March 2018 Imaging Case of the Month

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Clinical History: A 56-year-old woman with no significant past medical history underwent routine breast imaging (MRI) which showed an abnormality outside the breast (images not shown). She has a sister with recently-diagnosed breast malignancy. The patient smoked for 30 years, quitting 10 years ago. Her surgical history is remarkable only for a tubal ligation and hysterectomy, and she is asymptomatic. Her medications consist only of vitamins and supplements.

Laboratory evaluation showed a normal complete blood count, electrolyte panel, and liver function tests. Frontal and lateral chest radiography (Figure 1) was performed.

Figure 1. Frontal (A) and lateral (B) chest imaging.

Which of the following represents the most accurate assessment of the frontal chest imaging findings?

1. Chest frontal imaging shows a focal right lung nodule
2. Chest frontal imaging shows basilar fibrosis
3. Chest frontal imaging shows mediastinal and peribronchial lymphadenopathy
4. Chest frontal imaging shows multiple, bilateral small nodules
5. Chest frontal imaging shows normal findings
The frontal and lateral chest radiographs show normal lung volumes; no evidence of basal fibrosis is present, nor is there evidence of peribronchial or mediastinal lymph node enlargement. However, a focal nodular opacity is present in the right upper lobe. There is no evidence of numerous, small, disseminated pulmonary nodules and only one nodule is seen, in the right upper lobe (Figure 2).

Figure 2. Initial chest x-ray with right upper lobe nodule (arrow).

Which of the following represents the most appropriate management step for the evaluation of this patient?

1. Obtain $^{18}$FDG-PET scan
2. Obtain prior chest radiographs or thoracic imaging for comparison
3. Obtain routine enhanced thoracic CT
4. Obtain surgical lung biopsy
5. Treat presumptively with antibiotics and reimage in 2 weeks
Correct!

2. Obtain prior chest radiographs or thoracic imaging for comparison

In most situations, when an indeterminate lung nodule is encountered at chest radiography, it is most rewarding to obtain prior chest imaging to determine if the nodule is stable. While short-term stability has relatively little meaning as regards the possibility of malignancy, demonstrating long-term stability, particularly greater than two years, is a strong predictor of a benign etiology for a lung nodule. Thoracic CT is a reasonable choice as well, but typically thoracic CT characterization of nodules is conducted using unenhanced technique. On occasion, intravenous contrast may be injected for solitary pulmonary nodule characterization using a specialized protocol. \(^{18}\)FDG-PET scanning is also useful for charactering solitary pulmonary nodules but is typically obtained after any prior imaging is obtained and reviewed and the nodule has been characterized with unenhanced thoracic CT. Focal solitary pulmonary nodules are rarely the result of active bacterial pulmonary infection; therefore, presumptive treatment with broad-spectrum antibiotics and repeating imaging within 2 weeks is unlikely to be a rewarding management approach.

No prior thoracic imaging was available for comparison.

Which of the following represents the most appropriate management step for the evaluation of this patient?

1. Obtain \(^{18}\)FDG-PET scan
2. Obtain surgical lung biopsy
3. Obtain thoracic MRI
4. Perform bronchoscopy
5. Perform unenhanced thoracic CT
Correct!

5. Perform unenhanced thoracic CT

Based on the foregoing discussion, performing unenhanced thoracic CT is typically the next step, after attempting to locate prior imaging to document nodule stability, in the evaluation of the indeterminate solitary pulmonary nodule. Thoracic MRI is typically less rewarding for evaluation of pulmonary nodules; while nodule enhancement can be appreciated at enhanced MRI, calcification within a nodule - a strong predictor of a benign etiology for the nodule - is far more readily detectable, and characterizable, using CT. As noted previously, $^{18}$FDG-PET scanning is also useful for charactering solitary pulmonary nodules, but is typically obtained after any prior imaging is obtained and reviewed and the nodule has been characterized with unenhanced thoracic CT.

The patient underwent unenhanced thoracic CT (Figure 2).

![Thoracic CT images](image)

Figure 3. Representative images from the thoracic CT scan in lung windows (A-F) and soft tissue windows (J-L) showing the right lung nodule (arrows).

Which of the following represents the most accurate assessment of the thoracic CT findings?

1. Thoracic CT shows that the solitary right upper lobe nodule contains calcium
2. Thoracic CT shows that the solitary right upper lobe nodule has a configuration consistent with an arteriovenous malformation
3. Thoracic CT shows that the solitary right upper lobe nodule has a configuration consistent with bronchial impaction
4. Thoracic CT shows that the solitary right upper lobe nodule is a pulmonary varix
5. Thoracic CT shows that the solitary right upper lobe nodule is cavitary
Correct!

