

BRIEF ARTICLE

Preventing Death Through the Gift of Life: A Case of Cryptococcosis and the Critical Role of Dermatology Consultation in Organ Donation Related Infection

Kaylin Beiter, MD, PhD¹, Kathyana P. Santiago Mangual, BA², Travis Benson, MD¹, Sweta Subhadarshani, MBBS, MD, MRCP(SCE)¹

¹ Department of Dermatology, University of Pennsylvania, Philadelphia, Pennsylvania, USA

² David Geffen School of Medicine, University of California Los Angeles, Los Angeles, California, USA

ABSTRACT

Background: Primary cutaneous cryptococcosis is rare, and cutaneous lesions are most often due to disseminated disease. Cryptococcosis primarily affects immunosuppressed patients, such as organ transplant recipients.

Case: The dermatology inpatient service was consulted for an immunosuppressed, subsequently deceased patient who was being evaluated for potential organ donor status. The patient had a history of liver transplantation and had initially presented to an outside hospital with incidental hyponatremia of unknown etiology and a pulmonary nodule of unknown significance. Her outside hospital course was complicated by loss of consciousness necessitating intubation and eventual brain death. She was transferred to our hospital for organ donation evaluation. The transplant team consulted dermatology with concern for varicella. Clinical evaluation demonstrated numerous indurated flesh-colored papules without significant epidermal change. Biopsy ultimately showed cryptococcosis.

Conclusion: Cryptococcosis among solid organ transplant patients most often presents as extrapulmonary or disseminated disease, with a spectrum of cutaneous manifestations including cellulitis, papules, nodules, or ulcerative lesions. In this case, the patient most likely passed from disseminated disease (explaining her pulmonary nodule and hyponatremia). In consultation and biopsy, the inpatient dermatology team not only helped provide closure for the bereaved family, but also identified and halted a potentially dangerous transplant that would have otherwise put multiple organ recipients at risk for disseminated cryptococcal infection.

INTRODUCTION

Cryptococcosis is a human disease due to *Cryptococcus*, an encapsulated yeast found in woods, soil, pigeons (*C neoformans*) and eucalyptus trees/forests (*C gatti*).¹ Inhalation leads to pulmonary infection with subsequent systemic dissemination.¹

Primary cutaneous cryptococcosis is rare, and cutaneous lesions are most often due to disseminated disease.^{1,2} *C neoformans* primarily affects immunosuppressed patients, with tacrolimus-treated solid organ transplant recipients being especially susceptible to skin, soft tissue, and osteoarticular manifestations.¹

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The United States has seen an increase in both the total number of organ donations and the waitlist for transplant recipients over the past 20 years.³ However, not all transplants go well: donor-derived fungal infections constitute a rare yet severe complication.⁴ Donors who are themselves immunosuppressed prior to death are still considered for organ explantation. In such cases, these chronically immunosuppressed donors may unknowingly host pathogens that can be transmitted to organ recipients during the transplant process. Given that organ recipients are iatrogenically immunosuppressed (to prevent organ rejection), such cases constitute a high risk for inadvertent transmission of opportunistic infections.

We present the case of an immunosuppressed, subsequently deceased patient who was a potential organ donor but was found to have cutaneous cryptococcosis.

CASE REPORT

The inpatient dermatology team was consulted for evaluation of suspected varicella infection in a brain-dead organ donor patient. The woman was in her early 50s and had a prior medical history of liver transplantation for alcoholic cirrhosis, on immunosuppressive therapy (mycophenolate, tacrolimus, and prednisone), insulin-dependent diabetes mellitus, shingles, hypertension, dilated pancreatic duct, and a recently identified 2.2 cm mass in her right upper lung lobe. She initially presented to an outside hospital for evaluation of acute back pain and was admitted for incidental hyponatremia (sodium of 121) of unknown etiology. Unfortunately, she quickly progressed (nadir sodium of 114), exhibiting multiple episodes of loss of consciousness, eventually requiring

intubation. She was stabilized and extubated briefly; however, she was then found unresponsive again with agonal respirations. Despite re-intubation, additional testing yielded severe cerebral dysfunction and anoxic brain injury on imaging. Brain death was confirmed with a nuclear medicine blood flow scan and physical examination. Following identification of brain death, the family elected for organ donation, for which the patient was transferred to our hospital.

