Original Research Article

Decoding Focal GGO (Ground Glass opacity) by High Resolution Computed Tomography (HRCT) Scans

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Abstract

Background: Ground Glass Opacity (GGO) has been a perplexing dilemma for radiologists and clinicians as they have been notoriously non-specific in leading us to their underlying etiologies. The study aimed to differentiate focal non-neoplastic GGO from focal neoplastic GGO with the aid of High Resolution Computed Tomography (HRCT) scans. **Materials and method:** A total of 100 cases with clinical diagnosis and HRCT scan of focal GGO were retrospectively analyzed. The sample included 70 males and 30 females ranging from 40 to 75 years with a mean age of 55 years. 40 cases with no prior clinical symptoms, and diagnosed at the time of routine physical examination; 30 cases with cough or sputum; 20 cases with chest pain or chest tightness; 10 cases with hemoptysis and 40 cases with difficulty in breathing were included in the study. **Results:** There were 20 lesions with a fairly well defined shape and absence of bronchovascular markings within the lesions and 80 lesions with ill-defined margins and evidence of bronchovascular lesions within the lesions. **Conclusion:** Mere evidence or lack of evidence of bronchovascular markings in focal GGO on HRCT lungs, could offer a useful and vital evidence to differentiate neoplastic from non neoplastic focal lung GGO, excluding the need for unnecessary lung biopsies.

Key Words: Ground Glass Opacity, Focal Ground Glass Opacity, Computed Tomography, High Resolution Computed Tomography, Bronchoalveolar Carcinoma.

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INTRODUCTION

Lung ground-glass opacity (GGO) presents as a mild increase in the density of the lung on the high resolution computed tomography (HRCT). [1] In the mediastinal or soft tissue window of a computed tomography (CT) scan, GGO is hardly seen or not seen at all. Bronchial vascular bundles may or may not be visible within the lesion. GGO is a non-specific characteristic that may be associated with various diseases, including bronchoalveolar carcinoma (BAC). These signs can also be present in inflammation, edema, hemorrhage, fibrosis, cancer and multiple other diseases. [1, 2, 3] On a HRCT scan, four types of GGO have been documented: Type I (Simple ground glass-like shadow); Type II (Uneven density); Type III (Central high density with peripheral burring GGO) and Type IV (Nodular GGO). With the development of HRCT, the detection and diagnosis rate of lung GGO lesions has improved significantly. The study aimed to compare and analyze focal GGO lesions with their corresponding clinico-pathological results, with the aim of improving diagnosis and differential diagnosis**.** The study aimed to centre around two main differentiating factors in the focal

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GGO.[1,4,5] Firstly, Type A: GGO with no bronchovascular markings within it, and bronchovascular markings abruptly cut off at the edges of the GGO and secondly, Type B: GGO with bronchovascular markings identified within the GGO.

MATERIALS AND METHOD

Study design, setting and duration: A retrospective study was conducted at the Department of Radiodiagnosis at Jaipur National University Institute for Medical Science and Research Centre (JNUMISRC), Jaipur, Rajasthan, India over a duration of 2 years from January' 2017 to July' 2020.

Sample size and sample population: A total of 100 cases with clinical diagnosis and HRCT scan of focal GGO were retrospectively analyzed. The sample included 70 males and 30 females ranging from 40 to 75 years with a mean age of 55 years. 40 cases with no prior clinical symptoms, and diagnosed at the time of routine physical examination; 30 cases with cough or sputum; 20 cases with chest pain or chest tightness; 10 cases with hemoptysis and 40 cases with difficulty in breathing were included in the study. Only focal GGO cases were included in the study. Diffuse GGO involving large portions of lungs were excluded from this study.

Methodology:

All patients underwent pulmonary multi slice spiral CT examination by using Toshiba Alexion 16 slice CT scan machine (Toshiba, Germany). Patients were scanned in the supine position at end-expiration. Scan range was from the apex to the base of the lung, including both sides of the chest wall and axillary. The scan parameters were as follows: Tube voltage, 120–140 kV and reconstructed slice thickness: 0.5–1 mm. 20 of these patients were injected with non-ionic iodinated contrast medium iohexol, omnipaque (350 mgI/ml, 1.0–1.5 ml/kg, flow rate of 3–4 ml/sec) into the ulnar vein with a binocular high-pressure rapid injector syringe for an enhanced CT scan. Patients were scanned at 25 and 75 sec after injection, for the vascular and parenchymal phases, respectively. 20 of the total number of included patients underwent subsequently CT guided FNAC (Fine Needle Aspiration Cytology)/Biopsy and remaining were followed after appropriate non-surgical medical treatment and were compared with follow-up HRCT to evaluate progress or regression of the lesion. GGO was categorized into four types according to CT scan observation: Type I, II, III and IV, and Type A and B ((based on bronchial markings) as described previously. The present study focused primarily with Type A and B forms of focal GGO.

