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PII: S2214-0271(22)00200-7
DOI: https://doi.org/10.1016/j.hrcr.2022.10.006
Reference: HRCR 1420

To appear in: HeartRhythm Case Reports

Received Date: 10 June 2022
Revised Date: 15 September 2022
Accepted Date: 3 October 2022


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Diffuse large B-cell lymphoma presenting as implantable cardioverter-defibrillator pocket swelling: A case report

Short title: DLBCL presenting as ICD pocket swelling

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Conflicts of Interest: All authors have no conflict of interest to disclose.

Word Count: 1136
Keywords: cardiac implantable electronic device; Diffuse large B-cell lymphoma; intracardiac mass; malignant neoplasm; non-Hodgkin lymphoma; implantable cardioverter defibrillator.
Introduction

The number of Cardiovascular Implantable Electronic Devices (CIEDs) has increased owing in part to the growing number of indications for their use and the increasing demand of the aging population.\(^1\) An estimated 1.2 million CIEDs are implanted annually worldwide, and 2.9 million CIEDs were implanted in the United States alone between 1993 and 2009.\(^2\) The growing incidence of device implantation requires familiarity with and recognition of device related complications. CIED infections are a feared complication reported, and familiarity with CIED pocket abnormalities including pain, swelling, inflammatory changes, and erosion is essential to identifying patients with possible device related infection. Non-infectious etiologies of device pocket inflammation including lymphoma are limited to case reports. The pathophysiology of malignant transformation of tissue surrounding the device pocket remains unknown. We report a case of diffuse large B cell lymphoma (DLCBL) in a 91-year-old male presenting with subacute swelling and inflammatory changes at his implantable cardioverter-defibrillator (ICD) pocket site.

Malignant neoplasms presenting as CIED pocket masses are extremely rare yet remain in the differential diagnosis.

Case Report

A 91-year-old male with a nonischemic cardiomyopathy status post dual-chamber implantable cardioverter-defibrillator (ICD) implantation in 2010 and upgrade to left pre-pectoral biventricular ICD in 2013, permanent atrial fibrillation, and essential thrombocythemia on hydroxyurea presented to an outside hospital for two weeks of progressive ICD pocket swelling and erythema. The patient denied pain at the ICD pocket site. Examination revealed an erythematous, swollen pocket with overlying telangiectasias. The patient was afebrile with mild
leukocytosis. Ultrasound of the pocket revealed an irregular fluid collection inferior to the ICD generator measuring 4 x 2.6 x 3.3 cm. The patient was treated empirically with broad spectrum antibiotics for presumed ICD pocket infection and transferred to our center for pocket exploration and possible extraction.

Pocket exploration revealed a solid mass with cystic components extending onto the ICD generator, leads, and surrounding tissues. A biopsy specimen was obtained. The device was left in position and the pocket was closed. Bacterial and acid-fast bacilli wound cultures showed no growth, and blood cultures remained negative. Antibiotics were discontinued given low clinical suspicion for infection and absence of supportive microbiologic data. Microscopy of the biopsy specimen revealed fragments of fibrous tissue with focal chronic inflammation and fibrosis. No malignant cells were observed.

The patient was seen in follow up approximately one month later for consideration of surgical excision of the ICD pocket mass. Computed tomography (CT) scan of the chest revealed a large complex fluid collection measuring up to 11.5 cm involving the ICD pocket, few top-normal mediastinal lymph nodes, and a rounded density within the left pectoralis muscle measuring up to 1.8 cm. The patient was admitted following this evaluation for worsening ICD pocket swelling and erythema. The patient underwent repeat pocket exploration and resection of the 418-gram, 14 x 8 x 6 cm mass including a segment of the left pectoralis major muscle. Microscopy revealed a partially necrotic tumor with diffuse proliferation of atypical cells with frequent mitotic figures and apoptosis extending into skeletal muscle. Flow cytometry revealed evidence of abnormal B cells confirming the diagnosis of diffuse large B-cell lymphoma (DLCBL), activated immunophenotype (Figure 1). An interdisciplinary team including the patient, oncology and
electrophysiology favored holding further staging and treatment due to poor functional status. The patient was transitioned to hospice care and expired.

**Discussion**

DLBCL is the most common histologic subset of Non-Hodgkin Lymphoma (NHL). Treatment of DLBCL includes cytotoxic chemotherapy with rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (RCHOP), radiation therapy for bulky disease, and may include additional treatments based on immunologic and molecular subtype. Prognosis is determined by the patient’s age, performance status, stage of malignancy, and serum lactate dehydrogenase.

NHL at the site of CIEDs is reported rarely in the literature, and most often present with swelling of the generator pocket. The pathophysiologic relationship of the CIED and NHL remains unknown.

Infections, namely Epstein Barr virus (EBV), Human Immunodeficiency virus (HIV), Hepatitis C virus (HCV), Helicobacter Pylori, Borrelia burgdorferi, Chlamyphilia psittaci, among others, have been well documented in the literature and linked to the development of lymphoma through chronic inflammation. Hojo et. al reported a case of DLBCL in a pacemaker pocket and suggested chronic inflammation as the culprit. Additionally, Kang and colleagues reported a case of squamous cell carcinoma in a chronic non-healing CIED pocket infection. Our patient did not have any known infections and was EBV negative. However, most of the reported cases in the literature did not mention a history of infection on inflammation at the site of CIED implant. CIED pocket malignancy may be initially misdiagnosed as infection. Atypical cases of CIED pocket swelling should prompt biopsy for pathologic diagnosis. Non-infectious etiologies require high clinical suspicion and should be on the differential diagnosis for CIED pocket swelling.
Provider familiarity with the spectrum of CIED pocket complications is critical to early
diagnosis and management of rare non-infectious causes of pocket swelling.

Acknowledgements: None

Funding: This research did not receive any specific grant from funding agencies in the public,
commercial, or not-for-profit sectors.

Disclosures: None
Figure 1
Surface appearance of CIED pocket swelling (A). Computed tomography (CT) scan of the chest in coronal (B) and axial views (C) showing a soft mixed density material surrounding the left anterior chest wall implantable cardiovascular electronic device. Pathology with H&E staining showing partially necrotic tumor with diffuse proliferation of atypical cells with frequent mitotic figures and apoptosis extending into skeletal muscle (D).
Key teaching points

- Malignancy should be considered in the differential diagnosis of patients presenting with CIED pocket swelling.
- Gross pathologic and histological analysis of tissue specimens from CIED generator pocket should be considered in atypical cases of CIED pocket swelling.
- Treatment includes a multidisciplinary approach and involves electrophysiology, surgery, and oncology to evaluate and treat CIED associated malignancies.