Bol Med Hosp Infant Mex. 2016;73(1):26–30

Boletín Médico del
Hospital Infantil de México

www.elsevier.es/bmhim

CLINICAL CASE

Epstein-Barr virus-associated hemophagocytic lymphohistiocytosis: response to HLH-04 treatment protocol

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Received 30 November 2015; accepted 3 December 2015
Available online 28 February 2016

KEYWORDS
Hemophagocytic lymphohistiocytosis;
Hemophagocytic syndrome;
Epstein-Barr virus;
Protocol HLH-04

Abstract
Introduction: Hemophagocytic syndrome, macrophage activation syndrome, reactive histiocytosis or hemophagocytic lymphohistiocytosis (HLH) represent a group of diseases whose common thread is reactive or neoplastic mononuclear phagocytic system cells and dendritic cell proliferation.
Clinical case: We present a case of an HLH probably associated with Epstein-Barr virus (EBV) in a 4-year-old male patient treated with HLH-04 protocol. Viral etiology in HLH is well accepted. In this case, clinical picture of HLH was assumed secondary to EBV infection because IgM serology at the time of clinical presentation was the only positive factor in the viral panel.
Conclusions: Diagnosis of HLH is the critical first step to successful treatment. The earlier it is identified, the less the tissue damage and reduced risk of multiple organ failure, which favors treatment response.

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http://dx.doi.org/10.1016/j.bmhimx.2015.12.007

PALABRAS CLAVE
Linfohistiocitosis hemogafocítica;
Síndrome hemofagocítico;
Virus Epstein Barr;
Protocolo HLH04

Linfohistiocitosis hemofagocítica asociada con el virus de Epstein-Barr: respuesta al tratamiento con el protocolo HLH-04

Resumen
Introducción: El síndrome hemofagocítico, síndrome de activación de macrófagos, histiocitosis reactiva o linfohistiocitosis hemofagocítica (HLH) representan un grupo de enfermedades cuyo factor común es la proliferación reactiva o neoplásica de las células mononucleares fagocíticas y del sistema de células dendríticas.
Caso clínico: Se presenta un caso de HLH sugestivo de tener una asociación con el virus del Epstein Barr (VEB) de un paciente masculino de 4 años de edad, tratado con el protocolo HLH-04. La etiología viral en HLH es reconocida. En este caso se asumió un cuadro de HLH secundario a una infección por VEB, ya que la serología de IgM en el momento de la presentación clínica fue la única positiva en el panel viral.
Conclusiones: El diagnóstico de la HLH es el primer paso crítico para el éxito del tratamiento. Entre más temprano se identifique, existe menor daño tisular y menor riesgo de falla orgánica múltiple, lo que favorece la respuesta al tratamiento.

1. Introduction

Hemophagocytic syndrome, also known as macrophage activation syndrome, reactive histiocytosis or hemophagocytic lymphohistiocytosis (HLH), represents a group of diseases whose common factor is reactive or neoplastic proliferation of phagocytic mononuclear cells and of the dendritic cell system.[1] The International Histiocytosis Society coined the term to refer to a genetic disease with severe systemic inflammation,[2] which occurs as the result of a recessive genetic disorder associated with either defects in perforin or chromosome X-linked. The disease affects the communication of the innate and adaptive immune response, causing a lack of removal of the inflammatory cells harmful to the body and that should be removed once the inflammatory process has concluded. It is estimated that there are ∼1.2 cases per million/year. These are uncommon cases, but its diagnosis is important because the clinical pictures are very aggressive and evolve in a fulminant manner and with multiple organ failure if a precise and timely diagnosis is not carried out.[3] In this disease, T and B lymphocyte count and circulating monocytes show normal values. However, the defect is found in the function of T-lymphocytes and natural killer cells (NK) as well as in the activation of CD4 + and CD8 + T lymphocytes.[4] Other altered functions are the response of lymphocytes to mitogen activation, oxidation of glucose in phagocytes and, in some cases, decrease of IgA[5] antibodies. Clinical onset may be spontaneous. Prior reports described that ∼17% of the cases are associated with viral infections, among these, the Epstein-Barr (EBV) virus.[6] This report presents a case of HLH suggested to be associated with EBV.

2. Clinical case

We present the case of a 4-year-old male patient. The patient's mother was 33 years of age, healthy and denied any drug addictions. The father was 35 years of age with a secondary school education. He was apparently healthy and admitted occasional smoking. There is an apparently healthy 11-year-old brother. The patient is originally from and resident of Ecatepec, State of Mexico. The family lives in their own home with all urban services. Overcrowding or coexistence with animals was denied. The patient demonstrated adequate hygiene and dietary habits. Vaccination schedule was incomplete because there was a lack of DPT booster vaccine. The patient showed appropriate psychomotor development although he did not attend any child development center (Centro de Desarrollo Infantil, CENDI). The patient was the product of a GII with regular prenatal control and the mother received iron and folic acid intake from the first trimester without complications. The patient was born by cesarean section at 39 weeks of gestation due to nuchal cord. Usual resuscitation maneuvers were carried out. Apgar score was 8/9. The infant cried and breathed at birth. Birthweight was 3150 g and length was 54 cm. The infant was discharged without complications.

In March 2014, the patient began with right earache. He was seen in consultation by a private physician. Treatment with acetaminophen, ambroxol and amoxicillin was prescribed for 7 days, without improvement. He also began with fever up to 38.9 °C. Treatment with trimethoprim with sulfamethoxazole was added due to the persistence of fever. Complete blood count was done. Parameters low for age were seen for hemoglobin, hematocrit and platelets: hemoglobin 10.5 g/dl (reference value: 11.60-15.30 g/dl), hematocrit 31.7% (reference value: 35.6-46.52%), leukocytes 4,920/μl (reference value: 4,290-12400/μl), neutrophils 1082/μl (reference value: 983-3231/μl), bands 27%, atypical lymphocytes 5%, platelets 97,000/μl (reference value 147-384,000/μl).[7] Physical examination observed retroauricular and inguinal lymph nodes, hepatosplenomegaly, and persistent fever. The patient was referred to hematology for study protocol with diagnosis of lymphoproliferative syndrome.