Q&A column, 5/15

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Submit your pathology-related question for reply by appropriate medical consultants. CAP TODAY will make every effort to answer all relevant questions. However, those questions that are not of general interest may not receive a reply. For your question to be considered, you must include your name and address; this information will be omitted if your question is published in CAP TODAY.

Q. I am a pathologist practicing in a small community hospital. I was involved with a patient who was declared brain-dead and subsequently designated a donor of multiple organs. The organ procurement agency ordered additional testing during the two days before the organ harvest, including a CT scan of the chest. The latter revealed a solitary pulmonary nodule.

On the evening of the harvest, I was asked to perform a frozen section assessment of the nodule. I refused initially but finally relented when hospital administration intervened on behalf of the procurement agency. The frozen section revealed a completely necrotic nodule; my differential diagnosis included caseating granuloma and necrotic tumor. Based on my frozen section diagnosis, harvesting was abandoned. The cryostat was decontaminated the next morning. Permanent sections demonstrated coccidioidomycosis.

Pathologists are rarely asked to do frozen sections on nodules to establish a new diagnosis. In most cases, the diagnosis has been established on a previous formalin-fixed biopsy. In a case of a potential explant of organs, even if I am 99.99 percent sure that a nodule is benign and noninfectious by frozen section, there is still a risk for a misdiagnosis, which would be disastrous for all recipients. It would be prudent to defer the frozen section at the time of organ harvesting. Therefore, what is the point of doing a frozen section assessment?

Since there was a two-day window of opportunity, a CT-guided biopsy of the pulmonary nodule could have been performed. This biopsy would have resulted in a definitive diagnosis, circumventing the need for organ harvesting. Is this a reasonable and feasible approach?

A. I agree that an intraoperative or frozen section consult is not the optimal way to diagnose unknown lesions in a potential organ donor. Particularly in a case like this one, with a couple of days available to plan, the most common-sense approach would have been to perform a diagnostic procedure prior to organ procurement to obtain material for a definitive workup. It sounds like in this case, the consulting pathologist handled an unpleasant situation appropriately. I'm not an expert in the clinical decision-making around transplantation, but it is possible that if a diagnosis of a necrotic granuloma due to coccidioidomycosis were obtained pre-transplant, a clinician may even then have approved a transplant from this donor (though not lung, obviously). This opportunity was forfeited due to the need to make a spot decision in the OR without the benefit of a definitive diagnosis. If a kidney or liver were needed, for example, the probability of disseminated coccidioidomycosis would have to be weighed against the urgency of need for a replacement kidney in the recipient.

This is not a decision a pathologist can or should make alone at night in the frozen section room. If the questioner works in a facility that regularly serves as an organ procurement organization site, it would be prudent for a multispecialty group within the institution to implement decision trees to plan for such issues. The group should include pathologists, oncologists, organ transplant clinicians (surgical and medical), and infectious disease specialists, since positive cultures from a donor may develop long after a completed transplant procedure. With the increasing incidence of organ and tissue transplantation, such situations will arise more frequently. The incidence of unexpected or previously undiagnosed malignancy at autopsy, in a forensic pathology practice setting, was

found to be seven percent in a 2009 U.S. study.1

All that aside, the risk of malignancy transferring from a donor organ to a recipient is extremely low; recent studies derive from our British colleagues. An incidence of transmitted cancers was estimated at 0.06 percent in a 2014 guideline published by the Advisory Committee on the Safety of Blood, Tissues and Organs (SaBTO).2 This guideline is helpful as it stratifies tumors from low risk (subcentimeter thyroid papillary carcinomas) to high risk (stage IV carcinomas). Another useful and recent reference is from the British Journal of Surgery.3 Both references emphasize that the risk of cancer transmission, however low, can never be zero, and any procedure has to be balanced against the risk of deferring transplant in a patient whose organ is failing. And the potential recipient must, of course, be counseled in the risks and be involved in the decision.

Not surprisingly, organ transplant recipients have an elevated risk for subsequently developing many malignancies post-transplant, including non-Hodgkin lymphoma and infection-related malignancies such as anal or other HPV-related tumors and Kaposi sarcoma. These are likely due to immunosuppression, but other factors may be involved. Recipients of liver, kidney, and lung transplants seem to have the most elevated risk for malignancies.4 Again, the relative risk of not performing a transplant and potential years gained must be weighed against performing a transplant from a patient with malignancy or a potentially infectious process.

There is probably never going to be an easy yes or no answer to this question. Each incidence will occur amid a unique set of variables, and the careful clinical judgment of many experts will be needed to assess the proper steps, in conjunction with the patient's wishes.

1. Sens MA, Zhou X, Weiland T, Cooley AM. Unexpected neoplasia in autopsies: potential implications for tissue and organ safety. *Arch Pathol Lab Med.* 2009;133(12):1923–1931.
2. Advisory Committee on the Safety of Blood, Tissues and Organs. Transplantation of organs from deceased donors with cancer or a history of cancer. http://odt.nhs.uk/pdf/transplantation_of_organs_from_deceased_donors_with_cancer_or_a_history_of_cancer.pdf. Published April 22, 2014. Accessed Aug. 1, 2014.
3. Dutkowski P, Clavien PA. Solutions to shortage of liver grafts for transplantation. *Br J Surg.* 2014;101(7):739–741.
4. Engels EA, Pfeiffer RM, Fraumeni JF Jr, et al. Spectrum of cancer risk among US solid organ transplant recipients. *JAMA.* 2011;306(17):1891–1901.

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