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Lead-dependent infective endocarditis: An old problem, a new name

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Abstract

This paper presents a literature review on right heart endocarditis in patients with a permanent pacemaker (PM) or implantable cardioverter-defibrillator (ICD). We postulate putting a great deal more emphasis on separation of lead-dependent infective endocarditis from other types of infective endocarditis. We stress the need for screening patients with PM/ICD and pulmonary signs using transesophageal echocardiography. Antibiotic therapy and PM/ICD removal is the treatment of choice in such patients. (Cardiol J 2010; 17, 2: 205–210)

Key words: right heart endocarditis, pacemaker, implantable cardioverter-defibrillator, percutaneous lead extraction

Introduction

The first reports on infective complications after permanent endocardial stimulation were published in the 1960s. The symptoms of infection were described as 'sepsis', i.e. the body's response to infection. The term 'sepsis' had at that time a different meaning (according to [1]). It comprised infections in the pacemaker pocket. Positive blood culture tests served as the basis for diagnosing general infection described as septicemia. Its main symptom was infection in the pacemaker generator pocket involving various sites of the abdomen and thorax that were used at that time. The infection affected also neck regions due to lead introduction sites into the venous system. The association of the infective endocarditis with any local symptoms along the passage of the lead from the entrance in the vein to the pacemaker pocket together with positive blood culture tests was deduced from later diagnosis established during cardiac surgery or post mortem examination.

These first publications referred to the classic picture of infective endocarditis described by Osler in 1885 [2]. Osler, being both a clinician and anatomopathologist, joined the previously observed symptoms in patients with the autopsy picture of their hearts and vessels. Since his publications it has been known that infective endocarditis is a disease of heart structures and great vessels, together with systemic symptoms. The introduction of echocardiography into clinical practice represents a diagnostic revolution that made the non-invasive discovery of indisputable disease symptoms in living patients possible. Only then were the elements justifying the diagnosis of infective endocarditis with the possibility of visualizing vegetations defined precisely, which was taken into consideration in the Duke criteria [3]. As it noted before, a huge group of patients with cardiac implants (a group exceptionally exposed to infective endocarditis) was added to the original Osler's description.

Apart from artificial valves and vascular prostheses, other cardiac devices to steer the heart rate

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such as pacemakers (PM) and implantable cardioverter-defibrillators (ICD) came into use. By 2008, endocardial leads for heart pacing had a history of 50 years. The widespread implantation of cardiac devices had resulted in 3.25 million functioning PM and 180,000 ICD across the world [4]. At the same time, progress in contemporary cardiology, including treatment of heart rhythm disturbances, resulted in a significantly prolonged lifespan for people with chronic cardiac diseases. Patients with cardiac devices undergo repeated exchanges of their PM/ICDs over the course of their increasingly long lifetimes. For that very reason, they are especially exposed to post-operative infective complications of the pockets, as well as the development of infective endocarditis related to the presence of the leads in their right heart chambers.

Pacemaker related infections

The rate of PM/ICD infections has been shown to increase by 124% within the last decade [5].

The classification of infections related to cardiac devices was proposed many years ago. Charles Byrd divided pacemaker-related infections into the following groups [6]:

— endocarditis;
— inflammation of myocardial tissue;
— infected vegetations;
— infected implanted foreign bodies;
— bacteremia without signs of endocarditis;
— local infections of subcutaneous tissue;
— chronic infections limited to the pocket area;
— superinfection of pacemaker pocket area;
— chronic pocket infection with granulation tissue.

Recent papers on PM/ICD-dependent infections appear to underestimate the distinctive role of right heart endocarditis as one of the most important infectious complications [7, 8].

Lead-dependent infective endocarditis

We can ask the question: is there a need to pay a closer look at a specific type of infective endocarditis caused by endocardial leads, which, despite being previously described, have been under-recognized so far?

