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CASE REPORT
Heart failure

A new approach to the treatment of advanced heart failure: a case report

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Background Autonomic imbalance characterized by sympathetic predominance and decreased parasympathetic transmission is a classic feature of heart failure (HF) with reduced left ventricular ejection fraction, leading to disease progression, exercise intolerance, ventricular remodelling, arrhythmias, and premature death. The underlying mechanisms to these processes are not yet fully understood, but the current treatments influence this dysregulation, towards an inhibition of sympathetic hyperactivation. New therapies, such as the stimulation of carotid baroreceptors, enhance this inhibition to restore autonomic balance and to be able to cope with these mechanisms.

Case summary We report the case of a 76-year-old male with advanced HF at an advanced stage, refractory to optimal treatment, and included in a programme of ambulatory infusions of Levosimendan as compassionate treatment. The patient presented with multiple episodes of decompensated HF secondary to ventricular arrhythmias. A multidisciplinary team decided to implant a baroreceptor stimulator device (Barostim Neo) in order to improve HF symptoms and quality of life, as well as trying to decrease the burden of arrhythmias. The procedure was performed with no complications and good therapeutic response, resulting in a significant reduction of arrhythmias.

Discussion Treatment with a baroreceptor stimulating device is presented as a safe and effective option in our patients with advanced HF refractory to conventional treatment, to improve their quality of life and reduce symptoms; in addition to appearing as a promising option in those with arrhythmic events, which are difficult to control with usual treatments and procedures.

Keywords Heart failure • Decompensated • Arrhythmic events • Baroreceptor stimulating device • Case report

Learning points

- Autonomic imbalance characterized by sympathetic predominance and decreased parasympathetic transmission is a classic feature of heart failure (HF) with reduced left ventricular ejection fraction.
- This dysregulation of the autonomic nervous system leads to disease progression, exercise intolerance, ventricular remodelling, arrhythmias, and premature death.
- New therapies, such as stimulation of the carotid baroreceptors, enhance this inhibition to restore autonomic balance and improve HF symptoms, quality of life, and reduce arrhythmic events.

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Introduction

Current treatment recommendations for symptomatic patients with heart failure (HF) with reduced left ventricular ejection fraction (LVEF) are based on progressive initiation and titration of angiotensin-converting enzyme inhibitors and beta-blockers, adding other treatments if the patient continues being symptomatic [aldosterone antagonists, sacubitril/valsartan, cardiac resynchronization therapy (CRT), Ivabradine].[1] Autonomic imbalance characterized by sympathetic predominance and decreased parasympathetic transmission is a classic feature of HF with reduced LVEF, leading to disease progression, exercise intolerance, ventricular remodelling, arrhythmias, and premature death.[2]

New therapies, such as stimulation of the carotid baroreceptors, enhance this inhibition to restore autonomic balance and enable coping with these mechanisms in HF patients.[2] This case demonstrates the influence of neurohormonal activation in the pathogenicity and natural history of HF, and the option to target it with newly available therapies.

Timeline

April 1998	Age 55	Non-ischaemic dilated cardiomyopathy with ventricular dysfunction
April 2005	Age 62	Implant of implantable cardioverter-defibrillator (ICD)
November 2012	Age 69	Multiple episodes of atrial fibrillation (AF), with unsuccessful cardioversions
May 2015	Age 72	Optimization with ICD-cardiac resynchronization therapy (ICD-CRT) and atrioventricular node ablation due to multiple episodes of AF, with unsuccessful cardioversions, resulting in a low percentage of biventricular pacing
April 2016 to October 2018	Age 73	Four admissions for arrhythmic storm Prolonged episodes of symptomatic atrial flutter with biventricular stimulation <90%
January 2018	Age 75	Ambulatory Levosimendan infusions every 4 weeks
October 2018	Age 75	Ongoing episodes of non-sustained and sustained ventricular tachycardia despite ablation of extrasystolic focus in the left ventricular outflow tract
Since December 2018	Age 76	Several episodes of decompensated heart failure (HF) in the context of respiratory infections and episodes of arrhythmias
July 2019	Age 76	Implant of Barostim Neo® device
Since August 2019	Age 77	No episodes of decompensated HF and spacing of ambulatory Levosimendan infusions beyond 6 weeks. Significant decrease in episodes of arrhythmias monitored with ICD-CRT, showing biventricular stimulation >96%

Case presentation

We report the case of a 76-year-old male with advanced HF due to non-ischaemic dilated cardiomyopathy with ventricular dysfunction since 1998 (*Videos 1* and *2*) .

