Myotonia Congenita with Painful Muscle Cramps
Nobuhiko Sunohara, Hideaki Tomi, Akinori Nakamura*, Kiichi Arahata* and Ikuya Nonaka**

A sporadic Japanese case of myotonia congenita with painful muscle cramps is reported. Electromyographic examinations disclosed myotonic discharge with dive bomber sounds at insertion, and high-amplitude, high-frequency motor unit potentials during the muscle cramps. Biopsied muscle specimens and EMG findings showed non-specific mild myopathic changes. There was no abnormal expansion of CTG repeat within the myotonic dystrophy gene. This patient’s disorder closely resembles Becker’s myotonia congenita Type II though the family history of was non contributory. (Internal Medicine 35: 507-511, 1996)

Key words: myotonia, cramp, myotonia congenita, non-dystrophic myotonia

Introduction
Becker (1, 2) described nine dominant inherited patients who had Thomsen-like myotonic signs and painful cramps that were elicited by strong movement and lasted from less than a minute to several minutes or even longer. He also stated that this is probably a separate disease entity, and classified it as autosomal dominant myotonia congenita Type II. However, this type of myotonia congenita has not been fully investigated. In this paper we describe such a patient who had both myotonia and true muscle cramps or ordinary muscle cramps without family history. ‘Muscle cramps’ include various categories of clinical manifestations. Clinical features of ‘true or ordinary muscle cramps’ (3) described in this paper are as follows: 1. Sudden forceful muscular contraction accompanied by pain which occurs after severe exercise. 2. During cramps the affected muscle is visibly and palpably firm and bulging, and afterward it may remain sore and tender. 3. Cramps are often terminated by stretching of the affected muscle. 4. Electromyographic examination during cramps revealed high-voltage, high-frequency, irregular bursts of motor unit action potentials.

Case Report
Patient (age 62 years old) had had painful cramps of his legs when climbing up stairs since the age of 20 years old. He was also aware of painless, slow relaxation after forceful grip at age 25 years old. The frequency of the cramps was once in three months, but that gradually increased (once a day at the age of forty). Initially, cramps were induced by exertion, but later occurred at rest. The severity of the myotonia remained unchanged. At age 56 years old he visited our hospital complaining of frequent painful cramps. He had never had muscle pain except for cramps, paralytic attack or history of pigmenturia. His unrelated parents, who had died earlier, three brothers and one sister had no similar symptoms. His two sons aged 29 and 28 years old were normal on clinical and electrophysiological examinations, and showed normal serum creatinine kinase (CK) values.

Physical examination revealed no frontal balding, testicle atrophy, cataract, contracture of the wrist and ankle joints or pes cavus. There was no muscle weakness, wasting, fasciculation or muscle hypertrophy. Percussion myotonia was present in the tongue, forearms, hands and legs. Grip myotonia was prominent, but there was no spontaneous myotonia in the craniobulbar, neck or trunk muscles. Paradoxical myotonia was not seen. Muscle stretch reflexes were normal. During manual test of the muscle strength, cramps with violent pain were elicited without fail in the biceps brachii, quadriceps femoris, tibialis anterior, gastrocnemius, small foot or flexor digitorum longus muscle. The cramping muscle was visibly and palpably firm and bulging, and after the painful cramps, myotonia without pain frequently followed. The painful cramps lasted for 30 seconds to 1 minute, but those could terminate passive stretching of the cramping muscle.

