DISSEMINATED HSV-2 INFECTION PRESENTING AS SECONDARY HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS WITH COMPLETE HEMATOLOGIC RECOVERY FOLLOWING ANTIVIRAL THERAPY

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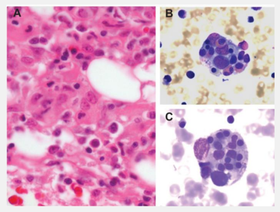
INTRODUCTION

Hemophagocytic lymphohistiocytosis (HLH) is a rare, life-threatening hyperinflammatory syndrome resulting from uncontrolled immune activation, excessive cytokine release, and multiorgan dysfunction. HLH may be primary or secondary (acquired), with secondary HLH triggered by infection, malignancy, autoimmune disease, or immunosuppression

AIM

The aim of this study was to explore a unique case of HLH triggered by HSV-2.



*Histopathology of HLH **(A)** Histopathology of a bone marrow section in HLH demonstrates marrow infiltration by macrophages (hematoxylin and eosin stained, 400x magnification). **(B, C) (1)***

HLH-2004 DIAGNOSTIC CRITERIA

Requires molecular diagnosis or 5 of 8 criteria

- Fever ≥ 38.5°C
- Splenomegaly ≥ 2 cm below costal margin
- Cytopenia affecting ≥ 2 cell lines
- Hypofibrinogenemia or hypertriglyceridemia
- Hyperferritinemia
- Hemophagocytosis in bone marrow
- Elevated soluble CD25
- Reduced or absent NK-cell activity

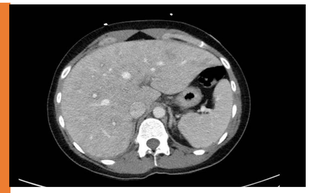
DISCUSSION

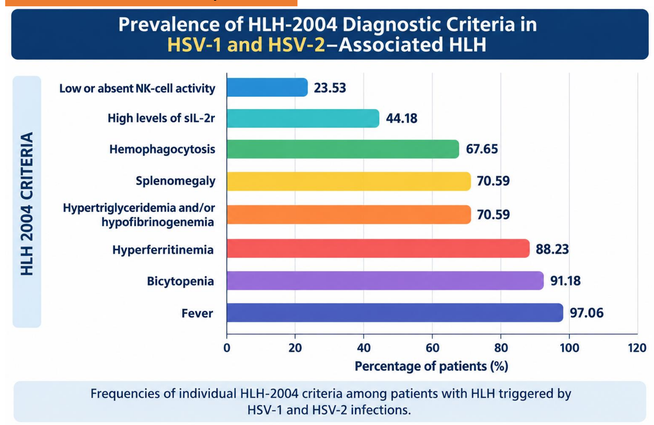
- **HSV-associated HLH is rare**, particularly in previously healthy adults, with reported mortality approaching **40%**.
- Identifying the **underlying infectious trigger** is critical for appropriate management.
- Reported HSV-associated HLH cases are commonly treated with **acyclovir and corticosteroids**, with additional HLH-directed therapy for severe cases.
- Our patient **improved with antiviral therapy alone**, without corticosteroids or HLH-directed immunochemotherapy.
- Following IV acyclovir and oral valacyclovir, **cytopenias resolved and ferritin normalized within 2 weeks**.
- **Early recognition and prompt antiviral therapy may be sufficient in selected clinically stable patients**, potentially avoiding the risks of immunosuppressive treatment.

CASE PRESENTATION

- 34-year-old previously healthy female. Recent travel to South America, with possible tick bite exposure, 6 weeks prior to symptom onset
- Initially presented to urgent care with acute onset fever and upper respiratory symptoms. Patient was diagnosed with, and treated for, a viral infection
- Returned to emergency department 1 week later with worsening high-grade fevers, fatigue, epigastric pain, nausea, nonproductive cough, and intermittent dyspnea lasting 7 days
- Bilirubin, INR, triglycerides within normal limits
- Imagining demonstrated hepatomegaly with periportal edema
- Infectious workup of viral serologies and PCR performed; **HSV PCR positive for HSV-2**; CSF positive for HSV-2 also
- **Bone marrow biopsy demonstrated hemophagocytosis**
- The patient met multiple HLH-2004 diagnostic criteria, including fever, cytopenia's, hyperferritinemia, and bone marrow hemophagocytosis.
- Treated empirically with IV acyclovir. Later transitioned to oral valacyclovir at discharge
- Following completion of antiviral therapy, pancytopenia resolved and ferritin levels normalized within 2 weeks

WBC	$1.7x10^9$/L
Hgb	10.6 g/dL
PLT	$103x10^9$/L
Bands	45%
AST	3500 U/L
ALT	1500 U/L
Ferritin	10,000 ng/mL
LDH	2400 U/L





Frequencies of individual HLH-2004 criteria among patients with HLH triggered by HSV-1 and HSV-2 infections.

CONTACT INFORMATION

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