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LETTER TO EDITOR

Hemophagocytic syndrome

Sir,

Hemophagocytic syndromes result from increased number of hemophagocytic macrophages with resultant cytopenias. Common clinical features are hepatomegaly, splenomegaly and fever.[1] The proliferating macrophages are reactive in most cases; however, they are rarely a part of a neoplastic clone. We present such a case in a 2-year-old female child.

A 2-year-old female child was presented with intermittent fever of 15 days along with passage of black stool and bleeding gums/lips since 3 days. There was no significant family history/past history. On clinical examination, the child was febrile, toxic with pedal edema. The examination of the oral cavity showed mucosal bleeding. Per-abdomen examination showed hepatosplenomegaly. Investigations showed Hb - 6.2 gm%, TC- 3,000 cells/mm^3, N65, L30, E4, M1 and platelet - 28,000 cells/cumm, indicating pancytopenia; Coombs test and ANA were positive. HIV, Widal test, Weil-Felix test, blood culture, stool culture malarial parasite, Dengue (IgM,IgG) and AFB culture were negative; Chest-X-Ray showed bronchopneumonia. Serum biochemical parameters were normal: fibrinogen - 88.6 mg/dl and D-Dimer - 958 ng/ml. The serial estimation of PT/APTT/INR values ranged from 15 to 50 s, 20 to 40 s, 1.19 to 2.68 S, respectively. The following values were noted: serum ferritin - 1800 mg/dl, serum triglyceride - 180 mg/dl and serum albumin - 0.5 mg/dl. Bone marrow aspiration (BMA) showed dilute marrow with marked reticuloendothelial hyperplasia along with erythrophagocytosis [Figure 1]. Bone marrow biopsy (BMB) showed cellular marrow with evidences suggestive of phagocytosis-? Virus-induced hemophagocytic syndrome (VAHS). Bone marrow culture showed the growth of candida (yeast) The patient was administered Inj. amphotericin on alternate days for 3 weeks leading to a remarkable recovery.

Hemophagocytic lymphohistiocytosis (HLH) is a severe systemic inflammatory reaction characterized by (uncontrolled) activation and proliferation of T cells and macrophages, with multiorgan infiltration and multiorgan dysfunction.[2] Risdall *et al.*[3] described 19 such patients. Active hemophagocytosis with normal appearing macrophages is the pathognomonic feature of HLH.[4] Hemophagocytic lymphohistiocytosis is further subdivided into the following: (1) Familial HLH, a familial disorder due to genetic mutations. (2) Secondary or acquired HLH - This includes virus-associated hemophagocytic syndrome (VAHS) and malignancy-associated hemophagocytic syndrome (MAHS). The following are included: viruses such as Epstein-Barr virus (EBV), cytomegalovirus (CMV), adenovirus, respiratory syncytial virus, parainfluenza virus and enteroviruses; bacterias (*Pseudomonas aeruginosa*, *Staphylococci*, *Streptococci*, *Escherichia coli* and *Brucella abortus*); parasites (*Leismania donovani*); and fungi such as *Histoplasma capsulatum* and *Penicillum marneffei*.

The diagnostic criteria laid down by Histiocytic Society to diagnose HLH[5] consists of (1) Clinical features (fever, hepato-splenomegaly) along with (2) laboratory features of cytopenia involving at least two cells lineages in the peripheral blood (Hb < 9 gm/dl, neutrophils < 1,000/cumm and platelets < 1,00,000 cells/cumm), hypertriglyceridemia (>160 mg/dl) and hypofibrinogenemia (<250 mg/dl) coupled with the demonstration of hemophagocytosis in the bone-marrow, spleen or lymphnodes. Based on review of literature, Revalli[5] found serum ferritin (>1000 mg/dl), triglycerides (>160 mg/dl) and fibrinogen (<250 mg/dl) to be the markers with highest sensitivity and specificity for the diagnosis of HLH. A quantification of soluble CD 163 by enzyme-linked immunosorbent assay (ELISA) has been suggested as a sensitive maker for HLH, CD 163 being highly specific for the monocyte-macrophage lineage.[5] The exact pathogenesis has not been elucidated;[2] however, quantitative or qualitative defect of natural killer cells (NK cells) and a persistent production of proinflammatory cytokines is suspected. Case reports of fungi-induced HLH have been reported in immunocompromised hosts. However, we report an unusual case of fungal (candida) activated HPS in an immunocompetent host. All patients who meet the diagnostic criteria for HLH should have genetic testing performed

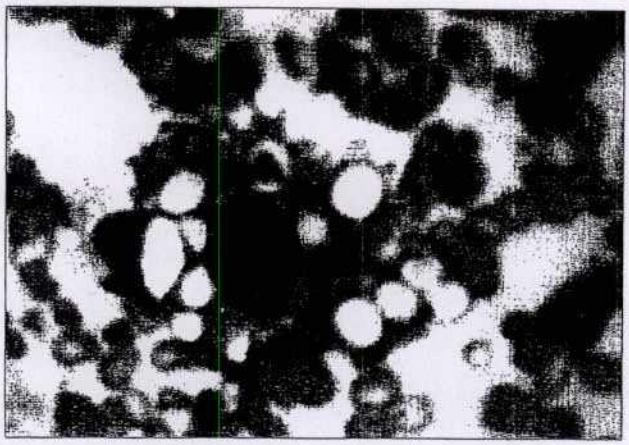

Figure 1: Photomicrograph showing erythrophagocytosis by bone marrow histiocytes (MGG, x1000)

because it is impossible to distinguish primary from secondary HLH on clinical grounds and familial HLH is uniformly fatal without bone marrow transplantation. A high level of vigilance and a comprehensive search for a potential infection is particularly important because the treatment of the infection can result in the rapid resolution of secondary HLH-associated signs and symptoms as highlighted by our case.

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