

Letters to the Editor

RE: Anesthetic Management for Resection of Hepatic Paraganglioma Metastatic From the Donor Organ in an Orthotopic Liver Transplant Recipient: A Case Report



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Transplant Proc 2013 Mar; 45(2):817–9

To the Editor: We would like to clarify the timeline of events described in this case report, comment on the pathology of the donor transmitted paraganglioma, and discuss potential implications of this case to future donation criteria.

As stated in the case report [1], this is the first published case of donor transmitted paraganglioma. Additional details of the case relevant to the behavior of the paraganglioma are briefly summarized below.

In 2002, at the age of 71, the patient underwent an orthotopic liver transplant (OLT) for cryptogenic cirrhosis. The donor liver came from a 39-year-old male with a history of hypertension and substance abuse who died of a cerebrovascular accident secondary to drug overdose. At the time of transplant, a 3 cm necrotic mass was found near the donor's aortic bifurcation, but there were no other gross lesions in the abdominal cavity. The histology and immunophenotype of the tumor were consistent with a paraganglioma.

Approximately 6 years post-transplant, the patient presented with abdominal pain, nausea, vomiting, and diarrhea. Computed tomography (CT) demonstrated three intrahepatic lesions, the largest of which measured 4.2 cm. A biopsy was performed and histologic examination revealed a paraganglioma. Subsequent radiofrequency ablations (RFA) and surgical management are detailed in the case report [1]. Postoperative CT scan showed a residual lesion in the left hepatic lobe which was resected approximately one year later.

Since the last surgery, the patient has been monitored with serial imaging. At the time of this writing, nearly 12 years post-transplant, there is no evidence of recurrent growth in the liver or metastases to other organs.

Gross examination of the resection specimen demonstrated an 11.7 cm paraganglioma with focal necrosis. Fluorescence in-situ hybridization (FISH) with X and Y centromere-specific probes confirmed the tumor to be of donor origin: 197 of 300 nuclei (65.7%) demonstrated a male (XY, donor) signal pattern. Interestingly, the remaining 103 nuclei (34.3%) demonstrated a tetraploid male-XXYY signal pattern of unclear significance.

Immunohistochemical analysis of the tumor showed loss of SDHB expression in tumor cells, which was consistent with a mutation of the SDHA, SDHB, SDHC, or SDHD genes [2]. SDHB (succinate dehydrogenase iron-sulfur subunit B) is one of four protein subunits that together with SDHA, SDHC and SDHD forms a mitochondrial succinate dehydrogenase complex that participates in the tricarboxylic acid cycle (Krebs cycle) [3]. Paragangliomas with mutations of these tumor suppressor gene(s) are commonly extra-adrenal [4,5]. Intra-abdominal extra-adrenal paragangliomas, such as the one in this case, tend to be the most aggressive. They are often associated with mutations of the SDHB gene and metastasize in at least 25% of patients.

It is well known that the shortage of donor livers has led to the increased use of expanded criteria donors. Of most interest to this case is the increasing consideration of transplanting organs from donors with a history of malignant disease [7]. Donor transmitted cancers have been described since 1965 [8] and it is these early case reports that have led to the recommendation that patients with a history of malignancy be excluded from the donation pool [9]. In 1999, the United Network for Organ Sharing (UNOS) Transplant Tumor Registry began to examine donor malignancy data and in their recent report of donor data between 2000 to 2005 four deaths from donor transmitted malignancies were identified [10]. The reported risk of donor tumor transmission rates have ranged from 0.01% [11] to 0.05% [12].

The need for more meaningful guidelines in donation with respect to transmitted malignancy led to the development of an ad hoc Malignancy Subcommittee of the Disease Transmission Advisory Committee (DTAC) to advise on this subject. The most recent DTAC report suggested risk categorization for specific tumor types as follows: no significant risk, minimal risk, low risk, intermediate risk, high risk, and unknown risk based on available data [7]. According to these guidelines, paragangliomas are considered "benign tumor[s] with malignant potential." However, as there are no histopathologic criteria to assess for

malignancy, without evidence of metastasis, these tumors fall under the category of “unknown risk.” This case report illustrates the difficulty in assessing the risk categorization of paragangliomas in donor transplant criteria. While there are no histopathologic criteria to assess for malignancy, many multi-factorial scoring systems may help in distinguishing tumors that pose a significant risk of metastasis from benign tumors [5,6]. In a study by Kimura et al [13], a scoring scale called the “GAPP” score (grading system for adrenal pheochromocytoma and paraganglioma) involving six factors: histological pattern, cellularity, comedo necrosis, vascular/capsular invasion, Ki-67 labeling index and catecholamine type, was used to classify tumors into well, moderate, or poorly differentiated types. Based on these criteria this donor tumor would be most consistent with a moderately differentiated type with 60% rate of metastasis [13].

Intriguing questions remain regarding this first known case of donor-transmitted paraganglioma. It's unclear what effect, if any, the immunosuppressive drug therapy had on the growth and behavior of this paraganglioma. It is also notable that despite the relatively large size of the tumor (almost 12 cm) and histologic features compatible with a higher than average risk of metastases, there has been no evidence of disease elsewhere in the recipient.

This case presented many unique challenges, highlighting the difficulty of assessing the risk of donor-transmitted malignancies and paragangliomas in particular. Perhaps future decision-making processes involving donors with paragangliomas may be aided by assessing the tumor location and use of a multi-factorial scoring system. The development of rapid intraoperative immunohistochemical staining procedures with the use of SDHB and Ki-67 antibodies would further aid in the assessment of the malignant potential of paragangliomas.

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<http://dx.doi.org/10.1016/j.transproceed.2015.07.012>

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(Note from the Editor: Our attempts to reach Drs. S. Sharma, C. Wray and H. Nourmand for comment have failed. Therefore this letter received from Dr. Sergei Tatishchev is published without response.)