CASE REPORT

Pacemaker lead-associated thrombosis in cardiac resynchronisation therapy

Jesmar Buttigieg,¹ Rachele Asciak,² Charles Mallia Azzopardi³¹Department of Medicine, Mater Dei Hospital, Malta, Msida, Malta²Mater Dei Hospital, Msida, Malta³Department of Internal Medicine and Infectious Diseases Medicine, Mater Dei Hospital, Msida, Malta**Correspondence to**
Dr Rachele Asciak,
rachasciak@gmail.com

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SUMMARY

Pacemaker lead-associated thrombosis is a possible complication of any cardiac implantable electronic device. We present a case of a middle-aged woman with a history of ischaemic left ventricular failure, who presented with fever and other non-specific symptoms 4 months after cardiac resynchronisation therapy. A transoesophageal echocardiogram confirmed a vegetation-like structure originating from the pacemaker lead in the right atrium. The patient was treated with intravenous antibiotics followed by open heart surgery in order to remove this mass as well as the pacing device, including all three pacing leads. Histology and culture of the retrieved mass confirmed a sterile thrombus with no features to suggest an infected mass (vegetation). The patient made an uncomplicated recovery and there were no long-term sequelae on follow-up during the 2 years after the event.

BACKGROUND

Symptomatic pacemaker lead-associated thrombosis is a relatively uncommon condition, especially in patients with cardiac resynchronisation therapy. Patients may present with a variety of non-specific symptoms, which, unfortunately, may lead to delayed diagnosis and, consequently, increased patient morbidity and mortality. It is therefore important that physicians are aware and consider the possibility of pacemaker lead-induced thrombus, especially in high-risk patients. A high index of suspicion is necessary for early diagnosis and prompt successful treatment.

CASE PRESENTATION

A 56-year-old postmenopausal Caucasian woman had suffered an extensive anterior myocardial infarction at 33 years of age, and had been diagnosed with diabetes mellitus at 50 years of age. She had left ventricular failure New York Heart Association (NYHA) class III, refractory to maximal antifailure treatment, with an echocardiogram that had shown a grossly dilated and hypocontractile left ventricle and an ejection fraction of <35%. ECG showed a prolonged QRS of 168 ms, and she had therefore been offered implantation of a cardiac resynchronisation therapy with defibrillator (CRT-D) device. The implantation had been uncomplicated, resulting in some improvement in her heart failure symptoms. She was on aspirin 75 mg once daily (OD), bumetanide 1 mg OD, simvastatin 40 mg OD, perindopril 8 mg OD and carvedilol 25 mg twice daily. Her glycaemic control was satisfactory on diet alone. She had no history

of hypertension or smoking but had a strong family history of ischaemic heart disease.

Four months after CRT-D insertion, the patient presented with a 6-week history of episodic low-grade fever associated with night sweats, lethargy, anorexia and weight loss of approximately 3 kg over the same period.

She had a temperature of 37.7°C, with a regular pulse rate of 100 bpm and a blood pressure of 110/70 mm Hg. Examination of the precordium, respiratory system, abdomen, neurology and musculoskeletal system revealed no abnormalities. She had no stigmata of infective endocarditis (IE) and there were no signs of local device infection. ECG showed atrial and ventricular pacing and her chest X-ray was normal. Absolute white cell count was $14.2 \times 10^9/L$, with a predominant neutrophilia, and C reactive protein was 41 mg/L (normal range 0–10 mg/L). The rest of the complete blood count, the liver function panel, thyroid function tests, autoimmune screen including antinuclear antibody, antineutrophil cytoplasmic antibodies and complement levels and urinalysis, were all within normal limits. Three sets of blood cultures from different sites (kept for prolonged incubation) were negative. A transthoracic echocardiogram (TTE) was carried out and all pacing wires were identified with no vegetations seen. The patient was kept off antimicrobials and observed for a week, during which time she remained afebrile, and her inflammatory markers normalised. The preliminary diagnosis at the time was a possible viraemia. She was therefore discharged home with a follow-up appointment scheduled for 3 weeks later.

