

Infectious Complications in Adult Patients with Hemophagocytic Lymphohistiocytosis: A Single Center Experience

Joanna K. Nelson, MD; Beth Martin, MD; Eric Lau, DO; Dora Ho, MD, PhD

(1) Division of Infectious Diseases & Geographic Medicine, (2) Division of Hematology, Department of Medicine, Stanford University School of Medicine, Stanford, CA; 3) Department of Medicine, Santa Clara Valley Medical Center, San Jose, CA, USA

Correspondence: Joanna Nelson, 300 Pasteur Dr., Lane Bldg., L134, Stanford CA 94305-2200
Phone: (650) 736-0768 / Fax: (650) 498-9876. joanna2@stanford.edu

Background

- Hemophagocytic lymphohistiocytosis (HLH) is a rare hematologic disorder which is characterized by excessive immune activation. In adults, it is typically secondary to an underlying process such as autoimmune disease, infection, or malignancy.
- Guidelines based on expert opinion suggest prophylaxis with antiviral, antibacterial, and/or anti-fungal agents for patients undergoing treatment for HLH.
- The incidence of infectious complications in patients with HLH is not known.

Objectives/Aims

- We aimed to study the scope of infection in patients with HLH to help determine the best strategy for antimicrobial prophylaxis.

Methods

- We performed a retrospective chart review of 56 adult patients who fulfilled clinical diagnostic criteria for HLH treated at Stanford University Hospital between 2012-2018.
- Infections diagnosed from 1 month prior to 6 months after a diagnosis of HLH were reviewed. Infection related variables were collected, and descriptive statistics were performed.

Limitations

- Majority of patients reviewed received some form of prophylaxis, which likely impacted the number and types of infection that developed.
- This was a single center study.

Results

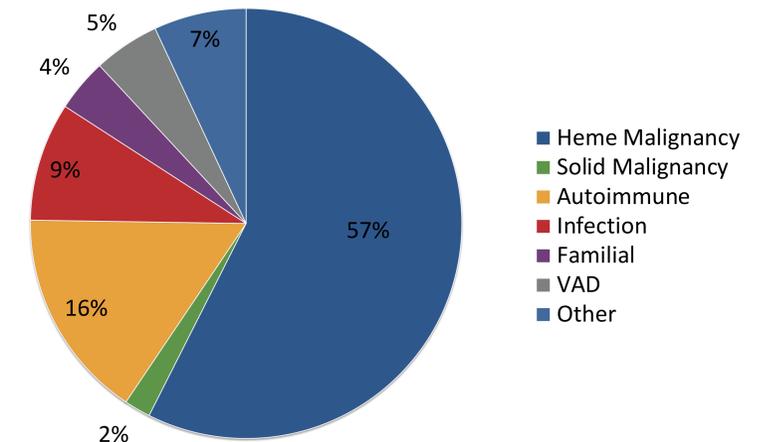
- A total of 94 infections were found in 33 of 57 episodes (58%) of HLH among 56 patients.
- 27 infections were diagnosed prior to HLH diagnosis and 67 infections were diagnosed after the diagnosis of HLH.
- The majority of infections pre-HLH diagnosis were viral, and most due to EBV (n=16). 13 of these had concomitant EBV-associated malignancies. Infection was thought to be a significant trigger of HLH in 5 cases: EBV (3), MAC (1), Histoplasma (1).
- Types of infections that occurred after the diagnosis of HLH:
 - Bacterial: n=46** (occurred in 44% of HLH episodes): Bacteremia (20), pneumonia (7), soft tissue (6), intraabdominal (5), urinary tract infection (6), other (2).
 - Fungal: n=11** (19% of HLH episodes): 9 proven and 2 possible (see Table)
 - Viral: n=10** (16% of HLH episodes): CMV (4), HHV6 viremia (3), H1N1 influenza (1), BK viruria (1), RSV (1)

Proven Fungal Infections

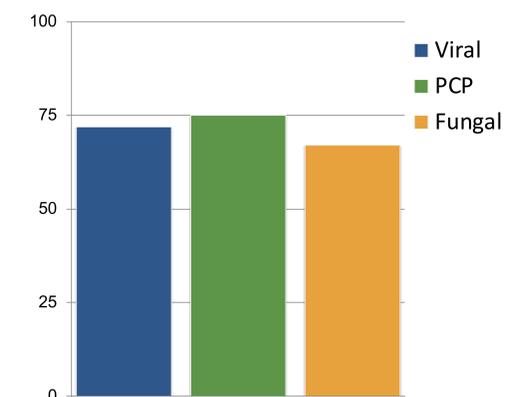
Diagnosis	Microbiology	Time of dx*	Cause of HLH	Days ANC <500	ANC at dx	Prophylaxis	Outcome: IFI related mortality
Fungemia	Rhodotorula mucilaginosa	70	T-cell lymphoma	10	1340	none	yes
Fungemia and retinitis	Candida albicans	44	T-cell lymphoma	17	0	posaconazole	no
Fungemia	Candida glabrata	115	T-cell lymphoma	26	1660	posaconazole	yes
Fungemia	Candida glabrata	20	MAC	11	0	posaconazole	no
Pulmonary and mediastinal mucormycosis	Rhizopus	28	T-cell lymphoma	20	1000	posaconazole	no
Orbital mucormycosis	Rhizopus	25	MM/MDS	0	8590	none	yes
Pulmonary and CNS Aspergillosis	Aspergillus fumigatus	15	DLBCL	14	600	fluconazole	no
Pulmonary mucormycosis	Syncephalastrum	65*	RA	n/a	0	caspofungin	yes
Disseminated mucormycosis	Rhizopus	12*	Stills dz	7	0	caspofungin	yes

+ days after HLH diagnosis made
* diagnosed post-mortem

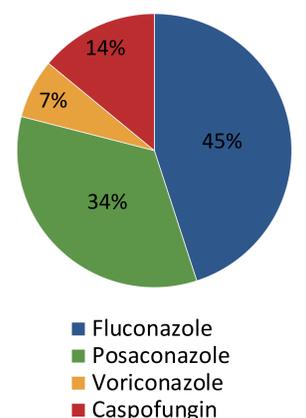
Etiology of HLH



Percentage of HLH patients started on prophylaxis



Fungal prophylaxis



Conclusions

- Infectious complications of HLH are common, and likely result from a combination of host immune factors related to underlying disease and induced by immunosuppressive chemotherapy.
- Most noteworthy is the high incidence of fungal infections which supports the use of antifungal prophylaxis in this patient population.
- Even with prophylaxis, breakthrough fungal infections, including with opportunistic molds, is not uncommon.