

# Autosomal Dominant Myotonia Congenita (Thomsen's Disease): A Report of the first Saudi Family and Literature Review

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**Objective:** To report the clinical and electromyographic profile of patients diagnosed with autosomal dominant (Thomsen's) myotonia congenita.

**Setting:** Neurology service at King Fahd Hospital of the University (KFHU), Al-Khobar, Saudi Arabia.

**Methods:** Review of a patient diagnosed with autosomal dominant (Thomsen's) myotonia congenita and his immediate family members.

**Results:** Autosomal dominant (Thomsen's) myotonia congenita was diagnosed in 3 members of the same family, mother and two offsprings (1 male, 1 female). The main features of the disease was autosomal dominant inheritance, painless myotonia that improved with exercise "warm up phenomenon", absence of weakness, muscle hypertrophy and myotonic discharges on electromyography.

**Conclusion:** The first Saudi family with Thomsen's myotonia congenita is reported. Further evaluation exploring the extent of the disease in this kindred is warranted.

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Myotonia is defined as delayed relaxation following skeletal muscle contraction either voluntarily or in response to mechanical or electrical stimulation. It is seen in a variety of dystrophic and non-dystrophic syndromes<sup>1</sup>. The dystrophic forms are part of the autosomal dominant myotonic dystrophy and proximal myotonic myopathy<sup>2</sup>. The non-dystrophic forms include myotonia congenita, hyperkalemic periodic paralysis and paramyotonia congenita<sup>1-3</sup>. Myotonia congenita is subdivided into an autosomal recessive (Becker's type) and an autosomal dominant (Thomsen's type)<sup>4</sup>. A genetic classification of the non-dystrophic myotonic syndromes based on abnormalities of the membrane ionic channel has recently been introduced<sup>5,6</sup>. No previous reports on myotonia congenita are available from the Kingdom of Saudi Arabia. This report describes the first Saudi family with autosomal dominant myotonia congenita who presented to the Neurology Clinic at King Fahd Hospital of the University (KFHU), Al-Khobar in December 1996.

## METHODS

AM is 5-year-old Saudi boy who was referred to the Neurology clinic for possible muscular dystrophy. He is a product of full term pregnancy and normal spontaneous vaginal delivery with a birth weight of 3.0 kg and an apgar's score of 9 and 10 at 1 and 5 minutes. The developmental milestones, feeding and sleep patterns were normal. At the

age of 2 years, he was noted to have difficulty in standing and walking. There was noticeable slowing at the beginning of walking but after a few steps became normal. These symptoms were exacerbated in winter. During this season the mother noted the occurrence of frequent falls. The patient has 5 brothers and sisters. One sister aged 4 years had similar complaints. The family history revealed a 28-year-old maternal female cousin, residing in Bahrain who suffered similar problems.

The general physical examination of the patient and his sister was unremarkable. The neurologic examination showed noticeable muscular development. Action and percussion myotonia were present. They both started to move slowly after standing but returned to normal walking pace after a few steps indicating a positive "warm-up" phenomenon.

Investigations including hemogram, coagulogram, serum biochemistry and liver function tests, serum creatinine kinase (CK), thyroid function tests and serum ammonia were normal. Nerve conduction studies of the tibial, peroneal and sural nerves were normal. Monopolar needle electrode examination showed diffuse frequent myotonic discharges (Fig 1). Cooling of muscle added no further information. Family screening was done including neurologic examination, serum CK levels, chromosomal analysis, nerve conduction studies and needle electromyography.