Fifteen days later the patient re-presented with fever. Once again, repeated multisite blood cultures

Figure 1 Transoesophageal echocardiogram showing a vegetation-like structure in the right atrium.

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Figure 2 Transoesophageal echocardiogram showing the right atrial thrombus prolapsing through the tricuspid valve.

(off antimicrobials) showed no growth. *Brucella* spp, *Mycoplasma* spp and *Legionella* spp serology were negative. The clinical suspicion of IE remained high despite a normal TTE, and therefore a transoesophageal echocardiogram was performed, following the latest European Society of Cardiology guidelines.¹ This showed a large vegetation-like structure (estimated size of 55 mm) in the right atrium, possibly originating from the pacemaker lead and prolapsing through the tricuspid valve (figures 1 and 2). A CT pulmonary angiogram showed no evidence of pulmonary embolism. A provisional diagnosis of pacemaker lead-induced culture-negative IE was performed. The patient was started empirically on meropenem 1 g 8 h, teicoplanin 100 mg OD and caspofungin 50 mg OD and was referred for early surgery 5 days into treatment. Prior to surgery, the atrioventricular delay of the CRT-D was prolonged with the aim to allow the ventricular intrinsic rhythm to take over. During surgery, cardiopulmonary bypass was used, and the right atrium was opened to reveal a large, mobile, irregular soft brown mass originating from the right atrial pacemaker lead. The mass together with all the pacemaker leads was removed and sent for histology and microbiology investigations. Gram stain and

culture of the mass showed no bacteria. Histological examination of the mass revealed a thrombus with no features to suggest a vegetation. Cultures of all the pacemaker lead tips were also negative. Although all cultures proved to be negative, the patient was still treated with the abovementioned antimicrobials for a total of 6 weeks. Caspofungin was replaced by fluconazole 400 mg OD 4 weeks into treatment. The patient was also treated with long-term anticoagulation. She made an uncomplicated recovery and was discharged from hospital to home, with regular follow-up appointments every 8 weeks. After 24 months of follow-up, the patient remained well, leading a relatively normal life, although with limited exercise tolerance in view of her poor left ventricular ejection fraction. The patient was very reluctant to have any device reinserted and remains without CRT-D.

DIFFERENTIAL DIAGNOSIS

Using the Modified Duke criteria for the diagnosis of IE, our case met only one major and one minor criterion, which is insufficient to diagnose definitive IE.¹ Nonetheless, we initiated empirical antimicrobial therapy after considering the possible catastrophic outcomes of not adequately treating a possible IE. Treatment consisted of teicoplanin to cover for *Staphylococci*, caspofungin to cover for fungal endocarditis, and meropenem to broaden the spectrum and cover for Gram negative organisms. Ultimately, microscopic examination revealed a sterile thrombus with no features to suggest an infected vegetation and, in light of this, our final diagnosis was that of pacemaker lead-associated thrombosis.

DISCUSSION

Thrombus formation is a recognised complication of any type of cardiac implantable electronic device (CIED). The clinical presentation can be fairly non-specific and often mimics IE. Chest pain, dyspnoea, congestive heart failure, syncope, cardiovascular shock, peripheral oedema, distended neck veins, fever and malaise, are some of the clinical features reported in the literature.^{2–5} Modern imaging modalities and postmortem studies have demonstrated that such thrombi can be entirely asymptomatic, incidental and indeed commoner than previously thought.^{6–10} Table 1 illustrates