Routine blood and urinary examinations were normal. Serum CK levels were 180 to 1,500 U/l (normal: 50–280). Serum aldolase and myoglobin levels were 4.2 to 10.4 U/l (normal:...
2.5–6.1 U/l, and 45 to 120 ng/ml (normal: less than 60 ng/ml), respectively. Serum values of electrolytes, lactate, pyruvate, immunoglobulins G, A and M, and metals were all within normal limits. Functions of thyroid, parathyroid, pituitary, gonadal and adrenal hormones were normal. RA factor, LE test, antinuclear antibody and antimitochondrial antibody were all negative. Peroral 75g-glucose tolerance test revealed a normal pattern. Deep cooling for 30 minutes with water at 10°C did not elicit myotonia, weakness or flaccid paralysis in the hand and forearm. Ischemic exercise, performed in the right arm, produced no unusual symptoms. A slit lamp examination disclosed no abnormality. An electrocardiographic examination showed normal findings. Examinations of muscle and brain CT scans, and muscle and brain MRIs disclosed no abnormality.

Specific Examination

Electrophysiological examination

On needle EMG examinations, insertion potentials were markedly increased and showed myotonic discharges with dive bomber sounds; the size of action potentials varied with polyphasic potentials (Fig. 1A). During mild muscle contraction, short-duration polyphasic potentials were observed (Fig. 1B). Needle electromyographic investigations during painful cramps showed high-amplitude, high-frequency discharges resembling motor unit potentials, and when the muscle pain was diminished, myotonic discharges frequently followed (Fig. 2). Sensory and motor nerve conduction velocities including the median, radial, posterior tibial and sural nerves were revealed to be within normal limits.

Study of biopsied muscle

Muscle biopsy specimens, obtained from the left biceps brachii muscle, were used for various histochemical stainings, and muscle enzyme analysis.

On pathological examination, there was a mild variation in fiber size and an increase in the number of central nuclei. Fibrous tissue in the interstitium was not increased in amount. Intermofibrillar networks were mildly disorganized in some fibers. PAS and oil-red O positive materials did not increase in amount. Type 1, 2A, 2B and 2C fibers comprised 35%, 19%, 45% and 1%, respectively. Other staining procedures including nonspecific esterase, acid phosphatase, alkaline phosphatase, phosphorylase, cytochrome c oxidase, phosphofructokinase, and adenosine monophosphate deaminase stains revealed no abnormal changes.

On biochemical study, activities of glycolytic enzymes were all within normal limits (Table 1). Lactate was fully formed when glycogen was added in the muscle homogenate in anaerobic state (Fig. 3).

DNA analysis

CTG repeat length within the 3' non-coding region of the myotonin protein kinase gene was studied using the method of Brook et al (4). Genomic DNA was isolated from peripheral blood leukocytes. The DNA was digested with the restriction enzymes SacI and PstI. The DNA probe, presented by Drs. DJ Shaw and PS Harper (4) was used. There was no abnormal expansion of CTG repeat length on PCR amplification, using the primers 101 and 102, presented by Drs. DJ Shaw and PS Harper (4), was performed. Analysis of the product obtained by PCR showed 5 and 11 CTG repeats in the DNA.

Discussion

Although the disorders accompanied by both myotonia and muscle cramps are extremely rare, a few cases have been reported. Stöhr et al (5) described four hereditary patients characterized by weakness and painful spasms during effort. Their cases, however, had no percussion myotonia and did not show electrical activity in the shortened muscles during the cramps. Sanders (6) stated a family which showed dominantly inherited myotonia congenita and painful muscle contractions. However, the muscle contractions, which were disclosed to be
Figure 2. Needle EMG findings during painful cramp. A) After the myotonic discharges diminished completely the patient was asked to plantar flex the foot with his maximal strength against resistance (arrows in Figure), and also the patient was asked to relax the muscle immediately at the same time when he had painful cramp. After the second arrow, high-amplitude, high-frequency motor unit potentials occurred. The discharges gradually increased and decreased in amplitude and frequency. After the painful cramp the myotonic discharges appeared. B) During a muscle cramp which occurs spontaneously high-amplitude, high-frequency motor unit potentials are observed.
Table 1. Activities of Glycolytic Enzymes

