An uncommon hematologic disorder in an adult Puerto Rican patient

Fernandez Francisco, Del Olmo Francisco, Fernandez Ricardo, Fernandez Rosangela, Torrellas Pedro, Hernandez Luis, Lozada Jose, Boodoosingh Dev

Abstract

We described a 24 years old man, born in Puerto Rico, with a history of type two diabetes mellitus, hypothyroidism and morbid obesity admitted after complaining of general malaise, dizziness, confusion, and unquantified fever of two weeks evolution. Pertinent clinical findings included hepatosplenomegaly and hypotension. Laboratories demonstrated leukocytosis, normocytic anemia, thrombocytopenia, high ferritin, increased lactate dehydrogenase (LDH) and elevated creatinine level along with hypertriglyceridemia. Further laboratories revealed bacteremia with Methicillin Resistant Staphylococcus aureus (MRSA). An abdominal sonogram confirmed an enlarged liver measuring 23.6 cm and a spleen 18.2 cm long. A bone marrow biopsy evidenced histiocytes with engulfed red cells and nucleated cells.

The patient was diagnosed with hemophagocytic lymphohistiocytosis (HLH) secondary to bacteremia with MRSA. He coursed with severe sepsis involving target organs such as kidneys, bone marrow, liver and spleen. Daptomycin and Methylprednisolone were prescribed for the bacteremia and the hematologic condition respectively, with a favorable overall clinical response.

HLH is an uncommon disorder with an estimated incidence of 1 in 50,000 lives births, having an equal male to female distribution. The current incidence in adults is unknown. Therefore, we like to share this case of an immune-competent, Hispanic adult with no history of familial immune deficiencies condition who presented an HLH secondary to bacteremia.

To our knowledge, there are no published studies describing this syndrome in an immune-competent adult from Puerto Rico, making this case very uncommon in our island.

Key words: Hemophagocytic lymphohistiocytosis, bacteremia, severe sepsis, anemia, histiocyte, Methicillin Resistant Staphylococcus aureus, hepatosplenomegaly.

Case report

A 24-year-old man, born in Puerto Rico, with a previous history of type two diabetes mellitus, hypothyroidism and morbid obesity who came to Emergency Room complaining of two weeks evolution of unquantified fever, general malaise, chills and headaches. Physical exam revealed a morbid obese man, oriented only in person, in no acute respiratory distress. Vital signs showed hypotension, tachycardia, fever and tachypnea. The oral mucosa was dry, and there was no palpable

From San Juan City Hospital, San Juan, Puerto Rico (Francisco Fernandez, Francisco Del Olmo, Ricardo Fernandez, Rosangela Fernandez, Pedro Torrellas, Luis Hernandez, Jose Lozada, and Dev Boodoosingh).

Address for correspondence:
Francisco Fernandez
San Juan City Hospital PMB # 79
P.O. Box 70344, San Juan, Puerto Rico 00936-8344
Tel: 787-378-1615
Email: frank1298@hotmail.com

lymphadenopathy. Auscultation showed tachycardia but the lungs were clear. Abdominal exam showed an enlarged liver palpated three centimeters below the right costal border as well as the spleen, palpated four centimeters below the left costal border. Initial laboratory results (**Tables 1** and **2**) revealed normocytic anemia and marked leukocytosis. The peripheral smear visualized anisocytosis and poikilocytosis. Thrombocytopenia was also noted, with levels at 16,000/μL.

A comprehensive metabolic panel was remarkable for acute kidney injury and elevated liver enzymes. Because of the abdominal findings, an ultrasound was performed which confirmed an enlarged liver 23.6 cm long and spleen 18.2 cm. Chest X ray and 2D echocardiogram were unremarkable.

In view of the significant laboratory findings suggestive of HLH, pertinent labs demonstrated (**Table 3** and **4**) high ferritin level (1777.1 μg/l), hypertriglyceridemia (552 mg/dl), elevated fibrinogen (750 mg/dl) and LDH (1,097 U/L) levels.

