PET-positive Mimics of Bronchogenic Carcinoma

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Learning objectives

1. Knowledge that some FDG avid pulmonary opacifications can mimic a bronchogenic carcinoma and are actually benign.

2. Make a diagnosis of some cases within the differential diagnosis with subsequent self assessment in an interactive case review format.

Background

PET/CT using FDG can increase the diagnostic accuracy to differentiate between benign and malignant lung lesions: it provides both functional and morphologic information. However, there are a number of known conditions that are FDG avid, but do not represent pulmonary malignancy. The differential diagnosis can be especially difficult if those conditions present with CT morphologic features that mimic a bronchogenic carcinoma.

In a malignant lesion FDG uptake depends on the number of malignant cells and their metabolic activity. Inflammatory granulomatous pulmonary lesions can also show increased FDG uptake as a result of the presence and activity of leukocytes. Therefore some FDG avid lesions actually are benign, but may easily be misinterpreted as bronchogenic carcinoma.

The differential diagnosis of such lesions include Wegener Granulomatosis, Sarcoidosis, Tuberculosis, Organizing Pneumonia, Rheumatoid Arthritis and Actinomyces infection.

Imaging findings OR Procedure details

Granulomatous disease in general causes increased FDG uptake on PET scan. This may not be misinterpreted as manifestation of progression of a suspected or known malignancy and causes differential diagnostic problems. Frequently only histology delivers final diagnosis.

Manifestations of granulomatous disease occur intrapulmonary and in mediastinal lymph nodes or in both. While morphology of the lymphadenopathy rarely provides diagnostic clues, morphology of the intrapulmonary lesions may exhibit some features that - in association with clinical information - allow for making the differential.
The exhibition summarizes a number of granulomatous diseases with immunological and infectious origin that causes increased FDG uptake and represent potential pitfalls in patients with suspected malignancy.

For each of the cases typical and for the diagnosis suggestive CT findings and associated clinical findings will be outlined (key findings are written in "italic"). Knowledge of them may help to avoid misinterpretation. A histologically proven bronchogenic tumor is shown first (fig. 1 and 2) for illustration.

Readers may now analyse figures 3-14 first and try to determine a diagnosis or differential diagnosis before continuing with the text that describes diagnoses and background information. Each case is shown with high resolution images and with a power point slide providing information about the imaging findings.

**Diagnosis of cases:**

Case Bronchogenic Carcinoma

Case 1. Actinomyces

Case 2. Tuberculosis

Case 3. Wegener's Granulomatosis

Case 4. Sarcoidosis

Case 5. Rheumatoid Arthritis

Case 6. Organizing Pneumonia

**Actinomyces**

Actinomyces is a chronic granulomatous infection, characterized by suppuration, sulfur granules and abscess formation. The organism is a normal inhabitant of the human oropharynx and is frequently found in dental caries. Mostly the disease is acquired by the spread from these sites, many patients are immunocompromised (e.g., alcoholics). The patient presents with low grade fever and productive sputum.
On CT scan there are focal or patchy areas of consolidation frequently containing areas of cavitations and typically associated with pleural thickening. Patients can also develop solitary or bilateral mass like consolidations, that imitate bronchogenic carcinoma. More often the lower lobes are involved. Two third of patients have mediastinal lymphadenopathy. Chest wall infections have to be differentiated from pulmonary infections. After intravenous contrast injection most patients show a ring-like rim enhancement around a central area of low attenuation. The first represents the wall of the abscess with increased vascularity within granulation tissue, the latter represents abscesses with inflammatory cells and sulfur granules.

**Tuberculosis**

The risk of developing active TB is greatest in patients with altered host cellular immunity, e.g., high age, malnutrition, cancer, immunosuppressive therapy (as in the patient exhibited here), HIV infection or endstage renal disease and diabetes.

