Transmission of Metastatic Glioblastoma Multiforme From Donor to Lung Transplant Recipient

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Abstract: This report describes a case in which a lung transplant patient presented with lung masses. After an extensive medical workup and biopsy, the masses were found to be caused by metastatic glioblastoma multiforme, which the patient acquired from the lung donor. This article will also review similar cases in the literature.

Key Words: gliobastoma multiforme, lung transplant, metastatic

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A 58-year-old man with severe end-stage chronic obstructive pulmonary disease underwent bilateral lung transplants in September 2005. One year later, the patient developed symptoms of productive cough and dyspnea. Imaging and clinical workup revealed multiple lung masses suggestive of metastatic disease or posttransplant lymphoproliferative disease (PTLD). Further workup including biopsy revealed metastatic glioblastoma multiforme (GBM) in the patient's lungs. Therefore, the patient underwent a magnetic resonance imaging of the brain, which revealed no evidence of primary GBM. However, review of the lung donor's medical records revealed that the donor had experienced an intracranial hemorrhage, and subsequent autopsy had revealed GBM. It was not known at the time of transplant that the cause of the intracranial bleed was secondary to the GBM. We present the details of this case and review the literature on the subject of donor-to-patient transmission of metastatic central nervous system (CNS) tumors.

CLINICAL INFORMATION

Approximately 1 year after bilateral lung transplant, the patient telephoned his clinician complaining of new onset of productive cough. The patient was treated with antibiotics, which resulted in improvement but not complete resolution of symptoms. Imaging workup was then pursued that included a chest radiograph, followed by a chest computed tomography (CT). Chest radiograph (Fig. 1) revealed two 3-cm densities in the region of the right middle lobe and small bilateral pleural effusions. Chest CT (Figs. 2–4) demonstrated multiple bilateral nodular lung nodules, with the 2 largest in the right middle lobe. Significant mediastinal lymphadenopathy was also present (Figs. 2 and 3). Given the bilateral lung nodules and associated mediastinal lymphadenopathy in a transplant recipient, PTLD was the leading consideration. Mediastinoscopy was performed with excision of a paratracheal lymph node. The pathology specimen underwent a series of immunohistochemical stains, which were strongly and diffusely positive for glial fibrillary protein and CD56, both of which are markers for GBM. The patient then underwent a magnetic resonance imaging of the brain, which revealed no evidence of primary GBM. However, review of the lung donor's medical records revealed that the patient had experienced an intracranial hemorrhage, and subsequent autopsy had revealed GBM, although that was not known at the time of organ harvest.

DISCUSSION

This case raises 2 important issues. First, is there a role for screening donor patients with imaging before transplantation in the proper clinical setting? In this particular case, the patient was not known to have a primary malignancy at the time of organ harvest. Radiological screening may have identified early lung metastases or the primary tumor before the transplant. This information could help clinicians in donor selection depending on the urgency of transplantation. The second issue is the safety of organ procurement in patients with malignant CNS neoplasms. However, the shortage of organ donors demands that some risks be taken to save the lives of potential recipients. In 1999, there were 6143 deaths on the waiting list, with nearly half of them (3059) occurring in candidates for life-saving organs such as liver, heart, and lung.[1] Because of the shortage of potential donors, use of marginal donors has been deemed acceptable, with at least 1 strategy being the use of patients with primary CNS tumors. However, patients with CNS tumors comprise a very small percentage of the donor population, for example, only approximately 0.5% of the approximately 13,000 patients who are dying from gliomas are procured and transplanted every year in the United States.[5] Review of the United Network for Sharing Organs showed that approximately 1% of American cadaver donors per year died of CNS tumors.[3] The data regarding the exact transmission rates of malignant CNS neoplasms in organ donors are not firmly established.

At least 1 prior case of metastatic GBM in the lung, transmitted from donor to recipient, has been reported in the literature. The case involved a 28-year-old man with progressive pulmonary fibrosis secondary to systemic sclerosis.

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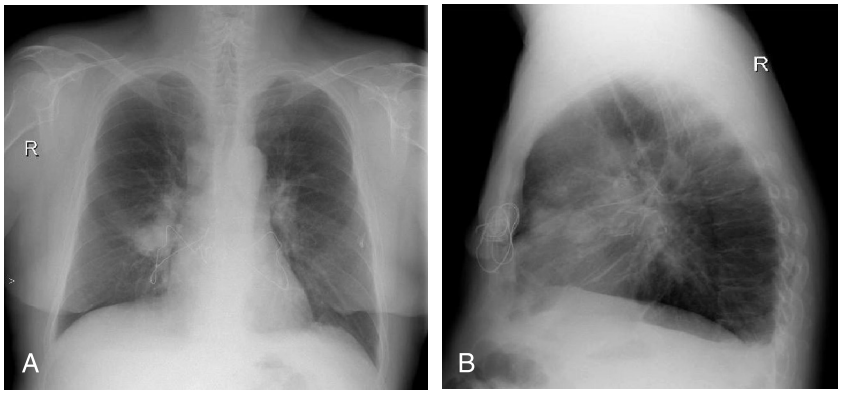

FIGURE 1. A and B, Chest radiograph showing right middle lobe mass, right paratracheal lymphadenopathy, and bilateral hilar lymphadenopathy.

