CASE REPORT

Electrical storm in a patient with Duchenne muscular dystrophy cardiomyopathy triggered by abrupt β -blocker interruption

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We present a case of a young man with Duchenne muscular dystrophy cardiomyopathy (DMDC) having an implantable cardioverter defibrillator for secondary prevention, who presented with electrical storm shortly after β -blocker interruption. The patient was stabilized and remained free of ventricular arrhythmias soon after reinitiating β -adrenoreceptor antagonists. The present case highlights the importance of sympathetic blockage in patients with DMDC due to existing pathophysiology of excess diastolic Ca^{2+} leak from sarcoplasmic reticulum as a result of ryanodine receptor dysfunction.

KEYWORDS

β -blocker, cardiomyopathy, duchenne muscular dystrophy, electrical storm, implantable cardioverter defibrillator

1 | CASE REPORT

A 23-year-old man with duchenne muscular dystrophy cardiomyopathy (DMDC) and an episode of syncope due to sustained ventricular tachycardia prompting ICD implantation 6 months ago was admitted urgently due to electrical storm. Device interrogation showed multiple VF episodes during the last 24 hr, with nine successfully delivered shocks, a few effective antitachycardia pacing therapies (ATP) within VF zone (>210 bpm) and numerous episodes of spontaneously terminated VF. (Figure 1) Clinically, the patient was severely distressed without significant hemodynamic impairment. Due to recurrent episodes of extremely fast ventricular tachycardia that was apparently detected within VF zone, the patient was started on esmolol and diazepam which led shortly to tachycardia termination. (Figure 2) Looking for potential reversible factors that may have contributed to the onset of electrical instability, a sudden interruption of β -blocker agent (bisoprolol 2.5 mg od) approximately 48 hr prior to electrical storm initiation was documented. No other than poor compliance to his medical therapy could explain the patient's decision to discontinue β -blocker medication.

According to the patient's medical history, the diagnosis of Duchenne Muscular Dystrophy (DMD) had been confirmed with

muscular biopsy indicating total lack of dystrophin as a result of a mutation in exone 5,254 at the age of 5 years. Left ventricle dysfunction was initially observed at the age of seventeen via transthoracic echocardiography whereas no other imaging modalities like cardiac magnetic resonance were used in order to detect early and occult alterations in systolic and/or diastolic cardiac function (Hor et al., 2009). Since then a progressive deterioration of left ventricle systolic function was observed despite ACE inhibitors and small dose of carvedilol administration. The patient underwent ICD implantation 6 months prior to his current admission due to a syncopal episode of sustained ventricular tachycardia. At that stage, carvedilol was replaced with bisoprolol 2.5 mg once a day and since then the patient remained free of arrhythmias except for an episode of nonsustained VT as the device arrhythmia logbook recorded.

A transthoracic echo confirmed a severely dilated left ventricle with severely reduced systolic function (EF 20–25%), and concomitant mild to moderate mitral valve regurgitation. For the rest of his hospitalization he remained asymptomatic taking bisoprolol, ACE-inhibitor, aldosterone antagonist and small dose of diuretics while no further arrhythmias were recorded in ICD holter. The patient continued to be asymptomatic without any recorded arrhythmic event for the following 6 months taking systematically β -blocker therapy.