1. Thoracic CT shows that the solitary right upper lobe nodule contains calcium

The unenhanced thoracic CT shows that the right upper lobe nodule, measuring 18 mm, is lobulated, unassociated with dilated feeding arteries or draining veins, but does contain a small focus of calcification along its lateral aspect (see Figure 2C and 2K). The nodule may be closely associated with a bronchus along its deep aspect, and the nodule does have a vaguely tubular shape, but the nodule is not clearly an uncomplicated impacted bronchus. The nodule morphology is not consistent with a pulmonary varix, and the nodule does not appear to be connected to a pulmonary vein. Often isolated pulmonary varices are more centrally located, commonly occurring in the context of various causes of elevated left atrial pressure, particularly mitral valve disease.

Given the unenhanced thoracic CT findings, which of the following represents the most appropriate management step for the evaluation of this patient?

1. Obtain $^{18}$FDG-PET scan
2. Obtain surgical lung biopsy
3. Obtain thoracic MRI
4. Perform bronchoscopy
5. Perform contrast-enhanced thoracic CT using a solitary pulmonary nodule protocol
Correct!
1. Obtain 18FDG-PET scan

Among the choices listed, 18FDG-PET scanning may represent the least invasive, most effective approach to nodule management for this patient. Performing contrast-enhanced thoracic CT using a nodule enhancement protocol could prove useful-negative findings, typically defined as less than 15 HU enhancement within the nodule at all 4, 1-minute time points, compared to baseline unenhanced imaging nodule attenuation, strongly predicts that the nodule is benign. However, false positive results are not uncommon and may occur with infectious granulomas (a consideration for this patient), and the nodule should be followed anyway to exclude growth even if the contrast-enhanced CT results are negative, limiting the utility of this approach. In contrast, positive 18FDG-PET scanning results may prompt biopsy, whereas negative results predict that a solitary nodule is likely benign (although the nodule is still typically followed to assure stability or resolution); furthermore, 18FDG-PET scanning can detect additional findings that may impact the relevant differential diagnostic considerations and also reveal abnormal findings that would be more readily accessible to a tissue diagnosis than the pulmonary nodule. Should the nodule prove to represent a bronchogenic malignancy, 18FDG-PET scanning is of proven value for lung cancer staging as well. The lesion is peripherally located and, while possibly accessible using navigational bronchoscopy, would probably be better approached using transthoracic percutaneous needle biopsy should a tissue diagnosis be desired. Surgical lung biopsy would no doubt be diagnostic but is needlessly invasive at this point. As noted previously, thoracic MRI has limited utility for the assessment of a solitary pulmonary nodule.

The patient underwent 18FDG-PET scanning (Figure 4).

Figure 4. Representative images from 18FDG-PET scanning.
Which of the following represents the most accurate assessment of the $^{18}$FDG-PET findings?

1. $^{18}$FDG-PET is degraded by artifact due to lack of pre-scan fasting state and therefore cannot be interpreted
2. $^{18}$FDG-PET scan shows hypermetabolic activity in the right upper lobe nodule
3. $^{18}$FDG-PET scan shows no significant metabolic activity in the right upper lobe nodule
4. $^{18}$FDG-PET scan shows no significant metabolic activity in the right upper lobe nodule but shows peribronchial and mediastinal lymph node metabolic activity
5. $^{18}$FDG-PET shows indeterminate tracer utilization within the right upper lobe nodule
Correct!

3. $^{18}$FDG-PET scan shows *no* significant metabolic activity in the right upper lobe nodule

The $^{18}$FDG-PET scan shows no significant metabolic activity in the right upper lobe nodule (standard uptake value= 1.8). No peribronchial or mediastinal lymph node tracer utilization was identified. The scan appears technically adequate - normal blood pool and muscle tracer activity is visible. No evidence of artifact to suggest that the $^{18}$FDG-PET scan cannot be accurately interpreted is noted.

Given the data available, which of the following represents the **most appropriate management step** for the evaluation of this patient?

1. Obtain thoracoscopic surgical lung biopsy
2. Obtain transthoracic percutaneous needle biopsy
3. Perform $^{68}$Ga – PET – CT dotate scan
4. Perform pleuroscopy
5. Serial imaging evaluation of the nodule to exclude growth
Correct!

5. Serial imaging evaluation of the nodule to exclude growth

$^{68}$Ga – PET – CT dotatate scanning is typically used for neuroendocrine malignancies, and, while peripheral large cell neuroendocrine malignancies and small cell malignancies do occur, they are uncommon and $^{68}$Ga – PET – CT dotatate scanning would be used in this context only after a diagnosis has been established. Pleuroscopy would not be of value for this patient as no pleural abnormality is present. Both thoracoscopic and transthoracic percutaneous biopsies could establish a definitive diagnosis for this patient, but the presence of calcification as well as the lack of tracer utilization at $^{18}$FDG-PET scanning predict that this nodule is benign; therefore, serial evaluation for nodule growth, rather than obtaining an invasive tissue diagnosis, may be the management strategy favored by the available data.

