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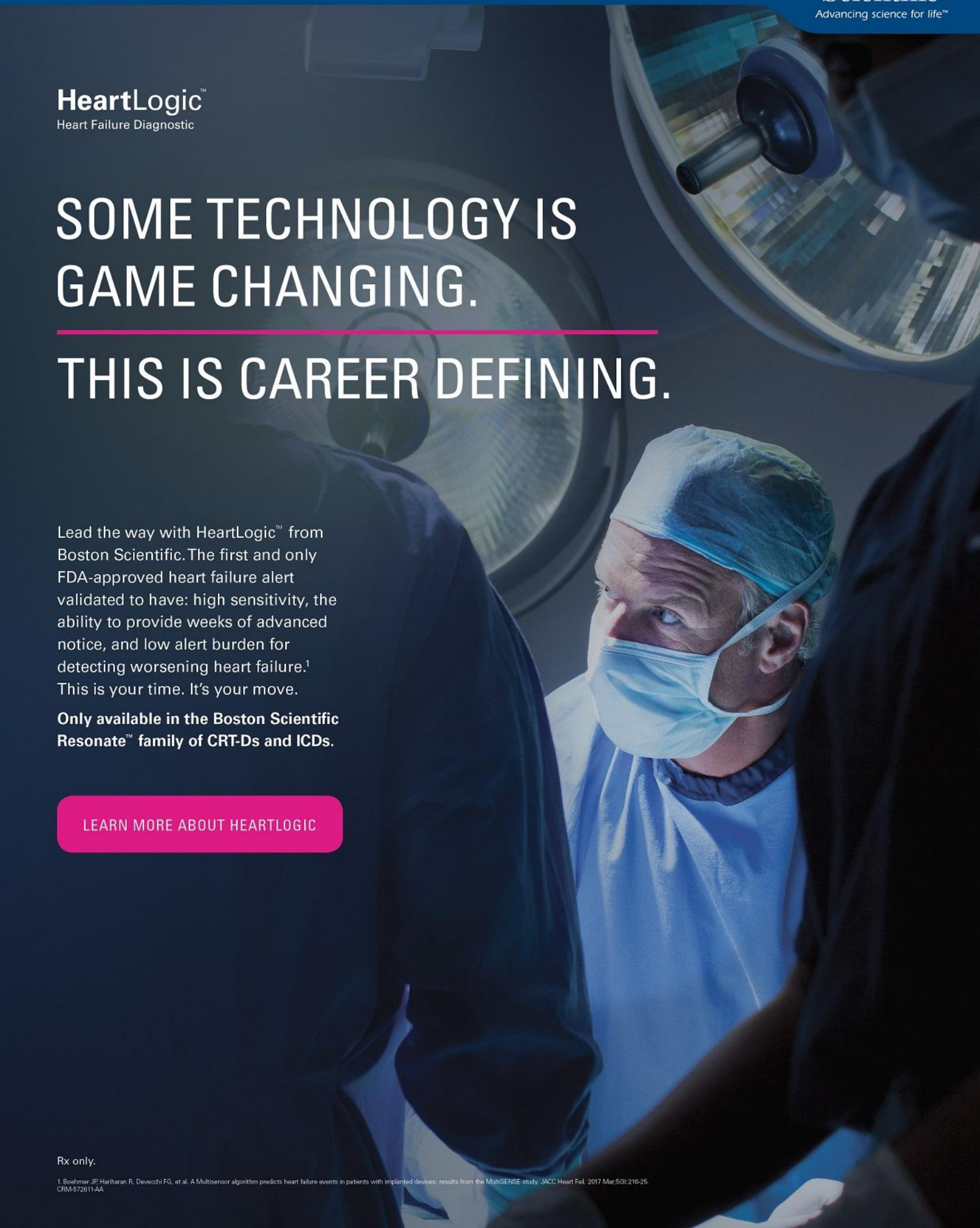

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Pacemaker Malfunctions in Danon's Disease

