RESPIRATORY CARE Paper in Press. Published on November 05, 2013 as DOI: 10.4187/respcare.02907

Atypical pattern of lung involvement in pacemaker endocarditis

Fotini C. Ampatzidou MD[1], Maria N. Sileli MD[1], Charilaos-Panagiotis C. Koutsogiannidis MD[2], Olga G. Ananiadou MD, PhD[2], Athanasios A. Madesis MD, PhD[2], Vassilis G. Michaelidis MD[3], George E. Drossos MD, PhD[2]

1. Cardiac surgery intensive care unit, General Hospital "G.Papanikolaou", Thessaloniki, Greece.
2. Cardiothoracic Surgery Department, General Hospital "G.Papanikolaou", Thessaloniki, Greece.
3. Department of Respiratory Care, General Hospital "G.Papanikolaou", Thessaloniki, Greece.

Dr Fotini Ampatzidou was in charge of patient's care and drafted the manuscript. Dr Maria Sileli provided the intensive care of the patient and also co-authored the manuscript. Dr Charilaos-Panagiotis Koutsogiannidis was involved in patient's care and provided writing assistance. Dr Olga Ananiadou and Dr Vassilis Michaelidis were involved in patient's care. Dr Athanasios Madesis was the surgeon of this case. Finally, Dr George Drossos is the department chair that provided general support. The case report was performed in General Hospital "G.Papanikolaou", Thessaloniki, Greece. The material presented in this article is original and is not under consideration by another journal. All authors have read and approved the manuscript and it presents no ethical problem or conflict of interest.

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Corresponding Author:

Charilaos-Panagiotis C. Koutsogiannidis

Cardiothoracic Surgery Department, General Hospital "G.PAPANIKOLAOU",

Exohi 57010, Thessaloniki Greece

tel: +302313307661, +306947563228

fax: +302313307667

e-mail: harisdoc76@yahoo.gr

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ABSTRACT

Pacemaker endocarditis has a high rate of morbidity and mortality and is associated with substantial healthcare cost. To maximize the effectiveness of treatment, diagnosis of pacemaker endocarditis should be made as early as possible. Medical treatment alone is not successful and the removal of the entire artificial pacing system is often required.

We present a case of a female patient with permanent transvenous pacemaker, recurring episodes of fever, chills, general malaise and a computed tomograph image of a solitary, tumor-like lesion indicating pneumonia. The symptoms subsided with empirical antibiotics but without improvement in the radiologic images. A wedge resection of the lesion by thoracotomy was performed revealing a necrotic lung lesion compatible with pulmonary infarct. Transesophageal echocardiography showed a mass that was adherent to the pacemaker lead. The therapeutic approach consisted of surgical removal of the complete pacing system along with long term antibiotic therapy and implantation of a new device with epicardial lead. Serial follow-up echocardiograms for one year period did not show any recurrence and the subsequent course was uneventful.

KEY WORDS

Infective endocarditis, pacemaker infection, echocardiography, pulmonary infarct, septic pulmonary emboli, management of cardiac device related infective endocarditis

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INTRODUCTION

The risk of pacemaker (PM) - related infective endocarditis (IE) has increased since the evidenced- based indications of these devices have progressively expanded. [1] Permanent PM infection is a serious complication with reported rates varying between 0.13%-19.9%. [2] PM endocarditis accounts for 10% of the PM- associated infections and has a mortality rate of 30-35%. [2, 3, 4, 8] Extended and serious forms of this infection may affect the leads, the cardiac valves or the endocardiac surface, and is called cardiac device related infective endocarditis (CDRIE). Its clinical presentation may vary, making diagnosis difficult. We report a case of CDRIE which diagnosis was delayed-because of its atypical presentation. A solitary pulmonary lesion revealed by chest computed tomography was initially misdiagnosed as round pneumonia.

