Recurrent perforation of an implantable cardioverter-defibrillator lead in a patient with vascular Ehlers-Danlos syndrome

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Introduction

Vascular Ehlers-Danlos Syndrome (vEDS) is a rare genetic connective tissue disorder with an estimated prevalence of 1:100,000 to 1:200,000.[1] It is caused by heterozygous pathogenic variants of the *COL3A1* gene encoding type III collagen. vEDS is phenotypically characterized by thin, translucent, and easily bruised skin and fragile blood vessels and organs, leading to arterial dissections or ruptures, spontaneous gastrointestinal perforations, and urogenital perforations, notably including uterine rupture during pregnancy or childbirth. Although primary myocardial involvement is uncommon in vEDS, surgical or invasive procedures are avoided unless critically essential because of the increased risk of vascular or organ rupture due to tissue fragility.[2] We report the case of a patient with vEDS who experienced recurrent right ventricular (RV) lead perforations complicated by chronic pericarditis after implantation of a primary prevention implantable cardioverter-defibrillator (ICD).

Case report

A 37-year-old woman (body mass index = 30) with a history of coronary artery and renal artery dissections and myocardial infarction complicated by ventricular fibrillation cardiac arrest in the setting of molecularly confirmed vEDS presented to our inherited heart disease clinic to establish care. In 2007, while in college, she presented with chest pain and was found to have ST-segment changes and elevated troponin levels, consistent with acute coronary syndrome. Given that this presentation preceded her vEDS diagnosis, her symptoms were attributed to possible vasospasm, and coronary angiography was not performed at that time. Left ventricular systolic function was preserved. In April 2015, she experienced a ventricular fibrillation cardiac arrest while running, for which she received bystander cardiopulmonary resuscitation. A subsequent coronary angiogram showed no obstructive disease, and the ventricular fibrillation arrest was attributed to myocarditis vs stress cardiomyopathy, given apical wall motion abnormalities and elevated troponin levels. In retrospect, recurrent spontaneous coronary artery dissections with a false-negative coronary angiogram should

KEY TEACHING POINTS

- Arterial and organ rupture is a hallmark of vascular Ehlers Danlos syndrome (vEDS): vEDS is characterized by a high risk of spontaneous arterial, intestinal, or uterine rupture, which can be life-threatening and requires immediate medical attention. A history of arterial or organ rupture and thin, translucent skin should alert the cardiac electrophysiologist of the possible presence of vEDS.
- Fragile vascular structures: Patients with vEDS are at a significantly higher risk of vascular complications, including lead perforation and poor wound healing during implantation of transvenous pacemaker or implantable cardioverter-defibrillator (ICD) leads. This fragility necessitates extra caution during device implantation and postoperative monitoring.
- Avoidance of transvenous ICD leads: Given the higher risk of perforation of transvenous ICD leads, subcutaneous ICD systems should be considered in patients with vEDS in the absence of pacing needs.

KEYWORDS ICD complication; RV perforation; Recurrent pericarditis; Vascular Ehlers-Danlos syndrome; Genetic connective tissue disorder

