Abstract

Within the thorax, a myriad of entities can demonstrate increased fluorodeoxyglucose (FDG) concentration; the goal of this article is to review benign pleural and chest wall entities that may mimic thoracic malignancy on positron emission tomography (PET)/CT. In addition, the article will review how clinical history, anatomic correlation, and imaging features can assist accurate identification of these thoracic malignancy mimickers. This review is divided into two parts: part 1 covers the pleura and chest wall; part 2 will cover lung parenchyma and mediastinum.

Positron emission tomography (PET) uses positron-emitting radionuclides to allow for the in vivo imaging of physiologic and pathologic processes. Multiple radiotracers may be used for PET/CT including fluorodeoxyglucose (FDG), F-18-sodium fluoride, prostate-specific membrane antigen, and dotatate. FDG PET/CT is particularly valuable in the management of pleural and chest wall abnormalities, as it can help contribute information to distinguish benign, malignant, primary, metastatic, localized, or disseminated diseases. This information is pivotal in determining prognosis, directing treatment, and assessing therapy response. However, pleural and chest wall abnormalities may be incidentally detected on a scan performed for an unrelated reason and may lead to management dilemmas.

Basics of PET/CT

The most commonly used radiotracer for oncologic imaging is FDG, a glucose analog that assesses tissue metabolism. FDG is a positron emitter with a half-life of approximately 110 minutes (about 2 hours), and when it decays, the nucleus emits a positron, which collides with an electron within the tissue. The basis of PET imaging is positron emission, where the positrons collide with electrons resulting in an annihilation reaction that produces two 511-KeV photons 180 degrees from one another. The amount of energy required for these annihilation photons must be 511 KeV for such a reaction to occur. The counts then detected 180 degrees from one another are recorded with a maximum intensity projection image constructed from this data. The scintillation crystals in PET cameras absorb the energy from the photons and emit light into electric signals, producing the raw nonattenuated PET data. A simultaneous CT is
due to its nonspecifcity, focal uptake on PET/CT can present a diagnostic dilemma.

**Mechanism of Action for FDG**

Hexokinase is an essential catalyst in the cellular metabolism of glucose. This enzyme has a high affinity for converting glucose into glucose-6-phosphate, which then results in increased facilitated diffusion of glucose through facilitative glucose transporters (GLUT 1-13). Cells with higher metabolic activity take up more FDG and demonstrate increased avidity on imaging. FDG is not specific for cancer cells, as any hypermetabolic cell with GLUT transporters will metabolize glucose and appear avid. This has allowed clinicians to capitalize on PET/CT not just for malignancy but to aid in diagnosing infectious/inflammatory processes such as hibernating myocardium, evaluation of discitis or osteomyelitis, or the identification of an infectious source in patients of unclear etiology. Due to its nonspecificity, focal uptake on PET/CT can be a diagnostic dilemma for the interpreting physician, and awareness of potential pitfalls is critical for accurate interpretation and further recommendations.

**Pitfalls of Pleural Entities on PET/CT**

There are a variety of benign etiologies that can mimic primary pleural malignancies and pleural metastasis, with select entities discussed below.

**Talc Pleurodesis**

Talc pleurodesis is a procedure to treat persistent pneumothorax and recurrent pleural effusions. Talc pleurodesis may cause false-positive interpretations because FDG is captured by pleural granulomas resulting in hypermetabolism, thus demonstrating increasing avidity on PET/CT (Figure 1). These findings may persist for years after pleurodesis is performed. The characteristic high CT attenuation of talc density helps to differentiate this entity from pleural tumors. Biopsy should be avoided as the imaging features are pathognomonic. Findings typically remain stable on follow-up imaging, and clinical history is often helpful in confirming the diagnoses.

**Desmoid-Type Fibromatosis**

Desmoid-type fibromatosis is a benign, noninflammatory fibroblastic tumor, which can occur in a variety of locations, most often intra-abdominally and within the abdominal wall. However, less common locations of desmoid-type fibromatosis include the pleura and chest wall. There is also an association with Gardner syndrome. Mesenteric desmoids can be seen sporadically or in an association with familial polyposis coli syndrome. On CT, desmoids often present as well-circumscribed masses and are relatively homogenous (Figure 2A). On PET/CT, desmoids are moderately hypermetabolic (Figures 2B and 2C). Less commonly, desmoids may exhibit partially ill-defined margins. Biopsy is generally indicated for confirmation as imaging features can be indistinguishable from other neoplasms, such as mesothelioma and sarcomas.
Benign mimics of primary pleural malignancy and pleural metastasis may include avidity after talc pleurodesis, desmoid-type fibromatosis, splenosis, rheumatoid arthritis, and asbestos-related pleural disease.

