A solitary pulmonary nodule (SPN) is defined as a single, well-circumscribed, spherical radiographic opacity that measures less than 3–4 cm in diameter and is surrounded completely by aerated lung. It is not associated with other, potentially related pulmonary pathology, such as hilar or mediastinal enlargement or a pleural effusion. Approximately 75% of pulmonary nodules are discovered incidentally on chest radiographs (CXR). The widespread adoption of computed tomography (CT), particularly spiral CT, has led to the detection of more and even smaller nodules in the lungs. More than 150,000 patients per year in the U.S. present with the diagnostic dilemma of an SPN.

The major question following detection of an SPN is whether it represents a benign or a malignant process. Although it is preferable not to subject a patient to a surgical removal of a benign lesion, it is more important to resect a localized non-small cell primary lung cancer, which is associated with an excellent prognosis following surgical resection.

Differential Diagnosis

In older patients the majority of SPNs are malignant, including primary lung cancer, solitary metastasis and carcinoid tumours. All cell types of primary lung cancer can present as an SPN, but it is seen most commonly with adenocarcinoma (including bronchoalveolar cell carcinoma) and, to a lesser extent, large cell carcinoma. Primary sites of extrapulmonary malignancy that are most likely to produce a metastatic SPN include malignant melanoma, sarcomas and carcinomas of the colon, breast, kidney and testicle. The vast majority of metastases to the lungs occur as multiple lesions. Benign etiologies for SPNs are infectious granuloma (tuberculosis and endemic fungi, especially histoplasmosis and coccidioidomycosis), hamartomas, rheumatoid nodules, intrapulmonary lymph nodes, plasma cell granulomas, pulmonary arteriovenous malformation and sarcoidosis.

Clinical Features Predicting Likelihood of Malignancy

The probability of an SPN being malignant rises with increasing age. The percentage of SPNs due to malignancy was reported to be 50–65% in patients 60 years of age or older, compared with 3–43% in those younger than 60 years. The possibility of an SPN being lung cancer is higher in patients with a history of smoking and asbestos or other occupational carcinogen exposure. A previously diagnosed malignancy increases the likelihood that an SPN may represent metastatic disease.

The size of a lung nodule is also a good indicator of the likelihood of malignancy; bigger nodules are more likely to be malignant. In older patients, the incidence of malignancy in a lung nodule > 3 cm is so great that all these lesions should be surgically resected unless medically contraindicated.
Clinical Management of the Solitary Lung Nodule in Older Adults†

1. Single pulmonary nodule seen on CXR
   - Previous CXRs showed no progression for > 2 years?
     - Yes → No further investigation
     - No → Spiral CT with and without contrast

2. Spiral CT with and without contrast
   - Typical benign features
     - Treat or serial follow-up
   - Possibly benign
     - Presence of high risk factors for cancer?*
       - Yes → High risk surgical complication?
         - Yes → Surgery
         - No → Serial follow-up
       - No → FDG-PET scan or TTNA
         - Positive → High risk surgical complication?
           - Yes → VATS approach or limited resection
           - No → Surgery
         - Negative → Serial follow-up
   - Possibly malignant
     - FDG-PET scan or TTNA
       - Positive → VATS approach or limited resection
       - Negative → Serial follow-up

†Based on the quantitative model to estimate the probability of cancer and the most recent cost-effectiveness analysis.
††Serial follow-up: CT at three, six, 12 and 24 months.
*High risk factors for cancer: smoking history, previous history of extrathoracic cancer, nodule > 10mm.
CXR: chest radiograph; TTNA: transthoracic needle aspiration; VATS: video-assisted thoracic surgery.

Imaging Features

CXR

Usually the presence of “benign” calcification or the absence of growth over a two-year time period are considered to be reliable indicators of benign disease. Benign calcification refers to central, diffuse, laminar or popcorn patterns. CXR may falsely suggest the presence of calcification. Furthermore, CXR is less sensitive than CT for detecting changes in size of an SPN, as a doubling in spherical tumour volume may result in a change in diameter of only a few millimeters.

