Hemophagocytic lymphohistiocytosis secondary to visceral leishmania, the first Italian report

[1]Gargiullo L, [1]Gramatica L, [1]Romani L, [1]Roma D, [1]Calò Carducci FI, [1]Bernardi S, [1]D'Argenio P

[1]Unit of Immunology and Infectious Disease University Hospital Pediatric Departement, Children Hospital Bambino Gesù, Rome (Italy), Italy.

Objectives

Hemophagocytic lymphohistiocytosis (HLH) is a life-threatening inflammatory disorder, which can be fatal if untreated. Visheral Leishmaniasis (VL) is a severe parasitic disease endemic in Mediterranean Europe, with overlapping clinical manifestations with that of HLH; this similarity can mislead to the right diagnosis and management. In literature no cases of VL-HLH in Italy are described. The goal of our study was to describe all cases of VL-HLH in the last six years in Bambino Gesù Children's Hospital of Rome.

Methods

We analyzed all clinical registers from October 2006 to October 2012 reporting HLH cases secondary to VL; we considered HLH diagnostic criteria as reported in the Guidelines 2004 of Histiocyte Society. We collected the following data: age, country, clinical presentation, laboratory values, microbiological and bone marrow features.

Results 1

We observed one case of HLH secondary to VL out of 15 cases of VL. The patient was a 1-year-old male admitted to our hospital after 8 days of fever and onset of neurological symptoms (irritability alternated with drowsiness). Physical examination revealed only hepato-splenomegaly, palpable laterocervical and inguinal lymphnodes. Laboratory findings included: white blood count (WBC) 2,860/mm3, with absolute neutrophils count 820/mm3, hemoglobin 8 g/dL, platelets (PLTs) 85,000/mm3, C-reactive protein (CRP) 9.56 mg/dl, erythrocyte sedimentation rate (ESR) 99 mm/h, fibrinogen 163 mg/dL; ferritin 11,830 ng/mL; alanine aminotransferase 2164 UI/L, aspartate aminotransferase 2002 UI/L, γ-glutamyl transpeptidase 92 UI/L, ammonia 360 mg/dL, mild elevation of triglycerides (236 mg/dl). The microbiological work-up showed no evidence of active or chronic infection. The bone marrow aspiration showed hemophagocytosis and absence of malignant cells; flow cytometric analysis of perforin expression and natural killer (NK)-cell activity was normal.

Results 2

Based on the presence of six of the eight diagnostic criteria (Tab.1), a diagnosis of secondary non-infectious hemophagocytic lymphohistiocytosis was performed; he started specific immunosuppressive treatment. The child had an initial good response. Yet, one month later he was readmitted for refractory fever, cytopenia (hemoglobin 8,9 g/dL, WBC 3,960/mm3, PLTs 139,000/mm3), and persisting organomegaly. Laboratory findings showed elevation of CRP (8,34 mg/dl), ESR (105 mm/h), LDH (810 UI/L), ferritin (895 ng/ml) and fibrinogen (711 mg/dl); furthermore a severe increase of both IgG (1,756 mg/dl) and IgM (1,168 mg/dl) was observed, along with the inversion of the albumin/gamma-globulin rate (0.54). A bone marrow aspiration was performed, and PCR on bone marrow aspirate led to the diagnosis of HLH secondary to VL. Treatment with Lyposomal Amphotericin B was started; the child rapidly recovered.

TAB.1 Diagnostic Guidelines for HLH (one of either 1 or 2 below must be fulfilled)

A molecular diagnosis consistent with HLH
Diagnostic criteria for HLH fulfilled (five out of the eight criteria below)
Fever
Splenomegaly
Cytopenias (affecting 2 of 3 lineages in the peripheral blood)
Hypertriglyceridemia and/or hypofibrinogenemia
Hemophagocytosis in bone marrow or spleen or lymph nodes
No evidence of malignancy

References

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Conclusions

Leishmania is the only etiology of secondary HLH with an effective treatment that leads to complete eradication of the disease. Special caution should be paid for the research for this infection because immune suppression may result very detrimental in patients with HLH-VL.