Thoracic Splenosis

Splenosis often occurs after trauma and/or splenectomy. Abdominal splenosis occurs in up to 65% of splenectomy cases after traumatic spleen rupture. Although thoracic splenosis is much less common, it occurs in about 18% of traumatic splenectomy cases (Figure 3). Thoracic splenosis should be considered in the setting of multiple, circumscribed unilateral pleural nodules in a patient with prior splenic injury. The left thorax is more often involved due to the location of the spleen. Scintigraphy with Tc-99m-labeled head-damaged red blood cells is the method of choice for the confirmation of splenic tissue.⁶

Rheumatoid Arthritis

Akin to other inflammatory processes, rheumatoid nodules can have increased FDG activity on PET (Figure 4). Rheumatoid arthritis (RA) is a multisystem inflammatory disorder that can present with both pleural and lung parenchymal abnormalities. RA can present with diffuse or nodular pleural thickening, pleural effusion, pulmonary nodules with or without cavitation, and interstitial lung disease. There are currently no established guidelines regarding hypermetabolism of rheumatoid nodules. Therefore, the interpreter should analyze for extra pulmonary findings of RA such as joint erosions, pericarditis, and cutaneous...
rheumatoid nodules. Correlation with the patient’s history and laboratory data is often helpful to suggest the findings are secondary to RA rather than a malignant process. In many cases, close monitoring or tissue sampling may be warranted where there is a high index of suspicion.

Asbestos-Related Pleural Disease

Asbestos-related pleural disease can demonstrate increased hypermetabolism on FDG PET/CT, creating a diagnostic dilemma (Figure 5). This benign cause of pleural disease can result in pleural effusions, diffuse pleural thickening, or classically multiple bilateral partially calcified pleural plaques that have a predilection for the diaphragmatic pleura. Asbestos-related pleural disease may also result in rounded atelectasis, which may mimic a pulmonary neoplasm. Most often, the typical imaging appearance precludes the need for further diagnostic testing. Correlation for a clinical history of occupational exposure is helpful in equivocal cases.

Silicone Granulomas

Silicone granulomas may lead to substantial expression of hexokinase in the granulomatous tissue and thus increasing the FDG avidity. Increased FDG activity can be seen around ruptured breast prosthesis due to the inflammatory process caused by free silicone (Figure 6). Silicone lymphadenopathy can also result in increased FDG avidity in the axillary or internal mammary compartments. MRI with silicone suppression can help confirm the diagnosis and exclude a neoplastic process. High attenuation on non-contrast CT and characteristic “snowstorm” appearance on ultrasound can also suggest the diagnosis without the need for biopsy.

Pitfalls of Chest Wall Entities on PET/CT

There are several benign chest wall processes that can be mistaken for malignancy. Select entities will be reviewed below.

Figure 3. Images obtained in a 59-year-old man with a history of right middle lobe mass (dashed arrows) and a remote history of motor vehicle accident requiring splenectomy. Fused PET/CT (A–D) illustrates a right middle lobe mass with increased FDG avidity. Multiple circumscribed left-sided pleural nodules (arrows) show mild FDG avidity. CT-guided biopsy of the right middle lobe mass was consistent with organizing pneumonia. The left pleural nodules were stable from remote prior CT examinations most consistent with benign thoracic splenosis given the patient’s history.
Benign chest wall processes that can be mistaken for malignancy include silicon granulomas, fat necrosis, hibernoma, and elastofibroma dorsi.

Fat Necrosis

On PET/CT, fat necrosis may demonstrate increased FDG uptake in the acute phase due to the presence of metabolically active inflammatory cells (Figure 7). This may occur in a variety of locations including chest wall, breasts,
Figure 7. CT and fusion PET/CT scans (A–E) in an 87-year-old woman with a history of lung cancer and a remote history of chest wall trauma. PET/CT shows avid pulmonary nodules within the right lower lobe and a left breast soft tissue mass with increased FDG avidity. Biopsy revealed fat necrosis with histiocytic and foreign body giant cell reaction. Follow-up CT demonstrates peripheral calcification.

