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CONDUCTION AND RHYTHM DISORDERS IN STEINERT DISEASE: A SERIES OF CASES AND LITERATURE REVIEW

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ABSTRACT

Introduction: The most prevalent muscular dystrophy in adults, Steinert's myotonic dystrophy, is a multisystem illness with autosomal dominant transmission. The cause is the growth of CTG triplets in the gene that codes for the enzyme known as "dystrophia myotonica protein kinase". It is distinguished by the existence of rhythm and conduction abnormalities, which may result in unexpected death. **Methods:** A total of 21 cases were gathered for this 13-year retrospective investigation. **Results:** The purpose of this study is to identify the conductive problems that are present during DM1 and to emphasize the value of doing thorough cardiac exams and electrophysiological investigation. Systematic cardiac exploration was beneficial for 21 DM1 patients. Cardiovascular symptoms affect 68% of the patients. In 28% of the patients, an intraventricular conduction problem predominated the ECG abnormalities, and in 33% of the cases, an entire AV block was seen. Hyperexcitability is evident in the atrial and/or ventricular levels of the Holter ECG. 95 % of patients have normal ETTs. Three symptomatic patients had electrophysiological explorations, which objectified a prolongation of the HV interval and resulted in the implantation of a dual-chamber pacemaker. **Conclusion:** To identify patients at risk for severe disease, rigorous clinical and diagnostic examination is crucial. This is demonstrated by conduction system anomalies, such as atrial or ventricular arrhythmias.

KEYWORDS: Steinert's myotonic dystrophy, cardiac conductive disorder, rhythmic disorder, cardiac stimulation.

INTRODUCTION

Steinert myotonic dystrophy is a systemic genetic disease with autosomal dominant transmission that affects 1 in 8000 individuals. It is the most common neuromuscular disease in adults.[1] Cardiac complications are well known and several disorders have been reported: conduction disorders, atrial and ventricular rhythm disorders, recurrent syncope, sudden death, heart disease and mitral valve prolapse.[2,3] There are several clinical forms of very variable severity. Among them, the most stable form in adults occurs between 20 and 25 years of age, characterized by myotonia of the hands and heart problems which can sometimes lead to sudden death.

MATERIALS AND METHODS

This is a retrospective, descriptive and analytical study of cases of Steinert's disease involving patients collected in the cardiology department B at the Souissi maternity hospital in Rabat over a period of 13 years from 2009 until January 2022.

- Inclusion criteria: The patients included in this study all met the Diagnostic Criteria – Task Force 2010. Only patients with a certain diagnosis were included in the study.

- Exclusion criteria: Patients for whom we did not have enough clinical and paraclinical information were excluded.

Data collection: These patients were initially seen in the Neurology department where the diagnosis of DM1 was made based on the clinical history, myotonia, electromyogram data and genetic study. The patients underwent an ophthalmological, endocrine and digestive examination and were then referred to our structure for systematic investigation of associated cardiac involvement.

Clinical and paraclinical data were collected from patients' medical files and available reports of the various examinations, the tracings were reread when available. These data include epidemiological, clinical, paraclinical, therapeutic and evolving variables.

RESULTS

Epidemiologically, we collected 21 cases over a period of 13 years from 2009 to 2022. We noted a slight male predominance with 11 men / 10 women. The average age at diagnosis is 38.2 +/- 14.3 years (range: 14 to 69 years).

81% of our patients were symptomatic, the main cause was palpitations. 23% had faintness, 14% had NYHA stage II dyspnea, 9% had syncope and 9% also had chest pain, however 19% were asymptomatic.

All our patients had ECG abnormalities: 28% of patients with BBD, 14% of patients had a microvoltage P wave, and 14% had sinus bradycardia, 33% had complete BAV, 4% had preexcitation. and 4% a negative T wave in V1, V2.

All our patients had a Holter ECG, showing: 14% presented ESV, 14% of patients had ESV, 4% atrial hyperexcitability and 4% ventricular hyperexcitability, 4% paroxysmal AF, 4% sinus bradycardia and 23 % had sinus dysfunction. 26% of patients had a normal Holter ECG.

Electrophysiological exploration was normal in all patients, with the exception of 4 patients who had a prolongation of the HV interval beyond 70 ms.

All patients underwent ETT which was normal in 17 patients. One patient had a prolapse of the small mitral valve which was responsible for a moderate regurgitation, one patient had a dilatation of the left ventricle (LV) with a moderate LV dysfunction, one patient had a dilatation of the trunk of the pulmonary artery which was associated with a moderate regurgitation, and another patient had dilated cardiomyopathy in moderate LV dysfunction.

Therapeutically, three patients explored, and whose HV interval > 70 ms, benefited from implantation of a pacemaker for prophylactic purposes.

