

SYSTEMIC LUPUS ERYTHEMATOSUS WITH ANTI-DFS70 ANTIBODIES

A. Chiron¹; A. Mathian²; JL. Charuel¹; D. Sterlin¹; P. Ghillani-Dalbin¹; J. Haroche²; S. Mudumba³; R. Burlingame³; G. Gorochov¹; L. Musset¹; Z. Amoura²; M. Miyara^{1,2}

¹Immunology department, Pitié Salpêtrière hospital, Paris, FRANCE; ²Internal medicine department 2, Pitié Salpêtrière hospital, Paris, FRANCE ³Genalyte Inc., San Diego, CA USA

Introduction

Anti-DFS70 antibodies (Dense Fine Speckled 70 kDa) are found in 3% of general population. Isolated anti-DFS70 reactivity i.e. without anti-extractable nuclear antigens (anti-ENA) or anti-double stranded DNA (anti-dsDNA) has been proposed as an exclusion marker for systemic autoimmune rheumatic diseases. However, anti-DFS70 antibodies can be found in patients with systemic lupus erythematosus (SLE). SLE patients with isolated anti-DFS70 antibodies have not been extensively described yet.

Patients and methods

Fifty-nine SLE patients followed-up at the internal medicine department 2 at the Pitié-Salpêtrière hospital presenting with at least 4 ACR97 or SLICC2012 classification criteria and positive for anti-DFS70 antibodies were included and separated in 2 groups: (1) isolated DFS group (n=31) with isolated anti-DFS70 antibodies and (2) DFS ENA/DNA group (n=28) with anti-DFS70 and anti-ENA and/or anti-dsDNA antibodies (Figure 1). Anti-DFS70 antibodies were screened by indirect immunofluorescence (IIF) on HEp-2000® cells (Immunoconcept) while anti-ENA were screened by ELISA (DiaSorin) and determined by multiplex assay (FIDIS™, Theradiag). Anti-DFS70 and anti-ENA antibodies were confirmed by photonic ring immunoassay (Maverick®; Genalyte). Anti-dsDNA were detected using either ELISA (DiaSorin) or RIA (InGen).

Results

Among the 1200 SLE patients of the active file of the department, the anti-DFS70 positive patients represented 4.8% (n = 59). The female/male sex ratio was 19/1, the average age at diagnosis 33 years, mean disease duration 6 years and mean follow up was of 4 years. The isolated DFS group had less ACR (4.3 +/- 0.2 vs 5 +/- 0.2) and SLICC (4.4 +/- 0.2 vs 5.6 +/- 0.3) classification criteria than the DFS ENA/DNA group (Figure 2, p < 0.05). There was no significant difference between the 2 groups in terms of clinical profile (Table 1), number of flares (Figure 3), treatment (Figure 4), anti-DFS70 titer or the presence of anti-phospholipid antibodies. All patients were treated with Hydroxychloroquine and the use of steroid treatment was also similar in the 2 groups (64 % of DFS DNA/ENA and 55 % of the isolated DFS group). The isolated DFS group presented less nephritis (n=2, 6 %) compared to the DFS ENA/DNA group (n = 7, 25 %, p = 0.07; Table 1). Antibodies associated with anti-DFS in the DFS ENA/DNA group were mostly anti-dsDNA antibodies (12.4 %, Figure 5)

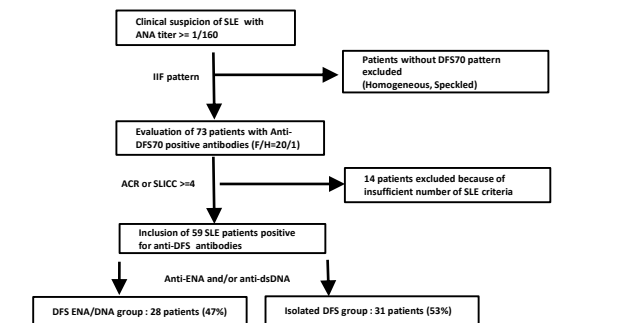


Figure 1. Patients inclusion The flow diagram depicts inclusion strategy for patients with SLE and anti-DFS70 antibodies

