



Incidentally Discovered Sub-centimetre Pre-invasive Ground Glass Adenocarcinoma of the Lung: A Case Report

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Abstract

Appropriate radiological imaging techniques including High Resolution CT scan of the chest (HRCT) are now available that detect ground-glass-opacities (GGOs) in the lung which are not detected by plain Chest X-rays. The aim of the study was to report a case of an-incidentally detected GGO during follow-up assessment for colonic cancer. A 54-year-old woman who had been having yearly appropriate radiological imaging follow-up assessments at yearly intervals pursuant to having colonic resection for colon cancer was found incidentally to have a sub-centimetre ground-glass-opacity in the lung which had subsequently increased in size minimally. Microscopic examination and immunohistochemistry of the excised lung lesion showed a primary adenocarcinoma of lung origin, in early in situ phase. Literature review had shown that GGOs have minimal or no invasive growth and limited resection of curative intent is justified, therefore it is important that these GGOs are detected by means of appropriate radiological imaging in order to provide minimal resection at an early phase of the disease. Developments in radiological imaging had enabled early detection of adenocarcinoma in situ of the lung in our case. Developments in radiological imaging techniques, now enables early detection of GGOs which enables limited curative resection of the lesions.

Key Words: Pre-invasive adenocarcinoma of the lung; ground glass opacities; TTF-1 antibody; immunohistochemistry; limited resection

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Introduction

Radiological imaging forms part of the follow-up assessment of patients who have

undergone various types of treatment for carcinomas. Targeted High Resolution CT scan of the chest (HRCT) is now used in the follow-up assessment of patients who have undergone treatment for carcinoma in addition to other imaging modalities. We report a case of an incidentally detected sub-centimetre GGO which subsequently minimally increased in size in the ensuing paper.

Case Report

A 54-year-old woman had undergone colonic resection for carcinoma of the colon and she had subsequently been undergoing follow-up investigations. She had radiological imaging (including chest X-ray and other imaging procedures) which revealed regional lymphadenopathy but no radiological evidence of distant metastasis. She had a follow-up CT scan of thorax, abdomen and pelvis 2

years later, which showed an incidental, small ground glass opacity in the upper lobe of the right lung. She had yearly follow-up CT scans at her 3, 4, 5, and 6 years follow-up which had shown minimal marginal increase in the size of the small ground glass opacity in the successive scans (see illustrations 1 to 9 which depict various stages of the imaging and explanations of steps taken). The ground glass opacity was PET/CT scan negative in the 4th year follow-up scan. Nevertheless, she underwent excision of the opacity in the 6th year. Pathological examination of the excised lung lesion showed a primary adenocarcinoma of lung origin, in early in situ phase, which was confirmed by the positivity of the tumour for TTF-1 antibody on immunohistochemical staining (see illustrations 10, 11 and 12 for the microscopic and immunohistochemistry features). As a result the regular radiological follow-up imaging, the incidental lung lesion was detected at an early stage and it was surgically excised.

Discussion

Ground glass opacities (GGOs) seen on radiological imaging can be attributed to a variety of causes. Some of the causes of GGOs that are seen on radiological imaging include: inflammatory disorders, primary and metastatic neoplasms. In order to establish the cause of a GGO, a biopsy of the lesion is often necessary for pathological examination. Gaeta et al. [1] undertook a retrospective study of 65 patients who had proven lung metastasis from gastrointestinal tumours. Gaeta et al. [1] stated that air-space lung metastasis from gastrointestinal tumours is uncommon but not rare. Gaeta et al. [1] indicated that the results of the retrospective study did reveal that based upon CT scan and microscopic examination, differentiating between air-space metastasis and bronchiolo-alveolar carcinoma (BAC) may prove impossible. The air-space metastases that were found by Gaeta et al. [1] in their study included: three from carcinoma of the pancreas, two from carcinoma of colon, and one from carcinoma of jejunum.

