

Case Report

The Snow Globe Effect

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Keywords

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- Malignant pleural effusion
- Tumor in pleural fluid

Abstract

Malignant pleural effusions often appear at the late stages of disease and can vary in severity of symptoms and volume. Timely diagnosis and etiology of pleural effusions are essential in achieving a favorable outcome; however there are instances when obtaining both are problematic. We report a case where immediate gross inspection of pleural fluid can allude to a diagnosis of malignancy.

A 68 year old male with HIV presented with 2-3 weeks of weight loss, shortness of breath and productive cough. Chest X-ray was consistent for bilateral patchy opacities with worsening adenopathy. Computed Tomography (CT) was positive for cavitating nodules, hilar adenopathy and bilateral pleural effusions. A right thoracentesis was performed revealing blood-tinged serosanguinous fluid with white, grainy specks of tissue. Cytologic analysis of the pleural fluid revealed the white grainy specks of tissue to be clusters of lung squamous cell carcinoma. This case is unique in the extent of the tumor spread at presentation and high degree of tumor burden that could be visualized on gross inspection of the pleural fluid. To the best of our knowledge, the presence of gross malignant clumps in the pleural fluid has not been described in literature. The cause of this unique pattern of pleural metastasis, which we have coined the "snow-globe effect", is unclear.

ABBREVIATIONS

CT: Computed Tomography

INTRODUCTION

It is estimated that between 150,000 and 175,000 patients in the US develop malignant pleural effusions each year. Breathlessness, cough and chest pain are common signs and symptoms of an effusion and the degree of impairment varies depending on the underlying disease. Chest radiographs and computed tomography help assist in evaluating the etiology and severity of the pleural effusion. When a malignant pleural effusion is suspected it is usually associated with a poor prognosis, a common complication of advanced metastasis is the production of a malignant pleural effusion.

Prompt diagnosis and the etiology of pleural effusions are critical and necessary to determine optimal treatment modalities. However, there are circumstances when determining a rapid diagnosis or etiology is difficult. In the present case gross inspection of pleural fluid may possibly contain characteristics associated with malignancy.

CASE PRESENTATION

A 68 year old male with HIV presented with 2-3 weeks of weight loss, shortness of breath and productive cough. His past medical history was significant for hypertension, tobacco use, and

previously treated syphilis and malaria over ten years ago. He was evaluated one week prior for admission at an outside facility where a chest x-ray revealed bilateral patchy opacities. His CD4 count at that time was 827, and he was given azithromycin without clinical response. Due to worsening symptoms, a helical chest CT was done 1 day prior to admission showing pulmonary infarcts, cavitating nodules, and hilar lymphadenopathy. He was admitted for further workup and management. Unfortunately, after approximately one week, he was transferred to the medical intensive care unit due to progressive hypoxic respiratory failure and acute loss of consciousness that required intubation.

On arrival to the ICU, the patient was unresponsive to noxious stimuli or commands. His lung exam was significant for bilateral coarse rhonchi, bibasilar decreased breath sounds and a moderately distended, soft abdomen with dullness to percussion. Chest CT done the day of transfer to the ICU showed increased size and number of the disseminated pulmonary nodules, new bilateral pleural effusions, and sub-segmental peripheral pulmonary emboli (Figure 1). Head CT revealed an acute infarct in the left anterior cerebral and middle cerebral artery territories. The patient was also found to have elevated cardiac markers, but heparin was not started due to concerns of converting the acute embolic stroke into a hemorrhagic stroke.

As part of his workup for worsening lung nodules, a right thoracentesis was performed and revealed blood-tinged

serosanguinous fluid with white, grainy specks (Figure 2). Additional laboratory findings included an abnormal D-dimer, elevated INR, and decreased fibrinogen suggestive of extensive clot formation. No infectious etiology was isolated from blood, sputum, urine or pleural fluid.

Cytologic analysis of pleural fluid revealed lung squamous cell carcinoma (Figure 3). The overall findings were interpreted as systemic venous and arterial thrombosis associated with metastatic squamous cell carcinoma. Based on the extent of the cancer, presence of multi-organ dysfunction, and the patient's previously stated end-of-life wishes, we extubated the patient, and he died. At autopsy, tumor was also found in his brain, heart and spleen.

DISCUSSION

Squamous cell carcinoma is the second most frequent subtype of non-small cell lung tumor. It often presents as a centrally-located endobronchial mass with distant metastases. No effective screening test currently exists, and patients often present with symptoms of advanced and widespread disease.

