AB0744

A "LOST-TO-FOLLOW-UP" AUTOANTIBODY FOR THE DIAGNOSIS OF AUTOIMMUNE DISEASE: PREVALENCE AND CLINICAL CHARACTERISTICS OF ANTI-NOR90/HUBF POSITIVE PATIENTS

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Background: Anti-nuclear antibody (ANA) patterns in indirect immunofluorescence testing (IIF) have been valuable in the diagnosis of autoimmune diseases. A pattern of speckling with fluorescent mitotic dots is considered to represent autoantibodies against nucleolar organising regions (NORs). Anti-NOR90 antibodies target the human upstream binding factor (hUBF) which activates RNA polymerase I-activated ribosomal RNA transcription. They have been anecdotally associated with systemic sclerosis (SSc), Sjögren's Syndrome (pSS) and rheumatoid arthritis (RA).

Objectives: To analyse the prevalence and clinical characteristics of patients found to be anti-NOR90 positive by immunology at The Dudley Group NHS FT (DGH) which also serves Worcestershire Acute Hospitals NHS Trust (WAH).

Methods: Clinical letters and electronic patient records of anti-NOR90 positive patients identified in the DGH immunology laboratory between July 2016 and October 2017 were reviewed. Advice was sought regarding ethical approval and consent; this was deemed unnecessary for this clinical survey. Anonymized patient data was collected on Excel. Anti-NOR90 was tested for when the characteristic ANA pattern was observed and as part of an extended SSc blot (EUROLINE SSc (Nucleoli) profile (IgG) – EUROIMMUN).

Results: We identified 11 anti-NOR90 positive patients among 8000 positive ANA results (estimated prevalence 0.0137%). Patient demographics, diagnoses and immunology are illustrated in table 1. Patients were in their vast majority female (10/11, 91%) and had a median age of 63 (IQR:53–74) years. The median anti-NOR90 titer was 111 (IQR:14–139) intensity units. 6/11 (54.5%) had a confirmed diagnosis of rheumatic disease. The most common clinical features were Raynaud's phenomenon (63.6%), sicca symptomatology (36.4%) and polyarthritides (36.4%). Interstitial lung disease (ILD) and oesophageal dysmotility (OD) were predominant clinical features in two cases (SSc, pSS). In general, patients lacked skin involvement (scleroderma, telangiectasias, calcinosis).

Abstract AB0744 – Table 1. Demographic, clinical and immunological characteristics of anti-NOR90 positive patients

Patient	Age/ Sex	Diagnosis	Rheumatoid Factor	ANA titre	ANA pattern	anti- NOR90 titre
1	82/F	SSc	-	weak positive	mitotic dots	positive
2	80/ M	pSS	-	1:320	speckled mitotic dots	11
3	35/F	UCTD	-	1:2560	nucleolar with mitotic dots	140
4	63/F	RA	+	weak positive	mitotic dots	positive
5	81/F	Bronchiectasis	-	1:1280	speckled mitotic dots	107
6	18/F	Raynaud's	-	1:1280	mitotic dots	139
7	68/F	Raynaud's	-	1:320	nucleolar with mitotic dots	130
8	56/F	UCTD	+	1:320	mitotic dots	11
9	66/F	Raynaud's	-	negative	negative	14
10	53/F	Raynaud's/ Crohn's disease	-	1:1280	nucleolar +homogenous with mitosis dots	151
11	52/F	Polyarthritides	-	weak positive	mitotic dots	111

Conclusions: Literature regarding anti-NOR90 auto-antibodies has been scarce and in the age of automated IIF ANA testing, it is plausible that their specific nucleolar pattern is frequently missed. In our survey, they were observed in the context of several rheumatic diseases and linked to Raynaud's, sicca symptoms and polyarthritides. Studies in larger relevant patient cohorts are needed to further clarify their clinical value.