Gaeta et al. [2] explored for patterns of CT scans in order to classify air-space lung metastases including air-space nodules, lung consolidation associated with an air-bronchogram with or without an angiogram sign, ground glass opacification (focal or diffuse), and nodules with a halo “sign”. Gaeta et al. [2] described the computerized tomography (CT) scan findings in a retrospective study of 18 patients who had a known bronchioloalveolar carcinoma (BAL) in the lung. Gaeta et al. [2] reported that out of

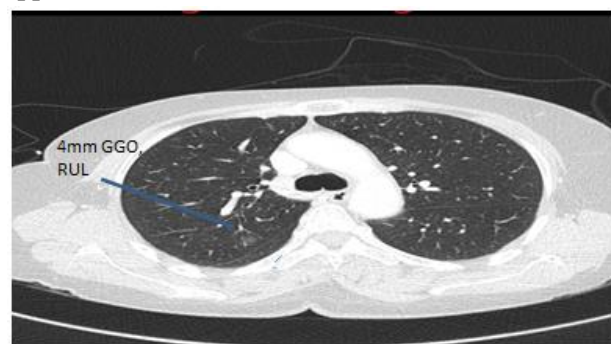
the 18 cases, the surgical specimens were available together with CT scan and histological correlation in 13 cases. Gaeta et al. [2] described three patterns which included: (1) Solitary pulmonary nodule (SPL), (2) lung mass / consolidation, (3) multi-centre or diffuse disease. Gaeta et al. [2] observed that many of the radiological features had been similar to other primary lung cancers and metastatic lung diseases. Gaeta et al. [2] recommended that BAL should be considered in the differential diagnosis of solitary pulmonary nodules (SPNs), multiple pulmonary nodules (MPNs), and chronic alveolar opacities. Gaeta et al. [2] iterated that the diagnosis of BAL is important, when it manifests as a SPN, in view of the fact that approximately 70% of the patients at this stage recover.

Illustration 1

HISTORY

- A middle age female with colon cancer with regional lymph nodes. No distant metastasis
- First survey Ct scan to look for metastasis showed: Incidental 4 mm ground glass opacity at the right upper lobe.
- Follow up CT scans revealed:
 - Very minimal increase in size in the subsequent four years, up to 6 mm
- PET CT scan was :negative, performed 2 years of the first presentation
- The ground glass opacity was excised after 4 years due to the persistence of this opacity, regardless of the negative PET scan

Illustration 2: First CT scan of the chest showing incidental small ground glass opacity at the right upper lobe.



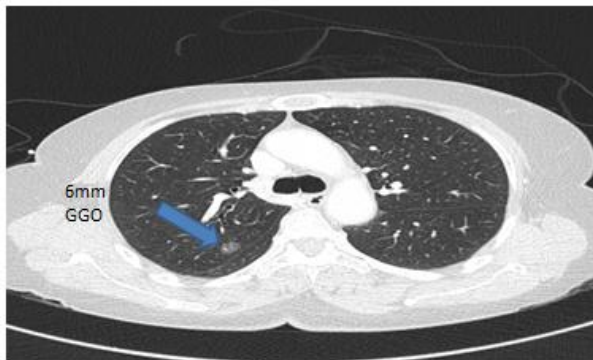
Mizuuchi et al. [3] reported a 57-year-old man, who had undergone surgical resection of a malignant melanoma of the right bulbar conjunctiva at the age of 51 years. He was referred for management of a ground glass opacity which was found in his lung in his follow-up investigation. The reports of the radiological examination of the nodule suggested that the lesion was an adenocarcinoma in

situ. He had a CT scan of the thorax, 9 months later which had shown that the nodule had increased in size from 6 mm to 8 mm and which had further grown and increased in size to 10 mm after another six months. The patient underwent partial resection of the lung nodule and histological examination of the specimen showed atypical cells with melanin granules proliferating in a lepidic-like fashion. Immunohistochemistry of the specimen revealed positive staining for S-100 which had indicated that the lesion was a pulmonary metastasis from malignant melanoma. Mizuuchi et al. [3] stated that the lesion was a solitary pulmonary metastasis from malignant melanoma which had presented as a pulmonary ground-glass nodule. Mizuuchi et al. [3] further stated that metastatic cancer from malignant melanoma can present as ground glass opacities and that metastasis from malignant melanoma should be considered in the differential diagnosis of ground-glass opacities.

