SUPPLEMENTARY MATERIAL

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Nicolás M. Maneiro-Melón,[a] Miguel González-Barbeito,[b] Francisco Estévez-Cid,[b] Jesús Peteiro-Vázquez,[c] José J. Cuenca-Castillo,[b] and Roberto Barriales-Villa[d,*]

[a]*Servicio de Cardiología, Complexo Hospitalario Universitario A Coruña, Instituto de Investigación Biomédica de A Coruña (INIBIC), Servizo Galego de Saúde (SERGAS), Universidade da Coruña, A Coruña, Spain*
[b]*Servicio de Cirugía Cardiaca, Complexo Hospitalario Universitario A Coruña, Instituto de Investigación Biomédica de A Coruña (INIBIC), Servizo Galego de Saúde (SERGAS), Universidade da Coruña, A Coruña, Spain*
[c]*Unidad de Imagen, Servicio de Cardiología, Complexo Hospitalario Universitario A Coruña, Instituto de Investigación Biomédica de A Coruña (INIBIC), Servizo Galego de Saúde (SERGAS), Universidade da Coruña, A Coruña, Spain*
[d]*Unidad de Cardiopatías Familiares, Servicio de Cardiología, Complexo Hospitalario Universitario A Coruña, Instituto de Investigación Biomédica de A Coruña (INIBIC), Servizo Galego de Saúde (SERGAS), Universidade da Coruña, A Coruña, Spain*

*Corresponding author:
E-mail address: rbarrialesv@gmail.com (R. Barriales-Villa).

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IgG4-related Disease Presenting as Cardiac Arrest

Enfermedad relacionada con IgG4 que se presenta como parada cardiaca

To the Editor,

Immunoglobulin (Ig) G4-related disease (IgG4-RD) is a fibroinflammatory process first described in 2003, with frequent multiorgan involvement, most often involving the pancreas, lungs, or retroperitoneum.[1] Cardiac manifestations, however, are rare, with only a few reported cases.[2]

We present the case of a 47-year-old previously healthy man, brought to our emergency department following resuscitation from out-of-hospital cardiac arrest in a shockable rhythm. An electrocardiogram after return of spontaneous circulation showed high-degree atrioventricular block with a varying escape rhythm.

On admission, he was awake and asymptomatic and, after exclusion of major echocardiographic abnormalities, a transvenous temporary pacemaker was implanted; a coronary angiogram showed no significant coronary artery disease. Backup pacing to allow for intrinsic rhythm was initially preferred, but the patient developed a *torsade de pointes*, which was promptly shocked. The pacemaker frequency was increased with no further arrhythmias, so that the initial arrest was interpreted as bradycardia-dependent.

Careful echocardiographic examination, complemented by transoesophageal imaging, displayed a nodular mass extending from the aortic root into the interatrial septum, without obstruction or valvular dysfunction; the mass was not opacified by ultrasonographic contrast (Figure 1A-B). Because the temporary pacemaker contraindicated magnetic resonance imaging, computed tomography was performed, showing a 36 × 37 mm mass with a density similar to that of the interventricular septum (Figure 1C-D).

After Heart Team discussion, a decision was made to attempt to distinguish a malignant neoplasm from a benign process to inform the choice between palliative care and a curative approach. An echo-guided percutaneous biopsy was performed, revealing only nonspecific inflammatory infiltrate. In the absence of evidence of malignancy, cardiac surgery revealed an inextricable tumoral mass at the center of the heart, closely related to the aortic, mitral, and tricuspid valves. A surgical specimen was collected (Figure 2A), with intraoperative frozen section examination suggesting a benign connective tissue neoplasm; a definitive pacemaker was implanted and the procedure terminated.

The patient was discharged with no other intercurrent events and remained asymptomatic. Histopathologic examination of the surgical specimen showed a fibrotic stroma with spindle-shaped cells in a storiform pattern and no significant atypia; obliterative phlebitis was also observed. This diffuse lesion was remarkable for the presence of an exuberant chronic inflammatory process with numerous plasma cells and polymorphonuclear leukocytes; immunohistochemistry showed the predominance of IgG4-producing plasma cells (274 per high power field; Figure 2B-C). This prompted further immunological evaluation that confirmed increased IgG4 serum levels (202 mg/dL).

