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POSTER ABSTRACTS

201.GRANULOCYTES, MONOCYTES, AND MACROPHAGES

Myelodysplastic Syndrome Associated Hemophagocytic Lymphohistiocytosis: A Retrospective Study of 15 Cases in a Single Center

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Introduction:
Hemophagocytic lymphohistiocytosis (HLH) is a life-threatening disorder characterized by excessive cytokine secretion, resulting in hyperinflammation and multiorgan dysfunction. It is classified into primary HLH, which is mainly caused by genetic defects, and secondary HLH, triggered by various underlying conditions. Malignancy-associated HLH (M-HLH) is a secondary form commonly observed in patients with hematological malignancies, such as lymphomas, T/NK-cell disorders, acute leukemias, lymphoproliferative diseases, and myelodysplastic syndrome (MDS). M-HLH can occur in up to 1% of patients with hematologic malignancies, with lymphoma being the most frequently associated malignancy. HLH initiated by MDS is a rare entity with only a few cases reported, leading to limited knowledge regarding its pathogenesis, diagnosis and optimal treatment strategies.
Methods:
In this retrospective study, we analyzed a consecutive series of MDS-HLH patients admitted to our center between March 1, 2019, and March 1, 2023. Bio-clinical data related with MDS and HLH were collected at diagnosis of MDS-HLH. Additional observational indicators encompassed the following: basic clinical characteristics of the patients (age at onset, gender, duration of MDS prior to HLH), correlation between the onset of HLH and MDS, treatment and response, and genetic defects associated with HLH and MDS. MDS risk classification was according to the Revised International Prognosis Scoring System (IPSS-R) and the WHO classification-based Prognosis Scoring System, while patients were categorized into two groups as higher-risk and lower-risk MDS-HLH group. The follow-up period started at the time of MDS-HLH diagnosis and ended at the date of death or last examination. Overall survival (OS) was calculated from the time of HLH diagnosis to the date of death from any cause.
Results:
A total of 15 patients diagnosed with MDS-HLH were included in the study, with a median age of 66 years (range, 33-83 years). The majority of patients (10/15, 67%) were over 60 years old. All patients exhibited typical features of aggressive HLH: fever, cytopenia and elevated serum ferritin in all patients, hepatomegaly/splenomegaly in 87% (13/15), hypofibrinogenemia/hypertriglyceridemia in 73% (11/15), hemophagocytosis in 73% (11/15), low NK-cell activity in 21% (3/14), and elevated levels of sCD25 in 93% of patients (14/15).
Additionally, four patients (27%) had concurrent Epstein-Barr virus (EBV) infection. Further analysis comparing the lower-risk and higher-risk MDS-HLH groups revealed interesting findings. In the lower-risk group, all patients developed HLH concurrently with the diagnosis of MDS. However, in the higher-risk group, the majority of patients (6/8, 62.5%) experienced HLH onset during MDS progression or relapse (p=0.014).
Among the 15 patients, 8 patients (53.3%) achieved remission of HLH. During the study period, 8 deaths occurred, all directly attributed to HLH or its complications. The majority of deaths (75%, 6/8) occurred within the first two months after HLH diagnosis. The median overall survival was 12.3 weeks (95%CI, 1.1-23.5). Patients who achieved complete or partial response had significantly prolonged overall survival compared to those who did not respond to treatment (p=0.002). In the multivariate analysis of prognosis, the remission status of HLH was the only factor which was significantly associated with survival (p=0.018, Exp(B)=0.003).
Conclusion:

This is the first comprehensive study focusing specifically on MDS-HLH, providing valuable insights into the clinical characteristics, treatment outcomes, and prognosis of MDS-HLH. The findings emphasize the need of considering revision of diagnostic criteria specially for MDS-HLH.
The pathogenesis of HLH in MDS-HLH differs based on the risk classification of MDS, with higher-risk cases driven by malignancy and lower-risk cases associated with immune dysfunction. The prognosis of MDS-HLH is generally poor. Achieving remission of HLH is crucial for improving the prognosis of MDS-HLH patients. Conventional chemotherapy regimens, including etoposide, have shown limited efficacy and safety in this context. Chemotherapy-free regimens should be preferred considering the features of ineffective hematopoiesis in MDS. The role of EBV infection in MDS-HLH development should be recognized.