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also be considered in the differential diagnosis. The patient underwent implantation of a single-chamber ICD with an active fixation RV lead. The procedure was complicated by pneumothorax and RV perforation, as evident by low R-wave sensing, high lead impedance, and diaphragmatic stimulation, causing a moderate-sized pericardial effusion and a left-sided pleural effusion. The patient then underwent removal and reimplantation of the RV lead in May 2015. Unfortunately, the patient developed a pocket infection with *Pseudomonas* and she underwent explantation of the left-sided transvenous device in October 2015, followed by implantation of a right-sided infraclavicular dual-chamber ICD system with active fixation right atrial and RV leads. In August 2016, she presented with dyspnea on exertion and subcostal pain that worsened on inspiration. Computed tomography scans of the chest and echocardiography suggested perforation of the RV lead with a small loculated effusion up to 0.5 cm at the apex of the right ventricle next to the tip of the RV lead. Of note, lead impedance and sensing were within normal limits. Given concerns for recurrent lead perforation in the setting of persistent chest discomfort and shortness of breath, the patient underwent explantation of the right-sided device and implantation of a Boston Scientific subcutaneous ICD. The patient's shortness of breath and pleuritic chest pain improved after removal of the ICD system. Genetic testing revealed a pathogenic *COL3A1* variant (p.Gly738Ser) consistent with vEDS. Both her siblings and children have tested negative for the familial *COL3A1* variant. Her parents did not undergo genetic testing, but did not have a history of complications typical of vEDS. The patient has a known pseudoaneurysm of the left vertebral artery. She likely also had a prior renal artery dissection that led to renal artery stenosis (status post angioplasty) with transient hypertension that occurred in 2004. Hypoplastic bilateral posterior tibial arteries were also observed. Computed tomography angiography in 2017 showed normal caliber aorta and no obvious residual dissections, and a subsequent computed tomography angiography of the head, abdomen and pelvis in 2018 was also normal. In 2020, her subcutaneous ICD experienced premature battery depletion and she underwent a generator change. The ICD implant site has healed well.

As a result of recurrent RV lead perforations, the patient developed pericarditis and experienced severe pleuritic chest pain in the first few months post arrest in 2015 and recurrent pericarditis in February 2022. Extensive vascular imaging in 2022 revealed no evidence of dissection or pulmonary embolism. Echocardiography revealed a left ventricular ejection fraction of 55% with apical septal and basal inferior wall hypokinesis, trivial pericardial effusion, abnormal septal motion, and annulus reversal concerning for constrictive physiology. Her workup included an elevated erythrocyte sedimentation rate of 44 mm/h, high-sensitivity C-reactive protein peaked at 97 mg/L with a cutoff of 3 mg/L, and troponin was slightly elevated at 15 ng/L with a cutoff of 9 ng/L. Autoantibodies, including antinuclear antibodies, double-stranded DNA, C3, C4, Smith, Sjögren syndrome–related antigen A and B were negative, as was viral testing for influenza, COVID-19, cytomegalovirus, Epstein-Barr virus, HIV, enterovirus, and Lyme disease. Initially, she was started on colchicine twice daily along with nonsteroidal anti-inflammatory drug therapy and Tylenol (Johnson & Johnson); however, her symptoms persisted. The decision was made to initiate anakinra, which was transitioned to 160 mg of rilonacept weekly. Overall, with the use of rilonacept, the patient has done very well without any return of pericarditis symptoms. In 2023, cardiac magnetic resonance imaging showed generally normal results except for thinning and akinesis of the apex and distal inferior wall, and mild enhancement of the pericardium without thickening, which is nonspecific and could be sequelae from prior pericarditis.

Discussion

vEDS can present with arterial dissection and rupture of muscular arteries, hemorrhages, and organ rupture.[3,4] Although vascular complications are encountered most commonly, ruptures of the chordae tendinae or myocardium are rare cardiovascular complications.[3] Due to the low prevalence of vEDS, experience with transvenous ICD leads in patients with vascular EDS is limited; however, elective surgery and routine colonoscopy for individuals with vEDS is generally discouraged due to the higher risk of surgical complications from inherent tissue fragility and risk of colonoscopy-associated bowel perforation, respectively. Complications during and after surgery are related to tissue and vessel friability, which result in recurrent arterial or bowel tears, fistulae, poor wound healing, and suture dehiscence.[3]

To our knowledge, this is the first report of ICD lead perforation in a patient with vEDS and the second report of a patient with an EDS condition.[5] There are additional risk factors that could contribute to a higher likelihood of perforations of transvenous leads, including female sex, use of active fixation leads, and RV free wall placement of the lead. Because vEDS presents with fragile blood vessels and organ walls, the high risk of complications during implantation of transvenous pacemaker or ICD leads, including vascular rupture, pneumothorax, RV lead perforation, and poor wound healing leading to a higher risk of infection, should be considered.

Conclusion

In the absence of pacing needs, transvenous ICDs should be avoided in patients with vEDS to minimize the risk of vascular complications and myocardial perforation.

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