We suggest giving it a name: LDIE (lead-dependent infective endocarditis), which may attract the attention of physicians to infective diseases in connection with endocardial leads. The positive answer is based on some facts related to the specific nature of the disease:

1. LDIE is the changes in the chambers and tissues of the right heart as well as in the veins introducing leads to the heart and arteries leading blood from the heart to the pulmonary circulation with the presence of one or more endocardial leads.
2. The symptoms of LDIE imitate pulmonary diseases.
3. Staphylococci are of special importance among pathogens.
4. For effective treatment of LDIE, it is necessary to remove the whole system i.e. PM/ICD with leads, independently of the chosen antibiotic therapy.

A specific feature of the disease is difficulty in its diagnosis due to the advanced age of the patients. This disease entity is not present in the cardiology textbooks despite the fact that it is rapidly increasing as a clinical and therapeutic problem. It is presented in case reports or retrospective analyses of small groups of patients (from less than ten to a few dozen patients) [7, 9–12]. First reports of bacterial right heart endocarditis appeared in the second half of the 20th century. Initially, the problem was only noticed in drug addicts and as a iatrogenic complication in patients with catheters in their right heart chambers or in association with prolonged hospitalization [7]. Right heart endocarditis in patients with permanent PM and ICD has also been reported [7, 9–12]. The reported rate of infection connected with a PM/ICD system ranges from 0.13% to 19.9%, and from 0.7% to 1.2% for LDIE.

Etiology of LDIE

From the pathomorphological viewpoint, right heart endocarditis is characterized by vegetations in the echocardiographic images — the fragile wart-like structures which are accumulations of microorganisms, thrombocytes, fibrin and inflammatory cells. In the antegrade flow vegetations can only migrate to pulmonary circulation, thus resulting in pulmonary embolism [7, 10–12].

The pathogenesis of vegetations on endocardial leads and/or right heart endocardium is unclear and deduced from the following hypotheses [6]:

1. Some breeds of bacteria, especially staphylococci, and perhaps other gram-position organisms, produce adhesins, thanks to which bacterial colonies can adhere to every smooth surface of a cardiac implant and create a biofilm to protect them from the host's immune system and antibiotic therapy. Also the formation of clots due to slow blood flow around the electrodes and turbulences caused by the presence of the electrodes may result in bacteria growth because the blood clots may then be colonized by bacteria appearing in the bloodstream during transient bacteremia related to personal hygiene (teeth brushing and gingival microinjuries) or therapeutic procedures (dental, urological, gynecological, etc.).

