Allergic reaction to pacemaker compounds: Case reports

Rogelio Robledo-Nolasco, MD,* Luis Gerardo González-Barrera, MD,*
Jesús Díaz-Davalos, MD,† Gerardo De León-Larios, MD,* Margarito Morales-Cruz, MD,†
David Ramírez-Cedillo, MD†

*From the *ISSSTE National Medical Center "November 20," Mexico City, Mexico, and †ISSSTE Regional Hospital "Dr. Valentín Gómez Farías," Guadalajara, Mexico.*

Introduction

Allergic reaction to permanent pacemakers or other cardiac implantable electronic devices (CIED) is extremely rare and is usually dismissed owing to confounding with an infectious process.[1] The components of the CIED most frequently involved are titanium, nickel, and epoxy resin.[2] A solution to this problem is the implantation of a new device covered in hypoallergenic material or one that does not contain the identified allergen. We report 3 cases of allergy to pacemaker components and final outcomes after implantation of covered generators: 1 with gold coating and the other 2 with a polytetrafluoroethylene (PTFE) membrane.

KEY TEACHING POINTS

- An allergic reaction to a pacemaker should be suspected after repeated exteriorizations without other evidence of a systemic inflammatory response.
- Type IV allergic reaction on tissue biopsy from the pacemaker pocket is the most characteristic finding of an allergic reaction to the pacemaker compounds.
- Covering the device with polytetrafluoroethylene, a widely available material, offers good results as treatment.

Case report

Patient 1

A 47-year-old man with a history of mechanical aortic valve implantation 26 years ago owing to a double aortic injury was admitted to our hospital in February 2008 for symptomatic Mobitz type II second-degree atrioventricular (AV) block. An Axios D bicameral pacemaker (Biotronik Co, Berlin, Germany; components of pacemaker: titanium and epoxy resin) was implanted via right subclavian vein. Three weeks later, the patient developed erythema and local swelling around the surgical wound without purulent discharge, fever, or leukocytosis. Treatment was based on intravenous antibiotics and removal of the pacemaker and leads. After 2 weeks, an identical generator was placed on the contralateral side. After a couple of months, the pacemaker generator exteriorized. The same generator model was implanted on the submuscular plane. After a month and a half, a vesicle was developed on the implant zone, which remitted after management with oral antibiotics; however, in March 2011 it was exteriorized once more. After complete removal of the device, an epicardial bicameral pacemaker (Vitatron T70 DR; Medtronic Inc, Minneapolis, MN; components of pacemaker: titanium and polyurethane) was implanted; however, it was exteriorized after 4 months.

Skin tests were performed on all pacemaker components, including titanium, which reported negative at 72 hours. Biopsies of the lesions were also taken during the device removal procedure, showing giant Langerhans cells and chronic granulomatous inflammation due to foreign body (type IV reaction) (Figure 1A).

A new implant was successfully done in March 2012, an endocardial bicameral pacemaker (Medtronic Adapta DR PVV, 24 karat gold, 0.45 mm minimum coating thickness; Medtronic Inc) (Figure 2A) in the left subclavian region. No complications were reported after a 9-year follow-up.

Patient 2

A 33-year-old woman with congenitally corrected transposition of the great arteries was implanted with a bicameral pacemaker (St Jude Regency™ model covered with parylene) in 2009 via right subclavian vein owing to complete AV block. After 10 years, the patient had a generator replacement (Medtronic Ensura DR MRI; components of pacemaker: titanium and

KEYWORDS Allergic reaction; Covered generator; Erythema; Exteriorization; Pacemaker; Polytetrafluoroethylene
(Heart Rhythm Case Reports 2022;8:410–414)

Funding Sources: None. Disclosures: None. **Address reprint requests and correspondence:** Dr Rogelio Robledo-Nolasco, ISSSTE National Medical Center, Avenida Felix Cueva 540, Colonia del Valle, Codigo, postal 03100, Ciudad de Mexico. E-mail address: rogelio_robledo@hotmail.com.

