Pulmonary Nodules: Review Article

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Abstract

In daily clinical practice, radiologists and pulmonologists are faced with incidental radiographic findings of pulmonary nodules. As the diagnosis of pulmonary nodules includes invasive procedures which can be relatively minimal, such as bronchoscopy or transthoracic aspiration or biopsy, but also more invasive procedures such as thoracic surgical biopsies, and as these procedures are linked to anxiety and to cost, it is important to have clearly defined algorithms for the description, management, and follow-up of these nodules. Pulmonary metastasis is seen in 20-54% of extra thoracic malignancies. Lungs are the second most frequent site of metastases from extra thoracic malignancies. Twenty percent of metastatic disease is isolated to the lungs. The development of pulmonary metastases in patients with known malignancies indicates disseminated disease and places the patient in stage IV in TNM (tumor, node, metastasis) staging systems.

The aim of this article is to provide a comprehensive review of the current knowledge on lung nodules.

Introduction

The incidental finding of lung nodule(s) in asymptomatic individuals is an increasingly common clinical dilemma encountered by radiologists and pulmonologists in daily clinical practice. Accurate identification and characterization of malignant lung nodules and development of clear algorithms for their management, permitting cure of early-stage lung cancer while avoiding morbidity, patient distress and increased costs caused by more invasive and unwarranted for benign disease approaches, remain a challenge [2]. Several scientific societies, including the Fleischner Society,[2] the British Thoracic Society (BTS),[3] the American College of Chest Physicians (ACCP),[4] and the National Comprehensive Cancer Network,[5] have published guidelines recommending algorithms for the management of lung nodules. Despite rather minor discrepancies, all proposed approaches take into consideration clinical risk factors for lung cancer, nodules imaging features, and previous imaging studies to assess the probability of malignancy and the most appropriate management. However, most of these recommendations are rather weak, relying on low-quality evidence, and current guidelines are only followed by a minority of clinicians (approximately 40%).[6] Moreover, the management of most patients presenting with incidental lung nodule(s) seems to rely largely on clinical judgment although evidence suggests that clear algorithms and a multidisciplinary approach are required.

Nodule management will become even more important, as evidence from the landmark National Lung Screening Trial (NLST) study, but also from the recently presented but yet unpublished NELSON trial, suggests that screening with low-dose computed tomography (CT) in high-risk individuals may reduce lung cancer mortality through the timely identification of malignant nodules corresponding to early-stage disease.[7]

The aim of this article is to provide a comprehensive review of the current knowledge on lung nodules.
Multi-detector CT Imaging of metastatic small pulmonary nodules

Practice Essentials;

Pulmonary metastasis is seen in 20-54% of extra thoracic malignancies. Lungs are the second most frequent site of metastases from extra thoracic malignancies. Twenty percent of metastatic disease is isolated to the lungs. The development of pulmonary metastases in patients with known malignancies indicates disseminated disease and places the patient in stage IV in TNM (tumor, node, metastasis) staging systems.[8]

This typically implies an adverse prognosis and alters the management plan. Imaging plays an important role in the screening and detection of pulmonary metastases. Imaging guidance is also used in histologic confirmation of metastatic disease. In patients with poor cardio respiratory function and co morbidities, imaging-guided thermal ablation procedures are an effective alternative to surgical resection to improve survival.[8]

Chest radiography (CXR) is the initial imaging modality used in the detection of suspected pulmonary metastasis in patients with known malignancies. Chest CT scanning without contrast is more sensitive than CXR. For patients with bone or soft-tissue sarcoma, malignant melanoma, or head and neck carcinoma, CT scanning of the chest should be performed as an initial evaluation.[9]

In patients with primary renal or testicular cancer, chest CT scanning should be performed based on the presence of metastatic disease elsewhere.[9]

CT scanning is the modality of choice for detection and follow-up of pulmonary metastasis (Fig.1,2), because of its higher spatial, temporal, and contrast resolution and lack of superimposition of adjacent structures. It has been shown to have higher sensitivity than chest radiography (CXR) in the detection of pulmonary metastases. [10]

CT scanning is performed using a multi-slice technique, and no intravenous contrast is required for the detection of pulmonary metastases. Contrast may be useful when a nodule is located adjacent to the hilum and mediastinum (Fig.3,4,5). [11]

