Pleural invasion in non-small cell lung cancer

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Abstract

Pleural invasion is a recognized adverse prognostic factor in non-small cell lung cancer. Here, we document a case of non-small cell lung cancer in a 66-year-old man presenting with direct invasion of the tumor through lung pleura into the mediastinum. Pleural invasion can proceed past the elastic layer of the visceral pleura and is classified as PL1. Less commonly, invasion to the surface of the visceral pleura or parietal pleura can occur and is classified as PL2 and PL3, respectively. Visceral invasion (PL2) is associated with increased mortality; patients have lower overall survival compared to those without visceral pleural invasion (HR = 2.447; 95% CI: 0.336,0.579) and those with only PL1 invasion (HR = 1.287; 95% CI: 1.114, 1.487). Treatment of non-small cell lung cancer with pleural invasion includes surgery, chemotherapy, radiation, and immunotherapy.

Keywords: lung neoplasms, non-small-cell lung carcinoma, visceral pleura, pleural invasion

Introduction

Pleural invasion is a known adverse prognostic factor in non-small cell lung cancer (NSCLC). Visceral pleural invasion can elevate NSCLC classification to a T2 descriptor in the tumor node metastasis (TMN) staging system, and parietal pleural invasion can elevate NSCLC classification to a T3 descriptor, significantly impacting expected prognosis and treatment of diagnosed NSCLC.[1] Here, we report a case of NSCLC in a 66-year-old man presenting with direct invasion of the tumor through lung pleura into the mediastinum. The case discussion reviews classification, prognosis, and treatment of pleural invasion in NSCLC.

Case

A 66-year-old white man was admitted directly to the Intensive Care Unit from an outside facility with cough, three days of hemoptysis, two weeks of dysphagia/non-bloody emesis, and an unexplained 30-pound weight loss over the prior six months. The patient denied hematochezia and pleurisy. No skin lesions or lymph nodes were appreciated. The patient's past medical history was significant for heavy tobacco use (50 pack-years), oropharyngeal cancer in 2019, occupational inhalational exposure to hydrazine gas (EPA probable human carcinogen), COPD, and alcoholic liver cirrhosis. On physical examination, coarse rhonchi were heard throughout the lungs, greatest at the right lateral base, and a prolonged expiratory phase was observed. Computed tomography (CT) scan of the chest showed prominent mediastinal and right hilar adenopathy, multifocal pneumonia, and areas of cavitation at the right lower lobe of the lung with one of the cavities eroding through the posterior wall of the right upper lobe bronchus into the mediastinum, abutting the esophagus (Figure 1). Bronchoscopy was performed with washings and brushings of the necrotic lesion in the right mainstem bronchus. It was noted that the pleura was visible on the bronchoscopy (Figure 2). Transbronchial needle aspirations were also performed in the left paratracheal area, subcarinal area, and hilum. Pathology reports indicated non-small cell carcinoma,

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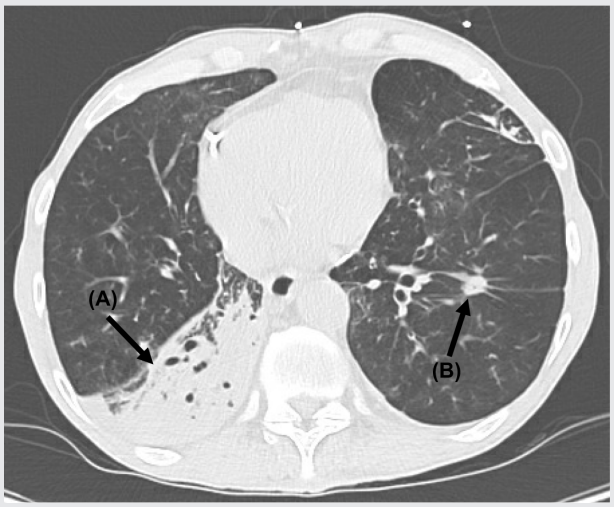

Figure 1. Chest CT Scans without contrast showing cavities in right lower lobe (A) and left sided pulmonary nodule (B).

favoring squamous carcinoma. Approximately one week into his hospital stay, the patient went into cardiac arrest. Emergency cricothyroidotomy was performed and airway was established, but the patient could not be resuscitated.

