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Infection of Cardiac Implantable Electronic Devices: A Moroccan Single-Center Experience

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Abstract **Original Research Article**

Background: Increasing of Cardiac implantable electronic devices (CIEDs) have induced several complications such as infections. Our aim was to investigate the frequency of CIED infection, analyze the microbiological status and determinate contributing factors in order to prevent it. ***Patients and methods****:* We conducted a retrospective and descriptive study of patients who underwent implantation of electronic cardiac device in cardiology B department from January 2011 to June 2019. A total of 23 cases of CIED infection were identified. For each patient, all data were recorded about initial implantation of device and about CIED infection. ***Results:*** Frequency of CIED infection in our study is 1.2%. According to British guidelines, isolated local infection (uncomplicated PI) is observed in 8 patients (34.7%), local infection associated with sepsis (complicated PI) is found in 8 cases (34.7%) and 5 patients (21.7%) presented with systemic signs (ICED-LE and ICED-IE). Infection involve 17 patients with primary implantation and 6 patients after generator replacement.78% of patients, male and 56% are young and (≤60 years) and 39% are diabetics series is characterized by largest number of patients (78%) who consult for local signs. Biological assessment and blood cultures didn't help to differentiate between local et systemic forms because blood tests were often negative. We noticed an increased negativity of bacteriological examinations. ***Conclusion:*** ICED-related infection affects, mainly, young male patients and frequently diabetics. These patients usually have been surgically revised for postoperative complications or underwent temporary wire before implantation. Often, it is systemic form induced by pocket infection. Biological and bacteriological tests are always negative. When the causative germ is isolated, it is often staphylococcus. Thus, implantation of CIED in these patients must be carefully performed especially in diabetics. Surgical revisions have to be avoided as much as possible.

Keywords: Cardiac implantable electronic device, Pocket infection, Risk factors, Percutaneous lead extraction.

INTRODUCTION

Cardiac implantable electronic devices (CIEDs) are used to treat cardiac arrhythmias since they can regulate myocardial contractions. Recently, the indications for using CIEDs have been expanded. As a result, we have noted a significant increase in survival and an improvement in the quality of life of appropriate patients [1]. However, the increase in the rate of implantations of CIEDs has resulted in an increase in the number of complications, such as infections [2]. Such infections are severe with high rates of mortality [3]. They are difficult to manage because they often involve elderly patients with comorbidities, which contribute to a poor prognosis. Moreover, differences between local infections and systemic device infections can make diagnosis and therapeutic strategies more difficult.

The aims of this study are: (1) to assess the prevalence of these infections in our center, (2) to define the bacteriological profile so that we can increase the effectiveness of antibiotic prophylaxis used preoperatively, and (3) to identify the risk factors so that we can reduce the incidence of infection.

METHODS

Study Population and Period

We conducted a retrospective descriptive study of patients who underwent implantation of electronic cardiac device in cardiology B department from January 2011 to June 2019.

A total of 23 cases of CIED infection were identified in the study period. Thirteen (13) patients had their devices implanted at our center and ten (10)

patients had their devices implanted outside hospital. There are no exclusion criteria for screening of patients.

Definitions

According to British guidelines for diagnosis, prevention and management of ICED infection established by A. T. Sandoe *et al*., [4], our patients were categorized into four groups:

- Early post-implantation inflammation
- Generator pocket infection (uncomplicated and complicated)
- ICED lead infection (ICED-LE)
- ICED-associated native or prosthetic valve endocarditis (ICED-IE)

Data Sources

We collected patients' data from medical records by following two steps:

- Data about initial implantation of device (date, type, first implantation or revision, indication of implantation, duration, complexity, procedural antibiotic use, postoperative complication). We don't know this information about six (6) patients operated outside the center.
- Data about CIED infection:
  - Demographic data (age, gender and origin)
  - Clinical data (co-morbidities, time of onset of infection compared to procedure, local or systemic symptoms)
  - Laboratory and microbiological data (blood cultures, device site cultures, complete blood count and inflammatory biomarkers tests)
  - Echocardiographic data (vegetation, localized thickening)
  - Treatment (intravenous antibiotic therapy, device extraction, reimplantation, surgery)

STATISTICAL ANALYSIS

The aggregated data was filled in an Excel sheet, then we conduct a statistical analysis upon it. We transformed all variables about patients' data into tables and figures.