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**Table 1: Non-dystrophic Myotonia's: Clinical Characteristics**

Character	Myotonia Congenita "Thomsen's"	Myotonia Congenita "Becker's"	Hyperkalemic Periodic Paralysis	Paramyotonia Congenita
Age of onset	Infancy and early childhood	Late childhood	Infancy, early childhood	Early childhood
Inheritance	Dominant	Recessive	Dominant	Dominant
Abnormal Chromosome	Chromosome 7	Chromosome 7	Chromosome 17	Chromosome 17
Muscle weakness	Absent	May be present	Present during attack	Present especially after exposure to cold
Muscle Hypertrophy	Present; usually generalized	Present; usually in legs	Absent	Absent
Distribution of Clinical Myotonia	Generalized	Generalized	Eyelids, Generalized	Eyelids
Precipitating Factor	Rest, Cold	Rest, Cold	Rest after exercise, ingestion of high K containing food, emotional stress	Repetitive activity, Cold
Ion channel affected	Chloride	Chloride	Sodium	Sodium
Pharmacologic Therapy	Quinine (25 mg/kg/day every 8 hrs) Phenytoin (3-7 mg/kg/day every 8 hrs) Procainamide (15-50 mg/kg/day every 3-6 hrs)	Quinine Phenytoin Procainamide	Thiazides (e.g. Chlorothiazide 250-100 mg/day) Acetazolamide (4-30 mg/kg/day every 6-8 hrs)	Mexilitine (150-190 mg/day) Tocanide (400-1200 mg/Day)

