

# Cardiomyopathy secondary to Steinert's dystrophy

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## Summary

*Myotonic dystrophy type 1 (MD1 or Steinert's disease) is a genetic syndrome with multisystemic repercussions, and it is usual to the patient to seek for several specialists before clinical suspicion. It is related a case of a 28 years old male patient admitted with congestive heart failure. MD1 has been diagnosed eight years before. At the time of the diagnosis, he presented syncope secondary to complete atrioventricular block. From that time on, he had a permanent pacemaker implanted. Etiological, pathophysiological and clinical aspects of MD1 with emphasis on cardiovascular manifestations are discussed.*

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**Keywords:** Steinert's disease - Myotonic dystrophy - Heart failure - Atrioventricular block - Artificial pacemaker.

## Introduction

Myotonic dystrophy (MD) is a progressive genetic syndrome, autosomal dominant, maternally inherited. MD is the most common neuromuscular disease in adults. It has a prevalence of 1:8000 births<sup>1</sup> and presents 2 types: type 1 (MD1 or Steinert dystrophy) and type 2 (MD2). MD1 is the most common type and is manifested in its classic form between 12 and 30 years of age. Patients present cardiac abnormalities such as atrioventricular (AV) block, atrial and ventricular arrhythmias and heart failure (HF). Other manifestations include hypogonadism and infertility, cataracts, sleep disorders, insulin resistance and hypothyroidism. Due to the multisystem context, it is common for the patient to try several specialists before the clinical suspicion of disease.

## Case report

### History and physical examination

A case of a man aged 28, born in Niterói (RJ, Brazil), unmarried and occupation: teacher. He was diagnosed with Steinert's dystrophy in 2003, after investigation of syncopal episode, culminating after diagnosis of AV block or complete grade 3, with implantation of a pacemaker (PM) bicameral. Their evolution was asymptomatic for the next five years. In 2008, he presented with dyspnea on great effort, diagnosed as IC. He began outpatient treatment with carvedilol, spironolactone, furosemide and digoxin. In 2011, he had worsened, with worsening of neuromuscular symptoms and signs of systemic congestion. Three months before admission, he presented

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## Discussion

progressive dyspnea, evolving from large to minimal effort (New York Heart Association -NYHA- functional class II-III), orthopnea, paroxysmal nocturnal dyspnea (PND), leg edema and increased abdominal volume. As family history, her mother was diagnosed as a carrier of DM1 and heart disease, with death at 33 years of age. Without any other cases of chromosomal diseases or sudden death in the family.

Physical examination showed: lucid and oriented with typical facies Steinert disease with atrophy of the temporal and masseter muscles. Had a heart rate of 60 bpm, a blood pressure of 90/60 mm Hg. Emaciated (body weight of 50.7 kg and BMI of 17.1 kg/m<sup>2</sup>). Tachypneic (22 rpm) without respiratory effort. No jugular venous distention at 45 degrees. Apical impulse visible in the 5<sup>th</sup> intercostals space, left midclavicular line, sustained 2 finger widths. Regular heart rhythm in four times for 3 and 4<sup>th</sup> sounds, no murmurs. He presented bilateral gynecomastia, symmetric and painless, venous collateral circulation in front of the chest, intercostal muscles consumed with costal arches visible. Pulmonary examination unchanged. His abdomen had a circumference of 76 cm and the presence of moderate ascites. Lower limb edema (3+/4+). Anisocoric pupils (left>right) and photoreactive. Absence of myotonic reflex. Static equilibrium and coordination preserved. Proximal muscle strength grade 4.0 in the upper and lower limbs and neck, and 4 - feet. Hyporeactive and symmetrical deep reflexes. Sensitivity preserved (Figures 1A and 1B).

### Complementary tests

Chest radiograph in posteroanterior and lateral evidenced cardiomegaly (cardiothoracic ratio= 0.53), MP bicameral lungs unaltered (Figures 2A and 2B). The electrocardiogram showed command of the pacemaker (Figure 3). The echocardiogram showed biatrial enlargement, biventricular dysfunction with severe diffuse hypokinesia of the left ventricle, mild mitral regurgitation and moderate tricuspid regurgitation, pulmonary artery systolic pressure estimated at 48 mm Hg; dilated inferior vena cava and AV dyssynchrony. Estimated creatinine clearance of 96 mL/min, serum sodium of 130 mEq/L, total bilirubin of 2.89 mg/dL with direct fraction of 1.69 mg/dL.