Quantitative variables are expressed in frequency (%) and qualitative variables are expressed in means and standard deviation and/or medians with inter-quartile ranges. We used two software in statistical study: "EPI Info version 3.6" and "SPSS version 13.0".

RESULTS

Patient Characteristics

The average age is 54.8 years ± 18.6. As shown in Figure-1, 56% of patients are young (under the age of 60). Moreover, the most affected age segment is 20-49 years. The sex ratio is 3.6 (78.2% men and 21.8% women). Nine patients are hypertensive and nine are diabetic. Two patients have valvular prosthesis and under anticoagulant therapy.

Procedure Prior to Infection

In our series, infection involves 21 pacemaker-implanted patients (PM) and 2 patients with implanted cardiac resynchronization therapy devices (CRT-D). 14 patients have a dual-chamber pacemaker while 7 patients are implanted with a single-chamber one. Implantation of pacemaker was indicated for high-degree atrioventricular block in 22 patients and for bradyatrial fibrillation in a single patient. It is a primary implantation in 15 patients, and it is a generator replacement for 6 patients.

Regarding CRT-D, it was indicated for a rhythmic dilated cardiomyopathy in one patient and *idiopathic dilated cardiomyopathy* in the other patient.

Conditions of the intervention before the occurrence of the infection were studied in patients operated in our formation (there are 13). We know initial circumstances of 4 patients whom operated outside our hospital. However, we ignore it for 6 patients.

The Infection

Incidence of Infection

In the study period, incidence of infection in patients operated in our department is 1.2%. This incidence doesn't include patients operated elsewhere.

Type of infection and clinical finding:

Isolated local infection (uncomplicated PI) was observed in 8 patients (34.7%), local infection associated with sepsis (complicated PI) was found in 8 cases (34.7%) and only 5 patients (21.7%) presented systemic signs (ICED-LE and ICED-IE).

Clinical Data

Fever was present in 6 patients, and shivers in 5patients. A poor state of health was reported by 4 patients. Two patients reported dyspnea and 3 had lipothymia.

Local signs of infection; 12 patients presented with purulent discharge, 3 patients with non-purulent serositis and skin erosion with risk of externalization in 15 patients. Skin erythema was present in 6 patients.

Symptoms Onset Delay

Patients who presented the infection after a first implantation of pacemaker (or CRT-P) are 17. The average time of onset of symptoms is 381.8 days ± 249.1. Patients who presented the infection after surgical revision are six. Within 4 patients, generator replacement was the only procedure that preceded the appearance of signs of infection. One patient underwent implantation of a new lead because of the fracture of the

ventricular simultaneously with generator replacement. Consequently, the infectious symptoms appeared 91 days after this procedure. The other 3 patient's manifest symptoms within 602 days on average after generator replacement.

After generator change, two patients were revised for lead dysfunction. The delay of symptoms onset is 19 days and 188 days respectively after resumption.

Biological Assessment

Inflammatory biomarkers test (C-reactive protein (CRP), white blood count (WBC), erythrocyte sedimentation rate (VS), procalcitonin serum levels (PCT) had returned positive for only 6 patients (26%). Skin swab of wound is negative in all patients. Cytobacteriological examination of pus is positive in 4 patients (17.4%). The germs found are staphylococcus in 2 patients, seratia Marcecens in 1 patient and Streptococcus sobrii in 1 patient. Cytobacteriological examination of the material is positive in 7 patients. The germs found are staphylococcus (4patients), pseudonomonas (2) and seratia mascecens (1). Blood cultures is positive in 9 patients: it is a staphylococcus (6patients), hemophilusparainflenza and inflenza (1), enterobactercloacae (1) and serratialiquefaciens (1). Figure-2 shows bacteriogical data of blood culture, microbiological *analysis of pus* and lead-tip culture.