Disclosure of Interest: None declared

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AB0745

MECHANICS OF EARLY VENTRICULAR IMPAIRMENT IN SYSTEMIC SCLEROSIS AND THE EFFECTS OF PERIPHERAL VASCULOPATHY

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Background: Multiple mechanisms commonly lead to severe cardiac involvement in systemic sclerosis (SSc), an autoimmune disease characterised by microvascular lesions, systemic inflammation and fibrosis.

Objectives: To examine the mechanics of right and left ventricles (RV, LV) at the early stage of possible impairment and test the hypothesis that peripheral arterial hemodynamics are associated with an early LV compromise.

Methods: Ninety-five asymptomatic SSc patients free of cardiovascular disease (88% women, 53±14 years) and 54 apparently healthy controls matched for age, gender, arterial hypertension, dyslipidaemia, and diabetes mellitus underwent echocardiography, including multilayer speckle-tracking, and tonometry-based pulse wave analysis of the peripheral arteries; 66 SSc patients were prospectively assessed after 32±7 months. Indices of ventricular and arterial structure and function, as well as LV-arterial coupling, were calculated.

Results: At baseline, patients presented RV diastolic/systolic impairment, as well as LV remodelling and diastolic/systolic impairment in terms of reduced deformation parameters versus controls. No association was evident between RV and LV strain within individual patients, whereas by multivariate analysis including age, gender and SSc characteristics we found that the global longitudinal strain of RV free wall was associated only with the presence of diffuse skin involvement (b=2.63, p=0.042) and both global longitudinal and circumferential strain of LV were correlated only with disease duration (b=0.14, p=0.001 and b=0.17, p=0.032, respectively). Both RV and LV abnormalities progressed independently during follow-up. Moreover, in the absence of differences in aortic stiffening and LV-arterial coupling between patients and controls, arterial pressure wave reflections assessing small vessel function and/or microcirculation were abnormal in SSc patients and strongly correlated with impaired indices of LV diastolic function and remodelling.

Conclusions: These novel findings show the mechanics of RV early impairment in SSc that develops and progresses independently from the concomitant LV impairment, which, in turn, may be influenced by peripheral microvascular abnormalities in the absence of macrovascular damage.

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AB0746

FREQUENCY AND CLINICAL ASSOCIATION OF RARE ANTIBODIES IN A LARGE CONNECTIVE TISSUE DISEASE COHORT

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Background: Connective tissue diseases (CTDs) are characterised by the presence of specific antibodies (Abs). These are useful in diagnosis and prognostic stratification. Rare Abs have been reported but their clinical significance is currently not as clear.

Objectives: To assess the diagnosis, and frequency of clinical features within each rare antibody subgroup in our CTD cohort

Methods: The immunology results for 5828 patients obtained over the past 17 years and patients positive for 1 of the rare Abs (Jo-1, PCNA, XR, PL-4, PL-7, PL-12, SRP, Ku, Mi-2, EJ, SL, PmScl, rRNP, Th/To, NuMa-1, OJ and hnRNP) were identified. Diagnosis and frequency of major organ involvement were reported.

Results: 758 patients (12.5%) were positive for at >1 rare Abs. Clinical information confirming a diagnosis of a CTD was available for 514 patients. The most frequent rare Ab in our cohort was PmScl (3.10%). The majority of patients had clinical features of overlap syndromes (33.8%), the 2nd most common diagnosis was systemic sclerosis (SSc) (31.10%). Interstitial lung disease (ILD) was more commonly seen in patients with PL-7+ (82.4%), PL-12+ (75%), Jo-1+ (70.8%) and SRP+ (66.7%). ILD was not reported in PCNA+, PL-4+, NuMa-1+ and hnRNP+. Pulmonary arterial hypertension (PAH) was most frequently seen in patients with XR+ (31.8%). Inflammatory myositis (IM) was found in all Jo-1+ and SRP+ patients, and in the majority of PL-7+ (88.2%) patients. Inflammatory arthritis was commonly reported in patients with PCNA+ (57.1%), NuMa-1+ (50.0%) and rRNP+ (40%). Renal involvement was classified as either glomerulonephritis (GMN) or scleroderma renal crisis (SRC). GMN was more common in patients with rRNP+ (60%), PL-4+ (45.4%) and PCNA+ (42.9%) patients. SRC was diagnosed in patients with SL+ (3.2%), PmScl+ (5.5%) and Th/To+ (2.5%) (table 1).

