

Letter

Improving Outcomes for Patients With Hemophagocytic Lymphohistiocytosis

To the Editor:

Hemophagocytic lymphohistiocytosis (HLH) is a rare syndrome of uncontrolled immune activation often triggered by genetic defects in the primary form, and also by infection, rheumatic diseases, and malignancy in the secondary form. It is characterized by fever, hyperferritinemia, cytopenias, hepatosplenomegaly, and multiorgan dysfunction.^{1,2} Although diagnostic criteria exist, the signs and symptoms of HLH being nonspecific often result in delayed diagnosis, which adversely affects the course and prognosis of the disease. HLH should be considered for children presenting with persistent fever, hepatosplenomegaly, and cytopenias, because initiation of a timely treatment to suppress the severe hyperinflammation is imperative to greatly increase chances of survival among these patients.³ Formation of a dedicated workgroup to HLH within a hospital system may aid in improving the approach to the diagnosis of HLH and increase awareness among providers. We note a recent study by Taylor et al that addressed the challenge of managing macrophage activation syndrome and HLH within an academic hospital institution through implementation of evidence-based guidelines that were established by consensus across multiple pediatric subspecialties.⁴ The described approach to the diagnosis and management of HLH by this hospital institution prompted us to take this opportunity to describe our preliminary findings of implementing a disease-specific multidisciplinary workgroup at Cook Children's Medical Center (CCMC).

A less-than-consistent diagnostic and therapeutic approach to suspected HLH within our hospital system led to the formation of this workgroup, preliminarily established to streamline the diagnostic approach and improve the management of HLH and related rare disorders. At CCMC, the workgroup was established in 2019 and consisted of specific members identified based on interest, including expertise from the following departments and specialists: hematology/oncology (attending and nurse practitioner), infectious disease, rheumatology, neonatal intensive care unit, pediatric intensive care unit, hospitalist group, and clinical pharmacists, as well as rotating medical students. Due to CCMC being a nonacademic institution, the support and resources of the workgroup have been driven primarily by motivated providers. Since formation, the HLH workgroup has met every 3 months to discuss cases within the hospital and any advancing research relevant to the diagnosis and management of HLH. The popularity of the workgroup within the hospital grew through newsletters that were circulated via emails sent on Fridays, called "Friday Facts," which included foundational information and the latest research on HLH.

As part of our endeavor to streamline laboratory workup surrounding this rare entity, an electronic order set specific to

the HLH diagnostic criteria was developed and implemented by our workgroup at our institution in 2019. The goal of implementation was to increase awareness across multiple pediatric subspecialties and improve outcomes of patients presenting with signs and symptoms suspicious of HLH. A quality improvement study is currently being planned to investigate the trends of use of the HLH order set and the impact on quality care metrics such as time to diagnosis, duration of illness, severity of illness, and completed treatment of patients with a suspected diagnosis of HLH.

To the best of our knowledge, evaluation of the effect of establishing a multidisciplinary team dedicated to HLH within a nonacademic institution, such as CCMC, has not been described. Disease-specific workgroups within a nonacademic institution are unique from those established in an academic institution, as nonacademic institutions do not have residents or fellows to support the group and, generally, there is limited funding for research and resources when compared to an academic institution. Considering the recent study finding associated improved clinical outcomes for children with HLH after the implementation of a streamlined approach to HLH,⁴ it is relevant to investigate the outcomes at other institutions. We hope to reinforce the importance of developing a collaborative approach to the diagnosis and management of HLH. Additionally, the goal is to encourage other nonacademic institutions to implement dedicated multidisciplinary workgroups and a disease-specific order set for HLH that can increase awareness of HLH and streamline the process of its diagnosis and management.

Meaghan Rousset¹ , BS

Anish Ray² , MD

¹Anne Burnett Marion School of Medicine at Texas Christian University;

²Department of Pediatric Hematology/Oncology, Cook Children's Medical Center, Fort Worth, Texas.

The authors declare no conflicts of interest relevant to this article.

Address correspondence to Dr. A. Ray, Department of Pediatric Hematology/Oncology, Cook Children's Health Care System, 1500 Cooper St., 5th floor, Fort Worth, TX, 76104, USA.

Email: Anish.Ray@CookChildrens.org.

REFERENCES

1. Henter JI, Horne A, Aricó M, et al. HLH-2004: Diagnostic and therapeutic guidelines for hemophagocytic lymphohistiocytosis. *Pediatr Blood Cancer* 2007;48:124-31.
2. Emile JF, Abl O, Fraïtag S, et al; Histiocyte Society. Revised classification of histiocytoses and neoplasms of the macrophage-dendritic cell lineages. *Blood* 2016;127:2672-81.
3. Kaçar AG, Celkan TT. Hemophagocytic Lymphohistiocytosis. *Balkan Med J* 2022;39:309-17.
4. Taylor ML, Hoyt KJ, Han J, et al. An evidence-based guideline improves outcomes for patients with hemophagocytic lymphohistiocytosis and macrophage activation syndrome. *J Rheumatol* 2022;49:1042-51.