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M.A. Karnaushkina*[1], A.V. Averyanov [2], V.N. Lesnyak[3]

[1] — I.M. Sechenov First Moscow State Medical University Moscow, Russia

[2] — Pulmonology Research Institute of Federal Medical and Biological Agency, Moscow, Russia

[3] — Department of Research, Federal Research Clinical Center of Federal Medical and Biological Agency, Moscow, Russia

GROUND GLASS OPACITY ON CT OF THE CHEST IN CLINICAL PRACTICE: PATHOGENESIS, CLINICAL RELEVANCE, DIFFERENTIAL DIAGNOSIS

Abstract

Ground glass opacity, mosaic perfusion and air-trapping signs on chest computed tomography are types of one of the most common CT patterns — the increased lung density pattern. It is important to remember that these signs require the differential diagnosis and are not a diagnosis itself. Differential diagnosis ranges widely, since this pattern commonly occurs in diseases that affect small bronchi, pulmonary vessels, alveoli and interstitial tissue. A combination of lesions of various components of the pulmonary parenchyma is often observed thus leading to CT patterns formation. The understanding of this formation helps the doctor find a clue to the correct diagnosis. Another problem in the evaluation of these patterns is the distinction between pathological and "healthy" areas of lung tissue. Thus, in certain diseases, areas of increased lung density may not be pathological. The objective of this lecture is to analyze the reasons of ground glass opacity, mosaic perfusion and air-trapping CT-signs formation normally and in pathology and to identify their distinctive features, which allow to determine lung parenchyma elements underlying the pathological process, and thereby to narrow the differential diagnosis.

Key words: *computed tomography, ground glass opacity, mosaic perfusion, air-trapping, differential diagnosis*

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Computed tomography (CT) of the chest

Introduction

Computed tomography (CT) of the chest is today one of the leading radiographic methods for the diagnosis of lung diseases, which have become widespread in clinical practice.

Many diagnostic centers, hospitals, and outpatient clinics are currently equipped with modern CT scanners. However, clinicians are still underinformed about the capabilities of computed tomography, including CT of the chest, and for them the radiography reports are often the final diagnosis. The reason is that the radiological terms for thoracic imaging are often difficult for clinicians to interpret due to their lack of knowledge of how CT images are formed. This prevents the doctor from fully mastering the approach to making the accurate diagnosis.

*Contacts. e-mail: kar3745@yandex.ru

This lecture is aimed to help the clinician to form the correct diagnostic algorithm based on one of the signs of CT pattern of increased lung density: ground-glass opacity (GGO). In the lecture, we outline the principles of the diagnostic imaging and interpretation of CT findings. This information is necessary for resident physicians, primary care doctors, general practitioners, and pulmonologists to understand the diagnostic value of the changes in lung parenchyma that are revealed during chest CT.

The CT Pattern of Increased Lung Density

There are many CT signs of pulmonary diseases, but in order to ease our understanding of them and classify them, four CT patterns can be distinguished:

- Increased lung density pattern.
- Decreased lung density pattern.
- The reticular pattern.
- Focal lung lesions pattern.

CT signs of increased lung density are presented in Table 1 [1, 2].

The main mechanism that creates this pattern is as follows. The healthy person's lung tissue density in CT scans is slightly higher than the density of air. It is determined by three components: the lung tissue itself, pulmonary vasculature, and the amount of air in the alveoli.

Therefore, the reasons for increased lung density are:

- The appearance of additional masses.
- Lung tissue that is more dense and less airy because the intralobular airways and/or interstitial space are filled with pathological inclusions, or atelectasis.
- Increased capillary blood volume.

Any of these mechanisms or a combination of these mechanisms can cause GGO.

Ground-Glass Opacity

Ground-glass opacity (GGO) is an insignificant increase in lung tissue density with preserved bronchial and vascular markings in the area of pathological changes [1, 3]. The GGO areas of pathological changes are clearly distinguished from the healthy lung tissue and look grayish. The bronchial contours appear to be "too black" in comparison with the surrounding lung tissue (Fig. 1).

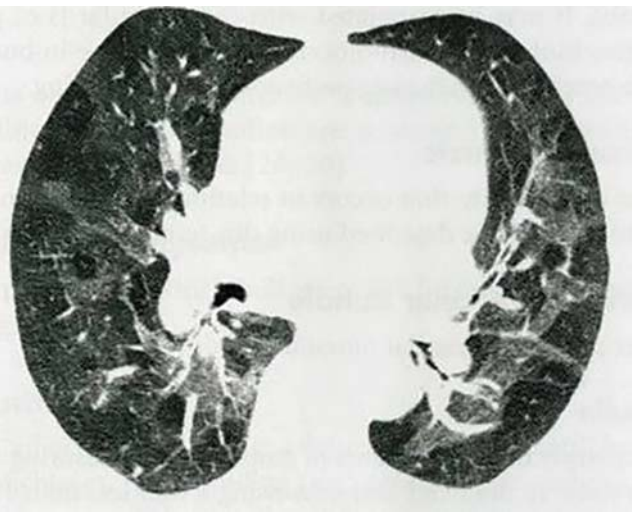

Figure 1. *High-resolution CT shows ground-glass opacity*

Table 1. *CT pattern – Increased Lung Density*

CT-pattern	CT signs of Increased Lung Density Pattern
Increased Lung Density Pattern	• Ground-Glass Opacity • Mosaic perfusion or "Mosaic lung" sign • Lung consolidation • Atelectasis • Soft-tissue density in the lungs ("expansive process")

It should be noted that the GGO is not always a sign of the pathological process in the lungs.

