Disseminated cutaneous coccidioidomycosis in a liver transplant patient

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INTRODUCTION

The increasing incidence of allogeneic transplants in *Coccidioides*-endemic areas such as the southwestern United States and Latin America highlights the importance of considering reactivation of donor coccidioidomycosis in transplant recipients. We report the case of a 42-year-old Nicaraguan woman who had multiple firm, violaceous subcutaneous nodules 1 month after her orthotopic liver transplant. Histopathology of a biopsy specimen, immunodiffusion assay, and donor serologic testing results were consistent with disseminated cutaneous coccidioidomycosis secondary to donor reactivation. Screening of donors in *Coccidioides*-endemic areas with serology, organ culture, and chest radiography should be considered before transplantation. Recipients in endemic areas may benefit from prophylactic antifungal therapy.

CASE REPORT

A 42-year-old Nicaraguan woman presented 3 months after orthotopic liver transplant secondary to autoimmune hepatitis with 2 months of headache, fever, and multiple firm, violaceous, subcutaneous nodules on the back, right buttock, and extremities (Fig 1). Lesions were tender and warm to palpation but lacked erythema, pallor, or fluctuance. Lymphadenopathy was not appreciated on physical examination. Her medications included tacrolimus.

Chest computed tomography found multiple pulmonary nodules; wedge biopsy of lung found a fibrocaseocalcific granuloma with Grocott's methenamine silver stain showing 4-μm budding oval yeast, suggestive of *Coccidioides* endospores. Liver biopsy findings were consistent with peliosis hepatitis. Results of HIV serology, Mantoux test, and hepatitis markers were negative. A biopsy of the left upper arm nodule found scattered round, thick-walled spores with granular cytoplasm, massive pseudoepitheliomatous hyperplasia, and granulomatous dermal inflammation on histopathology (Fig 2). Direct microscopy found spherules containing endospores dispersed in the dermis with surrounding infiltrate rich in chronic inflammatory cells, neutrophils, and granulomatous inflammation, consistent with coccidioidomycosis (Fig 3). Culture on Sabouraud's dextrose agar showed suedelike, greyish growth.

Histologic findings were corroborated by IgM^+-modified immunodiffusion. The donor tested positive for IgG *Coccidioides* antibody despite remaining symptom free, indicating latent infection and introducing the possibility that this patient was afflicted by reactivated donor-derived *Coccidioides*. The patient's lesions resolved completely with 500 mg voriconazole twice daily for 3 months, after initially not responding to 4 months of 800 mg of daily fluconazole.

DISCUSSION

Differential diagnoses include erythema nodosum, lipomas, cutaneous lymphoma, pseudolymphoma, and disseminated coccidioidomycosis. Additional infectious causes should be considered in a transplant patient with eruptive subcutaneous nodules, such as histoplasmosis, cryptococcosis, paracoccidioidomycosis, and leishmaniasis.

The diagnosis of donor coccidioidomycosis in this case highlights the importance of considering reactivation in posttransplant care, as there is an emerging incidence of allogeneic transplants in *Coccidioides*-endemic areas such as the southwestern United States and Latin America. There are few reported cases of donor-derived coccidioidomycosis outside of the dermatology literature.[1-6] Fewer than 5% of donors

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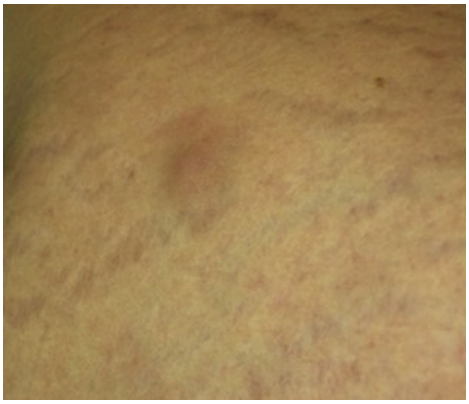

Fig 1. Cutaneous coccidioidomycosis. One of multiple firm, violaceous subcutaneous nodules.

