# A Myotonic Dystrophy Type I patient with Predominant Proximal Muscle Weakness without Action Myotonia- A Case Report and Review of Pathology

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**Abstract**

***Purpose:*** Early distal muscle weakness and myotonia are typical clinical presentations in type I myotonic dystrophy (DM1). We present a DM1 case with unusual predominant proximal weakness without action myotonia.

***Case report:*** The chief complaint of this 48-year-old female was difficulty in raising her arms and frequent falling in recent years. On neurological examination, proximal muscle weakness was more pronounced than the distal muscle groups, in addition to facial involvement. Although she did not experience any action myotonia throughout her life, hand and tongue myotonia were readily inducible by percussion during neurological examination. The diagnosis of DM1 was later supported by electromyography and neuropathological studies, and confirmed by molecular testing. The pathological findings in this patient and the characteristic features in typical DM1 patients were briefly reviewed.

***Conclusion:*** The unusual presentation of this DM1 patient suggests the importance of comprehensive neurological examination including percussion of thenar and tongue muscles, even in a patient with atypical distribution of muscle weakness and without a clear personal and family history of myotonia. In addition to molecular testing, muscle biopsy remains supportive in making the diagnosis.

***Keywords:*** Myotonic dystrophy, DM1, muscle pathology.

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## INTRODUCTION

Myotonia is one of the earliest symptoms in type I myotonic dystrophy (Dystrophia Myotonica; DM1) and the pattern of weakness involves mainly distal muscles. Here, we present an adult DM1 female whose weakness was more prominent in the proximal muscles. In addition, no action myotonia was noted throughout her life.

## CASE PRESENTATION

The chief complaint of this 48-year-old single female

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was her inability to raise both arms for the past few years. Since adolescence, she has been bothered by a gait problem and frequent falling, but she thought that was the consequence of scoliosis. Her performance in school was normal and her cognitive function was fair even until now, and hypersomnia was not serious during working hours. She did not recognize episodes of palpitation, nor did she have diabetes, blurred vision or irritable bowel symptom. Although power of hand grip was affected, the muscle weakness was more pronounced in the proximal muscles. Besides, she has not experienced any myotonic episodes, either spontaneous during voluntary movement or accidentally evoked by any stimulation, since she was young. Her parents passed away early and currently none of her relatives have shown similar symptoms.

On examination, the facial droop, temporal muscle atrophy and tented mouth were all characteristics of myopathy (Figure 1A). She could barely raise her arms (Figure 1B), nor could she stand up from squatting position without help, due to reduced muscle power in the deltoid muscle (MRC: 3/3) and the quadriceps (MRC: 4-/4-). Muscle strength of distal muscle groups was relatively preserved (hand grip 4/4; wrist extensor 4/4+; feet extensor 4/4) compared to proximal muscle