Clinical and biological features	Total (N=59)	Isolated DFS70 group (N=31)	DFS ENA/DNA group (N=28)
Arthritis	50 (84%)	28 (90%)	22 (79%)
Skin rash	42 (71%)	23 (74%)	19 (68%)
Acute cutaneous lupus	19 (32%)	11 (35%)	8 (29%)
Subacute cutaneous lupus	7 (12%)	5 (16%)	2 (7%)
Photosensitivity	22 (37%)	14 (45%)	8 (29%)
Nephritis	9 (15%)	2 (6%)	7 (25%)
Seritis	13 (22%)	4 (13%)	9 (32%)
Pericarditis	10 (17%)	3 (10%)	7 (25%)
Pleuritis	3 (5%)	1 (3%)	2 (7%)
Myocarditis	2 (3%)	1 (3%)	1 (3%)
CNS lupus	4 (7%)	2 (6%)	2 (7%)
Mucosal involvement	10 (17%)	5 (16%)	5 (18%)
Allergic	22 (37%)	12 (39%)	10 (36%)
Associated APS	9 (15%)	5 (16%)	4 (14%)
Cytopenia	32 (54%)	16 (52%)	16 (57%)
AHA	3 (5%)	0 (0%)	3 (11%)
Thrombocytopenia	3 (5%)	0 (0%)	3 (11%)
Leukopenia	18 (31%)	9 (29%)	9 (32%)
Lymphopenia	22 (37%)	11 (35%)	11 (39%)

Table 1. Lupus with isolated anti-DFS70 antibodies display clinical features similar to lupus with anti-ENA. AHA: Autoimmune hemolytic anemia, APS: antiphospholipid syndrome, CNS: central nervous system

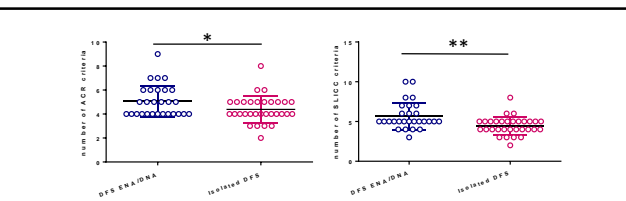


Figure 2. Isolated anti-DFS positivity is associated with lower SLE classification score. Comparison of the number of SLE classification criteria between the DFS ENA/DNA and the isolated DFS groups: ACR criteria (left) and SLICC criteria (right). *: p<0.05; **: p<0.005

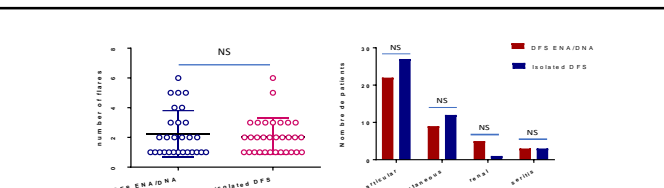


Figure 3. Absence of difference in the number or in the types of flares between patients with lupus and isolated antiDFS70 antibodies and patients with lupus with antiDFS70 and anti ENA or antiDNA. Comparison of the number (left) and type (right) of flares between the DFS ENA/DNA and the isolated DFS group. NS: not significant

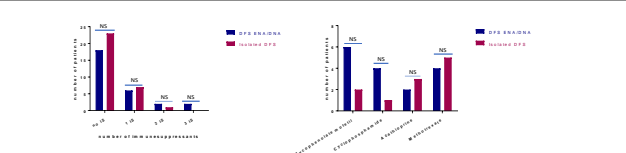


Figure 4. No difference in the immunosuppressant therapy between the isolated anti-DFS group and the anti-ENA and/or anti-dsDNA group. Comparison of the number (left) and type (right) of immunosuppressant drugs between the DFS ENA/DNA and the isolated DFS group. NS: non significant

- DFS positive with anti-ENA 4 (14%)
 - +3 (11%) Anti-SSA
 - +1 (4%) Anti-Ro52 & anti-Sm & anti-RNP
- DFS positive with both anti-ENA & anti-dsDNA and/or anti-nucleosome 10 (36%)
 - +2 (7%) anti-SSA & anti-dsDNA
 - +2 (7%) anti-Ro52 & anti-dsDNA
 - +3 (11%) anti-SSA & anti-RiboP & anti-dsDNA
 - +1 (4%) anti-Ro52 & anti-Sm & anti-RNP
 - +1 (4%) anti-SSA & anti-Nucleosome anti-RiboP anti-dsDNA
 - +1 (4%) anti-SSA & anti-Sm & anti-RNP & anti-RiboP & anti-dsDNA
- DFS positive with anti-dsDNA and/or anti-Nucl14 (50%)
 - +12 (43%) anti-dsDNA
 - +2 (7%) anti-dsDNA & anti-Nucleosome

Figure 5. Anti-ENA auto-antibodies associated with anti-DFS in the ENA/DNA group; anti-RiboP: anti-ribosomal P proteins;



Figure 6. Proposal for Diagnostic algorithm for SLE with ANA and anti-DFS70 antibodies

Conclusion

SLE patients with isolated anti-DFS antibodies have a clinical phenotype comparable to the one of patients with anti-DFS antibodies associated with usual SLE antibodies. Although not statistically significant, renal involvement is less frequent in the absence of anti-ENA and anti-dsDNA. We conclude that the diagnosis of SLE cannot be excluded in the presence of isolated anti-DFS70 antibodies. We propose here a diagnostic algorithm for lupus based on the observed clinical features of SLE and anti-DFS positivity (Figure 6).