CASE REPORT

Evaluation of pure ground glass pulmonary nodule: a case report

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A pulmonary nodule is a single, nearly spherical, well-circumscribed pulmonary opacity up to 30 mm in diameter and surrounded by aerated lung tissue. In radiographs, pulmonary nodules may appear as solid, completely obscuring the lung parenchyma, or as subsolid, not completely obscuring adjacent tissues. A subsolid pulmonary nodule may be further subclassified as a pure ground glass nodule (pGGN) or a part solid nodule, a mixture of ground glass components and focal opacity obscuring the adjacent tissues. Guidelines for evaluation of solid pulmonary nodules are based on nodule size, recommending vigilance and non-operative management for small nodules (less than 8 mm in diameter) and diagnostic biopsy for nodules with a diameter of 8 mm or more. However, subsolid ground glass pulmonary nodules are an exception to this rule. Although small in size, persistent subsolid nodules are potentially premalignant or malignant. We present the case of a non-smoker who was found to have an incidental pulmonary pGGN. We then discuss the radiologic appearance, histology, clinical outcomes, and evaluation and management strategy of subsolid pulmonary nodules compared with solid nodules.

Keywords: pulmonary nodule; subsolid; papillary adenocarcinoma

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A 55-year-old man with a medical history of hypertension and hyperlipidemia was referred to a pulmonologist for evaluation of a persistent asymptomatic pulmonary nodule. Seven months before presentation, an abdominal CT scan obtained to evaluate constant perirectal pain showed a pure ground glass nodule (pGGN), 2.4 × 2.6 cm in size, in the left lower lobe of the lung. At that time, chest CT confirmed the presence of the pGGN and showed no other pulmonary lesions (Fig. 1). A combined PET/CT scan showed no abnormal uptake of FDG tracer by the nodule. Subsequently, the patient underwent surgical resection of the perirectal abscess and had an uneventful recovery. A 6-month follow-up CT scan of the chest showed no change in the pulmonary nodule and prompted the pulmonary consultation. The patient had no prior history of pulmonary disease and no exertional dyspnea, cough, wheeze, or other chest complaints. The patient had no history of cigarette smoking but reported occasional pipe smoking in the remote past. His examination showed normal vital signs, oxygen saturation of 98% while inspiring room air, and an entirely normal lung and general physical examination.

The pulmonary consultant and the thoracic surgeon he consulted agreed that the appearance of this nodule was suspicious for malignancy and gave the patient the options of early surgical resection versus ongoing observation. Based on personal preference, the patient opted for early surgical resection. On histologic examination, the surgical specimen revealed moderately differentiated papillary adenocarcinoma (Fig. 2). The patient had an uneventful recovery from the surgery and no other treatment was recommended. He remains disease free at 3 years after surgery.

The clinical decision in this case, which was made 4 years ago, is consistent with the 2013 management algorithm (1) for subsolid pulmonary nodules, which is discussed below.

Discussion

A pulmonary nodule is a single, nearly spherical, well-circumscribed pulmonary opacity up to 30 mm in diameter and surrounded by aerated lung tissue (2). Pulmonary nodules may appear as solid, completely obscuring the lung parenchyma, or as subsolid, not completely obscuring adjacent tissues. A subsolid pulmonary nodule may be further subclassified as a pGGN or a part solid nodule, a mixture of ground glass components and focal opacity obscuring the adjacent tissues (Fig. 3).
Eighty percent of pulmonary nodules are solid, and 20% are subsolid (3).

Subsolid nodules may be benign [such as inflammatory, hamartoma, focal hemorrhage, or focal interstitial fibrosis (4)], or they may be malignant or premalignant. Of subsolid nodules, 40–70% resolve spontaneously in 3 months and upon resolution are presumed to have been benign (5). Subsolid nodules that persist for more than 3 months are considered potentially malignant, with a crude malignancy rate for part solid nodules and pGGN of 63% (10/16), and 18% (5/28), respectively, compared with the rate of 7% (14/189) for solid nodules (3). One study found that 75% of 53 non-resolving pGGNs were either bronchoalveolar carcinomas (BAC) or adenocarcinoma with a predominant BAC component; 6% were atypical adenomatous hyperplasia (AAH), and 19% were benign (6). AAH is a less common pathologic finding in surgically resected pGGNs and is a premalignant precursor of adenocarcinoma that is characterized by proliferation of epithelial cells without

Fig. 1. Initial chest CT of the pulmonary nodule with lung (a) and mediastinal window (b). A 2.4 × 2.6 cm pure ground glass nodule (pGGN) was present in the left lower lobe of the lung.

Fig. 2. The pathology slide from resection tissue reveals well-differentiated papillary adenocarcinoma at the low power field (a). High-powered field slide demonstrates the typical acinar pattern of glandular differentiation (b). The tumor is strongly and diffusely TTF-1 positive (c), as is characteristic of primary adenocarcinoma of the lung.
invasion into the adjacent tissues (7). BAC has been described in the 1999 and 2004 World Health Organization classifications of lung adenocarcinoma as a type of adenocarcinoma with lepidic growth pattern (along intact alveolar septa) with minimal, if any, PET-FDG uptake and occurring in relatively low-risk (such as non-smoking) patients. Patients with BAC have varied prognosis, with some having excellent survival and others progressing from early stage to more advanced stage during the 2–4 years before attempted surgical resection (3, 8).