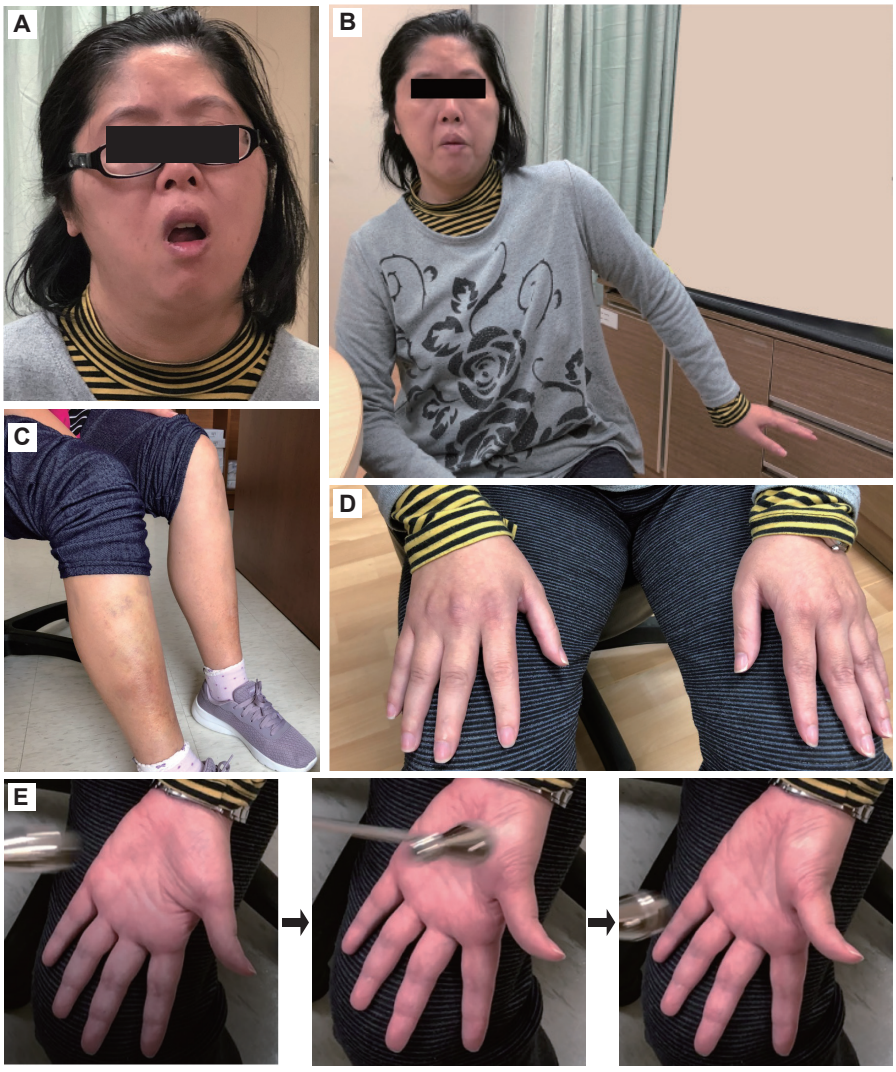


**Figure 1.** The DM1 patient. (A) Myopathic face with temporal muscle atrophy and tented mouth. (B) Failure in raising arms due to proximal muscle weakness. (C) Muscle status of both legs. (D) Muscle status of both hands. (E) Percussion myotonia of left thenar muscle: before (left), during (middle) and after (right) the percussion with a hammer.

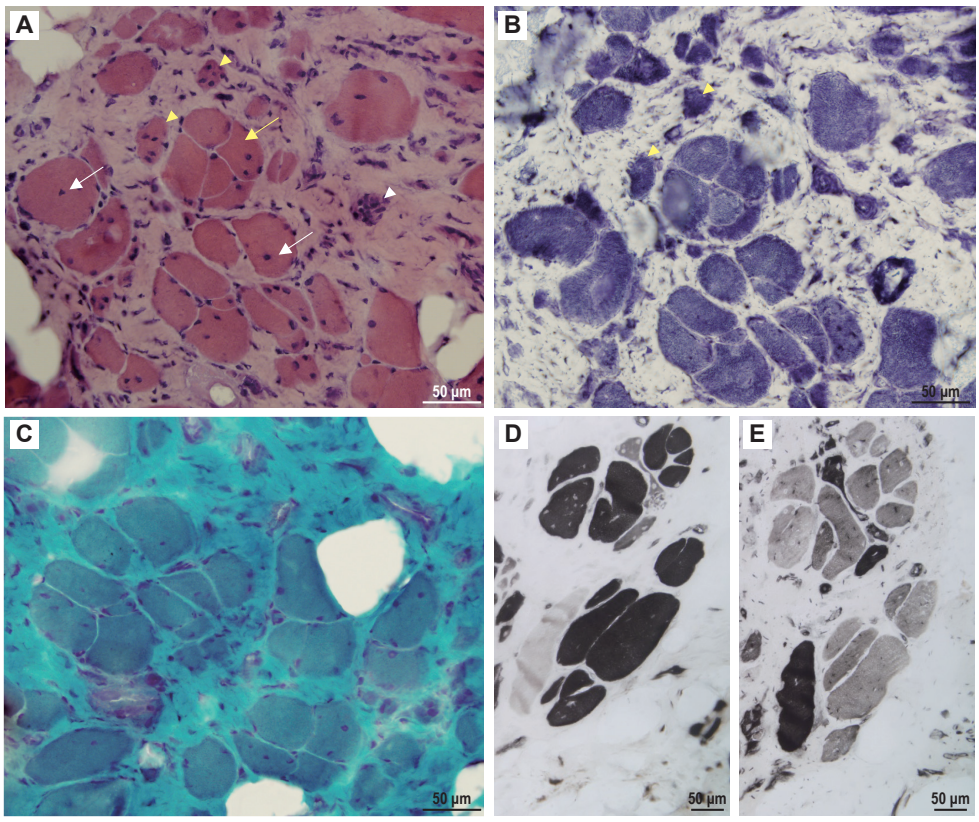


**Figure 2.** Muscle biopsy in this DM1 patient. (A) The H&E stain showing pyknotic nuclear clumps (white arrow head), internal nuclei (white arrows), type I muscle atrophy (yellow arrow heads) and muscle fiber splitting (yellow arrow). (B) NADH-TR stain showing dark type I muscle atrophy (yellow arrow heads) and disorganized intermyofibrillary network pattern. (C) Modified Gomori trichrome stain. (D) ATPase stains at pH 4.3 (dark: type I muscle fiber) and (E) pH10.8 (dark: type II muscle).

