Late Electrode Sepsis: Clinical Features, Diagnostics and Management. Clinical Cases

Vera Yu. Zimina, Gevorg R. Airapetian, Yuri N. Grishkin, Sergey A. Sayganov

1 North-Western State Medical University named after I.I. Mechnikov, Saint Petersburg, Russia;
2 Pokrovskaya Hospital of Saint Petersburg, Russia

In clinical practice diagnostics and treatment of infection of cardiac implantable electronic devices (CIEDs) is connected with significant difficulties, because distinctive features of electrode sepsis are extremely low information content of Duke criteria, disease propensity for a long flow in various clinical forms as well as in the form of a septic syndrome. An important practical issue in management of patients with CIEDs remains working out of effective strategies to prevent occurrence of late electrode sepsis (arising in a year or more after implantation of the device). The article describes two cases of typical course of late recurrent infection of the CIEDs.

Keywords: infective endocarditis; electrode sepsis; infection of cardiac implantable electronic devices.

To cite this article: Zimina VYu, Airapetian GR, Grishkin YN, Sayganov SA. Late electrode sepsis: clinical features, diagnostics and management. Clinical cases. Cardiac Arrhythmias. 2021;1(1):25–32. DOI: https://doi.org/10.17816/cardar71367
Поздний электродный сепсис: особенности клинического течения, диагностики и ведения. Клинические случаи

В.Ю. Зимина1, Г.Р. Айрапетян2, Ю.Н. Гришкин1, С.А. Сайганов1

1 Северо-Западный государственный медицинский университет им. И.И. Мечникова, Санкт-Петербург, Россия;
2 Городская Покровская больница, Санкт-Петербург, Россия

Диагностика и лечение пациентов с инфекцией имплантированных в сердце устройств в клинической практике сопряжены с существенными трудностями, поскольку отличительными особенностями электродного сепсиса считаются крайне низкая информативность критериев Duke, склонность заболевания длительно протекать в виде ряда клинических масок, в том числе септического синдрома. Важным практическим аспектом ведения пациентов с имплантированными в сердце устройствами остается выработка эффективной стратегии профилактики позднего электродного сепсиса (возникающего через год и более после имплантации устройства). В статье приведено описание двух случаев типичного течения позднего рецидивирующего одонтогенного инфекционного эндокардита имплантированного в сердце устройства.

Ключевые слова: инфекционный эндокардит; электродный сепсис; инфекция имплантированных в сердце устройств.

Как цитировать: Зимина В.Ю., Айрапетян Г.Р., Гришкин Ю.Н., Сайганов С.А. Поздний электродный сепсис: особенности клинического течения, диагностики и ведения. Клинические случаи // Cardiac Arrhythmias. 2021. Т. 1, № 1. С. 25–32. DOI: https://doi.org/10.17816/cardar71367
INTRODUCTION

Modern cardiology is impossible without implantation of intracardiac devices, such as cardiac pacemakers, resynchronization therapy devices, implantable cardioverter-defibrillators. Meanwhile, as the number of implanted devices increases, so does the number of cases of their infection [1]. At present, sufficient clinical material has been accumulated, demonstrating the obvious features of the course of this type of IE, leading to late diagnosis, the spread of infection to the tricuspid valve and, as a result, to a poor prognosis. The frequency of purulent complications after implantation of pacemakers is from 0.6 to 5.7%; mortality rate varies from 0.13% in local purulent inflammation to 19.9% in bacterial endocarditis and sepsis [2].

Abroad, term electrode sepsis is widely used to reflect the main features of the course of cardiac implantable electronic device infection, which are the predominance of systemic inflammation symptoms and the long-term absence of heart damage signs.

We present two typical cases of the course of cardiac implantable electronic device infection, illustrating the difficulties of diagnosing and treating this disease.

CLINICAL CASE 1

Patient A., 27 years old. At the age of 15, he was implanted with a two-chamber pacemaker for congenital (as it was regarded at that time) subtotal AV block. Seven years later, the pacemaker power supply was replaced due to exhausted battery. Five years later, in September 2018, the patient developed night sweats and rises in body temperature to 40–41°C. He denied invasive interventions, diseases or other conditions that could be accompanied by bacteremia over the past 6 months.