Initial medical management included aggressive hydration with isotonic solutions, which eventually improved the hemodynamic status and the renal function. Platelet transfusion was required as well in view of further worsening of thrombocytopenia and risk for bleeding. Because the patient presented with systemic inflammatory syndrome (SIRS) with high suspicion of an occult infection he was started on empiric antibiotic therapy with meropenem 1 gram intravenously every 12 hours. Later in his hospital course, the blood cultures confirmed an infectious process in which an MRSA was identified. Therefore, the treatment was changed to daptomycin.

Despite all of the above measures, the patient persisted with hematological abnormalities reason why a bone marrow biopsy was performed. The procedure was significant for histiocytes with engulfed red cells and nucleated cells (**Figure 1** and **2**), consistent with HLH. With these findings, the patient was started on methylprednisolone 60 mg intravenously every 8 hours for three weeks. After all of the mentioned treatment, the patient's clinical status along with the abnormal laboratories were basically resolved.

Discussion

Hemophagocytic lymphohystiocytosis, also called hemophagocytic syndrome, is a life threatening condition in which there is an abnormal hypercytokinemia due to a highly stimulated but ineffective immune process producing phagocytosis by macrophages of cells including the erythrocytes, neutrophils, platelets and their precursors in the bone marrow and other tissues. (1) It is more common in the pediatric population, especially from Sweden with an estimated incidence of 1 in 50,000 lives births, with a similar male to female distribution. (2) The epidemiologic studies in adults are scant and the incidence is not clearly known. This condition may be associated with malignancies, autoimmune disorders, infections or familial. It also may be classified as primary, when caused by genetic mutations, and secondary to causes such as infections, immunodeficiences and malignancies. (3)

Common symptoms include fever, hepatomegaly, splenomegaly, neurologic, and lymphadenopathies. Other important findings are cytopenia, hypertriglyceridemia, hypofibrinogenemia, high ferritin level, low fibrinogen level, and hemophagocytosis. (3) Five or more of these features make this diagnosis highly suggestive. Our patient had a secondary type of HLH, acquired as a result of an infectious process, being the blood as the focus of infection by an MRSA. However, no specific cause of the bacteremia was identified.

Regarding prognostic factors, there are studies such as the one described by Kaito et al, in which thrombocytopenia (less than 100,000 μ/l platelets), anemia (hemoglobin less than 10 g/dl) and high ferritin (more than 500 ng/ml) are usually seen. (4)

Another atypical detail in our case was the fact that no viral etiology (Epstein Barr, Cytomegalovirus or Parvovirus) was identified as the secondary cause of HLH since usually these are the most common triggered factors. (5)

Early diagnosis is imperative since it may have a better prognosis when treated properly.

Table 1. Complete blood count

Hemoglobin	9.3 g/dl
Hematocrit	26.9%
WBC	15,900/ L
Platelets	16,ooo/ L
MCV	79.5 fl
RDW	18.8%
Neutrophils	93%
Bands	9%
Lymphocytes	3%
Monocytes	3%
Eosinophils	1%
Peripheral smear	No schistocytes. Poikilocytosis, anisocytosis

Table 2. Comprehensive metabolic panel

Sodium	131.7 mmol/l
Potassium	3.5 mmol/l
Chloride	94.7 mmol/l
Bicarbonate	22.3 mmol/l
BUN	36 mg/dl
Creatinine	2.3 mg/dl
Glucose	170 mg/dl
AST	68 IU/L
ALT	141 IU/L
Alkaline phosphatase	214 IU/L
Total bilirrubin	1.1 mg/dl

Table 3. Lipid panel

Cholesterol	196 mg/dl
Triglycerides	552 mg/dl
HDL	18 mg/dl
LDL	67.6 mg/dl
VLDL	110.4 mg/dl

Table 4. Further laboratories

LDH	1,097 U/L
ESR	68 mm/hour
C3; C4	76.10 mg/dl; 18.10 mg/dl, respectively
Rheumatoid factor	22.9 IU/mL
ANA screen	Negative
Citomegalovirus IgM & IgG	Negative
Parvovirus B19 IgG	Negative
Parvovirus B 19 IgM	5 Index (0-0.8)
HIV 1 & 2 antibody	Non reactive