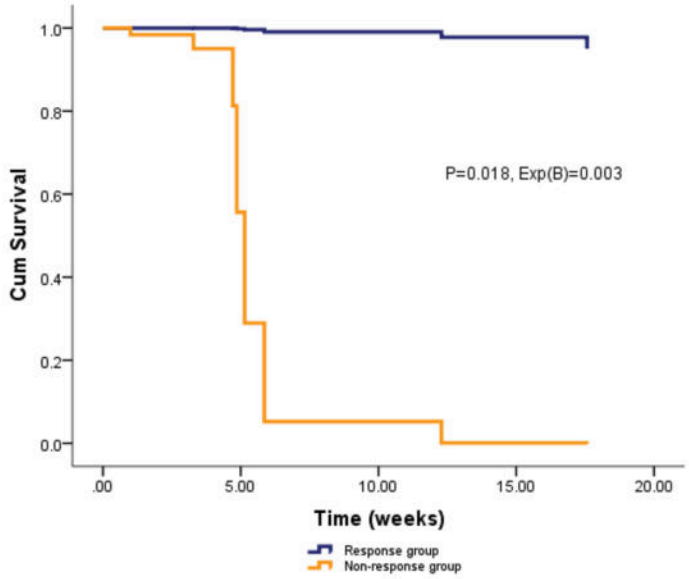
Disclosures No relevant conflicts of interest to declare.

Table 1 Clinical characteristics of the patients between lower-risk and higher-risk MDS-HLH groups.

Clinical features	Lower-risk MDS-HLH	Higher-risk MDS-HLH	p valve
	(n=7)	(n=8)	
Age, years			
Median	73	55.5	0.196
Range	[33, 83]	[44, 71]	
Gender			0.782
Male (n)	4	4	
Female (n)	3	4	
MDS status at HLH			0.026
New diagnosis	7	3	
Progress/Relapse	0	5 (62.5%)	
Fever (T>38.5℃)	7 (100%)	8 (100%)	
Splenomegaly (n)	6 (86%)	7 (88%)	1.00
Haemophagocytosis (n)	6 (86%)	5 (63%)	0.569
WBC (*10^9/L)	2.22 [1.17, 4.06]	1.12 [0.43, 52.46]	0.232
HGB (g/L)	85 [62, 120]	61 [54, 97]	0.121
PLT (*10^9/L)	45 [16, 83]	15.5 [8, 24]	0.014
ALT (U/L)	37.9±17.5	66.6±77.9	0.358
AST (U/L)	44.1±22.5	67.25±71.1	0.426
LDH (U/L)	416±189	645±540	0.308
Total bilirubin (μmol/L)	16.8±5.1	29.5±28.2	0.264
TG (mmol/L)	2.04±0.89	2.35±1.32	0.620
Fbg (g/L)	2.68±1.09	2.70±1.09	0.973
Ferritin (ng/mL)	7555±8234	8875±9797	0.784
sCD25 (pg/mL)	28330±27904	24559±21760	0.773
IL-6 (pg/ml)	46.9 [6.7, 164.3]	45.8 [4.4, 452.2]	0.949
IL-10 (pg/ml)	404.3 [2.4, 2625.0]	35.1 [7.9, 4304.7]	0.848
IFN-r (pg/ml)	4.2 [0, 114.4]	10 [0.4, 534.4]	0.655
Decreases NK cell activity, n	1/7 (14%)	2/7 (29%)	0.515
EBV-positive	1/7 (14%)	3/8 (38%)	0.569
Genetic defects related with HLH	1/4 (25.0%)	1/3 (33.3%)	0.809
Genetic defects related with MDS (>10%)	1 (14.3%)	7 (87.5%)	0.010
Chemotherapy contained	1 (14.3%)	2 (25.0%)	0.605
Remission of HLH	4 (57.1%)	4 (50%)	0.782
Outcome			
Death	4 (57.1%)	4 (50%)	0.782
Survival	5.1w [95%CI (4.2, 6.0)]	17.6w [95% (0, 40.9)]	0.365

the valve was expressed as median [range] or mean± standard deviation.

Figure 1 Survival function of MDS-HLH patients (COX analysis).



The remission status of HLH was significantly associated with survival in the multivariate analysis with COX analysis. MDS-HLH patients achieving at least partial remission having a better prognosis (p=0.018, Exp(B)=0.003).

Figure 1

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