Conclusions: Our data from a large CTD cohort suggest that rare Abs associate with distinct features in particular ILD and inflammatory myositis. A majority of these patients fulfil the criteria for overlap syndrome and SSc.

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AB0747 INTERSTITIAL LUNG DISEASE IS INDEPENDENTLY ASSOCIATED WITH INCREASED FAECAL CALPROTECTIN LEVELS IN SYSTEMIC SCLEROSIS

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Background: Interstitial lung disease (ILD) is one of the leading cause of death in systemic sclerosis (SSc).

Objectives: The aim of this paper was to evaluate the relationship between faecal calprotectin (FC) and ILD.

Methods: 129 outpatients with SSc were enrolled. Data about disease characteristics, in particular lung involvement, were collected and FC was measured.

Results: Eighty-seven patients (67.4%) had a limited subset with a mean disease duration of 13.3 (7.1) years. Anti-Sc170 antibodies were found in 35 (27.1%) patients. GI tract involvement was severe/end stage in 3 cases (2.4%). ILD affected 35 patients (27.1%). Median levels of FC were 80 µg/g (157 µg/g). FC was found to be higher in patients with a moderate/severe/end stage score for gastrointestinal tract (p=0.046) and on steroids (p=0.015). In addition, it positively correlated with age (p<0.001).

Other than well-known risk factors such as higher mRSS or diffuse subset, patients with ILD had higher values of FC (p<0.001). In multivariate analysis correcting also for factors affecting FC levels (i.e. disease duration, mRSS, Valentini activity score, total Medsger severity score, proton pump inhibitor, anti-Sc1-70 antibody, diverticulosis, limited cutaneous subset, faecal calprotectin levels, steroid treatment), diffuse disease subset (p=0.001), higher mRSS (0.04), longer disease duration (0.046), higher severity scores (0.026), higher FC levels (p=0.003) and steroid treatment (0.014) were associated with increased risk of ILD, while diverticulosis was protective. In addition, we ran a second multivariate analysis considering the 110 cases with FC level <275 µg/g, in order to correct for a possible small intestine bacterial overgrowth. Increased FC levels (p=0.019), steroid treatment (p=0.03), higher severity scores (p=0.016) and diffuse disease subset (p=0.002) were confirmed to be associated with ILD.

Conclusions: in this paper we have found a possible link between gut inflammation and ILD. Many hypothesis may be done but it is intriguing that these data further support what previously found by other authors (Andreasson et al. 2016), that is a correlation between gut inflammation and dysbiosis and non-gastrointestinal disease manifestation. Our study may support the hypothesis of a role of gut

dysbiosis in triggering a pathologic immune response leading to ILD. It may also be that increased FC simply reflects a more severe disease but this still doesn't explain why only ILD was found to be linked with FC. Is it because lung is a filter of molecule (i.e. antigens, cytokines, metabolites, etc.) produced in the gut? Further studies with longitudinal evaluation are warranted.

Disclosure of Interest: None declared

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AB0748 POLIAUTOIMMUNITY IN SCLERODERMA: DATA FROM DE SPANISH SCLERODERMA REGISTRY

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Background: Systemic sclerosis (SSc) is a disorder with a well-known autoimmune base. There is evidence suggesting a common background with other connective tissue diseases, thus predisposing to the development of other autoimmune disorders in these patients, that is, poliautoimmunity (PAI).

Objectives: To assess PAI in a cohort of SSc patients.

Methods: A nationwide, cross-sectional study was performed including the 1928 patients enrolled in the Spanish SSc Registry (RESCLE). Ethics Committee approval was obtained by all participating centres.