groups (biceps 4-/4-; hip flexion 4-/4-), without distinct muscle wasting in both lower and upper limbs (Figure 1C&D). The results of her laboratory investigations, including serum creatine kinase and thyroid function tests, were within normal limits. No myotonia was observed after shaking hands forcefully. Surprisingly, myotonia was readily inducible by percussion of her tongue and bilateral thenar eminence muscles (Figure 1E). Later, electromyography revealed waxing and waning myotonic discharges with the characteristic "dive bomber" sound. The muscle biopsy sample from left biceps brachii showed variable fiber sizes, fat replacement of myofibrils and increased connective tissues in hematoxylin-eosin (H&E) stain. Pyknotic nuclear clumps, fiber splitting, type I muscle atrophy and numerous internal nuclei were observed and also found in nicotinamide adenine dinucleotide-tetrazolium reductase (NADH-TR) and modified Gomori trichrome stains (Figure 2A, B and C). In addition, the ATPase stains at pH4.3 and pH10.8 showed centralized nuclei in both type I and type II muscle fibers (Figure 2D&E). Also, enzymatic activity in the NADH-TR stain exhibited moderate disorganization of intermyofibrillar network pattern (Figure 2B). Later, repeat-primed polymerase chain reaction identified a (CTG)n repeat expansion within the dystrophia myotonica protein kinase (*DMPK*) gene. This result was further confirmed by Southern blotting and an accurate estimated number of (CTG)n repeat was 145. On the other hand, the genetic test of (CCTG)n repeat length within *CNBP* gene for type II myotonic dystrophy (DM2) was within the normal range.

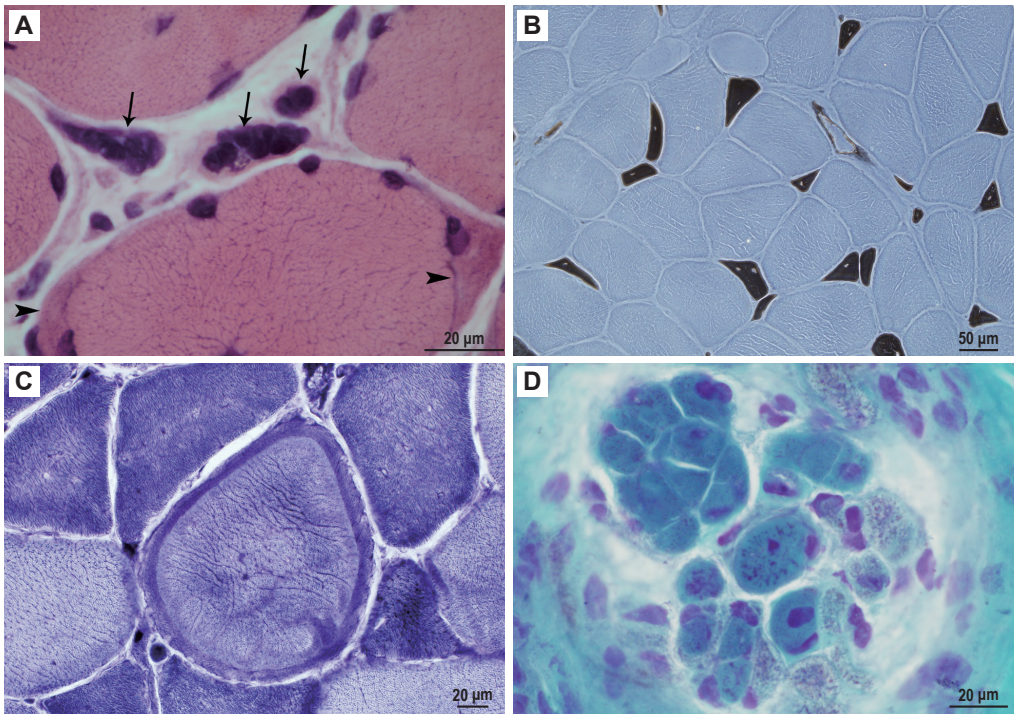


**Figure 3.** Muscle biopsy sample acquired from other DM1 patients. (A) H&E stain showing pyknotic nuclear clumps (arrows) and sarcoplasmic masses (arrow heads) (B) ATPase pH4.3 stain showing atrophic type I muscle fibers. (C) Ring fiber demonstrated by NADH-TR stain. (D) The muscle spindle in Gomori trichrome stain showing increase amount of intrafusal fibers.

