Pseudomonas sepsis with neutrophagocytosis in a premature newborn

Didem Aliefendioğlu, Deniz Aslan, Gülsevin Tekinalp, Aytemiz Gürgey

Department of Pediatrics, Hacettepe University Faculty of Medicine, Ankara, Turkey

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Secondary hemophagocytic syndrome may develop during certain severe infections commonly due to viral infections, but is rarely associated with bacterial infections, and its appearance in a premature newborn is uncommon. We present a case of hemophagocytosis during Pseudomonas aeruginosa septicemia in a premature infant. After sepsis treatment with imipenem-cilastatin and aminoglycoside, remission of hemophagocytosis was achieved.

Key words: hemophagocytosis, newborn, Pseudomonas.

Secondary hemophagocytic lymphohistiocytosis (HLH) is more often associated with an infectious episode, particularly with viruses of the herpes group, and tends to occur in older individuals who may have received immunosuppressive therapies. Secondary HLH is also referred to as infection associated hemophagocytosis[1] .

The association of hemophagocytic syndrome with bacterial infection is rare[2] and its appearance in a premature newborn is uncommon. We present a premature infant with bacterial sepsis due to Pseudomonas. Her clinical picture and findings were consistent with secondary hemophagocytosis. She was treated only with antibacterial therapy and remission was obtained.

Case Report

A female infant was born to a 40-year-old healthy mother by spontaneous vaginal delivery at 31 weeks of gestation. The pregnancy was complicated by premature rupture of membranes and chorioamnionitis. The mother had neither a family history for hemophagocytic syndrome nor was there parental consanguinity.

Her clinical and radiological findings were compatible with respiratory distress syndrome (RDS) and she was given surfactant therapy. Her clinical status deteriorated and she developed sclerema and jaundice on the 2nd day of life. She was diagnosed as having clinical sepsis; a single blood volume exchange transfusion was performed and empirical antibiotic therapy was started immediately. On the 7th day of life, hepatosplenomegaly was noted (the liver was palpable 5 cm below the right costal margin and the spleen was palpable 3 cm below the left costal margin). Later, liver and spleen sizes increased further, and on the 15th day the liver and spleen were palpable at 7 cm and 8 cm below the costal margins, respectively. Laboratory investigation showed hemoglobin 10.5 g/dl, platelets 9,000/mm^3, and leukocyte count 15,500/mm^3. On the peripheral blood smear neutrophils were 67%, and lymphocytes 33%, and vacuolated blood cells were seen. Plasma triglyceride and transaminating enzymes were increased. Coagulation test results were within normal ranges. Bone marrow aspiration revealed proliferation of histiocytes and hemophagocytosis; neutrophagocytosis was especially prominent. Viral investigation showed no exposure to Epstein-Barr virus (EBV), cytomegalovirus (CMV), rubella, herpes simplex virus (HSV), toxoplasma, hepatitis B and C, or parvoviruses. Lymphocyte subset analysis revealed no abnormality. Metabolic investigation (galactosemia spot test, amino acid chromatography) was normal.

Tracheal aspirate, bronchoalveolar lavage, and blood cultures revealed Pseudomonas aeruginosa. According to the antibiogram, broad spectrum antibiotic regimen (imipenem-cilastatin and

aminoglycoside combined therapy) was started on the 15th day. Hepatosplenomegaly regressed and platelet count normalized within ten days. The treatment was discontinued and the patient was discharged on the 39th day of life.

Discussion

Hemophagocytic lymphohistiocytosis is a reactive disorder of the histiocytes, characterized by their increased hemophagocytic and proliferative activity against erythrocytes, leukocytes and platelets in the liver, spleen, lymph nodes and bone marrow. The main features of HLH are persistent fever, cytopenia, liver dysfunction, hepatosplenomegaly, jaundice, coagulopathy and sometimes central nervous system symptoms. Bone marrow examination permits diagnosis with characteristic presence of macrophages with signs of active hemophagocytosis[3]. Although phagocytosis of only erythrocytes is a common process[4], neutrophagocytosis was prominent in our patient (Fig. 1).

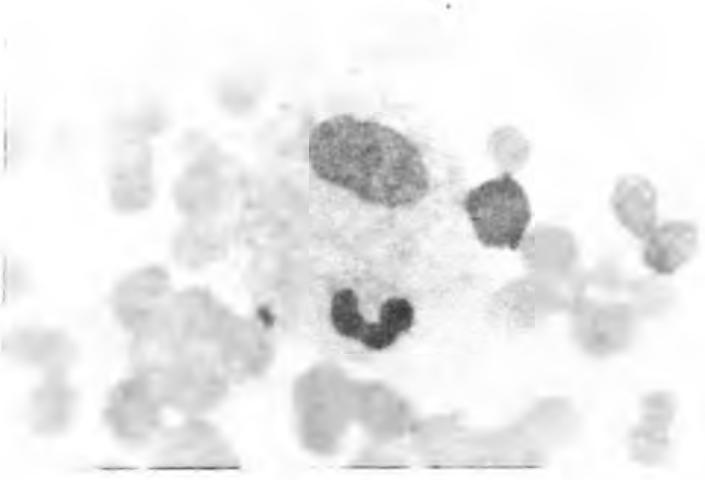

Fig. 1. Histiocyte with neutrophagocytosis.

The pathophysiology is thought to be mediated through a defect in the immunomodulation, resulting in an unrestricted release of inflammatory cytokines. The clinical and laboratory findings are consistent with these cytokines[5] . The clinical findings of our case were compatible with HLH, except for the absence of fever. The febrile response is believed to reflect enhanced metabolic activity and to be related to the release of endogenous pyrogens (i.e. cytokines, interleukin-1 and TNF) from the host's leukocytes, which then trigger a hypothalamic response. Because these pathways are not particularly well developed in the neonate, fever is not a valuable sign of infection[6] nor probably of HLH in this age group.

Patients with congenital or acquired immunodeficiency are at risk of having hemophagocytosis and of developing a hemophagocytic syndrome with or without associated infection. Acquired immunity in the newborn is affected by qualitative and quantitative deficiencies and, as newborn infants are at increased risk of serious infections, this situation may cause the newborn to be vulnerable to HLH.

This syndrome encompasses both primary (familial) and secondary HLH, which are frequently difficult to distinguish from each other[4]. The clinical course and the prognosis of secondary HLH are more favorable than in familial HLH. A previously affected sibling and/or history of consanguinity and an early onset may reveal a familial basis. In our case, there was neither a family history for HLH nor parental consanguinity, and the disease was self limited with the treatment of underlying bacterial sepsis. These findings led us to the diagnosis of secondary HLH in this patient.

Secondary HLH is more often associated with an infectious episode. Viral infections probably play a major role in secondary HLH; however, bacterial infections (tuberculosis, Leishmania, brucellosis, syphilis)[7] have rarely been reported. We were unable to find any other report of Pseudomonas infection associated with HLH.

In conclusion, hepatosplenomegaly, cytopenia, liver dysfunction, jaundice, coagulopathy, and

central nervous system symptoms exist in patients with both HLH and neonatal sepsis. In patients where hepatosplenomegaly and cytopenia resist appropriate antibiotic and supportive treatment, HLH should be kept in mind, and bone marrow aspiration should be performed for the diagnosis. In addition, in patients where neutrophagocytosis predominates, bacterial infection should be suspected as the cause of secondary HLH.

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