6. McCutcheon IE, Eng DY, Logothetis CJ: Brain metastasis from prostate carcinoma: Antemortem recognition and outcome after treatment. Cancer 86: 2301-2311, 1999

7. Sutton MA, Watkins HL, Green LK, et al: Intracranial metastases as the first manifestation of prostate cancer. Urology 48:789-793, 1996

8. Tsai V, Kim S, Clatterbuck RE, et al: Cystic prostate metastases to the brain parenchyma: Report of two cases and review of the literature. J Neurooncol 51:167-173, 2001

9. Mintz ER, Smith GG: Autopsy findings in 100 cases of prostatic cancer. N Engl J Med 211:479-487, 1934

10. Olson ME, Chernik NL, Posner JB: Infiltration of the leptomeninges by systemic cancer: A clinical and pathologic study. Arch Neurol 30:122-137, 1974

11. DeAngelis LM, Boutros D: Leptomeningeal metastasis. Cancer Invest 23:145-154, 2005

12. Freilich RJ, Krol G, DeAngelis LM: Neuroimaging and cerebrospinal fluid cytology in the diagnosis of leptomeningeal metastasis. Ann Neurol 38:51-57, 1995

13. Collie DA, Brush JP, Lammie GA, et al: Imaging features of leptomeningeal metastases. Clin Radiol 54:765-771, 1999

14. Wasserstrom WR, Glass JP, Posner JB: Diagnosis and treatment of leptomeningeal metastases from solid tumors: Experience with 90 patients. Cancer 49:759-772, 1982

15. Kaplan JG, DeSouza TG, Farkash A, et al: Leptomeningeal metastases: Comparison of clinical features and laboratory data of solid tumors, lymphomas, and leukemias. J Neurooncol 9:225-229, 1990

16. Grossman SA, Moynihan TJ: Neoplastic meningitis. Neurol Clin 9:843-856, 1991

17. Gleissner B, Chamberlain MC: Neoplastic meningitis. Lancet Neurol 5:443-452, 2006

18. Chamberlain MC: Cytologically negative carcinomatous meningitis: Usefulness of CSF biochemical markers. Neurology 50:1173-1175, 1998

19. Pentheroudakis G, Pavlidis N: Management of leptomeningeal malignancy. Expert Opin Pharmacother 6:1115-1125, 2005

20. Mencel PJ, DeAngelis LM, Motzer RJ: Hormonal ablation as effective therapy for carcinomatous meningitis from prostatic carcinoma. Cancer 73:1892-1894, 1994

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Transmission of Glioblastoma Multiforme After Bilateral Lung Transplantation

In December 2006, a 57-year-old male presented to the outpatient department with cough and dyspnea. Past medical history was significant for end-stage emphysema requiring bilateral lung transplantation in September 2005. His pulmonary function improved dramatically following the transplantation and he remained fully functional without supplemental oxygen on a regimen of prednisone, tacrolimus and mycophenolate mofetil to prevent rejection. He had been monitored with home spirometry and periodic surveillance transbronchial biopsy without abnormal findings. Review of systems was otherwise unremarkable. Physical examination revealed a resting tachycardia and clear lungs on auscultation. Laboratory tests showed mild anemia, elevated serum creatinine, worsening pulmonary function, and therapeutic levels of tacrolimus. A chest computed tomography (CT) scan revealed multiple bilateral round opacities, pleural effusions and mediastinal adenopathy (Fig 1). The largest pulmonary nodules measured 3.5 × 2.3 cm in the right middle lobe and 3.0 × 2.6 cm in the right lower lobe. A positron emission tomography/CT scan revealed intense [18F]fluorodeoxyglucose uptake in the enlarged mediastinal and right internal mammary lymph nodes and the multiple pulmonary nodules. The patient underwent bronchoscopy with transbronchial biopsy and fine needle aspiration of the subcarinal lymph nodes, which were nondiagnostic. Subsequent thoracentesis and a CT-guided biopsy of a lung nodule revealed a poorly differentiated carcinoma. Additional tissue was obtained by mediastinoscopy and paratracheal lymph node biopsy to further classify the cancer. The tumor cells were strongly and diffusely positive for glial fibrillary acidic protein (GFAP, Fig 2) and CD56, and were negative for cytokeratin (AE1/AE3), thyroid transcription factor-1, melanoma marker HMB-45, cytokeratins 7 and 20, chromogranin, CD45, CAM5.2, and prostate-specific antigen. The histology and special stains were consistent with glioblastoma multiforme (GBM). Further work-up included an magnetic resonance imaging of the brain and a CT scan of the abdomen and pelvis, both of which were normal. The lung donor for this patient was a 47-year-old male who died of an acute intracranial hemorrhage. His lungs, heart, liver, pancreas, and kidneys were harvested, appeared grossly normal, and were transplanted into five patients in need of the organs. A full autopsy was subsequently