His family history includes HF and sudden cardiac death in his maternal grandmother, and in his mother and brother at an early age (45 and 60 years, respectively). Four healthy sons with normal clinical studies [electrocardiogram (ECG) and echocardiogram]. In genetic study requested, no pathogenic variants were found (dilated cardiomyopathy panel with 121 genes using the latest generation sequencing technique).

As personal background point out former long-term smoker, arterial hypertension, dyslipidaemia, chronic obstructive pulmonary disease, and chronic kidney disease.

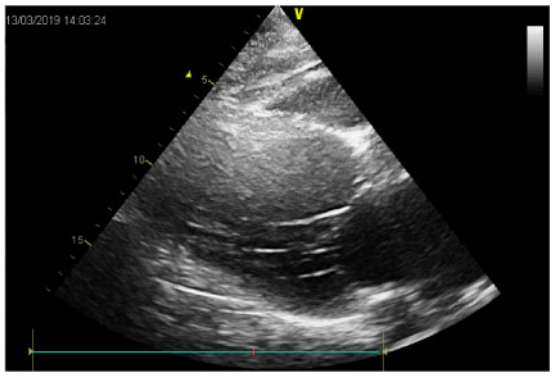
Physical examination revealed mild signs of pulmonary congestion and peripheral oedema. The LVEF was severely depressed (<20%) with no changes despite therapeutic optimization.

Implant of implantable cardioverter-defibrillator (ICD) in 2005, with later optimization to ICD-CRT and with atrioventricular node ablation due to multiple episodes of atrial fibrillation (AF), with unsuccessful cardioversions and causing a low percentage of biventricular pacing.

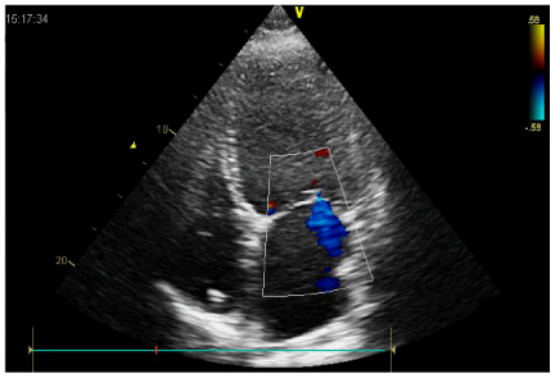
In optimized medical treatment with Bisoprolol 5 mg/8 h, Eplerenone 25 mg/24 h, and Sacubitril/Valsartan 24/26 mg/12 h (maximum doses tolerated due to blood pressure and renal dysfunction) and in treatment with Levosimendan ambulatory infusions every 4 weeks since January 2018.

The patient presented four admissions for arrhythmic storm since 2016, the last one in October 2018, with ablation of the extrasystolic focus in the left ventricular outflow tract, without achieving the disappearance of arrhythmic episodes, continuing with non-sustained ventricular tachycardias (NSVT) and sustained ventricular tachycardias (VT) with appropriate ICD therapies, both in the form of antitachycardia pacing (ATP) and defibrillation shocks. In addition, prolonged and symptomatic episodes of atrial flutter with a rapid ventricular response since 2017, requiring adjustment of medical treatment and parameters of ICD-CRT without achieving an optimal percentage of biventricular stimulation, staying below 90% (*Figure 1*) (ECG of the arrhythmic episodes in the Supplementary material online).

In addition, our patient suffered several episodes of decompensated HF in the context of respiratory infection and the arrhythmic episodes described above, with more than eight visits to the



Video 1 Dilated left ventricle with severe ventricular dysfunction.



