To the Editor:

We read with interest the article in CHEST (October 2011) by Raschke and Garcia-Orr, reporting three cases of hemophagocytic lymphohistiocytosis (HLH) in patients in ICUs and reviewing the relationship between HLH and septic shock. HLH is a rare but potentially life-threatening disorder that results from natural killer and cytotoxic T-cell dysregulation leading to cytokine overproduction and hemophagocytosis. Severe HLH is responsible for multiple organ failure (MOF) mimicking septic shock and requiring admission to the ICU. Also, pictures of hemophagocytosis are encountered in ≤4% of patients with septic shock. Indeed, HLH and sepsis may share common features and overlap, but we believe these disorders must be differentiated. HLH in adults is a syndrome resulting from cytokine-driven macrophage activation secondary to various triggers (infections, malignancies, or autoimmune diseases) in patients with preexisting immune deficiencies. It requires a specific treatment based on corticosteroids, etoposide, and the treatment of the underlying cause. Therefore, it is essential that intensivists promptly recognize HLH in patients admitted to the ICU with MOF. As reported in the article by Raschke and Garcia-Orr, the differential diagnosis between HLH and septic shock was challenging because these conditions may not be fully and early discriminated by the HLH-2004 diagnostic criteria. However, we have a slightly different experience at a teaching hospital specifically dedicated to the treatment of patients with malignant diseases.

We report the clinical course of nine patients (seven men and two women), mean age 49 years (range, 43-54), admitted to our ICU with HLH. The study was conducted after approval by the appropriate institutional review board. All patients needed vasopressor support, and all were believed to have septic shock. They received broad-spectrum empirical antibiotics, but none of them had clinically or microbiologically documented infection. The disease evolution was marked by the development of MOF: All patients but one (89%) received mechanical ventilation, and all had at least three organ dysfunctions. The median simplified acute physiologic score II was 63 (range, 56-73).

In the patients, the mean number of the HLH-2004 criteria was 6 (range, 5-6), the mean body temperature was 38.5°C (range 38.3°C-40°C), eight patients (86%) had spleen enlargement, the mean hemoglobin count was 7.7 g/L (range, 7.3-8.6 g/L), the mean platelet count was 27 × 10^9/L (range, 26-29), the mean WBC count was 4.4 × 10^9/L (range, 3.3-7.8), the mean triglyceridemia level was 2.6 mmol/L (range, 1.9-3.5 mmol/L), and the mean ferritidemia level was 4,246 μg/L (range, 2,424-7,612 μg/L). All patients had hemophagocytosis on bone marrow smears. Finally, all patients received etoposide. The mean length of stay was 7 days (range, 3-14 days) in the ICU and 21 days (range, 8-28 days) in the hospital. Three patients (33%) died in the ICU, and hospital mortality was 56% (five deaths).

We believe it is of critical importance for ICU physicians to be aware that severe HLH can lead to specific MOF mimicking septic shock from cytokine hyperproduction in a context of exaggerated and paradoxical response. Making an HLH diagnosis translates into specific therapy, along with prompt and aggressive organ support. Also, HLH carries different outcomes than septic shock. In our experience, the HLH-2004 criteria are sufficiently sensitive to detect HLH in patients in the ICU, especially when combined with the identification of a precipitating factor (infection, malignancy, or connective tissue disease) on a background of known or quiescent immune deficiency.

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REFERENCES