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CASE REPORT

A case of anti-Ku myositis mimicking limb girdle muscular dystrophy

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Abstract

Anti-Ku is a myositis associated antibody. Histopathology of anti-Ku myositis shows significant muscle fibre necrosis imitating immune mediated necrotising myositis as well as muscular dystrophies. A presentation of isolated proximal muscle weakness with muscle biopsy evidence of muscular dystrophy could mislead the clinician. We present a case of anti-Ku myositis with lower limb predominant weakness, absent extra-muscular manifestations and with an equivocal Anti-Nuclear antibody titre, whose muscle biopsy report came as muscular dystrophy. We would like to highlight the importance of considering anti-Ku myositis as an important differential in biopsies showing significant muscle destruction.

KEYWORDS

Myositis associated antibody, anti-Ku myositis, muscular dystrophy

INTRODUCTION

Inflammatory myopathies are a phenotypically diverse group of diseases. Isolated muscle involvement at presentation, is not unheard of. Extra muscular manifestations may develop over time. Limb girdle muscular dystrophies (LGMD) on the other hand are genetically driven diseases confined to the structural realm of muscles. The former is associated with antibodies, myositis specific as well as associated and the latter, with genetic mutations. Anti- Ku is a myositis associated antibody that is well described in cases of systemic sclerosis-myositis overlap. Both anti-Ku myositis and muscular dystrophies show significant destruction of muscle fibres on histopathology. In the absence of immunophenotyping that allows tagging and identifying the pathogenic proteins or cutting-edge genetic studies, diagnosis of LGMD becomes strictly clinical.

CASE PRESENTATION

We describe a 17-year-old boy who came with a progressive proximal muscle weakness over six months involving both hip and shoulder girdles. On admission he had a Medical Research Council power grading of 3/5 around the hip and 4/5 around the shoulder girdle. The distal muscle power, sensory system and deep tendon reflexes were spared. Muscle wasting, pseudo hypertrophy and fasciculations were absent. General and systemic examination was unremarkable with no rashes, lymphadenopathy, arthritis or abnormal lung sounds.

History revealed an insidious onset of weakness in the absence of oral ulcers, joint pain, rashes, dactylitis, sicca symptoms or definite Raynaud's phenomena. Initial investigations were significant for a creatine phosphokinase (CPK) of 14 684 U/L, an erythrocyte sedimentation rate (ESR) of 14 mm/hr and anti-nuclear antibodies (ANA) positive at a titre of 1: 80. Electro-myography demonstrated a myopathic pattern with no fibrillations or spontaneous activity. The muscle biopsy showed significant destruction with fibrosis and minimal lymphocytic infiltration; with a conclusion of the possibility of a muscular dystrophy (Figure 1). The entire work up was suggestive of an autosomal recessive LGMD.

TABLE 1 Myositis antibody panel of the patient

Mi-2a	Negative	PM-Scl 75	Negative
Mi -2b	Negative	Jo-1	Negative
TIF 1	Negative	SRP	Negative
MDA5	Negative	HMGCR	Negative
NXP2	Negative	PL7	Negative
SAE1	Negative	PL-12	Negative
Ku	Strongly positive	EJ	Negative
PM-Scl100	Negative	OJ	Negative
CN-1A	Negative	Ro-52	Negative

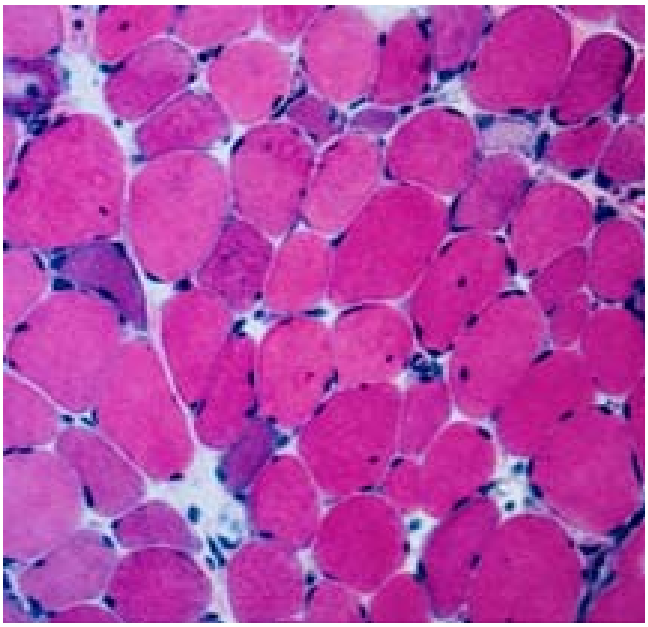

FIGURE 1 Muscle biopsy of the patient showing necrosis.