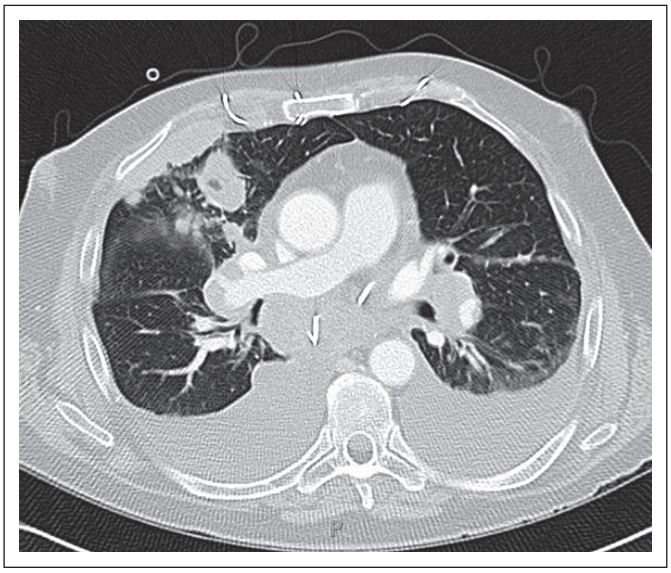

Fig 1.

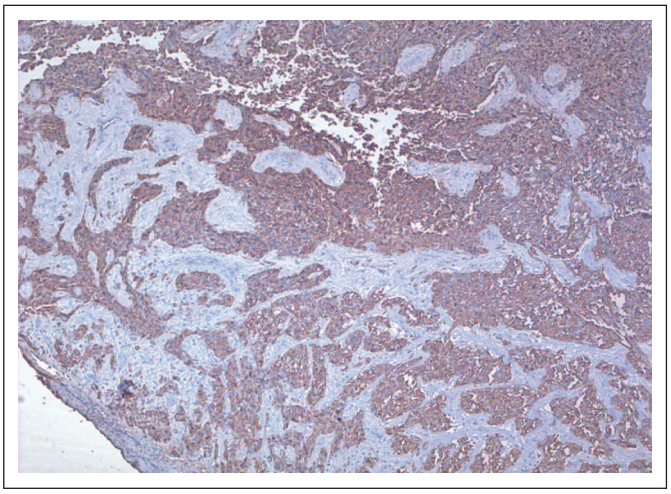

Fig 2.

conducted which revealed a neoplasm in the region of the bleed in the left frontal lobe. Pathologically this was determined to be a GBM with strongly positive GFAP by immunohistochemistry. The lung recipient was informed of the autopsy results and refused retransplantation. The patient's clinical status rapidly deteriorated shortly after the diagnosis was determined. He developed severe hypoxia and large, recurrent malignant pleural effusions requiring placement of a drainage catheter. As a result, chemotherapy was not initiated and he died two months after presentation (17 months after the lung transplant). The recipients of other organs from the same donor remain free of GBM. One recipient had his transplanted kidney removed after learning of the donor's diagnosis.