A diagnosis of IgG4-RD of the heart was made and a positron emission tomography-scan obtained, confirming the presence of the hypermetabolic intracardiac mass; no extracardiac metabolically active tumoral lesions were found (Figure 2D). The patient was started on prednisone, with no additional symptoms and normalization of IgG4 serum levels, but imaging follow-up at 1 year showed no significant response. Rituximab was attempted as second-line therapy, although without mass reduction, and consequently a watchful approach was decided.

Although infrequent, cardiovascular involvement in IgG4-RD has been described in cases of aortic aneurism, aortitis, pericarditis, and coronary artery pseudotumors[2,3]; intracardiac pseudotumors, however, are found only in exceedingly rare reports.[4–6] The latter usually present as heart failure, due to valvular dysfunction, associated in 2 cases with atrioventricular conduction distur-

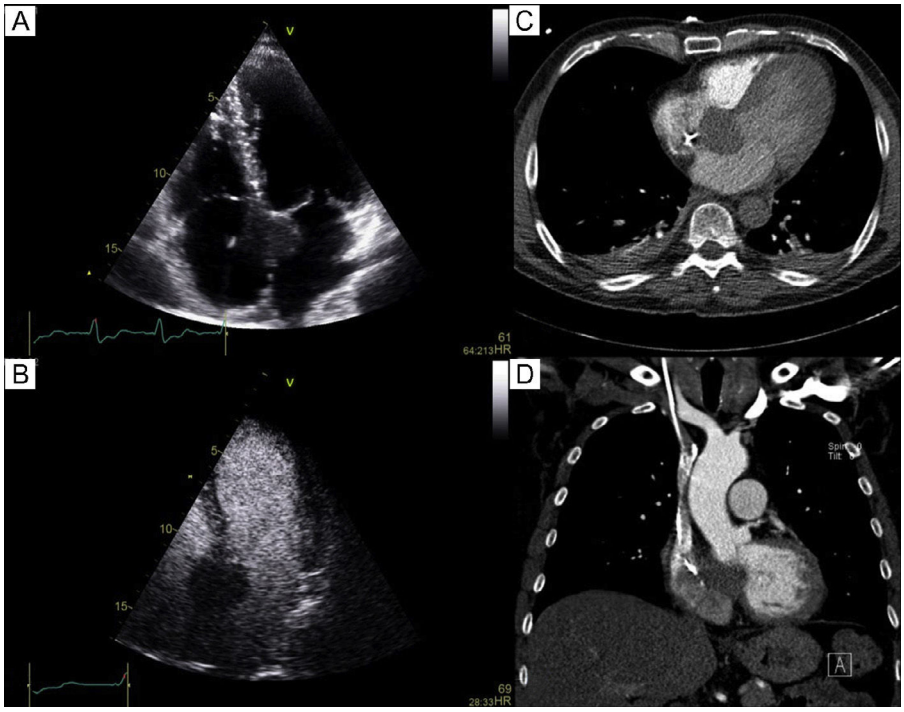

Figure 1. A: transthoracic echocardiography revealing the nodular mass in the interatrial septum, near the mitral and tricuspid valves, without opacification after ultrasonographic contrast administration (B). C, D: computed tomography displayed the 36 × 37 mm mass with a density similar to that of the interventricular septum.

