Multisystem Febrile Illness in a Cord-Blood Transplant Recipient
(See pages 716–717 for the Photo Quiz.)

Figure 1. Bone marrow smear showing *Toxoplasma gondii* tachyzoites (arrows).

Diagnosis: Acute disseminated toxoplasmosis in a cord-blood transplant recipient.

Figure 1 shows *Toxoplasma gondii* tachyzoites, whereas Figure 2 portrays a cystic form within a macrophage. *T. gondii* was confirmed by polymerase chain reaction detection in bone marrow and blood specimens. *T. gondii* is an intracellular parasite with a worldwide distribution. Seroprevalence is usually reported to be ~15% in the United States but >50% in southern Europe. Recipients of allogeneic hematopoietic stem cell transplants (HCTs) are profoundly immunocompromised and represent a patient population at risk for severe infection. However, toxoplasmosis following HCT is infrequently reported and is usually caused by reactivation of latent infection in seropositive patients. The overall incidence of reactivation in allogeneic HCT is 1% [1–3]. Reactivation toxoplasmosis typically occurs in the second to third month after receipt of the transplant, and patients usually have an AIDS-like presentation with central nervous system lesions [2]. In contrast, seronegative recipients usually develop acute primary infection. Acute infection in this population generally results from the allograft itself (from a seropositive donor) or the direct infusion of contaminated blood or blood products (survival of organisms in stored citrated blood has been documented for up to 2 months). Acute toxoplasmosis presents in the immediate period after engraftment (3 weeks to 3 months) and is of greater severity than reactivation disease. The clinical picture is often one of disseminated disease, as demonstrated by multisystem organ failure, isolation of the organism from numerous body sites (brain, liver, lungs, bone marrow, heart, spleen, omentum, and intestines), and widespread involvement at autopsy [3, 4]. Definite diagnosis is made by pathologic examination of an infected organ; however, molecular diagnosis by detection of *T. gondii* DNA in blood is possible, because parasitemia is common in the compromised host [5, 6]. Effective therapy consists of the combination of pyrimethamine plus sulfadiazine or pyrimethamine plus clindamycin [7].

In HCT, trimethoprim-sulfamethoxazole is usually used for *Pneumocystis carinii* pneumonia prophylaxis, and this combination also offers protection against *T. gondii*. However, in cord-blood HCT, myelosuppressive drugs, such as trimetho-
prim-sulfamethoxazole, are preferably avoided, because this type of transplantation is associated with delayed engraftment. Although toxoplasmosis appears to be rare after HCT, specific chemoprophylaxis for cord-blood transplant recipients can be obtained with atovaquone.

Disseminated forms of toxoplasmosis are frequently unrecognized, as evidenced by a number of studies in which the diagnosis was often made postmortem [2–4]. This is probably because the disease presentation is often nonspecific and mimics other causes of fever that are much more common after allogeneic HCT, such as acute graft-versus-host disease (GVHD). Our patient was ultimately proved to have disseminated toxoplasmosis. The type of transplantation predisposed to a fulminant clinical course, because cord-blood HCT is associated with prolonged and severe impairment of cellular immunity. Whether the appearance of fever and rash on day 39 represented a sign of toxoplasmosis or of GVHD is uncertain.

Skin biopsy specimens are widely used in the diagnosis of GVHD. However, it should be emphasized that skin pathology is not pathognomonic. The administration of methylprednisolone for presumed GVHD in our case doubtless contributed to a widely disseminated high-grade infection.

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Konstantinos Liapis, Ioannis Baltadakis, Konstantinos Balotis, and Dimitrios Karakasis

Department of Hematology, Bone Marrow Transplantation Unit, Evangelismos Hospital, Athens, Greece

References


Reprints or correspondence: Dr Konstantinos Liapis, Dept of Hematology, Bone Marrow Transplantation Unit, Evangelismos Hospital, 45-47 Ippilandou St, Athens, 10676, Greece (koliapis@hotmail.com).

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