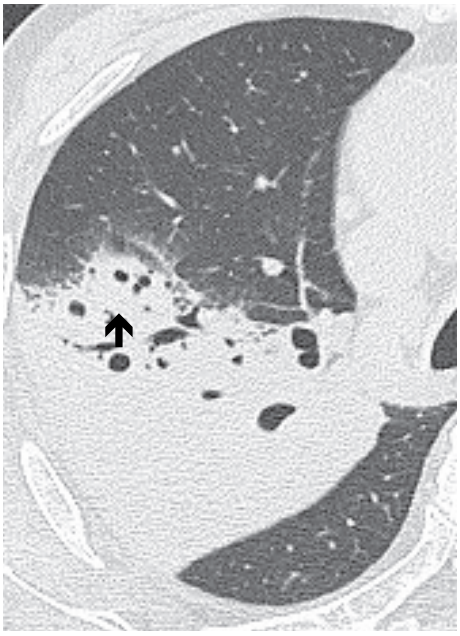

Figure 5: Mycobacterium tuberculosis. Computed tomography scan showing right lobe with diffuse airspace consolidation and a cavity (arrow), which is peripheral in distribution. Pleural effusion is also present.

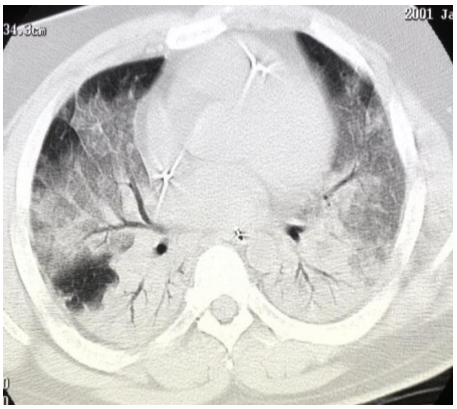

Figure 6: Measles. Computed tomography scan of a patient demonstrates extensive bilateral ground glass opacities and consolidation. Pleural effusion is also present.

In contrast to these other pathogens already mentioned, *Chlamydia pneumoniae* pneumonia presents as a centrilobular or peribronchovasular pattern with segmental distribution of airspace abnormalities on CT scans [22]. It has been reported that chest CT findings in patients with *C. pneumoniae* pneumonia consist mainly of ground-glass attenuation and acinar patterns. Acinar patterns and pleural effusions were observed significantly more frequently than in patients with *M. pneumoniae* pneumonia. Additionally, CT findings of centrilobular nodules and bronchial wall thickening were significantly less common than in the *M. pneumoniae* pneumonia patients The CT finding of acinar patterns, although nonspecific, can be considered suggestive of *C. pneumoniae* pneumonia.

Segmental consolidation is also the most commonly observed pattern in *M. pneumoniae* pneumonia, although a non-segmental distribution pattern can also be observed in children [23,24]. Reittner et al. have reported that in 28 patients with *M. pneumoniae* pneumonia, the most common finding was airspace opacification (24/28), which was segmental in 9 patients and non-segmental in 15 patients [23].

Figures 5-8 are all examples of clinical cases to further illustrate the concept of non-segmental distribution pattern seen in consolidation caused by tuberculosis, measles, viral pneumonia and *Chlamydophila psittaci* pneumonia respectively.

Non-segmental Consolidation in non-infectious Inflammatory Diseases

Non-segmental distribution pattern is observed in conditions other than infectious pneumonia. Non-segmental peripheral distribution of

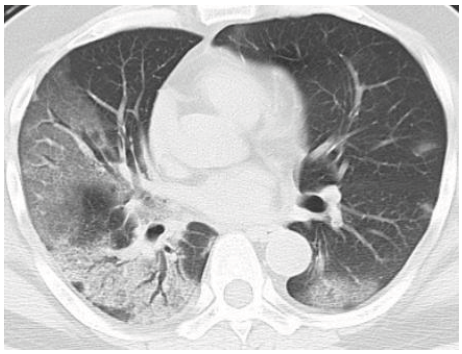

Figure 7: Influenza viral pneumonia. Computed tomography scan showing bilateral extensive ground glass opacities with peripheral non-segmental distribution.

