Ground-glass opacification (GGO)

Introduction

Ground-glass opacification/opacity (GGO) is a descriptive term referring to an area of increased attenuation in the lung on computed tomography (CT) with preserved bronchial and vascular markings.

It is a non-specific sign with a wide range of aetiology including infection, chronic interstitial disease and acute alveolar disease.

Ground glass opacification is also used in chest radiography to refer to a region of hazy lung radio-opacity, often fairly diffuse, in which the edges of the pulmonary vessels may be difficult to appreciate .

The use of the term ground glass derives from the industrial technique in glassmaking whereby the surface of normal glass is roughened by grinding it.

Aetiology

Ground-glass opacities have a number of causes:

- Normal expiration

  On expiratory acquisitions, which can be detected if the posterior membranous wall of the trachea is flattened or bowed inwards

- Partial filling of air spaces
- Partial collapse of alveoli
- Interstitial thickening
- Inflammation
- Oedema
- Fibrosis
- Lepidic proliferation (a pattern of cell proliferation along the lining of the alveolar structures of the lung) of neoplasm

Infections

Opportunistic

- Pneumocystis pneumonia
- Cytomegalovirus (CMV) pneumonia
- Herpes simplex virus (HSV) pneumonia
- Respiratory syncytial virus (RSV) bronchiolitis: type of infectious bronchiolitis
- Other infectious causes

Non-opportunistic

- viral pneumonia

Coronaviruses

- COVID-19
- Middle East respiratory syndrome coronavirus (MERS-CoV) infection
- severe acute respiratory syndrome (SARS)

Patterns of GGO

There are seven general patterns of ground-glass opacities.

When combined with a patient's clinical signs and symptoms, the GGO pattern seen on imaging is useful in narrowing the differential diagnosis.

It is important to note that while some disease processes present as only one pattern, many can present with a mixture of GGO patterns.

1] **Diffuse**

The diffuse pattern typically refers to GGOs in multiple lobes of one or both lungs.

Broadly, a diffuse pattern of GGO can be caused by displacement of air with fluid, inflammatory debris, or fibrosis.

Cardiogenic pulmonary oedema and ARDS are common causes of a fluid-filled lung.

Diffuse alveolar haemorrhage is a rarer cause of diffuse GGO seen in some types of vasculitis, autoimmune conditions, and bleeding disorders.

Inflammation and fibrosis can also cause diffuse GGOs. *Pneumocystis pneumonia, an infection typically seen in immunocompromised (e.g. patients with AIDS) or immunosuppressed individuals, is a classic cause of diffuse GGOs.*

Many viral pneumonias and idiopathic interstitial pneumonias can also lead to a diffuse GGO pattern. Radiation pneumonitis, a side effect of pulmonary radiation therapy, can lead to pulmonary fibrosis and diffuse GGOs.

2] Nodular

There are numerous potential causes of nodular GGOs which can be broadly separated into benign and malignant conditions.

Benign conditions potentially leading to the formation of nodular GGOs include aspergillosis, acute eosinophilic pneumonia, focal interstitial fibrosis, granulomatosis with polyangiitis, IgA vasculitis, organizing pneumonia, pulmonary contusion, pulmonary Cryptococcus, and thoracic endometriosis.

Focal interstitial fibrosis presents a unique challenge when differentiating from malignant nodular GGOs on CT imaging. It is typically persistent over long-term imaging follow-up and shares a similar appearance to malignant nodular GGOs.

Pre-malignant or malignant causes of nodular GGOs include adenocarcinoma, adenocarcinoma in situ, and atypical adenomatous hyperplasia (AAH).

AAH is a pre-malignant cause of nodular GGO and is more commonly associated with lower attenuation on CT and smaller nodule size (<10 mm) compared to adenocarcinoma.

In addition, AAH often lacks the solid features and spiculated appearance that are often associated with malignant growths.

In contrast, as adenocarcinoma becomes invasive it will more often cause retraction of adjacent pleura and may show an increase in vascular markings.

Nodules >15 mm almost always represent an invasive adenocarcinoma.

3] **Centrilobular**

Centrilobular GGOs refer to opacities occurring within one or multiple secondary lobules of the lung, which consist of a respiratory bronchiole, small pulmonary artery, and the surrounding tissue.

A defining feature of these GGOs is the lack of involvement of the interlobular septum.