Illustration 3: CT scan of the chest, one year later, showing minimal increase in size of the GGO up to 5 mm



Illustration 4: CT scan of the chest 2 years later showing minimal increase in size up to 6 mm



Oikonomou et al. [4] reported a patient who had never smoked and who was found to have a solitary ill-defined nodule, (a ground-glass-opacity) in the middle lobe of the lung. The nodule (area of

opacity) was resected and histological examination of the specimen showed a well differentiated adenocarcinoma. Oikonomou et al. [4] also reported that the lung cancer was associated with neurofibromatosis type 1. Oikonomou et al. [4] further reported that the patient who did not receive any chemotherapy or radiotherapy was alive and free of disease after 18 months.

Illustration 5

PET SCAN showing no avid uptake at the location of the GGO(NEGATIVE TEST)

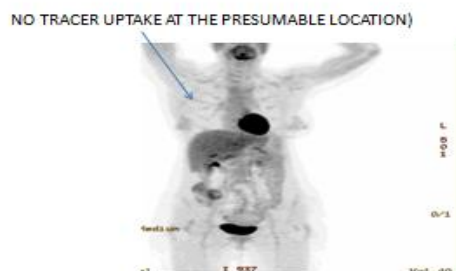
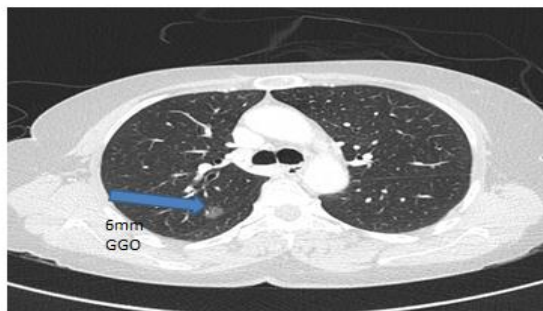


Illustration 6

CT scan of the chest performed 3 years later, showing no interval growth



Chun et al. [5] examined 68 ground-glass-nodules of 45 patients who had undergone PET/CT scan within 1 week pursuant to having CT scan of the chest. A definite diagnosis was established upon histological examination of specimens of the resected nodules. The reported histological examination findings of the nodules included: adenocarcinoma, bronchiolo-alveolar carcinoma (BAC), low-grade lymphoma, metastatic mucinous adenocarcinoma, and unknown low-grade malignancy. Inflammatory ground-glass-nodules (GGNs) were confirmed as pneumonic infiltration in view of the fact that they resolved on subsequent follow-up CT scans and the fact that there were often associated compatible clinical features of chronic inflammation. Chun et al.

[5] stated that the Standard Uptake Value (SUV) was determined for each nodule and that with regard to part-solid nodules the maximum SUV was significantly higher in inflammation. Nevertheless, paradoxical results did occur in part-solid inflammatory nodules with positive FGG-PET making their differentiation from malignant nodules difficult.

Illustration 7: Last CT scan 4 years later, revealing no change compared to last exam

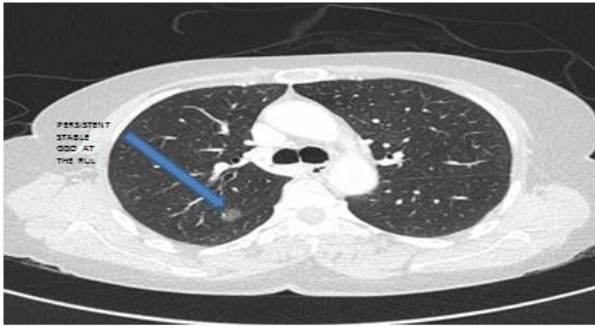
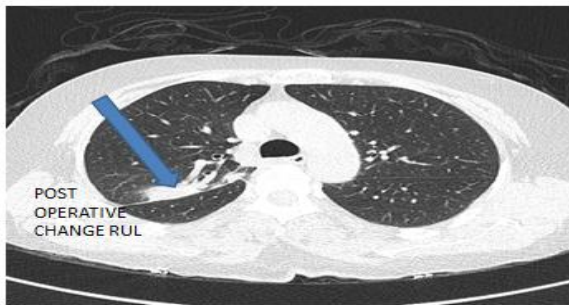


Illustration 8

- Due to persistent opacity in the lung, excision was recommended, despite the negative PET scan

Illustration 9

CT scan of the chest, post excision with post operative changes



Asamura et al. [6] reported a study of 1769 lung tumours which were discovered based on HRCT scans over a period of ten years. They reported that many more faint sub-centimetre lesions were discovered which were unlikely to be picked up on routine chest X-rays. Asamura et al. [6] showed that sub-centimetre ground-glass opacity (GGO) lesions (both non-solid and part-solid) were true early lung cancers. Asamura et al. [6] stated that in view of the fact that GGOs have minimal or no invasive growth, surgical procedure of limited resection is justified.