The presence of very high CPK values, the relatively faster progression, lack of family history and a history of Raynaud's like phenomenon led to the repetition of the ANA titre, this time recorded as 1:1280. The extractable nuclear antigen antibody panel was negative. By virtue of the very high ANA, he was started on high dose oral steroids (1g/kg).

There was a marked steroid responsiveness in the muscle strength. He was able to climb stairs without support. Immune mediated necrotizing myopathy was suspected. The myositis antibody panel was done yielding a strong positivity for anti-Ku antibodies.

He underwent a two-dimensional echocardiogram, lung function testing and a high-resolution computed tomography scan. Cardiomyopathy and interstitial lung disease was excluded. Methotrexate was introduced while slowly tailing prednisolone off. The patient was able to resume the daily activities of an active young man at the end of two months.

DISCUSSION

Anti-Ku antibodies were associated with rare cases of polymyositis – systemic sclerosis overlap, first described in 1981.[1] They are now identified with other systemic connective tissue diseases such as systemic lupus erythematosus, overlap syndromes and rheumatoid arthritis. The initial presentation could be isolated muscle weakness. Later, arthritis, interstitial lung disease, cutaneous manifestations and cardiac involvement may ensue.[1,2] The hallmark histopathological feature of anti-Ku myositis is myofibre necrosis with minimal inflammation, thereby mimicking immune mediated necrotising myopathies.[1-3] Similarly, muscular dystrophies too show significant myofibre destruction on histopathology. Minimal to moderate inflammation is seen on the biopsy of dysferlinopathies (LGMDR2) and fukutinopathies (LGMDR9). Recessive forms of LGMD (LGMDR) especially dysferlinopathies are known to have very high levels of creatinine phosphokinase like cases of immune mediated necrotising myopathies. Several cases of misdiagnoses between inflammatory myositis and limb girdle muscular dystrophies are described.[4-6] The short temporal progression, absence of family history, presence of abundant inflammatory and minimal fibro-fatty infiltrates, on histopathology and magnetic resonance imaging are suggestive of an inflammatory myositis.[7] In most cases

LGMDs were misdiagnosed as inflammatory myositis. Reports of misdiagnosis vice versa are rare. The authors believe that this may mostly be due to the avidity of treating physicians to proactively treat reversible causes and partly due to the obvious extra muscular manifestations, antibody profiles and electromyography (EMG) evidence that come along with inflammatory myositis.

The most frequently used maintenance treatment modalities are low dose steroids, hydroxychloroquine and methotrexate.[8] Mycophenolate mofetil, azathioprine, tacrolimus and cyclosporin A have also been used in isolated cases.[9] A negative Extractable Nuclear Antigen (ENA) antibody panel does not confer additional protection against developing extra-muscular manifestations, especially interstitial lung disease.[10] Therefore, it is important to follow up the patient closely.

CONCLUSION

Anti-Ku myositis as well as immune mediated necrotising myopathies show a significant amount of muscle fibre destruction on biopsy thereby mimicking a LGMD. In a resource rich setting, immunophenotyping of muscle, targeted next generation sequencing or whole exome sequencing together with the array of myositis specific and associated antibodies would guarantee an exact diagnosis. Unfortunately, the absence of these liberties in a resource poor setting have led to the conundrum of whether to start the patient on steroids. The lack of extra-muscular manifestations per se cannot be taken for granted. The way forward for a shrewd clinician in a similar situation is to pursue serological or imaging (magnetic resonance imaging (MRI)) evidence of muscle inflammation. Repetition of ANA levels was the most crucial diagnostic step in the above case.

The purpose of this description is to highlight the importance of considering inflammatory myositis in biopsies with significant myofibre destruction, to be persistent with out of the box presentations and to consider a therapeutic trial of steroids in such clinical ambiguities.

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