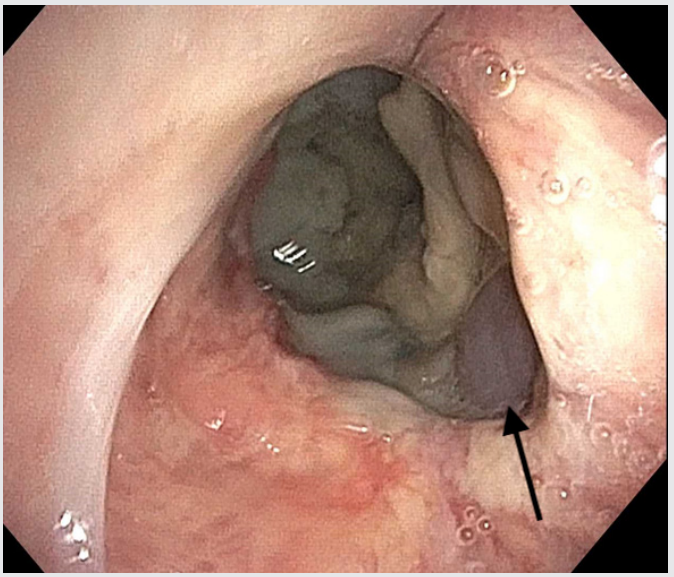

Figure 2. Bronchoscopy imaging of right mainstem bronchus with necrotic lesion and visible pleura (see arrow).

Discussion

Pleural invasion has been recognized as an adverse prognostic factor in non-small cell lung cancer (NSCLC) and is included in the Eighth Edition American Joint Committee on Cancer (AJCC) tumor node metastasis (TNM) staging system.[1,2]

Pleural invasion can be classified as PL1, PL2, PL3 or PL0. A PL0 classification carries the least risk of adverse effects of this classification and is defined as invasion that does not proceed past the elastic layer. The PL0 level of involvement is not considered visceral pleural invasion (VPI) and is not considered a T descriptor in the TNM staging system.[1,3] PL1 is defined as invasion proceeding past the elastic layer of the visceral pleura but not evident on the pleural surface, while PL2 classification indicates invasion to the pleural surface, as presented in this case.[3] Although PL1 and PL2 are distinct classifications, both indicate VPI and are T2 descriptors in the TNM staging system.[4] PL3 is defined by invasion of the parietal pleura and is a T3 descriptor in the TNM staging system.[4] To evaluate VPI in NSCLC, histologic sampling of the pleura in a lung cancer resection specimen should be obtained and can subsequently be evaluated by a pathologist with routine elastic tissue staining and hematoxylin and eosin (H&E) staining; the extent of invasion may be difficult to discern with (H&E) staining alone.[5]

Patients with NSCLC VPI rated PL1 or PL2 had poorer survival than patients rated PL0 (HR = 1.555; 95% CI: 1.399, 1.730; HR = 2.447; 95% CI: 1.913, 3.130), based on a 2016 meta-analysis by Wang et al. Patients with VPI rated PL2 have even poorer overall survival than PL1 patients (HR = 1.287; 95%: CI 1.114, 1.487). Patients with VPI rated PL1 or PL2 also have a lower 5-year survival rate than PL0 patients (OR = 0.515; 95% CI:0.415, 0.640; OR = 0.441, 95% CI: 0.336, 0.579), and patients with VPI rated PL2 had even lower 5-year survival rate than PL1 patients (OR = 0.706; 95% CI: 0.545, 0.915).[2] However, there have been contradictory reports in existing literature regarding the statistical differences in adverse risks of PL1 and PL2 classification classes.[6,7]

The poor prognosis due to VPI in NSCLC has been attributed to its significant association with mediastinal lymph node metastasis; it has been proposed that VPI results in drainage of tumor cells through pleural lymphatics into the mediastinal lymph nodes.[3,8] Kondo et al. reported pleural lavage cytology was positive in 14% of patients with PL1 invasion and 37% of patients with PL2 invasion.[9] However, Shimizu et al. establishes VPI as an independent poor prognostic factor regardless of N status and demonstrates associations between VPI and aggressive tumor characteristics, such as vascular and lymphatic invasion, moderate/poor differentiation, high nuclear atypia grade, high mitotic index, and high serum carcinoembryonic antigen levels, suggesting additional factors contribute to adverse outcomes in VPI.[10]

A range of treatment modalities are available for pleural invasion in NSCLC, including surgery, chemotherapy, radiation therapy, immunotherapy, and targeted therapy.[11] NSCLC with pleural invasion is classified as Stage 1B at a minimum, and NSCLC with parietal invasion is classified as Stage IIB at a minimum.[12] Stage 1 and 2 NSCLC should be treated with surgical resection when not contraindicated, optimally lobectomy though some studies indicate favorable outcomes with wedge resection or segmentectomy in peripheral N0 cancers measuring 2 cm or less. Positive margins following surgery can be addressed with a second surgery, chemotherapy, or radiation therapy. Adjuvant chemotherapy may be used following surgery to lower risk of cancer return.[11] Stage 1B, T2aN0 margin-negative NSCLC with VPI or the presence of other high-risk features should be treated with adjuvant chemotherapy.[13] Stage 3 and 4 NSCLC treatment varies widely and can include a combination of chemotherapy, radiation, immunotherapy, and surgery.[11]

In summary, this patient had necrosis in her right mainstem bronchus and the pleural surface was obviously during bronchoscopy. This information changed her tumor classification and demonstrates importance of careful airway inspection during all bronchoscopies.

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