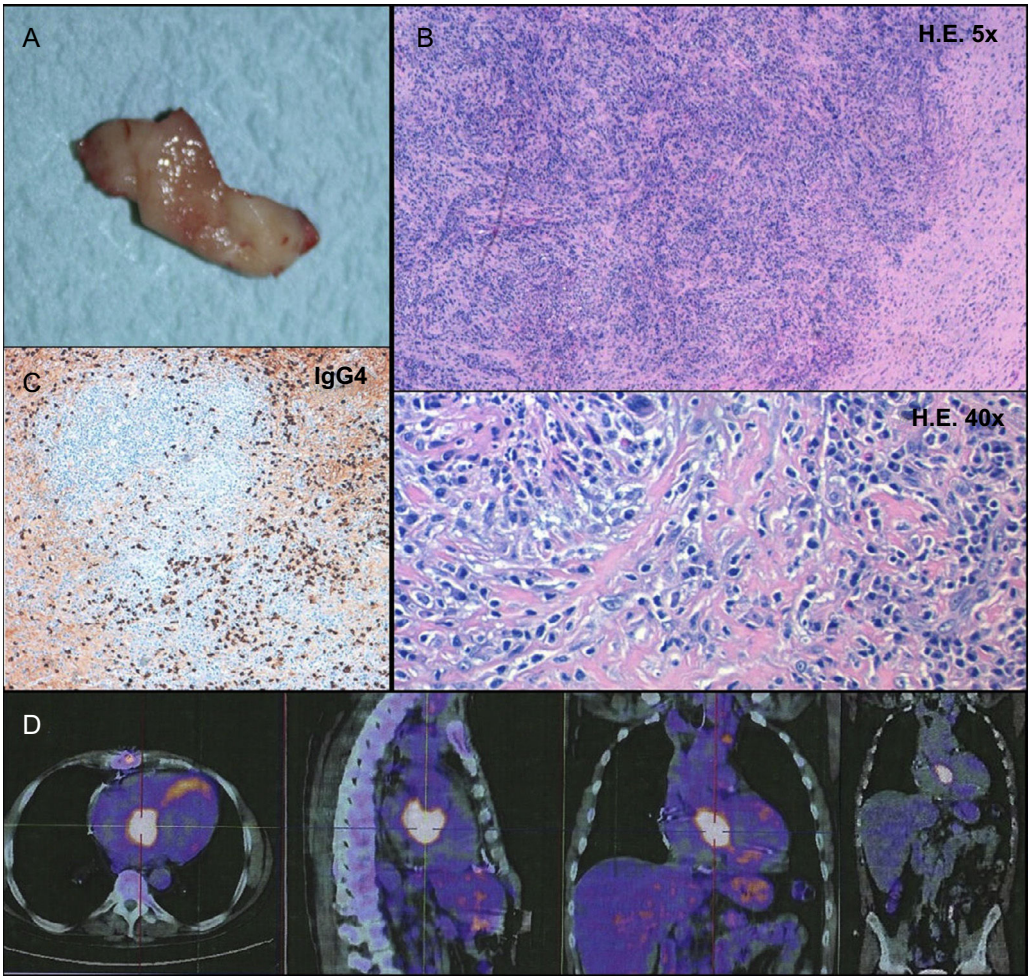

Figure 2. A: macroscopic appearance of the surgical specimen. B: hematoxylin-eosin (HE) staining demonstrated a fibrotic lesion with a storiform pattern and a rich inflammatory infiltrate. C: a large population of plasma cells was evidenced on immunohistochemistry, with an elevated number of IgG4-producing cells (274 per high power field). D: positron emission tomography scan confirmed the hypermetabolic cardiac lesion, without extracardiac involvement.

bances.[4,5] Cardiac arrest has been described as a result of ischemia in the context of coronary involvement.[2]

Some authors have reported successful steroid therapy for the reduction of residual lesions after surgery,[4] but there are also cases in which these agents were only able to stop tumoral growth[6] and even 1 patient who developed symptoms under steroid therapy for extracardiac disease.[5]

To the best of our knowledge, this is the first reported case of cardiac IgG4-RD presenting as nonischemic cardiac arrest. It is also the first to report the use of rituximab, a B-cell depleting agent currently regarded as second-line therapy in IgG4-RD. While clinically stable, our patient showed no signs of mass reduction; we hypothesize that these therapeutic strategies act on the inflammatory component of the lesions, but are probably unable to reduce the established fibrotic reaction.

