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CASE REPORT

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Prompt treatment of disseminated HSV-2 infection in a patient with compromised cellular immunity: A case of aborted hemophagocytic lymphohistiocytosis?

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Abstract

Recognition of unusual manifestations such as disseminated HSV or HSV-related hemophagocytic lymphohistiocytosis among individuals with impaired cellular immunity and prompt treatment initiation are essential for a favorable outcome.

KEYWORDS

disseminated HSV-2, fingolimod, hemophagocytic lymphohistiocytosis, herpes simplex virus type 2

1 | INTRODUCTION

Unusual manifestations of HSV-related disease are becoming increasingly common in the era of modern immunosuppressive therapies. A high degree of clinical suspicion in the predisposed patient is essential for prompt treatment initiation. We present a case of disseminated HSV-2 infection in a patient with multiple sclerosis on treatment with fingolimod.

Disseminated type 2 herpes simplex virus (HSV-2) infection and related complications such as multiorgan dysfunction and hemophagocytic lymphohistiocytosis (HLH) is an uncommon entity increasingly encountered among individuals with impaired cellular immunity.[1]

2 | CASE REPORT

A 55-year-old man, with a history of multiple sclerosis under daily fingolimod 0.5 mg treatment for the past year, was admitted with a 3-day history of fever and disseminated rash. Physical examination revealed multiple vesicles and pustules in the genital area, trunk, extremities, and face, some of which were crusted (Figure 1). The patient was febrile (axillary temperature 39.1°C). Systematic physical examination was unremarkable. Laboratory tests revealed elevated ferritin, liver enzymes, and lactate dehydrogenase (LDH), and marginal platelet count. Blood and urine cultures, and HIV-1/2 and HBV/HCV serologic testing were negative. A direct immunofluorescence assay for HSV-2 antigen of trunk

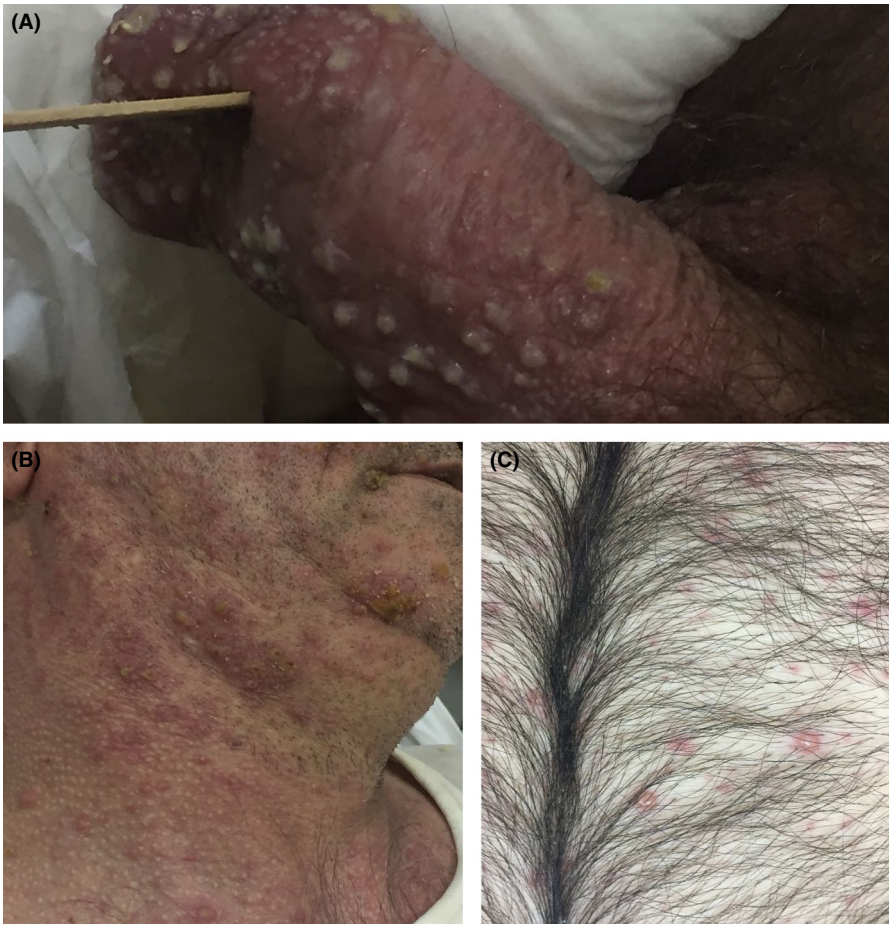

FIGURE 1 Initial skin lesions during presentation: multiple vesicles and pustules in genital (A), cervical-facial (B), and abdominal (C) areas