Upon transfer, the primary transplant team noted multiple linearly arranged papules on the patient's leg, and dermatology was consulted for evaluation with a suspicion for varicella/shingles. Physical exam revealed involvement of left anteromedial leg and thigh with numerous indurated flesh-colored papules and nodules without significant scaling, crusting, or surrounding erythema (**Figure 1**). The lesions were not confined to a single dermatome (rather, spanned L2-L4) and were oriented length-wise along the patient's anterior thigh. Our differential at the time of evaluation included infectious etiology as well as cutaneous metastases, given the patient's history of immunosuppression, known pulmonary nodule of unknown significance, and lack of exact cause of death.

Multiple lesions were biopsied for pathology, tissue culture, and fresh frozen evaluation. Initial assessment of the fresh frozen sample by the on-call surgical pathologist demonstrated numerous yeast forms and a decision was made to cancel the transplant process. Further review of the permanent pathology section led to a final diagnosis of cutaneous cryptococcosis upon examination of the Hematoxylin and Eosin, Mucicarmine, and Grocott stains (**Figure 2**). In all of these stains, the round yeast forms can be appreciated; the Mucicarmine and Grocott stains confirm the diagnosis via highlighting

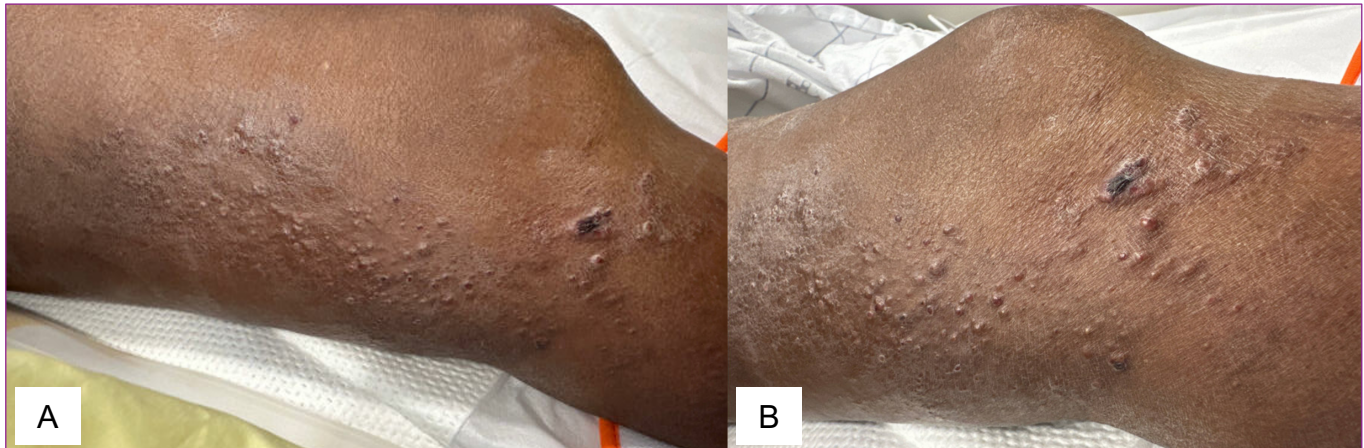


Figure 1. (A) View of the left medial leg demonstrates extensive burden of disease including indurated, flesh-colored papules. The relative cephalon-caudal distribution across multiple dermatomes can be appreciated. (B) A closer view of the left medial leg reveals that the lesions are not truly umbilicated but do demonstrate occasional superficial crusting.

the mucopolysaccharide-rich capsule and polysaccharide fungal cell wall, respectively.

DISCUSSION

Cryptococcosis among solid organ transplant patients most often presents as extrapulmonary or disseminated disease, with a spectrum of cutaneous manifestations including cellulitis, papules, nodules, or ulcerative lesions.²

When organ donation is planned using deceased donors, rapid infectious testing becomes critical to mitigate transmission risk.⁵ In particular, samples should be assessed via fresh frozen processing to streamline workup for the advancement of the organ transplant process. While fresh frozen sampling cannot always provide definitive diagnosis (e.g., for melanocytic lesions), it is a standard of care that should be attempted on the day of consultation so as to avoid delays in organ explantation. In addition, evaluation of biopsy specimens should be performed in consensus with a trained dermatopathologist, given that misdiagnosis portends differences in risk

stratification by the transplant team and informed consent discussions with organ recipients. In this case, the inpatient dermatology team, in collaboration with the surgical and dermatopathology services, identified and halted a potentially dangerous transplant that would have otherwise put multiple organ recipients at risk for disseminated cryptococcal infection.