### Evolution

He was admitted to cardiology and was given intravenous furosemide, carvedilol, spironolactone and digoxin, which was later discontinued due to elevated digoxinemia (3.5 ng/mL). The patient remained hospitalized for eight days, with clinical and laboratory improvement. Return to NYHA functional class II, with remission of PND. The patient presented regression of edema of lower limbs (1/4 +), discrete reduction of ascites and abdominal volume (74 cm) and significant decrease in body weight loss of 1.7 kg was discharged with improved symptoms and regression of the signs.

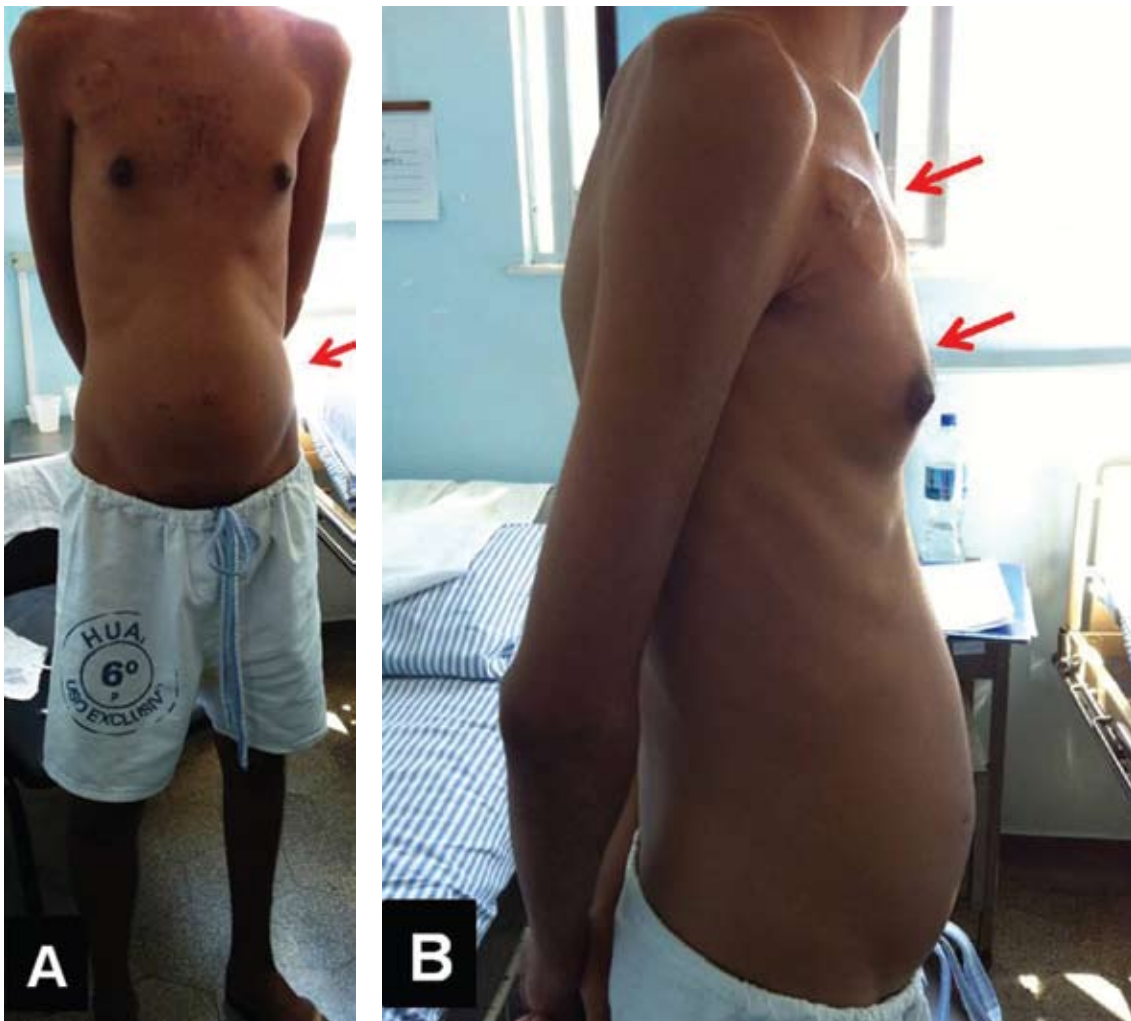
The clinical presentation of DM1 varies with the number of repetitions of the chain tyrosine-guanine-cytosine (TGC) in the gene of the protein-kinase. The number of repetitions determines the occurrence of mild clinical forms (50-150 repeats), classical(100-1000) or severe (500-2700)<sup>1</sup>. Patients with DM1 have classic profile of symptom onset between 12 and 30 years of age, presenting muscle weakness and atrophy, myotonia, cataracts, alopecia and cardiac conduction defects<sup>1</sup>. Although the patient in this case was not conducted genetic research, presented history and clinical manifestations suggestive of classic phenotype, ie, abnormal gait, maintenance of the muscles of the hands, typical facies, including ptosis and atrophy of the masseter muscle and dysphagia for solids. DM1 predominates in distal progressive muscle weakness, difficulty making fine movements with hands and feet. The characteristic facies depends on the weakness of facial muscles. The flexor muscles of the neck are often involved. It presents injury adrenergic neurons of the ascending reticular formation and may be accompanied by neuropathias<sup>2</sup>. The commitment of the gastrointestinal tract leads to reduced motility of the hypopharynx and proximal esophagus, resulting in dysphagia and pneumonia aspiración<sup>1-5</sup>. Other clinical features described, but absent in this patient are: cataract, alopecia, insulin resistance, irritable bowel syndrome, cholecystitis and miotonia<sup>1</sup>.