CT scanning is not required if CXR shows multiple nodules in a patient with a known primary malignancy. In a patient with known malignancy, chest CT scanning is performed if (1) CXR shows a solitary nodule, (2) CXR shows an equivocal nodule, (3) CXR findings are negative but the extra-thoracic malignancy has a high risk of lung metastasis (eg, breast, kidney, colon, bladder), or (4) CXR shows multiple nodules, but biopsy or definitive treatment by mastectomy, chemotherapy, and radiation is planned.[8]

In patients with high-risk tumors such as bone and soft-tissue sarcomas, testicular tumors, and choriocarcinomas, CT scanning is recommended every 3-6 months for 2 years. [42 8]

The radiation dose from frequent CT scanning can be reduced by using several dose-reduction techniques such as low kV, low mAs, adaptive-tube current modulation, and iterative reconstruction algorithms. The sensitivity of nodule detection can be increased by using post processing tools such as maximum-intensity projection (MIP) or volume rendering (VR) or using cine viewing of data sets. [8]

High-resolution CT (HRCT) scanning is used for detection of Lymphangitic carcinomatosis. In this technique, spatial resolution is maximized by narrow collimation (1-2 mm) and high-resolution reconstruction algorithm.[ 8]
Fig.1) Axial CT scan in a 58-year-old man with malignant melanoma shows multiple round nodules and masses of varying sizes in both lungs, consistent with metastases. There are also small bilateral pleural effusions.[12]

Fig.2) Coronal CT scan in a 58-year-old man with malignant melanoma shows multiple, predominantly basal nodules of varying sizes, consistent with metastatic disease.[12]

Fig.3) Axial CT scan in a 62-year-old woman with malignant ovarian tumor shows predominantly sub-pleural metastatic nodules of varying sizes.[12]
Fig. 4) Coronal CT scan in a 62-year-old woman with malignant ovarian tumor shows predominantly peripheral sub-pleural metastatic nodules of varying sizes. [12]

Fig. 5) Axial CT scan in a 67-year-old man with a history of spindle cell sarcoma of the thigh shows a heterogeneously enhancing mass in the right lower lobe that is extending to the mediastinum and into the chest wall. [12]

**Physics, Principals and Limitations of Maximum intensity projection**

While significant progress has been made with technological advancements resulting in today’s multi-detector CT scanning techniques, human perception errors continue to be a significant hurdle in the detection of small intrapulmonary nodules. To that end, there are commercially available techniques such as MIP and VR that allow displaying a sub-volume of the 3-dimensional data set. [13]

In MIP, only voxels with the maximum intensity are displayed along a projection line from the viewer’s eye through the 3-dimensional volume of interest. On the other hand, the VR technique incorporates the assignment of opacity values to CT numbers, meaning high opacity values produce an appearance similar to surface rendering and low opacity values allow the user to “see through” structures. [13]
With this technique, a MIP image is created when a specific projection (e.g., antero-posterior) is selected and then rays are cast perpendicular to the view through the volume, with the maximum value encountered by each ray recorded on a 2D image. [14]

As a result, the entire volume is “collapsed” and only the brightest structures are visible. Variations of this approach include the minimum intensity projection (Min IP), useful for visualizing airways, and the raysum or average projection, which sums all pixel values encountered by each ray to provide an image similar to a radiograph.[15]

Note that the MIP technique preserves high attenuation structures (e.g. nodule) in the final image and displays the continuity of high attenuation structures running obliquely through the slab (e.g. blood vessel) but obscures oblique low attenuation structures (e.g. airway lumen).[16]

A limitation of MIP, however, is that bones or other structures that are more attenuative than contrast-enhanced blood vessels, will obscure the blood vessels. Two approaches to address the limitations of obscuration are slab-MIP and pre-rendering editing: Slab-MIP images are created when a plane through the data is defined and then “thickened” perpendicular to the plane. The process with which the plane is thickened can be MIP, Min IP, raysum, or VR.[17]

By selecting a slab orientation that does not result in overlap of structures with extremely high attenuation (e.g., bones, metal) on structures of interest (e.g. blood vessels), the latter can be clearly visualized without the need for time-consuming and operator-dependent editing.[17]

This approach, however, is generally limited to imaging through slabs that are 5-30mm thick. If an MIP image of a larger sub-volume of the data is desired, then the data must first be edited to remove obscuring structures (“pre rendering editing”).[17]