The most common CT findings of postprimary pulmonary TB are centrilobular nodules and branching linear and nodular opacities (tree-in-bud), patchy or lobular areas of consolidations and cavitation. Around 25% of patients, however, present with the so called fibronodular pattern consisting of poorly defined nodules and linear opacities. Mediastinal lymphadenopathy is seen in 10 to 30%. The differential diagnosis of the ill-defined nodules is especially challenging if they are not associated with signs of endobronchial spread (tree-in-bud) or cavitating consolidations. It has to be noted that postprimary TB may result from reactivation of organisms in an old focus, but may also result from reinfection by new organisms, e.g., during a period of immune suppression.

Especially in cases of incomplete clinical history, the interpretation of PET findings may cause problems: the increased uptake was initially interpreted as suspicious for malignancy (in this particular case as lymphoma) and not as infection (see case 2). Knowing the history of immunesuppressive therapy made the finding much more suggestive for an infection.

**ANCA-associated granulomatous vasculitis**

(former Wegener granulomatosis).

Wegener granulomatosis affects the sinuses, kidneys and lungs resulting in the classic triad of symptoms comprising sinusitis and/or tracheobronchitis, pathological CXR (with or without hemoptyisis) and microhematuria. However, any part of the body may be affected. Females and males are affected equally and at any age (mostly age 40-55). Airway involvement is more frequent in men. The most common cause of death is renal failure. With treatment, the 24 months survival is 80%.
Histologic findings include necrotizing granulomatous vasculitis of small to medium vessels without associated infection. Serologically, up to 90% of patients are positive for c-ANCA (circulating antineutrophil cytoplasmic antibodies).

The most frequently seen pulmonary abnormalities are multiple nodules with or without a CT halo sign (hemorrhage). Cavitations have thick walls. Peripheral wedge shaped consolidations represent infarcts that may also cavitate. Diffuse consolidations or ground glass represent pulmonary hemorrhage. Fibrotic changes reflect preexisting disease.

Clinical features and also CT findings are mostly suggestive and causes rarely difficulties for the differential diagnosis from malignancies. Yet, a patient may undergo PET CT for diagnostic work up of a focal pulmonary lesion and knowledge of Wegener´s disease as possible underlying disease for increased FDG uptake is mandatory.

In addition there may be a concentric thickening of tracheal or bronchial walls with diameter reduction potentially causing atelectasis.

**Sarcoidosis**

In many cases sarcoidosis presents with typical nodular parenchymal densities in perilymphatic distribution that facilitates the correct interpretation of FDG avid lymphadenopathy and avoid misinterpretation. Nodular densities may also be localized in clusters or in conglomerates of larger nodules with satellite nodules around (galaxy sign).

It has been described that some malignancies, e.g., Hodgkin´s disease or NSCLC under chemotherapy may present with simultaneous granulomatous manifestations named sarcoid-like reaction. It represents hypermetabolic tissue with increased FDG uptake on the PET scan that may not be misinterpreted as tumor recurrence or progression. Patients with lymphoma may develop typical patterns of sarcoidosis including parenchymal perilymphatic nodular changes or sarcoid-like reactions with mediastinal lymphadenopathy.

The use of 18F-fluorodeoxyglucose-positron emission tomography (FDG-PET) for staging non-small cell lung cancer is widely recognized, whereas the value of fluorodeoxyglucose-positron emission tomography imaging in the evaluation of response to induction chemotherapy is still controversial. A sarcoid-like reaction during induction chemotherapy with pathological bilateral nodal FDG uptake may not be interpreted as progression of nodal disease without histological confirmation.

**Nodular opacities in Rheumatoid arthritis**

Patients with rheumatoid arthritis may develop intrapulmonary nodules, mostly located in the periphery and with cavitations in about 50%. They can be solitary or multiple, may be as large as 7 cm and show a predominance for the upper lobes. They are seen more
frequently in men than in women and the majority of patients are known with established disease. Occasionally nodules calcify (as in the case exhibited).

They represent necrobiotic nodules that are pathologically identical to subcutaneous rheumatoid nodules and 80% of patients with pulmonary nodules have also subcutaneous nodules. Histologically they consist of a necrotic center surrounded by pallisading histiocytes (epitheloid cells), plasmacells and lymphocytes.