The physiological GGO can be observed in the gravity-dependent (lower) parts of the lungs, due to an increase of their blood filling due to the gravitational force [2]. This phenomenon is often found in patients with obesity. If such a patient undergoes CT scanning in a prone body position, the posterior segments of the lungs in which changes were detected in a supine body position will become translucent again (Fig. 2). However, the areas of infiltrative or fibrotic changes remain unchanged regardless of the position of a patient.

The GGO can be observed when a healthy person expires and when all the pulmonary fields acquire an even grayish color. This phenomenon occurs due to the physiological expiratory decrease of the lung airiness [2]. It can be easily distinguished from pathological changes in the lung tissue. Since the healthy person's expiratory decrease of the lung airiness occurs almost evenly, the X-ray attenuation coefficient (the gray scale) is even for the whole pulmonary field (Fig. 3), which is unlike what is true of the pathological process, which has a mosaic pattern (Fig. 4).

Ground-glass opacity can be found in CT images of patients who have increased lung tissue density

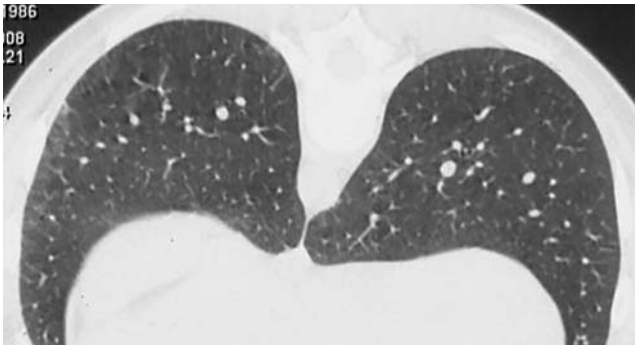

Figure 2b

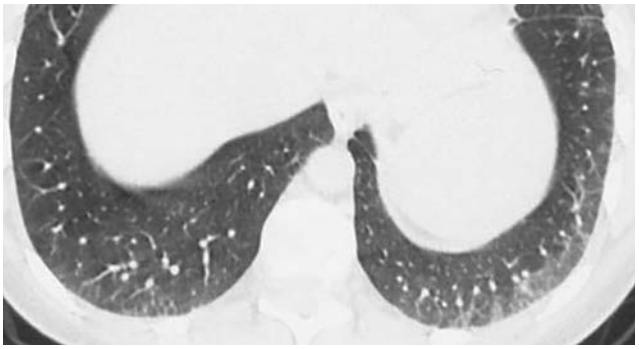

Figure 2a

Figure 2. *High-resolution CT of the normal lung at upper and middle levels in supine (**2a**) and at lower level in prone (**2b**) body positions*

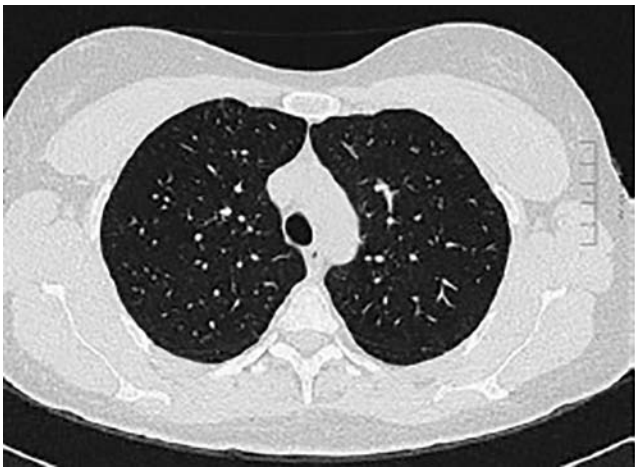

Figure 3a

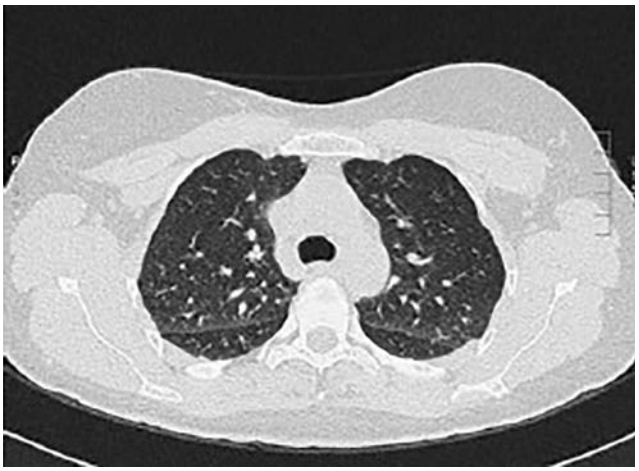

Figure 3b

Figure 3. *High-resolution CT of the normal lung (**3a** – suspended deep inspiration; **3b** – suspended deep expiration) [2]*