Video 2 Mitral regurgitation.

Emergency Department and the Cardiology Day Hospital between the beginning of 2018 and June 2019, with intravenous diuretic treatment and adjustment of outpatient regimen.

Given this situation of multiple decompensations and arrhythmic episodes despite optimized treatment, the possibility of implanting a Barostim Neo® device for symptomatic improvement and the possibility of reducing arrhythmic events was considered, because we had no more possibilities for medical treatment or device optimization. The case was presented in session with a multidisciplinary Heart Team (cardiology, cardiac surgery, and anaesthesiology), approving the procedure, which was carried out in July 2019 without incidents (*Figure 2*).

After device activation, there were no complications or discomfort associated with the implant or therapy. Blood pressure remained stable and without interaction with the ICD-CRT function, being monitored both at implantation and activation and at each control visit (*Figure 3*).

In the follow-up after activation of the device, the patient has not had any decompensation of HF, without consulting the emergency room or increasing diuretic therapy, and with outpatient infusions of Levosimendan every 6 weeks instead of every 4 weeks.

In addition, a very significant decrease in arrhythmic episodes monitored with ICD-CRT was observed: more than 480 episodes of NSVT were monitored prior to implantation, with three episodes of VT with adequate ICD therapy (with ATP, without shock), a 7.4% of the time in AT/AF, and with <90% biventricular stimulation. The number of arrhythmic episodes had decreased to almost disappear in the last revision of the device in October 2019, without the need for ICD therapy and increasing the percentage of biventricular stimulation reaching almost 97% (*Figure 4*). An improvement in N-terminal of the pro-natriuretic peptide type (NT-proBNP) and renal function levels had also been observed. There were no significant changes in the distance covered in the 6-min walk test (*Figure 5*). Signs of pulmonary congestion and peripheral oedema gradually disappeared on subsequent visits.

Discussion

Autonomic imbalance characterized by sympathetic predominance and decreased parasympathetic transmission is a classic feature of HF with reduced LVEF, leading to disease progression, exercise intolerance, ventricular remodelling, arrhythmias, and premature death.[2] The underlying mechanisms to these processes are not yet fully understood, but the current treatments recommended by the ESC HF guidelines[1] influence this dysregulation of the Autonomous Nervous System, towards an inhibition of sympathetic hyperactivation. New therapies, such as stimulation of carotid baroreceptors, enhance this inhibition to restore autonomic balance and to be able to cope with these mechanisms.

Baroreceptors are anatomical structures located in carotid sinus and aortic arch, and when they are active they initiate a reflex arc of activation of the parasympathetic nervous system direct and afferent inhibition of the sympathetic nervous system. The Barostim Neo® device consists of a pulse generator similar to a pacemaker and a carotid sinus cable that ends in a small circular electrode and produces direct and afferent activation of these baroreceptors. The implantation procedure is simple, by exposing the right carotid artery and mapping the area to find the point of greatest response that is represented by the decrease in heart rate and systolic blood pressure, suturing the electrode in that position. Finally, a subcutaneous pocket is created in the infraclavicular chest wall for the pulse generator and the cable is tunnelled towards it.

Several studies have shown promising results with this therapy[3–5] in symptomatic patients despite optimal treatment, showing significant improvements in the 6-min walk test, quality of life scales, and New York Heart Association (NYHA) functional class. In addition, these studies have shown a reduction in NT-proBNP levels, lower rates due to decompensated HF, and shorter duration of hospital admissions. The tolerance and safety of the implant and the therapy have also been tested in these studies, as well as the possibility of using it in patients with CRT. In addition, the BeAT-HF trial is being actively carried out recruiting patients with NYHA class II–III HF and LVEF ≤35% despite optimal treatment, randomized to patients to be implanted the device or continue only with conventional treatment. The results that are described in this study corroborate those previously described, together with evidence of the decrease in other cardiovascular events such as the presence of arrhythmias (reduction of 54%), ischaemic events (reduction of 50%), and presyncope. and syncope (reduction of 66%), which has led to approval by Food and Drug Administration for the use of this device in patients with HF.[6]