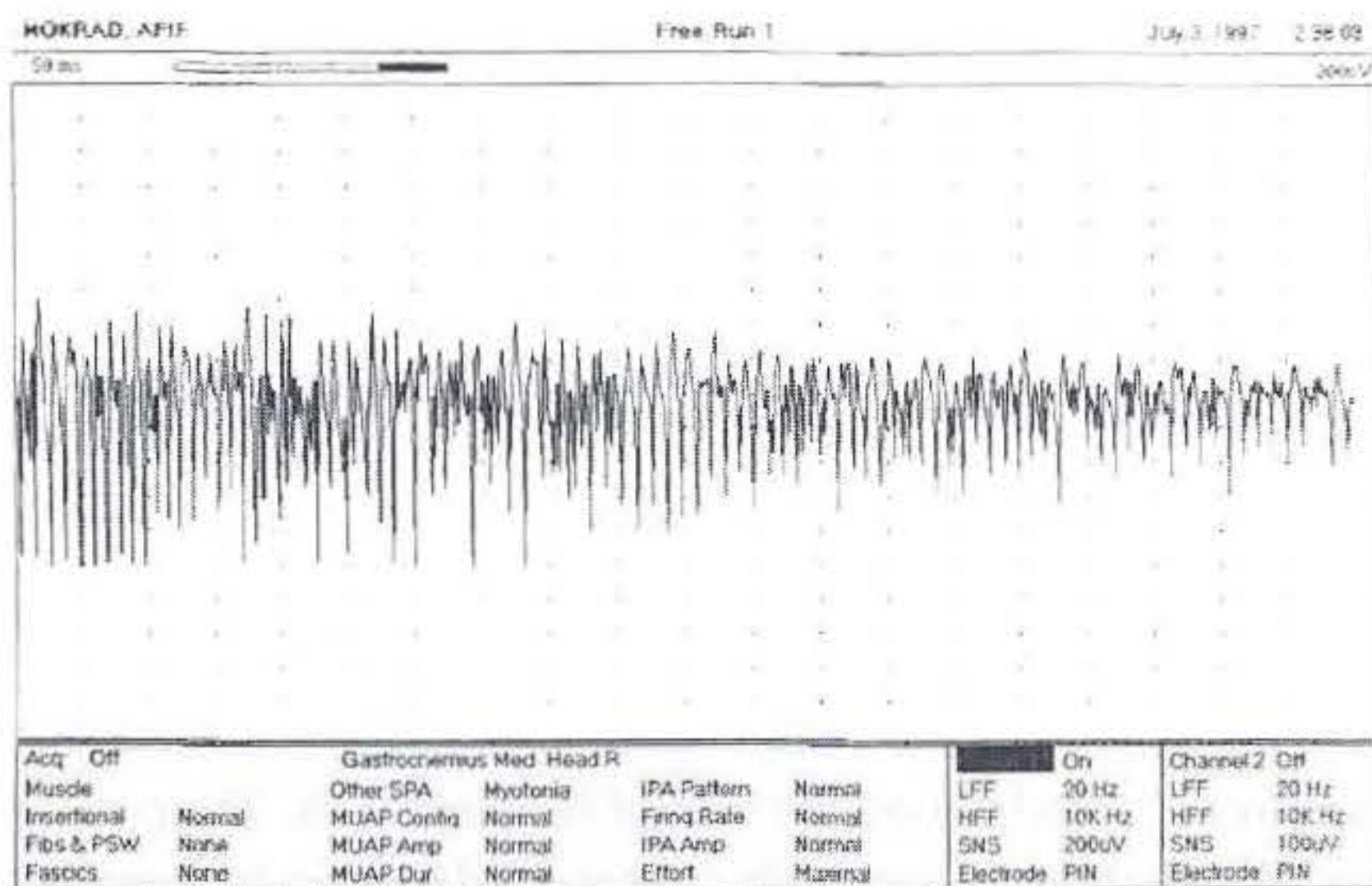


Figure 1. Shows example of myotonic discharges recorded from the medial head of the gastrocnemius muscle using monopolar needle electrode. (Sweep Speed: 50 msec, Sensitivity: 200 uv)

The screening included the father, mother and the 5 siblings. The mother also had well developed muscles, positive clinical and electrophysiological myotonia. The father and the other four siblings were normal.

**DISCUSSION**

The phenotype of myotonia congenita (Thomsen's disease) is characterized by autosomal dominant inheritance, painless myotonia that improves with exercise "warm up phenomenon", absence of weakness, muscle hypertrophy, clinical myotonia and myotonic discharges on electromyography<sup>7</sup>. All these characteristics were present in our patients. On the other hand autosomal recessive inheritance of myotonia congenita indicate Becker's type in which weakness may occur<sup>4</sup>. The differential diagnosis of myotonia congenita includes other non-dystrophic forms of myotonia including hyperkalemic periodic paralysis and paramyotonia congenita<sup>1,3,4</sup> (Table 1).

Hyperkalemic periodic paralysis is seen in infancy and early childhood but the myotonia is associated with episodic

weakness that is precipitated by rest after exercise, emotional stress or ingestion of food with high content of potassium<sup>8</sup>. The serum and urinary excretion of Potassium are often elevated. Histologically the muscle may exhibit vacuoles or degenerating or atrophic fibers<sup>9</sup>.

Paramyotonia congenita is frequently seen in the 1st decade of life<sup>1,10</sup>. In this disorder myotonia worsens with activity hence, it has been termed paradoxical myotonia<sup>11</sup>. Cold temperatures also exacerbate myotonia<sup>9</sup>. Laboratory tests are usually normal<sup>12</sup>. However, electromyography unveils the typical waxing and waning repetitive potentials characteristic of myotonic discharges. Both hyperkalemic periodic paralysis and paramyotonia congenita are dominantly inherited and the abnormality map to chromosomes<sup>17</sup> and results in sodium channel abnormalities<sup>13</sup>. The sodium channel perturbation leads to an abnormally large sodium conductance, accumulation of sodium intracellularly and thereby persistent depolarization and hyperexcitability<sup>14-16</sup>.

The molecular basis of both Thomsen's and Becker's forms of myotonia congenita have been shown to result from mutations in a gene encoding a voltage-sensitive, skeletal-muscle chloride channel on chromosome 7<sup>17-19</sup>. The mutation known to cause myotonia congenita abolished chloride conductance<sup>20</sup>. The reduced chloride conductance will reduce the normally high influx of the negatively charged chloride ions down their concentration gradient in the depolarized membrane, leading to failure of re-polarization and hence membrane hyperexcitability<sup>20</sup>. This manifests clinically as delayed relaxation of skeletal muscles.

The main mode of therapy in myotonia congenita is administration of "membrane stabilizing" drugs that may ameliorate myotonia<sup>4</sup>. Studies of drug treatment have not differentiated the various types of non-dystrophic myotonia's. The most commonly used drug is phenytoin. However, a number of other drugs were found useful to varying degrees

including: quinine, procainamide, mexilitine, tocanide and acetazolamide<sup>21,22</sup>.

## CONCLUSION

**This study reports the first Saudi family with Thomsen's myotonia congenita. The clinical and electrophysiological features of this syndrome seems similar to those from the west.**

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