CASE REPORT

Undiagnosed gastric adenocarcinoma causing progressive respiratory failure

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Abstract

Pulmonary tumor thrombotic microangiopathy (PTTM) is a rare manifestation of malignancy. Pulmonary tumor emboli and associated fibrous intimal hyperplasia cause widespread pulmonary vascular stenosis/occlusion, which in turn increase pulmonary vascular resistance and lead to pulmonary hypertension. Gastric cancer is the most common underlying malignancy that leads to PTTM, and patients may present with dyspnea or other features of pulmonary hypertension prior to the diagnosis of cancer. In this short report, we describe a case of pulmonary hypertension due to gastric cancer-associated PTTM. Endoscopic and histopathologic findings are shown, and a brief review of the literature is presented.

Case Presentation

A 45-year-old previously well woman with a past history of Osler–Weber–Rendu syndrome and well-controlled asthma presented to a regional hospital with 4 months of progressive dyspnea and unintentional weight loss of 10 kg. This was associated with 2 months of worsening dysphagia but no other upper gastrointestinal symptoms. She was not anemic, with hemoglobin of 135 g/L and mean corpuscular volume of 85 fL (ref 80–97). On initial assessment, she was hypoxic, with evidence of right ventricular strain on an electrocardiogram and with lymphadenopathy but no pulmonary embolus or arteriovenous malformations on computed tomography (CT) pulmonary angiography. A transthoracic echocardiogram (TTE) was performed, which revealed severe pulmonary hypertension and right ventricular dilatation. Due to escalating oxygen requirements, she was transferred to our tertiary statewide heart and lung transplant center for further workup and management.

A repeat TTE was performed, confirming severe pulmonary hypertension with a negative contrast bubble study. Right heart catheterization confirmed pulmonary arterial hypertension of 83/48 mmHg with a normal pulmonary capillary wedge pressure. Her respiratory failure continued to progress, and she was commenced on veno-arterial extra-corporeal membrane oxygenation (ECMO).

During this time, further CT imaging was performed, which showed prominent mediastinal, hilar, and retroperitoneal lymphadenopathy along with skeletal lesions. Her CA19-9 was 208 617 kU/L (ref 0–37). In this setting, an esophagogastroduodenoscopy was performed, which revealed a normal esophagus and duodenum, and ulcerative gastritis with a loss of rugal definition from the gastric body to the cardia (Fig. 1a–c), suspicious for linitis plastica. Multiple biopsies were taken, which confirmed infiltrative adenocarcinoma with a signet ring appearance (Fig. 1d). No alternative or reversible cause of her pulmonary hypertension was identified, and given her compromised cardiorespiratory state, she was not fit for chemotherapy. She was transitioned to comfort care and died peacefully.

A limited postmortem examination showed metastatic gastric signet ring adenocarcinoma in enlarged hilar and mediastinal lymph nodes, and widespread pulmonary vascular changes including tumor thrombi, eccentric intimal hyperplasia causing stenosis and occlusion and tumor in lymphatic spaces (Fig. 1e,f).
The final diagnosis was metastatic gastric adenocarcinoma with pulmonary tumor thrombotic microangiopathy (PTTM) causing pulmonary hypertension and progressive right heart failure.

Discussion

PTTM is a rare manifestation of malignancy with histopathological features of pulmonary tumor emboli and fibrous intimal hyperplasia causing widespread pulmonary vascular stenosis/occlusion.\(^1\) These changes are thought to lead to the development of increased pulmonary vascular resistance and right heart failure. Gastric cancer is the most commonly implicated malignancy, although other malignancies have been described.\(^2\)

The pathophysiology of PTTM is poorly understood. Embolic tumor cells are thought to induce endothelial damage and cause inflammation, coagulation, and intimal proliferation through a variety of growth factors and cytokines.\(^3,4\) The prevalence of PTTM is unknown—post-mortem estimates are of 1–3% in autopsy series of patients with a history of malignancy.\(^3,4\)

Patients typically present with subacute, progressive dyspnea over days to weeks. Other symptoms may include fatigue, weight loss, pain, fever, cough, and hemoptysis.\(^5\) Patients often die within weeks of developing dyspnea. While histopathological diagnosis is the gold standard, tissue sampling may be prohibited by the clinical state of the patient. Other investigations may assist but are often normal or nonspecific.

The optimal management of PTTM is unclear. Aside from supportive care, previous experiences described in case reports have included chemotherapy, anticoagulation, steroids, oxygen therapy, and medications used to treat pulmonary arterial hypertension with variable success.

In summary, PTTM is an oft overlooked cause of newly diagnosed pulmonary hypertension in the setting of a recently diagnosed or as-yet undiagnosed malignancy. Gastric cancer is the most common underlying malignancy leading to PTTM. Clinicians should exercise a high index of suspicion to facilitate prompt diagnosis and treatment.

Ethics Statement

Provided by our local human research ethics committee (Project 118/22) on 10 March, 2022. Due to the patient being deceased, surrogate consent was also provided by the patient’s next-of-kin (her husband).

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