Evolution: the patient with 1st degree atrioventricular block (BAV) and paroxysmal atrial fibrillation presented with lipothymia after a year of progression and died of a respiratory illness before an electrophysiological exploration (EEP) could be performed.

The patient who had a short PR showed faintness and palpitations after a year of progression, with a left bundle branch block on the baseline ECG, the EEP concluded that his pre-excitation was benign. Only one patient in our series who was stimulated and who died following respiratory damage.

DISCUSSION

Steinert disease, also known as myotonic dystrophy type 1 (DM1), is a member of the group of muscular dystrophies. It is characterized clinically by its multisystem distribution and by a large inter- and intra-familial variability, namely the age of onset and clinical manifestations. The clinical severity and prognosis vary, ranging from the severe form in newborns to the late form in adults. In its classic form, it combines varying degrees of muscular (myotonia and weakness of distal skeletal muscles), respiratory, cardiac (rhythm and conduction disorders, sudden death), endocrine (hypogonadism, carbohydrate intolerance), ocular damage. (cataract), central neurological (hypersomnia, cognitive disorders) as well as premature baldness.

Steinert's disease is due to a genetic anomaly located on chromosome 19. It involves the repetition in high quantities of a small DNA sequence (CTG nucleotide triplet) in the DMPK gene (for dystrophia myotonica protein kinase). The existence of this excessively repeated sequence disrupts the activity of proteins which control muscular, cardiac, nervous, hormonal functioning, etc. The transmission of Steinert myotonia is autosomal dominant with an anticipation phenomenon. Indeed, there is a tendency to worsening and early onset of the disease in each descending generation. This anticipation phenomenon would be linked to an amplification of the CTG gene. The number of repeats of the CTG triplet also seems to influence the occurrence of cardiac complications.

Cardiac involvement is a frequent and important occurrence in DM1. It is estimated that 75 to 80% of patients have some degree of cardiac involvement with a clinically variable spectrum, ranging from mild electrocardiogram (ECG) abnormalities to severe arrhythmias leading to sudden death. In fact, up to a third of deaths in these patients are due to cardiac causes.

Conduction disorders are estimated at 40%. They can affect any stage of the conduction system; however, the His-Purkinje system is most commonly affected (4,6). Minor conduction abnormalities are commonly observed on standard electrocardiograms (ECGs) and His-Bundle studies such as 1st degree BAV detected on the ECG or during electrophysiological studies (5, 6). These minor defects can progress to more serious conduction defects often associated with shortness of breath, dizziness, fainting, syncope, and sudden death (4). Supraventricular tachyarrhythmias are a common finding on 12-lead ECG or 24-hour Holter monitoring, often asymptomatic. The most common arrhythmias are atrial flutter and fibrillation, seen in up to 25% of patients in nonsustained and sustained form (7). Ventricular arrhythmias such as ventricular tachycardia (VT) and ventricular fibrillation can also occur in patients with DM1.

The prevalence of Steinert's disease varies from 10 to 12 people affected per 100,000 individuals. In our series over a period of 13 years, 21 cases were collected. The average age in our series is 38 years old. By comparing the data from other series, we conclude that the epidemiological data of our series match those of the literature: Wahbi et al: average age at diagnosis: 38 with a sex ratio of 1.

All our patients had neurological symptoms, and the cardiac involvement was diagnosed afterwards. 81% of our patients were symptomatic. This rate agrees with the Nishioka series which is around 89% of patients (8). In

the literature, cardiac damage, which often precedes that of the skeletal muscle, occurs in 80% of DM1 patients and represents the second cause of death, after respiratory causes. In our series the major symptom is palpitations which is also the most frequent in the literature, as stated by Nguyen and Hiromasa, it is linked to the frequency of rhythm disturbances.

Conduction system disease is the most common cardiac manifestation of DM1. Atrioventricular blocks were identified in 28 to 45% of patients at the time of diagnosis. Our study reveals a high prevalence of BAV.

Conduction disorders on the resting ECG are most frequently encountered in our series, with 33% of 1st degree BAV. These results generally correspond to those of the literature. It was described in 16 cases by Fragola, 9 cases by Haweley, and 7 cases by Prystowsky. Right bundle branch block is present in 23% of cases in our series. This was described in 2 cases by Fragola, 3 cases by Haweley and a single case by Prystowsky. By comparing the data from other series, we conclude that the atrioventricular conduction disorders in our series are similar to those in the literature, of which the BAV is the main disorder observed.

As for electrophysiological exploration, its indications are broad in Steinert's disease. It is indicated mainly in the event of symptoms or abnormalities on the surface ECG. However, some authors who performed it systematically in all their patients with DM1 obtained an HV interval greater than 70 ms in asymptomatic patients and with normal surface ECG in 13 to 30% of cases.[11–12] In our series, the number of patients with prolonged HV interval is 16.