https://doi.org/10.1016/j.hrcr.2022.03.003

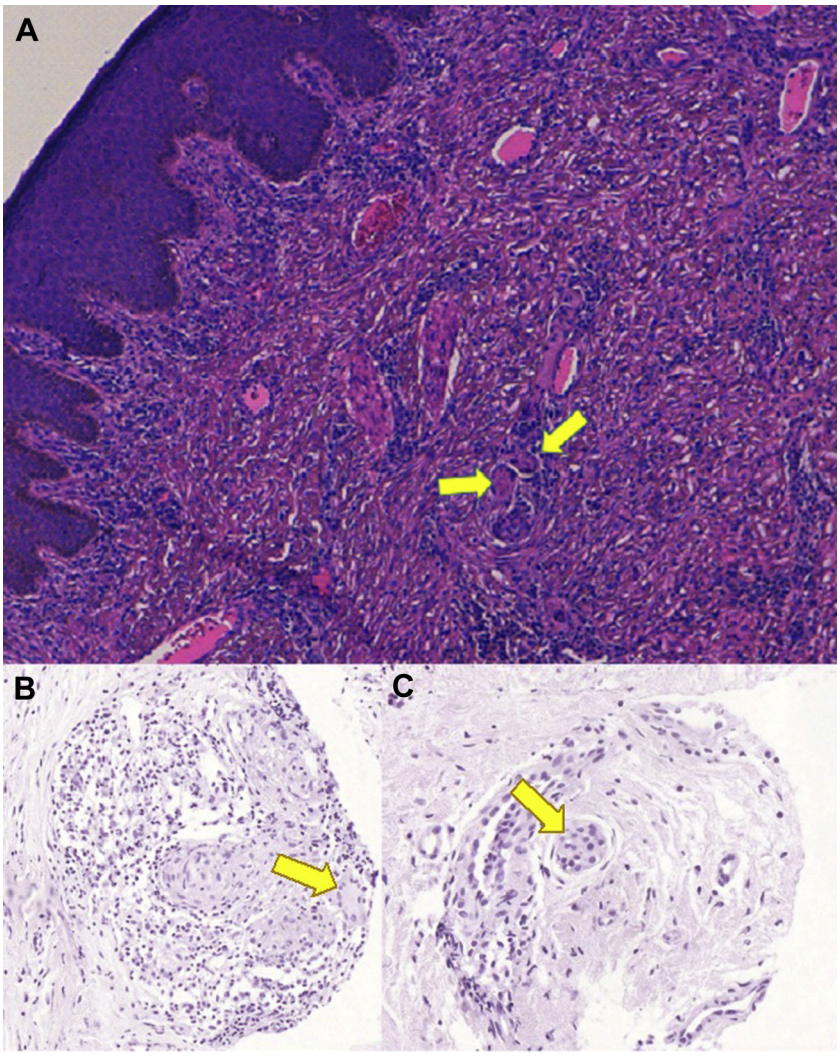

Figure 1 Pacemaker pocket tissue biopsy. Classic type IV reaction is shown, characterized by chronic granulomatous inflammation and Langerhans cells (*yellow arrows*). Pathology findings were consistent in the 3 reported cases. **A:** Case 1. **B:** Case 2. **C:** Case 3.

polyurethane). After 5 months, the pacemaker generator exteriorized and an erythema appeared on the pocket zone, without clinical evidence of systemic inflammatory response. The device was removed and a new one (same model) was implanted on the left subclavian region, leaving the 2 original leads. A month later, the patient developed fever, redness at the pocket zone, and exteriorization; a computed tomography angiography was performed, which revealed a wide interventricular communication. All 4 pacemaker leads migrated to different locations: 1 from the right subclavian crossed the interatrial septum and anchored to the morphologically right ventricle (located on the left); the second lead, also from the right subclavian, was in the right appendage; and the other 2 leads migrated through the brachiocephalic venous trunk, 1 to the right atrium and the other to the apex of the morphologically left ventricle (located on the right). The echocardiogram reported both ventricles with preserved systolic function, and the patient opted for the complete extraction of the device. In December 2019, the 4 leads were extracted and an external permanent pacemaker with active fixation lead placed via the right jugular vein.