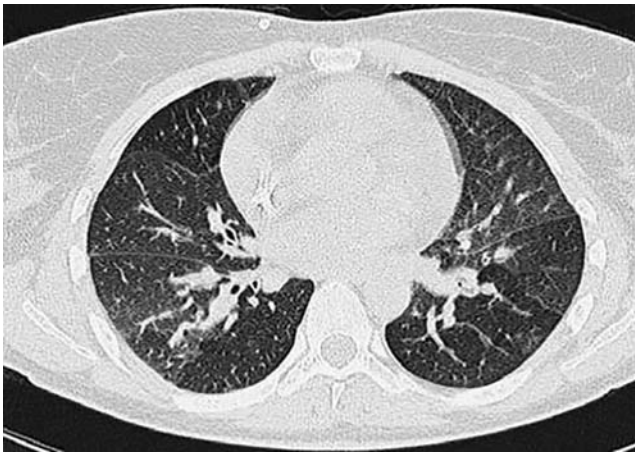

Figure 4a

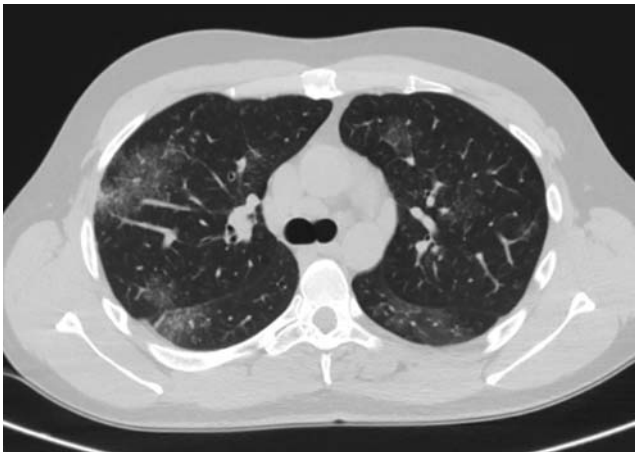

Figure 4b

Figure 4. *High-resolution CT of the lung (**4a** – COPD (areas of air-trapping); **4b** – pneumonia (ground-glass opacity)).*

due to bronchopulmonary disease. This sign can be both true and false in a patient with respiratory pathology.

True Ground-Glass Opacity Sign

Morphological substrate: True GGO develops due to three main mechanisms [1, 2, 4, 5]:

1. Figure 5 demonstrates the mechanism of formation of the pathological substrate in interlobular septa (septal interstitium) and the intralobular interstitium (most often of inflammatory origin). At the same time, the air-containing spaces (alveoli and bronchioles) remain almost completely airy. The diameter of the vessels in the areas with different densities is not changed.
2. Partial filling of alveolar spaces with cellular masses, exudate, transudate, or other pathological inclusions. If the alveoli are completely filled with liquid instead of air, the ground-glass opacity is transformed into a pulmonary consolidation (Fig. 6).

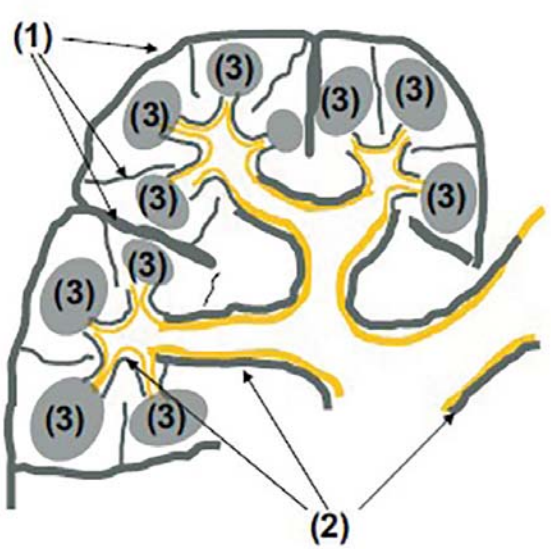

Figure 5. *The pulmonary interstitium can be divided into three component parts that communicate freely: (1) the peripheral connective tissue; (2) the axial connective tissue; (3) the parenchymatous connective tissue [2]*

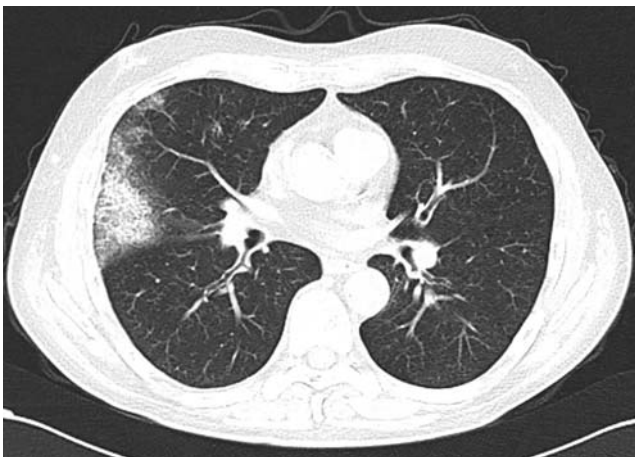

Figure 6. *Pulmonary haemorrhage in the right lobe in a patient with an injury after a car accident. Ground-glass opacity and areas of lung consolidation [2]*

Table 2. *Differential diagnosis of ground-glass opacity [4-9]*

Clinical Course	Disease
Acute disease	Pulmonary edema
	Pulmonary haemorrhage
	Acute respiratory distress syndrome, viral pneumonia, acute interstitial pneumonia
	Pneumonia (bacterial, viral, Mycoplasma pneumonia, Chlamydia pneumonia)
Subacute disease	Pneumocystis jiroveci pneumonia
	Fungal pneumonia
	Hypersensitivity pneumonitis
	Cryptogenic organising pneumonia
	Desquamative interstitial pneumonia
	Eosinophylic pneumonia (chronic)
	Micobacteriosis
Chronic disease	Nonspecific interstitial pneumonia
	Usual interstitial pneumonia (UIP): idiopathic pulmonary fibrosis and disease associated UIP
	Vasculitidis (Churg-Strauss syndrome)
	Sarcoidosis
	Bronchioloalveolar carcinoma (mucinous)
	Alveolar proteinosis

3. The decrease of lung airiness due to pathological processes (hypoventilation, respiratory depression, pulmonary fibrosis).