Prior to biopsy, no definitive cause of death had been identified for the patient. While there is no official recommendation for routine screening for cryptococcosis among organ donors,^{2,5} cryptococcosis should be suspected in cases of immunosuppression (including non-HIV infected hosts), pulmonary nodules of unexplained significance, and meningoencephalitis of unclear etiology.⁶ We suspect that the patient's altered mental status, hyponatremia and pulmonary nodule could all be explained by disseminated cryptococcosis with central nervous system (CNS) involvement. The hyponatremia likely resulted from syndrome of inappropriate antidiuretic hormone (SIADH), which has been previously reported as a diagnostic sign of coccidioidomycosis infection of the CNS.⁷ The risk of

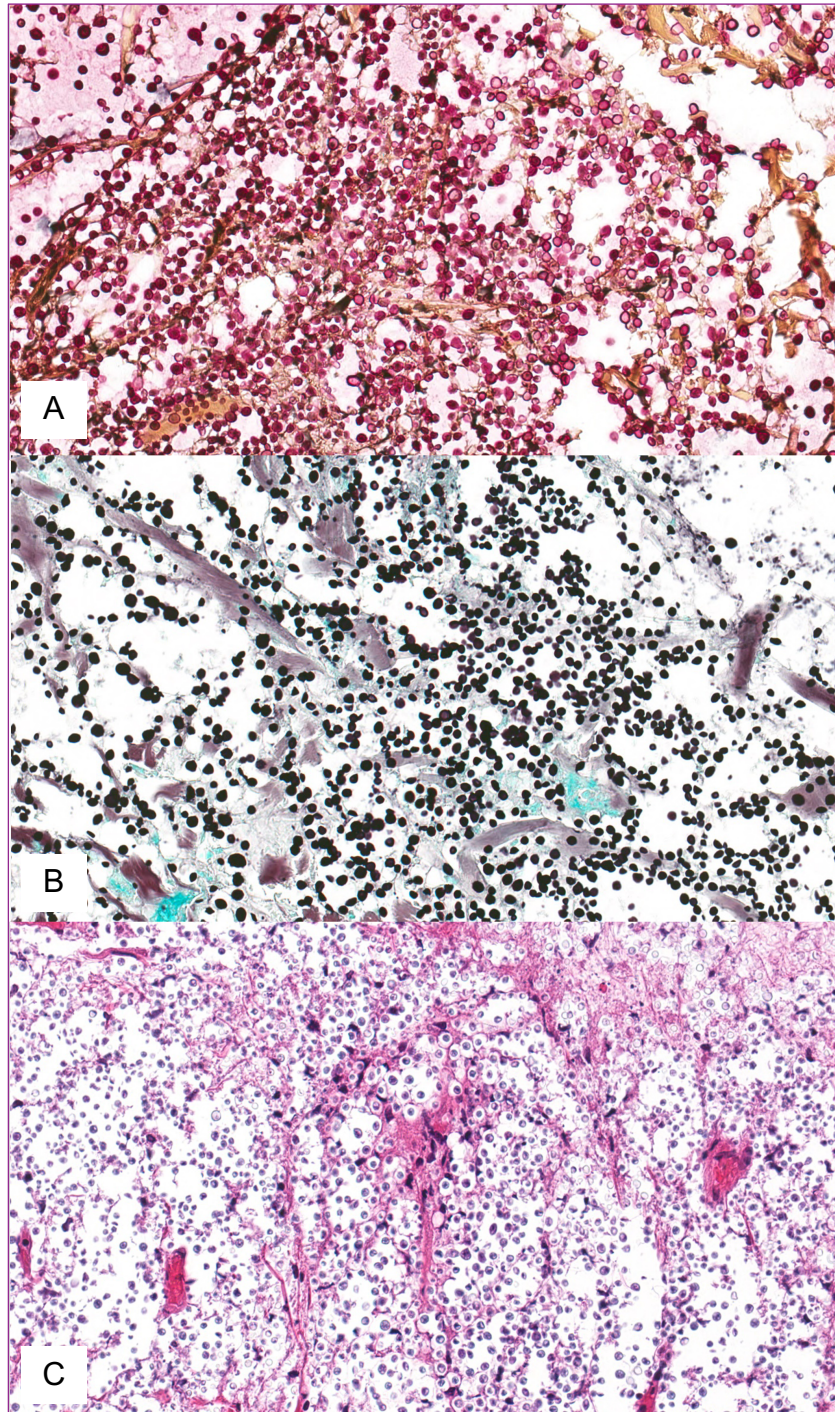


Figure 2. (A) Mucicarmine stain at 40x magnification. Mucicarmine is particularly useful in demonstrating the mucopolysaccharide-rich capsule of *Cryptococcus*. The capsule can be appreciated with this stain as a bright red to pink coloration. (B) Grocott stain at 40x magnification. This stain targets the fungal cell wall polysaccharides, and thus demonstrates the round yeast-like fungal organisms with black coloration against the green background. (C) Standard H&E at 40x. Use of hematoxylin and eosin is standard in assessing fresh frozen specimens. The cryptococcal yeast forms are seen as round bodies against the pink-stained stroma.

cryptococcosis from transplantation of organs from an untreated cryptococcal-infected host is very high (greater than 40% in cases of *C neoformans* and up to 70% for *C gatti*), and transplant is only recommended if the risk of death among the organ recipient outweighs infectious risk.^{4,6}

In general, the most common dermatologic abnormalities precluding transplant identified during physical exam of deceased organ donors include injection marks concerning for substance use and suspected malignancy (most commonly melanoma, abnormal lymph nodes, or breast lesions).⁸ Infectious etiologies can be similarly catastrophic (including fungal as above, bacterial, and varicella), though are not always absolute contraindications if appropriate treatment is rendered prior to transplantation.⁹

