Pulmonary Tumor Embolization after Renal Transplantation

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Dear Sir,

Malignancies are recognized complications after renal transplantation. We would like to report an unusual presentation of adenocarcinoma of the stomach in a 38-year-old lady, 9 years after renal transplantation, manifesting as cor pulmonale secondary to pulmonary thromboembolism.

Our patient was a 38-year-old Southern Chinese female. She presented at the age of 28 with end-stage renal failure of unknown etiology. Her past health and family history was unremarkable apart from her being a chronic carrier of hepatitis B surface antigen with persistently normal transaminase levels. After 6 months of hemodialysis, she received a renal allograft from her sister, with one haplo-type match. The postoperative course was uneventful, with no rejection. The levels of serum creatinine, urea, transaminases, alkaline phosphatase, gamma glutamyl trans-peptidase, albumin, globulin, and alpha-feto-protein, as well as hemoglobin, white cell count, platelet count, prothrombin time and activated partial thromboplastin time were monitored every 4-6 weeks and had remained persistently normal. Her clinical condition remained stable for 9 years after renal transplantation, with serum creatinine 100 $\mu\text{mol/l}$ (1.14 mg/dl) and hemoglobin 15.7 g/dl at the most recent follow-up. Maintenance immuno-suppression consisted of prednisolone 7.5 mg daily and azathioprine 50 mg daily. There was no history of oral contraceptive intake.

In February 1992, she presented with cough and scanty purulent sputum for 1 week, which cleared after a week's course of oral amoxicillin and sulbactam. The sputum culture was negative. However, she developed progressive dyspnea on exertion over the following week. Physical examination showed blood pressure 110/70 mm Hg, elevated jugular venous pressure, and resting sinus tachycardia of 100/min. The pulmonary second sound was loud, with no murmur. She had resting tachypnea with a respiratory rate 20/min. Her breath sounds were normal and symmetrical, and there was no adventitious sound. Examination of the abdomen did not reveal any abnormality. There was no clinical evidence of deep vein thrombosis or cutaneous vasculitis. Arterial blood gas showed PaO_2 6.3 kPa on room air, which increased to 9.3 kPa with 50% O_2 , PaCO_2 3.1 kPa, and bicarbonate level 16 mmol/l .

Electrocardiogram showed the new development of 1-mm ST depression and T wave inversion over leads II, III, aVF, V4-6, without P pulmonale, or other features of right ventricular hypertrophy. Chest X-ray showed a prominent pulmonary conus, with clear lung fields. Echo-cardiogram showed right ventricular dilatation and hypertrophy, with impaired contraction. The pulmonary arterial trunk was dilated. Heart valves were normal. Ventilation-perfusion lung scan showed multiple small peripheral perfusion defects. There was no evidence of deep vein thrombosis on Doppler study of the lower limbs. The overall features were compatible with cor pulmonale secondary to chronic pulmonary vasculopathy. Her clotting time, prothrombin time, activated partial thromboplastin time, and platelet counts were normal. Hemoglobin level was stable at 15.2 g/dl, as were serum iron and ferritin. Neither lupus anticoagulant nor anti-cardiolipin antibodies were detectable. On the 2nd day after admission, her condition deteriorated. Despite the administration of volume expanders, inotropic support with dopamine was required to maintain blood pressure at 100/70 mm Hg. Oxygen supplementation was increased to 70% in order to maintain PaO₂ at 9 kPa. Eight hours later, she developed sudden cardiac arrest and failed resuscitation. Postmortem examination showed a malignant ulcer 2.5 cm in diameter at the gastric fundus. Histologic examination showed adenocarcinoma arising from the gastric mucosa, with prominent distension of submucosal lymphatics by tumor cells (fig. 1). Tumor infiltration was observed in lymph nodes along the lesser curvature, the lumbar paravertebral lymph nodes, as well as the bone marrow. There was extensive tumor embolization to the distal pulmonary vasculature and multiple small wedge-shaped hemorrhagic infarcts, with features of organization and recanalization in some arterioles (fig. 2). Tumor invasion of the pulmonary arteries was not observed. There was only one focus of hepatic metastases, measuring 0.5 cm in diameter, without involvement of the hepatic vein, the portal vein, or the inferior vena cava. The right ventricle was dilated with increased trabeculation. Our patient presented with respiratory insufficiency and features suggestive of cor pulmonale secondary to pulmonary thromboembolism. In the absence of risk factors such as oral contraceptive intake, immobility, family history of thrombophilia, or deep vein thrombosis, it was important to determine the underlying etiology, as spontaneous pulmonary thromboembolism is rarely encountered among Chinese in our locality. Pulmonary radionuclide ventilation-perfusion scanning can be useful, as the demonstration of un-

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Fig. 2. A pulmonary arteriole showing recanalization after tumor

Fig. 1. An infiltrating adenocarcinoma arising from the gastric mucosa. The submucosal lymphatics were distended by tumor cells, embolization. HE. $\times 1,000$. HE. $\times 100$.

matched perfusion defects would suggest thromboembolic occlusion of major pulmonary arteries. The demonstration of smaller perfusion defects, however, is much less specific. Although multiple small subsegmental perfusion defects in a 'segmental contour pattern'

have been described in cases of pulmonary tumor embolization or lymphangitis carcinomatosa, similar findings have been reported in patients with primary pulmonary hypertension [1-3]. Pulmonary angiography may reveal pruning of the peripheral pulmonary arteries in thromboembolic disease as well as in idiopathic pulmonary hypertension [4], and it may fail to visualize vascular occlusions of 1 mm or less in diameter [5]. Furthermore, pulmonary angiography in patients with markedly elevated pulmonary arterial pressure can have fatal complications [6]. In view of this, for patients with a history of malignancy, when the perfusion lung scan showed multiple small perfusion defects, a lung biopsy had been the recommended investigation instead of pulmonary angiography to distinguish between pulmonary thromboembolism and tumor embolization to the pulmonary vasculature [4].

Carcinoma of the stomach accounted for 0.9% of all malignancies that had developed in organ transplant recipients [7]. The absence of clinical features such as anemia or epigastric pain in our patient could be accounted for by the relatively small size of the primary tumor. Dyspnea secondary to extensive pulmonary tumor embolization as the only presenting symptom has been reported in patients with carcinoma of the liver, carcinoma of the breast, or choriocarcinoma [8, 9], but has never been associated with carcinoma of the stomach or with renal allograft recipients.

It has been suggested that pulmonary tumor embolization in patients with carcinoma of the liver, choriocarcinoma, or renal cell carcinoma was secondary to venous invasion by these tumors. For tumors which had a low propensity for venous invasion, such as carcinoma of the breast and stomach, pulmonary tumor embolization correlated with extensive hepatic metastases, suggesting that the latter were the source of tumor microemboli [9]. Tumor embolization to the lungs via the vena cava was unlikely in our patient in view of the absence of vascular invasion by the primary tumor, and the single hepatic metastasis which did not involve the portal or hepatic veins. It is more probable that the tumor had spread to the pulmonary vasculature by lymphatic drainage via the thoracic duct, in view of the prominent lymphatic invasion.

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