Hemophagocytic Syndrome in a Patient with Unexplained Cytopenia

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Abstract
Hemophagocytic syndrome (HPS) is a pathologic immune activation defined by clinical signs and symptoms of excessive inflammation. The most typical findings are fever, splenomegaly, cytopenia, jaundice and hemophagocytosis in bone marrow and other organs (phagocytosis by macrophages of erythrocytes, leukocytes, thrombocytes and other precursors) and less commonly clinical and neurological findings. We diagnosed HPS on the basis of high fever, cytopenia and ferritin elevation. Etoposide and dexamethasone were used in treatment. This case report revealed that HPS should be considered in patients with high fever and abnormally elevated ferritin values and pancytopenia. The mortality is high in undiagnosed cases but early diagnosis and treatment can be life-saving.

Keywords: Hemophagocytic Syndrome; Hyper Ferritinemia; High Fever; Splenomegaly; Jaundice

Case
A 22-years-old male patient presented with rising fever with shivering and sore throat. His history revealed that these symptoms had commenced seven days previously and that non-steroid anti-inflammatory drug and broad spectrum antibiotic therapies prescribed by the physicians to whom he presented had not proved beneficial. He was born in Mardin which is a city located in southeast of Turkey and he was a student in a university. There is no family history of genetic disorders. He had no history of a chronic disease, immunosuppressive drug use, smoking, alcohol use and had never travelled to abroad. He was hospitalized when the severity of the symptoms increased. At physical examination axillary body temperature was 38.9°C (35.5-37.0), and at oropharyngeal examination both tonsils were hypertrophic and hyperemic. Blood pressure was 100/60 mmHg, heart rate 115/min and respiration rate 20/min. The patient was tachypnoeic and rales were detected in the right lower lung zone. At abdominal examination the liver projected 4 cm beyond the costal arch and was soft in texture, while 1 cm of the spleen was palpable. There was no rash, joint pain, lymphadenopathy or evidence of serositis. Other system findings and neurological examination were normal. At laboratory investigation, hemoglobin was 8.1 g/dl, red blood cell count 3.5 × 10⁶/mm³, platelets 51 × 10⁹/mm³ and white blood cell count 2,700/mm³, and 62% neutrophils, 23% lymphocytes and 15% monocytes were present at peripheral smear. C-reactive protein (CRP) was 148 mg/dl and ESR (Erythrocyte Sedimentation Rate) 30 mm/hour. At biochemical investigation, BUN (Blood Urea Nitrogen) was 15 mg/dl, creatinine 0.7 mg/dl, AST (Aspartate Aminotransferase) 414 IU/L (10-35), ALT (Alanine Aminotransferase) 193 IU/L (13-40), LDH (Lactate Dehydrogenase) 15 61 IU/L (230-460), GGT (Gamma Glutamyltransferase) 50 IU/L (5-55), ALP (Alkaline Phosphatase) 184 IU/L (40-150), total bilirubin 3.5 mg/dl (0.2-1), Ferritin 49078 ng/ml (30-400), triglyceride level 400 mg/dl, PT (Prothrombin Time) 22 sec (10-14), aPTT (activated Partial Thromboplastin Time) 44 sec (25-35) and fibrinogen 100 mg/dl. At bone marrow aspiration investigation, elevated histiocyte numbers (figure 1A) and erythrocytes phagocytized by histiocytes (figure 1B) were observed in some areas. Brucella IgM, CMV (Cytomegalovirus) IgM, HSV (Herpes Simplex Virus) IgM, ANA (Antinuclear Antibodies), anti-ds-DNA (anti-double stranded DNA), PPD (Purified Protein Derivative) investigated in terms of the etiology of hemophagocytic HPS were negative. Bacteriological cultures, ASO (Anti-streptolysin O) or Widal tests were also yielded negative. Clinical and bone marrow findings suggested a diagnosis of secondary HPS. Diagnostic criteria for HPS used in the HLH-2004

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Figure 1: Hemophagocytosis on bone marrow aspirate.
Hemophagocytic syndrome is a pathological immune activation defined by clinical signs and symptoms of excessive inflammation [2]. The most typical findings are fever, splenomegaly, cytopenia, jaundice and hemophagocytosis in bone marrow and other organs [3] (phagocytosis of erythrocytes, leukocytes, thrombocytes and other precursors by macrophages) and less commonly clinical and neurological findings. Studies have also reported that ferritin levels rise significantly in HPS and that elevated ferritin levels can assist with diagnosis [4]. It is associated with various viral, bacterial, fungal and parasitic infections and collagen tissue diseases and malignant diseases, and also frequently with Epstein-Barr virus (EBV) infection [5]. In our study we investigated the etiology of HPS and all of the tests were negative in our patient. Although we examined many viral agents such as EBV, CMV, Rubella, HIV, HBV, HCV and HSV, we didn’t test the patient for arboviruses and Dengue fever because they are not endemic in our country. Chemotherapeutics, and particularly etoposide and dexamethasone, have been reported to be effective in treatment [6].

We diagnosed HPS on the basis of high fever, cytopenia and ferritin elevation. Etoposide and dexamethasone were used in treatment. This case report is intended to remind colleagues that HPS should be considered in patients with high fever and abnormally elevated ferritin values, pancytopenia. The mortality is high in undiagnosed cases but early diagnosis and treatment can be life-saving.

**Conflict of Interest**

The authors declare that they have no conflict of interest.

**Ethical Approval**

All applicable international, national, and/or institutional guidelines for the care and use of human were followed.

**References**


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