Echocardiography Data

Vegetation is found in 10 patients. It is localized on the atrial lead in 4 patients and on the ventricular lead in 6 patients. Its average size is 12mm ranging from 5mm to 30mm. Local *thickening* of the *lead* of pacemaker is found in 5 patients, it is located on the atrial lead in 2patients and ventricular lead in 3patients.

Therapeutic Approach

Administration of antibiotic therapy began one day before the device extraction. We administered vancomycin with gentamycin within 11 patients, targocid with genta in 2patients and ceftriaxone with gentamycin in 9patients because of the unavailability of vancomycin. The average duration of antibiotic treatment is from 4 to 6 weeks. One patient underwent local revision without extraction. Percutaneous lead removal and reimplantation on the contralateral side has been considered in 12 patients. Reimplantation was considered with an average delay of 18.1 days compared to the date of removal. Three patients underwent extraction without reimplantation. Seven patients underwent open surgery removal that was indicated for difficulties of removal in two patients, large lead-associated vegetation in 3 patients and total externalization in 2patients.

Evolution

We noticed a good evolution, with no reappearance of infection in 21 patients. Two patients have been re-infected; one underwent removal of the device with surgical reimplantation and the other underwent extraction without reimplantation because he remained asymptomatic. No death reported in our series.

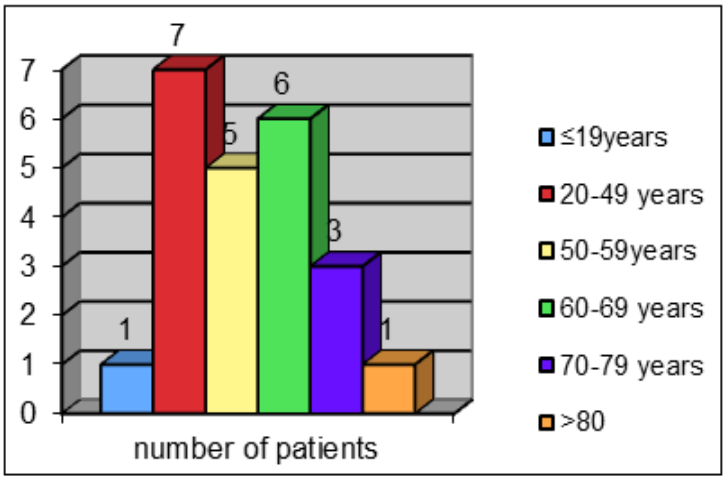

Fig-1: Different age groups of series

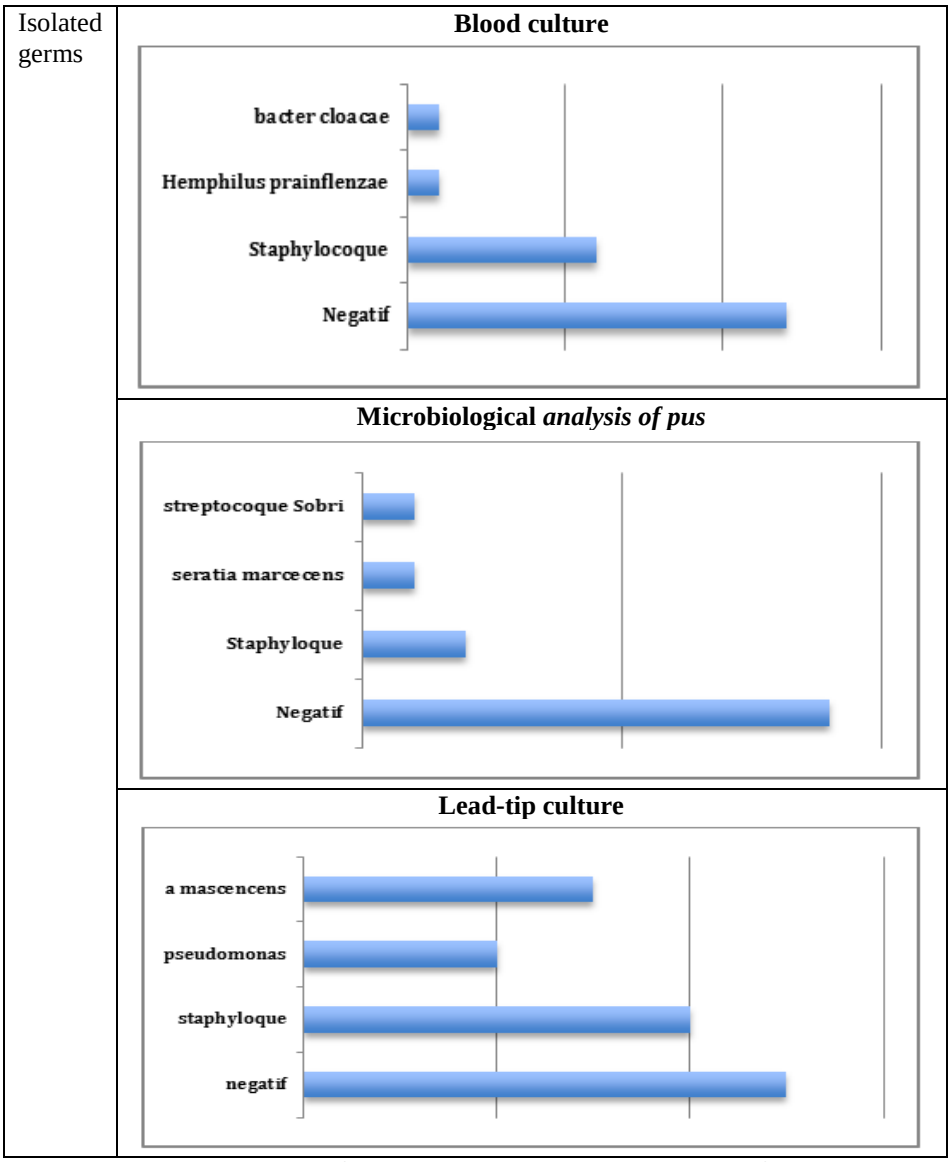

