Measles and Secondary Hemophagocytic Lymphohistiocytosis

To the Editor: We found interesting the article by Lupo et al. about a case of fatal measles in an immunocompetent 29-year-old woman (Fatal measles without rash in immunocompetent adult, France; http://dx.doi.org/10.3201/eid1803.111300). Perhaps, however, the possible diagnosis of secondary hemophagocytic lymphohistiocytosis (HLH) should also have been considered in that setting.

HLH is a potentially fatal hyperinflammatory syndrome characterized by histiocyte proliferation and hemophagocytosis. HLH may be inherited (i.e., primary, familial, generally occurring in infants) or may occur at any age secondary to infection, malignancy, or rheumatologic disease. Secondary HLH is determined according to clinical criteria from the HLH Study Group of the Histiocyte Society, which require ≥5 of the following for a diagnosis: fever; splenomegaly; cytopenia (affecting ≥2 cell lineages); hypertriglyceridemia or hypofibrinogenemia; hemophagocytosis in the bone marrow, spleen, or lymph nodes; low or absent natural killer cell cytotoxicity; hyperferritinemia; and elevated levels of soluble CD25.

We conducted a PubMed search and found 5 articles that described 6 cases of HLH in patients with measles (1–5). Pneumonia was described in all of them (1–5), and central nervous system involvement was described in 3 (1,4). Four cases occurred in children, 3 of them immunocompetent (1,3–5). The 2 adults were an immunocompetent 18-year-old man who had acute respiratory distress (2) and a 19-year-old man with acute lymphocytic leukemia who had measles pneumonia and acute hemorrhagic leukoencephalitis (1). The only fatal case occurred in an immunocompromised 8-year-old boy with giant-cell pneumonia (3).

The identification of hemophagocytosis in bone marrow aspirate represents only 1 of the 5–8 criteria needed for a diagnosis of HLH; conversely, a bone marrow aspirate lacking hemophagocytosis does not rule out the diagnosis of HLH. Still, we believe HLH should be considered for any patient with fever and pancytopenia, especially in the presence of respiratory distress or multiorgan dysfunction. An appropriate therapy could save the patient (Secondary hemophagocytic syndrome in adults: a case series of 18 patients in a single institution and a review of literature; http://dx.doi.org/10.1002/hon.960).

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In Response: We thank Iaria et al. (1) for their comments on our letter reporting an unusual case of fatal measles without rash in an immunocompetent woman who manifested cytopenias and an intractable acute respiratory distress syndrome (2). The authors suggest that secondary hemophagocytic lymphohistiocytosis (HLH) could have been considered in this patient.
Our reply supplies supplementary clinical and laboratory findings that could be useful for discussion.

During our patient’s hospitalization, we were able to investigate 6/8 diagnostic criteria for HLH proposed by the Histiocyte Society (3). Of these, only 2 or 3 were found: persistent fever at 38.5°C; hypertriglyceridemia at 267 mg/dL (analysis performed at day 7); and cytopenias, which preferentially affected erythrocytes and lymphocytes. (Thrombocytopenia was moderate at >100 × 10^9 platelets/L, and no neutropenia was found [≥2 × 10^9 neutrophils/L].) Liver function was not affected; no hepatomegaly was found, and alanine aminotransferase, aspartate aminotransferase, and bilirubin levels remained within reference ranges. Physical examinations did not detect splenomegaly, and laboratory findings did not show hypofibrinogenemia or ferritin level exceeding 500 ng/mL. A bone marrow biopsy performed on day 2 of hospitalization did not show hemophagocytosis. Studies of natural killer cell function and soluble CD25, which are also proposed diagnostic criteria for HLH, were not performed.

Overall, we found that the arguments in favor of HLH were too limited to consider this diagnosis and initiate an aggressive therapeutic approach based on immunosuppressive drugs. Even if, in the event of HLH, an early and appropriate treatment can be life-saving, the destruction of the remaining immune functions might also be lethal for the patient.

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Contaminated Soil and Transmission of Influenza Virus (H5N1)

To the Editor: Highly pathogenic avian influenza (H5N1) virus has been responsible for 603 confirmed human cases worldwide, including 356 that resulted in death, and for >7,000 epizootic outbreaks (1,2). Direct contact between hosts is the main mechanism of transmission for avian influenza viruses, but the possible role of the environment as a source of HPAI virus (H5N1) infection has been rarely studied, particularly in the context of countries where the virus is enzootic or epizootic (3–7). To determine if contaminated soil contributes to the transmission cycle of HPAI virus (H5N1), we used experimental and simulated field conditions to assess possible transmission in chickens.

All experiments were conducted by using HPAI virus (H5N1) strain A/chicken/Cambodia/LC1AL/2007 (GenBank accession nos. HQ200574–HQ200581). All animal experiments were conducted in the biosafety level 3 laboratory of Institut Pasteur in Cambodia (IPC), in compliance with the European Community 86/609/CEE directive and approved by the Animal Ethics Committee of IPC (permit: AEC/IPC/003/2010). Specific pathogen-free (SPF) chickens were provided by the National Veterinary Research Institute of Cambodia.

We used 3 types of soil: 1) sandy topsoil collected from around rice fields in Phnom Penh Province, Cambodia; 2) building sand purchased from a local building company; and 3) soil-based compost purchased from a local tree nursery. Physicochemical and microbiologic parameters were measured for water extracts obtained for each type of soil (online Technical Appendix Table, www.cdc.gov/EID/pdfs/12-0402-Techapp.pdf), and low- and high-dose contamination protocols (online Technical Appendix Figures) were used to experimentally contaminate each soil type. In brief, we seeded the soil samples with 1–56 infectious units of contaminated feces; 1 infectious unit was defined as 1 g feces from an SPF duck mixed with 1 × 10^7.8 50% egg infective dose of HPAI virus (H5N1) particles. The contaminated soil was then sprinkled on the bottom of an isolator (surface area 0.2 m^2) in which the chickens were housed. Oropharyngeal and cloacal swab samples and feathers were collected daily from the chickens and underwent quantitative reverse transcription PCR (qRT-PCR) testing targeting the H5 hemagglutinin gene (8). Surviving birds were killed humanely at the end of the experiments, and postmortem examination and collection of serum and organ samples were conducted on all animals. Organ samples were tested by using qRT-PCR, and serum samples were tested...