Pulmonary tumor embolism syndrome from occult colonic adenocarcinoma

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Pulmonary tumor embolism syndrome is a rare phenomenon that can occur in patients who have an occult neoplasm that metastasizes. We describe a case of an elderly woman with an undiagnosed colon cancer who suffered from respiratory distress and compromised pulmonary blood flow from micro-metastasis in the pulmonary arteries.

Cancer is one of the leading causes of death in the elderly. It can present in a variety of ways, some more subtle than others. This case illustrates the value of traditional autopsy in discovering subtle underlying pathologic processes that explain a patient's clinical outcome, despite extensive diagnostic, supportive, and therapeutic clinical efforts.

CASE DESCRIPTION

A 76-year-old white woman was transferred to our tertiary care center following a short hospital course characterized by bronchitis, dehydration, and failure to thrive. She had cough, fever, poor oral intake, and a general decline in her overall status for several weeks despite antibiotics and intravenous hydration. She was known to have type 2 diabetes mellitus, hypertension, chronic systolic heart failure, and Alzheimer's dementia. She had lived at home with her husband and was able to perform most activities of daily living without assistance. On presentation to our hospital she was lying in bed moaning but unable to communicate with the medical team or follow commands of any sort. She was found to have multiple laboratory abnormalities (*Table 1*).

Chest radiograph showed cardiomegaly and vascular congestion. Ultrasound examination of her abdomen showed increased hepatic echogenicity consistent with hepatic steatosis as well as renal cortical thinning consistent with medical renal disease. Computed tomography of the brain revealed senescent changes and an air fluid level in the sphenoid sinuses. Trans-thoracic echocardiogram showed changes consistent with mild pulmonary hypertension and left ventricular hypertrophy. The patient was started on broad-spectrum empiric antibiotics. Electroencephalogram showed periodic epileptiform discharges and

Table 1. Laboratory values

Serum test	Result	Cerebrospinal fluid test	Result
Hemoglobin (g/dL)	8.5	Erythrocyte count (cells/ μ L)	720
Platelets (n/ μ L)	75,000	Leukocytes (n/ μ L)	2
Blood urea nitrogen (mg/dL)	109	Glucose (mg/dL)	103
Serum creatinine (mg/dL)	4.1	Protein (g/dL)	300
Potassium (mEq/L)	5.6	Bacterial Gram stain and culture	negative
AST (U/L)	375	Fungal culture	negative
ALT (U/L)	177	Cryptococcal antigen	negative
GGT (U/L)	204	Histoplasma antigen	negative
Total bilirubin (mg/dL)	1.1	Herpes simplex virus PCR	negative
Alkaline phosphatase (U/L)	1400	Varicella zoster virus PCR	negative
D-dimer (mg/L)	35.2	Parvovirus B19 PCR	negative
Fibrin split products (μ g/mL)	>20	West Nile virus PCR	negative

ALT indicates alanine aminotransferase, AST, aspartate aminotransferase; GGT, gamma-glutamyl transpeptidase; PCR, polymerase chain reaction.

moderate to marked generalized slowing. Levetiracetam therapy provided no clinical improvement. Analyses of the cerebrospinal fluid are shown in Table 1, and there was no evidence of acute infection to explain her encephalopathy. Through the remainder of the hospitalization, the patient's respiratory distress and renal failure worsened, and she died.

Autopsy disclosed a 1.5-cm, well-circumscribed, dark brown subdural nodule overlying the left parietooccipital region of the brain. The heart weighed 520 g, and the right side was dilated. Her coronary arteries were widely patent. She had arteriolar nephrosclerosis and an atherosclerotic aorta. She had focal necrosis of the distal great toes bilaterally. The cecum contained a 4-cm fungating tumor mass (*Figure 1*), as well as multiple

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Figure 1. Gross examination of the cecum revealed a several-centimeter tumor extending intraluminally. A cut through the center of the tumor (arrow) demonstrates the transmural thickness (double arrow).

Figure 2. Microscopic examination of the tumor revealed anaplastic cells with glands consistent with poorly differentiated adenocarcinoma (hematoxylin and eosin stain, 100 $\times$).

firm mesenteric lymph nodes, histologically typical of poorly differentiated adenocarcinoma with prominent lymphovascular invasion (*Figure 2*). Metastases were present in the liver, bone marrow, adrenal glands, thyroid gland, sphenoid sinus, brain, dura, and lungs. All lobes of the lungs contained intravascular collections of poorly differentiated adenocarcinoma. Tumor

Figure 3. Sections of the pulmonary arteries revealed intravascular collections of fibrin and markedly anaplastic tumor cells consistent with poorly differentiated adenocarcinoma (hematoxylin and eosin stain, 100 $\times$).

cells were present within small arteries, arterioles, and septal capillaries (*Figure 3*). Many tumor emboli were seen associated with intravascular fibrin.

DISCUSSION

Pulmonary tumor embolism syndrome (also known as pulmonary tumor thrombotic microangiopathy) has been reported to be found in 3% to 26% of autopsies conducted on patients with solid tumors (1–4). Numerous case reports have been published (5–13), and in most cases the diagnosis is not made until after death. The incidence is highest in patients with gastric adenocarcinoma, and fewer cases have been reported with adenocarcinoma of the colon (14–16).

Pulmonary tumor embolism syndrome can present in a variety of ways, ranging from acute hypoxia due to large proximal emboli to indolent pulmonary hypertension developing from lymphatic or microvascular invasion (14). Patients can present with a wide range of symptoms including dyspnea, chest pain, and cough. Patients can have electrocardiographic signs of right-sided heart strain and dilated right ventricles. Arterial blood gases can reveal hypoxia with an associated respiratory alkalosis from hyperventilation. Patients who present with signs and symptoms of subclinical cor pulmonale often progress to death within 4 to 12 weeks (17). Chest radiographs or computed tomography are often normal or, in the case of lymphatic invasion, may show signs of interstitial infiltration. Pulmonary arteriography is usually not diagnostic (16, 18). Typical ventilation perfusion mismatches appear as subsegmental defects. These findings are often numerous, peripherally located, symmetric mismatches that are distinct in comparison to the defects caused by venous thromboemboli and have been described as “checkerboard” like—the so-called “checkerboard sign” (19).

Definitive diagnosis can be made premortem. Roberts and associates (1) described obtaining an aspirate from the distal port of a right-sided heart catheter that had been placed in the wedge position. This sample was stained with the Papanicolaou method, and metastatic carcinoma cells were identified. Patients

with this syndrome usually die quickly. Treatment is usually unhelpful. Thrombolysis has been attempted but usually causes more harm than benefit (20).

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