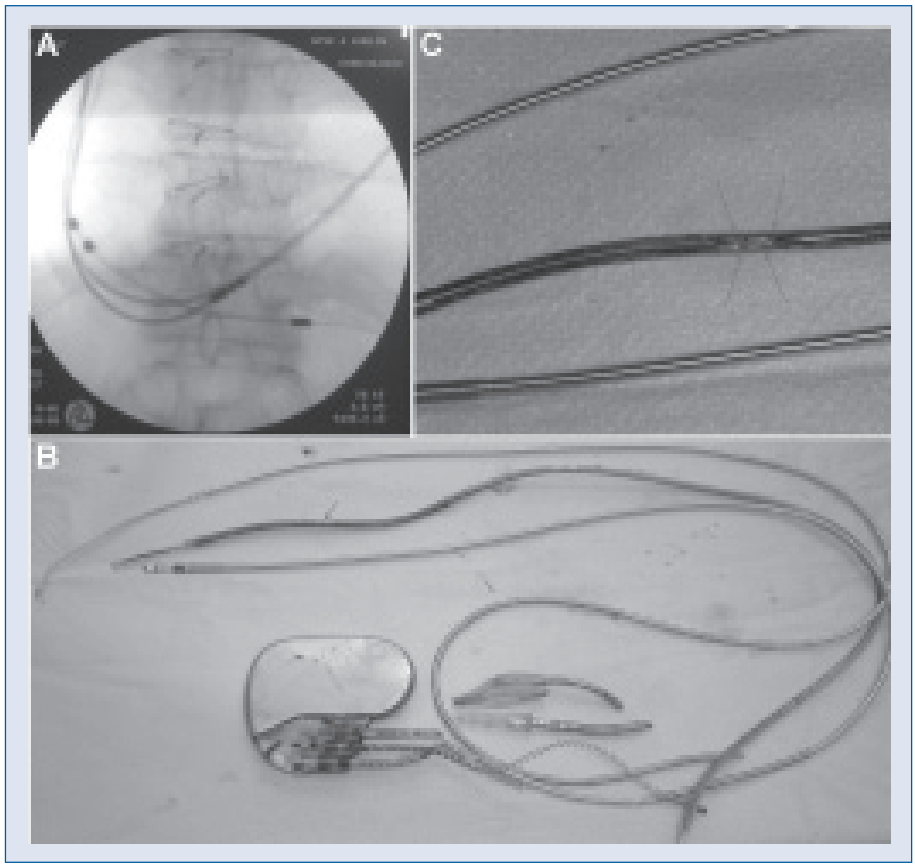

Figure 1. A. Fluoroscopy before the stimulation system removal. The contact place of leads in the right atrium is in the circle. There are two leads visible: the 11 year old VDD lead (Biotronik SL 60/13 BP), a two year old lead, active fixation in the coronary sinus outlet track (Biotronik Selox BP), and two year old left-ventricle lead (Biotronik Corox UP); **B, C.** Perioperative picture of removed endocardial leads. The arrows show the site of abrasion of a silicone insulation of the 11 year old lead with a typical thinning of the insulation close to tearing and discoloration of the metal wire inside the lead.

2. Localized infection of the PM/ICD pocket via the electrodes and vessels and the formation of vegetations as a result of the activation of the immune and coagulation system by bacterial colonies.

The new phenomenon i.e. endocardial lead abrasion, published recently by our group is complementary both to the first and second concept of vegetation formation and accounts for the failure of antibiotic therapy in LDIE without prior removal of old and abraded electrodes [13]. We describe two cases of LDIE which display the complexity of the disease, its probable etiology and results after complete removal of all endocardial leads.

Case 1

A 72 year old man has been suffering from recurrent fever of three months' duration despite repeated antibiotic therapy combined with periods of hospitalization. Initially, lab tests revealed only C-reactive protein (CRP) level to be elevated, and transesophageal echocardiography (TEE) suspected vegetations being associated with right atrium leads. Only the *Staphylococcus epidermidis,* confirmed by blood culture tests, and pulmonary embolism, confirmed in computed tomography, determined us to remove the leads. The patient's stimulation system consisted of one atrio-ventricular (AV) lead and two additional leads. The AV lead was implanted 11 years previously due to the AV block — a complication after aortic artificial valve implantation, whereas two additional leads were installed nine years later, during planned pacemaker exchange with coexisting indications for resynchronization stimulation. Both new leads, the atrial and the left-ventricle one, were placed in the coronary sinus (Fig. 1A). After the removal of the stimulation system, we discovered the endocardial abrasion of silicone insulation of the 11 year-old AV lead