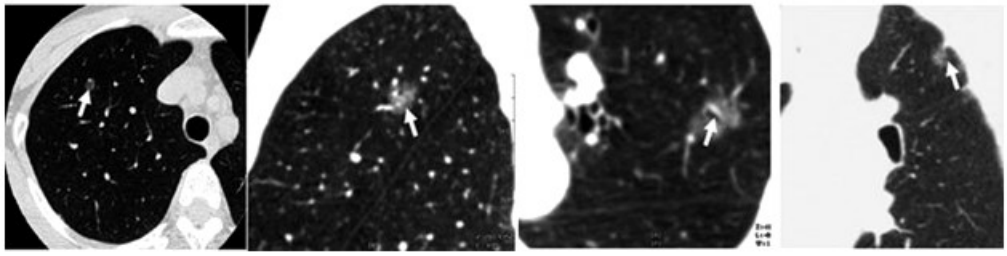
Analysis: Descriptive analysis was done**.** The location, size, shape (round, oval, irregular), edges (lobulated, burring, spinous process), side surface (clear, rough, fuzzy) and surroundings (vascular convergence, pleural indentation) of lesions were analyzed with plain and enhanced CT scan. Bronchovascular markings in and around the focal GGO were analyzed. For Bronchoalveolar carcinoma (BAC) analysis, CT guided FNAC / Biopsy tissues were preserved in formaldehyde and sent to department of pathology.

Ethical approval and consent: Approval was sought and obtained by the Institutional Ethics Committee and informed consent was taken from the included sample of patients, prior to conducting this study.

RESULTS

Patterns of focal GGO

Amongst a total of 100 cases, 28 lesions in the right upper lobe, 20 lesions in the right middle lobe, 10 lesions in the right lower lobe, 12 lesions in the left upper lobe, 10 lesions in the left middle lobe and 20 lesions in the left lower lobe were reported. Out of them, 10 lesions with diameter less than 1.0 cm, 30 lesions with diameter of 1.0–1.5 cm, 20 lesions with diameter of 1.6–2.0 cm, 20 lesions with diameter of 2.0–3.0 cm and 20 lesions with diameter of 2.5–4.0 cm were reported. In all these lesions, the focus of the present study was on the presence or absence of bronchovascular markings within the focal GGO irrespective of their shapes and sizes. There were 20 lesions with a fairly well defined shape and absence of bronchovascular markings within the lesions and 80 lesions with ill-defined margins and evidence of bronchovascular lesions within the lesions. There were 20 lesions with a fairly well defined shape and absence of bronchovascular markings within the lesions and 80 lesions with ill-defined margins and evidence of bronchovascular lesions within the lesions.



A B C D

Figure 1: Types of focal GGO on HRCT imaging [4]

DISCUSSION

Ground-glass opacity (GGO) is a radiological term indicating an area of hazy increased lung opacity through which vessels and bronchial structures may still be seen. It is less opaque than consolidation, in which such structures are obscured. Most commonly, diffuse GGOs are associated with widespread inflammatory or infiltrative lung disorders. GGO is a hazy, dense shadow in the lung that appears on high-resolution CT of the bronchus or pulmonary vasculature. [5, 6, 7] This manifestation is non-specific and can be seen in inflammation, injury, edema, hemorrhage, focal fibrosis, cancer or atypical adenomatous hyperplasia. GGO formation results in incomplete filling of air cavity, mild interstitial thickening and partial alveolar depression. An increasing number of patients are clinically diagnosed with lung GGO, for unknown reasons. Timely detection and diagnosis of GGO is critical to future treatment and prognosis. Figure 1 describes the types of focal GGO on HRCT imaging. [4] Figure 1A displays Nodular GGO in the right lung with round shape and no burring edges. Figure 1B shows burring edge with confirmation of BAC on pathological analysis. Figure 1C shows GGO with air bronchogram. Figure 1D shows GGO under visceral pleura with surrounding pleural indentation sign with confirmation of BAC on pathological analysis. In the current study, it is our endeavour to analyze focal GGO purely on the basis of visualization or non visualization of bronchovascular markings within the GGO, as the sole criteria to differentiate non-neoplastic from neoplastic GGO. Based on the association between GGO and its pathology, GGO was categorized into four types according to CT scans (Figure 2).[4] Type I GGO is simple (Figure 2A, 2B, 2C, 2D); Type II GGO is with uneven density (Figure 2E and 2F), Type III is with central high density and peripheral burring and Type IV is nodular (Figure 2G and 2H). Pathology of Type IV GGO revealed the tumor was solid, with no air filling, proliferation of elastic fibers and interrupted or destroyed reticular structure in the tumor. The malignancy ratio was 68.0% in GGO type I, 61.7% in type II, 73.6% in type III and 70.5% in type IV.[4]