The patient was examined in a hospital (from September 27, 2018 to October 11, 2018) and the diagnosis of community-acquired left-sided lower-lobe pneumonia was established based on lung X-ray data. Lung Multispiral CT was not performed. Blood tests showed leukocytosis, left shift, 10-fold increase in CRP, Staphylococcus Haemolyticus was found in blood cultures. According to transthoracicECHO-KG, no pathology was revealed. The patient underwent a 12-day course of ceftriaxone and leflobact with positive dynamics of clinical, instrumental and laboratory data: during the week before discharge, there was no fever, pneumatization of the lungs according to the control radiographs recovered completely, the level of leukocytes and CRP returned to normal. Control blood cultures were not performed. However, just one week after discharge, the patient was re-hospitalized due to recurrence of fever. Again, leukocytosis and left shift were observed, procalcitonin exceeded normal values by 150 times. This time Staphylococcus Aureus was found in blood cultures (October 19, 2018). On the fourth day of hospitalization with echocardiography, vegetation was first detected on one of the pacemaker electrodes. Based on the data obtained, acute IE associated with the implanted pacemaker was diagnosed. The total duration of antibiotic therapy was 25 days. Unfortunately, there was no detailed information on the antibiotics used in the discharge reports.

In order to find out the primary source of infection, the patient was examined by a dentist. An orthopantomogram (OPTG) revealed multiple granulomas of the upper and lower jaws. There were signs of periodontitis on teeth 15, 13, 12, 11, 21, 22, 23, 26, 27, 37, 35, 46; signs of chronic pulpitis 24, 25, 35, 34, 33, 43, 44 (Fig. 1). It turned out that the...
patient himself did not attach much importance to the state of the oral cavity and had not visited the dentist in recent years. Considering the large extent of the lesion, a phased debridement of the oral cavity was started. By the time of discharge (November 13, 2018), there were no symptoms, the CBT and procalcitonin values returned to normal. The control culture showed the absence of microflora growth, with the control TTE there were no reliable vegetations in the area of the electrodes. Indications for surgical treatment of IE have not been formulated.

A month after discharge, fever recurred, and this time, in addition to the symptoms already listed earlier, there was hyperemia and soreness in the area of the pacemaker bed. In early December 2018, the patient was hospitalized with a diagnosis of “pacemaker bed abscess”. In control TTE and TEE, no reliable vegetation was found in the projection of electrodes, valves, and free endocardium. There was only uneven compaction and thickening of some areas of the electrode (Fig. 2). Staphylococcus Aureus was re-isolated in blood cultures. The therapy was carried out with vancomycin (1 g) with gentamicin (80 mg) for 25 days. After sanitation of the abscess and with antibiotic therapy, regression of all symptoms was again noted, with complete normalization of blood counts.

Diagnosis at discharge (December 28, 2018): Subacute infectious odontogenic endocarditis with the formation of a pacemaker bed abscess.

Sanitation of the oral cavity was accompanied by standard antibiotic therapy: on the day of the dental intervention, the patient received a single oral dose of 2 g of amoxicillin orally, or 600 mg of clindamycin. In addition, intravenous gentamicin courses were repeated due to recurrent fever. Each course was accompanied by a rapid normalization of the clinical condition, normalization of temperature and laboratory parameters. In repeated cultures of blood, there was no growth, reliable vegetation on the electrodes was absent. The surgical stage of treatment for this patient was postponed until the complete sanitation of the oral cavity. Moreover, the opinions of the doctors involved regarding the need for surgical treatment were by no means unambiguous. Sanitation, including the phased removal of the infected teeth, took a considerable amount of time.

By April 2019, the patient’s condition deteriorated rapidly: weight loss (~8 kg), febrile rises in temperature, enlargement of the liver and spleen, severe weakness, a tendency to arterial hypotension (90–80/60–55 mm Hg), severe anemia, lungs X-ray showed pneumonic infiltration again. Blood tests revealed an increase in anemia, thrombocytosis, leukocytosis, and an increase in ESR by 4.2 times. The growth of Staphylococcus epidermidis was noted in blood cultures. ECG revealed large loose vegetation on the electrodes in the immediate vicinity of the MC (Fig. 3), however, there were no reliable signs of the involvement of MCs in the infectious process.

It was during this hospitalization, with the background of massive antibiotic therapy, that the oral cavity sanitation was urgently completed, and on May 07, 2019, 7.5 months after the onset of the disease, during an open surgical intervention, the system of constant electrocardiostimulation was completely removed and the heart chambers were sanitized while extracorporeal circulation and cold cardioplegia. On both electrodes, multiple vegetations were found, both ordinary — large formations on the “stem” fixed to the electrodes, and vegetation of the “sleeve” type (Fig. 4). During the surgical revision, vegetation was revealed on the anterior cusp of the TV, which necessitated partial resection and suture plasty of the anterior cusp of the TV. Fortunately, there were no indications for pacemaker reimplantation, since in the preoperative period it turned out that the patient was predominantly in sinus rhythm, there were no signs of AV block (both subtotal and complete). The early postoperative period was complicated by two episodes of ventricular tachycardia on the 2nd and 4th days after surgery.