Table 1 The incidence of electrode-attached intracardiac thrombus associated with CIED				
Study	Type of study	Investigation modality	Incidence of CIED associated thrombosis	CIED age
Rahbar <i>et al</i> ⁷	Case control retrospective study	Echo: TTE/TOE	15/1086 patients (1.4%) 6/15 RA lead 8/15 RV lead 1/15 LV lead	52.0±36.2 months
Novak <i>et al</i> ⁸	Retrospective postmortem studies	Postmortem studies	26/78 patients (33%) 22 BC/UCV leads 11 RA lead 11 RV lead 12 exhibited thrombi simultaneously on large vein leads, RA and RV leads	4.0±3.3 year
Supple <i>et al</i> ⁹	Retrospective observational cohort study (all patients had arrhythmias)	ICE	26/86 patients (30%) 25 thrombi on RA lead 5 thrombi on RV lead Total 30 thrombi identified in 26 patients	n/a
Korkeila <i>et al</i> ¹⁰	Prospective consecutive patients referred for first PM/ICD	TOE/Venography	6/66 patients (9%) RA or SVC-atrial junction on TOE 12/66 patients (18%) SC/BC vein on venography	6 months
BC, brachiocephalic; CIED, cardiac implantable electronic device; ICD, intracardiac defibrillator; ICE, intracardiac echocardiography; LV, left ventricle; PM, pacemaker; RA, right atrium; RV, right ventricle; SC, subclavian; SVC, superior vena cava; TOE, transoesophageal echocardiogram; TTE, transthoracic echocardiogram; UCV, upper caval vein.				

the incidence of electrode-attached intracardiac thrombi associated with CIED in some studies conducted in the past 10 years.

The treatment of pacemaker lead-associated thrombosis remains controversial. Given the size and mobility of the mass, and the high risk of fatal pulmonary embolism, our patient was referred for open heart surgery after 5 days of antimicrobial treatment. Other treatment options that have been described in the literature include anticoagulation and thrombolysis with reverse tissue plasminogen activator, streptokinase or urokinase.^{11–15} Open heart surgery has been the most commonly employed treatment option when dealing with relatively large thrombi or in cases of unsuccessful lysis.

It is thought that permanent implantation of pacemaker leads in the myocardium can lead to increased local thrombogenicity by causing endothelial trauma and by increasing blood turbulence. This, combined with relative blood stasis in the presence of depressed ventricular function, may increase the risk of thrombosis. The pacemaker leads themselves may produce a foreign-body-type reaction with inflammation and fibrosis along the course of the wire, which may lead to thrombus propagation along the pacing lead.⁶ Moreover, a higher incidence of venous thrombosis has been found in patients who had a previous transvenous temporary pacemaker lead.¹⁶ Other factors associated with pacemaker lead-associated thrombosis include coagulopathies such as protein S and C deficiency,⁶ oral contraceptive use, heparin-induced thrombocytopenia, polycythaemia vera, the pacemaker material itself and fractured retained pacemaker lead.^{17–21}

Studies have shown that patients with left ventricular ejection fraction (LVEF) of $\leq 40\%$ have a higher incidence of venous thrombosis in the 6 months after pacemaker implantation.¹⁶ In patients with LVEF $\leq 40\%$ or a temporary pacing system ipsilateral to the permanent implant, warfarin therapy prophylaxis seems to lower the incidence of venous lesions after CIED.²² These findings do raise the question of whether one should anticoagulate high-risk patients after such devices are implanted. Larger multicentre trials are therefore needed to study the risks versus benefits of lifelong anticoagulation in such patients. In such circumstances, there are also no clear recommendations regarding the timing or site of reimplantation of CRT-D device after the original device has been removed.

Learning points

- ▶ Symptomatic intracardiac pacemaker lead-associated thrombosis is an uncommon condition and may present with various non-specific symptoms, and it is therefore easily missed.
- ▶ Physicians should keep a high index of suspicion of cardiac implantable electronic device associated thrombosis, especially in high-risk patients and in cases of presumed pacemaker-related infective endocarditis with negative blood cultures.
- ▶ A transoesophageal echocardiogram should be requested if clinical suspicion remains high despite a negative trans-thoracic echocardiogram.
- ▶ Given that cardiac resynchronisation therapy is frequently instituted in patients with dilated and hypocontractile left ventricular function, long term anticoagulation should be considered.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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