This patient had clinical disease (DM1) at 20 years of age and reported that the same disease caused the death of his mother, after 33 years of her age. Several studies showed that the life expectancy of these patients is below the average for the general population. The immediate causes of mortality, in decreasing order, are: (1<sup>st</sup>) pneumonia, (2<sup>nd</sup>) neuromuscular weakness, (3<sup>rd</sup>) cardiovascular compromise or sudden death attributed to conduction disturbances, and (4<sup>th</sup>) cáncer<sup>6-8</sup>. The average age of death from the literature is 54 years, with stories of survival to age 80, with increased longevity attributed to a mild form of the disease.

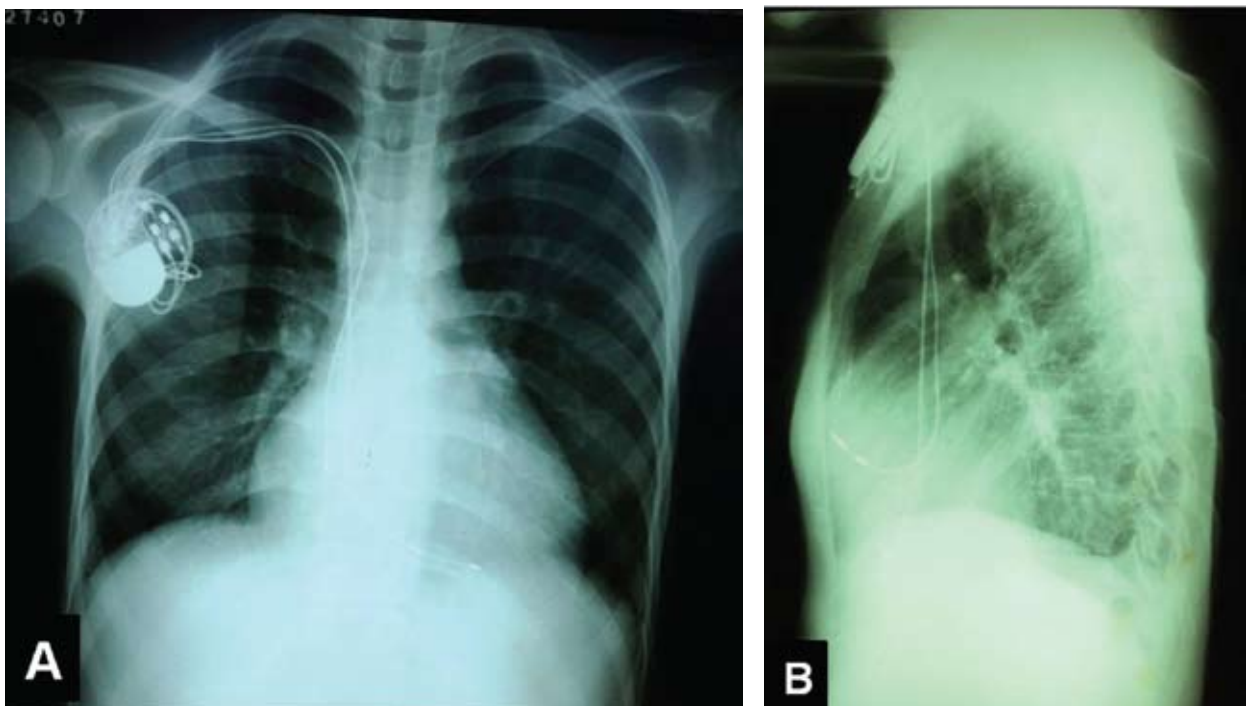
Life expectancy of DM1 differs from other neuromuscular diseases such as Duchenne muscular dystrophy (DMD), which has a significantly lower life expectancy. Repeated infections and thromboembolic complications increases the rate of mortality in these patients<sup>9-11</sup>.