Fig. 3. Echocardiogram of patient A., 04.2019 A — Four-chambered apical section; B — Three-chambered subcostal modified section. The arrows indicate a large loose vegetation located on the electrode near the TV structures.

Fig. 4. Postoperative photography: fragments of removed electrodes. There are two types of vegetation fixed on electrodes: classic giant vegetation, reaching a length of 5.5 cm (green arrow); vegetation, braiding the electrode like a “sleeve” or “stocking” (blue arrow).
CLINICAL CASE 2

Patient B., 64 years old. Suffers from diabetes mellitus. In 2015, a complete AV block developed, complicated by Morgagni-Adams-Stokes attacks, which is why a two-chamber pacemaker was implanted. There were no other invasive interventions, injuries, or infectious diseases. Since the fall of 2017, the patient periodically (once a week) experienced attacks of chills and pronounced “night” sweating, as well as a decrease in body weight. Since December 2018, unexplained sudden rises in temperature up to 38.5°C have appeared. According to the patient, the local therapist diagnosed angina and prescribed a course of antibiotic therapy with a positive effect. Over the next two months, the state of health remained satisfactory.

In March 2019, fever and night sweats resumed, and therefore the patient was hospitalized with a diagnosis of ARVI, acute bronchitis. In laboratory data, leukocytosis, a twofold increase in ESR, and a 12-fold excess of CRP were noted. Blood cultures were not performed. Lung x-ray showed no pathology. Within 17 days the patient received the following treatment: ceftriaxone 2 g, levofloxacin 500 mg, metronidazole 500 mg. By the time of discharge, the clinical condition and laboratory readings had returned to normal. For the next 4 months after the discharge, the patient felt well. However, in mid-July 2019, fever and bouts of night sweats resumed. By the beginning of August 2019, shortness of breath again joined the general symptoms of inflammation, and therefore the patient was again hospitalized. In laboratory tests, leukocytosis, a 55-fold increase in CRP, and mild anemia were present. Staphylococcus epidermidis was isolated from blood cultures. Orthopantomogram revealed signs of chronic periodontitis 26, 43, 47 teeth. Contrast multispiral CT of the lungs revealed embolic, destructive left-sided lower lobe pneumonia complicated by abscess, as well as multiple PE (segmental branches) on both sides. The finding with transthoracic echocardiography was initially regarded as a vegetation in the projection of the TV, although later, with TEE, classical vegetations on the atrial and ventricular pacemaker electrodes were reliably identified (Fig. 5), as well as local uneven thickening and echogenicity of the electrode fragments, regarded as 'sleeve' type vegetation (Fig. 6). There were no reliable signs of TV damage.

The duration of antibiotic therapy, including blood cultures and doxycycline 100 mg 2 r/day and ciprofloxacin 200 mg 2 r/day, was 6.5 weeks. With the antibiotic therapy, a rapid positive clinical dynamic was observed — manifestations of respiratory failure disappeared, temperature and laboratory changes returned to normal.

Nevertheless, even after a 6.5-week course of antibiotic therapy, according to EchoCG and TEE, vegetation on the intracardiac electrodes in the immediate vicinity of the TV valves was present. All ECGs showed P-dependent ventricular pacing. With the planned programming of the pacemaker, the patient’s dependence on the stimulator was confirmed.

On 10.10.2019, 11 months after the onset of the disease, the pacemaker endocardial system was extracted, and the
permanent pacemaker was reimplanted into the epicardial position under artificial circulation. Intraoperatively, the presence of massive vegetation of ‘sleeve’ type on the electrodes was confirmed (Fig. 7), and vegetation on the TV was also detected, which required its removal and plastic surgery of the TV according to De Vega.

In the postoperative period, the patient underwent a 2-week course of antibiotic therapy with vancomycin, 2 g/day. Over the next 6 months, the patient’s condition remained stable, there were no complaints, there were no markers of inflammation, and the body temperature did not rise.

CASE DISCUSSION

IE is known to often develop as a result of bacteremia, the cause of which can be identified by taking anamnesis: invasive procedures (dental, urological, gynecological) or obvious concomitant infectious diseases. Meanwhile, it is often overlooked that spontaneous activation of chronic foci of infection can become the cause of bacteremia. In particular, odontogenic foci are the most frequent sources of microflora that causes the development of infective endocarditis.

