Arq Neuropsiquiatr 1995, 53(1):114-117

AUTOSOMAL RECESSIVE NONDYSTROPHIC MYOTONIA

REPORT OF A CASE WITH UNUSUAL CLINICAL COURSE

UMBERTINA C. REED, SUELY K. NAGAHASHI MARIE*, MARIO WILSON I. BROTTO*, CARLOS ALBERTO MARTINEZ*, PAULO E. MARCHIORI*, ARON DIAMENT*, JOSÉ ANTONIO LEVY**

SUMMARY - We describe the case of a girl with a probable autosomal recessive form of nondystrophic hereditary myotonia whose clinical findings are more compatible with the dominant ones mainly myotonia congenita of Thomsen or myotonia fluctuans. Besides the clinical aspects of the atypical form presented by our patient, the efficacy of the more available drugs employed for the treatment of myotonia congenita is briefly discussed .

KEY WORDS: myotonia congenita, myotonia congenita of Becker, myotonia congenita of Thomsen, myotonia fluctuans, antimyotonic treatment.

Miotonia congênita não distrófica autossômica recessiva: relato de um caso com aspectos clínicos atípicos

RESUMO - As miotonias não distróficas hereditárias podem ser divididas em um grupo mais heterogêneo, de herança autossômica dominante, que inclui a miotonia congênita de Thomsen, a paramiotonia congênita, a miotonia fluctuans e a paralisia periódica hipercaliêmica; e em uma forma mais rara, de herança autossômica recessiva, que é a miotonia congênita de Becker. É descrito o caso de uma adolescente com uma forma de miotonia de herança provavelmente autossômica recessiva, cujos achados clínicos, entretanto, são mais compatíveis com as formas de herança autossômica dominante, principalmente a miotonia congênita de Thomsen ou a miotonia fluctuans. Além do quadro clínico atípico apresentado pela paciente, são discutidos os aspectos principais do tratamento medicamentoso mais empregado atualmente para aliviar o fenômeno miotônico.

PALAVRAS-CHAVE: miotonia congênita, miotonia congênita de Becker, miotonia congênita de Thomsen, miotonia fluctuans, tratamento da miotonia.

The nondystrophic hereditary myotonias can be divided into a more heterogenous autosomal-dominantly inherited group that includes the myotonia congenita of Thomsen (MCT), the paramyotonia congenita (PMC), the myotonia fluctuans (MF) and the hyperkalemic periodic paralysis (HPP) and in a rarer autosomal recessive form, the myotonia congenita of Becker (MCB). Our patient, in spite of the probably autosomal recessive pattern of inheritance, shows a benign clinical course that was not influenced by the use of different drugs against myotonia. The aim of this report is to analyse briefly the main clinical and therapeutic aspects of this rare group of diseases in childhood.

CASE REPORT

SOF, a 13-year-old girl with consanguineous first cousins parents presented from 11 months of age stiffness in her right leg 3 to 4 times a week for about 2 minutes. Occasionally the stiffness had caused her to

*Department of Neurology, Hospital das Clínicas , Faculty of Medicine, University of São Paulo, Brazil.
Aceite: 31-agosto-1994.

Dra. Umbertina C. Reed - Divisão de Clínica Neurológica, Hospital das Clínicas, FMUSP - Av. Dr. Enéas de Carvalho Aguiar 255 - 05403-900 São Paulo SP - Brasil.

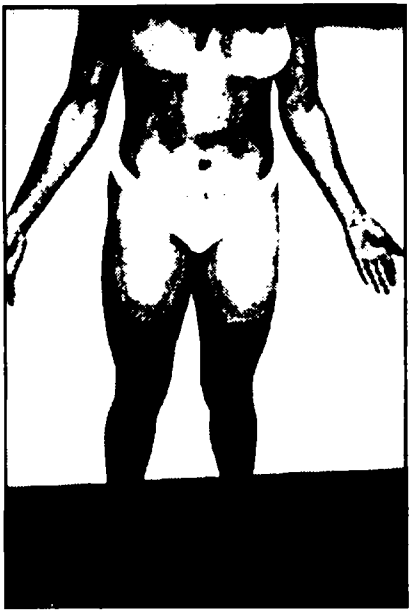

Fig 1. Patient SOF. Hypertrophy in the proximal muscles of the limbs.