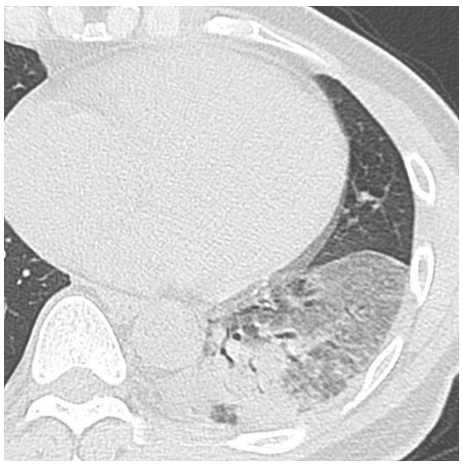

Figure 8: *Chlamydophila pssitaci* pneumonia. Computed tomography scan of left lower lobe showing ground glass opacities and airspace consolidation. Pleural effusion is also present. Airspace abnormalities are predominantly peripheral in distribution.

ground-glass opacification and consolidation is a typical CT feature seen in COP. COP is an inflammatory disease which is defined by the presence of buds of granulation tissue in lumen of distal airspaces which lead to obliteration of bronchioles. Although proper diagnosis of COP demands typical histological features (Figures 9 and 10), detailed analysis of CT scans can also play an important role in the diagnosis of a COP [25,26]. Johkoh et al. [8] have reported that non-segmental distribution with peripheral predominance of ground-glass opcaification and consolidation with an air-bronchogram are the prominent CT findings in COP [8]. Distribution is typically subpleural, basal and sometimes bronchocentric and perilobular. In addition, it may be encountered secondary to infection. Priedler et al. [27] concluded that of all 15 patients studied with COP, a non-segmental consolidation with peripheral predominance was present on their CT scans [27]. Pleural effusion however, was not seen in any of the cases.

CEP is a condition that presents with similar features on CT scans as COP (Figure 11). In a detailed study about eosinophilic lung diseases by Jeong et al. [28], it was reported that CEP is characterized by non-segmental airspace consolidations with peripheral predominance [28]. This distribution is not common in other types of eosinophilic pneumonias. An air-bronchogram in consolidation is also seen in CEP, whereas pleural effusion is rarely present. The percentage of eosinophils in peripheral blood and bronchoalveolar lavage along with

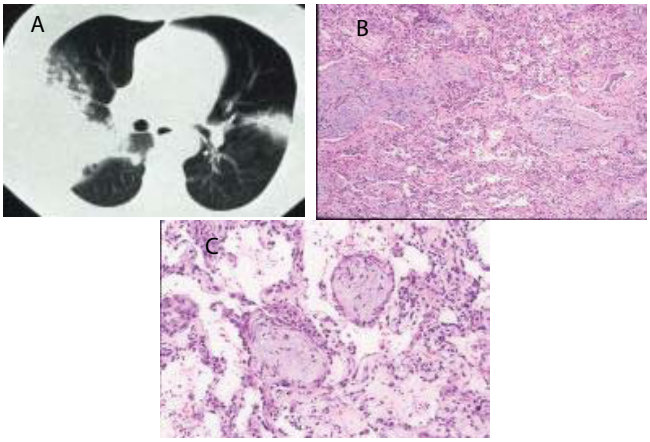

Figure 9: COP. (A) Computed tomography scan of a patient with cryptogenic organizing pneumonia showing consolidation and ground glass opacities with peripheral distribution. (B) Lung biopsy specimen showing organization of inflammatory exudates in airspaces.

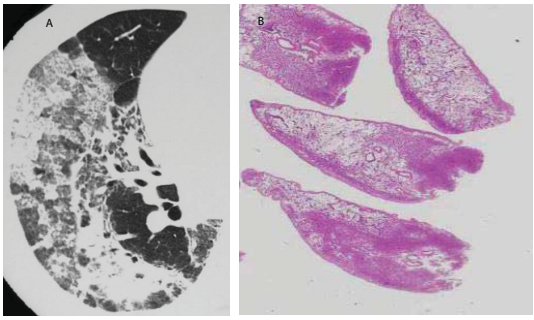

Figure 10: COP. Computed tomography scan (A) is of the of right lower lobe shows diffuse airspace consolidation and ground-glass opacification with a peripheral non-segmental distribution, features suggesting COP. Lung biopsy specimen (B) displays COP with organization of inflammatory exudates in respiratory bronchiolar airspaces near the pleura. The alveoli far from the inflammatory bronchioles are relatively normal.

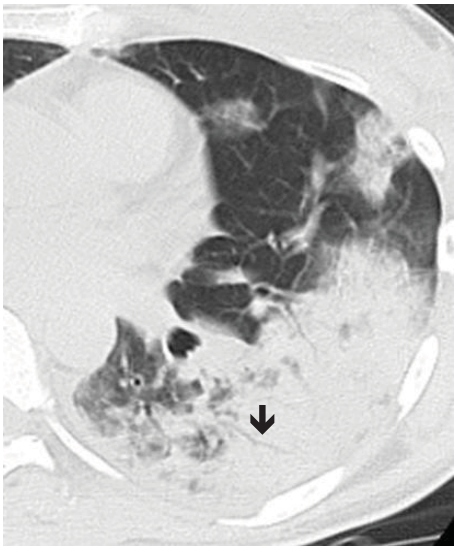

Figure 11: Chronic eosinophilic pneumonia. Computed tomography scan showing left lobe patchy sub-pleural consolidation and ground glass opacities. Pleural effusion is also present, as well as air bronchogram (arrow).

