Overlap of systemic lupus erythematosus and myositis is rare in anti-Ku antibody-positive patients

Anti-Ku antibodies were originally reported as scleroderma-poly myositis (PM) overlap syndrome-related autoantibodies. However, they are also frequently found in various connective tissue diseases (CTDs) and their clinical significance has not been conclusively determined. Moreover, there are few studies on anti-Ku in Asian CTD cohorts. Recently, Spielmann *et al*[1] published a notable report of a French single-centre large-cohort study which tried to classify anti-Ku-positive patients with various CTDs and was able to identify two distinct subgroups of patients: 'anti-Ku-positive patients with elevated serum creatine kinase (CK) levels' and 'anti-Ku-positive patients with anti-double-strand DNA antibodies (anti-dsDNA)'. Patients in the former group were at high risk of developing interstitial lung disease and those in the latter were at high risk of developing glomerulonephritis.

In the present study, we retrospectively screened sera from 600 Japanese patients with CTDs who visited our institute[2] by immunofluorescence patterns for anti-Ku-positivity, as performed in a previous study.[1] Sera suspected of being anti-Ku-positive were then screened by anti-Ku70 and anti-Ku80 ELISAs and verified by immunoprecipitation-immunoblot. We found 10 anti-Ku-positive patients and analysed their clinical and laboratory findings (table 1). Their average age was 47.2±23.9 years. Nine were female and their average follow-up period was 5.7 years (0.5–26 years). Five patients showed CK elevation and were diagnosed with PM or dermatomyositis (DM). Two of the five PM/DM patients had developed systemic scleroderma (SSc) and PM simultaneously. Of the other five patients without CK elevation, three had been diagnosed with systemic lupus erythematosus (SLE), one of whom had developed SSc after a 20 year disease history. None of the 3 SLE patients among the present 10 anti-Ku-positive patients showed CK elevation. These results are consistent with the findings reported by Spielmann *et al*.[1] There are two studies supporting the lower frequency of myositis overlapping SLE in anti-Ku-positive patients.[3 4] Among 46 anti-Ku-positive CTD patients, 17 had myositis (PM or DM) and 9 had SLE spectrum (anti-phospholipid syndrome or SLE), but there was only 1 case with overlap syndrome of PM and SLE.[3] Another retrospective CTD-screened study reported that only 1 myositis/SLE overlap patient was seen among 30 anti-Ku-positive patients, including 11 myositis patients (inflammatory myopathy, inclusion body myositis and PM) and 8 SLE-spectrum patients.[4] These characteristics seen in myositis patients or SLE-spectrum patients are consistent with the findings reported by Spielmann *et al*.[1]

We also collected the data on anti-dsDNA for all 10 anti-Ku-positive patients. Four of them were positive for anti-dsDNA. Surprisingly, of the four anti-dsDNA-positive patients, three were CK-elevated patients. In contrast, all three SLE cases were negative for anti-dsDNA. Thus, anti-dsDNA positivity and SLE were mutually exclusive in the present anti-Ku-positive patients. In contrast, a previous international study compared the clinical and laboratory characteristics of 22 anti-Ku-positive SLE patients with those of 209 anti-Ku-negative SLE patients.[5] In both anti-Ku-positive and anti-Ku-negative SLE groups, frequencies of anti-dsDNA were similar: 31.8% and 32.2%, respectively. Furthermore, Spielmann *et al*[1] reported that anti-dsDNA was very often found in anti-Ku-positive SLE patients (89%, 7/8). This discrepancy might be due to a difference of genetic backgrounds. Since anti-dsDNA are not so frequently found (around 30%) in anti-Ku-positive SLE[5] in addition to the presence of anti-dsDNA in 'anti-Ku with elevated CK patients' in our study, we might have to be careful in using the results of anti-dsDNA for differential diagnosis. We also found anti-ssDNA in 9 of the 10 anti-Ku-positive patients in the present study. Previous studies did not investigate anti-ssDNA in anti-Ku-positive patients. Future study is necessary to clarify whether anti-ssDNA could be a marker for anti-Ku in antinuclear antibody-positive sera with speckled/homogenous staining patterns.

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Table 1 Clinical and laboratory information of anti-Ku-positive patients with various connective tissue diseases

Case	Age	Sex	Diagnosis	Serum CK	Cancer	ILD	Nephritis	Arthralgia	Lupus rash	Hypo C.	Raynaud	ssDNA	dsDNA	Other autoantibody
1	70	F	PM+SSc+SS	2095	–	+	–	–	–	+	+	+	–	PL-7
2	14	F	PM+SSc	3682	–	–	–	+	–	–	NA	+	+	–
3	80	F	PM	2710	–	+	–	–	–	–	–	–	–	–
4	76	F	PM	2263	–	+	–	+	–	–	NA	+	+	SRP
5	20	F	DM	1263	–	–	–	+	–	NA	–	+	+	–
6	35	F	MCTD→SSc	261	Lung	+	–	–	–	–	+	+	+	U1RNP
7	17	F	SLE→SSc	31	–	–	+	–	+	+	+	+	–	U1RNP ACA
8	44	F	SLE	105	–	+	+	+	+	+	+	+	–	U1RNP
9	25	M	SLE	111	–	–	+	+	+	+	–	+	–	SSA
10	52	F	UCTD	180	–	+	–	+	–	–	–	+	–	P-ANCA

ACA, anti-centromere antibody; ANCA, anti-neutrophil cytoplasmic antibody; Hypo C., hypocomplementemia; CK, creatine kinase (U/l); DM, dermatomyositis; ILD, interstitial lung disease; MCTD, mixed connective tissue disease; NA, information not available; PM, polymyositis; SS, Sjögren's syndrome; SSc, systemic sclerosis; UCTD, undifferentiated connective tissue disease.

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