fall. From 4 years of age she experienced the same disorder in the right leg and from 10 years of age the hands were also affected. However, in spite of this dissemination of symptoms, their intensity gradually decreased and presently the patient consideres her illness not much disabling. From the beginning the manifestations were unrelated to the exposure to the cold and were noticed only sporadically after exercise. Familiar history revealed many relatives with cataracts (mother, 2 maternal uncles, maternal grandmother and paternal great-grandmother), all of them only with cataracts, without any of the classical manifestations of myotonic dystrophy (Steinert disease), as dystrophic muscle involvement with myotonic sign, cardiac dysfunction, endocrine abnormalities, mental retardation or frontal balding. The neurological examination evidentiated a gait with lack of associated movements and a slight hypertrophy of the proximal muscles of the limbs with no myotonic sign (Fig 1). An electromyographic investigation (EMG) was performed in proximal and distal muscles of the limbs bilaterally and demonstrated typical runs of myotonic discharges in all muscles examined (Fig 2). A muscle biopsy and routine blood studies were normal. The creatine kinase level (measured in Sigma Units/mL) was 30 SU/mL (normal level for children 0-14 years of age: until 20 SU/mL). As there was familiar history of cataract, the girl was submitted to DNA analysis that showed normal result, excluding the unstable fragment of DNA specific to individuals with myotonic dystrophy. The patient did not develop any manifestation after oral administration of 5 g potassium chloride. An EMG was performed in both patient's parents and revealed no abnormalities. Over a period of 18 months the patient was treated sucessively with diphenylhydantoin, carbamazepine, diazepam, quinidine, placebo, nifedipine and mexiletine. Each treatment phase was maintained for at least 2 months except for dyphenylhydantoin and carbamazepine that were discontinued in few days due to allergic manifestations. During the first month of its utilization nifedipine had a favourable effect but the relief of symptoms was temporary.

COMMENTS

The type of myotonia congenita presented by our patient is difficult to characterize. Since a recessive pattern of inheritance (consanguineous parents) is more probable, a diagnosis of MCB

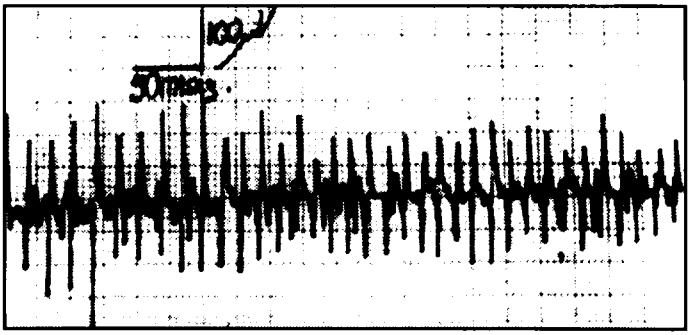

Fig 2. Patient SOF. Electromyography of the left quadriceps femoris and anterior tibialis muscles after mechanical stimulation with needle electrode. Note myotonic discharges, consisting of short low voltage potentials with typical features of waxing and waning of potential amplitude and discharge frequency.

should be considered. However, onset of MCB tends to occur later in childhood[2,4] and the course is often progressive and disabling. Occasionally patients may show slight weakness and wasting during adolescence[2,4,10]. The normal result of the EMG performed in the patient's parents removes the remote possibility of an autosomal dominant pattern of inheritance and that the consanguinity could be only an occasional finding. Anyway, the clinical manifestations of our patient would be atypical even for the diagnosis of MCT. In this form the degree of myotonic stiffness is relatively evident and constant in infancy and action or percussion myotonia may occur in almost any muscle. Exposure to cold, prolonged rest, stress and puberty may increase the myotonia, whereas exercise improves it[2,4]. Our patient does not exhibit any of these findings.

PMC is an autosomal dominant form of myotonia with development of stiffness after exposure to cold and cold- or exercise-induced weakness or paralysis[9,11]. Therefore, PMC cannot be considered in this case either.

