THE CLINICAL CHARACTERISTICS OF ACYCLOVIR-RESISTANT HERPES SIMPLEX VIRUS INFECTION IN IMMUNOSUPPRESSED PATIENTS

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INTRODUCTION

Herpes simplex virus (HSV) infection is common among immunosuppressed patients, especially following hematopoietic cell transplantation (HCT). Prophylaxis and treatment of recurrent infection relied primarily upon acyclovir (ACV). Infections due to ACV-resistant HSV strains have been reported in HCT patients. Those infections might be severe and even life-threatening and perceived as a challenge in the management of HCT patients.

Given the poor clinical outcomes and lack of documented cases of ACV-resistant HSV infections in immunosuppressed patients, our study aims to comprehensively describe this clinical condition.

METHODS

Medical records of patients diagnosed ACV-resistant HSV between the years 2009-2022 were retrieved and evaluated. The diagnosis was based on the clinical features and plaque reduction assay (figure 1) performed at the Sheba Medical Center Virology laboratory.

The demographics, medical background, clinical features of HSV infection and outcome of anti-viral treatment were recorded.

The study was approved by the Sheba Medical Center Institutional Review Board.

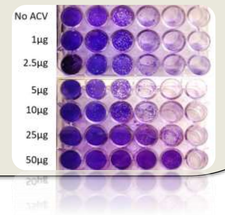

Figure 1: plaque reduction assay

RESULTS

	Age	Gender	Time from HCT to HSV (month)	ACV prophylaxis at HSV oral manifestation	*First line treatment duration (days)	**Second line treatment duration (days)	Disseminate infection	Outcome at follow-up
Patient 1	34	F	4	No	28	14	Brain	Deceased
Patient 2	42	F	3	No	14	50	Vaginal	Deceased
Patient 3	30	M	1	Yes	7	14	Eyes	Partially recovered
Patient 4	21	F	2	No	3	21	-	Recovered
Patient 5	52	F	1	No	3	7	-	Recovered
Patient 6	33	F	8	Yes	30	30	GI	Deceased
Patient 7	53	M	2	No	4	27	GI	Recovered
Patient 8	65	F	33	No	14	7	-	Deceased
Patient 9	32	M	3	Yes	180	-	-	Recovered
Patient 10	21	F	5	Yes	27	40	-	Recovered

*Table: Patients characteristics. * First line treatment- ACV low/high dose. ** Second line treatment- Foscarnet, Ganciclovir*

A total of 10 ACV resistant HSV cases were reviewed. All patients (7 females and 3 males) were diagnosed with hematological malignancies and underwent HCT. Median age at hematological diagnosis was 38 years (range 21-65). Oral manifestations of ACV-resistant HSV occurred within the first year post-HCT in most cases; only one patient developed a later infection (3 years post-HCT). At HSV diagnosis, only four received ACV prophylaxis. Among majority of cases (90%) oral manifestation was multifocal and presented with atypical lesions (figure 2). One case was localized. Disseminate infection was noted in half of the cases including the gastrointestinal tract (2 patients), genitalia (1 patient), eye (1 patient) and cerebral spinal fluid (1 patient). The average first line treatment duration with ACV was 31 days and 23 days for the second line treatment. At follow-up, 5 patients fully recovered, 1 patient demonstrated signs of HSV infection (eye) and 4 patients deceased.

Figure 2A: Multifocal atypical appearance of ACV-resistant HSV (patient 8)

Figure 2B: Partial heling after 5 days of high dose ACV

CONCLUSIONS

Our preliminary results are aligned with the literature regarding ACV-resistant HSV in patients during their first year post-HCT. In any case of long-standing, multifocal, atypical lesions in post HCT patients, ACV-resistant HSV should be considered. Other organs (e.g. brain, eyes, genitalia, GI) may be involved. Second-line antiviral therapy is necessary in most cases. The side effects associated with such treatment endanger this group of patients. Additional preventive treatments such as daily mouth rinses, may be considered to reduce viral infectivity. Further research is needed to fully understand the mechanism associated with resistance development.

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