Even after the issues of obscuration have been addressed, some limitations of the MIP technique remain. MIP does not permit the appreciation of depth relationships and, in regions of complex anatomy such as at the neck of an aortic aneurysm, it can be difficult to be confident when the true origin of a branch is visualized versus shortened branch due to overlap of its proximal extent with the aorta itself.[17]

A study by Jankowski et al. showed that the sensitivity of nodule detection was higher with MIP than with 1-mm axial images or computer-aided detection (CAD) for all nodules.[18]

For nodules larger than 3 mm, sensitivities were higher with 1-mm images or MIP than with CAD (P<.0001). In addition, MIP was the least time-consuming technique, and CAD was the most time-consuming technique. MIP and CAD reduced the number of overlooked small nodules. [18]

Using MIP reduces the number of overlooked small pulmonary nodules (Fig.6,7,8), especially in the central lung and in junior-reviewer detection of pulmonary nodules. [19]

Kawel et al. showed that the sensitivity of nodule detection was superior for 8-mm MIP than for 11-mm MIP and all thicknesses of volume-rendered images, independent of nodule localization and size.[20]

Fig.6 (A,B) False-negative thoracic nodule detection. Thoracic CT in a 5-year-old with Wilms’ tumor. A right lower lobe nodule (arrow) adjacent to a vessel was missed on axial CT images (A) but identified on MIP image (B).[21]
Fig. 7) Thoracic CT in a 12-year-old with osteosarcoma. A 2-mm peripheral left lower lobe nodule (arrow) was missed on axial CT image (A) but identified on MIP image (B).[21]

Fig. 8) A 1.25-mm thick transverse CT section reveals two 4-mm rounded opacities appearing as lung nodules (arrows in top image). A 7-mm thick TS-MIP centered on the transverse section above reveals that only the posterior of the two opacities is a lung nodule (arrow in bottom image) and the anterior opacity corresponds to a part of a normal blood vessel (bottom).[21]

**Degree of confidence**

CT scanning has much higher sensitivity than CXR in the detection of pulmonary metastases. However, studies have reported that CT scanning has underestimated the pulmonary metastatic involvement discovered in surgery by 25-38%. [57,58 22-23]

Another study showed that surgery discovered 22% more malignant nodules than those detected by helical CT scanning. [24]

Hence, manual palpation is recommended during surgery to detect subtle lesions.[19]

CAD is also available for chest CT scanning, most often as a second look after the radiologist has reviewed the study. It has been shown to detect 82.4% of known pulmonary nodules. [24]

Although CT scanning is very sensitive, the finding of a nodule is not specific. False-positive results may be caused by hamartomas, granulomas (eg, tuberculosis, histoplasmosis, Wegener granulomatosis), sarcoidosis, silicosis, small infarcts, small areas of fibrosis, and intrapulmonary lymph nodes. [24]

**The specificity of CT scanning depends on the following:**

- Propensity of the primary malignancy to metastasize to the lung
- Stage of primary malignancy
- Age
Smoking history
- History of prior treatment
- History of granulomatous disease
- Prevalence of benign nodules in the population

**Features that are more favorable of malignancy are as follows:**
- Non calcified nodule
- Spherical or ovoid shape rather than linear or irregular shape
- Close relationship to adjacent vessel
- Lesion with decreased attenuation distally
- Lesion with reticular changes
- Doubling time of metastases from 2-10 months

Size is not useful in distinguishing benign and malignant nodules. Although a direct correlation exists between nodule size and malignancy, the size should be evaluated in the context of a known malignancy. In patients with known malignancy, it should be noted that nodules smaller than 1 cm can also be metastasis.[25]

Temporal assessment of nodules is useful in determining malignancy. However, nodule measurements have significant inter-observer and intra-observer variability, which can be reduced by automated or semi-automated measurements. Three-dimensional volume measurement may be more accurate and reproducible, but it is also prone to precision errors. [25]

Doubling times less than 20-30 days are suggestive of infections or rapidly growing metastasis. Doubling times greater than 400 days are benign lesions. Nodules being stable for at least 2 years is an indicator of benignity (with the exception of sub solid nodules). Nodule enhancement can be also used to distinguish benign nodules from malignant nodules. [6126]

Thin-section CT images are obtained through the nodules before and after 1, 2, 3, and 4 minutes following administration of contrast at 2 mL/second. Enhancement of 15 HU or less is suggestive of a benign lesion, while higher degrees of enhancement are suggestive of malignancy or inflammation. This technique has 98% sensitivity for malignancy and 58% specificity for benignity.[26]