ZOOM View™ Arrhythmia Logbook Report					ZOOM View™ Arrhythmia Logbook Report				
Device: INOGEN MINI ICD D010/ 208551 Tachy Mode: Monitor - Therapy					Last Office Interrogation: 19 Sep 2016 Implant Date: 20 Apr 2016				
Event	Date/Time	Type	Therapy	Duration Minutes	Event	Date/Time	Type	Therapy	Duration Minutes
V-56	18 Sep 2016 23:23	VF	ATPx1	00:00:15	V-49	18 Sep 2016 23:14	VF	ATPx1	00:00:16
V-57	18 Sep 2016 23:22	VF	No Therapy	00:00:13	V-48	18 Sep 2016 23:12	VF	ATPx1	00:00:15
V-56	18 Sep 2016 23:21	VF	No Therapy	00:00:14	V-47	18 Sep 2016 23:12	VF	No Therapy	00:00:16
V-55	18 Sep 2016 23:20	VF	No Therapy	00:00:20	V-46	18 Sep 2016 23:09	VF	ATPx1	00:00:15
V-54	18 Sep 2016 23:17	VF	ATPx1, 41J	00:00:49	V-45	18 Sep 2016 23:09	VF	ATPx1	00:00:15
V-53	18 Sep 2016 23:17	VF	ATPx1	00:00:15	V-44	18 Sep 2016 23:07	VF	ATPx1	00:00:15
V-52	18 Sep 2016 23:17	VF	ATPx1	00:00:15	V-43	18 Sep 2016 23:06	VF	ATPx1	00:00:15
V-51	18 Sep 2016 23:15	VF	ATPx1, 41J	00:00:52	V-42	18 Sep 2016 23:05	VF	ATPx1	00:00:15
V-50	18 Sep 2016 23:14	VF	ATPx1	00:00:15	V-41	18 Sep 2016 23:04	VF	ATPx1	00:00:15
Page 1 of 5					V-40	18 Sep 2016 23:03	VF	ATPx1	00:00:15
					V-39	18 Sep 2016 22:46	VF	41J	00:00:50
					V-38	18 Sep 2016 22:42	VF	No Therapy	00:00:14
					V-37	18 Sep 2016 22:40	VF	ATPx1, 41J	00:00:59
					Page 2 of 5				
Event	Date/Time	Type	Therapy	Duration Minutes	Event	Date/Time	Type	Therapy	Duration Minutes
V-36	18 Sep 2016 22:38	VF	No Therapy	00:00:13	V-23	18 Sep 2016 21:59	VF	ATPx1	00:00:15
V-35	18 Sep 2016 22:37	VF	ATPx1	00:00:15	V-22	18 Sep 2016 21:56	VF	No Therapy	00:00:12
V-34	18 Sep 2016 22:35	VF	41J	00:00:45	V-21	18 Sep 2016 21:54	VF	No Therapy	00:00:12
V-33	18 Sep 2016 22:34	VF	No Therapy	00:00:15	V-20	18 Sep 2016 21:46	VF	41J	00:00:54
V-32	18 Sep 2016 22:33	VF	No Therapy	00:00:15	V-19	18 Sep 2016 21:45	VF	No Therapy	00:00:20
V-31	18 Sep 2016 22:32	VF	ATPx1	00:00:15	V-18	18 Sep 2016 21:44	VF	No Therapy	00:00:13
V-30	18 Sep 2016 22:27	VF	No Therapy	00:00:15	V-17	18 Sep 2016 21:44	VF	No Therapy	00:00:12
V-29	18 Sep 2016 22:25	VF	ATPx1	00:00:15	V-16	18 Sep 2016 21:40	VF	41J	00:00:41
V-28	18 Sep 2016 22:24	NonSustV	NonSustained	00:00:12	V-15	18 Sep 2016 21:38	VF	41J	00:00:45
V-27	18 Sep 2016 22:24	VF	No Therapy	00:00:15	V-14	18 Sep 2016 21:37	VF	No Therapy	00:00:16
V-26	18 Sep 2016 22:14	VF	No Therapy	00:00:14	V-13	18 Sep 2016 21:34	VF	41J	00:00:41
V-25	18 Sep 2016 22:10	VF	No Therapy	00:00:16	V-12	18 Sep 2016 21:30	VF	41J	00:00:41
V-24	18 Sep 2016 22:08	VF	ATPx1	00:00:15	V-11	18 Sep 2016 21:29	VF	41J	00:00:41
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FIGURE 1 Arrhythmia logbook report showing the arrhythmic clustering and the various therapies delivered by the ICD

Worth noting that no mechanical or noninvasive ventilation support has been used before or instituted after hospital discharge due to the patient satisfactory respiratory condition.

2 | DISCUSSION

DMD is the most common X-linked disorder which results from dystrophy deficiency due to nonsense (Koenig et al., 1987). The cardiac involvement is progressive, leading finally to severe ventricular dysfunction characterized by cardiomyocytes' hypertrophy, atrophy, fibrosis and ventricular dilation. Even though an increased survival has been attained over the past three decades as a result of proactive management of complications and early administration of appropriate drugs, respiratory failure and cardiomyopathy complications like heart failure and arrhythmias remain the most common causes of death (Chiang et al., 2016; Van Ruiten et al., 2016).

Regarding our case, it is striking the excessive electrical instability following β -blocker interruption. The key point may lay in calcium channels dysfunction that has been described in dystrophic hearts (Hopf, Turner, & Steinhardt, 2007; Jung, Martins, Niggi, &

Shirokova, 2008). Structural and functional remodeling of the cardiac sarcoplasmic reticulum (SR) Ca^{2+} release channel/ryanodine receptors (RyR2) has been demonstrated in mouse model of DMD. RyR2 have been found depleted of calstabin 2, resulting in a diastolic SR Ca^{2+} leak. When this depletion was inhibited, Ca^{2+} leak and arrhythmias in vivo were prevented (Fauconnier et al., 2010; Koenig et al., 2014). To the contrary, sympathetic stimulation following isoproterenol administration induced ventricular tachycardia due to triggering of abnormally leaky RyR2 channels (Parvatiyar et al., 2015). This is a mechanism resembling that of catecholaminergic polymorphic ventricular tachycardia (CPVT) (Priori & Chen, 2011). Consequently, β -adrenoreceptor antagonists is expected to have a critical role in preventing malignant ventricular arrhythmias (Matsumura, Tamura, Kuru, Kikuchi, & Kawai, 2010) which is supported in our case by the impressive arrhythmias abolition soon after β -blockade administration.

Although we cannot exclude an additive beneficial role of aldosterone antagonist (Raman et al., 2017) and ACE-Inhibitor, the immediate arrhythmia abolition with β -blockers reinstitution strongly supports their critical role in continuing electrical stability in our case.

FIGURE 2 Twelve-lead ECG presenting the mode of ventricular tachycardia initiation. The spontaneous onset supports triggered activity as the putative arrhythmogenic mechanism

To conclude, the absence of sympatholytic agents in patients with DMD may facilitate the initiation of malignant ventricular arrhythmias at least in patients with manifest cardiomyopathy. The use of adrenoceptor antagonists may need to be proposed as strictly as in patients with CPVT.

CONFLICT OF INTEREST

None.

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