Clinical Infectious Diseases

PHOTO QUIZ

Anthony Amoroso and Ajit P. Limaye, Section Editors

Disseminated Skin Lesions After Allogeneic Hematopietic Stem Cell Transplantation

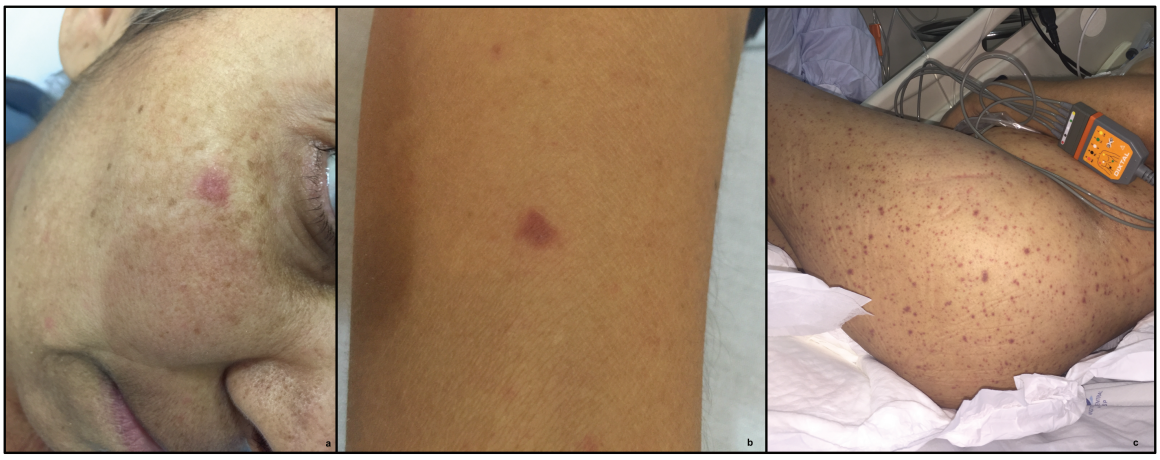

Figure 1. *A, B,* First skin lesions on the patient's face and arm on day 5 after transplantation. *C,* Disseminated skin lesions on day 10.

A 40-year-old woman with a history of chronic myeloid leukemia, which progressed to acute myeloid leukemia in August 2015, underwent allogeneic hematopietic stem cell transplantation (in April 2016) from an unrelated donor after conditioning with busulphan and fludarabine. On day 1 after transplantation a fever developed, followed by skin lesions with a diffuse erythematous maculopapular rash on day 5 (Figure 1). Skin biopsy was performed. Blood cultures were negative, but fever persisted despite treatment with broad-spectrum antibiotics (meropenem, vancomycin, polymyxin, voriconazole and Lipossomal amphotericin). Even with intensive treatment, the patient died on day 12, owing to septic shock followed by multiorgan failure.

What is your diagnosis?

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ANSWER TO THE PHOTO QUIZ

Anthony Amoroso and Ajit P. Limaye, Section Editors

Disseminated Skin Lesions After Allogeneic Hematopietic Stem Cell Transplantation

Diagnosis: Disseminated cutaneous toxoplasmosis.

Before transplantation, the patient was found to have a positive serum immunoglobulin (Ig) G titer for *Toxoplasma gondii*, whereas the donor was IgG negative. Postmortem skin biopsy showed *T. gondii* bradyzoites (Figure 2). Results of serum and tissue *T. gondii* reverse-transcription polymerase chain reaction (PCR) were positive, with parasite counts of 10^3/mL and 10^2/mL, respectively.

Compared with men in the United States, the seroprevalence of *T. gondii* was 4 times higher (56% vs 13%) among men in Brazil, and antibody titers were also higher in magnitude [1]. The ingestion of oocysts from the environment and the consumption of meat infected with tissue cysts are the 2 most common routes of transmission for *T. gondii.* The environment in many areas in Brazil is highly contaminated by oocysts. Based on a population of 12 million cats, a seropositivity of 25%–50%, and shedding of 1 million oocysts per cat, there could be large numbers of oocysts in the environment in Brazil [2–4]. Brazilian epidemiological surveys, especially in preteen children, indicate that the environment is highly contaminated with oocysts, especially in lower socioeconomic communities and among pregnant women, persons with a lower level of education, older persons, those who handle soil, and those in contact with cats [1–5].

The risk of *Toxoplasma* reactivation among persons undergoing hematopietic stem cell transplantation (HSCT) varies by regional seroprevalence. The incidence ranges from 0.4% to 8.7% of seropositive recipients, 0.3% in the United States, 5% in France and 5.9% in Brazil [6–8].

