CHEST

Special Features

CHEST IMAGING

A Practical Algorithmic Approach to the Diagnosis and Management of Solitary Pulmonary Nodules

Part 1: Radiologic Characteristics and Imaging Modalities

Vishal K. Patel, MBBS; Sagar K. Naik, MBBS; David P. Naidich, MD, FCCP; William D. Travis, MD, FCCP; Jeremy A. Weingarten, MD, FCCP; Richard Lazzaro, MD; David D. Gutterman, MD, FCCP; Catherine Wentowski, MD; Horiana B. Grosu, MD; and Suhail Raoof, MBBS, FCCP

The solitary pulmonary nodule (SPN) is frequently encountered on chest imaging and poses an important diagnostic challenge to clinicians. The differential diagnosis is broad, ranging from benign granulomata and infectious processes to malignancy. Important concepts in the evaluation of SPNs include the definition, morphologic characteristics via appropriate imaging modalities, and the calculation of pretest probability of malignancy. Morphologic differentiation of SPN into solid or subsolid types is important in the choice of follow-up and further management. In this first part of a two-part series, we describe the morphologic characteristics and various imaging modalities available to further characterize SPN. In Part 2, we will describe the determination of pretest probability of malignancy and an algorithmic approach to the diagnosis of SPN.

CHEST 2013; 143(3):825–839

Abbreviations: ATS = American Thoracic Society; ERS = European Respiratory Society; FDG = ^{18}F-2-deoxy-2-fluoro-D-glucose; GGN = ground glass nodule; IASLC = International Association for the Study of Lung Cancer; NPV = negative predictive value; NSCLC = non-small cell lung cancer; PPV = positive predictive value; SPN = solitary pulmonary nodule; SUV = standardized uptake value

The solitary pulmonary nodule (SPN) is defined as a radiographic opacity ≤ 3 cm in diameter with at least two-thirds of its margins surrounded by lung parenchyma.[1,2] Implied in this definition is the exclusion of lymph nodes, atelectasis, and postobstructive pneumonia. However, it may be difficult at times to exclude intraparenchymal lymph nodes based on just radiologic appearance. SPNs have been noted in 0.09% to 7% of all chest radiographs.[3-5] A review of eight large studies on lung cancer screening using CT imaging[6-13] documented the prevalence of SPN from 8% to 51%, and the prevalence of malignancy from 1.1% to 12%.[14] The etiologic spectrum of SPN represents a veritable minefield of diseases, including benign conditions such as hamartomas to potentially fatal ones such as primary lung cancer (Table 1). Establishing the etiology of a SPN in a timely and accurate manner, therefore, assumes critical importance, since surgical resection in a patient with early-stage lung cancer provides the highest chance of cure. By the same token, avoiding thoracic surgery for a benign SPN whenever possible does obviate significant morbidity. We will describe an algorithmic approach to diagnosis of SPN in Part 2 (see page 840).[15]

Clinical Evaluation

A SPN does not typically herald its presence with clinical symptoms, nor does it lend itself to self-awareness like melanoma or a breast lump. Although the SPN may be insidious, a variety of clinical risk factors such as advancing age and history of smoking have been associated with a higher OR of the SPN being malignant.[15-19] Elucidating a thorough history of prior malignancy is crucial; the majority of SPNs detected in patients with a history of prior malignancy are malignant.[20-22] Interestingly, the malignant SPNs are equally or more likely to represent primary lung cancer rather

than metastasis from the extrapulmonary malignancy, with the notable exceptions of sarcoma, melanoma, and testicular carcinoma (Table 2). The presence of mediastinal lymph node enlargement on CT scan strongly suggests a new primary lung cancer rather than metastasis.[20] Interstitial lung diseases, such as idiopathic pulmonary fibrosis, asbestosis, and scleroderma are associated with an increased incidence of lung cancer.[23] The prevalence of lung cancer in idiopathic pulmonary fibrosis, for example, ranges from 9% to 38%, with a predilection for peripheral lung areas in the lower lobes in elderly male smokers.[24-29] Finally, residence in or travel to an area with endemic fungal pathogens could suggest a benign, infectious SPN in the correct clinical context. For example, coccidioidomycosis is endemic in the southwestern United States and Mexico, and often presents as a SPN on chest CT scans.[30] *Cryptococcus*[31-33] infection and histoplasmosis can also present as a SPN.

Radiographic Characteristics: CT Scan

Specific morphologic characteristics of SPNs on imaging may help differentiate benign from malignant SPNs. It is recommended that CT images be thin section, with contiguous 1-mm images through nodules. Both lung and mediastinal windows should be obtained, the former for the edges, the latter for solid components. Low-dose (milliamperes second [mAs] <80) CT scan can be used for this purpose.

Growth Rate

Malignant, solid SPNs have a volume doubling time of 20-400 days,[34-38] with a majority having volume doubling times of significantly <100 days.[39] A volume doubling time >400 days suggests slow growth and is usually associated with benign SPNs, whereas volume doubling time <20 days indicates very rapid growth, usually attributable to infectious processes.[40] It is important to realize that since the volume of a sphere equals $4\pi r^3/3$, an increase in nodule diameter by only 26% indicates doubling of volume. In other words, a

Table 1—*Differential Diagnosis of Solitary Pulmonary Nodules*

Infectious
TB (tuberculoma)
Round pneumonia, organizing pneumonia
Lung abscess
Fungal: aspergillosis, blastomycosis, cryptococcosis, histoplasmosis, coccidioidomycosis
Parasitic: amoebiasis, echinococcosis, *Dirofilaria immitis* (dog heartworm)
Measles
Nocardia
Atypical mycobacteria
Pneumocystis jiroveci
Septic embolus
Neoplastic
Benign
Hamartoma
Chondroma
Fibroma
Lipoma
Neural tumor (Schwannoma, neurofibroma)
Sclerosing hemangioma
Plasma cell granuloma
Endometriosis
Malignant
Lung cancer
Primary pulmonary carcinoid
Solitary metastasis
Teratoma
Leiomyoma
Vascular
Arteriovenous malformation
Pulmonary infarct
Pulmonary artery aneurysm
Pulmonary venous varix
Hematoma
Congenital
Bronchogenic cyst
Lung sequestration
Bronchial atresia with mucoid impaction
Inflammatory
Rheumatoid arthritis
Granulomatosis with polyangiitis (Wegener)
Microscopic polyangiitis
Sarcoidosis
Lymphatic
Intrapulmonary or subpleural lymph node
Lymphoma
Outside lung fields
Skin nodule
Nipple shadows
Rib fracture
Pleural thickening, mass or fluid (pseudotumor [ie, loculated fluid])
Miscellaneous
Rounded atelectasis
Lipoid pneumonia
Amyloidosis
Mucoid impaction (mucocele)
Infected bulla
Pulmonary scar

Manuscript received June 12, 2012; revision accepted October 10, 2012.
Affiliations: From the New York Methodist Hospital (Drs Patel, Naik, Weingarten, Lazzaro, Wentowski, Grosu, and Raoof), Brooklyn, NY; New York University Langone Medical Center (Dr Naidich), New York, NY; Memorial Sloan-Kettering Cancer Center (Dr Travis), New York, NY; and Medical College of Wisconsin (Dr Gutterman), Milwaukee, WI.
Correspondence to: Suhail Raoof, MBBS, FCCP, New York Methodist Hospital, Department of Pulmonary and Critical Care, 506 Sixth St, Brooklyn, NY 11215; e-mail: suhailraoof@gmail.com

DOI: 10.1378/chest.12-0960