

## Anti-dense fine speckled 70 antibodies in primary Sjögren's syndrome

Sirs,

Antinuclear antibodies (ANA) represent a defining trait of many connective tissue autoimmune disorders (CTDs). Anti-dense fine speckled 70 (DFS70) antibodies have been reported with a higher prevalence among healthy individuals, suggesting that a diagnosis of CTD is quite unlikely in case of anti-DFS70 positivity (1).

Nevertheless, current medical literature displays a paucity of data on this topic and the clinical relevance of DFS70 is still a matter of debate. In this regard, we retrospectively assessed their frequency in a cohort of patients who underwent minor salivary glands biopsy and ANA testing and extractable nuclear antigens (ENA) screening in our Unit from March 2011 to December 2019, in the suspicion of primary Sjögren's syndrome (pSS). Patients affected by other CTDs and infectious diseases were excluded from the study. Salivary glands samples were assessed using the Chisholm and Mason grading system and/or the Focus score, while ACR/EULAR classification criteria were used for the definitive diagnosis of pSS (2). ANA were determined by indirect immunofluorescence (IIF) on Hep2 cells (Euroimmune, Lubeck, Germany), whereas anti-ENA were detected by fluoroenzymeimmunoassay (FEIA-ThermoFisher).

A total of 1113 patients, 85 males and 1028 females, were included; ANA were present in 492 subjects and DFS70 pattern was observed in 9 of them (titre  $\geq 1:160$ ). Two of them were positive, at various titres, for rheumatoid factor, 2 for anti-Ro/SSA-52 kDa and the remaining 5 only for anti-DFS70 antibodies.

A definite diagnosis of pSS was established in 7 out of 9 (77.8%) anti-DFS70 positive patients. No other significant laboratorial abnormalities, nor an extra-glandular involvement were assessed in these patients. Table I summarises their demographic and serological characteristics. No statistically significant differences in terms of DFS70 positivity emerged between pSS patients and healthy controls ( $p=0.495$ ).

Bizzaro *et al.*, in a large multicentric study, found that 4 out of 172 (2.3%) DFS70 positive patients were affected by pSS. Among 200 patients affected by various CTDs, DFS70 was found in 3 subjects (1.5%). Interestingly, 2 out of 30 (7%) patients with pSS were found to be positive for anti-DFS70 antibodies (3).

In a large Japanese cohort, 64 out of 597 healthy subjects (11%) were positive for anti-DFS70, notably 54% of the ANA posi-

**Table I.** Demographic and laboratory characteristic of anti-DFS70 positive patients.

Patient	Age	Gender	Diagnosis	ANA dilution	Concomitant antibodies
1	62	F		1:640	RF
2	81	F	pSS	1:1280	-
3	52	F	pSS	1:320	-
4	55	F		1:640	RF
5	77	F	pSS	1:320	-
6	33	F	pSS	1:640	-
7	58	F	pSS	1:640	Ro/SSA
8	64	F	pSS	1:640	Ro/SSA
9	65	F	pSS	1:160	-

pSS: primary Sjögren's syndrome; RF: rheumatoid factor.

tive ones. Thus, the authors suggested using this specific pattern to rule out any autoimmune disease (4).

Similar percentages were reported in a cohort of 500 patients affected by various CTDs, where DFS70 was found in 8 out of 71 (11.2%) subjects affected by pSS, 7 of whom were also positive for anti-Ro/SSA (5). Such findings were not confirmed by the large cohort by Carbone *et al.*, in whom no DFS70 patient displayed a Ro/SSA positivity nor received a diagnosis of pSS (6). Mahler *et al.* found an overall anti-DFS70 prevalence of 1.62%, significantly higher among healthy individuals (8.9%) than in the ones affected by CTDs. Interestingly, none of the patients affected by pSS, exhibited an anti-DFS70 pattern (7).

The overall prevalence of DFS70 in our cohort (0.8%) was similar to the one reported by Bizzaro *et al.* Nevertheless, they considered ANA test to be positive when titres were  $>1:40$ , while we considered ANA titres  $\geq 1:160$ .

More in detail, in our study anti-DFS70 frequency was 1.82% among ANA positive subjects, 1.08% among pSS patients and 0.45% among healthy individuals. Conversely, 7 out of 9 (77.8%) anti-DFS70 positive subjects, received a diagnosis of pSS, while in only 2 of 9 (22.2%) no definite diagnosis was established.

According to our findings, which should always be interpreted in the context of a retrospective chart review and the relatively small sample size, the presence of anti-DFS70 antibodies should not be considered as an exclusion criterion for CTDs.

Indeed, a considerable percentage of anti-DFS70 positive patients was found to be affected by pSS. In case of a strong suspicion of pSS, further diagnostic work-up should not be discouraged even when an ANA pattern resembling DFS70 is encountered.

Despite tremendous advances in the comprehension of the pathogenesis of pSS, further studies are needed for a better patients stratification according to their autoimmune profile (8).

E. CONTICINI, MD

J. SOTA, MD

P. FALSETTI, PhD

F. BELLISAI, MD

M.R. BACARELLI, PhD

S.G. AL-KHAYYAT, MD

L. CANTARINI, MD, PhD

B. FREDIANI, MD, PhD

Rheumatology Unit, Department of Medical Sciences, Surgery and Neurosciences, University of Siena, Italy.

Please address correspondence to:

Edoardo Conticini,

Department of Medical Sciences,

Surgery and Neurosciences,

Rheumatology Unit, University of Siena,

Policlinico Le Scotte,

viale Bracci 16, 53100 Siena, Italy.

E-mail: conticini.edoardo@gmail.com

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