Fig-2: Bacteriogical data from blood culture, Microbiological *analysis of pus* and

Table-1: Clinical sign of sepsis, laboratory findings and echocardiographic data depending of types of infection: +: present,-: absent

Types of infection	Nb of patients (%)	Fever	chills	GB	CRP	Blood culture	vegetation	Lead culture
Uncomplicated pocket infection	8	1 patient	1patient	-	-	-	-	+ in 2 patients
Complicated lead pocket infection (10patients)	4(40%)	-	-	-	-	-	+	+ in 3patients
	3 (20%)	-	-	-	-	+	+	+ in 1 patients
	2 (20%)	+in 1patient	+ in 1patient	+	+	+	_	+
	1 (20%)	+ in 1patient	-	+	+	-	+	+
ICED-LI	1	+	+	+	+	+	+	+
ICED-IE	1	+	+	+	+	+	+	+

Table-2: Risk factors found in our series

Risk Factor of infection		Number of patients (%)
Host related Risk factor	Male sexe	18 (78%)
	Age<60	13 (56.5%)
	Diabetes mellitus	9 (39.1%)
	Anticoagulation	2 (8.69%)
Procedure related risk factor	Need of reintervention (for lead dysfunction, post-operative haematoma.)	8 (34.6%)
	Use of temporary pacemaker prior to implantation	6 (26%)
	Prolonged time of procedure(complexity)	3 (11%)

DISCUSSION

Incidence

The frequency of device-related infections in our center is 1.2%. Similar results were reported by Olsen *et al.*, (1.19%) based on data from a Danish register of CIEDs [5]. In Japan, a survey of 129 institutes led by Nakajima *et al.*, [6] found an incidence rate as low as ours (1.12%). However, other studies have reported much higher infection rates, ranging from 1.9% [7] to 2.4% [8]. The low rate of infection in our center is due to systematic antibiotic prophylaxis prior to undertaking the procedure, local expertise, and fewer implanted CRTs.

