Fever, Shock, and Pancytopenia in a Patient Treated with Alemtuzumab
(See page 1540 for the Photo Quiz.)

Figure 1. May-Grünewald-Giemsa staining (original magnification, ×1000) of the patient’s bone marrow aspirate (left panel), showing unstained oblong shapes (white arrows) in the cytoplasm of several macrophages, and Ziehl-Neelsen staining of the same area (right panel), revealing the unstained objects to be acid-fast bacilli (black arrows).

Diagnosis: hemophagocytic syndrome due to disseminated tuberculosis.

May-Grünewald-Giemsa staining of the bone marrow aspirate revealed a predominance of macrophages with occasional hemophagocytosis and ≤1% lymphocytes. Moreover, unstained oblong shapes were seen in the cytoplasm of macrophages infiltrating the bone marrow. Counterstaining of the bone marrow aspirate by Ziehl-Neelsen staining revealed these shapes to be acid-fast bacilli (figure 1.) Culture of the bone marrow aspirate for mycobacteria showed growth of *Mycobacterium tuberculosis* that was susceptible to all first-line tuberculostatics.

*Mycobacteria* cannot be demonstrated directly with Gram or May-Grünewald-Giemsa staining, because the lipid-rich cell wall of mycobacteria prevents penetration of the dyes. However, mycobacteria may be visible as so-called ghosts, or defects in these stains [1].

Our case fulfilled the criteria for hemophagocytic syndrome, also called macrophage activation syndrome or hemophagocytic lymphohistiocytosis, as defined by the Histiocyte Society [2]. In particular, our patient had an extremely elevated serum ferritin level (247,008 μg/L; normal range, 10–150 μg/L), which is one of these criteria. Secondary forms of hemophagocytic syndrome can be caused by infection [3]. An inability of the host’s immune system to deal with an invading pathogen is thought to lead to an uncontrolled immune response that causes proliferation and tissue invasion by activated macrophages.

A fulminant course of disseminated tuberculosis without evidence of massive tuberculosis, frequently accompanied by pancytopenia, has been described [4]. This syndrome predominantly occurs in immunocompromised patients and is sometimes called Landouzy septicemia, after the author of the first description [5]. One could question whether tuberculosis-associated hemophagocytic syndrome is an entity essentially different from Landouzy septicemia. In Landouzy septicemia, absence of granuloma formation has also been described, but the classical histological picture consists of necrosis without inflammatory reaction [6], instead of massive infiltration with macrophages.

Our case illustrates that disseminated tuberculosis should be part of the differential diagnosis of fever and pancytopenia, even when there are no pulmonary abnormalities and the pa-
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References


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