When studying the role of chronic focal infection of the oral cavity in the development of infective endocarditis, it was found that foci of stomatogenic infection were detected in 93.7% of cases [3], and in 70.9% these foci were chronic. These foci were recognized to be the immediate cause of the development of infective endocarditis in 22.2% of cases [4]. A study by S.N. Krutov (2010) revealed a direct correlation between the microbial DNA of the gingival sulcus and the DNA of the IE causative agent from vegetation [5].

An important aspect of the preoperative preparation of any cardiac surgery (including the implantation of intracardiac devices) is the sanitation of chronic foci of oral cavity infection at least 2 weeks before the intervention, which significantly reduces the risk of developing infectious complications in the postoperative period. This rule is strictly observed when performing major cardiac surgery such as implantation of valve prostheses or vascular grafts. Unfortunately, it seems that this rule is not always fulfilled regarding the implantation of endovascular and intracardiac devices.

For a long time, the main manifestation of the disease is septic syndrome, the course of which has changed and does not always correspond to previous ideas. In many cases, modern septic syndrome is characterized by a chronic or subacute course, under one or more masks, successively replacing each other, or stably combined with each other. Typical masks of IE APU are rheumatologic syndrome, local infection of the device bed, and respiratory syndrome. We shall consider each of these masks in sequence.

Rheumatological syndrome includes fever, night sweats, arthralgias, unexplained weight loss, polyserositis, moderate enlargement of the liver and spleen, and changes in urinary sediment.

In young people and middle-aged people, a febrile increase in temperature is typical, while in elderly and weak people, high fever is often absent, giving way to a prolonged subfebrile condition. A stable manifestation of septic syndrome in such patients can only be a change in daily body temperature by more than one degree. Abnormal temperature is usually accompanied by profuse night sweats. Over time, patients experience weight loss. When performing instrumental studies, manifestations of polyserositis in the form of minor hydrothorax and hydropericardium can be detected. The septic syndrome is also characterized by the addition of nephritis. In patients with multiple comorbidities, such findings are usually interpreted as manifestations of chronic pathology.

Local infection of the bed of the intracardiac device is often perceived as a local and potentially curable infection. This belief is supported by the fact that during therapy, usually all local symptoms undergo rapid regression, creating the illusion of recovery. Meanwhile, it should be noted that infection of the device pocket can only be called a local infection, since in the overwhelming majority of cases of local inflammation in the area of the device bed, the infection eventually spreads to the intracardiac electrodes. So, in the study by D. Klug et al. (2007) demonstrated that in patients with isolated infection of the stimulator bed and the absence of obvious manifestations of generalized infection, cultures from intravascular segments of the electrodes were positive in 72% of cases [6]. Thus, any infectious process in the area of extracardiac elements of the device is potentially a manifestation of CIED and should be the reason for the removal of the entire system (recommendation class I, level of evidence C).

Respiratory Syndrome. One of the earliest and most typical complications of electrode sepsis is infarction pneumonia, the manifestations of which vary widely: from asymptomatic to clinically severe pneumonia. The source of embolism is fresh vegetation formed on the electrodes, which are located in the right chambers of the heart. Since until recently the main method for diagnosing community-acquired pneumonia remained the x-ray of the chest, which is not sensitive enough to detect pneumonia infarction in comparison with multispiral CT of the lungs, the embolic nature of pneumonia for the time being remains unclear, and patients for some time are being treated against common community-acquired pneumonia or bronchitis. Unfortunately, multispiral CT in routine clinical practice is usually performed much later, with recurrent pneumonia. Meanwhile, the presence of CIED infection in a patient with suspected inflammatory lung disease is the basis for performing MSCT as a first-line method to exclude infarction pneumonia and stratification of the risk of IE.

Comprehensive consideration of all clinical masks of IE is a more sensitive approach than taking into account the Duke criteria, which are not very informative in relation to ES. The latter can proceed for a long time without the formation of classical vegetation — mobile, rather large formations on the electrodes, similar to those that occur with valvular
lesions. With CIED infection, a typical vegetation “braids” the electrode like a “sleeve” and looks atypical during EchoCG examination, in the form of extended seals on the electrode, falsely perceived as fibrous tissue on the electrode. In the early stages, classical vegetation is unstable and, probably, can come off and disappear, including against the background of ongoing therapy, which is often mistakenly interpreted as positive dynamics or even recovery. Massive, obvious, persistent vegetation on the electrodes is most likely characteristic of the late stage of IE, associated with an extensive clinical picture of sepsis and the probable spread of infection to the TV. Another feature of CIED infection diagnostics is significant difficulties in early detection of TV lesions. In both presented cases, TV vegetation was detected only intraoperatively, because Artifacts of the electrodes and/or vegetation located on the electrodes in the immediate vicinity of the TV make it difficult to assess the valve itself, and the absence of significant tricuspid regurgitation speaks against the leaflet lesions. The described clinical cases have shown that with ES duration ≥ 6 months, TV is usually involved into the infectious process. However, it is impossible to say for sure that exactly six months is the period after which the TV is always affected, since there is no serious evidence base / large studies on this. The duration of ES is undoubtedly directly proportional to the likelihood of TV infection, being an additional argument in favor of the earliest possible removal of CIED in case of suspected ES.