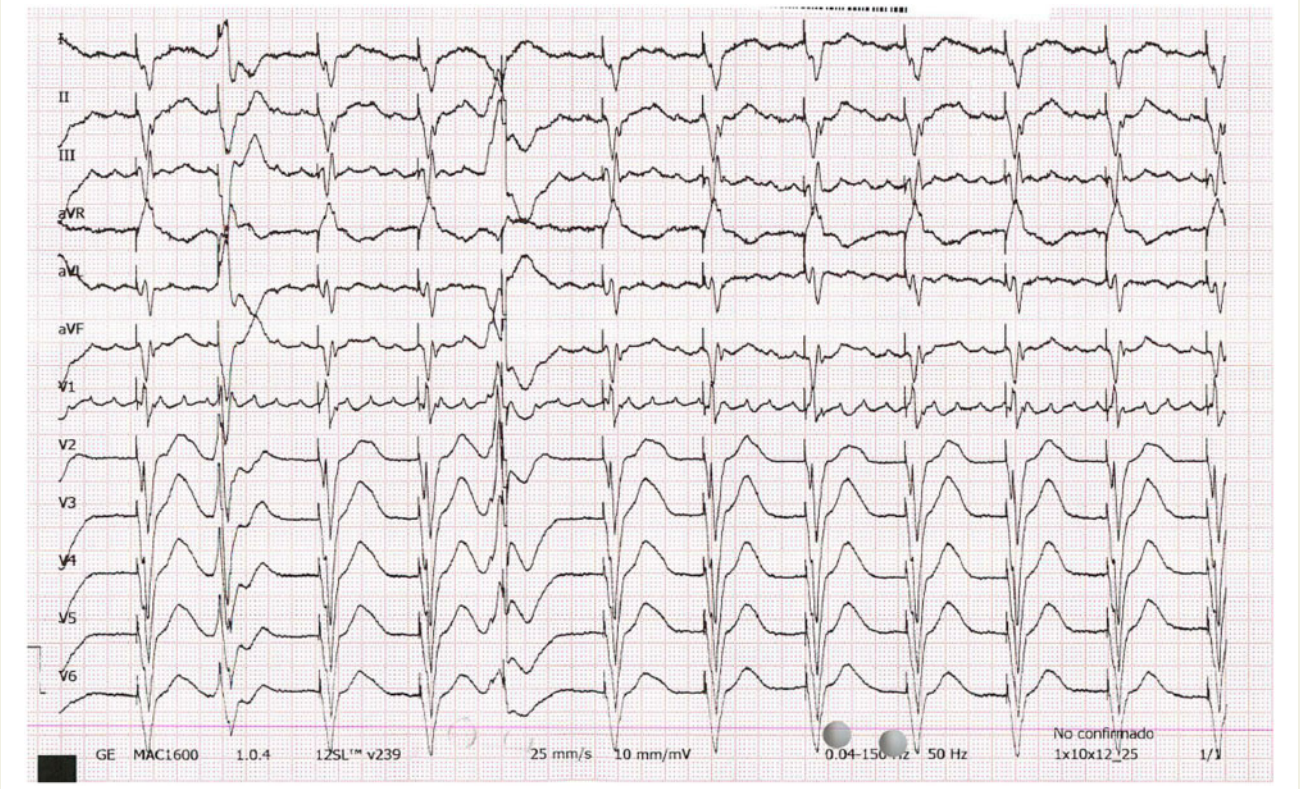


Figure 1 Ventricular stimulation by implantable cardioverter-defibrillator-cardiac resynchronization therapy at 70 b.p.m. Atrial rhythm of atrial/flutter tachycardia at about 110 b.p.m. Frequent ventricular extrasystoles with right bundle branch block morphology.