Another autosomal dominant type of myotonia is MF that shows benign clinical course with an unusual degree of fluctuation of the stiffness[9]. In this form the myotonia can manifest itself only occasionally and increases with potassium loading. The induced grip myotonia decreases following repeated muscle contractions, but gradually returns after 15 minutes of rest. This phenomenon is called exercise-induced delayed-onset myotonia[9]. Our patient in spite of the benign fluctuating course of the myotonia differs from those with MF not only by the recessive pattern of inheritance, but also by the lack of worsening with cold, sensitivity to potassium loading and exercise-induced delayed-onset myotonia.

Finally, HPP is easily excluded by the lack of transient episodes of paralysis.

The treatment of myotonia is based on the knowledge that in myotonia congenita there is an abnormality of chloride conductance across the muscle fiber membrane[1] whereas in PMC, in MF and in HPP there is a membrane defect in the sodium channels system[1,6]. The first abnormality is probably dependent of genetic defect at chromosome 7q, whereas the second is associated to the chromosome 19q[8].

Recently, Ptacek et al.[8] discussed if the MCB-causing mutation could be analogous to that observed in the ADR mouse, an animal model of the recessive form of myotonia congenita. In affirmative case the mutation would result in the disruption of chloride conductance across the muscle membrane by different ways. To explain the autosomal recessive transmission, these authors[8] considered that the defect would be a "loss of function" mutation in which a single normal copy may be sufficient to confer the normal phenotype.

At present time there is no effective pharmacological agent that acts on chloride conductance[1]. So, the more useful drugs against myotonia have been a variety of agents that act on sodium channel activity: quinidine, diphenylhidantoin, procainamide, tocainide and mexiletine[1,4,5,7,8]. Calcium-channel antagonists, such as nifedipine, have also been used to treat myotonia that was unresponsive to other medication[1]. This drug, acting on T-tubular calcium transport, would inhibit the mechanisms of muscle contraction[3]. Most agents utilized in our patient were uneffective in controlling the stiffness. We did not try procainamide in accordance with the cardiologist because of its side effects. Tocainide is not avaliable in our country. Some authors questioned the treatment of myotonia during childhood because of the side effects of most avaliable drugs[5,7]. According with the literature[2,4,7], it is our opinion that treatment is superfluous when myotonia does not interfere significantly with daily activities. The benefits and the risks of treatment must be carefully considered[5]. In our patient the results of treatment were disappointing and the beneficial effect of nifedipine lasted only a month, a fact already emphasized by Bethlem & Knobbout[2].

REFERENCES

1. Barchi RL. Myotonia. Neurol Clin 1988, 6: 473-484.
2. Bethlem J, Knobbout CE. Neuromuscular diseases. Oxford: Oxford Univ Press, 1987, p 107-119.
3. Cook JD, Henderson-Tilton AC. Beneficial responses to a calcium channel antagonist in myotonic syndromes. Neurology 1984, 34 (Suppl 1): 193-194.
4. Gutmann L, Phillips LH. Myotonia congenita. Semin Neurol 1991, 11: 244-248.
5. Kwiecinski H, Ryniewicz B. A comparative study of disopyramide, diphenylhydantoin, mexiletine and tocainide in the treatment of myotonia. J Neurol Sci 1990,98 (Suppl): 113.
6. Lehmann-Horn F, Rüdel R, Ricker K. Membrane defects in paramyotonia congenita (Eulenburg). Muscle Nerve 1987,10: 633-641.
7. Moxley RT III. New therapies for the nondystrophic hereditary myotonias and paramyotonias. J Neurol Sci 1990,98 (Suppl): 111.
8. Ptacek LJ, Johnson KJ, Griggs RC. Genetics and physiology of the myotonic muscle disorders. N Engl J Med 1993, 328: 482-489.
9. Ricker K, Lehmann-Horn F, Moxley RT III . Myotonia fluctuans. Arch Neurol 1990,47: 268-272.
10. Rüdel R, Ricker K, Lehmann-Horn F. Transient weakness and altered membrane characteristic in recessive generalized myotonia (Becker). Muscle Nerve 1988, 11: 202-211.
11. Streib EW. Paramyotonia congenita. Semin Neurol 1991, 11: 249-257.