Figure 2: GGO CT classifications. (A) and (B) Simple GGO nodules in the upper lobe with clear boundary and shape, without burring. (A) GGO type IV and (B) type III were indicated. (C) Bronchial vascular bundle shown in GGO type II. (D) Pathology demonstrated incomplete filling of air cavity, mild interstitial thickening and partial alveolar depression, with pathology of BAC (GGO type I). (E) CT image showed nodules of uneven density (GGO type I). (F) Pathology indicated alveolar collapse and severe hyperplasia of elastic fibers in tumor (GGO type II). (G) CT image showed nodules of homogeneous soft tissue density (GGO type IV). (H) Pathology showed elastic fiber proliferation in tumor with interrupted and destroyed reticular structure, and pathology of lung cancer.[4]

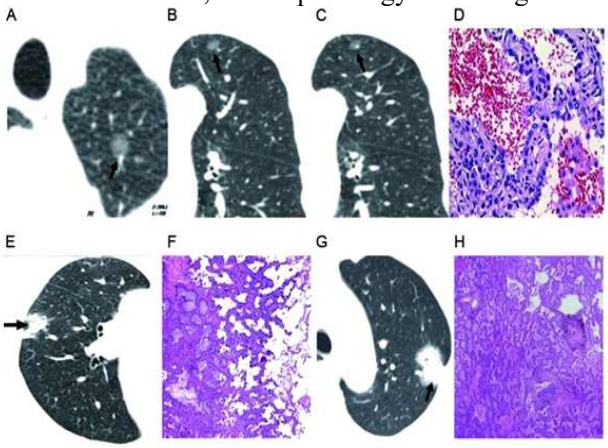


Figure 2: A,B,C,D,E,F,G,H

GGO lesions can be caused by numerous pathological changes, which generally present as incomplete filling of the alveolar cavity with cells and liquids (such as edema and hemorrhage), or lung interstitial thickening due to inflammation, edema, fibrosis or cancer. At end-expiration, the volume of alveolar air is reduced; lung interstitial volume is normal and the number of alveolar follicles in the alveolar unit increases. However, with a small amount of liquid or early gas-liquid presence in alveoli, and restricted spatial resolution of high-resolution CT, it is hard to distinguish these pathology changes from the thickening of the alveolar walls. Lung focal GGO is usually associated with atypical adenomatous hyperplasia (AAH) and BAC.[4, 5] It has previously been reported that AAH is a precancerous lesion of lung cancer. This type generally consists of smaller lesions, with no leaf or burring edges on CT. Simple GGO can also end being BAC. The BAC lesions were larger than AAH, with high density, air bronchogram, burring and leaf edges, thus these two types of cancer can be differentiated by CT.

Yang *et al.* reported that out of 55 cases of BAC, 56% showed air bronchogram. [8] If BAC is of peripheral type, pleural indentation may be visible. Solid GGO is generally shown in adenocarcinoma, which is usually larger than an AHH lesion. BAC can also show heterogeneous density with strips or patchy shadows and pleural indentation, with a smaller proportion of solid GGO compared with adenocarcinoma. It has been reported that mixed GGO density is of higher lung cancer incidence. Therefore, mixed GGO density should be considered as high-risk and surgical intervention is highly recommended. GGO can also be a sign of inflammation[4, 5], thus regular follow-up is important to determine the nature of the lesions and further treatment. When GGO is reported on a

