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LETTER TO THE EDITOR

Screening for Myositis Antibodies in Interstitial Lung Disease

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To the editor,

We read with interest the recent article from Fidler et al. [1] published online in LUNG (March 2019) and the previous article from De Sadeleer et al. [2] (March 2018) examining the role of myositis antibodies (MA), which characterize idiopathic inflammatory myositis (IIM), in the evaluation of idiopathic interstitial pneumonia (IIP). In IIM, the lung is the most frequent extra-muscular organ involved. [3] Interstitial lung disease (ILD) occurs in 50% of patients and often presents before connective tissue disease (CTD) features are evident, so the identification of autoantibodies can aid diagnosis in otherwise complex cases [3].

Fidler et al. examined 165 patients with idiopathic ILD and excluded patients with known CTD. 26.7% were identified as having myositis-specific antibodies (MSA) or myositis-associated antibodies (MAA). Fourteen patients (8.5%) had a change in diagnosis as a result of screening. The presence of MA was associated with current smoking ($p=0.008$) and DLCO < 70% predicted ($p=0.03$). Age, gender and patient-reported CTD symptoms failed to predict the presence of MA, and current recommended serology [anti-nuclear antigen (ANA), Rheumatoid factor (RF) and anti-CCP] was negative in the majority (57.1%). Usual interstitial pneumonia (UIP) was the most common radiological pattern [1].

Similar to Fidler et al. [1], De Sadeleer et al. evaluated MSA prevalence in an IIP cohort ($n=68$), but in contrast included only those with specific interstitial lung disease patterns [non-specific interstitial pneumonia (NSIP), organizing pneumonia (OP) or lymphocytic interstitial pneumonia (LIP)] [2]. 17.6% were positive for MSA [2]. In contrast to Fidler et al. [1], female gender was identified as a predictive factor for MSA identification. MSA was found frequently in those who satisfied diagnostic criteria for interstitial lung disease with auto-immune features (IPAF), occurring in approximately 1 in 3 [2].

In our institution, we recently sought to evaluate the prevalence of MA in IIP, the impact of MA on multidisciplinary diagnosis (MDD) and whether identification of MA in patients with ILD, altered clinician's treatment decisions. Over a 3-year period (2014–2016), all patients who tested positive for MA at a large tertiary referral center (Cork University Hospital, Cork, Ireland) had their cases reviewed. *Euroline Autoimmune Inflammatory Myopathies immunoblot*® was utilized to detect antibodies (*MSA*: anti-Jo-1, anti-PL-7, anti-PL-12, Anti-Mi-2, anti-MDA-5, anti-TIF1, anti-Mi-2, Mi2α, Mi-2β; *MAA*: anti-NXP2, anti-PM/Scl 75, anti-PM/Scl100, anti-Ku and anti-Ro52).

Out of 179 screening tests sent, a total of 44 were positive (24.6%). Thirty-one patients (16 females, mean age 65.2 ± 6.5, range 26–86) had subclinical or clinical evidence of ILD and were included for review (Table 1). Nineteen patients had MSA: [(anit-Jo-1 ($n=2$), anti-PL-7 ($n=4$), anti-PL-12 ($n=2$), anti-MDA-5 ($n=2$)] or MAA: [anti-PM-Scl75 ($n=6$), anti-PM/Scl-75/PM/Scl-100 ($n=2$), anti-Ku ($n=1$)] associated with progressive ILD. ANA, RF, anti-CCP were positive in 41.9, 9.7 and 6.5%, respectively. The majority ($n=29$) reported respiratory symptoms (cough and dyspnea) at initial review. Features of CTD were observed in 48.4% with Raynaud's phenomenon the most common. In contrast to Fidler et al. [1], NSIP was the predominant radiological pattern ($n=16$, 51.6%).