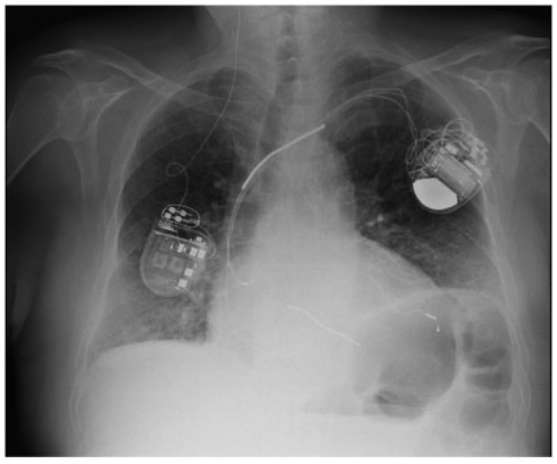


Figure 2 Chest X-ray shows implantable cardioverter-defibrillator-cardiac resynchronization therapy (left) and the Barostim Neo® device (right).

In conclusion, treatment with a baroreceptor stimulating device is presented as a safe and effective option in patients with advanced HF refractory to conventional treatment, to improve their quality of life and reduce symptoms; in addition to appearing as a promising option in those with arrhythmic events, which are difficult to control with the usual treatments and procedures.

Lead author biography

Dr Ainhoa Robles-Mezcua acquired her medical degree at 'University of Granada, Spain', and Specialization in Cardiology at the Hospital Virgen de la Victoria, Malaga. Actually, she works as Cardiologist in the Heart Failure and Heart Disease Unit. Cardiology Service, Hospital Virgen de la Victoria, Malaga, Spain.

Supplementary material

Supplementary material is available at *European Heart Journal - Case Reports* online.