Potential causes of centrilobular GGOs include pulmonary calcifications from metastatic disease, some types of idiopathic interstitial pneumonias, hypersensitivity pneumonitis, aspiration pneumonitis, cholesterol granulomas, and pulmonary capillary hemangiomastosis.

4] **Mosaic**

A mosaic pattern of GGO refers to multiple irregular areas of both increased attenuation and decreased attenuation on CT.

It is often the result of occlusion of small pulmonary arteries or obstruction of small airways leading to air trapping.

Sarcoidosis is an additional cause of a mosaic GGOs due to the formation of granulomas in interstitial areas.

5] **Crazy paving**

The crazy paving pattern may occur when there is both interlobular and intralobular widening. This sometimes resembles a road paved with irregular bricks or tiles.

It is typically diffuse, involving larger areas of one or multiple lobes.

There are a variety of potential causes, including Pneumocystis pneumonia, late-stage adenocarcinoma, pulmonary oedema, some types of idiopathic interstitial pneumonias, diffuse alveolar haemorrhage, sarcoidosis, and pulmonary alveolar proteinosis.

COVID-19 has also been shown to occasionally cause GGOs with a crazy paving pattern.

6] **Halo sign**

A halo sign refers to a GGO that fills the area around a consolidation or nodule.

This is a most commonly seen in various types of pulmonary infections, including CMV pneumonia, tuberculosis, nocardia infection, some fungal pneumonias, and septic emboli. Schistosomiasis, a parasitic infection, also commonly presents with the halo sign.

7] **Reversed halo sign**

A reversed halo sign is a central ground-glass opacity surrounded by denser consolidation. According to published criteria, *the consolidation should form more than three-fourths of a circle and be at least 2 mm thick*.

It is often suggestive of only 20% of patients with organizing pneumonia.

It can also be present in lung infarction where the halo consists of haemorrhage, as well as in infectious diseases such as tuberculosis, and aspergillosis, as well as in granulomatosis with polyangiitis, lymphomatoid granulomatosis, and sarcoidosis.

Approach to GGO

History

Noted to be are:

- Fever
- Duration
- Smoking
- Industrial exposure suggestive of ILD
- Unprotected sexual exposure
- Response to regression with antibiotic course
- **SAARS CoV2 report – a must in this pandemic era.**

Nature of GGO

Nonpolygonal shape, apparent radial growth and clear-cut margins were associated with a malignant histology.

The stepwise approach adopted in the present study increased the diagnostic specificity and reduced time to definitive diagnosis. Whenever GGOs are seen in CT.

- Antibiotics - (levofloxacin 500 mg daily for 8 days) –and repeat CT to check if still persisting
- Diagnostic procedures –Bronchoscoy/ Mediastonoscopyetc as the situation (history) demands.
- Transthoracic needle aspiration biopsy –if no other non-invasive diagnostic procedure gives a way out.

Ground-glass opacity (GGO in the era of COVID-19

Thoracic imaging is fundamental in the diagnostic route of Coronavirus disease 2019 (COVID-19) especially in patients admitted to hospitals. In particular, chest computed tomography (CT) has a key role in identifying the typical features of the infection. **Ground-glass opacities (GGO) are one of the main CT findings, but their presence is not specific for this viral pneumonia.**

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In fact, GGO is a radiological sign of different pathologies with both acute and subacute/chronic clinical manifestations.

In the evaluation of a subject with focal or diffuse GGO, the radiologist has to know the patient's medical history to obtain a valid diagnostic hypothesis.