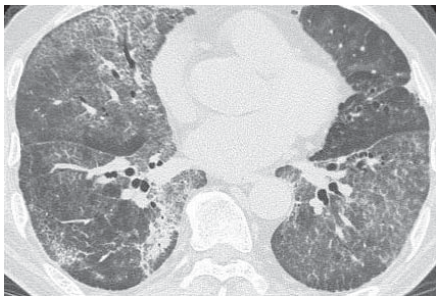

Figure 12: Alveolar proteinosis. Computed tomography scan demonstrates bilateral patchy ground glass opacities. Septal thickening is also seen in abnormal areas. Air space abnormalities are peripheral in distribution.

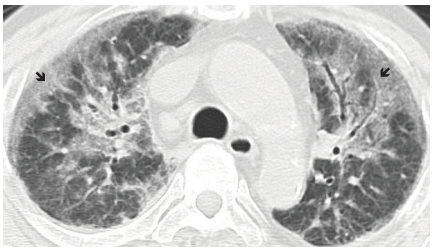

Figure 13: ANCA-related pulmonary hemorrhage. Computed tomography scan of a 50-year-old male showing bilateral peripheral ground-glass opacfication (arrow) with a non-segmental distribution pattern and interlobular septal thickening in both lobes.

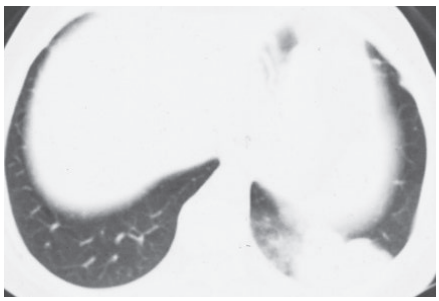

Figure 14: Bronchioloalveolar carcinoma. Computed tomography scan of a patient with bronchoalveolar carcinoma showing diffuse consolidation with a peripheral distribution.

typical CT findings facilitates in the diagnosis of CEP [28,29]. Simple pulmonary eosinophilia also consists of transient and migratory areas of consolidation that are non-segmental, may be single or multiple, usually have ill-defined margins, and often have a predominantly peripheral distribution [28].

Pulmonary Alveolar Proteinosis (PAP) is a rare and enigmatic disorder that is characterized by abnormal intraalveolar surfactant accumulation and a variable natural history [30-32]. On chest CT scans, characteristic features of PAP include patchy airspace ground-glass opacities or consolidation with non-segmental distribution pattern and thickening of intralobular septa, resulting in a crazy-paving pattern [30] (Figure 12).

Non-segmental Consolidation in Other Pulmonary disorders

One rare differential diagnosis of the non-segmental pattern of consolidation is ANCA-related pulmonary hemorrhage. In ANCA-related pulmonary vasculitis, an intense infilteration of activated neutrophils result in dissolution of vessel walls, which can lead to serious pulmonary hemorrhage [12]. It can present on CT scans as bilateral ground-glass opacifications and consolidation with a peripheral predominance and non-segmental distribution (Figure 13). Other findings include interlobular septal thickening.

Bronchoalveolar carcinoma can have a varied appearance on CT scans. Patsios D et al. [33] has recently reported that there are three different radiological patterns of BAC: (1) solitary nodule or mass of varying density; (2) focal consolidation; and (3) multifocal or diffuse disease[33].It was noted that mucinous BAC is more likely to appear as multifocal and diffuse disease. A combination of air-filled bronchi within areas of persistent unresolving lobar consolidation with multiple ill-defined nodules and areas of ground glass opacity are characteristic features of diffuse BAC (Figure 14).

Summary

In summary, this pictorial review has emphasized the importance of varied appearances when it comes to non-segmental distribution pattern of consolidation. Different examples of non-segmental distribution of consolidation are explained by recent clinical cases of respiratory abnormalities. Although chest radiograph is often the first imaging study performed in patients with pulmonary pathology, but it has limited role regarding etiology of various respiratory pathologies [7]. Chest CT is more useful in assessment of the thoracic findings. If a detail evaluation of type of consolidation is done it gives a clue about the causative agent in case of infectious pneumonia and finally helps the physician to narrow the long list of differential diagnosis of respiratory pathologies.

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