Haemophagocytic syndrome due to Ebstein-Barr virus

Sir,

Haemophagocytic syndrome is a clinicopathological syndrome characterised by uncontrolled activation of lymphohistiocytic system resulting in multisystem organ involvement. The disease though common in children can affect all age groups and is characterised by haematological, pulmonary, cutaneous, hepatobiliary and neurological involvement. Ebstein–Barr virus constitutes an important triggering factor of this condition, as is illustrated by the following case.

A 52-year-old male patient presented with high-grade fever on and off since the last 1 month not associated with cough, difficulty in breathing, burning micturition, pain abdomen, loose motion, vomiting, headache and joint pain. On examination, the patient had fever, pallor, edema, bleeding from oral cavity and hepatosplenomegaly as positive findings. Blood investigation revealed haemoglobin 6.8 g/dL, white blood cell (WBC) 500/mm^3 and platelet count 10,000/mm^3. Blood and urine cultures and tests for malaria, typhoid, dengue, leptospirosis, hepatitis B, hepatitis C, HIV and hepatitis A were negative, as were the Mantoux test, antinuclear antibody and double-stranded DNA. X-ray chest and echocardiography were unremarkable, and ultrasonography of the abdomen revealed hepatosplenomegaly.

The patient was treated with broad-spectrum antibiotics and blood and platelet transfusion along with granulocyte-monocyte colony–stimulating factor, but his condition did not improve. Bone marrow biopsy was done which revealed erythroid and megakaryocytic hyperplasia with moderate haemophagocytosis. Serum ferritin (>1000 ng/dL) and triglyceride level (227 mg/dL) were both increased.

Thus, he was diagnosed to be a case of haemophagocytic syndrome and treated as per haemophagocytic lymphohistiocytosis (HLH) protocol with dexamethasone (10 mg/m^2) and etoposide (150 mg/m^2) injection. Serology for Ebstein–Barr virus along with polymerase chain reaction was sent which came positive. The patient was treated for further 8 weeks with the HLH protocol following which he became afebrile with gradual improvement in WBC, haemoglobin and platelet count, and he was subsequently discharged with stable haematological parameters.

Haemophagocytic syndrome is a life-threatening condition characterised by excessive immune system activation.[1] It can be primary or familial when the condition is inherited or secondary

precipitated by infection, autoimmune conditions and malignancies.[2] Among the infections, bacterial (Gram-negative bacteria, rickettsia, leptospira, salmonella, tuberculosis), viral (Ebstein–Barr virus, dengue virus, cytomegalovirus, HIV, parvovirus, herpes simplex, varicella), fungal and parasite (malaria, leishmaniasis) constitute the major triggering factor for this condition. The mechanism includes stimulation of T cells, natural killer cells and generation of interleukin (IL) 2, interferon-a and IL6 causing activation of macrophage histiocytic system.[3]

The diagnosis of this condition is based on HLH-2004 trial in which five of the following must be present:[4] fever ≥38.5°C; splenomegaly; peripheral blood cytopenia, with at least two of the following: haemoglobin <9 g/dL, platelets <100,000/mm^3, absolute neutrophil count <1000/mm^3; hypertriglyceridemia (fasting triglycerides >265 mg/dL) and/or hypofibrinogenemia (fibrinogen <150 mg/dL); haemophagocytosis in bone marrow, spleen, lymph node or liver; ferritin >500 ng/mL; and elevated soluble CD25 (soluble IL-2 receptor alpha) two standard deviations above age-adjusted laboratory-specific norm.

Alternately, the H6 score developed by Fardet *et al.* can be used.[5]

As far as the treatment is concerned, HLH protocol 2004[6] consists of initial therapy for 8 weeks with dexamethasone (10 mg/m^2) and etoposide (150 mg/m^2) followed by maintenance therapy with the same regime dexamethasone (10 mg/m^2) for 3 days every 2 weeks and etoposide (150 mg/m^2).

In both primary and secondary HLH, central nervous system (CNS) involvement (30%–73% of all HLH) in the form of seizures (33%–83%), encephalopathy (31%–47%) and focal neurological signs in the form of hemiparesis and cranial neuropathies are frequent findings at disease onset and are confirmed by magnetic resonance imaging of brain where multifocal and bilateral abnormalities are seen in T2-weighted image study. The treatment is the same as induction therapy along with intrathecal methotrexate which is given weekly from 3 to 6 weeks in patients who had clinical symptoms of CNS disease progression after 2 weeks of systemic treatment or in those with worsening or unchanged CNS symptoms.[7]

Haemophagocytic syndrome should always be considered in any patient presenting with fever, multisystem involvement and haematological abnormality so as to diagnose and treat it as early as possible.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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REFERENCES

1. Larroche C. Hemophagocytic lymphohistiocytosis in adults: Diagnosis and treatment. Joint Bone Spine 2012;79:356-61.
2. Henter JI, Horne A, Arico M, Egeler RM, Filipovich AH, Imashuku S, *et al*. HLH-2004: Diagnostic and therapeutic guidelines for hemophagocytic lymphohistiocytosis. Pediatr Blood Cancer 2007;48:124-31
3. Gupta S, Weitzman S. Primary and secondary hemophagocytic lymphohistiocytosis: Clinical features, pathogenesis and therapy. Expert Rev ClinImmunol 2010;6:137-54.
4. Henter JI, Horne A, Aricó M, Egeler RM, Filipovich AH, Imashuku S. HLH-2004: Diagnostic and therapeutic guidelines for hemophagocytic lymphohistiocytosis. Pediatr Blood Cancer 2007;48:124-31.
5. Fardet L, Galicier L, Lambotte O. Development and validation of a score for the diagnosis of reactive hemophagocytic

syndrome (H Score). Arthritis Rheumatol 2014;66:2613-20.
6. Tothova Z, Berliner N. Hemophagocytic syndrome and critical illness: New insights into diagnosis and management. J Intensive Care Med 2015;30:401-12.
7. Trottestam H, Horne A, Arico M, Egeler RM, Filipovich AH, Gadner H, *et al*. Chemoimmunotherapy for hemophagocytic lymphohistiocytosis: Long-term results of the HLH-94 treatment protocol. Blood 2011;118:4577-84.

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