Figure 2. Catheterization of the patient with visualization of a filling defect of the left coronary artery.

therapy, digoxin, carvedilol, acetylsalicylic acid, and nasogastric feeding. During his clinical course, he was admitted several times to the pediatric intensive care unit for cardiac decompensation in the presence of catarrhal symptoms. He was included on the transplant list at 12 months of life and received a transplant 5 months later, with good outcome. Histopathology of the explanted heart showed a dilated left ventricle, with extensive areas of fibroelastosis, and almost half of the external myocardium in the free wall had been replaced by adipose tissue and fibrosis. No coronary obstruction was detected.

Acute myocardial infarction in the neonatal period is exceptional and represents a considerable diagnostic and therapeutic challenge for clinicians and cardiologists. Early diagnosis via electrocardiography, echocardiography, and catheterization is important for adequate treatment and to promote coronary reperfusion because these patients often lack adequate collateral circulation. Prompt treatment could avoid the irreversible myocardial necrosis[3,6] that culminates in heart transplantation,

as in our patient. Various therapeutic options have been described, but there is no universal consensus because few such patients have been described and because newborns are highly susceptible to immaturity-related complications.[2] The most recent articles advocate local thrombolytic treatment with low-dose intracoronary r-TPA, together with the administration of intravenous heparin, with good results and without complications.[2,4–6]

SUPPLEMENTARY MATERIAL

Supplementary material associated with this article can be found in the online version available at doi:10.1016/j.rec.2015.06.012.

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Familial Paralysis of the Atrium Due to a Mutation in *SCN5A*

### Parálisis auricular familiar debida a una mutación en *SCN5A*

To the Editor,

We present a family with a history of atrial arrhythmias requiring a pacemaker (PM) due to sick sinus syndrome (SSS) and paralysis of the atrium. Genetic study revealed the presence of the *SCN5A*[p.Arg219His] variant already associated with familial paralysis of the atrium (FPA), conduction disorders, and dilated cardiomyopathy. To the best of our knowledge, this is the first report of FPA in a Spanish family.

The index case (III.3) was a 30-year-old man with no relevant medical history who was admitted for dizziness; on arrival at hospital, the electrocardiogram (ECG) revealed absence of atrial

activity and idioventricular rhythm (Figure 1A). The echocardiogram showed a severely dilated left atrium (60 mL/m^2), while the other chambers were of normal size. The left ventricular ejection fraction (LVEF) in the magnetic resonance imaging study was 48% and there was no late enhancement. A dual-chamber PM was implanted. The patient improved without any complications and left ventricular ejection fraction completely recovered after 9 months of ramipril therapy.

The patient's father (II.3) required a PM at the age of 31 years, also for paralysis of the atrium. In the most recent ECG, sinus rhythm alternated with VVI pacing (Figure 1B). A paternal aunt (II.2) required a PM aged 62 years and his son (III.1) had a stroke aged 38 years and required a PM for SSS. A first cousin (III.3) had atrial fibrillation and atrial flutter from the age of 29 years, with several cardioversions, and ablation of the cavotricuspid isthmus, after which he was in sinus rhythm with propafenone (Figure 1C).
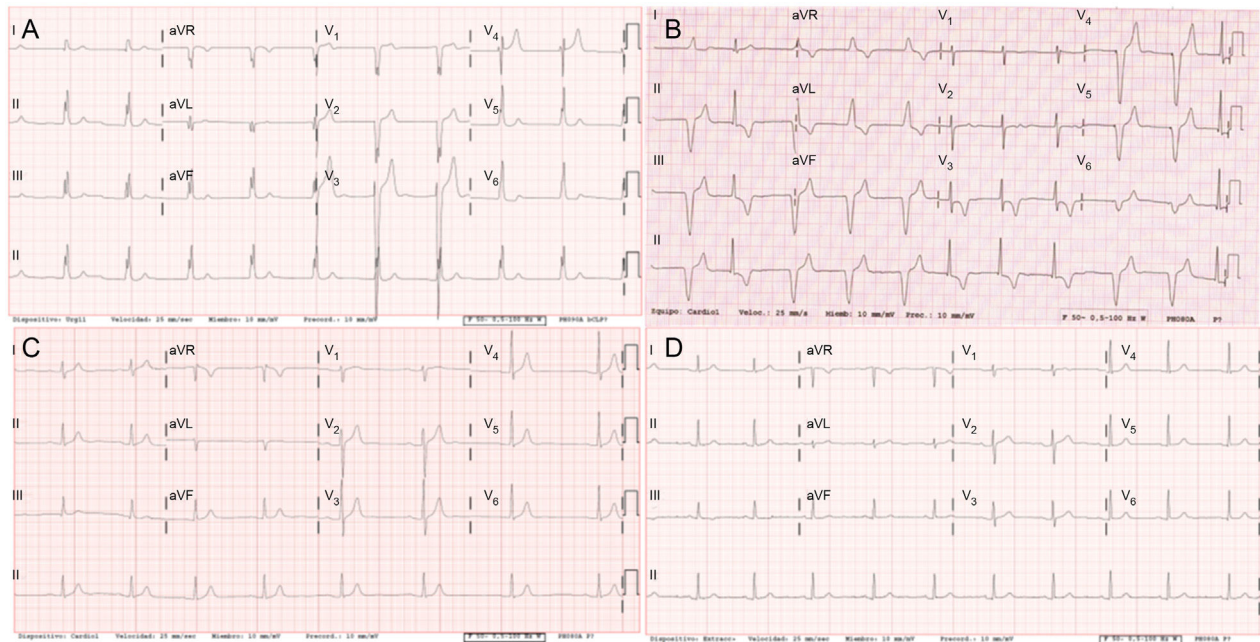
Figure 1. Electrocardiograms of several carriers of the p.Arg219His mutation in *SCN5A*. A, electrocardiogram of the index case III.3 (at age 30 years). B, electrocardiogram of case II.3 (age 62 years). C, electrocardiogram of case III.8 (age 32 years). D, electrocardiogram of the asymptomatic carrier II.8 (age 58 years).

