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Poster A Novel Inflammatory Index is Sufficient to Identify Hemophagocytic Lymphohistiocytosis in Adult Patients with Hematologic Malignancies

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INTRODUCTION

Hemophagocytic lymphohistiocytosis (HLH) is a life-threatening hyper-inflammatory syndrome which may occur in adults with hematologic malignancies (HM). The diagnosis of HLH in this context (HM-HLH) is hindered by the fact that currently used HLH 2004 diagnostic criteria are derived from pediatric patients with genetic lesions, a very different population than adults with cancer. Moreover, most parameters used for diagnosis of HLH are directly impacted by the underlying HM and may reflect the presence of the malignancy rather than an inflammatory process.

OBJECTIVES

In this study we determine the diagnostic value of the laboratory components of the HLH 2004 diagnostic criteria and establish optimal cutoffs for the diagnosis of HM-HLH in HM patients.

METHODS

A multicenter, retrospective study of adult patients with HM included patients in whom sCD25 was measured. We established the optimal cutoffs for laboratory parameters used for the diagnosis of HM-HLH using receiver operating curves (ROC) in a discovery cohort and tested their performance in a validation cohort. We then examined the performance of each parameter in each cohort by using a contingency table and Chi-square and Fisher's exact test to determine the diagnostic performance of established cutoffs.

RESULTS

212 adults with HM with or without HLH in whom testing for HLH was performed were included in the study. Despite considerable overlap in laboratory values (figure 1) ferritin and sCD25 had the greatest discriminatory power. ROC analysis (figure 2) revealed an optimal cutoff value of >5,600 U/mL for sCD25. Combining the two markers to create a novel inflammatory index (HLH-INFL) yielded superior diagnostic ability (AUC =0.86). Using HLH 2004 cutoff levels the HLH-INFL index had a sensitivity of 94% and NPV of 94% and when using the optimal cutoff levels, it had a specificity of 92% and PPV of 90% (Table 1).

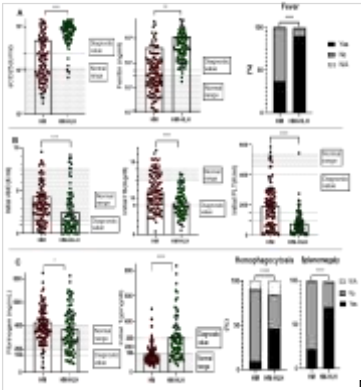
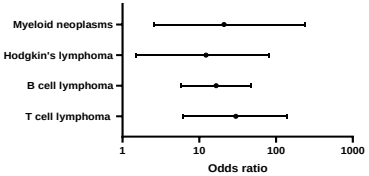


Figure 1. A significant overlap in the distribution of all HLH 2004 diagnostic markers exists between patients with uncomplicated hematologic malignancies and patients with malignancies complicated by HLH

	Discovery cohort N = 120					Validation cohort N = 52				
	Sens	Spec	PPV	NPV	LR	Sens	Spec	PPV	NPV	LR
sCD25 >2,460 U/mL	0.88	0.81	0.67	0.94	2.9	0.86	0.82	0.7	0.94	2.6
Ferritin >500ng/mL	0.88	0.37	0.43	0.87	1.3	0.85	0.41	0.7	0.94	1.5
sCD25 >5,600 U/mL and ferritin >500 ng/mL	0.94	0.79	0.78	0.94	4.5	0.86	0.77	0.78	0.85	4.1
sCD25 >5,600 U/mL	0.81	0.79	0.75	0.84	3.7	0.84	0.77	0.77	0.84	3.6
Ferritin >1,000 ng/mL	0.81	0.75	0.73	0.9	3.6	0.86	0.75	0.74	0.88	3.5
sCD25 >5,600 U/mL and ferritin >1,000	0.8	0.93	0.9	0.88	13.4	0.73	0.94	0.91	0.79	11.6

Table 1. A novel inflammatory index (HLH-INFL) comprising ferritin and sCD25 levels improves diagnostic accuracy. PPV- positive predictive value; NPV- negative predictive value; LR- likelihood ratio.



HLH-INFL index is associated with HLH across all types of malignancies

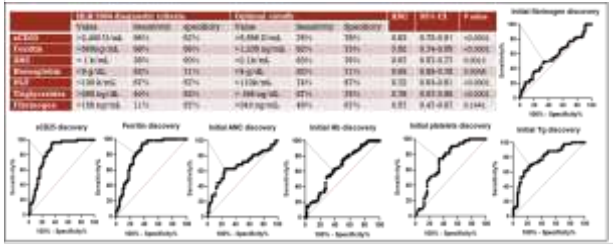


Figure 2. Inflammatory markers rather than other diagnostic criteria discriminate better between patients with uncomplicated hematologic malignancies and patients with HLH in the context of hematologic malignancies

CONCLUSIONS

1. Ferritin and sCD25, though nonspecific, are the most sensitive markers for diagnosing HLH in patients with hematologic malignancies.
2. An index of optimized sCD25 and ferritin is highly accurate for identifying patients with HLH in the context of hematologic malignancies.