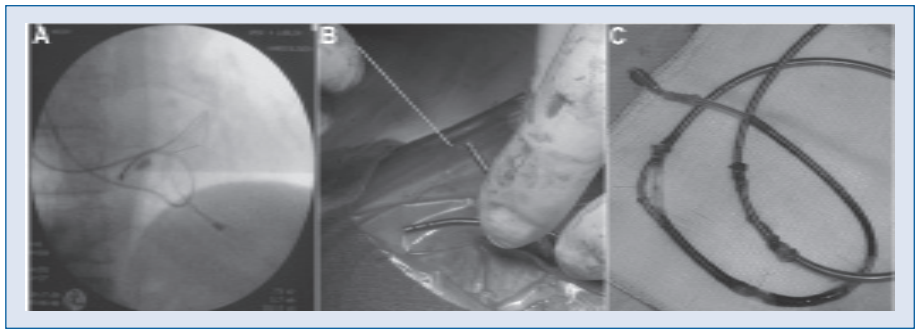

Figure 2. A. Fluoroscopy before the stimulation system removal: the atrial lead, Biotronik YP BP active, implanted to the coronary sinus outflow track and the ventricular lead, Biotronik Synox BP, implanted to the right ventricle apex. Arrows show the mutual dynamic contact of leads' loops resulting from the leads being too long; **B, C.** Perioperative pictures; **B** — pus outflow from the atrial lead, **C** — multiple abrasions of a silicone insulation of the atrial lead, Biotronik YP BP, with exposition of the metal wire and its discoloration.

at the contact place with other leads on the right atrium level (Fig. 1B, C). After recovery from LDIE, a new pacing system was implanted from the access on another side of the thorax.

Case 2

In a 65-year old man with a seven year-old AV two-lead pacing system, we decided to remove the system despite the negative blood culture tests and no changes in the stimulation pocket. Diagnosis of LDIE was based on a recurrent fever of six months' duration and on the presence of 1cm vegetations in the right atrium and right ventricle, both being in connection with the leads. The X-ray scan of the thorax, apart from the limited concentration of pulmonary tissue in the upper and middle lobe, revealed the leads being too long in the heart and the lead loop in the right ventricle (Fig. 2A). Such a situation is caused by the lack of efficient fixation of leads in the stimulation pocket during the procedure of stimulation system implantation. On attempting to insert the fixing stylet into the leads, pus came out of the atrial lead. The pus contained *Staphylococcus aureus* which was proved in later examination (Fig. 2B). The removed atrial lead revealed endocardial abrasions of its silicone insulation in several sites. Abrasion sites were connected with mutual contact places of looped leads, seen before in fluoroscopy (Fig. 2A, arrows). The removal of the stimulation system resulted in the subsidence of the recurrent fever.

The risk factors of an infection associated with PM/ICD systems include fever 24 hours before implantation, temporary stimulation prior to permanent, repeat procedure i.e. exchange/revision of the device, early repair, and lastly the lack of antibiotic prophylaxis before device implantation [9].

Despite the widely-accepted hypotheses of PM/ICD pocket infections, including the most dangerous LDIE, the presence of the pacemaker/cardioverter system together with endocardial leads is not considered as an indication for antibiotic prophylaxis when a high risk procedure is performed [14].

Symptoms of LDIE

The classical symptoms of LDIE are [10–12, 15]:

— local PM/ICD pocket infection (with varying percentage of occurrence);
— pulmonary symptoms: cough and pain in the thoracic cavity, pleural in character, dyspnoea, symptoms of pneumonia, atypical X-ray changes in the lungs suggesting pulmonary embolism caused by infected vegetations (26–41%);
— severe systemic inflammation: persistent fever (80%), shivers (75%), weakness, fatigue (75%), anorexia (36%), excessive perspiration (32%), pale, 'café au lait', sallow complexion (late stage);
— lab test signs of LDIE such as: positive blood cultures (80%), anemia (66%), leukocytosis (59%), high erythrocyte sedimentation rate, CRP (59%), erythrocyturia and albuminuria are unspecific signs of the disease. These symptoms are presented in Table 1.

This particular disease lacks the typical symptoms of minor Duke criteria, i.e. the symptoms of embolism in systemic circulation caused by left heart vegetations. Vegetations and emboli are still present in the pulmonary circulation, however. Due to the instability of many symptoms, this disease is

Table 1. Symptoms of lead-dependend infective endocarditis.

Year	Author	No. of patients	Pocket infection	Fever	Results of blood culture tests
2008	Sohail MR, Mayo Clinic [10]	44	80%	80%	Positive blood culture 77% Staphylococcus coagulation negative 41% Aureus 41%
2008	Greenspon AJ, Philadelphia [11]	51	22%	51%	Positive blood culture 92% Staphylococcus coagulation negative 22% Aureus 53%
2007	Massoure P-L, Bordeaux FR [12]	60	35%	78%	Positive blood culture 68% Staphylococcus epidermidis 68% Aureus 17%

usually diagnosed at a late stage, or remains unrecognized until the patient's death.