Results: Prevalence of PAI was 45%, with 32% having more than one association. Most of these patients were women (93%, p<0.001), with older age at diagnosis (53.7±14.7 years, p=0.027). Regarding subtypes, PAI was significantly more frequent in limited cutaneous SSc (48%, p=0.004) and pre-SSc (47%, p<0.001). Sjögren's syndrome was by far the most common association (55%), followed by global autoimmune thyroid disorders (31%), autoimmune liver disorders (17%) and inflammatory myopathies (12%). Clinical features are shown on table 1.

Abstract AB0746 – Table 1. Diagnosis and clinical features in patients positive for rare antibodies

Antibody(n, %)	Diagnosis					Clinical features					
	SSc	SLE	SS	IM	Overlap	UCTD	ILD	PAH	IM	Arthritis	Renal
Jo1(72)	0	0	0	51 (70.8)	21 (29.2)	0	51 (70.8)	11 (15.3)	72(100)	21 (29.2)	0
PCNA ⁽⁷⁾	1 (14.3)	6 (85.7)	0	0	0	0	0	1 (14.3)	0	4 (57.1)	3 (42.9)
XR ⁽²²⁾	9 (40.9)	6 (27.3)	0	0	7 (31.8)	0	9 (40.9)	7 (31.8)	3 (13.6)	6 (27.3)	1 (4.5)
PL-4(11)	0	11(100)	0	0	0	0	0	0	0	0	5 (45.5)
PL-7(17)	2 (11.8)	0	0	9 (52.9)	6 (35.3)	0	14 (82.4)	0	15 (88.2)	5 (29.4)	0
PL-12 ⁽¹²⁾	2 (16.7)	2 (16.7)	1 (8.3)	5 (41.7)	2 (16.6)	0	9 (75.0)	0	6 (50.0)	4 (33.3)	1 (8.3)
SRP ⁽⁹⁾	0	0	0	5 (55.6)	4 (44.4)	0	6 (66.7)	2 (22.2)	9 (100.0)	1 (11.1)	0
Ku ⁽⁴⁷⁾	14 (29.8)	5 (10.6)	0	2 (4.3)	21 (44.7)	5 (10.6)	21 (44.7)	2 (4.3)	8 (17.0)	16 (34.0)	4 (8.5)
MI-2(7)	0	0	0	6 (85.7)	1 (14.3)	0	4 (57.1)	0	1 (14.7)	0	0
EJ ⁽²⁾	1 (50.0)	0	0	0	1 (50.0)	0	1 (50.0)	0	0	0	0
SL(94)	33 (35.1)	34 (36.1)	10 (10.6)	1 (1.1)	10 (10.7)	6 (6.4)	16 (17.0)	9 (9.6)	12 (12.7)	36 (38.3)	14 (14.9)
Pm/Sc1(182)	70 (38.7)	2 (1.1)	1 (0.6)	6 (3.3)	99 (54.7)	3 (1.7)	75 (41.4)	11 (6.1)	94 (51.9)	35 (19.3)	10 (5.5)
rRNP ⁽⁵⁾	0	5 (100)	0	0	0	0	1 (20.0)	0	0	2 (40.0)	3 (60.0)
Th/To ⁽⁴⁰⁾	34 (85.0)	0	0	1 (2.5)	4 (10.0)	1 (2.5)	16 (40.0)	10 (25.0)	5 (25.0)	2 (5.0)	1 (2.5)
NuMA-1(2)	2 (100.0)	0	0	0	0	0	0	0	0	1 (50.0)	0
OJ ⁽¹⁾	0	0	0	1 (100.0)	0	0	1 (100.0)	0	1 (100.0)	1 (100.0)	0
hnRNP ⁽³⁾	0 (0.0)	2 (66.7)	0 (0.0)	0 (0.0)	0 (0.0)	1 (33.3)	0 (0.0)	0 (0.0)	0 (0.0)	3 (100.0)	0 (0.0)