Type of the lung disease: acute, subacute or chronic clinical course leads to the appearance of additional CT signs, which help to perform a differential diagnosis.

Table 2 shows the main diseases that lead to the formation of the true ground-glass opacity and additional CT signs of corresponding pathology (Table 2).

If the clinical course is acute or subacute, GGO is mostly represented on CT scans as:
1. Pure GGO (Fig. 1).
2. GGO + consolidation (Fig. 7). The common cause of lung tissue consolidation is the

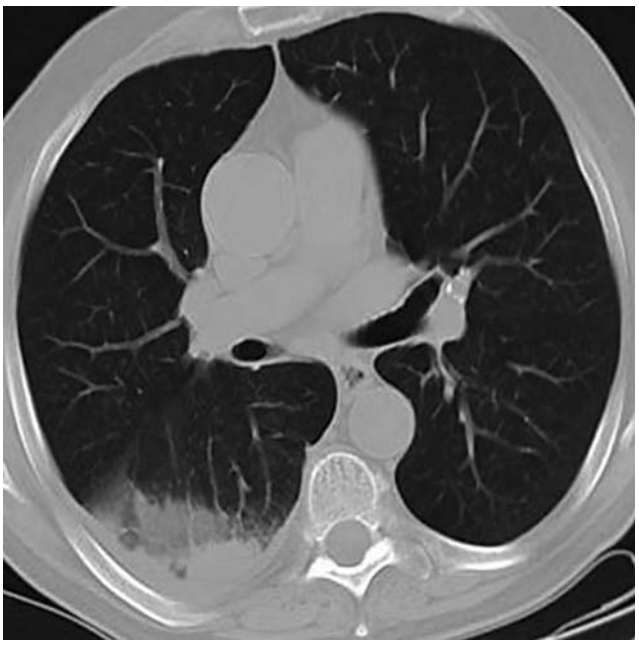

Figure 7. *The combination of ground-glass opacity and lung consolidation*

replacement of air in alveoli with liquids, cells or tissue. However, GGO is found along the consolidation area periphery if lung airiness is partially preserved and the interstitial component is predominant.

1. GGO + bronchiolitis (Fig. 8). Bronchiolitis is characterized by Y-structures with widening at the ends. It resembles the buds on tree branches. This symptom is associated with the filling of intralobular bronchioles with liquid (usually it is an inflammatory liquid), their dilation, and the thickening of their walls.

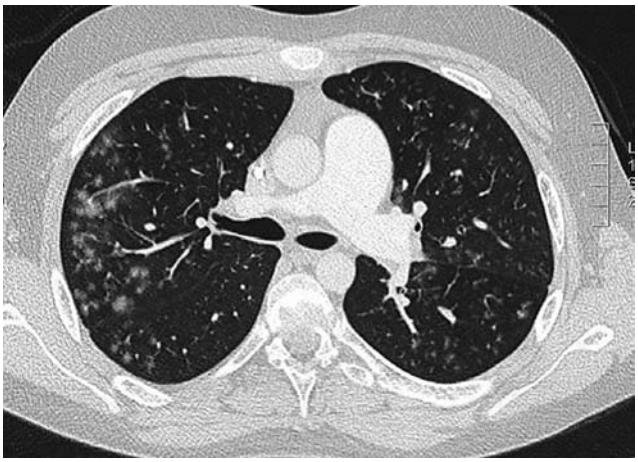

Figure 8. *Infectious bronchiolitis ("tree-in-bud" sign) with ground-glass opacity in a patient with Mycoplasma pneumonia*

The detection of GGO without signs of fibrosis, traction bronchiectasis, and lung tissue structural damages thus means the development of an active, most often reversible process in the lung tissue (Fig. 9).

If the clinical course is subacute or chronic, the GGO is represented on CT scans on the background of reticular (fibrotic) changes [4–9] as:

1. GGO + reticular changes (Fig. 10).
2. "Crazy paving" pattern (Fig. 11). It is a bilateral lung lesion, imaged as GGO, combined with the reticular pattern caused by interlobular and parenchymal interstitium thickening and peripheral lobular air space filling with the pathological inclusions.

The "crazy paving" pattern is specific for pulmonary alveolar proteinosis, but it also occurs in other diseases, including acute diseases (nonspecific interstitial pneumonia, cryptogenic organising pneumonia, vasculitides, eosinophilic pneumonia) (Table 3).

3. GGO + bronchiectasis and/or bronchiolectasis (Fig. 12).
4. GGO + cysts (Fig. 13).

Note that the appearance or expansion of the ground-glass opacity area in subacute and chronic diseases may indicate the degree of the pulmonary pathological process activity [4, 8, 10, 11].