vesicle fluid was positive. A working diagnosis of disseminated HSV-2 infection was established, and treatment with intravenous acyclovir at 10 mg/kg/8 h was initiated. It should be noted that the patient was sexually inactive for a considerable time and there was no clear medical history of past HSV infection.

During the first 48 hours, he remained febrile and his complete blood counts diminished, and he developed marked hyperferritinemia raising the possibility of incipient HLH (Table 1). In further support of this scenario, the H-score attributed an 85% (calculated online at http://saintantoine.aphp.fr/score/) probability of HLH in our patient 48 hours after his admission. On the third day, however, a prompt improvement in his overall clinical status was observed, accompanied by a gradual normalization of his laboratory panel. Due to the rapid clinical improvement, no HLH-specific treatment was administered and the patient was discharged in a very good clinical condition after completion of 10 days on intravenous acyclovir.

TABLE 1 Patient's hematology and biochemistry profile during hospitalization period

	Day before admission (at another institution)	Admission	48 h after admission	Discharge
White blood cells(K/μL)	5340	8870	4.310	7760
Lymphocytes(K/μL)	390	549	459	690
Hemoglobin (g/dL)	16	16.2	13.5	14.1
Platelets (K/μL)	220	140	108	550
Aspartate transaminase (U/L)	-	117	150	28
Alanine transaminase (U/L)	-	139	171	56
Gamma-glutamyl transferase (U/L)	-	115	147	115
LDH (U/L)	-	363	537	139
Ferritin (ng/mL)	-	1924	3596	495

3 | COMMENT

Hemophagocytic lymphohistiocytosis is a rare and severe condition, which leads to uncontrolled hemophagocytosis because of activated and rapidly proliferating lymphocytes or histiocytes and cytokine overproduction. It can manifest itself either as a primary (familial) disorder, or as a secondary disorder to malignant, autoimmune, or infectious diseases, including herpetic infections.[2] Existing diagnostic criteria[3] include parameters that are seldom obtainable in unspecialized centers. Recently, a probability score (H-score) implementing clinical and routine laboratory features has been proposed and validated for adults.[4] On the grounds of a compatible clinical setting, a high probability of HLH as suggested by the H-score warrants further investigation to confirm the diagnosis or even initiation of emergency treatment in severe cases. In our case, it can be hypothesized that the irreversible cascade of events leading to HLH was intercepted by early treatment of the HSV-2 infection.

In the literature, few cases of HSV-2-associated HLH have been described.[5] Ikumi et al[6] described a fatal case of HSV-2-associated HLH in a 56-year-old man with MS on treatment with fingolimod. The identification of HSV-2 was achieved postmortem, by polymerase chain reaction in autopsy specimens. It can be presumed that in both our case and the one described by Ikumi et al, T cell–mediated immunity was severely impaired because of fingolimod treatment, resulting in dissemination of the HSV-2 infection. Despite its rarity, the possibility of disseminated HSV-2 and related complications such as HLH must be considered in a patient presenting with a compatible clinical picture. As in our patient, early identification and initiation of treatment can be decisive for a favorable outcome.

CONFLICT OF INTEREST

The authors declare no potential conflict of interest.

AUTHOR CONTRIBUTIONS

AT: wrote the original draft and conceptualized the study. DT: wrote the original draft and edited the manuscript. ER: conceptualized the study. EZ: reviewed the manuscript. DR: underwent supervision. EN: wrote, reviewed, and edited the manuscript.

CONSENT

Written informed consent was obtained from the patient for publication of this case report.

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