Figure 1. Histiocyte with engulfed red cell

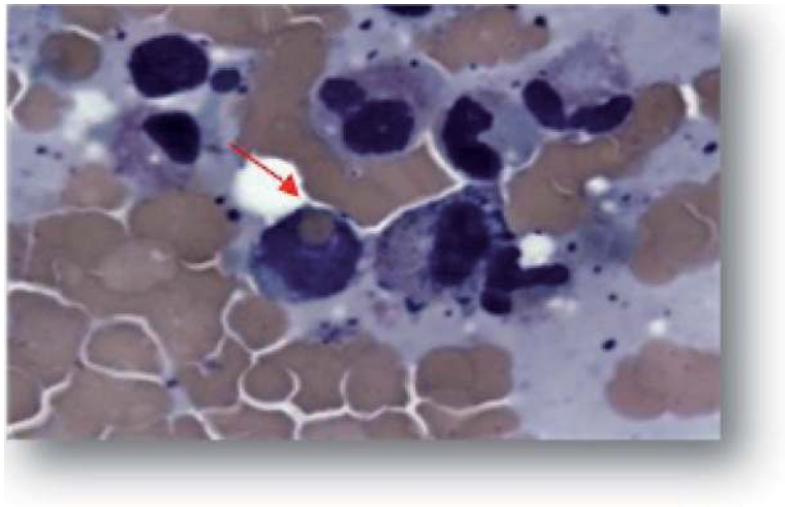
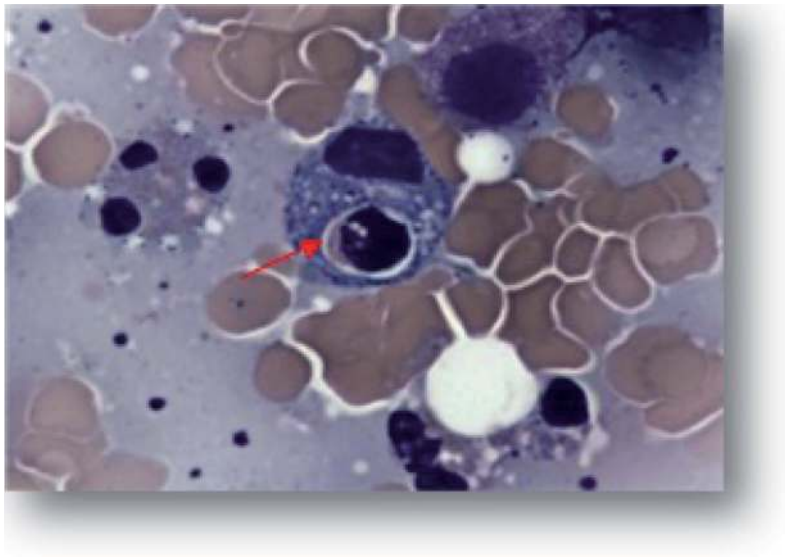


Figure 2. Histiocyte with nucleated cell



References

1. Janka G. Hemophagocytic lymphohistiocytosis: when the immune system runs amok. Klin Padiatr 2009;221:278.
2. Henter JI, Elinder G, Söder O, Ost A. Incidence in Sweden and clinical features of familial hemophagocytic lymphohistiocytosis. Acta Paediatr Scand 1991;80:428.
3. Janka GE. Familial and acquired hemophagocytic lymphohistiocytosis. Eur J Pediatr 2007;166:95.
4. Kaito K, Kobayashi M, Katayama T, Otsubo H, Ogasawara Y, Sekita T, et al. Prognostic factors of hemophagocytic syndrome in adults: analysis of 34 cases. Eur J Haematol 1997;59:247.
5. McClain K, Gehrz R, Grierson H, Purtilo D, Filipovich A. Virus-associated histiocytic proliferations in children: frequent association with Epstein-Barr virus and congenital or acquired immunodeficiencies. Am J Pediatr Hematol Oncol 1988;10:196.