



## Dengue fever, a revisit of the virus associated hemophagocytic syndrome

Hemophagocytic lymphohistiocytosis (HLH) is a result of uncontrolled macrophage activation with prominent phagocytosis of platelets, erythrocytes, and lymphocytes, and hematopoietic precursors. Attempt should be made to establish or rule out HLH in patients presenting with fever, multisystem inflammation, and varying degrees of unexplained pancytopenia. Apart from EBV, dengue infection, especially in epidemics, has emerged as an important cause of HLH. Early recognition of infection-associated HLH in the tropical Asian populations should stimulate a search for common infections, and early institution of specific treatment and aggressive supportive care, which is essential for reducing morbidity and mortality.

HLH, a macrophage-related hyperinflammatory disorder is of two types: Primary (familial) and secondary or reactive HLH (associated with infections, autoimmune disorders, or malignancy). Despite a high incidence of tropical infections in India, studies on secondary HLH are sparse and limited to case reports. The main reasons are a lack of clinical suspicion and awareness and non-availability of genetic and other molecular studies in most developing countries. Diagnosis is usually delayed, which has a negative effect on the morbidity and mortality. Both types of HLH can be triggered by infections, and hence it was not possible to exclude familial HLH in our case.<sup>[1]</sup>

In a Thailand study of 15 pediatric cases with infection-associated HLH, several of the infections known to be associated with the disorder including salmonellosis, dengue virus, and *P. marneffei* infection were identified.<sup>[2]</sup>

The recent increase in manifest cases of dengue and its complications revisits the hemophagocytosis syndromes. The hematological manifestations of neutropenia and thrombocytopenia are wakeup calls. Hemophagocytosis is regarded as one of the causes of thrombocytopenia.

Macrophages are activated by dengue virus infection, and serum ferritin a macrophage activation marker is highly elevated in dengue. These activated macrophages destroy the target cells by engulfing the antibody-coated platelets.<sup>[3]</sup>

In adults, the immune response is stronger, and hence those with autoimmune diseases, diabetes, and chronic renal failure have a higher fatality rate in elderly.

The lack of clinical awareness of this association delays the suspicion of HLH. In literature, only a handful of cases have been reported of this association. In practice, when a suspected case of dengue fever does not subside within a week, HLH must be suspected with raised serum ferritin levels and LDH.

K. R. Chatura

Department of Pathology, JJMMC, Davangere, Karnataka, India.  
E-mail: chaturakr@gmail.com

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