Illustration 10

Hematoxyline and Eosin section at X200. The inset shows hyperchromatic columnar cells lining thin septa X400.

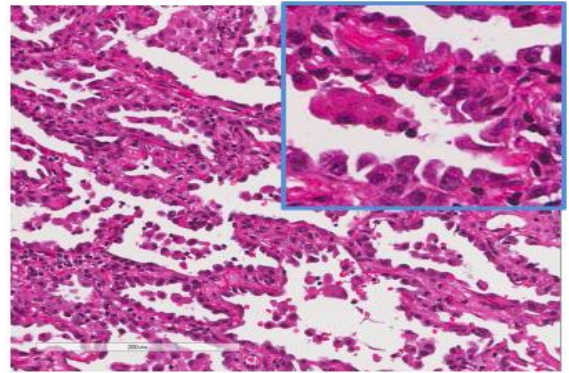


Illustration 11

Low power whole slide image WSI. There is a well demarcated sub pleural lesion, sized 1.0 cm (Blue circle)

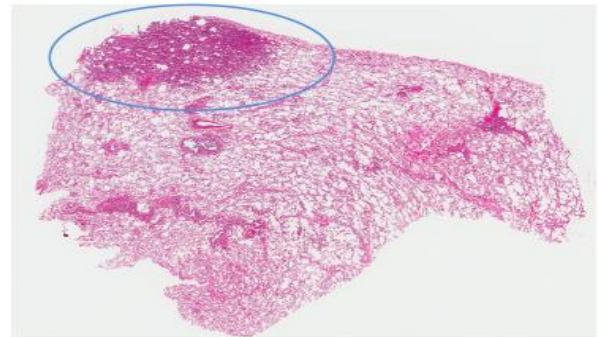
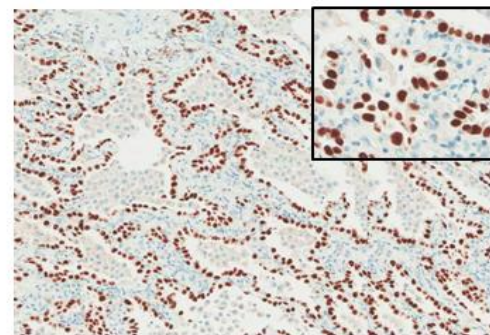


Illustration 12

The tall columnar cells lining the alveolar septae are stained positive for TTF-1 antibodies, this confirm that they are pneumocytes X200. The inset show pleomorphism X400



The International Association for the study of Lung Cancer / American Thoracic Society / European Respiratory Society International Multidisciplinary Classification of Lung Adenocarcinoma [7] have issued new guidelines IASLC/ATS/ERS on the classification of lung adenocarcinoma in resection

specimens. This new classification includes the following: (1) Pre-invasive lesions with two subtypes which comprises atypical adenomatous hyperplasia and carcinoma in situ (less than or equal to 3cm, formerly called BAC), (2) minimally invasive adenocarcinoma, (3) invasive adenocarcinoma, (4) variants of invasive adenocarcinoma.

Documentations of our miscellaneous narrations from the preceding reported publications do indicate that the use of dedicated targeted HRCT scans has resulted in the discovery of many faint sub-centimetre ground-glass-opacities (GGOs) which are not seen on routine chest X-rays. Some of these sub-centimetre GGOs are seen in low-risk population and non-smokers, while in others, these lesions do represent second lung cancers. Many of these GGOs have minimal or no invasive growth, and limited surgical resection for cure can be justified.

Conclusion

The use of dedicated targeted High Resolution CT scan of the chest (HRCT) has resulted in the discovery of many sub-centimetre faint ground glass opacities which are usually not seen in routine chest X-rays.

Conflict of Interest: None

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