The patient failed to perform their work activities after two years of this hospital. The clinical manifestations of DM1 can affect state behavior, emotional and cognitive, social interaction difficult and the degree of learning, impairs daily activities and reducing the quality of life. In patients with DM1, the commitment of mental status and the presence of behavioral factors that influence the management of treatment and consequently in the prognosis<sup>12</sup>, but they were not present in this case.

Cardiac involvement is one of the main features of the development of DM1. Cardiac histopathology can demonstrate fibrosis of the conduction system and AV node, hypertrophy of cardiomyocytes and fatty infiltration. There are bands I prominent myofibrillar degeneration electron



**Figure 1.** Photos of front (A) and side (B). Steinert's disease patient. Evidence muscle atrophy, secondary to spironolactone gynecomastia, ascites, and pacemaker generator.



**Figure 2.** Chest X-ray front (A) and side (B). Cardiothoracic ratio of 0.53 and pacemaker.

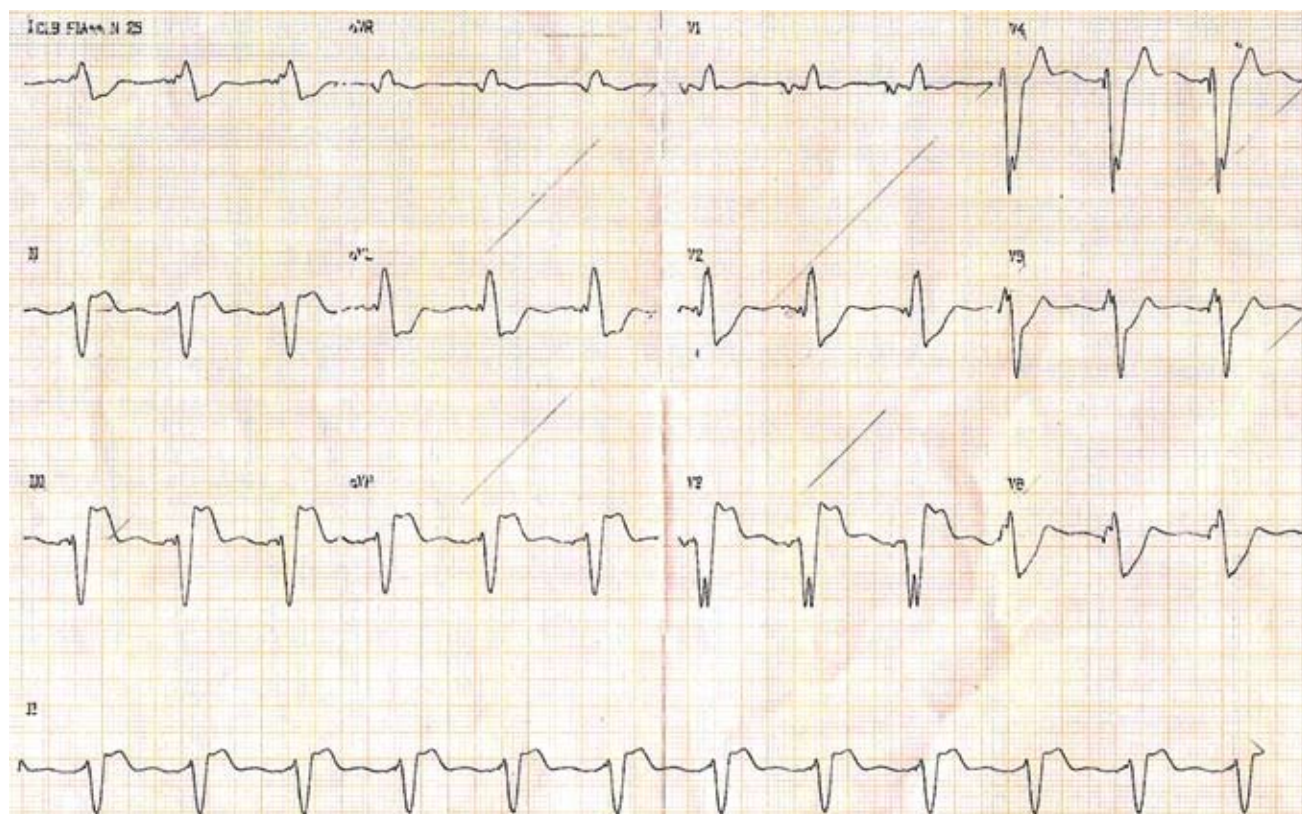


Figure 3. The basal electrocardiogram hospitalization shows pacemaker rhythm.

microscopy. Myocardial fibrosis and degeneration of the conduction system may lead to AV block, asystole, ventricular tachyarrhythmia or death súbita<sup>11</sup>. The conduction disturbances are common, mainly in the His-Purkinje system, with significant increase in PR interval and QRS prolongation. Despite its high incidence, these alterations are usually subclínicas<sup>13</sup>. Atrial or ventricular arrhythmias may be present, usually benign. There is a clear dissociation between the prevalence of electrocardiographic abnormalities with a low frequency of symptoms cardiovasculares<sup>14</sup>. There is no established correlation between the degree of symptoms of cardiovascular and musculoskeletal symptoms. It is believed that in the classical form, the more early neuromuscular manifestations occur -while being only myotonia in the second decade of life- greater the commitment of His-Purkinje system. Moreover, cardiac conduction disorders probably correlate with the evolution time and the degree of phenotypic variation in disease when the onset of neuromuscular symptoms is later (between the third and fourth decade of life). The presence of cardiac conduction disturbances in the case reported is considered a factor prognostic worse<sup>13</sup>.

The selection criteria for pacemaker implantation in these patients were not yet established, but it was shown that early use may prevent sudden death. Dilated cardiomyopathy can be early, but asymptomatic, and the difficulty of the exercises is a parameter of late presentation of HF, as the restriction of effort, due musculoskeletal dysfunction, precludes the practice of vigorous exercise in these patients. The proportion of patients with DM1 and HF with

