Hemophagocytic Lymphohistiocytosis Singularity: A Multicenter Retrospective Study

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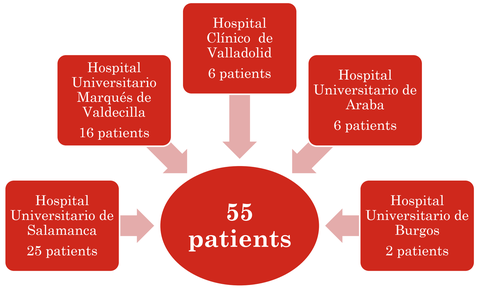
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Background

Hemophagocytic lymphohistiocytosis (HLH) is characterized by an excessive inflammatory response due to aberrant activation of macrophages and T lymphocytes[1]. Cases of primary HLH (genetic mutations) are usually diagnosed in childhood, while secondary cases (due to neoplasms or infections, among others) appear predominantly in adults[2]. Early diagnosis and treatment are essential to reduce the high mortality rate associated with this syndrome[3].

Materials & Methods

A retrospective multicenter analysis of 55 patients diagnosed with HLH between 2004 and 2021 in five Spanish centers was performed. The main etiologies, treatment strategies employed and the evolution of the patients were collected.



Results (1)

Median age at diagnosis was 54 years (range 0-82). All patients in whom the determination was performed presented hyperferritinemia (>10000ng/mL in 56.5%). Bone marrow hemophagocytosis was observed in 87.3%.

Table 1. Main characteristics of patients who met diagnostic criteria for HLH.

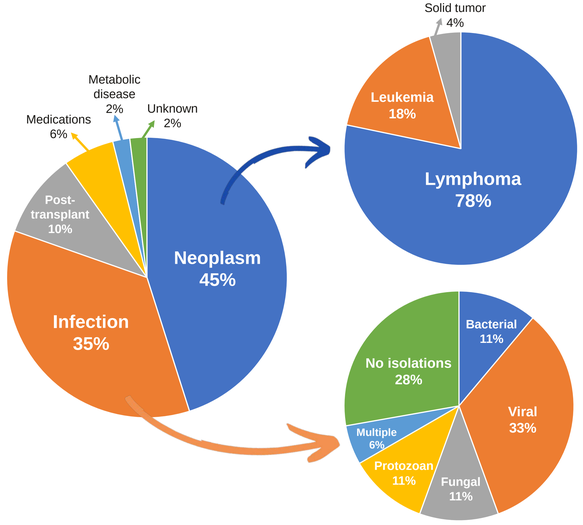
Variable	Present	Absent	Not available	Median (range)
Fever*	49 (89.1%)	6 (10.9%)	0	
Splenomegaly*	41 (74.5%)	14 (25.5%)	0	
Cytopenias† involving two or more cell lines*	49 (89.1%)	6 (10.9%)	0	
Triglycerides >265mg/dL*	36 (65.5%)	14 (25.4%)	5 (9.1%)	332 (92-1343)
Fibrinogen <150mg/dL*	25 (45.45%)	25 (45.45%)	5 (9.1%)	161 (43-1021)
Ferritin >500ng/mL*	46 (83.6%)	0	9 (16.4%)	10418
>10000ng/mL	26 (47.3%)	20 (36.3%)	9 (16.4%)	(941-90670)
Hemophagocytosis*	48 (87.3%)	6 (10.9%)	1 (1.8%)	
sCD25>2400U/L*	11 (20%)	5 (9.1%)	39 (70.9%)	
Decreased NK-cell activity*	5 (9.1%)	6 (10.9%)	44 (80%)	
Liver enzyme alteration	52 (94.5%)	3 (5.5%)	0	
LDH>250	49 (89%)	4 (7.2%)	2 (4.8%)	772 (132-6570)
Leukoerythroblastic syndrome	8 (14.5%)	35 (63.8%)	12 (21.7%)	
HS score>169	52 (94.5%)	3 (5.5%)	0	230 (164-321)

* Diagnostic criteria; † Hb<9g/dL, neutrophils <1000/mm^3 or platelets <100000/mm^3

HLH was primary in 4 patients (3 of them belonged to the same family and had a homozygous mutation in the *UNC13D* gene) and the remaining 92.7% were secondary, with the most frequent causes being neoplasms (23 patients, 45.1%) and infections (18 patients, 35.3%).

Results (2)

Figure 1. Etiologies of secondary HLH

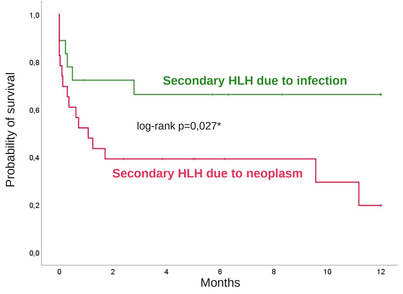


Of the patients who were able to receive treatment, 18 (42%) achieved complete response (CR), with a median of 23 days to response, and only 2 of these patients (13%) relapsed.

First-year overall survival (OS) was 40%. Patients with HLH secondary to neoplasia had significantly lower OS than those secondary to infection (30.4% vs. 66.7%; p=0.027).

Results (3)

Figure 2. Comparison of first-year OS in patients with secondary HLH



It should be noted that 42% of the patients died within the first month of diagnosis and that 27% were diagnosed with necropsy.

Conclusions

- In HLH a high diagnostic suspicion is essential in order to identify and treat the underlying etiology.
- The prognosis of the disease continues to be disappointing, so efforts should focus on early diagnosis and the search for new therapeutic strategies.

References

1. Hemophagocytic lymphohistiocytosis: An update on pathogenesis, diagnosis, and therapy. *Best Pract Res Clin Rheumatol.*
2. Hemophagocytic lymphohistiocytosis: Pathogenesis, diagnosis, and management. *Pediatr Int.*
3. Hemophagocytic Lymphohistiocytosis. *Annu Rev Pathol.*