The addition of MA serology findings changed the MDD in 20 (64.5%) cases. Younger patients and those with CTD features at presentation were more likely to undergo a change in diagnosis (Table 1). Treatment decisions were significantly affected by the presence of MA. In total 35.5% ($n=11$) had a treatment change. This was more pronounced in the subgroup of patients with MA associated with progressive ILD ($n=19$), where a treatment change occurred in 47.4% ($n=9$), consisting of commencement ($n=3$) or escalation ($n=6$) of immunosuppression (IS). One patient changed from anti-fibrotic therapy to IS.

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Table 1 Patient characteristics and comparison between patients with a change in diagnosis at MDD and those that did not with the addition of myositis antibody screening

	Total cohort ($n=31$)	Change in MDD ($n=20$)	No change in MDD ($n=11$)	p value
Age [years (±SD)]	65.2±6.5	60.9±16.4	73±10.3	0.04
Gender (female)	16 (51.6)	12 (60)	4 (36.4)	0.27
Lung function				–
FVC [% (L)]	84 (2.6)	82.16 (2.6)	91.6 (2.7)	0.273
DLCO (%)	50.1	48.4	53.6	0.458
Radiological pattern				–
NSIP	16 (51.6)	13 (65)	3 (27.3)	0.06
UIP	7 (22.6)	7 (22.6)	8 (72.7)	0.07
Smoking status				–
Current	6 (19.4)	3 (15)	3 (27.3)	–
Ex	9 (29)	5 (25)	4 (36.4)	–
Never[a]	16 (51.6)	12 (60)	4 (36.4)	0.273
CTD features present at diagnosis	15 (48.4)	14 (70)	1 (9.1)	0.002
Raynaud's phenomenon	8 (25.8)	7 (35)	1 (9.1)	0.203
Rash	6 (19.4)	6 (30)	0 (0)	0.066
Myalgia/muscle weakness	6 (16.4)	6 30)	0 (0)	0.066
Arthralgia	3 (9.7)	2 (10)	1 (9.1)	>0.99
Early morning stiffness	3 (9.7)	3 (15)	0 (0)	0.535
Fever	3 (9.7)	3 (15)	0 (0)	0.535
Dysphagia	2 (6.5)	1 (5)	1 (9.1)	0.99
Creatinine kinase (umol/l)	1055.8	1226.2	431.3	0.367
Serology				–
MSA	11(35.5)	7 (35)	4 (36.4)	>0.99
MAA	15 (48.4)	10 (50)	5 (45.5)	>0.99
MSA/MAA	5 (16.1)	3 (15)	2 (18.1)	>0.99
ANA	15 (48.4)	10 (50)	5 (45.5)	>0.99
Lung biopsy	9 (29)	5 (25)	4 (36.4)	0.683

Data are presented as n (%) unless otherwise stated

MDD multidisciplinary diagnosis, *FVC* forced vital capacity, *DLCO* diffusing capacity of the lung for carbon monoxide, *NSIP* non-interstitial idiopathic pneumonia, *UIP* usual interstitial pneumonia, *CTD* connective tissue disease, *MSA* myositis-specific antibodies, *MAA* myositis-associated antibodies, *ANA* antinuclear antigen

[a]Never smokers compared to current or ex-smoker

Our study compliments the two previous studies [1, 2] whereby a high prevalence of MA was found. The addition of testing had significant clinical implications, leading to a change in diagnosis in 1 in 9 [our study] to 1 in 12 [1] patients tested. This has cost saving and patient benefits, eliminating the need for more invasive testing such as surgical lung biopsy.

In conclusion, the aforementioned studies [1, 2] and the additional study from our institution suggest that given the heterogeneity of IIM-ILD, with no conclusive correlations between antibodies, radiological pattern and clinical features, screening for MA should be considered early to avoid diagnostic and treatment delays. MA detection impacts MDD and may prevent erroneous diagnosis and potentially costly and dangerous treatment strategies. Lung biopsy should be reserved for patients who still have no MDD, despite clinical, radiological and serological review. Further large-scale multicenter studies should correlate clinical phenotypes with serology (MA) in order to optimize patient care.

Compliance with Ethical Standards

Conflict of interest None.

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