The patient underwent serial clinical and imaging evaluation assessment. Coccidioidomycosis serologies were negative. Pulmonary function testing showed nonspecific proportionate reductions in forced vital capacity and forced expiratory volume in 1 second, with carbon dioxide diffusion capacity 73% predicted. Resting and exercising blood oxygenation was normal. The patient underwent bronchoscopy, and biopsy showed a “rare” granuloma in the normal-sized right paratracheal lymph node but was otherwise non-diagnostic. The patient was schedule for repeat unenhanced thoracic CT, performed 6 months later (Figure 5).

![Figure 5. Representative images in lung windows from the repeat thoracic CT scan performed 6 months after the initial CT scan.](image)

Which of the following represents the most accurate assessment of the thoracic CT findings?

1. New numerous pulmonary nodules have developed
2. The right upper lobe nodule appears decreased in size
3. The right upper lobe nodule appears slightly enlarged and now shows cavitation
4. The right upper lobe nodule appears unchanged
5. The right upper lobe nodule now shows extensive surrounding ground-glass opacity, suggesting hemorrhage
3. The right upper lobe nodule appears slightly enlarged and now shows cavitation

Repeat thoracic CT, at about 6 months following initial presentation, shows slight interval enlargement of the subpleural right upper lobe nodule (increased from 18 mm to 23 mm maximum dimension) with development of central cavitation. While there is some mild ground-glass opacity on the margins of the enlarging nodule, the ground-glass opacity is not extensive enough to suggest an actively hemorrhagic lesion. No significant new nodules are present.

Given the data available, which of the following represents the most appropriate management step for the evaluation of this patient?

1. Obtain thoracoscopic surgical lung biopsy
2. Obtain transthoracic percutaneous needle biopsy
3. Perform dynamic contrast-enhanced thoracic CT
4. Perform right upper lobe surgical resection
5. Serial imaging evaluation of the nodule to exclude growth
Correct!

2. Obtain transthoracic percutaneous needle biopsy

Although the nodule showed no significant tracer accumulation at $^{18}$FDG-PET and showed a small focus of calcification - both strong predictors of a benign etiology - the lesion has clearly shown growth and developed cavitation, indicating that it is an active process. The growth and cavitation are certainly not specific for malignancy - active infection, most likely fungal or mycobacterial, could present in this fashion. Because the lesion is active and both malignancies and infections, the latter requiring mutually exclusive therapies that prohibit an empiric approach, suggest that a tissue diagnosis is required. The lesion should be amenable to percutaneous transthoracic fine needle aspiration biopsy, and that approach is the least invasive of the options listed, although clearly the surgical options would provide a definitive diagnosis. In fact, one could argue that the pre-test probability of primarily malignancy is high enough in this patient - a growing cavitary nodule in an adult with a significant smoking history, with an $^{18}$FDG-PET scan showing no metastatic disease - to resect the right upper lobe on the assumption that the lesion is malignant. Nevertheless, in practice, even high pre-test probability lung nodules undergo pre-operative tissue sampling to confirm a malignant diagnosis before definitive surgical therapy is often undertaken. Given that the nodule has shown growth, serial evaluation to exclude further growth is generally a less rewarding approach.

The patient was referred to thoracic surgery and underwent repeat $^{18}$FDG-PET scanning, as part of the pre-operative evaluation which now showed the right upper lobe nodule to be hypermetabolic but no increased metabolic activity was seen in the regional or mediastinal lymph nodes (Figure 6).

![Figure 6. Representative images from the repeat 18FDG-PET scan done as part of the pre-operative evaluation showing increased tracer utilization in the right upper lobe nodule (standard uptake value = 4.7). No evidence of increased mediastinal or peribronchial tracer activity is noted.](image)

![A](image)  ![B](image)  ![C](image)  ![D](image)
The right upper lobe was resected, showing moderately-differentiated adenocarcinoma without lymph node involvement. The right upper lobe also showed areas of necrotizing granuloma formation, areas of organizing pneumonia, and patchy bronchiolocentric scars.

**Diagnosis:** Primary bronchogenic malignancy - moderately differentiated adenocarcinoma (with initially false negative $^{18}$FDG-PET results)

**References**

5. Berger WG, Erly WK, Krupinski EA, Standen JR, Stern RG. The solitary pulmonary nodule on chest radiography: can we really tell if the nodule is calcified? AJR Am J Roentgenol. 2001;176(1):201-4. [CrossRef] [PubMed]