CASE REPORT

We report a case of a 55 year old female, thalassemia carrier, with a medical history of arterial hypertension, type II diabetes mellitus, and a known allergy to cephalosporins. The patient received an implanted permanent transvenous pacemaker (St Jude Medical, mode DDDR, rate 60/min) due to sick sinus syndrome. Three years later she developed a high grade fever (39º C) and chills. Associated symptoms included general malaise and musculoskeletal pain in the lower limbs. Laboratory tests revealed elevated white blood cells count, and the plain chest X- ray demonstrated right lower lobe (RLL) infiltrate, which was diagnosed as pneumonia. She had been treated with empirical antibiotic therapy for community acquired pneumonia as an outpatient by the family doctor. While her symptoms improved, she still suffered from musculoskeletal pain. Three months later, she was referred to our hospital because of a persistent high fever and RLL infiltrate. On admission, physical

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examination revealed no pathological findings. Chest CT scan revealed a solitary, tumor-like, consolidation located in the posterior basal segment of the RLL (5.5x4.5 x3 cm) abutting the pleura (Figure 1). This was interpreted as round pneumonia. The two PM leads were in normal positions. Electrocardiogram showed a good functioning pacemaker. The patient received moxifloxacin for a week. She became afebrile with a normal white cell count, but the other markers of inflammation, such as erythrocyte sedimentation rate and the C- reactive protein, were still elevated. Further investigations, including multiple blood and sputum cultures, immunology tests, and screening for vasculitis, were all negative. The patient underwent bronchoscopy with normal findings. Both a microbiological and cytological analysis of bronchoalveolar lavage, along with a protected bronchial brushing were negative as well. However, the diagnosis of infection related to the PM had not been considered in differential diagnosis.

Upon a follow up examination, the patient showed no radiological improvement. Two months later the tumor-like solitary pulmonary nodule was still present. She underwent right thoracotomy and a wedge resection of the lesion was performed. Macroscopic evaluation of the resected tissue revealed a necrotic lesion. Microscopic examination showed coagulation-type necrotic tissue, recanalization, a large amount of eosinophilic material and nuclei degradation. The necrotic area was surrounded by fibrotic tissue. Inside the necrotic lesion, ghost vessels and vessels with intraluminal obliteration and hemosiderin-containing alveolar macrophages were recognised. These findings were compatible with pulmonary infarct.

On the 10th postoperative day, she became febrile again (max 40^{o}C) with an elevated white blood cell count. She was complaining for malaise, anorexia and weight loss. Although there were no local symptoms of inflammation at the site of pacemaker

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implantation, pacemaker endocarditis was suspected due to on-going fevers and the histopathologic findings. As a result, the patient underwent a transthoracic echocardiography (TTE) exam, but this did not yield a diagnosis. Further investigation using transesophageal echocardiography (TEE) revealed a large oscillating intracardiac mass in the right atrium (11.8x 8.7mm) attached to the pacemaker lead (Figure 2). Systolic function was normal and there was moderate tricuspid regurgitation. Blood cultures were again negative. Therefore, empirical intravenous anti-staphylococcal therapy for endocarditis was initiated (vancomycin 15mg/kg/12 hours and gentamicin 1mg/kg/8 hours) since staphylococci are involved in the majority of these infections.

Surgical removal of the entire pacing system using extracorporeal circulation (ECC) was the decided course of action. The patient underwent median sternotomy. The PM device and leads were extracted under ECC (cardiopulmonary bypass time: 30 min) and were replaced by epicardial atrioventricular PM since the patient was PM - dependent. Intraoperative TEE showed complete removal of the vegetation leaving intact valves and endocardiac surfaces. Cultures from the extracted PM leads and vegetation were negative. Antimicrobial therapy with vancomycin continued for a total of 6 weeks.

The postoperative period was uneventful. The patient remained afebrile with normal white blood cell count. There was no recurrence 1 year after she discharged from the cardiothoracic department.

DISCUSSION

As noted, reported rates of permanent PM infection may reach 19.9%. [2] PM endocarditis accounts for 10% of the PM- associated infections and is a potentially

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lethal complication. [2, 3, 4, 8] Factors contributing to a higher incidence of infection include age, diabetes mellitus, immunosuppression, neoplasm, the use of anticoagulants, intravenous catheters, temporary pacing, early reintervention after PM implantation, dermatological diseases, absence of periprocedural antibiotic prophylaxis and other infectious foci before implantation.