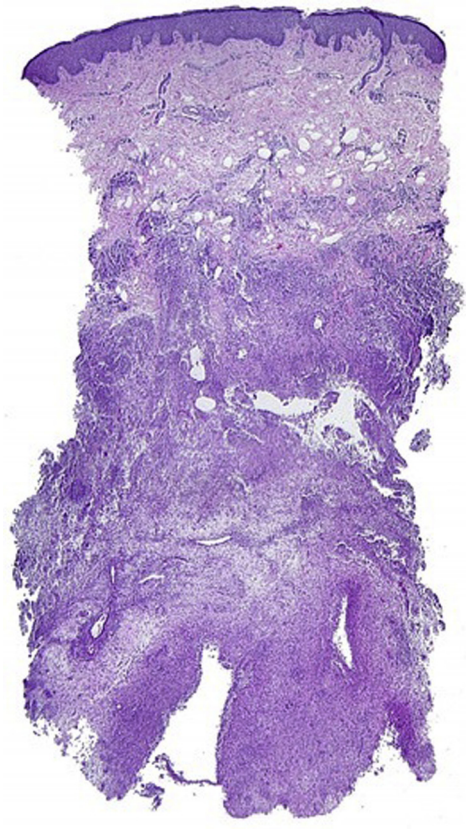

Fig 2. Cutaneous coccidioidomycosis. Massive pseudoepitheliomatous hyperplasia and granulomatous dermal inflammation. Careful searching at high power is often needed to find the spherules, which are 100 μm in diameter. (Hematoxylin-eosin stain.)

in endemic areas have active coccidioidomycosis infection, and 70% of those with active infection have a reactivation of the disease instead of a primary infection.[7] Infection risk is amplified by posttransplant immunosuppressant therapy, and risk is greatest within the first posttransplant year, as 70% of

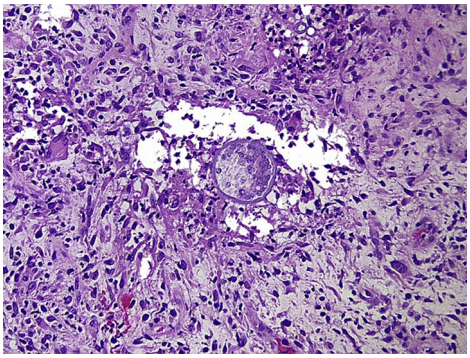

Fig 3. Cutaneous coccidioidomycosis: Spherule containing endospores, with surrounding infiltrate rich in chronic inflammatory cells, neutrophils, and granulomatous inflammation. (Hematoxylin-eosin stain.)

disseminated coccidioidomycosis cases occur during this time.[8] Donors in endemic areas should be screened with serology, organ cultures, and chest radiography. Cases of *Coccidioides* transmission, despite such precautionary measures, have been reported[9]; prophylactic antifungal therapy is, therefore, recommended for patients undergoing transplant in *Coccidioides*-endemic areas.

Choices for initial treatment include fluconazole, itraconazole, voriconazole, and posaconazole.[10] Our patient was treated with voriconazole after not responding to a fluconazole trial.

REFERENCES

1. Tripathy U, Yung GL, Kreitt JM, Thistlethwaite PA, Kapelanski DP, Jamieson SW. Donor transfer of pulmonary coccidioidomycosis in lung transplantation. *Ann Thorac Surg*. 2002;73:306-308.
2. Wright PW, Pappagianis D, Wilson M, et al. Donor- related coccidioidomycosis in organ transplant recipients. *Clin Infect Dis*. 2003;37:1265-1269.
3. Miller MB, Hendren R, Gilligan PH. Posttransplantation disseminated coccidioidomycosis acquired from donor lungs. *J Clin Microbiol*. 2004;42:2347-2349.
4. Brugiere O, Forget E, Biondi G, et al. Coccidioidomycosis in a lung transplant recipient acquired from a donor graft in France. *Transplantation*. 2009;88:1319-1320.
5. Blodget E, Geiseler PJ, Larsen RA, Stapfer M, Qazi Y, Petrovic LM. Donor-derived *Coccidioides immitis* fungemia in solid organ transplant recipients. *Transpl Infect Dis*. 2012;14:305-310.
6. Dierberg KL, Marr KA, Subramanian A, et al. Donor- derived organ transplant transmission of coccidioidomycosis. *Transpl Infect Dis*. 2012;14:300-304.
7. Braddy CM, Heilman RL, Blair JE. Coccidioidomycosis after renal transplantation in an endemic area. *Am J Transplant*. 2006;6:340-345.
8. Blair JE, Logan JL. Coccidioidomycosis in solid organ transplantation. *Clin Infect Dis*. 2001;33:1536-1544.
9. Keckich DW, Blair JE, Vikram HR, Seville MT, Kusne S. Reactivation of coccidioidomycosis despite antifungal prophylaxis in solid organ transplant recipients. *Transplantation*. 2011;92:88-93.
10. Blair JE. Approach to the solid organ transplant patient with latent infection and disease caused by *Coccidioides* species. *Curr Opin Infect Dis*. 2008;21:415-420.