Dermal tests of the pacemaker components were negative. The biopsy of the pocket lesions demonstrated chronic granulomatous inflammation and multinucleated giant cells (Figure 1B). After analyzing the results, it was decided to implant an epicardial pacemaker covered with an expanded polytetrafluoroethylene (ePTFE) bag (Gore-Tex cardiovascular patch) made by the surgery team (Figure 2B). No complications or symptoms were reported after 2 years of follow-up.

Patient 3

A 17-year-old female patient, at 4 years of age (2008), had an epicardial unicameral pacemaker (St Jude Regency model covered with parylene) implanted owing to complete congenital AV block. In July 2018, the generator was changed by depletion and upgraded to a dual-chamber endocardial pacemaker (St Jude, Endurity Core; components of pacemaker: titanium, epoxy resin, and polysulfone) via left subclavian. Fifteen days post suture removal, she developed erythema around the pacemaker pocket and dehiscence of the surgical

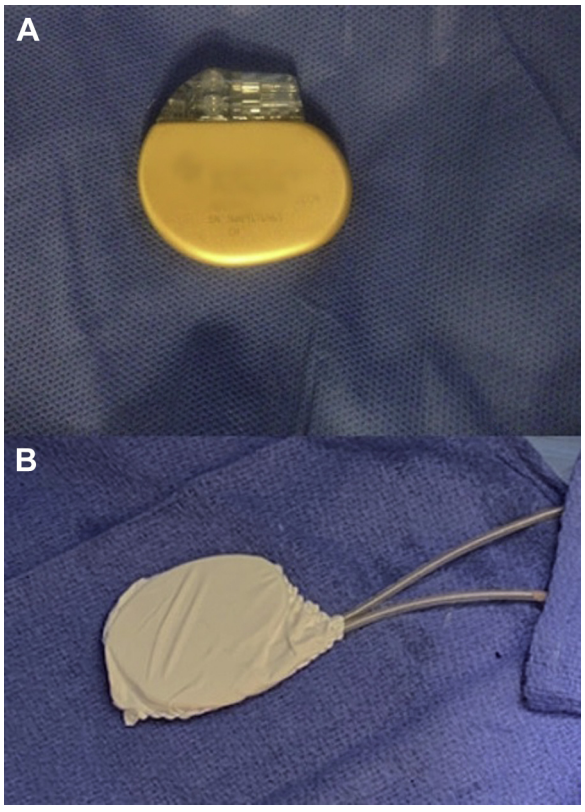

Figure 2 Pacemaker generators covered. **A:** The gold-coated pacemaker generator implanted in the first case (patient 1). **B:** The polytetrafluoroethylene-wrapped generator used in the second case (patient 2).

wound with exposure of the generator; white blood cell count was normal and there was no fever. The patient was treated with an antibiotic regimen and wound care for a year and a half. In January 2020, the entire system was removed and the patient treated with antibiotics to implant a new contralateral submuscular pacemaker (St Jude Endurity Core). One month later the system exteriorized; it was removed and a different scheme of intravenous antibiotics was applied, and a bicameral epicardial pacemaker (Biotronik, Effecta DR; components of pacemaker: titanium, epoxy resin, and silicone) was implanted after the patient completed 15 days of medication. Dehiscence of the surgical wound and a third exteriorization occurred. In May 2020 the device was removed and a new pacemaker (same model as the previous one) was implanted via right subclavian. Fifteen days later, similar complications from previous implants were observed: erythema, dehiscence of the surgical wound, and a fourth exteriorization.

The dermal tests concluded rejection to nickel; therefore in August 2020 the implantation of an epicardial pacemaker was chosen, with the casing covered by a PTFE bag. The leads (Greatbatch Medical Myopore Bipolar Sutureless Myocardial Pacing Lead) were fixed in the right atrium and in the anterior face of the right ventricle. The bicameral generator used (Endurity Core; St Jude) was wrapped in an ePTFE bag made by the surgical team. At a 10-month follow-up, the patient has remained with the surgical wound adequately healed, with satisfactory outcomes. The pocket tissue biopsy reported findings consistent with the 2 previous cases (Figure 1C).