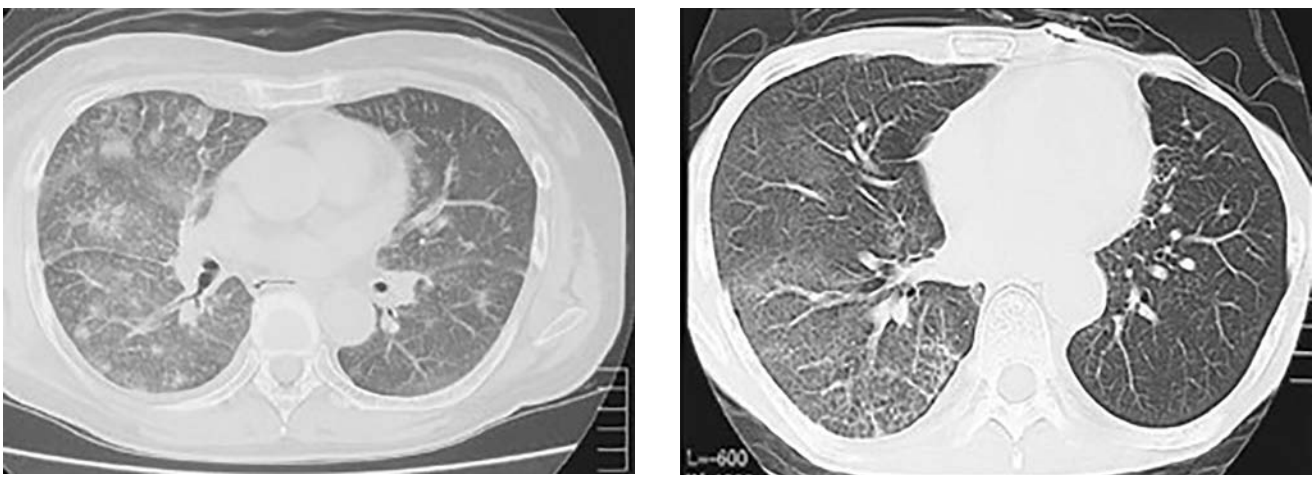

Figure 9. *Dynamics of ground-glass opacity sign in a patient with hypersensitivity pneumonitis before and after corticosteroids therapy (3 months) [1]*

The decrease of lung tissue density on CT images as an insignificant lung tissue density increasing with preserved bronchial and vascular markings in the area of pathological changes may be associated not only with interstitium thickening and partial filling of alveoli with the pathological inclusions ("true GGO"), but also with a perfusion defect, the "air trapping" occurrence. This phenomenon is called "false GGO" or the "mosaic lung" sign [1, 11], since its X-ray pattern on inspiratory CT scan is very similar to true GGO.

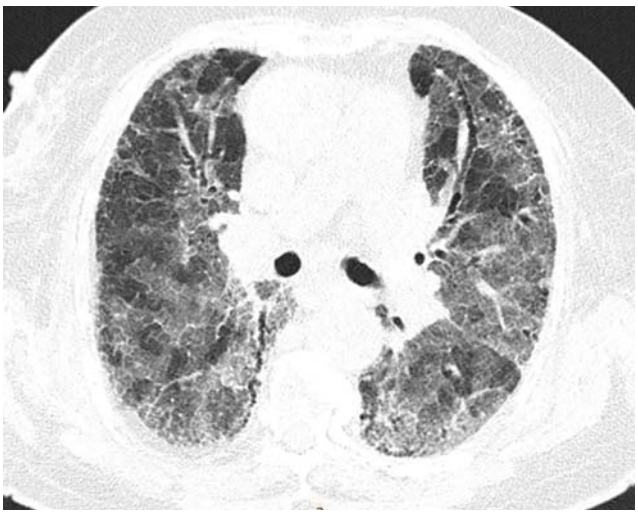

Figure 10. *Diffuse ground-glass opacity and the reticular pattern in a patient with hypersensitivity pneumonitis*

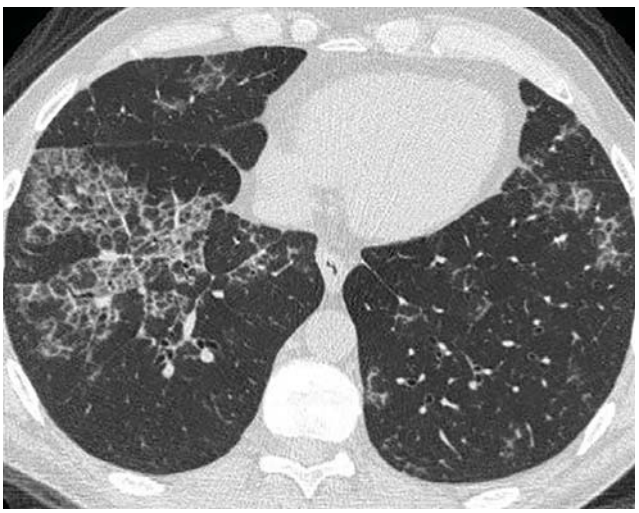

Figure 11. *The combination of ground-glass opacity and intra- and interlobular lines creates the crazy-paving pattern, in a patient with alveolar proteinosis*

Table 3. *Diseases than can cause the crazy-paving pattern formation [2, 4, 9-11]*

