

# Anti-Ku autoantibodies

## Series of 5 cases

Krzysztof Gryga, Mamert Milewski, Marek Żółciński, Andrzej Dyczek, Jacek Musiał

Department of Internal Medicine, Jagiellonian University Medical College, Kraków, Poland

### KEY WORDS

anti-Ku, clinical presentation, neuropathy

### ABSTRACT

Autoantibodies directed against nuclear protein Ku are infrequently detected. If present, they are found in high titers in patients with connective tissue overlap syndromes. This article describes 5 patients with anti-Ku antibodies in whom systemic lupus erythematosus, Sjögren's syndrome, idiopathic lung fibrosis or scleroderma – polymyositis overlap syndrome were diagnosed. Interestingly, signs and symptoms of transient cranial neuropathy involving trigeminal and facial nerves were reported by 3 patients. Cranial nerve neuropathy has not been described in patients with anti-Ku autoantibodies previously.

**INTRODUCTION** Antibodies against Ku protein were first reported in 1981 in a patient with polymyositis/scleroderma overlap syndrome. At that time the term Ku was derived from the initials of the patient's name.<sup>1</sup>

The Ku protein is a heterodimer found mainly in a cell nucleus and consists of two subunits with mass of 70kD (p70) and 86kD (p86), which attach to the terminal sections of double stranded DNA. This protein is a constituent of the DNA-dependent protein kinase and plays an important role in the process of repair and recombination of DNA. It also participates in the regulation of gene transcription processes.<sup>2,3</sup>

The incidence of anti-Ku antibodies is not so high. As few as 1 out of 3500 positive results for anti-nuclear antibodies (ANA) is detected by immunoblotting.<sup>4</sup> When present, they usually reach a high titer (>1:10,000). Clinically, anti-Ku antibodies are most often associated with symptoms of muscle damage (*myositis*), skin (*sclerodactylia*, *microstomia*) and joint involvement and the presence of Raynaud's syndrome, rarely lung fibrosis and disturbances in the upper gastrointestinal tract.<sup>5,6</sup>

Of note, there exists a possibility of demographic differences in clinical symptoms. Anti-Ku in the North American population (especially in Afro-Americans) is detected more frequently in patients with systemic lupus

erythematosus (SLE), while in the European population it is observed in patients with overlap syndromes (most commonly with scleroderma and polymyositis).<sup>7-9</sup>

**CASE REPORTS** In 5 women hospitalized in 2007 in the II Department of Internal Medicine, Jagiellonian University Medical College in Kraków, ANA at a very high titer (>1:10,000) were detected by indirect immunofluorescence (Myositis Profile test, Euroimmun, Germany), and the immunoblot test confirmed the presence of anti-Ku antibodies at high titers.

Patient number 1, aged 37, with SLE diagnosed in 2005, complained of osteoarticular pains, recurrent left-sided numbness of the face and tongue, and, transient hyperesthesia in this region. Magnetic resonance imaging (MRI) of the brain was normal.

Patient number 2, aged 58, with a mixed connective tissue disease, accompanied with sicca syndrome and Raynaud's symptoms diagnosed in 2006, presented muscle weakness of the shoulder and hip girdles, muscle atrophy, bone and joint pain, numbness of the hands, scleroderma and persistent heartburn. Further studies revealed increased muscle enzyme activity and myoglobin level. pH-metry showed gastroesophageal reflux disease, and pulmonary fibrosis was diagnosed with high resolution chest computed

Correspondence to:  
Krzysztof Gryga, MD, Oddział  
Kliniczny Kliniki Alergii i Immunologii Szpitala Uniwersyteckiego,  
Uniwersytet Jagielloński,  
Collegium Medicum, ul. Skawińska 8,  
31-066 Kraków, Poland,  
phone: + 48-12-430-52-66,  
fax: + 48-12-430-53-14,  
e-mail: grykry@mp.pl  
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TABLE Clinical symptoms in patients with anti-Ku autoantibodies

No.	Diagnosis	Sicca syndrome symptoms	Raynaud's syndrome symptoms	Skin symptoms	Osteoarticular symptoms	Symptoms concerning skeletal muscles	Laboratory features of skeletal muscle damage	Pulmonary symptoms	Neurological symptoms	Gastroenterological symptoms
1	SLE	+	+	-	+	-	-	-	+	-
2	MCTD	+	+	+	+	+	+	+	+	+
3	Sjögren's syndrome	+	-	-	+	-	+	-	+	-
4	Pulmonary fibrosis	-	-	-	-	-	-	+	-	-
5	Overlap syndrome: polymyositis/systemic sclerosis	-	+	+	+	+	+	-	-	-

Abbreviations: MCTD – mixed connective tissue disease, SLE – systemic lupus erythematosus

tomography. No anti-Scl 70 antibodies were found.

Patient number 3, aged 47, with Sjögren's syndrome diagnosed in 2007, apart from symptoms of sicca syndrome and osteoarticular pains, complained of mouth twisting, inability to close her left eye lid and left-sided facial hypoesthesia. The MRI of the brain was normal, and laboratory tests showed features of skeletal muscle damage.

Patient number 4, aged 69, with idiopathic pulmonary fibrosis diagnosed in 2002, apart from exertion dyspnea did not report any other symptoms.

Patient number 5, aged 32, with the overlap syndrome diagnosed in 2007, i.e. polymyositis/scleroderma, presented with typical symptoms of Raynaud's syndrome, bone and joint pains, scleroderma (*sclerodactylia*, *microstomia*) with digital pitting ulcers, muscle atrophy, along with features of skeletal muscle damage in laboratory tests. No anti-Scl 70 antibodies were reported.

**DISCUSSION** The cases described in this paper reflect the variety of clinical manifestations observed in patients with autoimmune diseases having anti-Ku antibodies (TABLE).

Firstly, the gender of patients should be mentioned because all the cases reported were women. Secondly, a broad spectrum of symptoms associated with anti-Ku antibodies does not allow us to assume that these antibodies are pathognomonic for any particular connective tissue disease. However, the analysis of these 5 cases seems to corroborate previous reports<sup>7,8</sup> that the presence of anti-Ku antibodies in the European population shows more commonly association with symptoms of polymyositis-scleroderma overlap syndrome than with SLE. Thirdly, if anti-Ku antibodies have been identified, their titer is high, more than 1:10,000. With the exception of anti-small nuclear ribonucleoprotein particles (anti-snRNP) antibodies, it is very rare that any other antibodies reach such a high titer. It should also be emphasized that usually other types of antibodies, except for anti-Ro52, do not coexist with anti-Ku antibodies.

The clinical symptoms associated with anti-Ku antibodies which have not been reported so far, are transient symptoms of cranial neuropathy involving trigeminal and facial nerves in 3 out of the 5 patients studied. It needs to be emphasized that these subjective complaints were short lasting, difficult to document in the MRI or in functional tests (electromyography), and they subsided spontaneously. Further studies are necessary to determine to which extent indeed they are typical of the presence of anti-Ku antibodies.

In conclusion, it should be stated that anti-Ku antibodies occur in a variety of systemic autoimmune diseases and are characteristic of none of them. Among patients with anti-Ku women definitely prevail, and antibodies detected in their

sera reach high titers. Clinically, they may present a variety of nonspecific symptoms – most often with myositis, skin lesions typical of scleroderma, osteoarticular pains, symptoms of sicca syndrome and Raynaud's syndrome, cranial polyneuropathy, and far less commonly – pulmonary fibrosis or esophageal dysmotility.

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