

# Malignant transformation of a chronically infected implantable cardioverter-defibrillator pocket



Donna Kang, MD, Khuyen Do, MD, Jonathan Nattiv, MD, Meena Zareh, MD, Rahul Doshi, MD, FHRS

*From the University of Southern California, Los Angeles, California.*

## Introduction

Device infection is a serious complication of cardiac implantable electronic device (CIED) implantation. Chronic non-healing cutaneous wounds can cause cutaneous squamous cell carcinoma (SCC).<sup>1</sup> This process is driven by chronic inflammation and immune activation of the underlying cutaneous tissue.<sup>2</sup> Here, we present a case of an 81-year-old man with chronic nonhealing device pocket infection that we believe transformed into cutaneous SCC.

## Case report

An 81-year-old man with ischemic cardiomyopathy—and history of dual-chamber implantable cardioverter-defibrillator placement 11 years prior—presented to a tertiary care facility for management of a suspected chronic nonhealing CIED pocket infection. This device was originally placed in the patient's left chest wall. Six years prior, the device was upgraded to a cardiac resynchronization therapy device. One year prior, the patient underwent a routine generator change. Soon after the generator change, the patient developed redness and pain over the device pocket site and was diagnosed with a cellulitis. As the referring physicians did not perform device extraction, this infection was initially treated with pocket revision and a prolonged course of intravenous antibiotics, but the infection persisted. He was then transferred to a tertiary care facility with lead extraction capabilities, where he subsequently underwent laser lead extraction of the old system and repeat pocket revision with debridement on the left side. He then had cardiac resynchronization therapy device placement on the right side of his chest with continued intravenous antibiotics for an additional 6 weeks. Despite multiple debridement procedures and courses of intravenous antibiotics, the infection on the left chest wall persisted with development of an abscess (Figure 1). The patient was referred to general surgery for

surgical exploration. Operatively, the chronic infection from the pocket site and skin was debrided and washed out, and the poorly healing skin of the pocket site was excised and sent to pathology; there were no retained foreign bodies noted. Pathology of this tissue revealed SCC of the cavity and the overlying skin (Figure 2). The patient subsequently had a full skin examination along with full-body computerized tomography, which did not demonstrate any other skin lesions or internal SCC that may have metastasized to the chest wall. The surgical resection margins were not complete; thus he required systemic chemotherapy. Unfortunately, the patient has had a long and protracted recovery period.

## Discussion

Infection is a serious complication of CIED implantation. The incidence of infection is 0.5% with the primary implant and this risk is increased to as high as 1.0% to 7.0% with repeat instrumentation, such as in generator changes, device upgrades, or revisions.<sup>3–7</sup> CIED infections are associated with significant morbidity, healthcare costs, and increased mortality.<sup>8</sup>

Preimplantation factors associated with increased risk for device infection include renal insufficiency, heart failure, diabetes, anticoagulation, corticosteroid use, and temporary pacemaker placement prior to the procedure. In turn, multiple leads, requirement for revision or upgrade, procedure time, and early reintervention for pocket hematoma are considered procedure-related factors that increase infection risk.<sup>9–13</sup>

While superficial infections and suture-related abscesses can be managed with antibiotics, deeper pocket infections and device-related endocarditis often require complete system extraction. In a study by Margey and colleagues,<sup>12</sup> among all patients with any device-related infection, the rate of recurrent infection after an antibiotic course without complete system extraction was 67%, vs 0% for those who underwent complete extraction.

In our patient, the initial treatment strategy for his post-generator change CIED infection was antibiotics alone, and the patient had recurrence of infection after the antibiotic course was complete. Although surgical exploration of the pocket was done, the device was maintained in the same left pectoral area and the leads were not extracted initially.

**KEYWORDS** Cardiac implantable electronic device; Chronic infection; Chronic inflammation; Malignancy transformation; Squamous cell carcinoma (Heart Rhythm Case Reports 2018;4:307–309)

**Address reprint requests and correspondence:** Dr Donna Kang, 1510 San Pablo St, Suite 322, Los Angeles, CA 90033. E-mail address: [donna.kang@med.usc.edu](mailto:donna.kang@med.usc.edu).

## KEY TEACHING POINTS

- Cardiac implantable electronic devices can be chronically infected.
- Chronic infection in this patient's device probably led to the development of cutaneous squamous cell carcinoma of the pocket.
- The possibility of this complication should be anticipated when considering patients, especially the elderly, for implantable cardiac devices.

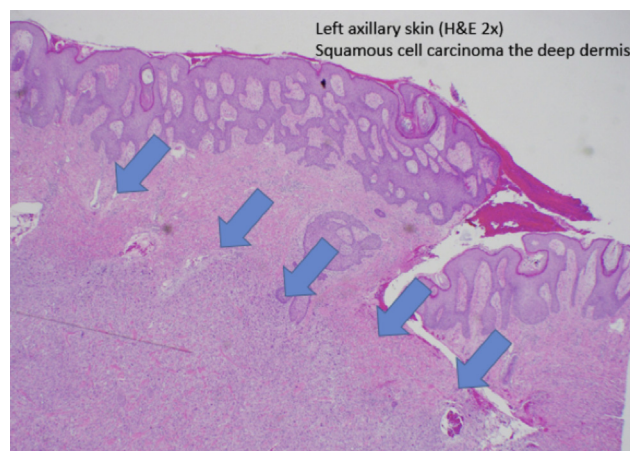
This led to chronic infection at the left pectoral pocket site that impaired wound healing and prevented eradication of the infection.

Chronic infection is a well-known risk factor for the development of malignancies.<sup>1</sup> Chronic inflammation, in turn, is a common mechanism through which chronic infection can lead to malignancy. In chronic inflammation, pathologic release of NF- $\kappa$ B from local immune cells leads to overexpression of inflammatory cytokines, including TNF- $\alpha$ , IL-1, IL-6, IL-17, and IL-23, which are known to promote cancer development.<sup>14</sup> This cascade is exacerbated as the released NF- $\kappa$ B acts on developing cancer cells by promoting survival mechanisms. STAT3, a transcription factor, is also activated by chronic inflammation and promotes survival via a similar mechanism. The ultimate consequence of these tissue changes is altered function of immune cells and epithelial cells, leading to dysregulated immunity, enhanced cell turnover and regeneration, and ultimately enhanced tumor cell survival and immortality.<sup>2</sup> This process has been demonstrated in numerous organ systems, including the skin.

Development of SCC of the pocket site was a worrisome occurrence in our patient. Regarding the etiology for SCC occurrence, it is possible that SCC developed independently of the chronic infection of the pocket site and then subsequently led to a poorly healing chronic wound. However,



**Figure 1** A photograph of the patient's chronic nonhealing device pocket infection on left chest wall.



**Figure 2** A hematoxylin-eosin stain of surgically resected chronically nonhealing device pocket infection showing squamous cell carcinoma (SCC) of the deep dermis. The arrows are pointing to the SCC.

the fact that the skin prior to generator change was completely normal argues for the reverse explanation—that the chronic inflammatory changes from chronic CIED infection over time led to malignant transformation of the tissue in the pocket area.

## Conclusion

This is the first case report of a chronic nonhealing device pocket infection most likely causing cutaneous SCC. Incomplete system extraction led to recurrent infections, which increased morbidity and mortality; thus it is essential to have complete system removal in all infected CIED. As the incidence of SCC of the skin rises dramatically with age,<sup>15</sup> this complication should be taken into consideration when an elderly patient is being evaluated for device placement.

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