Hemophagocytic Lymphohistiocytosis in a Patient of Scrub Typhus

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Abstract
Hemophagocytic lymphohistiocytosis (HLH) is a rare but aggressive and potentially fatal condition characterized by excessive immune activation. It can occur as primary/familial and secondary/sporadic/acquired form. Infections can play a role as triggers in the secondary form of HLH. A case of Hemophagocytic lymphohistiocytosis (HLH) in a patient of Scrub typhus is being reported here. Such association of scrub typhus and HLH is rare.

Introduction
Hemophagocytic lymphohistiocytosis (HLH) is a rare but aggressive and potentially fatal condition characterized by excessive immune activation. It has variable clinical presentation and lack specific symptoms and signs but prompt initiation of treatment is essential for the survival of affected patients. It can occur as primary/familial and secondary/sporadic/acquired form. Infections can play a role as triggers in the secondary form of HLH. A case of HLH associated with scrub typhus is being reported here. Such association of scrub typhus and HLH is rare.

Case Report
An 18 years old male youth was admitted in medical ward with complaint of high grade continuous fever since 10 days. There was history of cough without sputum production since 3 days along with yellow discolouration of eyes. On the day of admission in hospital, he also developed petechiae over the limbs and trunk. There was no past history of such illness/drugs ingestion/any significant medical illness. On examination he was conscious, cooperative. His vitals were-pulse 108/minute, blood pressure 114/76 mm of Hg, temperature 102F, respiratory rate 22/minute with thoraco-abdominal respiration and oxygen saturation was 94% at room air. Clinical examination revealed tender hepatomegaly and splenomegaly (2 cm below costal margin) along with fine crepitations at base of right lung.

Discussion
Hemophagocytic lymphohistiocytosis (HLH) is a rare but aggressive and potentially fatal condition characterized by excessive immune activation. Many patients with HLH have a predisposing genetic defect, and/or an immunologic trigger, which can include infection, malignancy, rheumatologic disorder (i.e. juvenile idiopathic arthritis) or disorders associated with immune dysregulation. Infections can play a role as triggers in the secondary form of HLH. HLH associated infections includes Epstein Barr virus, cytomegalovirus, parvovirus, herpes simplex virus, varicella zoster virus, measles virus, human herpes virus8, H1N1 influenza virus, and HIV.

The diagnosis of secondary HLH is based on fulfilling five of eight diagnostic criteria. These 8 criteria include 1. Fever ≥38.5°C, 2. Splenomegaly, 3. Peripheral blood cytopenia, with at least two of the following: hemoglobin <9 g/dL (for infants <4 weeks, hemoglobin <10 g/dL), platelets <1Lac/µL; absolute neutrophil count <1000/µL, 4. Hypertriglyceridemia (fasting triglycerides >265 mg/dL) and/or hypofibrinogenemia (fibrinogen <150 mg/dL), 5. Hemophagocytosis in bone marrow, spleen, lymph node, or liver, 6. Low or absent NK cell activity, 7. Ferritin >500 ng/mL, 8. Elevated soluble CD25 >2400 U/mL.
When a diagnosis of secondary HLH is established, patient should be evaluated for a possible infectious trigger/immunological/rheumatologic or malignant disease. In our case the patient was positive for scrub typhus. Scrub typhus is a rickettsial disease, caused by Orientia tsutsugamushi. The pathognomic finding in scrub typhus, a necrotic eschar at the inoculating site of the mite, is rarely seen in South East Asia region including Indian subcontinent. There are only few case reports showing scrub typhus as a trigger for HLH. The peculiar finding in our case was leucocytosis which is seen in 25% cases of HLH and the same has not been reported in case reports of scrub typhus with secondary HLH. Association of scrub typhus and HPLS in adult patient is rare.

HLH should be suspected in non-responding cases of Scrub typhus associated with persistent cytopenias/leucocytosis despite optimal treatment of scrub typhus.

**References**