The most recent echocardiogram showed dilatation of 2 chambers (left atrium 45.5 mL/m^2) with normal biventricular function.

The familial cluster of SSS requiring a PM at a young age led to suspicion of the presence of a genetic condition of autosomal dominant transmission (Figure 2). A genetic ultradeep sequencing study of 132 genes associated or potentially associated with arrhythmias and cardiomyopathies was ordered for the index case. Two heterozygous mutations not present in controls were found in 2 genes previously associated with conduction disorders: NC_000003.11:g.38655281C>T in *SCN5A* and NC_000015.9:g.73615231C>T in *HCN4*, as well as the polymorphism NC_000021.8:g.35821680C>T in *KCNE1* associated with acquired prolonged QT interval.

The *SCN5A*[p.Arg219His] mutation has been reported in 2 families in Switzerland and Japan.[1,2] Clinically, in addition to SSS, supraven-

tricular and ventricular tachyarrhythmias may be present and a PM may need to be implanted at a young age, particularly in men. In one of the families, cosegregation of the mutation with dilated cardiomyopathy was demonstrated.[1,2]

In contrast, the *HCN4*[p.Arg1068His] variant had not been described previously. The *HCN4* gene encodes subunit 4 of the HCN channels, which carry the native I_f current. These channels participate in the generation and modulation of the cardiac activity of the PM. Certain mutations in *HCN4* are associated with a faster channel deactivation time, leading to loss of function and bradycardia.[3] The in silico study of *HCN4*[p.Arg1068His], was inconclusive.

A clinical-genetic study was offered to the families prior to signing the informed consent. Echocardiogram and ECG studies were conducted in 10 family members and genetic studies (when indicated) were performed in 7.
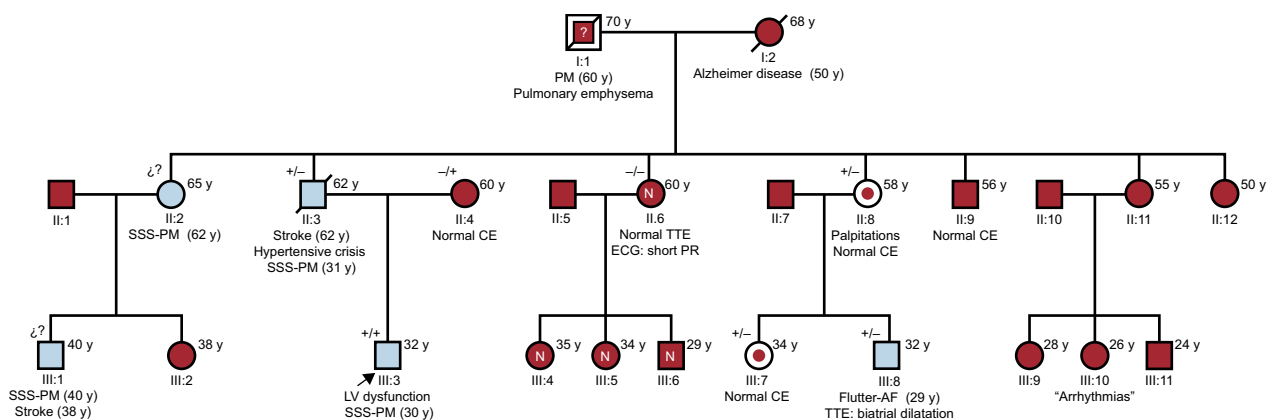
Figure 2. Family tree and study of *SCN5A*[p.Arg219His] and *HCN4*[p.Arg1068His] mutations. The boxes and circles represent males and females, respectively. The shaded symbols indicate affected individuals. A dot inside the symbol indicates an individual not affected. The letter N inside the symbol indicates an individual who is not a carrier and is not affected. The symbols + and – represent carriers and noncarriers, respectively, of the mutations in individuals with available genetic studies. A diagonal line through the symbol indicates an individual who has died. The age of the individual at the time of the event is shown in parenthesis. The actual age or age on death is shown at the top right of the symbol. AF, atrial fibrillation; CE, clinical examination; ECG, electrocardiogram; LV, left ventricular; PM, pacemaker; SSS, sick sinus syndrome; TTE, transthoracic echocardiography; y, years. *SCN5A*[p.Arg219His] (pathogenic)/*HCN4*[p.Arg1068His] (variant of unknown significance).