Morphologically the nodules are indistinguishable from malignancy. PET scan may show an increased uptake and unless histological proof is available a careful acquisition of patient history is necessary associated with a follow up of the nodules.

**Organizing Pneumonia**

Organizing pneumonia (OP) represents a reparative reaction of the lung to various injuries including infection, drug toxicity, inhalational injury, etc. Histopathologically it is characterized by *granulation tissue within the distal bronchioles, alveolar ducts and alveoli*. Clinically patients present with low grade fever, weight loss and nonproductive cough.

The most frequent imaging features are patchy nonsegmental consolidations that may be located subpleurally or along the bronchovascular bundle. It is more frequently multifocal and bilateral than unilateral and solitary. Yet, especially the latter may have a mass like appearance with spiculated margins that make them indistinguishable from a malignancy. Increased FDG uptake is not a differentiating feature in these in cases.

Suggestive for the diagnosis of organizing pneumonia are:

a) bilateral distribution.

b) sharp demarcation of consolidations by interlobular septa.

c) dilated and air filled bronchi within the consolidations (a lack of air bronchograms does not mean that OP can be excluded).

d) combination of ground glass and consolidation.

e) imaging signs as the `reversed halo sign` or the `interlobular pattern`.

**Images for this section:**
Fig. 1: Case Bronchogenic Carcinoma

Fig. 2: Case Bronchogenic Carcinoma in the left lower lobe: hi resolution images
Case 1

69 yrs male; smoker, weightloss, thoracic pain, productive cough, low-grade fever and blood-tinged sputum.

- subsegmental “infiltrative” consolidation
- multiple peribronchovascularmodular densities
- air bronchogram, no destruction
- tree-in-bud suggestive for endobronchial spread of infection

Fig. 3: Case 1
Fig. 4: Case 1: hi resolution images

Fig. 5: Case 2

35 ys. male; History: Crohn for which immunosuppressive therapy, weight loss, smoking, cocaine, fever, night sweats, hemoptysis, headache.

- unilateral peribronchial round and sharply defined opacities in lingula
- perifocal tree-in-bud (endobronchial spread)
- hilar/ mediastinal lymphadenopathy (left> right) with peripheral enhancement
Fig. 6: Case 2: hi resolution images
Fig. 7: Case 3

67 ys male; malaise, fever, weightloss, sinus pain, epistaxis.

- multiple nodular densities in subpleural distribution
- no perifocal ground glass
- emphysema and bronchopathy (mucoid impaction)
Fig. 8: Case 3: hi resolution images.
Fig. 9: Case 4

52 yrs male; dyspnoe, cough, fever, arthralgia.

- small nodules in *peri-lymphatic* distribution
- confluent to perihilar consolidations
- *predominance in upper lobes* and along peri-bronchovascular interstitium
- symmetric hilar lymphadenopathy with calcifications
Fig. 10: Case 4: hi resolution images.
Fig. 11: Case 5

Case 5

71 yrs female; patient is known with *arthritis*.

- nodular densities with calcifications and perifocal retraction in both upper lobes

- sharply defined, non-calcified nodule in left lower lobe

- no lymphadenopathy
**Fig. 12:** Case 5: hi resolution images.
Case 6

59 yrs female; low grade fever, non-productive cough, malaise, shortness of breath.

- sharply demarcated sub-segmental consolidations in subpleural location

- perifocal ground glass

- bilateral distribution

- narrowed air filled bronchi within opacification, but no underlying distortion

- small hilar/ mediastinal lymphadenopathy

Fig. 13: Case 6
Fig. 14: Case 6: hi resolution images.
Conclusion

Awareness of focal pulmonary opacifications that are FGD avid, yet benign is crucial to avoid misinterpretation. Integration of clinical information, CT findings and FDG uptake is essential to make the correct diagnosis.

CT findings may be suggestive supported by clinical information, though a lung biopsy may be needed for final diagnosis.

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