With the development of better correlation between radiographic appearance of subsolid nodules and the invasiveness of the tumor, in 2011 the International Association for the Study of Lung Cancer/American Thoracic Society/European Respiratory Society (IASLC/ATS/ERS) has reclassified BAC into the subtypes adenocarcinoma in situ (AIS), minimally invasive adenocarcinoma (MIA), and lepidic predominant adenocarcinoma (LPA) (9). The new pathology terminology has been adopted to better identify BAC on the continuum of premalignant precursor (AAH), adenocarcinoma in situ (AIS and MIA),

**Table 1. Guidelines for evaluation of pulmonary nodules**

| Pure GGN less than 8 mm |
|-------------------------|
| If less than 5 mm, no follow-up |
| If greater than 5 mm, annual CT for at least 3 years |
| **Part solid nodules** |
| If less than 8 mm, CT at 3, 12, 24 months, then annual CT for 1–3 years |
| If greater than 8 mm, repeat CT at 3 months, followed by PET, needle biopsy, and/or surgical resection |
| **Solid nodules less than 8 mm without risk factors** |
| If less than 4 mm, no follow-up |
| If 4–6 mm, reevaluate at 12 months, if unchanged |
| If 6–8 mm, reevaluate between 6 and 12 months, then between 18 and 24 months, if unchanged |
| **Solid nodules less than 8 mm with risk factors** |
| If less than 4 mm, reevaluate at 12 months |
| If 4–6 mm, reevaluate between 6 and 12 months, then between 18 and 24 months, if unchanged |
| If 6–8 mm, reevaluate between 3 and 6 months, then between 9 and 12 months, and again at 24 months, if unchanged |
| **Solid nodules, 8–30 mm, with low to moderate pretest probability** |
| Consider PET, needle biopsy as initial work up; if negative, then serial CT scans at 3–6, 9–12, 18–24 months |
| Consider PET, needle biopsy as initial work up; if positive, then surgical resection unless contraindicated |
| **Solid nodules, 8–30 mm, with high pretest probability** |
| PET is not recommended to characterize the nodule, prefer surgical diagnosis |
| **Dominant nodule and one or more additional small nodules** |
| Each nodule should be evaluated individually; curative treatment not be denied unless proved to be metastasis |

*Table summarizes diagnosis and management of pulmonary nodules as described by Gould et al. (1).*
and invasive lung adenocarcinoma (10). Patients with AAH, AIS, or MIA have a good prognosis, with near 100% 5-year disease-free survival after complete resection. Patients with LPA have 86–90% 5-year disease-free survival after surgical resection (10), whereas patients with invasive adenocarcinoma have 67% 5-year disease-free survival after surgical resection (11). The classification system of early-stage pulmonary adenocarcinoma may improve future clinical trials designed to stratify patients to expectant observation, surgical resection, and/or adjuvant chemotherapy.

In 2013, Gould et al. described a management algorithm for individuals with both solid and subsolid pulmonary nodules that takes into account size, radiologic appearance, and independent risk factors for malignancy (older age, current or past smoking history, and extrathoracic cancer) (1). Generally, the likelihood of invasiveness correlates with the initial size of the pulmonary nodule [e.g., the prevalence of malignancy is less than 1% for nodules less than 5 mm in diameter, 6–28% for nodules between 5 and 10 mm in diameter, and 64–82% for nodules over 20 mm in diameter (12)], observed growth, or the development of a solid component within the nodule. Certain pathologic types of pulmonary nodules may correlate with radiographic appearance. For example, AIS typically presents as a pGGN and MIA is more likely to present as a part solid nodule, whereas invasive adenocarcinomas may present as a solid nodule, a part solid nodule, or occasionally a pGGN (9).

Studies support using this more stringent evaluation and treatment algorithm for subsolid pulmonary nodules. A study showed that 59% of 320 subsolid malignant nodules occur in never-smokers, whereas 25% of solid malignant nodules occurred in never-smokers, a statistically significant difference (13). A recent study of 46 resected pGGNs using the new classification system found that 41% were AISs, 20% were MIAs, and 39% were invasive adenocarcinomas (14). Although PET scan has relatively good sensitivity and specificity (87 and 83%, respectively) for distinguishing cancer from non-cancer in solid pulmonary nodules (1), the sensitivity of PET scan in subsolid nodules is lower (50%) (15, 16). Also, the accuracy of transthoracic biopsy is lower in patients with pGGNs, with accuracy rates of (67, 85, and 95% for pGGNs, subsolid nodules, and solid nodules, respectively) (17). The current case highlights the importance of early consideration of surgical resection for subsolid pulmonary nodules consistent with the 2013 management guidelines (1) (Table 1).

However, further studies are needed to weigh the benefits and risks of immediate surgical resection versus serial low-dose CT scan follow-up and to determine the optimal duration of CT scan follow-up for those patients not undergoing immediate resection. Based on our current understanding of the radiographic, pathologic, and clinical correlates of subsolid nodules, clinicians should consider an individualized diagnostic strategy accounting for the nodule’s radiographic characteristics and the patient’s comorbidities and personal preferences.

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