Hemophagocytic syndrome in patients from SLE Registry from the Spanish Society of Rheumatology (RELESSER)

A Lois-Iglesias[1], I Rua-Figueroa[2], F deToro-Santos[1], A Zea-Mendoza[3], J López-Longo[4], J Calvo[5], M Galindo[6], E Uriarte-Isacelaya[7], J Pego-Reigosa[8,9], on behalf of EASSER-RELESSER

[1]University Hospital A Coruña, A Coruña; [2]Hospital Universitario Dr Negrin, Gran Canaria; [3]UniversityHospital Ramón y Cajal; [4]HGUGregorio Marañón, Madrid; [5]Hospital, Araba; [6]University Hospital 12 de Octubre, Madrid; [7]University Hospital Donostia, Donostia; [8]Hospital Vigo; [9]IISGS, Vigo, Spain

Background Systemic Lupus Erythematosus (SLE) is an autoimmune systemic rheumatic disease that, in our area, presents hematologic manifestations in approximately 70% of cases[1]. Some of them are very rare so there are no large series whose analysis could provide relevant information.

Objectives To study the characteristics of patients with Hemophagocytic Syndrome (HS) in a large sample of SLE patients.

Methods SLE patients from RELESSER database were studied. We analysed SLE manifestations present at 12 different domains (mucocutaneous, renal, musculoskeletal, constitutional, hematologic, vascular, cardiac, respiratory, neuropsychiatric, gastrointestinal, ophthalmic and serological) before, during and after HS diagnosis and until the last available assessment. We also studied activity (SELENA-SLEDAI) and damage (SLICC/ACR DI) indices at those moments.We evaluated the treatment received, HS recurrences and the number of deaths by this entity.

Results 3,656 SLE patients (≥4 ACR criteria) from 45 Rheumatology Units across Spain were studied. Seven patients (<0.5%) with HS were identified. 71.4% were women, with a mean age (± S.D.) at SH diagnosis of 35.1 (± 17.1) years. In 5 of the 7 cases the HS occurred 115.5 (± 162.9) months after SLE diagnosis. In the other 2 cases the diagnosis of both entities was simultaneous. The main triggers of HS were infections, followed by SLE activity flares. At the time of HS diagnosis, they had high SLE activity with a mean SLEDAI score of 13.1 (± 11.3) and 1.4 (± 2.3) SDI score.
Clinically, 100% of the patients presented fever and alterations of the liver profile, 85.8% cytopenias and 71.5% dermatological manifestations. Respiratory manifestations and hemolytic anemia were present in 57.2% of the cases, both; lymph nodes and coagulopathy in 42.9%. Hepatomegaly was detected in 28.6%, as well as neuropsychiatric, digestive and renal manifestations. Splenomegaly was detected in 14.3%. The mean hemoglobin level was 8.6 (± 1.1) g/dl, platelets 85,585 (± 83,390)/mm^3, ferritin 7,410 (± 6,470) ng/ml and triglycerides 404.7 (± 235.6) mg/dl. All patients were admitted and undergonebone marrow study, requiring a mean of 2.2 (± 1.5) treatment lines, using 2.8 (± 1.7) drugs. One patient died during the HS episode by the HS itself and another 2 patients had 2 and 3 recurrences, respectively.

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7
Number of organ systems affected by SLE before HS diagnosis	9	4	5	5	6	Simultaneous diagnosis of SLE and SH	Simultaneous diagnosis of SLE and SH
Number of organ systems affected by SLE at HS diagnosis	4	1	2	4	2	4	3
Number of organ systems affected by SLE until last assessment	Died	2	2	Follow-up lost	1	5	1
SLEDAI//SLICC-ACR DI at HS diagnosis	4//6	4//0	5//0	29//3	4//1	25//0	21//0
SLEDAI//SLICC-ACR DI 1 year after HS	*	0//0	0//0	*	2//1	0//0	2//13
SLEDAI//SLICC ACR DI at last assessment	*	0//0	0//0	*	0//1	2//0	2//13
Number of treatment lines	1	0	3	2	2	4	3
Number	2		5	3	2	4	4
Treatments administered	GC and CsA	0	GCs, etoposide, iv Ig, CsA, platelets,red cells	GC, CYP and iv Ig	Amphotericin B, miltefosine	GC, iv Ig, CsA, MM	GC, Cs A, anakinra and CYP
Relapses	0	2	0	3	0	0	0
Deaths	Yes	No	No	No	No	No	No
Follow-up time (months)	Died	45	80	Follow-up lost	Unknown	26	24
GC:Glucocorticoids, iv Ig: intravenous immunoglobulins, CYP: Cyclophsphamide, CsA:Ciclosporine A, MM: Mycophenolate mofetil							

Conclusions HS is a rare life-threatening SLE manifestation. It must be suspected in SLE patients with persistent fever who do not respond to antibiotics, cytopenias and evidence of multiorgan involvement. Relapses and death are common in HS associated to SLE.

References

[1] Pego-Reigosa JM, Rua-Figueroa I, Lopez-Longo FJ, Galindo-Izquierdo M, Calvo-Alen J, Olive-Marques A, et al. Analysis of disease activity and response to treatment in a large Spanish cohort of s with systemic lupus erythematosus. Lupus 2015;24:720–9.

Acknowledgements Work supported by Spanish Society of Rheumatology, FIS/ISCIII (PI11/02857), BIOCAPS from the European Union 7th Framework Programme/REGPOT-2012–2013.1 (316265), GSK, Roche, Novartis, UCB.

Disclosure of Interest None declared