Figure 8. Staging fusion PET/CT (A–B) in a 78-year-old woman with a history of adenocarcinoma of the colon demonstrates an FDG-avid mass in the left chest wall/axillary region. The corresponding CT scan shows a circumscribed mass of fat attenuation without soft tissue components, compatible with a hibernoma.

Figure 9. CT and fusion PET/CT scans (A–C) in a patient with a history of colon cancer show a soft tissue mass like the adjacent skeletal muscle in the right infrascapular region, deep to the serratus anterior and latissimus dorsi with increased FDG avidity. Given the typical location and CT appearance, a diagnosis of elastofibroma dorsi was made, and no biopsy was performed.

and mediastinal compartments. The CT appearance is often diagnostic, revealing central fat attenuation with a peripheral soft tissue rim, fat stranding, and calcification in the later stages. Correlation with a history of trauma or surgery is helpful to suggest the diagnosis, but in equivocal cases, further evaluation with diagnostic imaging such as mammography and follow-up imaging may be needed.8

Hibernoma

Hibernomas are benign rare adipocytic tumors, which contain metabolically active brown fat. Due to the large number of mitochondria within brown adipocytes, these tumors demonstrate intense FDG hypermetabolism (Figure 8). CT will exhibit features similar to lipomas including homogenous fat attenuation, circumscribed margins, and lack of invasive features. However, unlike lipomas,
hibernomas may demonstrate internal branching vessels and hypervascularity.

**Elastofibroma Dorsi**

Elastofibroma dorsi is a benign soft tissue tumor classically located within the infrascapular region, deep to the serratus anterior and latissimus dorsi muscle. It typically demonstrates mild to moderate increased avidity on FDG PET/CT usually equal to or less than liver \(^9\) (Figure 9). Elastofibroma dorsi is bilateral in up to 60% of cases. The typical location and CT appearance of a striated poorly defined mass with interspersed fat allows for a confident diagnosis without the need for biopsy.

**Conclusion**

Several hypermetabolic benign entities exist within the thorax, specifically involving the pleura and chest wall, many of which may mimic malignancy. Awareness of these pathologies and potential pitfalls can offer a noninvasive confident diagnosis when possible or recommend histologic confirmation with a biopsy when appropriate.

**References**

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1. Which one of the following entities represents a benign soft tissue tumor classically located within the infrascapular region, deep to the serratus anterior and latissimus dorsi?
   A. elastofibroma dorsi
   B. hibernoma
   C. thoracic splenosis
   D. desmoid-type fibromatosis

2. Which one of the following imaging modalities is the method of choice for diagnosis of thoracic splenosis?
   A. CT
   B. MRI
   C. scintigraphy
   D. ultrasound

3. Fat necrosis is commonly depicted on CT imaging as
   A. striated, poorly defined masses with interspersed fat.
   B. well-circumscribed homogenous soft tissue masses.
   C. calcified pleural plaques.
   D. central fat attenuation with peripheral calcification.

4. The most likely diagnosis in the patient in Figure 10 is
   A. elastofibroma dorsi
   B. hibernoma
   C. silicone granulomas
   D. desmoid-type fibromatosis

5. High-attenuating pleural nodules demonstrating increased FDG uptake, as depicted in Figure 11, are characteristic of
   A. rheumatoid arthritis
   B. hibernoma
   C. thoracic splenosis
   D. talc pleurodesis

6. Which one of the following is the most commonly used radiotracer agent for oncologic PET imaging?
   A. Tc-99m sulfur colloid
   B. Ga-68 dotatate
   C. F-18-fluorodeoxyglucose (FDG)
   D. F-18-labeled sodium fluoride

7. Rounded atelectasis, a known mimicker of pulmonary neoplasm on PET/CT imaging, is associated with
   A. asbestos-related pleural disease
   B. fat necrosis
   C. elastofibroma dorsi
   D. hibernoma

8. Which one of the following disease entities commonly presents with extra pulmonary clinical findings such as pericarditis and cutaneous nodules?
   A. rheumatoid arthritis
   B. asbestos-related pleural disease
   C. desmoid-type fibromatosis
   D. thoracic splenosis