Dermatologists should be included in the organ donation process for both living and deceased donors prior to organ donation, as their expertise is critical in identifying potential contraindications to donation.⁸ Inter-departmental collaboration and referrals are essential and should be prioritized given the ease and minimal risk of performing skin examinations relative to the risks of transplantation of malignant or infected tissues for living donors. By examining the skin of deceased organ donors, dermatologists have the unique opportunity to help protect and save the living.

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Corresponding Author:

Subhadarshani, MBBS, MD, MRCP(SCE)
3400 Civic Center Blvd, Philadelphia, PA 19104
Phone: 215-662-2737
Email: shweta.aiims07@gmail.com

1. Maziarz EK, Perfect JR. Cryptococcosis. *Inf Dis Clin of North America*. 2016;30(1): 179-206. doi:10.1016/j.idc.2015.10.006
2. Baddley JW, Forrest GN, AST Infectious Diseases Community of Practice. *Clin Transplant*. 2019;33(9): e13543. doi:10.1111/ctr.13543
3. Spardy J, Concepcion J, Yeager M, Andrade R, Braun H, Elkbuli A. National Analysis of Recent Trends in Organ Donation and Transplantation in the United States: Toward Optimizing Care Delivery and Patient Outcomes. *Am Surg*. 2023;89(12):5201-5209. doi:10.1177/00031348221135776
4. Elhaj Mahmoud D, Hérivaux A, Morio F, et al. The epidemiology of invasive fungal infections in transplant recipients. *Biomed J*. 2024;47(3):100719. doi:10.1016/j.bj.2024.100719
5. Fischer SA, Avery RK; AST Infectious Disease Community of Practice. Screening of donor and recipient prior to solid organ transplantation. *Am J Transplant*. 2009;9 Suppl 4(Suppl 4):S7-S18. doi:10.1111/j.1600-6143.2009.02888.x
6. Singh N, Huprikar S, Burdette SD, et al. Donor-Derived Fungal Infections in Organ Transplant Recipients: Guidelines of the American Society of Transplantation, Infectious Diseases Community of Practice. *Am J Transplant*. 2012;12(9): 2414-2428. doi:10.1111/j.1600-6143.2012.04100
7. Branigan GL, Ozgur HT, Lim J, Riaz T. Syndrome of inappropriate antidiuretic hormone release secondary to central nervous system coccidioidomycosis with vasculitis. *BMJ Case Rep*. 2024;17(3):e258915. Published 2024 Mar 29. doi:10.1136/bcr-2023-258915
8. Chandrasekar A, Lomas R, Sánchez-Ibáñez J, et al. Physical Examination of Potential Deceased Organ and Tissue Donors: An Overview of the European Landscape. *Transpl Int*. 2023;36:11394. Published 2023 Jul 21. doi:10.3389/ti.2023.11394
9. Vinson AJ, Chauhan P, Daley C, et al. Successful Use of Kidneys from a Deceased Donor with Active Herpes Zoster Infection. *Case Rep Transplant*. 2021;2021:7719041. Published 2021 Aug 16. doi:10.1155/2021/7719041

References: