Enteric Fever Presenting as Hemophagocytic Lymphohistiocytosis (Macrophage Activation Syndrome)

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Abstract

Macrophage Activation Syndrome is a rare, fatal disease which needs to be considered in patients with a SIRS (systemic inflammatory response syndrome) like clinical presentation. Here, we report a case of enteric fever masquerading as hemophagocytic syndrome for its rarity and unusual presentation.

Introduction

Hemophagocytic lymphohistiocytosis (HLH) or macrophage activation syndrome is a rare and potentially fatal disorder of normal overactive histiocytes1,2,3. In hemophagocytic lymphohistiocytosis there is an abnormal activation of normal T cells and macrophages resulting in clinical and hematological alterations. Many clinical features of this syndrome mimic SIRS and death is inevitable in the absence of treatment1,2,3. This case is being reported to enlighten the general physicians regarding the clinical entity of macrophage activation syndrome especially in patients presenting with fever unresponsive to antibiotics, unexplained cytopenia and liver dysfunction with elevated ferritin. Hemophagocytic syndrome has been uncommonly reported in association with enteric fever4,5,6,7,8. Moreover, acquired infection associated HLH has a high fatality rate of 50% in children. If a treatable organism is found, appropriate therapy should be given but anti-infectious therapy may not be sufficient to control HLH. The immediate aim of treatment is to suppress hypercytokinemia.9

Case

An 18 year old female was admitted in our emergency ward with ten days history of continuous fever associated with chills, rigors and sweating. Subsequently patient developed cough which was productive of mucopurulent sputum. Apart from fever and pallor, general physical examination was unremarkable.

Systemic examination revealed rales in right infrascapular area and splenomegaly 3cm below left costal margin. Hemogram revealed: [Hb à 8.6gm/dl, TLC à 2200/ml, DLC à N54 L37 M9, Platelet à 34000/ml, MCV à 87 fl., ESR à 35mm, PBF à marked pancytopenia with normocytic normochromic anemia]. Except for transaminits [SGOT =115 and SGPT =135], her serum chemistry was normal. Chest skiagram, electrocardiogram, urinalysis, septic screen (blood/urine cultures) were unrewarding. Abdominal sonography revealed splenomegaly of 15cm. Widal reaction was positive in titres of TO 1:320 and TH 1:160. Brucella Serology and evaluation for tuberculosis was negative. In view of fever, splenomegaly and pancytopenia, bone marrow aspiration was performed which revealed hypercellular marrow with myeloid hyperplasia with an increase in hemophagocytic macrophages. Erythropoiesis was normoblastic. Bone marrow culture yielded salmonella typhi after 48 hours of incubation. Serum ferritin (2229.95ng/ml) and serum triglycerides (286mg/dl) were markedly increased. In view of history, examination and laboratory parameters, a diagnosis of hemophagocytic lymphohistiocytosis (macrophage activation syndrome) secondary to typhoid fever was entertained.

Patient received ceftriaxone 1gm IV BD for 10 days. Patient became afebrile on 4th day after receiving treatment. Serial blood counts revealed a rising trend till they became normal before the end of second week.

Discussion

Hemophagocytic syndrome is of two types (a) Primary HLH with no obvious precipitating cause (b) Secondary HLH (acquired HLH) which occurs after strong immune activation as in systemic infection (virus, bacteria, and protozoa), autoimmune disorders, or underlying malignancy1,2. In hemophagocytic lymphohistiocytosis there is overwhelming activation of normal T cells and macrophages. The clinical entity has to be suspected when patient presents with fever unresponsive to antibiotics, general fatigue, falling ESR, cytopenia of unknown origin and liver dysfunction with elevated ferritin. The diagnostic
criteria proposed by Histiocyte Society for inclusion in the International Registry for hemophagocytic lymphohistiocytosis is as follows10.

(1) Fever - Seven or more days of a temperature as high as 38.5°C (101.3°F).

(2) Splenomegaly

(3) Cytopenia - Counts below the specified range in at least 2 of the following cell lineages:
- Absolute neutrophils less than 1000/mL;
- Platelets less than 100,000/mL;
- Hemoglobin less than 9.0 g/dL

(4) Hypofibrinogenemia or hypertriglyceridemia

(5) Hemophagocytosis

(6) Rash

At least five criteria need to be present to have a definite diagnosis. For confirmation tissue diagnosis is needed. Hemophagocytosis must be demonstrated in the bone marrow, spleen, or lymph nodes. Macrophage activation syndrome should be considered in patients with a SIRS like clinical presentation. Hyperferritinaemia >10000 μg/l seems to be a good marker for defining patients with or at risk of developing MAS (and should be completed with a morphological assessment of hemophagocytosis) as well as an indicator for emergency administration of IVIG. But low ferritin does not rule out the condition as it may possibly reflect ferritin measurements some time after the peak of macrophage activation. This may be the reason for the relatively less elevated ferritin in our patient.

In the absence of prospective controlled trials, corticosteroids, cyclosporin A, and etoposide have been used with varied success. Recent reports show promising results with an anti-TNF-α and plasmapheresis.10

References

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