Risk Factor of Infection

In our data, 78% of the patients infected were male. Male predominance has been noted in several studies. This is probably due to gender differences in bacterial skin colonization [9]. A younger age has also been associated with CIED infection [10, 11, 5], but the reasons remain unclear [5]. Conversely, the infection rate has been correlated with older ages in some studies [12, 13]. Diabetes mellitus is known to be a risk factor for infection. In our data, 39.1% of the patients infected were diabetic. Similarly, Deniz *et al.*, [13] found that 25.5% of patients infected were diabetic. This higher rate of infections for diabetics is due to several mechanisms that disrupt and delay wound healing [14, 13]. Olsen *et al.*, [5] demonstrated that postoperative procedures relating to the device (such as fixing a lead dysfunction or draining a postoperative hematoma), except for changing the generator, contribute to an increased infection rate and can shorten the delay in the onset of symptoms. In fact, some patients quickly become infected after such postoperative procedures.

Six of our patients had a temporary wire fitted before implantation of their pacemaker. The rates of infections following the insertion of a temporary pacemaker range from 2% to 18% [15], which is probably related to bacteremia and occult sepsis induced by the external leads. In a prospective multi-center survey, we found that when a temporary wire was used, the odds ratio of infection was 2.46 (95% CI 1.09–5.13) [16].

Local infections are more frequent

In our data, most patients (78%) had signs of a local infection. Such infections may be limited to the wound site (i.e., an uncomplicated pocket infection) or be accompanied by systemic signs (i.e., a complicated pocket infection). Similarly, Marwan Refaat *et al.*, [17] found that 59.1% of patients presented signs of generator pocket infection. Souhail *et al.*, found that 69% of patients had such symptoms [18].

Table-1 shows that for four patients, a biological assessment and blood culture did not help in the diagnosis of complicated forms of infection, which were revealed only by the presence of vegetation. According to Golzio *et al.*, [19], vegetation is frequently observed in patients with only local symptoms. These authors concluded that transesophageal echocardiography should be mandatory for patients with local signs, even if there has been a negative biological assessment. In fact, infections often involve the whole stimulation system and are not limited to the generator pocket [19]. Therefore, looking for vegetation is justified even when a patient has signs of only local infection.

Inflammatory Biomarkers in Local Forms

Inflammatory biomarkers have a low sensitivity in detecting cardiac device infection [18]. Contrary to what Lennerz *et al.*, [20] found, CRP and procalcitonin did not help in diagnosis, particularly for complicated pocket infections. Therefore, in our opinion, testing for inflammatory biomarkers should not initially be considered for local cases of infection.

Negative Bacteriological Results

Another characteristic of our data is the number of bacteriological examinations with negative results of infection. Given the reasonable distance between the bacteriology laboratory and our center, the longer delivery times for samples may contribute to germs not being isolated. Preparing cultures with samples from the lead tip culture is the most sensitive form of bacteriological examination. Similarly, based on the available data on causative agents [20, 21], staphylococci remain the most isolated forms of bacteria.

Management

Patients with uncomplicated PI underwent local surgical revision and targeted antibiotic therapy. If signs of infection persisted, we often extracted the device. A systemic infection requires an immediate percutaneous extraction of the lead. Nevertheless, in the absence of any technical protection of the pulmonary bed, surgical extraction should be considered for a large vegetation.

Reimplantation is recommended if the necessity of CIED implantation is confirmed. According to the guidelines, reimplantation must be delayed to reduce the risk of reinfection [4, 22]. In our clinical practice, even with local forms of infection, reimplantation is delayed until all clinical and bacteriological signs of infection have resolved.

CONCLUSION

In our context, ICED-related infection affects, mainly, young male patients and frequently diabetics. These patients usually have been surgically revised for postoperative complications or underwent temporary wire before implantation of cardiac device. Often, it is systemic forms induced by pocket infection. Biological et bacteriological tests are always negative. When the causative germ is isolated, it is often a staphylococcus. Thus, implantation of CIED in these patients must be carefully performed especially in diabetics. Surgical revisions have to be avoided as much as possible.

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