The patient's lung donor was a 29-year-old man who had a known 9 × 7-cm parietal GBM and eventually had a fatal intracranial hemorrhage. Four months after receiving the transplant, the patient developed interstitial infiltrates and mediastinal lymphadenopathy that was histologically proven GBM. The patient died shortly after.[2]

Metastases from primary CNS tumors, not in the setting of transplant, are rare, and literature has shown that most documented cases of metastases have involved disruption of the blood-brain barrier by surgical intervention or ventricular shunting.[3] One study evaluated the potential risk of transmission of glioblastomas in transplant recipients. The study revealed that the transmission rates were determined by the grade of the tumor and other risk factors including prior surgical disruption of blood-brain barrier and ventricular shunting. In this study, 26 donors with primary glioblastomas were reviewed. Fifteen patients received organs from a donor with at least 1 risk factor for disease transmission (prior surgical intervention or high-grade [grade 4] GBM). In the 15 recipients, 8 transmissions were identified between periods of 2 and 15 months posttransplant. This study also analyzed the overall risk of transmission for CNS neoplasms as a group (astrocytomas, glioblastomas, medulloblastomas, and other). Transmission risk with no risk factors was 7%; with 1 risk factor, 36%; and with 2 risk factors, 43%. With a high-grade tumor as an independent factor, risk of transmission was 43%.[4] It should be noted that other studies have shown lower transmission rates. For example, a published study using the Australia and New Zealand Organ Donation Registry evaluated 26 donors with malignant brain tumors, of whom there were 96 recipients of organs from these donors. A mean follow-up of 40 months in recipients revealed no cases of donor tumor recurrence. Of the donors, however, only 4 had glioblastomas.[5] In the literature, metastases of primary CNS tumors have been documented in liver, kidneys, and lung of transplant recipients.

CONCLUSIONS

This case illustrates the potential for tumor transmission from donor to recipient in patients receiving organs from

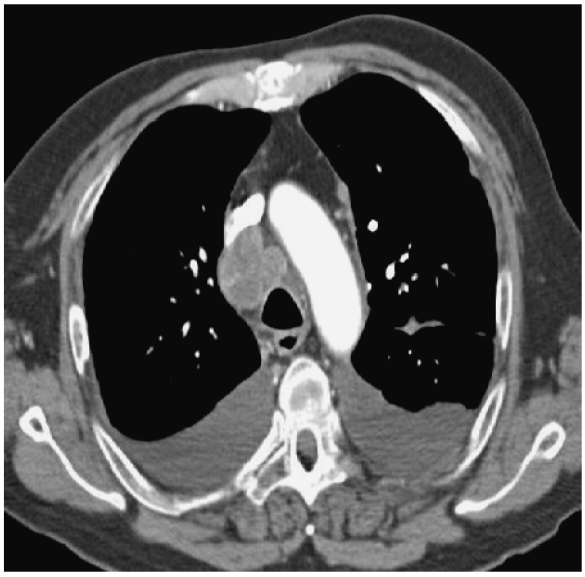

FIGURE 2. Chest CT with contrast showing large right paratracheal lymph node.

FIGURE 3. Chest CT showing bilateral hilar lymphadenopathy and subcarinal lymphadenopathy.

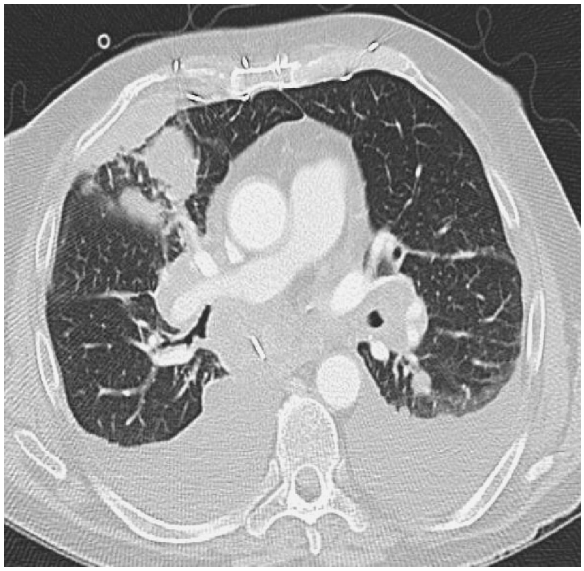

FIGURE 4. Chest CT showing right middle lobe mass.

patients with primary CNS malignancies. The radiological presentation was bilateral lung nodularity, mediastinal lymphadenopathy, and bilateral pleural effusions. The differential diagnosis in this patient included PTLD, primary lung cancer, metastases from another primary site, and atypical infection. Posttransplant lymphoproliferative disease and nonmelanoma skin cancers are the most common and recognized neoplastic complications of organ transplant. Both are thought to be secondary to immunosuppression and are recipient derived.[2] Despite PTLD and nonmelanoma skin cancers being more common, the radiological presentation of new cancer in an organ transplant recipient should include transmission of primary cancer from the organ donor.

Additionally, this case raises the issue of the use of screening donor patients with imaging before transplantation in the proper clinical setting. In this particular case, the patient was not known to have a primary malignancy at the time of organ harvest. Radiological screening may have identified early lung metastases or the primary tumor before the transplant. This information could help clinicians in donor selection depending on the urgency of transplantation.

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