preserved ejection fraction has not been described in the literature. The pathogenesis of myocardial dysfunction occurs only by muscle weakness or is aggravated by dyssynchrony in these patients. It is likely that the placement of an PM without resynchronization function could aggravate ventricular dyssynchrony and consequently worsen cardiac dysfunction. Steinert's disease should be considered as differential diagnosis in young patients with syncope associated with AV block. In addition, the patients diagnosed must be performed serial ECG<sup>15</sup>.

Research in genetic diagnosis of DM1 advanced since 1992, with the availability of a molecular biology test. Several studies have been published, with the expansion of an unstable CTG repeat in the DM protein kinase gene<sup>16-20</sup>, now considered the gold standard for diagnosis of DM1. It is appropriate to initiate diagnostic confirmation with genetic analysis, rather than making a electroneuromiography (ENMG). In general, information of a ENMG is limited, however, may be useful for atypical cases where there is no apparent clinical myotonia or when DM molecular tests are normal. In this case, the diagnosis of DM1 was based on clinical impression, practical support in the literature. Usually, the diagnosis can be established by muscle weakness and myotonia, added to a positive family history. The patient in this case presented, initially, a cardiac conduction disorder, although they have a history of positive family history and neuromuscular symptoms.

Treatment of DM1 was performed by symptomatic and multidisciplinary support. Orthopedic prostheses, eye surgery, physical therapy to control motor and medicines out

of myalgia, such as anti-inflammatory drugs, gabapentin, antidepressant, methylxanthines and glucocorticoids in low doses are employed in these patients<sup>21</sup>. This therapy is not applied to this patient because their neuromuscular symptoms were milder.

## Conclusion

DM1 is a serious disease with frequent cardiovascular compromise. Patients should be monitored for cardiovascular lesions, especially cardiomyopathy and conduction disorders, as are common in these patients and usually are underestimated given the magnitude of neuromuscular symptoms. Screening tests are recommended to address early diagnosis of this disease, even asymptomatic from the cardiovascular standpoint, however, the prognosis is reserved in most cases.

## Financial resources

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## Conflict of interest

The authors have no conflicts of interest to declare.

