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Case Report

Hilly or mountainous surface: a new CT feature to predict the behavior of pure ground glass nodules?

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ABSTRACT

Persistent pure ground-glass nodules (pGGNs) typically show an indolent course with very slow growth rates. These slow-growing lesions exhibit different growth patterns regardless of their initial computed tomography (CT) features. Therefore, predicting the aggressive behavior of pGGNs on initial CT remains a diagnostic challenge. The literature reports that computerized analysis and various quantitative features have been tested to improve the risk stratification for pGGNs.

The present article describes the long-term follow-up of two pGGNs with different behavior and introduces, for the first time, a new computerized method of analysis that could be helpful for predicting the future behavior of pGGNs.

1. Introduction

Subsolid nodules (SSNs) manifest on thin-section computed tomography (CT) as focal ground-glass opacities. SSNs are classified as part solid or pure ground glass nodules (pGGNs) according to the presence or absence of a solid component within the lesion [1].

SSNs represent a major diagnostic challenge, as they may be the manifestation of benign and malignant conditions [2]. Malignancies exhibiting ground glass opacity (most often lepidic predominant adenocarcinoma) may remain unchanged for years [2] or show heterogeneous growth patterns with a trend toward a progressive increase in size over time [3].

Persistent SSNs have a high likelihood to represent pre-invasive or invasive adenocarcinomas, particularly part-solid nodules [3–5]. As a result, the updated Fleischner Society guidelines for the management of SSNs, published at the beginning of 2017, recommend a follow-up period for every pGGN or part-solid nodules ≥ 6 mm in diameter [1]. Conversely, for SSNs smaller than 6 mm in diameter, no routine follow-up is recommended [1].

The literature reports that approximately 80% of pGGNs remain unchanged for an extended period [2]; therefore, conservative monitoring of these lesions is justified. However, some authors demonstrate that more than 40% of pGGNs with initial size ≥ 10 mm exhibited growth during follow-up [6]. In addition, other authors reported that persistent pGGNs ≥ 10 mm in diameter should be considered as early adenocarcinomas or their precursors, until proven otherwise [7]. However, it is unclear whether all such lesions should be surgically resected, as most of these lesions will never become clinically evident [2]. As a result, for pGGNs ≥ 10 mm in diameter, a CT follow-up at 6 months and then every 2 years until 5 years is recommended to confirm the absence of growth [1].

Previous studies on the natural history of pGGNs showed that initial size and development of a solid component within the lesion were associated with nodule growth [6,8]. However, a recent study reported that growth was independent from the initial CT features (such as diameter, volume, mean CT attenuation, and mass) and that only the doubling times may provide information on a nodules' aggressiveness [3]. Thus, predicting the aggressive behavior of pGGNs on initial CT remains a complex diagnostic challenge.

The current report describes the natural course of two pGGNs with an initial size close to 10 mm and long-term CT follow-up periods of 7 and 10 years. One pGGN remained stable in size without the development of a solid component, while the other pGGN showed significant growth with the development of an intralesional solid component and bubbly lucencies. The retrospective computerized analysis of these two pGGNs performed on initial thin-section CT images using a three-

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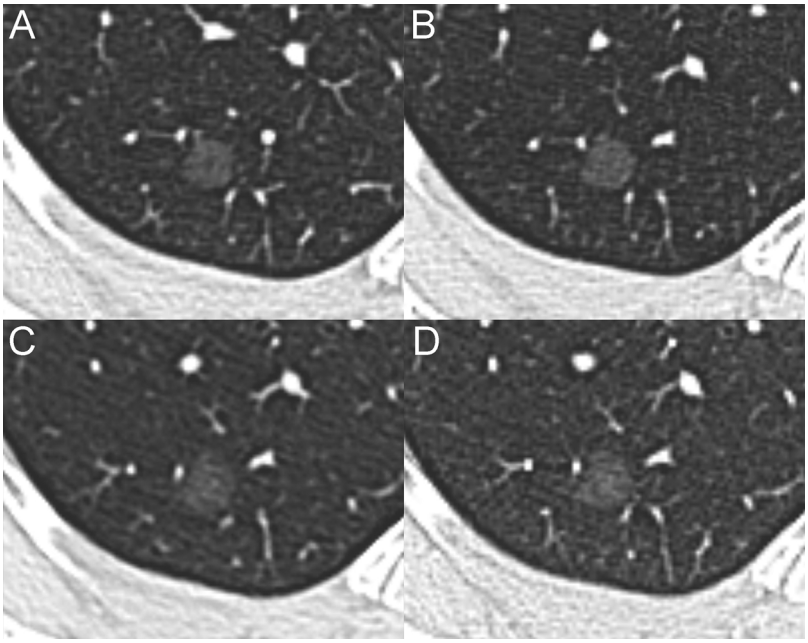