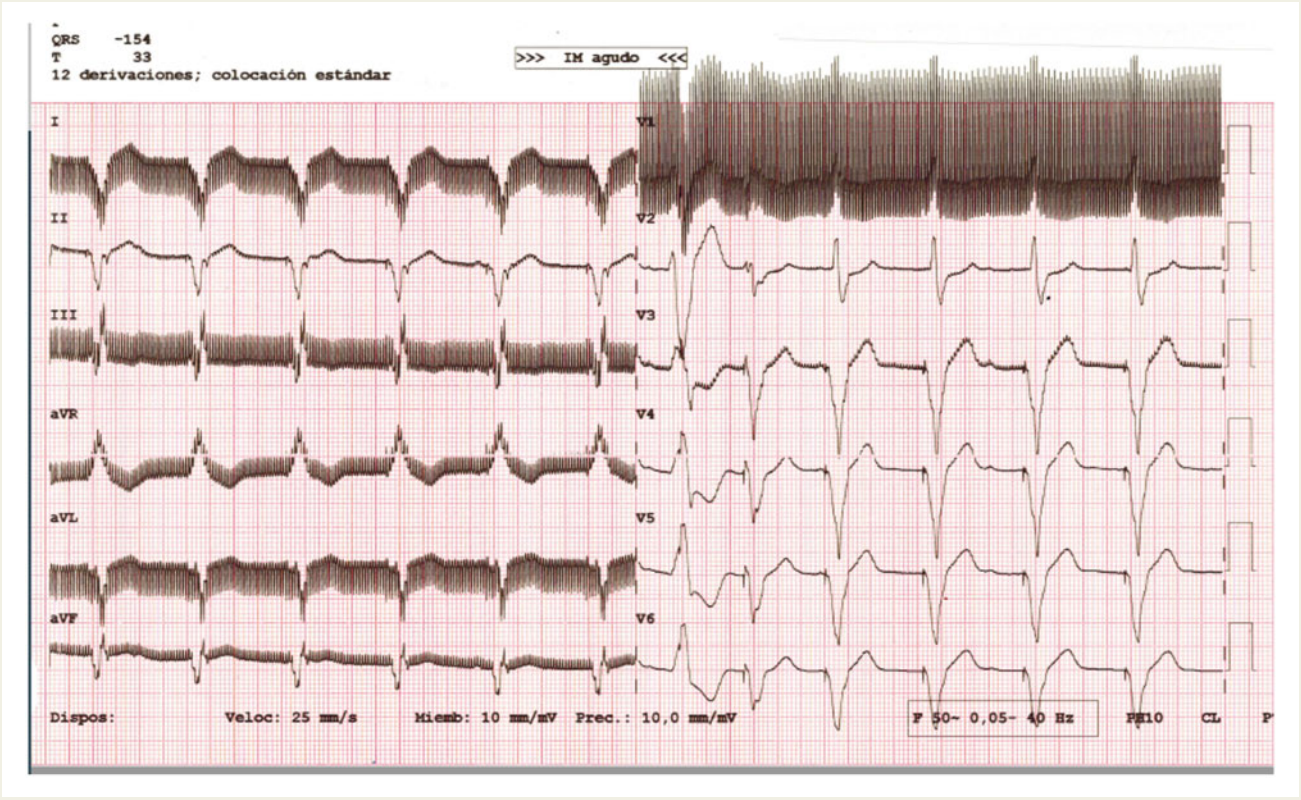


Figure 3 Electrocardiogram shows activity of the Barostim device without interfering in the pacing by cardiac resynchronization therapy.

	July 2019
Therapy	
FV	0
TVR (Desac)	
TV	3
Monitor	
TV (Desac)	
TV-NS (>4 latidos, >143 min-¹)	489
Frecuencia alta-NS	0
TSV: Terapia de TV/FV retenida	0
Sobredetección V-Terapia de Onda T detenida	0
Sobredetección V-Terapia de ruido detenida	0
TA/FA	262
AF Time	1.8 h/d (7.4%)
Longest AF episode	36 minutos
Patient activity	**Last Week** 1.6 h/día

% Pacing	
VP total	89.6%
AS-VS	12.3%
AS-VP	87.7%
AP-VS	0.0%
AP-VP	0.0%

	October 2019
Therapy	
FV	0
TVR (Desac)	
TV	0
Monitor	
TV (Desac)	
TV-NS (>4 latidos, >143 min-¹)	19
Frecuencia alta-NS	0
TSV: Terapia de TV/FV retenida	0
Sobredetección V-Terapia de Onda T detenida	0
Sobredetección V-Terapia de ruido detenida	0
TA/FA	0
AF Time	0.0 h/d (0.0%)
Patient activity	**Last Week** 1.3 h/día

% Pacing	
VP total	96.8%
AS-VS	3.7%
AS-VP	96.3%
AP-VS	0.0%
AP-VP	0.0%

Figure 4 Arrhythmic episodes recorded by the implantable cardioverter-defibrillator before (July 2019) and after (October 2019) of Barostim therapy.

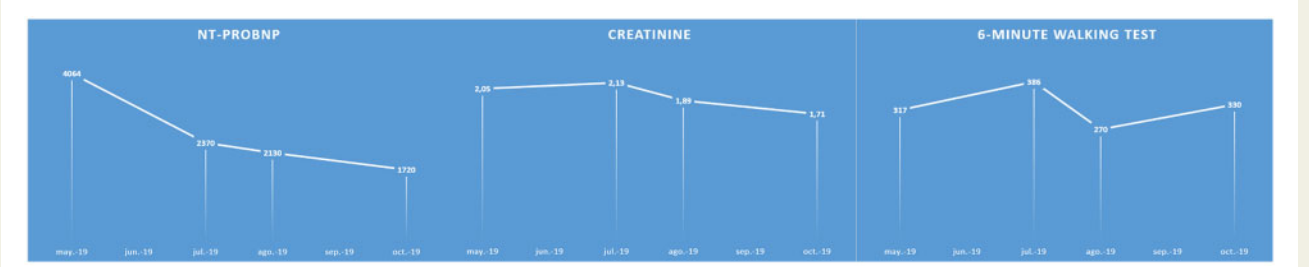


Figure 5 Evolution of the values of NT-proBNP, creatinine, and distance in the 6-min walk test.

Slide set: A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

Consent: The authors confirm that written consent for submission and publication of this case report including images and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: None declared.

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