Discussion

As previously mentioned, allergy to any permanent pacemaker component is extremely rare.[1] To our knowledge, this is the first series of cases published in the literature with medium- and long-term follow-up.

The diagnostic approach is challenging, as the allergy is commonly mistaken for an infection process, and this last complication is seen much more frequently in clinical practice.[2] Nery and colleagues[3] reported an incidence of infection of 1% in a case-control study that included 2417 patients who underwent CIED implantation over a 4-year period, whereas the incidence of allergy to any one specific component of the pacemaker still unknown.

The data in our case series are based on 2 centers with a high volume of device implants; from 2008 to date, a total of 5526 pacemakers have been implanted in both centers, resulting in an estimated incidence of allergic reaction of 0.05%.

The dermal signs that occur in infection and allergy to pacemakers are similar; in infection, erythema occurs in 41% and skin erosion in 21%.[4] These signs are common in titanium allergy or other CIED components, and therefore making an accurate diagnosis is more difficult. In all 3 cases presented in this case report, dermal lesions appeared, and the exteriorization of the pacemaker generator occurred in the first weeks following the device implant.

The first case of allergy associated with pacemaker components was documented in 1970 by Raque and Goldschmidt.[5] In this patient, silicone was the allergen reported by the tests performed. Since then, several cases have been reported. In 2002 Déry and colleagues[6] analyzed 21 cases reported worldwide up to that time; 5 of them had presented allergies to nickel, 4 to titanium, and 3 to epoxy, and the other cases were related to cobalt, chromium, mercury, silicone, cadmium, and parylene, but in 6 patients the dermal tests were negative. The latter is not surprising, as dermal tests with titanium and other CIED components have low sensitivity and therefore can lead to false-negative results.[7]

In other words, the fact that these tests are negative does not exclude the possibility of allergic reaction to some CIED material. In the first 2 cases of our case report, the dermal tests were reported with negative results, and in the third case the tests were positive for nickel. It is worth mentioning that in patients 2 and 3 the allergic reaction occurred until the second implant. We consider that the device (St Jude Regency model, covered with parylene) used in both cases initially played a particularly important protective role.

The definitive treatment of this pathology is the removal of the allergenic material, but this is not possible in patients with an indication for a pacemaker.[6] In some cases, partial resolution has been achieved with topical steroids, but their

Table 1 Summary of the clinical characteristics of the present case series

Characteristics	Patient 1	Patient 2	Patient 3
Sex	Male	Female	Female
Age	47	33	17
Pacemaker indication	Second-degree AV block Mobitz II	CHB	CHB congenital
Time to rejection[†]	21 days	15 days	25 days
Cutaneous reaction	Local erythema; local inflammation	Local erythema; local inflammation	Local erythema; local inflammation
No. of exteriorizations	4	2	4
Skin test[‡]	Negative	Negative	Nickel
Treatment	Gold cover	Cover of ePTFE	Cover of ePTFE
Implant approach	Endocardial	Epicardial	Epicardial
Follow-up	9 years	2 years	10 months
History of skin allergies[§]	Denied	Denied	Denied
Peripheral blood and pocket tissue cultures[‖]	Negative	Negative	Negative

AV = atrioventricular; CHB = complete heart block; ePTFE = expanded polytetrafluoroethylene.
[†]Involves only the first device related to the reaction.
[‡]Included all components of the pacemaker.
[§]No history of previous dermatological hypersensitivities.
[‖]Include aerobic, anaerobic, and atypical microorganisms.

long-term use may have other complications.[5,8] To date in most of the case reports, the definitive treatment has been the implantation of a pacemaker generator covered with gold, silicone, or PTFE manufactured during the procedure.[1,2,6,8–14]

Of the cases we report here, the first one involved implantation with a gold-covered pacemaker generator and the other 2 implants were wrapped in ePTFE; none of the cases have shown allergy data again during their follow-up. In our experience, the use of PTFE has provided an adequate alternative, since it is a much more viable material and no allergic reactions have been reported despite its greater use in other surgical procedures.[15] It is also much more difficult to get a device covered with gold, since there is only 1 manufacturer in the world and silicone is a material with little use in surgeries today.

