Association of anti-Ro52 autoantibodies with interstitial lung disease in connective tissue diseases

We read with great interest the article by Sabbagh *et al* demonstrating that anti-Ro52 autoantibodies were connected with the development of interstitial lung disease (ILD) in patients with juvenile myositis.[1] Anti-Ro52 has been found in a variety of connective tissue diseases (CTDs) and drawn considerable attention from rheumatologists in recent years. Besides myositis, these autoantibodies have also been reported to be related to ILD in several other CTDs, but with great discrepancy across the studies.[2] In addition, it remains unclear how the incidence of ILD differs in the presence of anti-Ro52 alone or in combination with anti-Ro60 (Sjogren's syndrome related antigen A), one of the most associated antibodies that may determine anti-Ro52 epitope mapping.[3]

To explore the clinical features of anti-Ro52 and its relationship with anti-Ro60, we retrieved the medical records of 1979 patients tested positive for anti-Ro52 and hospitalised between January 2016 and September 2017 in the Drum Tower Hospital. Both anti-Ro52 and anti-Ro60 were routinely measured using an immunoblotting method (EUROLINE, EUROIMMUN AG, Germany). The majority of our cases were female (1457, 73.6%) and the average age was 53.0±16.8 years old. Totally 1321 (66.8%) patients were diagnosed as having CTDs and 658 (33.2%) diagnosed as non-CTDs.

Distribution of ILD in patients with various diseases is summarised in table 1. In this cohort, ILD occurred in 37.1% of anti-Ro52 positive CTD patients and 10.9% of anti-Ro52 positive non-CTD patients. Among CTDs, idiopathic inflammatory myopathy (IIM) was the most often seen underlying disease (85.4%), followed by undifferentiated connective tissue disease (UCTD), systemic sclerosis, rheumatoid arthritis (RA) and primary Sjögren's syndrome (pSS). As for systemic lupus erythematosus, only 6.5% anti-Ro52 positive patients presented ILD, consistent with its low incidence in this prototypic autoimmune disease.[4]

There was no discussion of the difference between anti-Ro52 single-positive and anti-Ro52/Ro60 double-positive in Sabbagh *et al*'s article.[1] Previously, it has been implied that the expressions of these two types of autoantibodies were related to different CTDs,[5] and those with isolated anti-Ro52 were more prone to IIM and inflammatory rheumatism.[6] Our data showed that the distribution of ILD was also varied between the two groups. The incidence of ILD was increased in both CTD and non-CTD patients with single-positive anti-Ro52 (OR 4.94, $p<0.0001$ and OR 3.41, $p<0.05$ by χ^2 and Baptista-Pike analysis). However, compared with those having both anti-Ro52 and anti-Ro60, patients with isolated anti-Ro52 were more likely to develop ILD in RA (OR 6.11), pSS (OR 4.50), polymyositis (PM) (OR 10.00) and UCTD (OR 3.71), but not other CTDs including dermatomyositis (table 1).

In conclusion, our data support that ILD is associated with anti-Ro52, yet the incidence is quite different among various CTDs. For patients with RA, pSS, PM or UCTD, the positivity of anti-Ro52 without anti-Ro60 may indicate the occurrence of ILD.

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Table 1 Distribution of ILD in anti-Ro52 positive patients with various underlying diseases

	Total	$Ro52^+Ro60^-$	$Ro52^+Ro60^+$	OR	95% CI	P value
CTD*	490 (37.1%)	352 (55.4%)	138 (20.1%)	4.94	3.88 to 6.31	<0.0001
IIM ‡	123 (85.4%)	99 (88.4%)	24 (75.0%)	2.54	0.93 to 6.77	>0.05
DM	84 (87.5%)	66 (86.8%)	18 (90.0%)	0.73	0.15 to 3.22	>0.05
PM	18 (66.7%)	15 (83.3%)	3 (33.3%)	10.00	1.42 to 48.96	<0.01
ASS	21 (100.0%)	18 (100.0%)	3 (100.0%)			
pSS	236 (38.2%)	157 (57.3%)	79 (23.0%)	4.50	3.17 to 6.31	<0.0001
SLE	18 (6.5%)	4 (7.4%)	14 (6.3%)	1.18	0.41 to 3.64	>0.05
RA	36 (43.4%)	29 (60.4%)	7 (20.0%)	6.11	2.12 to 15.16	<0.001
SSc	15 (51.7%)	11 (57.9%)	4 (40.0%)	2.06	0.44 to 8.04	>0.05
UCTD	49 (64.5%)	44 (69.8%)	5 (38.5%)	3.71	1.16 to 11.61	<0.05
MCTD/overlap syndrome	7 (46.7%)	3 (30.0%)	4 (80.0%)	0.11	0.01 to 1.50	>0.05
Vasculitis	6 (35.3%)	5 (38.5%)	1 (25.0%)	1.88	0.21 to 28.67	>0.05
Non-CTD†	72 (10.9%)	68 (12.2%)	4 (3.9%)	3.41	1.25 to 8.95	<0.05

Data were shown as number (percentage of ILD patients for each disease). $Ro52^+Ro60^-$: anti-Ro52 positive and anti-Ro60 negative, $Ro52^+Ro60^+$: both anti-Ro52 and anti-Ro60 positive.
*Diagnosis of CTDs was in accordance with the international criteria for classification.
†Patients without a definite CTD during the hospitalisation, of which tumour, infection, ILD and chronic kidney disease were the most common disease types.
‡including DM, PM and ASS.
ASS, anti-synthetase syndrome; CTD, connective tissue disease; DM, dermatomyositis; IIM, idiopathic inflammatory myopathy; MCTD, mixed connective tissue disease; PM, polymyositis; pSS, primary Sjögren's syndrome; RA, rheumatoid arthritis; SLE, systemic lupus erythematosus; SSc, systemic sclerosis; UCTD, undifferentiated connective tissue disease.

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