This technique is suitable for nodules between 7 mm and 3 cm and for non-calcified nodules. Peak attenuation of nodules correlates positively with micro vessel density and vascular endothelial growth factor staining on pathology. (Malignant lesions have higher vascular endothelial growth factor expression).[26]

With the advent of dual-source CT scanning, simultaneous 80 kV and 140 kV images can be obtained, which helps in identifying areas of fat, bone, soft tissue, and iodinated contrast. Virtual unenhanced images can be generated, which then can be subtracted from contrast-enhanced scans to evaluate areas of enhancement, yielding an estimate of tumor perfusion. [25]

CT may miss nodules that are centrally located (either within bronchi or adjacent to vessels), are small, have faint attenuation, are at a lower lobe location, or are adjacent to or within parenchymal abnormalities. Sensitivity may be improved by using MIP, VR, or cine viewing of datasets.[25]

**Radiological differential diagnosis of pulmonary nodules**

**A) Distribution:**
When the nodules are numerous, they are distributed diffusely throughout the lungs in a random pattern without any specific anatomic distribution; when nodules are few, they are predominantly sub-pleural. [27]

Multiple pulmonary nodules in a patient with known malignancy are highly suggestive of metastasis. Of multiple pulmonary nodules detected with CT scanning, 73% are shown to be metastases. While 80-90% of patients with multiple metastatic nodules have a history of malignancy, some do not have a malignancy at the time of diagnosis, and in few rare cases, the primary may never be found. [27]
The most common CT pattern of pulmonary metastasis is the presence of multiple pulmonary nodules. These nodules are in a random distribution and are of varying sizes, because of multiple episodes of tumor embolization or different tumor growth rates.\(^{(6227)}\)

**B) Margins:**
Nodules of the same size are believed to be due to a shower of emboli that occurred at the same time. The margins can be smooth or irregular and can be either well defined or ill defined. The nodule has soft-tissue attenuation and can have a prominent pulmonary vessel heading into it, which is called the feeding-vessel sign. They are more common in the lung bases because of higher vascular supply.\(^{(27)}\)

The margins of the pulmonary metastatic nodules are well circumscribed because, histologically, the tumor cells invade peri-vascular interstitium and have clear, smooth margins. However, once the tumor grows out of the vessels into the adjacent interstitium and alveolar space and proliferates, the margins become irregular.\(^{(27)}\)

A radiologic-pathologic correlation study showed that well-defined, smooth-margined metastasis corresponded to an expanding alveolar space-filling type (eg, hepatocellular carcinoma); poorly defined, smooth-margined metastasis corresponded to an alveolar cell type (adeno-carcinoma); and poorly defined, irregular-margined metastasis corresponded to an interstitial proliferating type (squamous carcinoma or metastases after chemo-therapy). Some correlation also exists between the histologic type of primary tumor and CT appearance of a lesion margin.\(^{(28)}\)

Because of this non specificity of margins, it is difficult to distinguish metastases from other confounding lesions. For example, some metastases have smooth margins and, hence, cannot be distinguished from benign lesions based on margins. Since some metastases have irregular margins, the margins cannot be used as a factor to differentiate primary cancer in a solitary pulmonary nodule.\(^{(28)}\)

The key factor of differentiating these from pulmonary metastatic disease is appropriate clinical history taking and a radiographic pattern showing the evaluation of ill-defined pulmonary opacities into organizing, more circumscribed nodules.\(^{(28)}\)

**C) Growth:**
Follow-up CT scanning in 6 weeks to 3 months will show progression of metastatic nodules, while benign lesions show no growth, decrease in size, or undergo complete resolution. While the classic features of lung metastases are extremely helpful in narrowing the differential mainly down to metastases, the atypical features can make it difficult to distinguish lung metastases from more benign lung pathology.\(^{(28)}\)

**D) Pattern:**
Cannonball metastasis refers to the presence of few, large, well-circumscribed, and round metastatic masses. It is usually seen in metastasis from renal carcinoma, choriocarcinoma, colon cancer, prostate cancer, or endometrial carcinoma. Miliary nodules refer to numerous, small (1-4 mm), same-sized nodular opacities that resemble millet seeds.\(^{(28)}\)