Acute disease	Subacute/chronic disease
Pulmonary edema	Alveolar proteinosis
Acute respiratory distress syndrom	Usual interstitial pneumonia (UIP): idiopathic pulmonary fibrosis and disease associated UIP
Pulmonary infection (bacterial, viral, Pneumocystis pneumonia, Mycoplasma pneumonia)	Nonspecific interstitial pneumonia
Pulmonary haemorrhage	Organising pneumonia
Acute interstitial pneumonia	Vasculitis (Churg-Strauss syndrome)
Radiation pneumonitis	Bronchioloalveolar carcinoma
Acute eosinophilic pneumonia	Chronic eosinophilic pneumonia
	Lipoid pneumonia
	Sarcoidosis

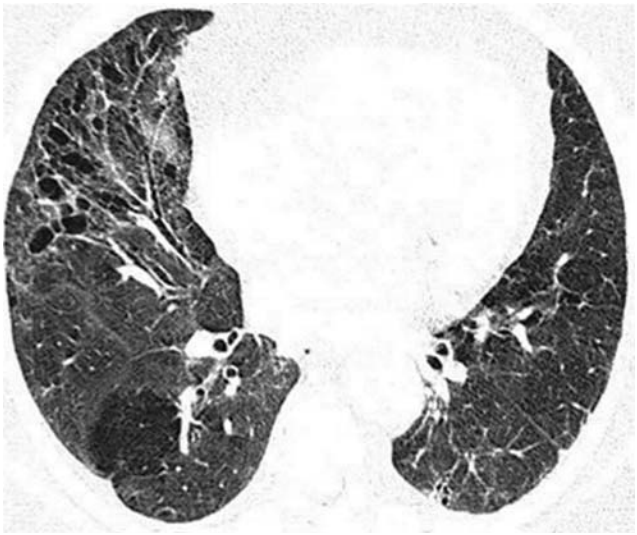

Figure 12a

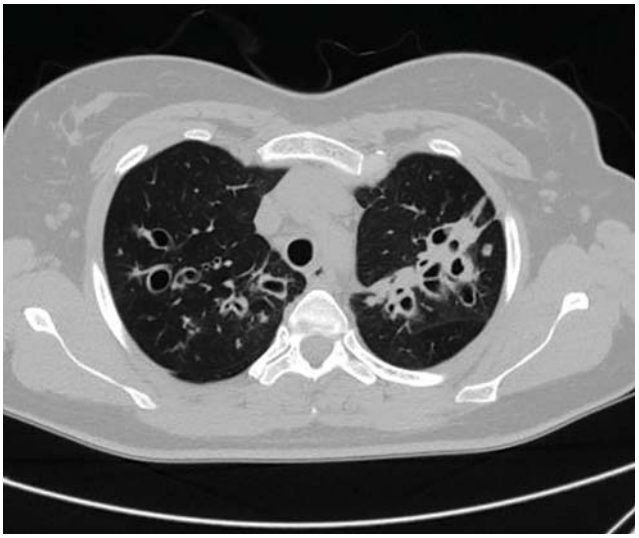

Figure 12b

Figure 12. *Ground-glass opacity in a patient with bronchiectasis (**12a** – diffuse ground-glass opacity and traction bronchiectasis in a patient with chronic hypersensitivity pneumonitis; **12b** – the combination of ground-glass opacity and cysts bronchiectasis)*

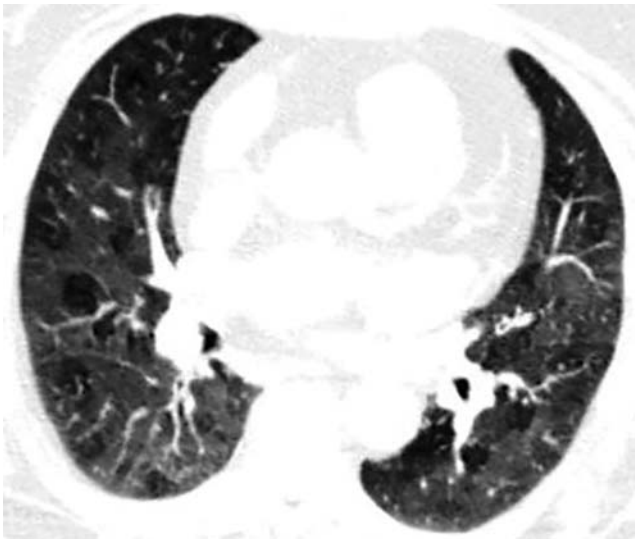

Figure 13. *Lymphocytic interstitial pneumonia. A few thin-walled cysts and GGO are seen in both lower lobes [10]*

«Mosaic Lung» Sign or Mosaic Perfusion (False Ground-Glass Opacity)

The «mosaic lung» sign or mosaic perfusion is a combination of areas with increased and reduced lung tissue density that are not associated with the decreased alveoli airiness or pulmonary interstitium lesions [1, 2, 11] (Fig. 14).

Morphological substrate: It occurs as a result of two mechanisms or a combination of mechanisms [1, 11]:

1. Affected by pathological changes in small bronchi with subsequent reflex vasoconstriction and redistribution of blood to healthy (well-aerated) areas of the lung tissue.
2. Affected by lobular arteriostenosis (obstruction, spasm).

The «mosaic lung» sign is a mosaic decrease of lung tissue density. It is very similar to true GGO in inspiratory CT images. In other words, it is manifested by a combination of increased and decreased density areas (alternating light gray and dark gray regions). However, the areas of true GGO reflect the lung tissue with preserved hemodynamics and reduced airiness, whilst mosaic perfusion occurs as a result of hemodynamic anomalies or pathology of small airways [1, 2, 11, 14].

