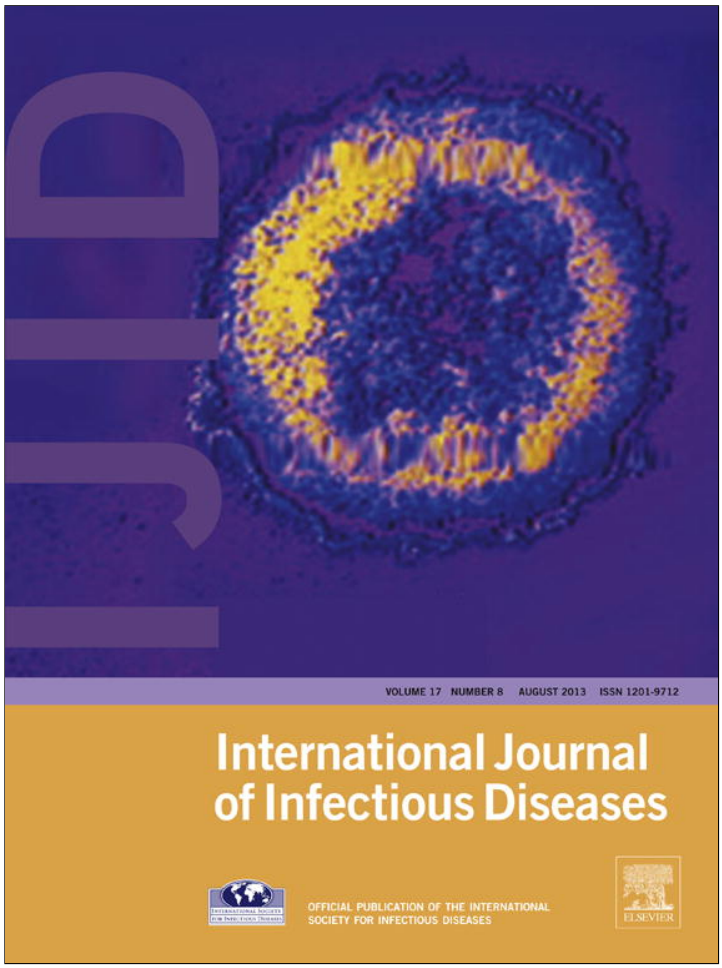

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Letter to the Editor

## Scrub typhus, acute respiratory distress, and hemophagocytic lymphohistiocytosis

We found the paper by Goswami et al., concerning a severe case of scrub typhus (disease caused by *Orientia tsutsugamushi*) complicated by acute respiratory distress syndrome (ARDS) and acute liver failure, very interesting.[1] 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 (primary, familial, generally occurring in infants) or secondary to infection, malignancy, or rheumatologic disease and occurring at any age. Secondary HLH is diagnosed using the following clinical criteria developed by the HLH Study Group of the Histiocyte Society; having five out of eight of the following: (1) fever, (2) splenomegaly, (3) cytopenia (affecting $\geq$2 cell lineages), (4) hypertriglyceridemia and/or hypofibrinogenemia, (5) hemophagocytosis in the bone marrow, spleen, or lymph nodes, (6) low or absent natural killer cell cytotoxicity, (7) hyperferritinemia, (8) elevated soluble CD25.[2]

In PubMed there are at least 12 papers describing cases of HLH in patients with scrub typhus (search strategy: (haemophagocytic, or haemophagocytosis, or hemophagocytosis, or hemophagocytic, or erythrophagocytosis, or macrophage activation syndrome) AND (scrub typhus OR tsutsugamushi OR orientia)), and ARDS was described in at least four of them,[3–6] and in one case was fatal.[6]

In PubMed there are at least 30 papers describing patients with scrub typhus and ARDS (search strategy: (ARDS OR acute respiratory distress syndrome OR acute respiratory failure) AND (scrub typhus OR tsutsugamushi OR orientia)), and many of them were also complicated by liver failure, multiorgan failure, and disseminated intravascular coagulation (DIC); anemia and thrombocytopenia were very often reported. Strangely enough, only in a few papers was a diagnosis of HLH considered in that setting.[3,5,7]

HLH is a life-threatening clinical syndrome. Liver involvement is more frequent in pediatric cases, but may be present in adults with variable levels of transaminases up to signs of acute liver failure and coagulopathy. Respiratory distress is frequently present and respiratory insufficiency represents a negative prognostic sign and may need assisted ventilation. HLH can be triggered by rickettsial diseases,[8–10] and it should remembered that the identification of hemophagocytosis in bone marrow aspirate represents only one of 5/8 criteria needed for the diagnosis of HLH and that a bone marrow aspirate lacking hemophagocytosis does not rule out the diagnosis of HLH.[2]

HLH should be suspected in every patient with rickettsial diseases, especially in the presence of respiratory distress or multiorgan dysfunction. An appropriate therapy could save the patient.

*Conflict of interest:* All authors: no conflicts.

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