Several mechanisms have been proposed to explain typical patterns of lung cancer growth and metastasis. Excess production of epidermal growth factor, stem-cell factor, macrophage stimulating protein, and vascular endothelial growth factor are known to modify tumor microenvironments [1]. These signaling



Figure 1 CT scan of the chest showing progressively enlarged nodules and bilateral pleural effusions compared to one week earlier.

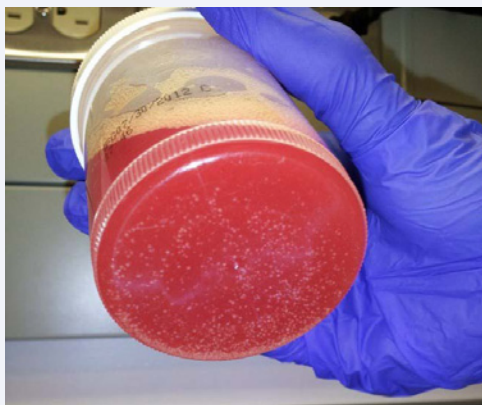


Figure 2 Pleural fluid from thoracentesis showing gross cellular clumps (the "snow-globe effect").

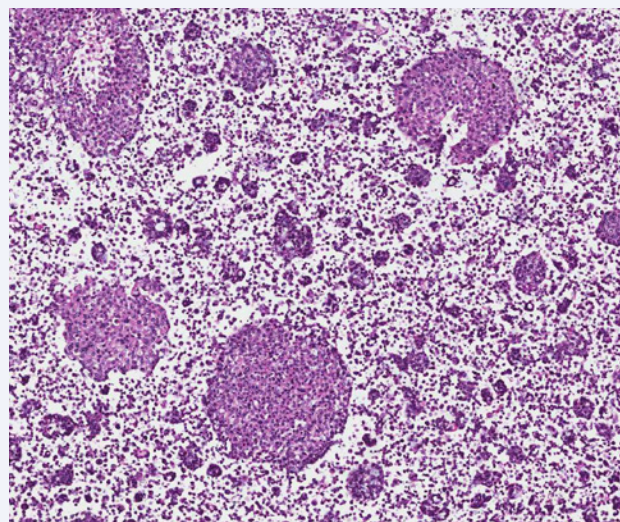


Figure 3 Pleural fluid cytology consistent with squamous cell carcinoma with clumps of malignant cells.

pathways and their receptors result in excess paracrine and autocrine signals that stimulate cancer growth and spread [2]. Distant metastases also require loss of intracellular adhesions, migration and eventual reattachment at distal sites to resume growth. Cell-cell adhesion abnormalities are central to successful metastasis.

This case was unusual in the extent of tumor spread at presentation, the degree of clot burden, and the bulk of tumor found in pleural fluid. We postulate that his impaired immune status is a large contributor to this unusual presentation. Low CD4 HIV-associated tumors include Kaposi sarcoma and non-Hodgkin lymphoma. In addition, lung cancer, Hodgkin's lymphoma, multiple myeloma, leukemia and oropharyngeal carcinoma occur at higher rates in HIV-infected individuals [3]. The etiology for this increased risk is unclear but may be due to immune dysfunction that is not reflected by CD4 depletion. As such it may also be related to impaired cell mediated immunity [4], immunosuppression, or direct cellular effects of HIV. Drug exposures and co-infection with oncogenic viruses such as human herpes virus and Epstein-Barr virus may also weaken cell repair mechanisms that protect against aberrant cell types [5]. Current literature suggests that lung cancer risk is two to four times greater in HIV patients than the general population. This risk remains even after accounting for tobacco use, CD4 count, or HIV viral load [6]. Studies also suggest that lung cancer in HIV patients progresses more rapidly than in HIV-negative individuals. This was certainly evident in the clinical course of our patient.

To the best of our knowledge, the presence of gross malignant clumps in the pleural fluid has not been described in the literature. The cause of this unique pattern of pleural metastasis, which we have coined the "snow-globe effect", is unclear. However, the combination of HIV infection, prior exposures, and genetic traits likely contributed. The case illustrates the heterogeneity of very aggressive tumor metastases with aberrant cell-to-cell interactions. These mechanisms were altered in a grossly visible way and led to systemic effects with multi-organ involvement.

CONFLICT OF INTEREST

We the authors have nothing to disclose (funding or conflict of interest: none), and agree that the work is original and that all authors had access to the data and had a role in writing the manuscript and accept responsibility for the scientific content of the manuscript.

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