Diagnostic criteria for allergic reaction to pacemaker

We recommend the following diagnostic criteria, based on the literature and the clinical characteristics of our case series (Table 1): (1) the appearance of erythema or eczema over the pacemaker area, accompanied by local inflammation but without evidence of systemic infection; (2) exteriorization of the device within the first 6 months postimplantation is highly suggestive; (3) exteriorization repeatedly on 2 or more occasions; (4) cultures of blood, pocket tissue, and device material are negative; (5) the presence of multinucleated giant cells in the pacemaker pocket tissue biopsy; (6) no recurrence of exteriorization after implantation of a generator covered with gold or PTFE.

Conclusion

There has been an expansion in the indications for CIED, which forces the clinician to be aware of complications. An unusual condition is allergy to the components of the device, which is confirmed when the dermal tests are positive; but when they are not, and strong clinical suspicion remains, we suggest several indicators that support an allergic reaction to some component of the pacemaker. A good treatment option in our experience, owing to its greater availability, is the implantation of a device wrapped in PTFE.

References

1. Syburra T, Schurr U, Rahn M, et al. Gold-coated pacemaker implantation after allergic reactions to pacemaker compounds. Europace 2010;12:749–750.
2. Goli A, Shroff S, Osman MN, et al. A case of gold-coated pacemaker for pacemaker allergy. J Innov Card Rhythm Manag 2012;3:944–947.
3. Nery PB, Fernandes R, Nair GM, et al. Device-related infection among patients with pacemakers and implantable defibrillators: incidence, risk factors, and consequences. J Cardiovasc Electrophysiol 2010;21:786–790.
4. Tarakji KG, Chan EJ, Cantillon DJ, et al. Cardiac implantable electronic device infections: presentation, management, and patient outcomes. Heart Rhythm 2010;7:1043–1047.
5. Raque C, Goldschmidt H. Dermatitis associated with an implanted cardiac pacemaker. Arch Dermatol 1970;102:646–649.
6. Déry JP, Gilles M, O'Hara G, et al. Pacemaker contact sensitivity: case report and review of the literature. Pacing Clin Electrophysiol 2002;25:863–865.
7. Wood MM, Warshaw EM. Hypersensitivity reactions to titanium: diagnosis and management. Dermatitis 2015;26:7–25.
8. Viraben R, Boulinguez S, Alba C. Granulomatous dermatitis after implantation of a titanium-containing pacemaker. Contact Dermatitis 1995;33:437.
9. Slim M, Neffati E, Lagren A, et al. Case report: a nine year follow-up for a pacemaker generator poly-tetra-fluoro-ethylene coating for allergic reactions to pacemaker compounds. F1000Research 2018;7:1460.
10. Kypta A, Blessberger H, Lichtenauer M, et al. Gold-coated pacemaker implantation for a patient with type IV allergy to titanium. Indian Pacing Electrophysiol J 2015;15:291–292.
11. Hayes DL, Loesl K. Pacemaker component allergy: case report and review of the literature. J Interv Card Electrophysiol 2002;6:277e8.
12. Iguchi N, Kasanuki H, Matsuda N, et al. Contact sensitivity to polychloroparaxylene-coated cardiac pacemaker. Pacing Clin Electrophysiol 1997;20:372–373.
13. Tamenishi A, Usui A, Oshima H, et al. Entirely polytetrafluoroethylene coating for pacemaker system contact dermatitis. Interact Cardiovasc Thorac Surg 2008;7:275–277.

14. Vodiskar J, Schnöring H, Sachweh JS, et al. Polytetrafluoroethylene-coated pacemaker leads as surgical management of contact allergy to silicone. Ann Thorac Surg 2014;97:328–329.

15. Begovac PC, Tomson RC, Fisher JL, et al. Improvements in GORE-TEX vascular graft performance by Carmeda BioActive surface heparin immobilization. Eur J Vasc Endovasc Surg 2003;25:432–437.