In order to distinguish between these two CT signs, it is necessary to:

1. Compare the diameters of the vessels in the light gray and dark gray regions of the lung parenchyma during the examination while the patient breathes in. The diameters of the

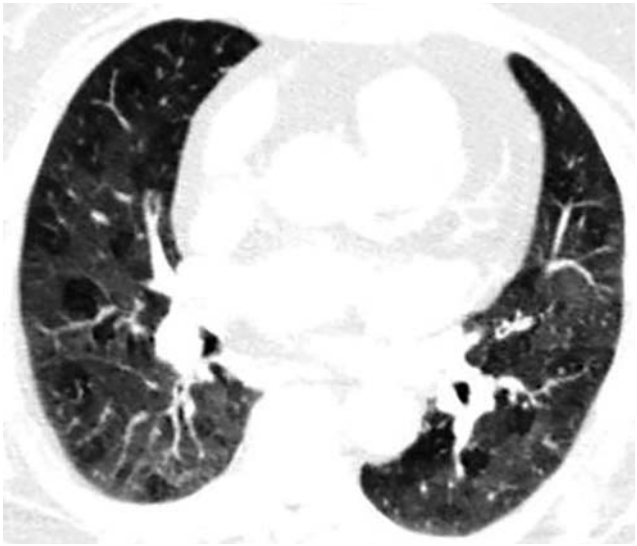

Figure 14. *Mosaic perfusion secondary to chronic pulmonary embolism. The areas of ground-glass opacity are «normal» lung regions with increased perfusion and increased blood volume*

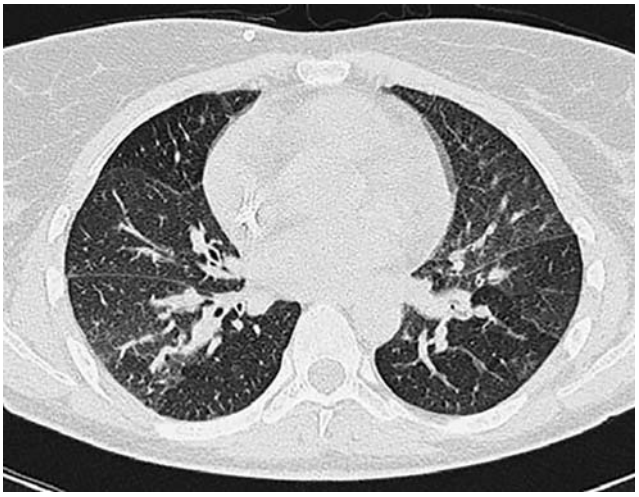

Figure 15. *Mosaic perfusion pattern*

vessels in different density areas are almost the same with true GGO in CT images of the chest. With false GGO, the diameters of the vessels in different density areas are not the same: they are less in decreased density areas (Fig. 15).

2. One of the best methods to distinguish the causes of the mosaic CT sign is the evaluation of the data obtained during inspiration and expiration. If the changes are related to hemodynamic anomalies and are presented as mosaic perfusion and true GGO, the density difference between these areas disappears or decreases: areas with a lower attenuation coefficient (darker regions) become more dense (become grayish like the healthy areas of the lung tissue) (Fig. 16).

If the «mosaic lung» sign is caused by the pathology of the small airways, pathological areas retain

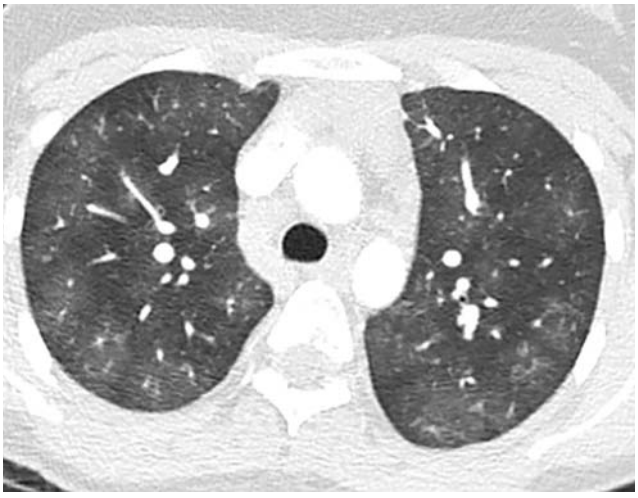

Figure 16a

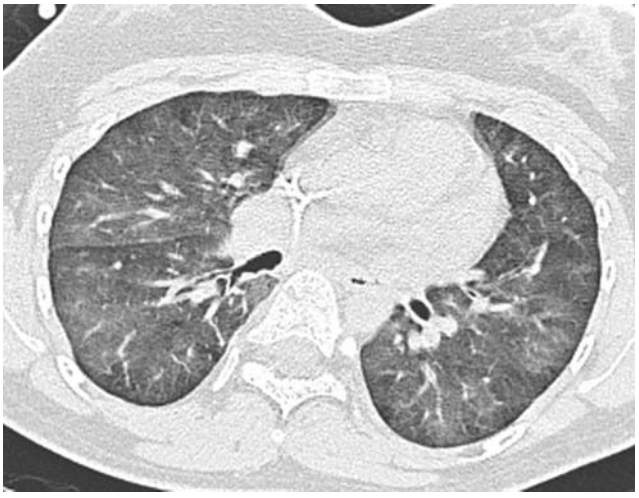

Figure 16b

Figure 16. *Multiple areas of mosaic perfusion in a patient with chronic pulmonary embolism. Differential diagnosis is predominantly based on normal vessel size in the high- and low-density areas: inspiration (16a) and expiration (16b)*

the same density irrespective of the respiratory phases, or the differences in the density of areas increase even more («air trapping») (Fig. 17).