They are believed to be caused by a single massive shower of tumor emboli. Miliary nodules are seen in a random distribution within the secondary pulmonary lobule and involve the sub pleural regions. The differential diagnosis for miliary nodules includes granulomatous infections such as tuberculosis, histoplasmosis, healed varicella pneumonia, sarcoidosis, silicosis, coal worker's pneumonoconiosis, hypersensitivity pneumonitis, and langerhans cell histiocytosis.\(^{(28)}\)

**E) Location:**
Histologic studies have described the distribution of a metastatic nodule within a secondary pulmonary nodule. The metastatic nodule initially proliferates from tumor emboli in the arteriole or capillary. Initially, a metastatic nodule is seen in a peripheral portion rather than the centri lobular structures; in one study, only 11-12% were shown to be located in the central bronchovascular bundle, with 60-68% located between central and peri-lobular structures and 20-28% in peri-lobular structures.\(^{(28)}\)

When the metastasis subsequently grows, it appears to be connected with the broncho-vascular bundle, which is called the mass-vessel sign.\(^{(28)}\)
F) Cavitation:
Cavitation is seen in 4% of metastases (vs 9% of lung primaries). Tumor necrosis and discharge of necrotic material is thought to be the primary mechanism behind cavitating lung metastases (excavating metastasis). [29]
These tumors initially are solid and later become a cavitary lesion with thick and irregular walls. Cavitation can also be caused by a check-valve mechanism of tumor infiltrating into bronchial structures. Head and neck cancers in males and genitalia cancers in females are the common causes. Squamous cell carcinomas are the most common (70%) primary tumor to cause cavitation, especially seen on radiographs, although adeno-carcinomas (GI tract, breast), transitional cell tumors, and sarcomas are also known to cavitate on CT scans. [30]
On CT scans, 10% of squamous carcinoma metastases were shown to cavitate, while 9.5% of adenocarcinoma metastases were also shown to cavitate. Cavitation can also be seen following chemotherapy of metastatic nodules. Cavitated metastasis usually has thick and irregular walls. Thin-walled cavities are seen in sarcomas, which are the ones that often result in pneumothorax. [31]
The differential diagnosis for cavitating nodules includes septic emboli (eg, septic patients, intravenous drug abusers), lung abscess, tuberculosis, angitis, Wegener granulomatosis, and rheumatoid nodules. Nine percent of primary lung tumors cavitate, most commonly squamous cell cancers. [30]

G) Associated pneumothorax:
Spontaneous pneumothorax is an uncommon presentation of pulmonary metastasis. Osteosarcoma is the most common tumor known to produce pneumothorax. Pneumothorax has been shown in 5-7% of osteosarcoma metastasis. Spontaneous pneumothorax in a patient with osteosarcoma should raise suspicion of pulmonary metastasis, which can be detected with CT scanning. Aggressive sarcomas and non sarcomatous tumors can also produce pneumothorax. [32]
The proposed theory behind spontaneous pneumothorax is tumor necrosis in peripheral sub-pleural nodules resulting in a broncho pleural fistula with subsequent pneumothorax. The differential diagnosis for pneumothorax includes rupture of a subpleural bleb, trauma, mechanical ventilation complications, and underlying lung diseases (eg, cystic fibrosis, tuberculosis, fibrosis, sarcoidosis). [30]
Multiple thin-walled cystic metastases are also seen in metastasis from angiosarcoma. This is the second most common type of presentation for angiosarcoma metastasis after multiple pulmonary nodules. [33]
Rupture of sub-pleural cystic metastasis may result in pneumothorax. Proposed mechanisms for thin-walled cysts are (1) cavation of a solid nodular lesion through discharge of necrotic tumor material, (2) infiltration of tumor cells into walls of pre-existing bulla, (3) a ball-valve effect caused by circumferential growth of tumor around small bronchioles resulting in bronchiolar obstruction, and (4) proliferation of tumor cells forming blood-filled cystic spaces anastomosing the network of sinusoids. [33]

H) Calcification:
Calcification of metastatic nodule is often seen only on CT scans. Calcification is seen in metastasis from osteosarcoma, chondrosarcoma, giant cell tumor of the bone, mucinous adenocarcinoma, and treated metastatic choriocarcinoma. [33]
Reasons for calcification vary but include bone formation in primary bone tumors, dystrophic calcification, and mucoid calcification. Punctate calcification may be seen following hemorrhagic necrosis in angiosarcoma. [33]
Calcification can also be seen following chemotherapy and radiation therapy. In osteosarcomas, dense, eccentric calcification/ossification is seen. In rare cases, calcification may develop at the site of pulmonary metastasis (typically from a testicular primary site) that has vanished after chemotherapy. CT scans cannot help differentiate calcifications or ossifications due to metastasis from calcifications or ossifications due to other lesions. [41 31]