## DISCUSSION

DM1 is the most common adult-onset muscular dystrophy worldwide but is relatively rare in Taiwan[1,2]. In DM1, weakness and atrophy occur most frequently in facial muscles and distal muscle groups, including intrinsic muscles. This is in contrast to DM2, also called proximal myotonic myopathy (PROMM), which involves mainly proximal muscles. In fact, DM2 is very rare in Asian countries[3,4], and patients with autosomal-dominant (AD) adult-onset myotonic myopathy in Taiwan are almost exclusively DM1. Early predominant proximal muscle weakness in DM1 patients has rarely been reported[5,6]. Most DM1 patients showed a distal to proximal gradient, only some patients may develop shoulder and hip girdle weakness at a much earlier time[7]. Scapular winging and dyskinesis were rare features in a subset of DM1 patients and has to be genetically differentiated with facioscapulohumeral muscular dystrophy (FSHD)[8].

The clinical presentation in our patient could be easily overlooked or misjudged. Throughout her 30 years of disease progression, she did not recognize myotonia on any occasion, either during speaking or hand grasping. Since most of the DM1 patients experienced myotonia as the initial symptom early in their lifetime[7], the absence of action myotonia was unusual. In a cross-sectional study of 278 adult DM1 patients, myotonia was complained in 90.3% of patients[9]. On the other hand, since the sizes of (CTG)n repeats in DM1 has been thought to be correlated with disease severity[10], an estimated 145 (CTG)n repeat on one allele in our patient should be long enough to cause distinct DM1 symptoms. Therefore, the absence of action myotonia is not due to relatively short extended repeats (e.g. n<100) that may only cause minimal symptoms. Intriguingly, factors predisposing the discrepancy between her profound weakness and absence of action myotonia were unclear. Severe muscle atrophy with fat replacement may be the cause.

Although genetic testing is required for the definite diagnosis of DM1/2, muscle biopsy alone is sufficient

for the diagnosis of DM, based on a few specialists' opinion[11]. Here, we briefly review the characteristic features of DM1 pathology. Central nucleation, which indicates a constant regeneration, is far more common than other muscular dystrophies. Pyknotic nuclear clumps (condensed myonuclei in severely atrophic fibers) (Figure 3A) may frequently be seen in late stage DM1 but can be seen relatively early in DM2. Both changes increase along with the disease progression. The predominantly atrophic type I muscle in DM1 could be identified with specific ATPase stain (Figure 3B). In contrast to DM1, predominant type II fiber atrophy can be seen in DM2 [12]. In addition, ring fibers (fiber running circumferentially and perpendicular to the myofibrial in a cross-section), which may develop during fiber splitting (Figure 3C) [13], and an increased amount of intrafusal fibers (Figure 3D), are more frequently seen in DM1 than other muscular disorders. Additional features such as sarcoplasmic masses (Figure 3A), moth-eaten fibers and small angular fibers are also relatively common in DM. Although there are many "characteristic" features, these findings are not DM-specific. For example, ring fibers could also be seen in mitochondrial myopathy or desmin myopathy[13,14]. Instead, the pathological diagnosis is based on the coexistence of these features and absence of inflammation or necrosis[15]. Ultrastructure studies may reveal myofibril and mitochondrial degeneration, changes of the sarcotubular system, or lipofuscin accumulation in DM2 patients, but they are non-specific and may be inconsistent[16]. The pathological investigation is helpful in excluding FSHD, limb-girdle muscular dystrophy that is similar to DM1 and DM2, and in children with congenital myopathies and anterior horn cell diseases that are similar to congenital DM (CDM)[17].

## CONCLUSION

We present a case with prominent proximal weakness without action myotonia during her entire life. The ambiguity of diagnosis was luckily resolved by comprehensive neurological examination with percussion, followed by electrophysiological approach, neuropathological study and molecular testing. Additionally, we reviewed the typical pathological presentation of DM1. The gold standard for DM1 diagnosis has been molecular detection of microsatellite mutation for decades. However, muscle biopsy remains informative for patients exhibiting myotonia with no affected family members; patients with DM-like symptoms but without distinct myotonia; or when molecular testing is not available. This case report followed the Declaration of Helsinki and was approved by the Medical Ethics Committee of CGMH, Taipei, Taiwan (IRB No.202002335B0).

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**Conflicts of interest statement**

We have no conflicts of interest to declare.

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