The first echocardiographic studies in Steinert's myotonia bring together 103 patients, and report mitral valve prolapse in 32% of cases, dilated cardiomyopathy in 4% of cases, alteration of systolic function parameters in 11.5% of cases, concentric hypertrophy of the left ventricle in 4% of cases. In contrast, echocardiography is within normal limits in nearly 48% of cases. These data are consistent with the data from our series, 4 patients had abnormalities on echocardiography, namely LV dilatation with moderate LV dysfunction, dilatation of the pulmonary artery trunk with moderate regurgitation, and prolapse of the small mitral valve responsible for moderate MI. Our study also stands out from others by the low incidence of ventricular systolic dysfunction.

According to Laurent's study, from a series of 46 patients, 39 patients with a prolonged HV interval were implanted, and none died of sudden death after a follow-up of 81 months. The indication for implantation in our patients was the same as that of the series mentioned above, any patient with a prolonged HV interval benefited from cardiac stimulation. The implantation rate in our series is 14%. This percentage is higher than the implantation rates reported in other series: Breton et al.[9] described a PMK implantation rate of 3.3% in a cohort of 428 patients with a median age of 33 years followed for an average of 11.7 years, while Lindqvist et al.[10] reported an implantation rate of 2.7% in 36 patients with a mean age of 45 (10) years followed for an average of 3 years.

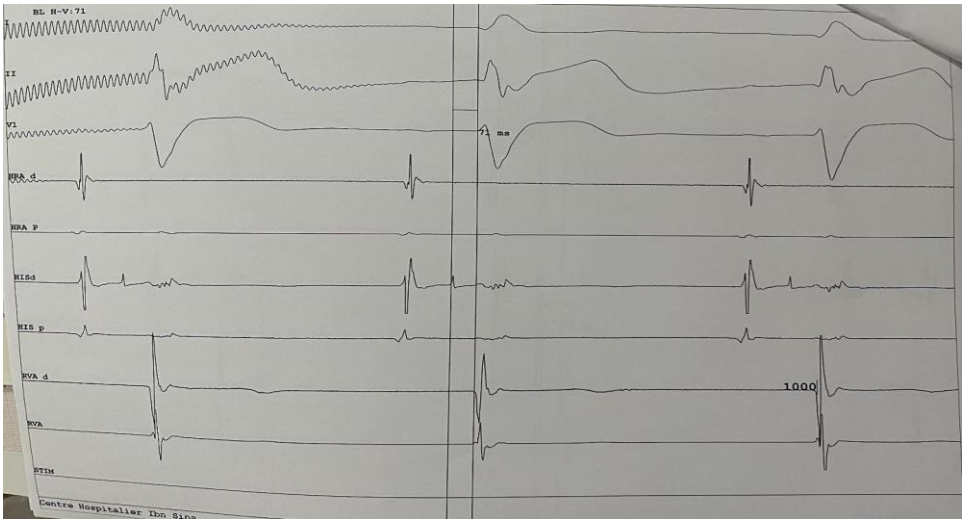
Comparison of our study with different works reveals similarities. All the studies showed that the most common conduction disorder was BAV, which was the case for our patients with a percentage of 33%. Regarding the rhythm disturbances observed in the different series, were flutter and atrial fibrillation. In our series, one patient developed atrial fibrillation. The majority of Holter ECGs in the literature showed abnormalities such as conduction or repolarization disorders. 74% of our patients also had abnormal ECG holters and only 26% were normal. Transthoracic echocardiography in our patients showed the same pathologies encountered in the literature, namely: prolapse of the mitral valve, dilatation of the LV with moderate LV dysfunction, dilatation of the pulmonary artery trunk responsible for insufficiency pulmonary.

CONCLUSION

Myotonic dystrophy is the most common hereditary neuromuscular disease of adult life. It is a multisystem disease with major cardiac involvement. The main features of myotonic dystrophy are myotonia, muscle weakness, cataracts, respiratory failure, and cardiac conduction abnormalities.

Conduction system abnormalities, atrial or ventricular arrhythmias, and less commonly, myocardial dysfunction are seen in patients with DM1 and may sometimes represent the initial manifestations of the disease, even in the absence of neuromuscular involvement.

Conversely, in all patients presenting with DM1, careful clinical and diagnostic evaluation should be performed to identify patients at risk for major cardiac events. A low-threshold attitude for invasive procedures is suggested, given the uncertain rate of progression of cardiac disease and the risk of sudden death in certain subsets of patients. However, several questions are still unanswered, hence the need to carry out several studies to improve the stratification of DM1 patients at high risk of sudden death and/or heart failure.



Figures: Electrophysiological exploration of a patient in our series showing a prolonged HV interval > 70 ms.

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