Fig. 1. Serial MDCT scans of the stable pGGN. (A) The baseline MDCT shows a pGGN (mean diameter, 10 mm) in the posterior segment of the right upper lobe. The follow-up CT scans performed at 23 (B), 61 (C) and 83 months (D) reveal the stability of the lesion.

dimensional (3D) surface plot revealed a new distinguishing feature. Therefore, we present this new distinguishing feature and its possible future prospects for differentiating pGGNs ≥ 10 mm that should be followed from those that should be resected.

2. Case report

2.1. Case 1

A 29-year-old Caucasian woman was referred to our radiology department for the monitoring of an endobronchial carcinoid previously located in the right main bronchus and treated with laser.

For this indication, a multidetector computed tomography (MDCT) scan with and without contrast was performed. The patient was asymptomatic and in good health. No sign of persistence or relapse of disease was found on the MDCT scan. However, a pGGN 10 mm in diameter (average of long- and short-axis diameters on the largest cross-sectional area of the lesion) was detected in the posterior segment of the right upper lobe (Fig. 1A). Possible radiologic diagnosis included inflammatory transient lesions and persistent lesions, such as atypical adenomatous hyperplasia and adenocarcinoma in situ. Follow-up CT scans performed 12 and 23 months later revealed the persistence of the nodule without a significant change in the axial diameter (Fig. 1B). Based on the age and history of the patient and the MDCT findings, a long-term follow-up was recommended. Follow-up CT scans at 61 and 83 months showed the stability of the lesion (Fig. 1C and D). Therefore, the patient was reassured, and no further follow-up was recommended.

2.2. Case 2

A 60-year-old Caucasian woman with a previous history of non-Hodgkin lymphoma was referred to our radiology department for the persistence of a consolidation in the left lower lobe.

For this, a MDCT scan without contrast was performed. The MDCT scan showed an irregular consolidation in the left lower lobe (Fig. 2) and a pGGN 12 mm in mean diameter in the anterior segment of the right upper lobe (Fig. 3A). Bronchoscopy and biopsy focused on the left irregular consolidation revealed squamous cell lung cancer. Therefore, a left lower lobectomy was performed with a histological diagnosis of squamous cell lung cancer (pT3N0M0).

For pGGN in the right upper lobe, possible radiologic diagnosis included inflammatory transient lesions and persistent lesions such as atypical adenomatous hyperplasia and adenocarcinoma in situ. A follow-up CT scan performed 12 months later revealed the persistence of pGGN with an initial change in the axial diameters (from 12 mm to 15 mm) (Fig. 3B). No sign of persistence or relapse of disease was found in the left lung. Based on the history of the patient and the MDCT findings, periodic follow-up was suggested. Follow-up CT at 25 and 42 months (Fig. 3C and D) revealed a progressive increase in size of the pGGN and the development of a bubbly lucency within the lesion. The subsequent CT follow-up scans, the last performed at 106 months from baseline, showed a further significant increase in the size of the lesion, numeric and dimensional growth of the bubbly lucencies and development of an intralesional solid component (Fig. 3E). The aggressive behavior of the lesion was considered highly suspicious for a radiological diagnosis of lepidic predominant invasive adenocarcinoma. Therefore, a bronchoscopy with transbronchial biopsy was recommended. The multiple transbronchial biopsies performed within the area of the lesion were negative for neoplastic cells. Despite this result, the lesion was still considered highly suspicious. Based on the comorbidities (chronic HBV-related liver disease, chronic kidney disease stage 3 A, peripheral arterial disease of the lower extremities, Raynaud syndrome) and the clinical status of the patient, surgical treatment was not recommended, and only periodic CT follow-up was suggested. The next CT follow-up scan, performed 120 months after baseline, revealed a significant change in the morphology of the lesion characterized by the collapse of the bubbly lucencies and a further significant increase in the solid component showing peripheral calcifications (Fig. 3F). The PET-CT scan, obtained 1 month later, showed fluorodeoxyglucose (FDG) uptake of the intralesional solid component (SUVmax 4.7) (Fig. 4). No other active lesions in the rest of the body were detected; particularly, non-pathological FDG uptake was observed in hilar or mediastinal lymph nodes. Based on the CT and PET-CT findings and the comorbidities of the patient, stereotactic radiotherapy or radiofrequency ablation was suggested as a valid therapeutic option.