The *SCN5A*[p.Arg219His] mutation was present in all affected persons in the paternal family. The phenotype was very similar to that described earlier, although in the literature, SSS was reported in unrelated patients.[1,2] This is therefore the first time that cosegregation of *SCN5A*[p.Arg219His] with familial paralysis of the atrium[1,2] has been reported (Figure 2). In addition, 2 women aged 58 years and 34 years (II.8 and III.7, respectively) were identified as asymptomatic carriers. This finding fits with the later clinical presentation in women (Figure 1D).

The *HCN4*[p.Arg1068His] mutation and the *KCNE1*[p.Asp85Asn] polymorphism were transmitted by the mother, whose clinical study was normal. It was not possible to study the other members of the mother's family. Given that lack of cosegregation with SSS, *HCN4*[p.Arg1068His] is considered a variant of unknown significance that does not explain FPA.

Sick sinus syndrome is defined as abnormal formation and propagation of the electric impulse in the sinus node. It is characterized by sinus bradycardia, sinoatrial block, sinus arrest, chronotropic incompetence, and/or atrial tachyarrhythmias (essentially atrial fibrillation). It is a common disorder in elderly individuals but rarely seen in young people. A permanent PM needs to be implanted in approximately 50% of affected individuals.[4] According to data from the Spanish Pacemaker Registry,[5] SSS and atrial fibrillation/atrial flutter with bradycardia account for approximately 36% of PM implantations. There does not appear to be any predominance of one sex or the other (ratio of men to women, 0.98) although atrial fibrillation/atrial flutter with bradycardia occurs predominantly in men (ratio, 1.7).[5]

We consider the *SCN5A*[p.Arg219His] mutation the cause of the familial condition as it shows cosegregation with the disease and has been described previously. The *HCN4*[p.Arg1068His] mutation is a variant of unknown significance that could act as a disease modifier, although it is not the cause. These findings would enable genetic counselling to be provided to individual carriers (Figure 2). In the case of asymptomatic patients, follow-up with electrocardiogram, Holter, and echocardiographic studies (given the association with dilated cardiomyopathy) were planned, and, depending on the symptoms, exercise testing was considered to detect chronotropic incompetence. The familial study, in this case, was essential to clarify which of the documented genetic variants was the cause of the familial paralysis of the atrium.

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Impella CP® Circulatory Support Device as a Bridge to Heart Transplantation: First Experience in Spain

Dispositivo de asistencia circulatoria Impella CP® como terapia puente a trasplante cardiaco: primera experiencia en España

To the Editor,

Death due to cardiogenic shock is still high (50%-80%) despite early coronary revascularization, intra-aortic balloon counterpulsation, and short-term mechanical ventricular assist devices (VADs; extracorporeal membrane oxygenator or Levitronix®).

One recently approved short-term percutaneous VAD, the Impella CP®, provides a theoretical flow of up to 4 L.

We report the case of a 37-year-old woman with cardiomyopathy after childhood thoracic chemotherapy and radiotherapy who had spent 6 months on the elective heart transplant list due to advanced heart failure. When the patient was admitted with refractory cardiogenic shock despite inotropic therapy (INTER-MACS level 2), it was decided to implant a VAD as a bridge to heart transplant. However, due to the history of thoracic irradiation, reduced size of the left ventricle (46 mL), and severe dysfunction of the right ventricle, she was a suboptimal candidate for a surgical VAD, and a percutaneous 4-L Impella CP® device was implanted. Implantation was performed without complications via a right femoral approach (Figure), and the mean flow achieved of 3 L improved her clinical and hemodynamic profile (Table). Given the cardiogenic shock and dependence on a short-term VAD, she was prioritized on the national emergency heart transplant waiting list. The device was stopped after 10 days because it displayed a "high motor current" alarm. Because the patient showed renewed hemodynamic deterioration, the dysfunctional device was removed and a new one was implanted. After 4 days with this second