

Pulmonary Manifestations of Nonpulmonary Solid Malignancies

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KEYWORDS

• Metastatic disease • Complications • Pulmonary metastases • Solid malignancies

KEY POINTS

- The lungs are a common site of metastatic disease and these include the lung parenchyma, airways, mediastinal lymph nodes, pleura, and vasculature.
- Metastatic disease may present without symptoms, with nonspecific symptoms, and with pulmonary symptoms, in addition to symptoms related to their anatomic origin.
- Treatment of pulmonary metastatic disease includes systemic therapy as well as local therapy based on the site of metastasis, including the airway and pleural space.

INTRODUCTION

The lungs are a common site of metastatic disease and these include the lung parenchyma, airways, mediastinal lymph nodes, pleura, and vasculature (Table 1). Metastatic disease may present without symptoms, with nonspecific symptoms such as anorexia or weight loss, and with pulmonary symptoms such as chronic cough, hemoptysis, dyspnea, and hoarseness, in addition to symptoms related to their anatomic origin.

Pulmonary metastases develop due to various mechanisms, including local blood flow and cellular or biochemical properties of tumor cells that thrive in an appropriate microenvironment for growth. These likely include growth factors and inhibitors, chemoattractants, and complex cellular interactions that may predispose tumor deposition based on distinct subtypes. Some diseases, such as melanoma, choriocarcinoma, and sarcoma, have thoracic metastatic invasion up to 80% to 100% of the time based on autopsy specimens. Other cancers with pulmonary metastatic lesions occurring more than 50% of the time

include those of the breast, prostate, kidney, thyroid, and testes.¹

PARENCHYMAL DISEASE

Metastatic disease is often identified as a solitary nodule, multiple pulmonary nodules, and infiltrates in a distribution consistent with lymphangitic spread. However, up to 50% of cases of lymphangitic spread may have normal chest radiograph, but are detected on computed tomography (CT).¹

Nodules may appear small (miliary), large (“cannonball”), cavitory, calcified, and be either well-defined or poorly defined. Examples are demonstrated in Fig. 1, including metastatic disease from breast cancer, osteosarcoma, and thyroid cancer. Although calcification often represents benign disease, it occurs with metastatic osteogenic sarcoma and chondrosarcoma, among others. Cavitation is most commonly seen with metastatic squamous cell carcinoma, and in this scenario may occur up to 75% of the time.¹ A recent study suggested the presence of multiple nodules and cavitation most commonly

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Table 1
Pulmonary manifestations of extrathoracic malignancies and treatment considerations

Site of Disease	Evaluation	Treatment Possibilities
Lung parenchyma	Biopsy (bronchoscopy, CT-guided, surgical resection)	Systemic therapy Metastatectomy Palliative care
Endobronchial disease	Bronchoscopy	Systemic therapy Radiation therapy Bronchoscopic including electrocautery, APC, laser, cryotherapy, stenting Palliative care
Mediastinal lymph nodes	EBUS EUS Mediastinoscopy CT-guided biopsies	Systemic therapy Palliative care
Pleural effusion	Thoracentesis Thoracoscopy CT-guided biopsies	Systemic therapy Thoracentesis Tunneled pleural catheter Pleurodesis Palliative care
Pericardial Effusion	Echocardiography	Systemic therapy Catheter drainage Surgical window Palliative care
Pulmonary vascular disease	CT angiogram V/Q scan	Systemic therapy Anticoagulation Palliative care
Paraneoplastic syndrome	PET scan Brain MRI	Systemic therapy Palliative care

Abbreviations: APC, argon plasma coagulation; CT, computed tomography; EBUS, endobronchial ultrasound; EUS, endoscopic ultrasound.

represented metastatic disease but suggested biopsy to confirm malignancy because almost 10% had nonmetastatic deposits.²

Lymphangitic features are characterized by reticular or reticulonodular infiltrates and nodular septal thickening without architectural distortion. This pattern is associated most frequently with adenocarcinoma, namely breast, prostate, stomach, and pancreas carcinomas.¹ An example of metastatic adenocarcinoma of the lung is shown in **Fig. 1**. The differential diagnosis includes infection or pulmonary toxicity from chemotherapy, and thus further investigation may be required in the form of bronchoscopy, transthoracic biopsy, or, occasionally, surgical biopsy.

Treatment for metastatic parenchymal disease is often systemic cytotoxic chemotherapy and/or hormonal manipulation aimed at the underlying malignancy. Radiation may be used as part of a palliative approach, such as those tumors causing significant hemoptysis.

Although surgery is often the primary treatment modality for limited stage cancer, occasionally pulmonary metastatectomy may be considered

for oligometastatic disease in the absence of extrathoracic sites of disease. In these cases of carefully defined oligometastatic disease, the number and site of metastatic tumors are limited and represent a distinct scenario from more extensive metastatic disease. As described by Weichselbaum and Hellman,³ “successful results of curative resection of lung metastases have been described for almost all types of cancer.” In the report from the International Registry of Lung Metastases, 4572 patients almost equally divided between epithelial tumors and sarcomas who underwent complete resection of metastatic tumors had a 5-year survival rate of 36% and a 10-year survival rate of 26%.⁴ Multiple studies have since been performed to identify specific cohorts with the greatest chance of benefit. In an analysis of 19 papers, investigators determined that patients most likely to benefit from pulmonary metastatectomy in colorectal carcinoma included those with smaller size and number of metastatic deposits, lower carcinoembryonic antigen levels, absence of intrathoracic lymph node involvement, and response to induction chemotherapy.⁵ In a

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