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Pulmonary Manifestations of Solid Non-Pulmonary Malignancies

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Jonathan Puchalski

The lungs are a common site of metastatic disease. Pulmonary metastases develop due to local blood flow and cellular or biochemical properties of tumor cells. Metastases develop from any type of malignancy and may occur via hematogenous, lymphatic, aerogenous, and/or direct spread. Metastatic disease may present with symptoms indistinguishable from primary lung cancer, including dyspnea, hemoptysis, and chest pain. Radiographically, these may present as parenchymal lung disease, mediastinal lymphadenopathy, airway obstruction, or pleural and vascular disease. No part of the thorax is spared from metastatic potential. This review highlights complications of non-pulmonary solid malignancies based on sites of anatomic metastases.

Pulmonary Manifestations of Lymphoma and Leukemia

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Lara Bashoura, George A. Eapen, and Saadia A. Faiz

Pulmonary manifestations of lymphoma and leukemia may involve multiple structures within the thoracic cavity. Malignant lymphoma typically originates in lymph nodes, but concomitant or primary presentations with parenchymal, pleural, or tracheobronchial disease may occur. Once infection is excluded, leukemic infiltrates may be related to malignancy, hemorrhage, or secondary pulmonary alveolar proteinosis. Confirmation with cytology or flow cytometry is recommended to diagnose malignant pleural effusions in hematologic malignancies. In chronic leukemia with progressive pulmonary findings, exclusion of a synchronous malignancy or Richter syndrome should be performed. Venous thromboembolism may present in patients with leukemia and lymphoma despite the presence of thrombocytopenia.

Complications of Cancer Treatment

Radiation Pneumonitis

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Trevor J. Bledsoe, Sameer K. Nath, and Roy H. Decker

Radiation-induced lung injury is a well-known complication of thoracic radiation for patients with breast, lung, thymic, and esophageal malignancies, and mediastinal lymphomas. Improvements in radiation technique, as well as the understanding of the pathophysiology of radiation injury, have led to lower rates of pneumonitis and improved symptom control. Here, the authors provide an overview of the pathophysiology, diagnosis, and management of patients with radiation pneumonitis as a complication of treatment of chest malignancies.

Pulmonary Toxicities from Conventional Chemotherapy**209**

Paul Leger, Andrew H. Limper, and Fabien Maldonado

Despite significant recent progress in precision medicine and immunotherapy, conventional chemotherapy remains the cornerstone of the treatment of most cancers. Chemotherapy-induced lung toxicity represents a serious diagnostic challenge for health care providers and requires careful consideration because it is a diagnosis of exclusion with significant impact on therapeutic decisions. This review aims to provide clinicians with a valuable guide in assessing their patients with possible chemotherapy-induced lung toxicity.

Pulmonary Toxicities from Checkpoint Immunotherapy for Malignancy**223**

Jennifer D. Possick

Checkpoint immunotherapy with agents targeting PD-1 and CTLA-4 has transformed the landscape of oncologic therapy. Immune-related adverse events (IRAEs), including significant pulmonary toxicities, have been observed in patients treated with these agents. The incidence, timing, clinical features, and outcomes of pulmonary IRAEs are quite variable, emphasizing the importance for clinical vigilance as these therapies become more ubiquitous in the treatment of a spectrum of malignancies. Outcomes are generally favorable when toxicity is recognized early and treated promptly.

Early Onset Noninfectious Pulmonary Syndromes after Hematopoietic Cell Transplantation**233**

Lisa K. Vande Vusse and David K. Madtes

This article reviews the noninfectious pulmonary syndromes that cause morbidity and mortality early after hematopoietic cell transplantation with an emphasis on risk factors, clinical manifestations, treatment, and outcomes. The first section covers idiopathic pneumonia syndrome and its subtypes: peri-engraftment respiratory distress syndrome, diffuse alveolar hemorrhage, delayed pulmonary toxicity syndrome, and cryptogenic organizing pneumonia. The second section covers pulmonary toxicities of chemotherapies and immunosuppressive agents used in this setting. The final section covers less common syndromes, including pulmonary alveolar proteinosis, venous thromboembolism, pulmonary cytolytic thrombi, pulmonary venoocclusive disease, and transfusion-related acute lung injury.

Late-Onset Noninfectious Pulmonary Complications After Allogeneic Hematopoietic Stem Cell Transplantation**249**

Anne Bergeron

Late-onset noninfectious pulmonary complications (LONIPCs), most of which occur between 3 months and 2 years following allogeneic hematopoietic stem cell transplantation (HSCT), have a significant effect on patient outcomes and are highly associated with mortalities and morbidities. LONIPCs can involve all anatomic lung regions: bronchi, parenchyma, vessels, and pleura; this diversity can lead to various clinical entities. Bronchiolitis obliterans syndrome is the most frequent LONIPC. Most LONIPCs are associated with graft-versus-host disease. Evaluation of prophylactic strategies for LONIPCs is necessary to improve outcomes in high-risk allogeneic HSCT recipients.