<table>
<thead>
<tr>
<th>Enzyme</th>
<th>Patient</th>
<th>Control</th>
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<tbody>
<tr>
<td>Phosphorylase (-AMP)</td>
<td>1.9</td>
<td>3.1 ±1.6</td>
</tr>
<tr>
<td>Phosphorylase (+AMP)</td>
<td>73.9</td>
<td>44.7 ±19.6</td>
</tr>
<tr>
<td>Phosphoglucomutase</td>
<td>228.5</td>
<td>261.1 ±70.1</td>
</tr>
<tr>
<td>Phosphohexoisomerase</td>
<td>981.6</td>
<td>838.9 ±221.1</td>
</tr>
<tr>
<td>Phosphofructokinase</td>
<td>16.6</td>
<td>19.9 ±11.1</td>
</tr>
<tr>
<td>Aldolase</td>
<td>519.4</td>
<td>380.6 ±112.0</td>
</tr>
<tr>
<td>Glyceraldehyde-3P-dehydrogenase</td>
<td>2,308.2</td>
<td>1,708.1 ±536.6</td>
</tr>
<tr>
<td>Phosphoglycerate kinase</td>
<td>1,154.1</td>
<td>770.6 ±172.8</td>
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<td>Phosphoglycerate mutase</td>
<td>1,208.2</td>
<td>820.4 ±191.3</td>
</tr>
<tr>
<td>Enolase</td>
<td>432.8</td>
<td>331.3 ±64.3</td>
</tr>
<tr>
<td>Pyruvate kinase</td>
<td>1,443.6</td>
<td>991.2 ±292.2</td>
</tr>
<tr>
<td>LDH</td>
<td>1,384.9</td>
<td>1,302.4 ±517.5</td>
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</tbody>
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nmoles of substrate utilization/min/mg protein.

Anaerobic glycolysis in vitro

Figure 3. Lactate content showed a sufficient increase when glycogen was added in the muscle homogenate obtained from the patient.

Electrically silent, were improved after thyroid replacement therapy.

Thornton et al (7) reported three cases of myotonic dystrophy with no trinucleotide repeat expansion. One of their cases showed stiff and painful muscles after athletic activities in addition to myotonia, cataracts, prominent calf muscle and mild muscular weakness. The painful muscle stiffness does not seem to be true muscle cramps. Brody (8) stated a syndrome of exercise-induced stiffness and cramping with some pain which causes difficulty in relaxing, but there is no grip or percussion myotonia and EMG reveals no myotonic discharges.

Becker's cases of autosomal dominant myotonia with painful cramps resemble those of the present patient (1, 2). However, it is not clear whether or not the disorders of our patient and Becker's cases were the same because the electrophysiologic findings during the painful muscle cramps were not described in Becker's cases, and our patient had no family history. While, our patient may be a sporadic case of autosomal recessive form of myotonia congenita, but muscle pain or cramps usually do not occur in the autosomal recessive form of myotonia congenita (9).

The clinical features and findings of the various examinations differed in our patient from cases of paramyotonia congenita, myopathy with tubular aggregates (10), a syndrome of painful cramps, fasciculation and muscle pain (11–14) or glycogen storage diseases.

The possibility that the myotonic disorder and the cramp disorder in our patient are coincidental cannot be entirely excluded. However, there is a convincing hypothesis that cramps are caused by hyperexcitability of the intramuscular terminal motor axons and the hyperexcitability of the intramuscular portion of the motor nerve terminals may occur by changes in volume or concentration of the extracellular fluid of the muscle fiber (15–18). While, it is well known that there are electrophysiologic abnormalities of the muscle fiber surface membrane in myotonic disorders. From those points, there is the possibility that the present case may have some abnormalities in the membrane of both the muscle fibers and the intramuscular motor nerve terminals, which are strongly influenced by the condition of the extracellular space. However, more detailed investigations are needed to clarify the pathogenesis of the muscle cramps and myotonia in this patient.

References
13) Lazaro RP, Rollinson RD, Fenichel GM. Familial cramps and muscle
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