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We describe a case of a 30-year-old man with Danon's disease, an X-linked genetic disorder due to deficiency of lysosomal-associated membrane protein 2 with secondary intracytoplasmatic glycogen and autophagic material storage. This disease is characterized by skeletal muscle involvement, mental retardation, ophthalmic abnormalities, and cardiac disease. In this patient, cardiac involvement was characterized by hypertrophic cardiomyopathy in young age, preexcitation, and parossistic atrioventriular block. The patient underwent to an implantable cardioverter defibrillator implantation for conduction disorders and for primary prevention of sudden death, a frequent event in Danon's disease. This case report describes cardiac involvement with conduction disorders and multiple pacemaker malfunctions in Danon's disease. (PACE 2008; 31:125–128)

electrocardiogram, pacing

Case Report

A 30-year-old man was admitted to our hospital because of syncope. He was affected by Danon's disease with relevant cardiac disease characterized by hypertrophic cardiomyopathy (HCM) diagnosed in young age. The patient's mother was also affected by Danon's disease and she underwent heart transplantation because of refractory heart failure. Danon's disease was diagnosed in both cases with muscular biopsy, which revealed typical vacuolar myopathy with glycogen content and with immunohistochemical analysis that showed deficiency of lysosomal-associated membrane protein 2 (LAMP-2 protein).

One month earlier, he underwent ICD implantation (Medtronic Intrinsic 7288, Minneapolis, MN, USA) in another hospital for parossistic paroxysmal complete atrioventricular heart block (AV block) and because of high risk of sudden death in this disease. Because of transient AV block, the antibradycardia therapy was programmed in DDD pacing with minimal ventricular pacing (MVP) activated. MVP is a new algorithm (Medtronic) that reduces unuseful ventricular pacing in patients with spontaneous rhythm and episodes of AV block (AAI pacing with DDD backup if AV block occurs).

One month after device implantation, the patient was admitted to our hospital because of sudden onset of dyspnea and profuse sweating. He was pale, he had mild muscle weakness, marked myopia and serum creatine kinase, and aspartate transaminase and alanine aminotransferase were increased. Electrocardiogram (ECG) at emergency room showed sinus rhythm, 2:1 AV block, Wolff-Parkinson-White (WPW) pattern, left ventricular hypertrophy, ventricular pacing failure, and oversensing of T-wave (Fig. 1). The echocardiogram showed hypertrophic cardiomyopathy with maximum of 20 mm of septal thickness, normal ejection fraction, and ventricular diameter. Subsequent implantable cardioverter defibrillator (ICD) control revealed high ventricular pacing threshold, normal atrial and ventricular sensing, paced rhythm $< 1\%$. No lead dislodgement was found at chest X-ray. Therefore, the patient underwent ventricular lead revision and replacement in another site because of high threshold in apex. Antibradycardia therapy was programmed in DDD and minimal ventricular pacing was activated.

Six months later, the patient was readmitted to our hospital because of syncope. ECG showed P-synchronous pacing with 2:1 AV block (Fig. 2). The AV block was transient and at ICD control, during ventricular pacing threshold, intracardiac electrogram (EGM) recorded from bipolar ring revealed high and different T-wave morphology with secondary inappropriate ventricular sensing only in paced complexes (oversensing of T-wave) (Fig. 3). To remove oversensing of T-wave, we tested reduction of ventricular sensitivity, but oversensing disappeared only with long ventricular refractory period (VRP was programmed at 300 ms). As upper rate in dual-chamber pacing with long VRP was low and in consideration of the presence of paroxysmal AV block (the total paced rhythm was $< 1\%$), in order to avoid T-wave oversensing, we programmed VRP at 300 ms and brady therapy backup VVI 40 bpm. One month later, the AV block evolved in symptomatic stable complete AV block. The device was then programmed in dual-chamber pacing, with VRP 300 ms and lower upper rate.

