H149 Two Cases of Fatal Pulmonary Tumor Thrombotic Microangiopathy

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After attending this presentation, attendees will have a better appreciation of the value of a thorough autopsy in the diagnosis of this rare cause of progressive respiratory insufficiency and death.

This presentation will impact the forensic science community by emphasizing the importance of complete autopsies in challenging cases of respiratory insufficiency. In particular, this presentation will increase the awareness of diagnosing a rare yet usually fatal cause of pulmonary hypertension through careful correlation of the clinical history with postmortem microscopy and immunohistochemistry.

Pulmonary Tumor Thrombotic Microangiopathy (PTTM) is a rare complication of metastatic cancer that may cause progressive respiratory insufficiency and pulmonary hypertension. PTTM was first described by von Herbay et al. to present with a variety of non-specific clinical manifestations ranging from acute hypoxia from large proximal emboli to pulmonary hypertension developing from microvascular invasion.[1] Other complications include right-sided heart failure and sudden death. PTTM has been reported in 3% to 26% of autopsies conducted on patients with solid tumors; the diagnosis is usually not made until postmortem examination. Generally, there are no distinguishing radiographic findings, and there is no grossly apparent pulmonary tumor metastasis or thromboembolism at autopsy. Microscopically, PTTM is characterized by tumor microemboli, intravascular thrombosis, and fibromuscular thickening of pulmonary small arteries and arterioles.

Vascular Endothelial Growth Factor (VEGF) is an angiogenic and hyperpermeability factor that may mediate the development of pulmonary hypertension in these cases. While the exact underlying mechanism of PTTM is not completely understood, it is theorized that abnormalities in VEGF may be involved in its development; VEGF is expressed more frequently in tumor cells associated with PTTM.

This report presents two cases of PTTM in patients with undiagnosed malignancies (gastric and colon carcinoma) who presented with respiratory distress and subsequent death. Both cases presented with non-specific clinical findings, including cough, hypertension, type 2 diabetes mellitus, and malaise. Chest radiographs were rather non-specific and demonstrated cardiomegaly and vascular congestion. Transthoracic echocardiogram revealed pulmonary hypertension and cardiomegaly. In one case, PE was suspected; however, a ventilation-perfusion scan showed a very low probability of PE and Doppler studies of the legs were negative.

Autopsy disclosed widely metastatic malignancies consisting of poorly differentiated adenocarcinoma. Neither case had grossly apparent pulmonary thromboembolism. Microscopic sections of the lungs found widespread intravascular collections of poorly differentiated carcinoma in small arteries and arterioles. Many of the tumor emboli were seen associated with intravascular fibrin. Arteriolar medial hypertrophy and intimal hyperplasia were present. VEGF-positive gastric adenocarcinoma tumor cells were demonstrated by immunohistochemistry in one of the cases.

These cases illustrate the importance of thorough autopsy, including microscopic studies when indicated, in cases of respiratory insufficiency with subsequent death, since PTTM does not result in large tumor metastases, which would be visible on imaging studies or at gross autopsy examination. Furthermore, antemortem serum analysis of VEGF levels has been suggested as a potential clinical test to aid in diagnosis of this rare complication.

Reference(s):

1. Von Herbay A., Illes A., Waldherr R., Otto H.F. Pulmonary Tumor Thrombatic Microangiopathy with Pulmonary Hypertension. *Cancer*. 1990;66:587-92.

Tumor Microangiopathy, Dyspnea, Metastatic Complications