

ANTI-DFS70 ANTIBODIES

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BACKGROUND

The anti-DFS70 antibodies were first described by Ochs et al in 1994 who has shown in immunofluorescence on HEp-2 cells a dense granular staining in interphase nuclei and mitotic chromosomes condensed giving the name of DFS to Dense Fine Speckles (fig 1). In immunoblotting, these antibodies react with an approximately 70 kDa, hence its name of DFS70. Finally, the patient serum was used to screen a cDNA expression library of a cell line of bladder cancer leading to isolate a gene encoding a protein whose sequence is identical to the transcription coactivator p75, also described as the Lens Epithelium p75-Derived Growth Factor (LEDGF/p75) (fig 2).

Currently, this protein is involved in many pathological processes without being specific for a disease. The higher prevalence of anti DFS70 has been described in patients with Vogt-Harada syndrome (66.7%) and atopic dermatitis (30%) followed by apparently healthy subjects (10%) while the prevalence of diseases chronic systemic rheumatic significantly lower (2-3%).

RESULTS

We evaluated the titer of the IIF of patients who came between 3 to 13 times (35% of samples). The titer is quiet stable in time, and less vary (fig 3). The dilution was quiet high (60% at titer 1/1280) (fig 4).

Among the aspects of IIF, we performed ENA in 228 cases, 217 were tested for nucleosome/ histone autoantibodies, and 49 for DNA (fig 5).

In 62% of cases, other autoantibodies were prescribed (as rheumatoid factors, or transglutaminase antibodies ...). All were negative, except a few cases for the rheumatoid factors (1,6 to 2.5%) and for CCP (5.1%).

The follow-up of patients shows that 18.6% of patients realize the same analysis during years after anti-DFS70 detection. Some have been controlled until 13 times (fig 6).

OBJECTIVE

To evaluate the follow-up of the DFS70 found in Indirect Immuno-Fluorescence (IIF) over a 5.5-year period by a retrospective study, and the possible relationship with other auto-immune diseases.

METHODS

From January 1, 2008 to October 1, 2013, we analyzed 49630 antinuclear antibodies in IIF. 441 samples were DFS70 positive (titer cut off 1/320) (0.9%) representing 279 patients and results were quantified by Elisa (MBL, Japan).

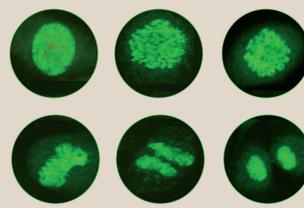
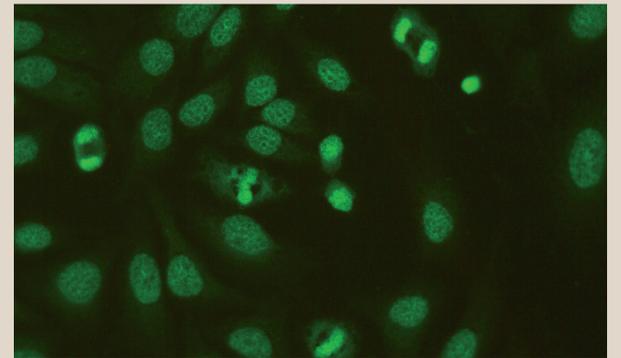


Fig. 1 : Staining of DFS70 in IIF



1 92 149 156 178 197 530

PWWP NLS AT hook IBD

Fig. 2 : Structure of DFS70-LEDGF/p75

titer	1/320	1/640	1/1280	1/2560	51/120
n	13	157	297	30	1

Fig. 4 : Titers of anti-DFS70 in IIF

numbers of patients	208	39	14	7	3	3	2	1	2
following of the patients	1	2	3	4	5	6	8	10	13

