G9 Sudden Death by Occult Metastatic Carcinoma

Stephanie A. Dean, MD, 350 E Willow Grove Ave, Apt. 711, Philadelphia, PA 19118; Benjamin Mathis, MD*, 555 NE 34th St, Apt 2002, Miami, FL 33137; Leslie A. Litzky, MD, 3400 Spruce St, Founders 6, Philadelphia, PA 19107; and Ian C. Hood, MBChB, JD, MEO, 4 Academy Dr, Westampton, NJ 08060*

After attending this presentation, attendees will learn about an unusual cause of natural sudden death from pulmonary hypertension as a result of an unusual pattern of pulmonary metastasis from an occult gastric adenocarcinoma.

This presentation will impact the forensic science community by illustrating a rare but important presentation of occult metastatic carcinoma which led to sudden death in a young patient. The objective is to inform forensic pathologists and medicolegal investigators of this bizarre mechanism and cause of death that can only be discovered through careful autopsy.

A 33-year-old Filipina female, with no significant past medical history, was admitted to the emergency room with a several-month history of a cough. She reported taking antibiotics without relief. Imaging revealed slight coarsening of the interstitial markings and no evidence of a pulmonary embolism. Laboratory values were remarkable for an elevated D-dimer (>5000). She was discharged from the emergency room with prescriptions for albuterol inhaler and oral prednisone. One month later, she returned to the hospital with a two-week history of abdominal pain, nausea, vomiting, dyspnea, lightheadedness, and chest pain. The CT was again negative for pulmonary embolus, showing bilateral infiltrates in her upper lung lobes. Her white blood count at that time was elevated to 15K/uL. She was admitted for presumed pneumonia; however, a rapid response was called within hours of admission due to an acute hypoxic episode and subsequent syncope when she tried to get to the bed from the bathroom. After approximately two hours of advanced cardiac life support, the patient expired.

Autopsy revealed an adult female with gross edema and scattered purpura from terminal resuscitation efforts but no significant trauma. Internal examination revealed a thickened stomach wall which, on microscopic examination, was infiltrated by poorly differentiated adenocarcinoma in a linitus-plastica type pattern. Grossly, multiple abdominal lymph nodes were involved by metastatic tumor. Immunohistochemical staining was strongly positive for CK7 and CK20, supporting the diagnosis of a primary gastric carcinoma.

The lungs were notable for fine reticular nodular densities bilaterally. Microscopic examination showed a tumor infiltrate involving the microvasculature, significant arteriolar fibrointimal hyperplasia, and interlobular septal lymphangitic spread. These findings are consistent with Pulmonary Tumor Thrombotic Microangiopathy (PTTM) with the additional finding of extensive extravascular compression by tumor cells.

PTTM is a well-described complication in patients with adenocarcinoma. The typical presentation involves acute pulmonary hypertension (as evidenced by progressive dyspnea, hypoxemia, cough, and hemoptysis), progression to right-sided heart failure and sudden death, often before the adenocarcinoma is discovered. It has been reported in 3% of patients who die with adenocarcinoma (breast, prostate, lung, pancreas) and 25% in patients who die with gastric adenocarcinoma; however, only 8% of patients with tumor emboli experience morbidity or mortality. The diagnosis of tumor emboli is typically not made until postmortem examination. Patients with PTTM develop rapidly progressive pulmonary hypertension secondary to tumor cells occupying a large proportion of small pulmonary arterioles. This in turn leads to fibrointimal hyperplasia and a significant reduction in the pulmonary vasculature available for gas exchange. The pathophysiology of PTTM remains elusive. It has been suggested that carcinoma cells may produce certain substances that influence the surrounding pulmonary vasculature.

Histologically, medium-sized peripheral pulmonary arteries and smaller arterioles are involved with acute and organizing platelet-fibrin thrombi, small artery intimal fibrosis, and adjacent intralymphatic tumor. These elements do not cause simple mechanical obstruction of the affected vessels. By adhering to the vascular endothelium, they are thought to activate the coagulation cascade and release inflammatory mediators, thus resulting in the formation of microthrombi, stimulation of subintimal proliferation, and smooth muscle colonization of these lesions. The result is a diffuse narrowing of the pulmonary arteriolar system, increased vascular resistance, and marked secondary pulmonary hypertension. The patient had both the classic clinical and histologic features of PTTM with the additional prominent feature of extravascular compression by intralymphatic tumor cells. These features undoubtedly caused her precipitous decline and the mechanism of death in this case is lethal pulmonary hypertension induced by underlying adenocarcinoma.

In the practice of forensic pathology, PTTM should be considered and recognized as a potential cause of pulmonary hypertension. Medical examiners must, therefore, search for occult malignancy via autopsy in order to identify or exclude metastatic cancer as the underlying cause of death.

Thrombotic, Microangiopathy, Adenocarcinoma

 ** Presenting Author*