Pulmonary Infections in Patients with Malignancy

Bacterial Pneumonia in Patients with Cancer: Novel Risk Factors and Management 263

Justin L. Wong and Scott E. Evans

Bacterial pneumonias exact unacceptable morbidity on patients with cancer. Although the risk is often most pronounced among patients with treatment-induced cytopenias, the numerous contributors to life-threatening pneumonias in cancer populations range from derangements of lung architecture and swallow function to complex immune defects associated with cytotoxic therapies and graft-versus-host disease. These structural and immunologic abnormalities often make the diagnosis of pneumonia challenging in patients with cancer and impact the composition and duration of therapy. This article addresses host factors that contribute to pneumonia susceptibility, summarizes diagnostic recommendations, and reviews current guidelines for management of bacterial pneumonia in patients with cancer.

Fungal Pneumonia in Patients with Hematologic Malignancies and Hematopoietic Cell Transplantation 279

Steven A. Pergam

Invasive fungal infections, which occur primarily as a consequence of prolonged neutropenia and immunosuppression, are a life-threatening complication seen among patients with hematologic malignancies. The routine use of triazole antifungal prophylaxis, enhanced diagnostics, and newer antifungal agents have led to improvements in the care of fungal pneumonias, but invasive fungal infections remain a major cause of morbidity and mortality. This article covers risk factors for major fungal infections, diagnostic approaches, and treatment options for specific fungal pathogens, including *Aspergillus* and Mucorales species, and discusses current approved strategies for prevention of common and uncommon fungal pneumonias.

Viral Pneumonia in Patients with Hematopoietic Cell Transplantation and Hematologic Malignancies 295

Margaret L. Green

Viral pneumonia is a common complication for patients with hematologic malignancies and after hematopoietic cell transplantation causing significant morbidity, and often mortality. Infections are predominantly caused by herpes viruses, either by reactivation of latent infection, or less commonly primary infection, or community respiratory viruses. High-resolution CT scan is useful for diagnosis but is nonspecific; generally, bronchoalveolar lavage is required. Prevention strategies are not pathogen-specific but include vaccination, chemoprophylaxis, preemptive treatment, and effective infection-prevention strategies during community outbreaks. Directed antiviral treatment is available for some pathogens. Toxicities and viral resistance are perennial challenges.

Evaluation of Pulmonary Disease in Patients with Malignancy

Pulmonary Function and Pretransplant Evaluation of the Hematopoietic Cell Transplant Candidate 307

Guang-Shing Cheng

Pretransplant pulmonary function tests provide baseline data by which to reference subsequent respiratory impairment, as well as important prognostic information, for

the hematopoietic cell transplant (HCT) recipient. Abnormalities in forced expiratory volume in 1 second and diffusing capacity of carbon monoxide are associated with early respiratory failure and increased all-cause mortality after allogeneic HCT. These parameters have been incorporated into risk assessment calculators that may aid in clinical decision making. This article discusses the clinical implications of pulmonary function parameters and other risk factors for pulmonary complications in the context of evolving allogeneic HCT practice.

Diagnostic Evaluation of Pulmonary Abnormalities in Patients with Hematologic Malignancies and Hematopoietic Cell Transplantation

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Bianca Harris and Alexander I. Geyer

Pulmonary complications (PC) of hematologic malignancies and their treatments are common causes of morbidity and mortality. Early diagnosis is challenging due to host risk factors, clinical instability, and provider preference. Delayed diagnosis impairs targeted treatment and may contribute to poor outcomes. An integrated understanding of clinical risk and radiographic patterns informs a timely approach to diagnosis and treatment. There is little prospective evidence guiding optimal modality and timing of minimally invasive lung sampling; however, a low threshold for diagnostic bronchoscopy during the first 24 to 72 hours after presentation should be a guiding principle in high-risk patients.

Critical Care of the Patient with Malignancy

Critical Care Prognosis and Outcomes in Patients with Cancer

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Ayman O. Soubani

Advances in cancer treatment and patient survival are associated with increasing number of these patients requiring intensive care. Over the last 2 decades, there has been a steady improvement in the outcomes of critically ill patients with cancer. This review provides data on the use of the intensive care unit (ICU) and short and long-term outcomes of critically ill patients with cancer, the ICU system practices that influence patients outcomes, and the role of the different clinical variables in predicting the prognosis of these patients.

Acute Respiratory Failure in Patients with Hematologic Malignancies

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Anne-Sophie Moreau, Olivier Peyrony, Virginie Lemiale, Lara Zafrani, and Elie Azoulay

Acute respiratory failure occurs in up to 50% of patients treated for hematologic malignancies and is associated with a high case fatality rate. Because of residual organ dysfunction and time spent receiving respiratory care, underlying disease control is affected. Early admission to an intensive care unit for acute respiratory failure has proven benefit because it is the best place for rapid implementation of noninvasive diagnostic and therapeutic strategies. This article reviews the clinical approach and diagnostic strategies for acute respiratory failure in patients with hematologic malignancies.

Palliative and End-of-Life Care for Patients with Malignancy

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Kathleen M. Akgün

Patients with cancer continue to have unmet palliative care needs. Concurrent palliative care is tailored to the needs of patients as well as their families to relieve

suffering. Specialty palliative care referral is associated with improved symptom management, improved end-of-life quality, and higher family-rated satisfaction. Optimal timing for palliative care referral has not been determined. Barriers to palliative care referral include workforce limitations, provider attitudes and perceptions, and potential ethnic and racial disparities in access to palliative care. Future work should focus on novel, patient-centered approaches to identify and address unmet palliative care needs for patients living with cancer.