Fig. 6 : Medical following of patients

Associated antibodies	% of positivity	Associated antibodies	% of positivity	Associated antibodies	% of positivity
ANCA	0	Anti-GH Ab	0	Anti-Nucleosome / His-	0
anti Ovary Ab	0	Anti-Gliadin Ab	0	Anti-Parietal Cells	0
Anti Pituitary Ab	0	Anti-IA2 Ab	0	Anti-Prolactine Ab	0
Anti-ACHol. R. Ab	0	Anti-Insulin Ab	0	Anti-Skin Ab	0
Anti-actin Ab	0	Anti-Intrinsic Factor Ab	0	Anti-TTG Ab	0
Anti-Adrenal Ab	0	Anti-Kydney Ab	0	Anti-VGCC Ab	0
Anti-CCP Ab	5,1 (5/98)	Anti-LC1 Ab	0	Antiphospholipid Sd	0
Anti-DNA Ab	1,4	Anti-LKM Ab	0	ASCA	0
Anti-ENA Ab	0,0	Anti-striated muscle Ab	0	Rhumatoid Factor IgA	1,7 (2/ 120)
Anti-GADII Ab	0	Anti-MusK Ab	0	Rhumatoid Factor IgM	2,5 (3 /119)
Anti-Ganglioside Ab	0	Anti-Myelin Ab	0	TRAK	0

Fig. 5 : Association of DFS70 antibodies with others antibodies prescribed in the same time



Fig. 3 : Titer of DFS 70 over time in 8 patients (Elisa)

CONCLUSIONS

The DFS70 pattern tended to appear at high titer and to be stable over years. Moreover, this pattern was not associated with other auto-antibodies. This antibody is not described associated with SARD so the repeated analyzes can be discussed but as autoantibodies are typically present many years before a diagnosis of immune disease, a clinical follow-up of these patients is necessary.



BIBLIOGRAPHY

Ochs RL, Stein TW Jr, Peebles CL, et al. Autoantibodies in interstitial cystitis. J Urol 1994;151(3):587-92. - Singh DP, Ohguro N, Kikuchi T, et al. Lens epithelium-derived growth factor: effects on growth and survival of lens epithelial cells, keratinocytes, and fibroblasts. Biochem Biophys Res Commun 2000;267:373-81. - Wu X, Daniels T, Molinaro C, et al. Caspase cleavage of the nuclear autoantigen LEDGF/p75 abrogates its pro-survival function: implications for autoimmunity in atopic disorders. Cell Death Differ 2002;9(9):915-25. - Ochs RL, Muro Y, Si Y, et al. Autoantibodies to DFS 70 kd/transcription coactivator p75 in atopic dermatitis and other conditions. J Allergy Clin Immunol 2000;105(6 Pt1):1211-20. - Ayaki M, Ohguro N, Azuma N, et al. Detection of cytotoxic anti-LEDGF autoantibodies in atopic dermatitis. Autoimmunity 2002;35(5):319-27. - Yamada K, Senju S, Shinohara T, et al. Humoral immune response directed against LEDGF in patients with VKH. Immunol Lett. 2001;78(3):161-8. - Watanabe A, Kodera M, Sugiura K, et al. Anti-DFS70 antibodies in 597 healthy hospital workers. Arthritis Rheum 2004;50(3):892-900. - Dellavance A, Viana VS, Leon EP, et al. The clinical spectrum of antinuclear antibodies associated with the nuclear dense fine speckled immunofluorescence pattern. J Rheumatol 2005;32(11):2144-9. - Mahler M, Parker T, Peebles CL, et al. Anti-DFS70/LEDGF antibodies are more prevalent in healthy individuals compared to patients with systemic autoimmune rheumatic diseases. J Rheumatol 2012;39(11):2104-10. - Mariz HA, Sato EI, Barbosa SH, et al. Pattern on the antinuclear antibody-HEp-2 test is a critical parameter for discriminating antinuclear antibody-positive healthy individuals and patients with autoimmune rheumatic diseases. Arthritis Rheum 2011;63(1):191-200. - Miyara M, Albesa R, Charuel JL, et al. Clinical phenotypes of patients with anti-DFS70/LEDGF antibodies in a routine ANA referral cohort. Clin Dev Immunol 2013;art ID 703759. - Mahler M, Fritzier MJ. The clinical significance of the dense fine speckled immunofluorescence pattern on HEp-2 cells for the diagnosis of systemic autoimmune diseases. Clin Dev Immunol 2012;art ID 494356.