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Gonçalo Pestana,[a,*] Teresa Pinho,[a,b] Catarina Costa,[b,c] Pedro Bernardo Almeida,[a,b] Paulo Pinho,[b,d] and M. Júlia Maciel[a,b]

[a]*Cardiology Department, Centro Hospitalar São João, Porto, Portugal*
[b]*Faculty of Medicine, Porto University, Porto, Portugal*
[c]*Anatomical Pathology Department, Centro Hospitalar São João, Porto, Portugal*
[d]*Cardiac Surgery Department, Centro Hospitalar São João, Porto, Portugal*

*Corresponding author:
E-mail address: gpestana.md@gmail.com (G. Pestana).

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Leadless Pacemaker Implantation in a Transplanted Heart

Implante de marcapasos sin cables en un corazón trasplantado

To the Editor,

Leadless pacemakers are a proven alternative to conventional pacemakers, with excellent outcomes in terms of safety and efficacy, a lower rate of complications, and optimal electrical performance in the short- and mid-term.[1–3] These outcomes have been reported in both pivotal studies and in the clinical practice setting.[2,3]

We present the case of a 54-year-old man who underwent orthotopic heart transplant with biatrial anastomosis for the indication of end-stage nonischemic heart disease in 2004. In the first 3 months after transplant, routine endomyocardial biopsies showed mild graft rejection (grade $\leq$ IA), which resolved after increasing the intensity of immunosuppressive therapy. The patient remained asymptomatic until 2016, when he was admitted to hospital with broad QRS tachycardia (Figure 1A). Transthoracic echocardiography showed normal ventricular function, slight right ventricular dilatation, moderate tricuspid regurgitation, and right atrial dilatation. In the electrophysiology study, supraventricular tachycardia with aberrant conduction was detected (Figure 1A). Activation mapping confirmed a right atrial macrore-entrant circuit involving the superior vena cava. Radiofrequency ablation was applied to this site (Figure 2A), with reversion to sinus rhythm without subsequent arrhythmic reinduction. The patient remained asymptomatic in treatment with β-blockers and calcium antagonists for 6 months before experiencing clinical tachycardia associated with heart failure. A second electrophysiology study was scheduled. This study revealed severe sinus dysfunction, prolonged infra-Hisian conduction (HV-interval), and alternating bundle branch block (Figure 1A and B). Programmed pacing was performed, without reinduction of clinical tachycardia or ventricular arrhythmias. In view of the limited efficacy of β-blockers in transplant patients and the possible negative effect of calcium antagonists, definitive pacemaker placement was considered the best option. Moreover, in view of the absence of atrial capture in the broad scarring area (Figure 2A) and immunosuppressive therapy, as well as the possible indication for a second heart transplant, a Micra leadless pacemaker (Medtronic Ibérica, S.A.) was implanted. The device was deployed in the mid-septal position after 3 attempts at different sites in the right ventricle, due to high thresholds; the acute parameters were impedance, 520 Ω; R wave, 7.2 mV; and threshold, 1.88 V at 0.24 ms. After placement of the Micra device, atrioventricular node ablation was performed in the same procedure (Figure 2B). During follow-up, the pacing parameters were stable at 6 and 10 months after implantation: impedance, 500 Ω; R wave, 7.9 mV; and threshold, 1.13 V at 0.24 ms. The ventricular pacing percentage was 100% and there were no infectious complications, embolisms, or readmissions due to heart failure.

Permanent electrical pacing is required in 5.8% of patients with orthotopic transplant,[4] and in the late period this requirement can be a sign of rejection or severe vascular disease in the graft. In this case, in which aggressive immunosuppressive therapy is needed, pacemaker placement may increase the risk of infection.[4] Leadless pacemaker placement is a promising alternative for transplant recipients given the lower risk of infection.[5]

It is important to note that the slightly increased pacing threshold in our patient could be due to diffuse cardiac fibrosis. This may call into question whether the strategy of atrioventricular node ablation and pacemaker placement in the same procedure is safe and more convenient for the patient or