Disclosure: none

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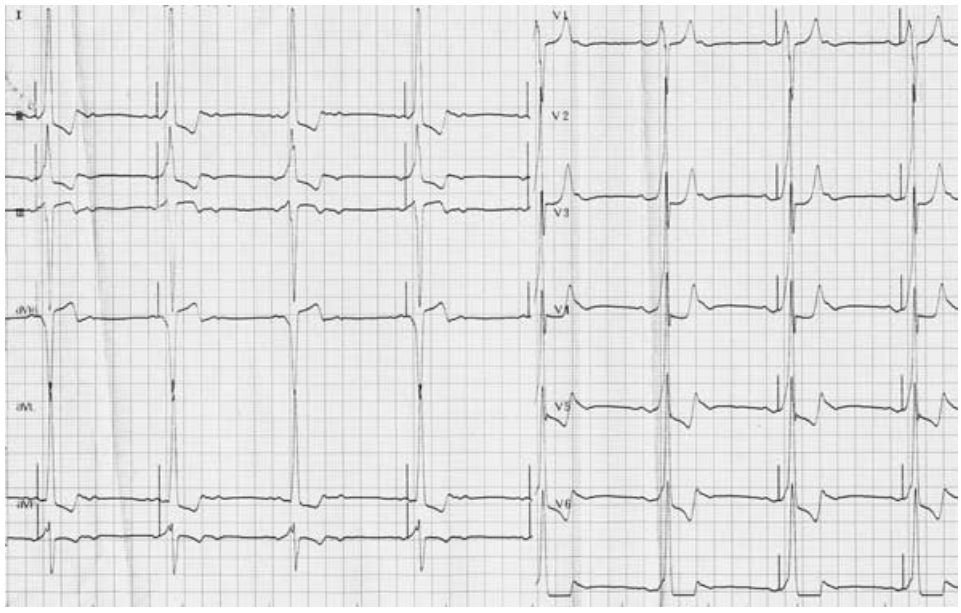

Figure 1. *Spontaneous ECG rhythm in emergency room: sinus rhythm with 2:1 AV block, preexcitation-like aspect, left ventricular hypertrophy, ventricular pacing failure (after conducted P-wave an inconstant ventricular spike is observed with pseudofusion complexes), and oversensing of T-wave in spontaneous complexes (after nonconducted P-wave no ventricular spike is observed). Preexcitation was mimicked by short PR and by slurring of the initial portion of QRS. 2:1 AV block excluded WPW syndrome and preexcitation is probably due to hypertrophic cardiomyopathy or to enhanced AV nodal conduction.*

At eight-month follow-up, the patient was asymptomatic for syncope and he complained only for mild dyspnea (like before device implant). He showed stable and complete AV block and no malfunctions in pacemaker therapy were found.

Discussion

Danon's disease is a very rare X-linked genetic disorder due to deficiency of LAMP-2, a glycoprotein of lysosome with secondary intracytoplasmatic glycogen and autophagic material

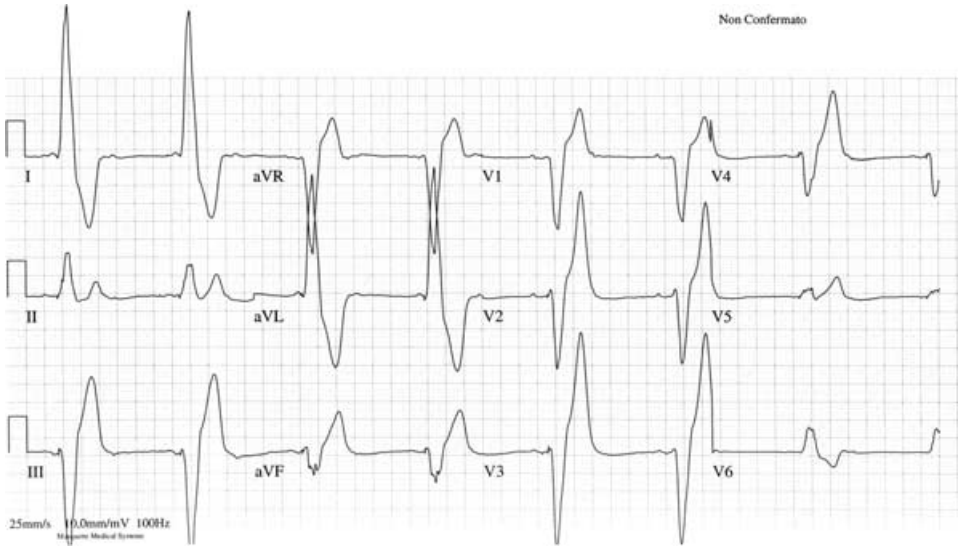

Figure 2. *P-synchronous ventricular pacing with 2:1 AV block. Note wide QRS and giant T-wave of paced complexes.*

