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Review article

Pulmonary manifestations of urothelial carcinoma of the bladder

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ABSTRACT

Urothelial carcinoma (Transitional cell carcinoma) of the bladder is the pre-dominant histological type of bladder cancer in the United States and Europe. Patients with bladder cancer usually present with painless hematuria. The diagnosis is often delayed, as the symptoms are similar to various other benign conditions such as urinary tract infection, prostatitis or renal calculi. In some patients, the metastatic lesions will cause the initial presenting symptoms. We conducted a MedLine/PubMED search identifying all relevant articles with “pulmonary manifestations”, “urothelial bladder cancer”, “manifestations of bladder cancer” or a combination of these terms in the title. The pulmonary manifestations of urothelial carcinoma of the bladder include metastatic disease including cavitary lesions, endobronchial, pleural, or lymph node metastasis pleural effusion and chylothorax. Pulmonary embolism and tumor embolism is another manifestation of this cancer. Intravesical Bacillus Calmette-Gurin therapy for bladder cancer has been associated with a range of adverse effects including the systemic spread of Bacilli Calmette-Guérin immunotherapy affecting the lungs. Other drugs used to treat bladder cancer can be associated with drug-related pneumonitis. Other rare manifestations include a sarcoid like reaction and systemic granulomatous disease to Bacilli Calmette-Guérin therapy. In this review we discuss the various pulmonary manifestations of urothelial carcinoma of the bladder. A high index of suspicion with these presentations can lead to an early diagnosis and assist in instituting an appropriate intervention.

Contents

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1. Introduction

Bladder cancer is the fifth most common carcinoma in the United States [1]. Urothelial carcinoma (transitional cell carcinoma (TCC)) of the bladder is the pre-dominant histological type accounting for 90% of all bladder cancers in the United States and Europe. Patients with bladder cancer usually present with painless hematuria. The diagnosis is often delayed, as the symptoms are similar to various other benign conditions such as urinary tract infection, prostatitis or renal calculi. While a majority of patients present with localized symptoms a few patients with advanced disease may present with pelvic or bony pain, lower-extremity edema from iliac vessel compression, or flank pain from ureteral obstruction. In a very few cases the metastatic process may be the reason for presenting complaint with the lung being a common area for metastatic disease. However due to insidious onset and vague symptomatology, in some patients with advanced disease, pulmonary manifestations are the initial presenting symptoms.

Patients with urothelial carcinoma of the bladder may present with various pulmonary manifestations, one of which may be due to metastatic disease. Some manifestations include endobronchial metastasis, metastatic disease to the lungs or lymph nodes, pleural effusion, pulmonary embolism amongst others, which have been outlined in Table 1. The purpose of this article is to review the pulmonary manifestations of urothelial cancer of the bladder.

2. Methods and materials

A search was conducted of the National Library of Medicine's MEDLINE/PubMed with the objective of identifying all articles published in English language between January 1980 and May 2016 with “Urothelial/Transitional Cell Carcinoma” and “pulmonary manifestations” in the title. Combinations of medical subject heading terms including “pulmonary metastasis,” “pleural effusion” and “manifestations of urothelial/transitional cell carcinoma” were used. We mainly selected recent publications, but did not exclude any older works that were widely referenced. We also searched the reference lists of all articles identified by this search strategy and selected those we judged to be relevant. All pertinent reports were retrieved and the relative reference lists were systematically searched in order to identify any potential additional studies that could be included. All data were accessed between January and May 2016. Our comprehensive PubMed/Medline search revealed a total of 278 manuscripts of which 222 were duplicates, not of the English language or not related to our focus and were excluded from our review. This yielded a total of 56 manuscripts that were completely assessed and incorporated into this review.

3. Pulmonary and mediastinal metastatic disease

The most common respiratory manifestation of urothelial cancer is metastasis to the pulmonary structures. As many as 50% of patients with muscle-invasive bladder cancer may have occult metastases that become clinically apparent within 5 years of initial diagnosis [2]. It is thought that spread of TCC of the bladder primarily occurs via regional lymphatics [3]. The patterns of pulmonary metastasis are variable and may range from parenchymal nodular disease, solitary mass lesions or interstitial micronodules [4]. In a study by Rovirosa et al. it was observed that in up to 4% of lung metastases there is evolution to a cavitary lesion [5]. The pathomechanism of cavitation is attributed to the necrosis occurring from insufficient blood supply to the tumor or due to the invasion of blood vessels by tumor cells [3,6]. Such patients will present with complaints of dyspnea, couch and hemoptysis. Cases of urothelial bladder cancer presenting as cavitary metastatic lesions have been outlined in Table 2. Thus, the presence of cavitary lung lesion in patients with a history TCC of the bladder should raise a suspicion for metastatic disease (Fig. 1) warranting further workup regarding the diagnosis, staging and treatment.

While uncommon, patients may also present with endobronchial metastasis (EBM) [9,10]. The presenting symptoms include cough, wheezing, dyspnea, stridor or hemoptysis. Bronchoscopy is a valuable diagnostic tool in such patients for identifying EBM from bladder cancer. Therapeutic bronchoscopy including the use of argon plasma coagulation may also be considered in such cases to improve quality of life [11].

Patients with bladder carcinoma can also present with mediastinal lymphadenopathy due to metastatic disease [12]. Mediastinal metastasis can either be asymptomatic or may produce symptoms such as superior vena cava syndrome or dysphagia from esophageal invasion/compression [13]. In a rare instance,

Table 1
Pulmonary manifestations of urothelial carcinoma of bladder.

Metastasis - Cavitary metastasis of the lung parenchyma [3] - Endobronchial metastasis [9,10] - Mediastinal Lymphadenopathy [12,13] -Pleural metastasis [4]
Pleural effusion & Chylothorax [15–17].
Vascular Manifestations - Pulmonary embolism - Pulmonary Tumor Thrombotic Microangiopathy (PTTM) [22–24] Adverse effects of Intravesical Bacillus Calmette-Guerin (BCG) therapy [30,31,35,36]. - Flu like symptoms, - Interstitial pneumonitis - Sepsis including miliary nodular spread to lungs. - Systematic granulomatous disease. Adverse effects of drugs used to treat urothelial bladder cancer - MVAC/GC: Acute respiratory distress syndrome (ARDS) [37] - Gemcitabine: Hypersensitivity pneumonitis [41]. - Methotrexate: Hypersensitivity pneumonitis, opportunistic lung infections, lymphoproliferative disease of lung [43] Sarcoid like Reaction [49]