I) Density:
Another atypical feature of metastatic disease is nodular density surrounded by a halo of ground-glass attenuation or ill-defined fuzzy margins (ie, the CT halo sign). This is seen in hyper-vascular primary
tumors such as choriocarcinoma (parenchymal hemorrhage), angiosarcoma (fragility of neo-vascular tissue resulting in rupture of vessels), or renal carcinoma.[30]

A ruptured vessel secondary to fragile neo-vascular tissue leads to hemorrhage, causing the ground-glass halo on CT scans. The differential diagnosis for this appearance includes invasive aspergillosis, candidiasis, tuberculosis, Wegener granulomatosis, minimally invasive adenocarcinoma, pneumonia, eosinophilic pneumonia, abscess and lymphoma in immune-compromised patients (due to fibrin, less dense inflammatory reaction, edema, or less densely arranged malignant cells histo-pathologically), or post biopsy.[31]

**J) Air-space pattern:**
An air-space pattern is another atypical presentation of metastasis. This can be due to lepidic growth of tumor along intact alveolar walls, which is seen in metastatic adeno-carcinoma from GI tract, ovary, or breast. Imaging features include consolidation with air bronchography, ground-glass opacities, and air-space nodules. Another mechanism is pulmonary infarction due to tumor embolism, which is seen in tumors of the liver, breast, kidney, stomach, and prostate, as well as in choriocarcinoma.[31]

The differential diagnosis for this air-space pattern includes infections, edema, hemorrhage, organizing pneumonia, eosinophilic pneumonia, minimally invasive adeno-carcinoma, lymphoma, and sarcoidosis, among other entities.[30]

**K) Tumor embolism:**
Tumor embolism is a less common presentation of metastatic disease. Although most pulmonary metastases result from microscopic tumor embolization, only a few survive to proliferate as metastases. With tumor emboli, the tumor is confined to the vascular tree, without proliferation of metastasis into extra vascular tissue. In an autopsy series, intravascular tumor emboli have been seen in 2.4 to 26% of patients with solid malignancy.[34]

Tumor emboli is seen in metastasis from liver, breast, renal, gastric, and prostatic cancers, as well as in sarcomas and choriocarcinoma. Tumor emboli are seen in small or medium-sized arteries. Large tumor emboli within main, lobar, or segmental pulmonary arterial branches are only rarely seen. Diagnosis may be difficult to make, even with HRCT scanning. On CT scans, multifocal dilatation and beading of the peripheral sub-segmental arteries are seen due to smaller tumor emboli. Also seen are peripheral wedge-shaped areas of infarction. Perfusion defects can be identified with dual-source CT scanning.[30]

Occasionally, tumor emboli may be seen within the larger pulmonary vessels. The differential diagnosis of tumor emboli includes pulmonary thrombo-embolism and pulmonary artery sarcoma. Pulmonary artery enlargement (>2.9 cm, or larger than the ascending aorta) may be due to large tumor emboli or the development of pulmonary hypertension from large or numerous tumor emboli.[31]

**L) Endo-bronchial metastasis:**
Endobronchial metastasis is rare (Fig.9, 10), seen in 2% of tumors. Primaries that cause endobronchial metastases are renal, breast, colorectal, and pancreatic cancers. Endobronchial involvement occurs through 2 routes: (1) direct endobronchial deposition through aspiration, hematogenous, or lymphatic spread or (2) by airway invasion of tumor into adjacent lymph nodes/parenchyma.[30]

The endobronchial lesion, as well as the consequences (eg, lobar atelectasis or, less commonly, complete collapse of a unilateral lung) can be identified on CT scans. The differential diagnosis includes primary neoplasms such as bronchogenic carcinoma, carcinoid, and granulomas such as in tuberculosis, histoplasmosis, foreign bodies, or bronchiolitis.[30]
Fig. 9) Axial CT scan shows an endobronchial mass within the bronchus intermedius, which is the cause of the collapse of the right upper and lower lobe. [12]