Patients with LDIE are often referred for pulmonary, internal or even oncological diagnostics because of atypical X-ray changes. Such changes may temporarily subside after antibiotic therapy, but almost invariably recur. Echocardiographic disappearance of vegetations is not synonymous with recovery if the leads are still in the heart chambers. This results in a totally different clinical picture, but the key point of the diagnostic procedure should be special attention to the cardiac implant (endocardial leads) in the right heart. The association between right heart vegetations and the endocardial leads is the basis for the diagnosis of this disease. Our experience shows that the individual course of LDIE varies. We have established a registry of about 300 patients who underwent percutaneous removal of the leads. Our observations revealed LDIE in almost 20% of patients qualified for endocardial lead removal [16]. A preliminary review of the registry was published in 2009 [17].

Treatment of LDIE

We believe that patients with PM/ICDs suspected of LDIE should be hospitalized in an electrotherapy center. The patient's blood culture tests as well as tests of the skin, nose, pharynx or from the incompletely healed wound or a fistula to the PM/ICD pocket, should be made. At the time of the PM/ICD system removal, blood culture samples should also be taken from the PM/ICD pocket incision site and from every removed lead. A febrile patient should be given antibiotics according to the results of blood culture tests, and vancomycin in the case of a negative test.

It should be underlined that echocardiography, including TEE, must be a basic diagnostic procedure. The course of treatment in a case of LDIE can be monitored using this particular diagnostic method.

In patients with pulmonary embolism caused by vegetations migrated from the right heart chambers, lung scintigraphy and computed tomography are valuable imaging tools. Unfortunately, the presence of leads in the right heart chambers is not considered as a risk factor of pulmonary embolism or an indication for antithrombolitic prophylaxis [18, 19].

After confirming the diagnosis, an initial decision to remove the whole system as well as the choice of technique (percutaneous or surgical) should be made. There should be no doubts whether to remove the system or adopt a 'conservative' approach. LDIE has already been a class 1 indication for removal of the whole lead and PM/ICD system for nine years [20, 21]. Mortality in cases of LDIE treated only with antibiotics is 66% compared to a three times lower percentage in cases of therapy combining antibiotics and the complete removal of the cardiac implant [6, 7].

The procedure of percutaneous lead removal carries a risk of 1–2%. Cardio-pulmonary bypass surgery carries a 10% risk of perioperative mortality, and it is a much more serious strain for the patient [22].

It should be emphasized that nowadays there are only four indications for cardiac surgery:

— the need for heart valve repair;
— 'giant vegetation' in the chambers of the right heart (vegetation of 2.5 cm on echocardiography);
— failure of percutaneous removal;
— complications after percutaneous removal.

An additional advantage of cardiac surgery under the above circumstances is the chance to implant the epicardial leads, whereas placing endocardial leads in the setting of persistent bacteremia or residual infected vegetation may be problematic and

may need to be delayed substantially. In pacemaker-dependent patients, in case of percutaneous removals, only temporary stimulation can be used, until the end of antibiotic therapy course and recovery from endocarditis.

A cardiac surgeon with special training and experience in lead extraction procedures, together with an anesthesiologist, comprise a team to secure percutaneous lead removal and to intervene immediately if complications occur.

A higher safety level of percutaneous PM/ICD system removal compared with cardiac surgery has resulted in expanding the indications for percutaneous procedures.

Conclusions

1. LDIE of the right heart in PM/ICD patients often goes undiagnosed.
2. Every PM/ICD patient with pulmonary symptoms should be screened for right heart LDIE and pulmonary embolism.
3. PM/ICD patients with known LDIE of the right heart should be given antibiotics and undergo removal of the stimulation system.
4. Percutaneous removal of the stimulation system is a safer and less invasive therapeutic approach than cardiac surgery.

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