## References

1. Turner C, Hilton-Jones D. The myotonic dystrophies: diagnosis and management. *J Neurol Neurosurg Psychiatry* 2010;81:358-67.
2. Krishnan AV, Kiernan MC. Axonal function and activity-dependent excitability changes in myotonic dystrophy. *Muscle Nerve* 2006;33:627-36.
3. Ronnblom A, Forsberg H, Danielsson A. Gastrointestinal symptoms in myotonic dystrophy. *Scand J Gastroenterol* 1996;31:654-7.
4. Ronnblom A, Andersson S, Hellstrom PM, Danielsson A. Gastric emptying in myotonic dystrophy. *Eur J Clin Invest* 2002;32:570-4.
5. Heatwole CR, Miller J, Martens B, Moxley RT. Laboratory abnormalities in ambulatory patients with myotonic dystrophy type 1. *Arch Neurol* 2006;63:1149-53.
6. Reardon W, Newcombe R, Fenton I, Sibert J, Harper PS. The natural history of congenital myotonic dystrophy: mortality and long term clinical aspects. *Arch Dis Child* 1993;68:177-81.
7. Schoser BG, Ricker K, Schneider-Gold C, Hengstemberg C, Durre J, Bultmann B et al. Sudden cardiac death in myotonic dystrophy type 2. *Neurology* 2004;63:2402-4.
8. Nazarian S, Wagner KR, Caffo BS, Tomaselli GF. Clinical predictors of conduction disease progression in type I myotonic muscular dystrophy. *Pacing Clin Electrophysiol* 2011;34:171-6.
9. De Die-Smulders CE, Höweler CJ, Thijs C, Mirandolle JF, Anten HB, Smeets HJM et al. Age and causes of death in adult-onset myotonic dystrophy. *Brain* 1998;121(8):1557-63.
10. Mathieu J, Allard P, Potvin L, Prévost C, Bégin P. A 10-year study of mortality in a cohort of patients with myotonic dystrophy. *Neurology* 1999;52:1658-62.
11. Groh WJ, Groh MR, Saha C, Kincaid JC, Simmons Z, Ciafaloni E et al. Electrocardiographic abnormalities and sudden death in myotonic dystrophy type 1. *N Engl J Med* 2008;358:2688-97.
12. Roig M, Balliu PR, Navarro C, Brugera R, Losada M. Presentation, clinical course, and outcome of the congenital form of myotonic dystrophy. *Pediatr Neurol* 1994;11:208-13.
13. Nishioka SAD, Filho MM, Marie S, Zatz M, Costa R. Distrofia miotônica e cardiopatia. Comportamento dos eventos arrítmicos e dos distúrbios da condução. *Arq Bras Cardiol* 2005;84(4):330-6.
14. Rodríguez IJP, Rivas EG, Cabello A. Repercusión cardíaca de las enfermedades neuromusculares. *Rev Esp Cardiol* 1997;50:882-901.
15. Melacini P, Buja G, Fasoli G, Angelini C, Armani M, Scognamiglio R et al. The Natural History of Cardiac Involvement in Myotonic Dystrophy: An Eight-Year Follow-Up in 17 Patients. *Clin Cardiol* 1998;11:231-8.
16. Brook JD, McCurrach ME, Harley HG, Buckler AJ, Church D, Aburatani H et al. Molecular basis of myotonic dystrophy: expansion of a trinucleotide (CTG) repeat at the 3' end of a transcript encoding a protein kinase family member. *Cell* 1992;69:799-808.
17. Buxton J, Shelbourne P, Davies J, Jones C, Tongeren TV, Charalampos A et al. Detection of an unstable fragment of DNA specific to individuals with myotonic dystrophy. *Nature* 1992;355:547-48.
18. Fu YH, Pizzuti A, Fenwick RG Jr, King J, Rajnarayan S, Dunne PW. An unstable triplet repeat in a gene related to myotonic muscular dystrophy. *Science* 1992;255:1256-58.
19. Harley HG, Brook JD, Rundle SA, Crow S, Reardon W, Buckler AJ et al. Expansion of an unstable DNA region and phenotypic variation in myotonic dystrophy. *Nature* 1992;355:545-6.
20. Mahadevan M, Tsilfidis C, Sabourin L, Shutler G, Amemiya C, Janses G et al. Myotonic dystrophy mutation: an unstable CTG repeat in the 3' untranslated region of the gene. *Science* 1992;255:1253-55.
21. Kurihara T. New classification and treatment for myotonic disorders. *Intern Med* 2005;44:102.