Fig. 10) Axial positron emission tomography scan of the same patient shows high uptake in the endobronchial mass, which was proven to be endobronchial metastasis. [12]

Solitary pulmonary nodule is a less common presentation of metastatic disease. Solitary pulmonary nodule is a round opacity that is at least moderately well marginated and less than 3 cm in maximum diameter. [35]

In brief, Solitary pulmonary metastasis is frequent in melanoma, sarcoma, and cancers of colon, breast, kidney, bladder, and testicle. Carcinoma of the colon, especially from the recto-sigmoid area, accounts for a third of cases with solitary pulmonary metastasis. Metastasis accounts for 2 to 10% of solitary nodules. [36]

The differential diagnosis is extensive, but the most common lesions are primary lung neoplasms, granuloma, hamartoma, and arteriovenous malformation. Granulomas (tuberculosis, histoplasmosis) show calcification, which is usually central, diffuse, or laminated. Hamartoma may have “popcorn” calcification, fat attenuation, or a combination. Arteriovenous malformation has a feeding vessel. [36]

In a patient with known malignancy, development of a solitary pulmonary nodule is a challenge (Fig. 11). Distinguishing between a primary and secondary neoplasm is important, since it has prognostic and therapeutic implications. At surgery, 0.4 to 9% of solitary pulmonary nodules are likely to be a metastasis in a patient with known extrathoracic malignancy. [37]
Fig. 11) Axial CT scan in a patient with laryngeal cancer shows a solitary pulmonary nodule in the apico-posterior segment of the left upper lobe. This was biopsy proven to be metastasis.[12]

Solitary pulmonary nodules seen on radiographs have a 25% chance of being a metastasis, while those seen on chest CT scans have a 46% chance of being a metastasis in a patient with known extra thoracic malignancy. It should be noted that CT scans may show additional lesions compared with a radiograph, in which case the diagnosis becomes easier.[30]

The likelihood of a solitary pulmonary nodule being a metastasis depends on the histopathology of the primary tumor and age of the patient. The incidence of a second primary lung malignancy is higher than a solitary metastasis in patients with cancers of the head and neck (8:1 ratio), bladder, breast, cervix, bile ducts, esophagus, ovary, prostate, or stomach (3:1 ratio for all these). This likelihood also exists for tumors of the salivary gland, adrenals, colon, kidney, thyroid, thymus, or uterus.[38]

There is a higher chance of metastasis (2.5:1) with melanoma, sarcoma, and testicular cancer. In patients with a melanoma or sarcoma, a solitary lung metastasis is more common than a second primary lung cancer.[14]

No reliable imaging features help distinguish a solitary pulmonary metastatic nodule from primary pulmonary neoplasms. Metastatic nodules may be round or oval, or they may have lobulated margins. Initially, it was thought that metastatic solitary pulmonary nodules have smooth margins compared with primary lung cancers, which can have speculated or lobulated margins.[39]

However, it is now known that margins are not helpful in distinguishing primary and secondary tumors, since a metastasis can also have irregular, speculated margins due to a desmoplastic reaction or tumor infiltration into the adjacent lymphatics or bronchovascular structures.[39]

Smooth borders and lobulated margins can also be seen in benign lesions such as hamartomas. Laminated, central, diffuse, and popcorn calcification are benign patterns, while stippled and eccentric calcifications are considered malignant. Solitary metastases are more common in lower lobes, while primary lung cancer is more common in upper lobes. [39]

Attenuation measurements may be of some value. In one study, the mean attenuation value of pulmonary metastasis from renal cancer was found to be higher than that of primary lung cancer nodules. The interval between appearance of initial tumor and solitary pulmonary nodule may be useful. An interval of more than 5 years in patients with osteosarcoma more likely represents a new primary tumor.[39]

However, in patients with carcinoma of the breast or kidney, pulmonary metastases may occur many years after the primary tumor is diagnosed. Biopsy is often required for histo-pathologic diagnosis in this scenario.[39]

Lymphangitic carcinomatosis refers to spread of a neoplasm through the lymphatics. It is most commonly seen in adeno-carcinomas, particularly primary tumors of breast, lung, stomach, pancreas, uterus, rectum, or prostate. It is seen in 35% of autopsies of patients with solid tumors. It occurs from hematogenous spread to the lungs, with subsequent lymphatic invasion or direct lymphatic spread from mediastinal and hilar lymph nodes.[28]
References


