

Pulmonary Involvement in Patients with Hematological Malignancies

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Acute pulmonary events are among the most common complications in patients with hematological malignancies. These events often raise difficult diagnostic and therapeutic challenges. In this book, readers faced with these challenges will find a vast array of clinically relevant information contributed by physicians in many specialties who have acquired considerable experience over the years. Pulmonary complications in patients with hematological malignancies may be related to many factors, including infection, tissue invasion by the malignant cells, toxicity and immune deficiency related to the disease or treatments. The multiplicity of the possible etiologies and frequent presence of more than one etiology in a given patient create diagnostic conundrums. Importantly, an early accurate diagnosis is crucial to improve patient outcomes. This book provides practical guidance on untangling complex diagnoses and selecting optimal treatments.

In addition to hematologists, intensivists, and pulmonologists, clinicians from many specialties may be called on to manage respiratory events in patients with hematological malignancies. This book was written to serve as an easily accessible source of information to primary-care physicians, emergency-room physicians, intensivists and physicians working in internal medicine, infectious diseases or pulmonary care departments. Furthermore, the problems encountered in patients with hematological malignancies are relevant to all specialties where patients

require immunosuppressant treatments for systemic inflammatory diseases, including clinical immunology, rheumatology, hepatology, gastroenterology, nephrology, dermatology, neurology, and solid organ transplantation.

This book has six parts. After an introduction by Dr Soubani, who presents a comprehensive overview of infectious etiologies of respiratory events in patients with hematological malignancies, the first part focuses on epidemiology. International leaders draw attention to important points such as the specificities of bone marrow transplant recipients and the possibility of non-infectious pulmonary involvement, most notably heart failure with pulmonary edema whose diagnostic and therapeutic management differ fundamentally from those of other etiologies of respiratory events in hematological patients. The second part addresses ongoing controversies about the best diagnostic strategies, which are largely fueled by the fast pace at which new diagnostic tools are being introduced. Renowned researchers discuss the latest information on the benefit/risk ratio of diagnostic tools ranging from the least invasive (clinical examination) to the most invasive (surgical lung biopsy). This careful attention to diagnostic tools is warranted, as mortality is higher when no cause to the respiratory symptoms is identified. In patients who are not receiving mechanical ventilation, noninvasive diagnostic testing may provide comparable diagnostic yields to those obtained using bronchoscopy with bronchoalveolar lavage. Attention is drawn to the valuable information that can be derived by the optimal use and interpretation of lung computed tomography. In the third and the fourth parts of this book, leading researchers describe the spectrum of pulmonary infections in hematological patients because of pathogens ranging from common bacteria to opportunistic pathogens, and the spectrum of

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noninfectious causes, including drug-related toxicity, pulmonary embolism, diffuse alveolar hemorrhage, and alveolar proteinosis. The fifth part provides new insights into treatments and difficult decisions for patients with hematological malignancies. Contributions from physicians in various specialties were assembled to shed light on the many facets of this topic. Opinion leaders provide recommendations on the use (or withdrawal) of various therapeutic strategies. Last, the sixth part presents 15 carefully selected case reports about clinical situations that are rare but important. The goal is to improve the diagnosis of rare but treatable conditions. For each clinical situation, a literature review is reported. These case reports may constitute valuable teaching material for discussing patients with unusual problems. The abundance of tables, figures, radiographs, and computed tomography scans in the book considerably enriches the written material.

Three methods can be suggested for using this book. First, you can look up a clinical situation you are interested in (e.g., pneumonia in patients with chronic lymphocytic leukemia or pulmonary infiltrates at the earliest phase of acute leukemia). Second, you can look for the diagnostic strategy that is best for evaluating a clinical suspicion of infectious or noninfectious pulmonary involvement (e.g., induced sputum, transbronchial biopsy, or core needle biopsy). Third, you can find a description of the clinical picture related to a given form of pulmonary involvement or a given pathogen (e.g., *Pneumocystis* pneumonia, cytomegalovirus pneumonia, cardiogenic pulmonary edema, diffuse alveolar hemorrhage, or transfusion-related acute lung injury). These three methods can complement one another. Therapeutic alternatives are also available for all these situations.

I hope this book will spread ten important messages. First, in patients with hematological malignancies who experience respiratory complications, treating every possible etiology is not the best way to ensure a favorable outcome. Instead, identifying the exact cause improves survival. Second, within the first few hours the most likely causes of the respiratory symptoms should be determined based on the clinical findings (see the DIRECT strategy) and recorded in the medical chart. Treatments appropriate for these causes should be given immediately, while waiting for the results of further investigations. Third, computed tomography may help to support a clinical suspicion

of an infectious or noninfectious cause and may also rule out a number of etiologies. However, computed tomography alone cannot establish a diagnosis. Furthermore, computed tomography should be performed only after a comprehensive clinical assessment, whose findings guide the choice of the imaging strategy.

Fourth, not all patients are at risk for all the possible etiologies. Knowledge of the specific risk factors for each cause is crucial. For instance, the type of immune deficiency indicates which pathogens are most likely to cause pulmonary involvement. A discerning risk factor assessment may show that some patients are at very low risk for some causes. Fifth, two diagnoses, cardiogenic pulmonary edema and bacterial infections, should be considered in all patients at all times during the course of the hematological malignancy. Sixth, positive tests (e.g., cytomegalovirus antigen test, PCR test for *Pneumocystis*, or virological studies of nasopharyngeal swabs) must be interpreted with great caution. A positive test does not always mean that the disease is present. Furthermore, several causes may be present in combination. For instance, even when the bronchoalveolar lavage fluid indicates alveolar hemorrhage, infections (e.g., aspergillosis, *Pseudomonas*, *Staphylococcus*, and other causes of necrotizing pneumonia), and noninfectious disorders (e.g., cardiogenic pulmonary edema, leukemic infiltrates, and drug-related toxicity) must be ruled out before accepting a diagnosis of diffuse alveolar hemorrhage and initiating the specific treatment for this condition. Another important point is that negative results do not always exclude diagnoses, such as cytomegalovirus pneumonia, *Pneumocystis* pneumonia, or invasive aspergillosis. The few diagnostic tests whose negative predictive value is close to 100% (e.g., PCR test for *Pneumocystis*) are extremely valuable. Seventh, thrombocytopenia does not protect against the occurrence of thromboembolic events. Eighth, core needle biopsy performed by an experienced operator can provide valuable diagnostic information. As with all invasive procedures, the ICU may be the safest place to monitor the patients before and after core needle biopsy. Ninth, each new diagnostic method must be carefully evaluated in a group of unselected patients with hematological malignancies. The diagnostic performance characteristics must be reported, together with the prevalence of the disease in the study group. Tenth, managing patients with pulmonary events and

hematological malignancies requires considerable clinical skill, close collaboration among medical specialties and with the laboratories, and easy access to the ICU. Among patients with hematological malignancies, more than half experience critical illnesses, and early ICU admission may be the best means of

providing them with optimal diagnostic and therapeutic care.

I owe an enormous debt of gratitude to the specialists who provided their valuable contributions to this book.

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