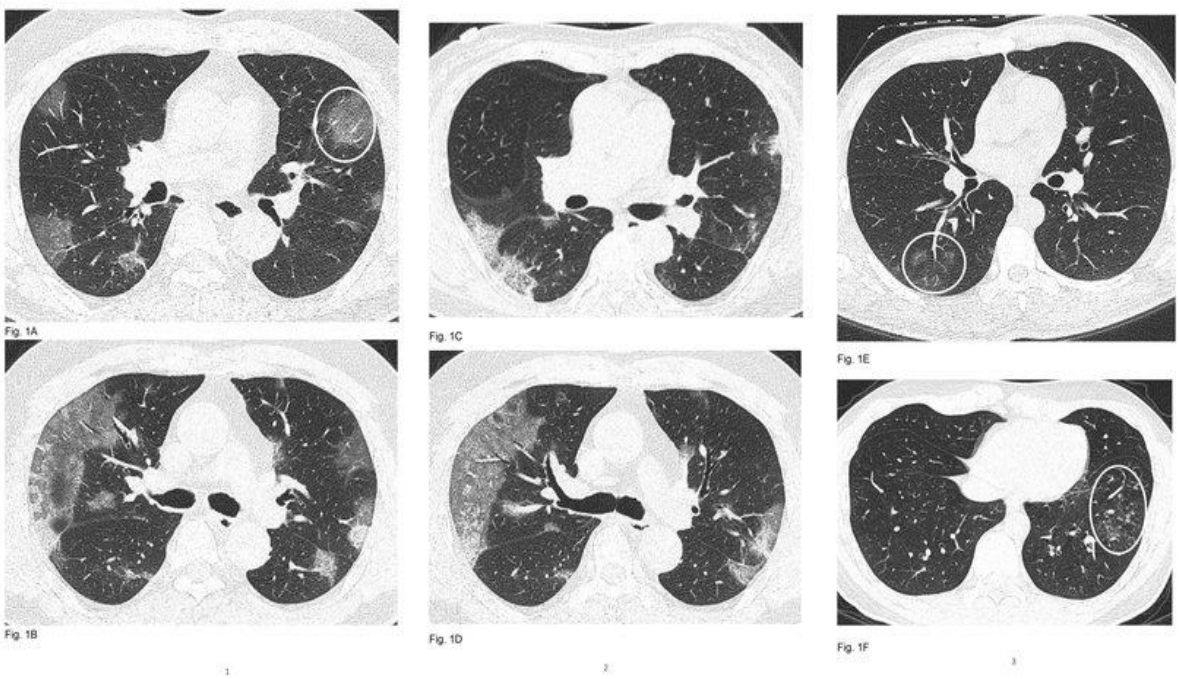
Points to be remembered before interpreting GGOs (in era of Covid)

- Clinical presentation
- History of fever and dry cough, diarrhoea o other systemic symptoms –Covid affects almost all systems of body.
- Degree of dyspnoea.
- Saturation levels at room air. Monitoring to see if it falls and patient starts air hunger requiring Oxygen.
- **Distribution of GGO –peripheral (lesions were mostly distributed bilaterally and close to the lower lungs or the pleura) – likely Covid and also the crazy-paving pattern and air bronchogram.**
- Pure GGO, vs GGO with consolidation - *Most of the COVID-19 lesions were located in multiple lobes in both lungs.*
- *Compared with that in the group with positive initial RT-PCR results, CT of the group with negative initial RT-PCR results was less likely to show pulmonary consolidation*
- The RT-PCR assay may be negative.Reasons are, either its early disease or not Covbid-19 but variants.

Conclusions

- GGO remains a diagnostic challenge.
- Although CT represents a fundamental diagnostic tool because of its sensitivity, it still needs to be integrated with clinical data to achieve the best clinical management.
- *In the presence of typical imaging features (e.g. GGO and consolidation), the radiologist should focus on the pandemic and manage a suspect patient as COVID-19 positive until proven to be negative.*
- When features were combined, GGOs with bilateral pulmonary distribution and GGOs with pleural distribution were more common among the positive patients
- The combinations with GGOs could be useful in the identification and differential diagnosis of COVID-19, alerting clinicians to isolate patients for prompt treatment and repeat RT-PCR tests until the end of incubation.

- *The main CT features were ground-glass opacity and consolidation with a sub pleural distribution (100%), in peripheral distribution is likely Covid GGOs.*
- *The less pulmonary consolidation found at CT, the greater is the possibility of negative initial RT-PCR results.*
- Thus chest CT is important in the screening of patients in whom Coronavirus disease is clinically suspected, especially those who have negative initial RT-PCR results.
- **But presence of GGO does not simply stamp the patient as a Covid –many issues discussed above needs to be considered**. Few examples are cited pictorially below.



1)APure GGO and Rounded GGO (circle)
2)B Mix GGO and consolidation
3)C Crazy-paving pattern
4)D Sub pleural band like areas of GGO Central (peribronchovascular) distribution (circle)

A-D are the images of COVID-19

5)ECentral (peribronchovascular) distribution (circle)
6)F Tree-in-bud sign(circle).

E-F are the images of non - COVID-19