Pulmonary Tumor Thrombotic Microangiopathy — Antemortem Diagnosis With Pulmonary Artery Wedge Blood Cell Sampling in a Recurrent Breast Cancer Patient —

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A 46-year-old woman with a 2-week history of progressive exertional dyspnea and dry cough was admitted to hospital with a diagnosis of severe hypoxia. She had a history of operation for breast cancer (left mastectomy and axillary lymph node dissection) 6 years earlier, and adjuvant chemotherapy (fluorouracil, epirubicin and cyclophosphamide followed by docetaxel), then endocrine therapy for 5 years because of clinical stage IIa invasive carcinoma of the left breast.

At the present admission the patient had sinus tachycardia...
(heart rate, 132 beats/min), with systemic hypertension (arterial blood pressure, 141/106 mmHg), tachypnea (respiratory rate, 32/min) and severe hypoxemia (oxygen saturation on pulse oximetry, 96% under 10 L/min oxygen flow rate). Arterial blood gas examination with the patient breathing under the condition of 10 L/min oxygen flow rate, indicated respiratory alkalosis (pO2, 111 mmHg; pCO2, 27 mmHg; pH, 7.32). Chest X-ray did not show pulmonary congestion (Figure A). Transthoracic echocardiography indicated severe right ventricular dilatation with left ventricular compression and elevated systolic pulmonary artery pressure (Figure B). Although there was no pulmonary embolism on enhanced computed tomography (CT), a diffuse patchy distribution of ground-glass opacity and diffuse thickening of the interlobular septa were also seen (Figure C–E). The patient’s general condition was so bad that lung perfusion scintigraphy could not be performed. Right heart catheterization indicated pulmonary hypertension, with a pulmonary artery pressure of 45/24 mmHg (mean, 33 mmHg), and pulmonary vascular resistance of 852 dyne·sec·cm⁻⁵. In contrast, pulmonary artery wedge pressure (PAWP) and cardiac index (CI) were almost normal (PAWP, 2 mmHg; CI, 2.64 L/min/m², respectively). D-dimer was increased to 37.2 μg/mL (normal, <1.0 μg/mL).

First, the patient was treated with diuretics (furosemide, 60 mg/24 h), dobutamine (5 μg·kg⁻¹·min⁻¹) and heparin sodium (12 U·kg⁻¹·h⁻¹) to improve circulation dynamics. In addition, we initiated treatment targeting pulmonary arterial hypertension (PAH), including ambrisentan (5 mg/day), tadalafil (20 mg/day) and beraprost (180 μg/day).

Despite this treatment, the patient’s general condition worsened. Therefore, for more precise diagnosis and intensive treatment, pulmonary artery wedge blood sampling was carried out, and 10 mL of blood submitted to the pathology department for cytology. On direct smear and cell block preparation (Figure F–H), several tight 3-D clusters of atypical cells were noted in the blood. These cells had a high nuclear-cytoplasmic ratio with periodic acid-Schiff-positive foamy cytoplasm and occasional prominent nucleoli, consistent with adenocarcinoma. On immunohistochemistry of the cell block, tumor cells were positive for cytokeratin (CK)7, negative for CK20, thyroid transcription factor-1, and napsin A. Estrogen receptor was positive in 10% of tumor cells, and progesterone receptor was positive in 50% of tumor cells. Taking the past history into account, these results were compatible with recurrence of breast carcinoma.

This patient presented with rapidly progressing dyspnea and acute pulmonary hypertension. Despite receiving medical treatment and endotracheal intubation, the respiratory condition worsened. This rapid progression cannot be explained by breast cancer metastasis only. CT showed a patchy distribution of ground-glass opacity and diffuse thickening of the interlobular septa. These findings are often caused by diffuse embolization of small pulmonary arteries and the resultant inflammation. Furthermore, pulmonary artery wedge blood cell sampling and cytodiagnosis confirmed recurrent breast carcinoma. The CT findings and the results of cytodiagnosis were compatible with pulmonary tumor thrombosis microangiopathy (PTTM). On this basis, the patient was diagnosed with recurrent breast cancer with PTTM.

Because of the patient’s poor general condition, anticancer agents could not be used. As noted, the patient’s respiratory condition rapidly deteriorated, and she died 7 days after admission. Autopsy was unable to be performed due to refusal by the family.

PTTM was first described by Von Herbay et al in 1990. It is a very rare cancer-related pulmonary complication, leading to pulmonary hypertension, heart failure and hypoxia. It is characterized histologically by tumor embolism and fibrocellular intimal proliferation of the small pulmonary arterioles, but the mechanism of PTTM is still unclear. PTTM is usually diagnosed on autopsy and is rarely diagnosed before death. Pulmonary artery wedge blood sampling with a pulmonary artery wedge catheter is a simple and useful diagnostic method. A Swan-Ganz catheter is inserted and located in the right pulmonary artery wedge position, and blood gently withdrawn from the wedge catheter.

Herein we have described a case of antemortem diagnosis of PTTM made using pulmonary artery wedge blood cell sampling in a patient with recurrent breast cancer. PTTM is a rare condition, but should be considered in the differential diagnosis of acute dyspnea or PAH in the presence or absence of a previous diagnosis of cancer. Pulmonary artery wedge blood cell sampling and cytodiagnosis should be performed in the case of rapidly progressing PAH and rapidly worsening respiratory failure under medications targeting PAH. Pulmonary microvascular cytology using a pulmonary artery wedge catheter is a good tool for use in the antemortem diagnosis of PTTM.

Disclosures

The authors declare no conflicts of interest.

References