The differential diagnosis of pulmonary nodules in patients following organ transplant is extensive. This represents the second reported case of metastatic GBM following bilateral lung transplantation from a donor with GBM.[1] Unlike the first case report, in which the donor had a known history of GBM and received radiation, in the current case the diagnosis of donor GBM was made only at autopsy. Due to the acuteness of the transplantation process, this information was not available to either the transplantation team or the recipient at the time of the transplantation. In addition, during the transplantation procedure of the first case, an enlarged hilar lymph node was found to contain GBM, indicating the extracranial dissemination of GBM. In this second case, the donor lungs appeared normal. Transmission of solid tumor through organ transplantation is rare as a history of cancer generally precludes organ donation.[2] However, patients with primary CNS tumors have been considered acceptable transplant donors given the low or negligible risk of systemic tumor dissemination and the high demand for organs.[3] Recent data from the Organ Procurement and Transplantation Network revealed that of a total of 202,233 deceased donor transplants from 1994 to 2004, one single-donor-transmitted GBM was identified that resulted in three deaths, with a tumor transmission rate of 0.8% from 128 donors with malignant CNS tumors and 1.4% out of 69 donors who had GBM.[4] Data from the Israel Penn International Transplant Tumor Registry reported on 30 organs from an unknown number of donors with GBM and suggested the incidence of tumor transmission could be as high as 40%.[5] Donor-transmitted GBM has been also reported following transplantation of liver and kidneys.[1,6-8] The onset of metastatic disease ranges from 2 to 18 months after transplantation and the outcome is uniformly fatal. In some cases, identification of histologic features[1] or molecular analysis with DNA sequencing[6] confirmed the cancer was transmitted through the transplanted organ making this a truly iatrogenic disease.[7] Different donor organs may be associated with different rates of tumor transmission. The lungs and liver are common sites of metastases in patients with solid tumors compared with the heart or kidneys. In our experience, using lungs from donors with high-grade gliomas appears to be of high risk to the recipients. From 2002 to 2007, 101 patients underwent lung transplantation at our institution and two of these lungs came from donors with cancer. Both donors had GBM and each recipient died of metastatic GBM. One of these patients had a known recurrence of his GBM and the second appeared to have had micrometastatic disease to the lungs when he died of an undiagnosed GBM. These cases and a previous review of systemic dissemination of these tumors suggest that high-grade primary CNS tumors are frequently associated with micrometastatic disease long before they die from progressive disease within the CNS.[1] The risk of tumor transmission from donors with high-grade CNS tumors is likely to be unacceptably high especially if organs with the highest probability of harboring these micrometastases, such as lungs and liver, are used for transplantation. As a result, use of these organs should be avoided.[9]

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

REFERENCES

1. Armanios MY, Grossman SA, Yang SC, et al: Transmission of glioblastoma multiforme following bilateral lung transplantation from an affected donor: Case study and review of the literature. Neuro Oncol 6:259-263, 2004

2. Ajithkumar TV, Parkinson CA, Butler A, et al: Management of solid tumours in organ-transplant recipients. Lancet Oncol 8:921-932, 2007

3. Orens JB, Boehler A, Perrot Md, et al: A review of lung transplant donor acceptability criteria. J Heart Lung Transplant 22:1183-1200, 2003

4. Kauffman HM, Cherikh WS, McBride MA, et al: Deceased donors with primary CNS malignancies: An underused organ source. Transplantation 82:330, 2006

5. Buell JF: Use of donors with central nervous system malignancies: Proceed with caution. Transplantation 77:1906-1907, 2004

6. Frank S, Muller J, Bonk C, et al: Transmission of glioblastoma multiforme through liver transplantation. Lancet 352:31, 1998

7. Healey PJ, Davis CL: Transmission of tumours by transplantation. Lancet 352:2-3, 1998

8. Punnett AS, McCarthy LJ, Dirks PB, et al: Patients with primary brain tumors as organ donors: Case report and review of the literature. Pediatric Blood Cancer 43:73-77, 2004

9. Kauffman HM: The United Network for Organ Sharing position on using donors with primary central nervous system malignancies. Transplantation 79:622-623, 2005

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