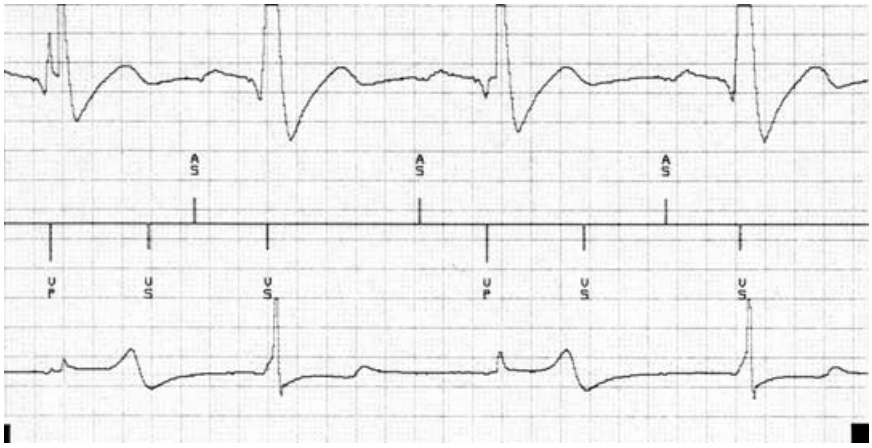

Figure 3. *EGM during ventricular pacing (below panel): the first and third beats are paced complexes with oversensing of T-wave. AS = atrial sensing; VP = ventricular pacing; VS = ventricular sensing.*

storage.[1–3] It is characterized by skeletal muscle involvement with variable myopathy, often serum creatine kinase, aspartate transaminase, and alanine aminotransferase increment, variable mental retardation, ophthalmic abnormalities, and chiefly cardiac disease. Cardiac disorder is determined by HCM, preexcitation, electrical conduction disorder, and heart failure.[4–8] Sudden death is frequent. The prevalence of Danon's disease in patients with previous diagnosis of HCM is 1%.[9] Diagnosis is based on muscle biopsy showing intracytoplasmatic vacuoles of glycogen and autophagic material and with demonstration of LAMP-2 deficiency by immunohistochemical analysis[2] or by genetic analysis.

Conduction disorders, such as AV block and WPW, were already described in Danon's disease and in other storage diseases (Pompe's disease, Fabry disease, and in glycogen storage cardiomyopathy due to mutations in PRKAG2, the gene encoding for $\gamma 2$ subunit of AMP-activated protein kinase).[7–15] However, in this case report management of AV block was problematic because of multiple pacemaker malfunctions and preexcitation ECG pattern was not related to WPW syndrome. We observed two different kinds of pacemaker malfunctions in this patient. The first malfunction was the high ventricular pacing threshold, likely secondary to the storage disease, since no lead dislodgements were found at chest X-ray. The other malfunction was the oversensing of giant T-wave only in paced complexes and was observed only after the development of stable complete AV block.

Notably, WPW pattern (shortened PR interval, delta wave, and widened QRS) in glycogen storage diseases is considered to be due to the presence of a bypass tracts, enhanced AV nodal conduction, fasciculoventricular connections, or ventricular conduction disease.[7,10–11] Recently, the WPW pattern is considered due to the presence of a bypass tracts produced by disruption of the annulus fibrosis by glycogen-filled myocites.[16] In this case, the contemporaneous presence of AV block and WPW pattern excludes the presence of bypass tract, and thus preexcitation-like conduction is probably due to enhanced AV nodal conduction or HCM.

Conclusion

Danon's disease is a rare disorder with important cardiac involvement in young patients. Hypertrophic cardiomyopathy in young people, heart failure, and sudden death are frequently observed. Electrical disturbances are also frequent and represented by preexcitation and conduction disorders. Preexcitation is not always due to the presence of bypass tract, but may be secondary to hypertrophic cardiomyopathy or enhanced AV nodal conduction. In this disease, management of conduction disorders may be troublesome, because of multiple pacemaker malfunctions.

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