It is necessary to examine the distribution of GGO in order to perform a proper diagnosis. It may be patchy or diffuse (Table 4).

The ground-glass opacity can also exhibit features of regional distribution in the lung parenchyma (Table 5).

Conclusion

The objective of this lecture was to explain to clinicians the pathogenic mechanisms by which the ground-glass opacity develops normally and in pathology. We presented the main approaches that are used to identify and conduct a differential diagnosis of true and false ground-glass opacity CT patterns in patients with lung diseases. We hope that this lecture will help you use the obtained knowledge for proper diagnosis and for

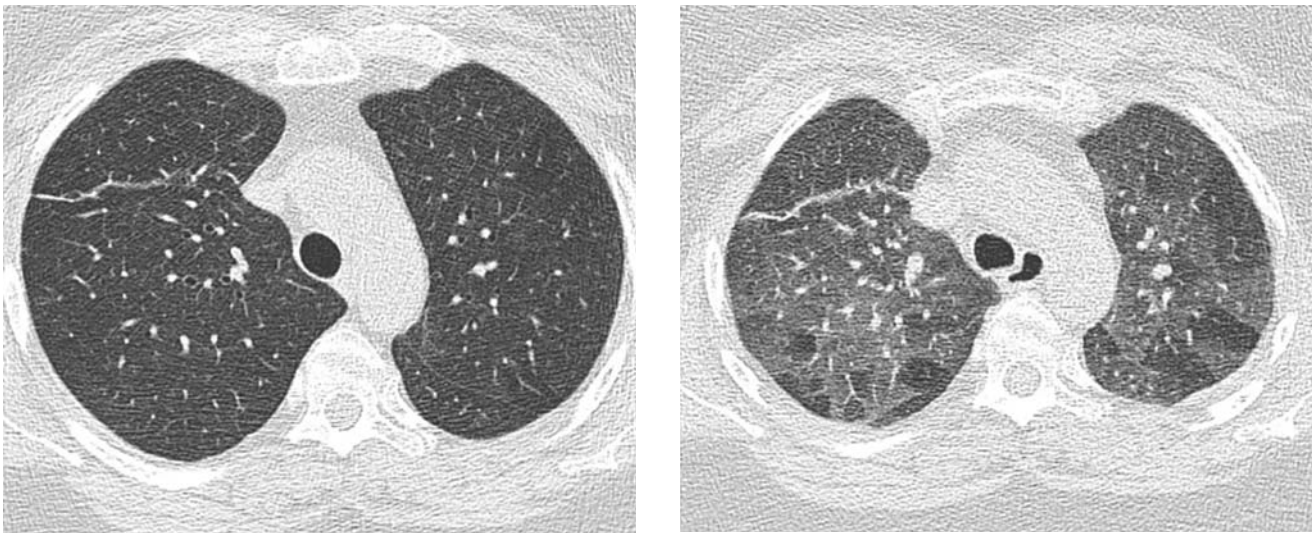

Figure 17. *Inspiration (a) and expiration (b) CT scans. Multiple large areas of air-trapping are seen in both lungs*

Table 4. *GGO distribution [2, 4, 11, 13]*

Patchy distribution	Diffuse distribution
Nonspecific interstitial pneumonia	Hypersensitivity pneumonitis
Desquamative interstitial pneumonia	Smoking related parenchymal lung disease, respiratory bronchiolitis (Respiratory bronchiolitis — interstitial lung disease, Desquamative interstitial pneumonia)
Hypersensitivity pneumonitis	
Alveolar proteinosis	Nonspecific interstitial pneumonia
Pulmonary embolism	Pneumonia (viral, bacterial, fungus)
Vasculitidis	Pulmonary edema
Sarcoidosis	Pulmonary embolism
	Acute respiratory distress syndrome
	Acute interstitial pneumonia
	Alveolar proteinosis

Table 5. *GGO localization [2, 4, 11, 13]*

Upper lung	Lower lung	Diffuse distribution
Sarcoidosis Туберкулез/Tuberculosis Chronic Eosinophilic pneumonia	Pulmonary edema Usual interstitial pneumonia [UIP]: idiopathic pulmonary fibrosis and disease associated UIP Nonspecific interstitial pneumonia Desquamative interstitial pneumonia Lymphocytic interstitial pneumonia (Sjögren syndrome, AIDS) Organising pneumonia Pulmonary embolism	Hypersensitivity pneumonitis Pneumonia (viral, bacterial, fungus) Sarcoidosis

developing the most optimal algorithm for choosing additional clinical and instrumental tests when you perform diagnoses. However, despite the knowledge about the formation mechanisms and radiographic features of CT sign of ground-glass opacity that you have learned, a doctor should primarily take into account the clinical picture of the disease when making a diagnosis.

Conflict of interests

Авторы заявляют, что данная работа, её тема, предмет и содержание не затрагивают конкурирующих интересов / The authors declare no conflict of interests.

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