Anti-Ku syndrome with elevated CK: association with myocardial involvement in systemic sclerosis

We read with great interest the paper by Spielmann et al describing a large cohort of anti-Ku-positive connective tissue disease patients.1 In their paper, the authors could identify two different subgroups of patients: ‘anti-Ku with elevated CK patients’, who are at risk of developing interstitial lung disease (ILD), and ‘anti-Ku with anti-dsDNA patients’, who are at risk of developing glomerulonephritis. Interestingly, the authors found an extremely low rate of myocarditis in both subgroups as only one patient in the C1 cluster (‘elevated CK’) was diagnosed with myocarditis. Of note, in our cohort of anti-Ku-positive systemic sclerosis (SSc) patients we found that the positivity for this rare antibody was invariably associated with myocardial inflammation. We indeed performed a retrospective review of anti-Ku-positive patients affected by SSc according to European League Against Rheumatism/American College of Rheumatology (EULAR/ACR) 2013 criteria2 followed-up at two referral centres for SSc. We routinely performed anti-Ku in all SSc patients without any detected positivity for other SSc-related antibodies, that is, antitopoisoenzyme I, anticientromere and anti-RNA polymerase III. All SSc patients with suspected myocardial inflammation (new onset cardiac signs and/or symptoms, raised troponin T and/or N-terminal pro-brain natriuretic peptide (NTproBNP)) routinely underwent cardiac magnetic resonance imaging (CMR) and 24-hour Holter-ECG tape. Myocarditis diagnosis was defined according to the Lake Louise Criteria3 on CMR. We identified four anti-Ku-positive SSc patients. All patients were female, and had been diagnosed with limited cutaneous SSc; mean age at diagnosis was 52.5±19.74 years. In all cases, the anti-Ku positivity was confirmed by immunoblotting. Mean delay between myocarditis and SSc onset was 79.2±48.1 months. In three out of four patients (75%), ILD was also present. Myositis was diagnosed in all patients by creatine kinase (CK) increase, electromyography and skeletal MRI, and in all cases it preceded the diagnosis of myocarditis. None of the patients had scleroderma renal crisis or pulmonary arterial hypertension. Two patients had subclinical presentation, while the other two had signs of heart failure. At presentation, troponin T serum levels were increased in all patients (mean levels: 82.4±21.1 ng/L), and NTproBNP was slightly raised in three patients (mean levels 317.5±4.6 pg/mL). A large cohort of anti-Ku-positive connective tissue disease patients and myocarditis is unequivocally associated with a dismal outcome. Importantly though, myocarditis could be asymptomatic or clinically subtle, as in the two patients of our cohort; thus, it needs to be actively investigated, especially in high-risk patients. An early recognition of inflammatory myocardial involvement is indeed of cardinal importance to allow a prompt therapeutic intervention, thus improving patient’s outcome.

Given the concomitant presence of elevated CK in all anti-Ku patients in our cohort, we suggest that not only ILD but also myocarditis, might be a specific feature of the anti-Ku with elevated CK subgroup and that all anti-Ku-positive SSc patients should be actively screened for potential myocardial involvement.

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Contributors CC: conceived the hypothesis, analysed data and drafted the manuscript. GDL: conceived the hypothesis, analysed data, critically revised the manuscript and gave the final approval. MDS: analysed data, critically revised the manuscript and gave the final approval.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; internally peer reviewed.

REFERENCE