The mortality rate among *T. gondii*–seropositive allogeneic transplant recipients is high (60%–90%) [8–11]. Most cases, however, are diagnosed only at autopsy, because histological evidence of invasive toxoplasmosis of the central nervous system (CNS) or other sites is rarely obtained before death. Bleggi-Torres et al [12] evaluated neuropathological complications in180 patients studied by autopsy after HSCT (allogeneic in 177, autologous in 3) and they found that CNS infections were documented in 27 patients (15%) and constituted the second most common cause of lesions. Toxoplasmosis was observed in 8 patients and was significantly more frequent in those who died of CNS causes [12].

Diagnosing toxoplasmosis in patients HSCT recipients is a challenge, because clinical features are nonspecific. In setting with focal CNS lesion, with a ring enhancement, the imaging can support a presumptive diagnosis, but in subjects with diffuse encephalitis, the lesions are nonfocal and nonspecific. Several case reports and case

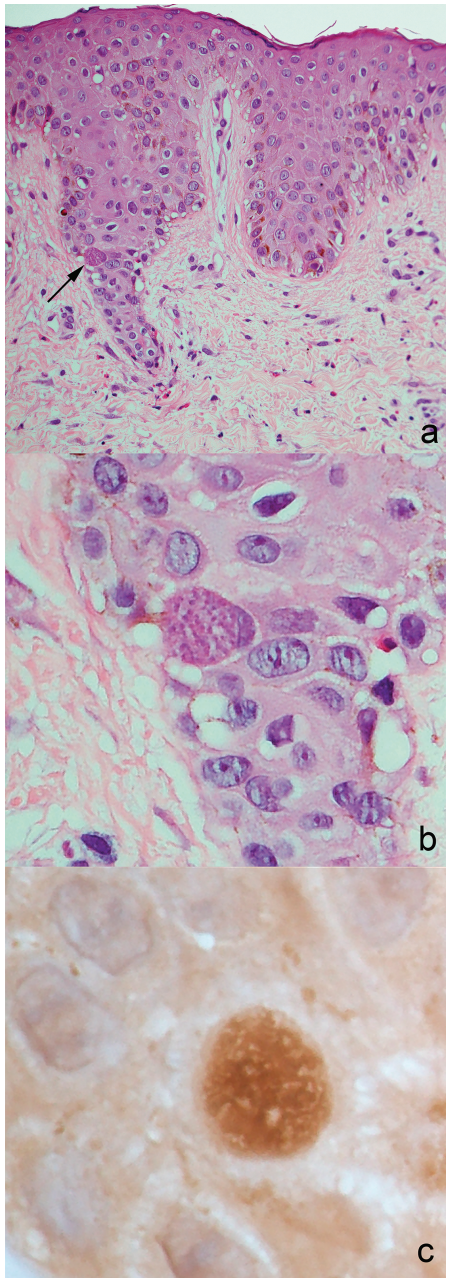

Figure 2. *A,* Histological examination of the skin showed many *Toxoplasma gondii* pseudocysts at the epidermis (*arrow*) and dermis (hematoxylin-eosin stain, original magnification ×20). *B,* Detail of the pseudocyst containing the bradyzoites of *T. gondii* with high magnification (hematoxylin-eosin stain, original magnification ×40). *C,* Photomicrography shows the immunohistochemical reaction with specific polyclonal antibody against *T. gondii.* (diaminobenzidine stain, original magnification ×100 oil-immersion objective).

series have suggested that the finding of *T. gondii* DNA in peripheral blood with PCR might help in diagnosis or, to enable early diagnosis before the disseminated stage, serum *T. gondii* PCR could be useful as a possible blood-based test for preemptive therapy [11, 13].

Toxoplasmosis cases observed at our HSCT center were difficult to diagnose and were confirmed only by pathological analysis (at cerebral biopsy or autopsy). We are now using real-time PCR as a screening test in high-risk (IgG-positive recipients), and positive results are interpreted based on clinical signs. The reactivation of toxoplasmosis is a rare but life-threatening complication that can occur after stem cell transplantation, and a high index of suspicion is needed in order to perform appropriate diagnostic tests and start therapy as soon as possible. Our main targets are patients with positive serum IgG titers and those receiving myeloablative conditioning.

The serological status of the donor must also be tested, because disseminated toxoplasmosis has occurred in seronegative recipients of bone marrow transplants from seropositive donors, even with autologous transplantation. Another controversial issue is the dosage of prophylaxis among these patients. In our institution, we start double-strength tablets daily for 6 months in recipients of allogeneic and 3 months in recipients of autologous transplantation.

Notes

Acknowledgments. We thank Dr Mirian Nacagami Sotto for the help in histological diagnosis.

Potential conflicts of interest. All authors: No reported conflicts of interest. The authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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Clinical Infectious Diseases® 2018;67(4):639–41

DOI: 10.1093/cid/ciy080