CT scan, inflammation should be ruled out first. Kodama showed that focal GGO resulting from acute inflammation or hemorrhage can be resolved in the first three months of follow-up. If the size or density of the lesion increases within 3–6 months, it is necessary to determine the nature of the lesions. If the lesion has remained the same size or slightly increased, combined with cancer history, malignancy is of a higher possibility. If the lesion has burring or leaf edges, lung biopsy should be conducted for diagnosis. In the follow-up, regardless of the GGO size, if soft tissue has increased, adenocarcinoma is possible and surgical intervention is recommended. Focal GGOs, also called nonsolid or part-solid nodules, are circumscribed areas of hazy lung opacity. Their association with early-stage bronchioloalveolar carcinoma (BAC) was first reported in the 1990s by Japanese and Korean investigators. Since then, a number of publications have addressed the clinical significance of focal GGOs and their relationship with atypical adenomatous hyperplasia (AAH), BAC and invasive adenocarcinoma. In spite of various studies since as early as 1990, GGO diagnosis has remained elusive. Through this study we hope to establish that irrelevant of shape, size and location of the GGO and the absence or presence of air bronchograms the sole criteria of existence of bronchovascular markings in the GGO indicate a non neoplastic lesion compared to the absence of bronchovascular marking in neoplastic GGO. As displayed in the HRCT of thorax[5] (Figure 3) it can be observed that, based on the principles of our present study, there are no bronchovascular markings seen in GGO in 3(a) and 3(c) which are hence neoplastic, and with bronchovascular markings traversing through the GGO in 3(b) and 3(d) which are non neoplastic GGO. This feature along with follow up scans and biopsy would exclude neoplastic from non neoplastic GGO. While reaching this conclusion in this study, the only criteria was the presence or absence of bronchovascular markings in the GGO, and no other criteria of shape, size , appearance or location was followed, thus enabling a simplified approach to analyzing GGO.[4, 5, 7] Figure 3: Benign and malignant ground-glass opacities (GGO) with close resemblance. a) GGO with irregular contours, clear-cut margins, and tiny air spaces. Diagnosed as adenocarcinoma. b) Similar lesion, with irregular contour, clear-cut margins, a minimal solid component and tiny air spaces. The biopsy yielded inflammatory tissue. c) GGO in the right lower lobe, with irregular shape and minimal solid component. The biopsy was suggestive of bronchioloalveolar carcinoma d) Similar lesion in the left lower lobe, with irregular shape and minimal solid component. The biopsy revealed inflammation and fibrosis. [5]

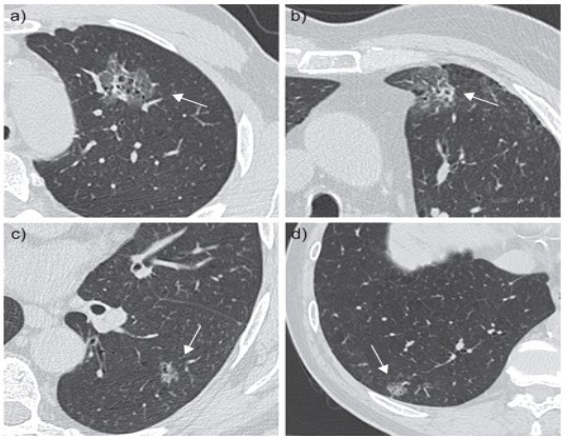


Figure 3: A, B, C, D

It was observed in this study that GGO which showed bronchovascular areas within the GGO were non neoplastic, compared to neoplastic GGO which had no evidence of bronchovascular markings within them. Again using the same principle as discussed earlier, in above Figure 4[5], it is seen that there are obvious bronchovascular markings in the GGO in 4(a) which according to our theory should be a benign lesion and is subsequently proved non neoplastic, supporting our theory. There is absence of bronchovascular markings in GGO seen in 4(b) indicating a neoplastic lesion, based on this study.

Figure 4: (a) GGO in the right lower lobe. Following antibiotic treatment, the lesion regressed (b) GGO with polygonal shape. This patient had adenocarcinoma.[5]

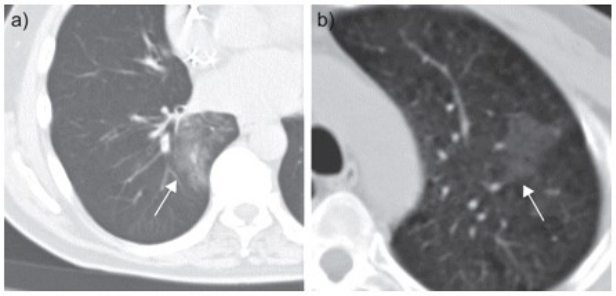


Figure 4: A, B

CONCLUSION

In conclusion, mere evidence or lack of evidence of bronchovascular markings in focal GGO on HRCT lungs, could offer a useful and vital evidence to differentiate neoplastic from non neoplastic focal lung GGO, excluding the need for unnecessary lung biopsies.

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