Chest CT and Magnetic Resonance Imaging

Spiral CT with or without IV contrast is an important tool in the evaluation of SPNs. CT is more sensitive than CXR in characterization of the nodule. In addition, chest CT is a useful tool for the assessment of chest wall, diaphragmatic invasion and mediastinal adenopathy. With the availability of low-dose spiral CT, it is more likely that spiral CT will replace routine CXR in the surveillance of benign SPNs in the future. However, due to the absence of mortality reduction, it is premature to recommend low-dose spiral CT as routine lung cancer surveillance at present.

Characteristics on CT that suggest a benign lesion include: a smooth border; fat within a nodule (hamartoma); diffuse, central, lamellate or “popcorn” calcification; SPN surrounded by small satellite lesions (infectious granuloma); presence
Solitary Lung Nodule

of feeding blood vessels (arteriovenous malformations, bronchopulmonary sequestrations); thin walled cavitating nodules (< 1mm); a dense “comet tail” (rounded atelectasis); and SPN within a cavity (fungus ball).14,15

Characteristics on CT that suggest a malignant lesion (Figure 1) include: ill-defined or irregular margins; spiculated and scalloped borders; corona radiate (fine linear striations extending perpendicular to the surface of the nodule into surrounding lung for a distance of 4–5mm); wall thickness > 15mm in cavitating lesion; predominantly ground glass opacification and air bronchograms (bronchoalveolar carcinomas, adenocarcinomas); and reticular, punctate, amorphous or eccentric calcifications.14,16,17

Magnetic resonance imaging (MRI) has little to offer in the evaluation of the SPN. However, it may be beneficial in patients who cannot tolerate IV contrast, and may allow better anatomic evaluation of the lung apices, thoracic inlet, chest wall or diaphragm due to its ability to provide sagittal, coronal and oblique images.18

Positron Emission Tomography

Positron emission tomography (PET) with 18-fluorodeoxyglucose (FDG) identifies malignant tumours based on their increased metabolic rate and has proven to be the most accurate mode of tumour imaging (Figure 2).19 PET scans also have a 96% sensitivity and 88% specificity, with 94% accuracy in the diagnosis of benign nodules.

The current generation of PET scans is unreliable for the investigation of an SPN < 1cm. False-negative PET studies may be due to relatively low tumour metabolic activity, such as with bronchoalveolar tumours, carcinoids and some well-differentiated adenocarcinomas; these tumours may not have high FDG uptake or uncontrolled hyperglycaemia may retard the uptake of FDG. False-positive results may be seen in lung lesions with an infectious or inflammatory etiology, such as tuberculosis, histoplasmosis or rheumatoid nodules.

PET is available only in large academic centres and is more expensive than other imaging modalities. For patients who are at average risk for surgical complications, FDG-PET should be used selectively when pretest probability and CT results are discordant. For patients at high risk for surgical complications and with low or intermediate pretest probability, FDG-PET should be used when CT results are possibly malignant. In most other circumstances, CT-based strategies result in similar quality-adjusted life expectancy and lower costs.20

Tissue Diagnosis

Transthoracic Needle Aspiration

Transthoracic needle aspiration (TTNA) is less invasive and has higher diagnostic yield than bronchoscopy and Wang transbronchial needle biopsy, especially for peripheral lung nodule.21 Relative contraindications to this procedure are pulmonary hypertension, uncorrected coagulopathy or bleeding diathesis, severe chronic obstructive pulmonary disease or vascular malformations.

Bronchoscopy

Bronchoscopy is ideal for obtaining tissue diagnosis in large, central lung lesion or endobronchial lesion. For a patient with a peripheral SPN, there is little role for bronchoscopy.

Surgery and Treatment Considerations

Surgical resection is the ideal therapeutic approach for an SPN, as it is both diagnostic and therapeutic. For the surgical candidate with an SPN proven to be non-small cell lung cancer (NSCLC), lobectomy and systematic mediastinal lymph node dissection is the standard of care for complete oncologic resection and staging.

For a patient who is a marginal surgical candidate and whose pulmonary or cardiac status can only tolerate a limited resection, thoracoscopic wedge resection or segmentectomy are acceptable for treatment of NSCLC.22 Radiation therapy can be offered for malignant SPN if the patient declines surgery.23 In the older patient, some of the malignant lesion may grow at a relatively slow rate to the extent that some patients may achieve several years of quality survival without any intervention.

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