In our opinion, a more important consequence of this pattern is the need to remove the entire pacemaker system not only with confirmed ES (which is very difficult to prove at the early stages), not only with local infection of the device bed, but also with a reasonable suspicion of a septic condition without a proven source in patients with CIED. This suspicion is the basis for considering the issue of complete removal of the “suspicious” CIED and prolonged antibiotic therapy according to the recommendations of the European Society of Cardiology 2015. An additional diagnostic tool for CIED-associated sepsis is a combined positron emission and X-ray computed tomography (PET/CT) scan with 18F-FDG [7]. The isolated use of antibiotics without radical removal of CIED worsens the prognosis, because persistent intracardiac infection ultimately leads to the progression of sepsis and the involvement of TV structures in the infectious process, which, even after the cure of CIED infection, becomes a severe clinical problem.

CONCLUSION

- The course of infective endocarditis of the device implanted in the heart differs from the classical clinical picture of valvular IE. The key to early diagnosis of electrode sepsis is knowledge of typical clinical CIED masks and the features of the modern course of septic syndrome.
- With a long course of electrode sepsis, the likelihood of involvement of tricuspid valve structures in infective endocarditis is directly proportional to the time from debut to surgery.
- Early and complete removal of CIED in combination with antibacterial therapy, the duration and volume of which corresponds to international clinical guidelines, is a guarantee of favorable short-term and long-term prognosis.
- In our opinion, the systematic sanitation of chronic foci of infection, especially odontogenic infection, can become an effective preventive measure against CIED infection.
- Thorough debridement of chronic foci of infection before ISU implantation should be as necessary a procedure as before open cardiac surgery.

ADDITIONAL INFORMATION

Funding source. There was not supported by any external sources of funding.

Competing interests. The authors declare that they have no competing interests.

Consent for publication. Written consent was obtained from the patients for publication of relevant medical information and all of accompanying images within the manuscript.

REFERENCES


DOI: https://doi.org/10.17816/cardar70497
СПИСОК ЛИТЕРАТУРЫ


4. Шелковский В.Н. Хирургическая санация очагов одонтогенной инфекции в лечении и профилактике инфекционных эндокардитов: автореф. дис. ... канд. мед. наук. СПб., 1999.

5. Крутоя С. Н. Особенности стоматологической подготовки больных инфекционным эндокардитом к операции на сердце: автореф. дис. ... канд. мед. наук. Тверь, 2010.


AUTHORS INFO

*Vera Y. Zimina, Candidate of Sciences in Medicine, Associate Professor; e-mail: ziminavu@mail.ru; ORCID: 0000-0002-5655-8981; SPIN code: 7202-1071

Gevorg R. Airapetian, Cardiologist, Interventional radiology; e-mail: goshabravo@mail.ru; ORCID: 0000-0003-3988-1880; SPIN code: 9102-1759

Yuri N. Grishkin, Doctor of Medical Sciences, Professor; e-mail: yurigrishkin@yandex.ru; SPIN code: 9997-2073

Sergey A. Sayganov, Doctor of Medical Sciences, Professor; e-mail: sergey.sayganov@szgmu.ru; ORCID: 0000-0001-8325-1937; SPIN code: 2174-6400

* Corresponding author / Автор, ответственный за переписку

ОБ АВТОРАХ

*Вера Юрьевна Зимина, кандидат медицинских наук, доцент; e-mail: ziminavu@mail.ru; ORCID: 0000-0002-5655-8981; SPIN-код: 7202-1071

Геворг Размикович Айрапетян, врач-кардиолог, врач по рентгенэндоваскулярной диагностике и лечению; e-mail: goshabravo@mail.ru; ORCID: 0000-0003-3988-1880; SPIN-код: 9102-1759

Юрий Николаевич Гришкин, доктор медицинских наук, профессор; e-mail: yurigrishkin@yandex.ru; SPIN-код: 9997-2073

Сергей Анатольевич Сайганов, доктор медицинских наук, профессор; e-mail: sergey.sayganov@szgmu.ru; ORCID: 0000-0001-8325-1937; SPIN-код: 2174-6400