Presentation of PM-associated infection includes acute endocarditis caused by virulent pathogens that may lead in severe sepsis and sub-acute or chronic infection with non-specific symptoms. This may obscure the initial assessment. Infection during the first year after implantation is characterized as surgical site infection. Beyond the first year, these infections are termed late –onset lead endocarditis. Permanent PM infection can be limited to the pocket of the cardiac device, characterized by local signs of inflammation, or it may cause a more extended and serious infection affecting the leads, the cardiac valves or the endocardiac surface, also called cardiac device related infective endocarditis. Early infections are most commonly caused by Staphylococcus aureus, while late infections are most commonly caused by coagulase negative staphylococci such as Staphylococcus epidermidis. Other pathogens such as gram positive cocci, gram negative bacilli and fungi (Candida) have been also described. [2, 4] Positive cultures, from the blood or the subcutaneous pacemaker pocket, have high diagnostic value and lead to appropriate treatment. Blood cultures are positive in 77% of patients suffering from CDRIE. Prior antibiotic administration or organisms with limited proliferation under conventional culture conditions may underlie many of the observed instances of culture negative endocarditis, often delaying the diagnosis and onset of treatment. Antibiotic selection should be based on the identified pathogen and guided by the antimicrobial susceptibility testing. The therapeutic scheme should be bactericidal and

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parenterally administrated for a long time for complicated infections. In the case of negative cultures where PM-related infected endocarditis is suspected, broad spectrum antibiotic therapy must be chosen. [2, 3, 4]

Transthoracic echocardiography (TTE) is an important diagnostic tool in detecting endocarditis, particularly when blood cultures are negative. Echocardiography is indicated for the measurement of vegetation size and is also useful for detecting complications such as valvular insufficiency, congestive heart failure, paravalvular abscesses and for predicting embolic events. When the TTE is negative or inconclusive and there is a high clinical suspicion of infective endocarditis, a transesophageal echocardiography (TEE) should be performed. In cases where pace wire endocarditis is suspected, determining whether tricuspid valve endocarditis, pacemaker lead infection or both are present, is difficult to assess by TTE. TEE has better diagnostic accuracy compared with TTE for this particular application, with high sensitivity (94% versus 23%, respectively). [5] There is a 5% possibility that the identified intracardiac mass that is adhering to the lead is a thrombus and not infected vegetation, and there is no need for lead removal or antibiotic treatment in these cases. Taken altogether, we conclude that in addition to positive echocardiographic findings, clinical features and laboratory data are essential to establish the diagnosis of endocarditis. In cases where surgical removal of the pacing system is deemed necessary, intraoperative TEE is recommended because it may provide additional diagnostic information and modify the surgical plan. Echocardiography should also be repeated after device extraction. [6]

CDRIE is a heterogeneous disease with variable clinical presentations. The use of modified Dukes criteria is suggested to correctly diagnosis condition. Our patient fulfills these criteria for definite diagnosis of infective endocarditis (1 major -

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Echocardiogram evidence of infective endocarditis and 3 minor – predisposition, fever, pulmonary infarct). Although they are of considerable use, they must not replace clinical judgment. CDRIE must be suspected in the presence of unexplained persisting fever in all patients with an implanted PM even in the absence of local signs of infection or negative blood cultures. In our case cultures from the extracted PM leads and vegetation were also negative. However, it has been reported that only 25.4% of cultured valves from patients with infected endocarditis could be true positive. [7]

In the case presented here, PM-lead infection was not initially considered in the differential diagnosis. The negative blood cultures, the absence of local signs of infection at the generator pocket site, the long time elapsed between PM implantation and the occurrence of infection, and the presence of specific findings in the chest CT scan which suggested pneumonia, significantly delayed the correct diagnosis. Infective endocarditis can cause pulmonary complications, especially septic emboli. Emboli to the lungs often present with IE. Patients with large vegetations (>10 mm) are at high risk of embolism, while the risk of new embolism is highest during the first days following the initiation of antibiotic therapy. Imaging along with clinical signs and laboratory tests, play a major role in the diagnosis of septic pulmonary emboli. Although radiographic abnormalities may be non-specific, typical lung CT findings include bilateral, poorly defined, parenchymal nodules or multifocal infiltrates, commonly involving peripheral lung zones, often associated with varying degrees of cavitation. [8] There is also a tendency for the septic nodules to change their appearance over time. Feeding vessels are observed in the nodules in 60-70% of patients. [9]

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In this case, although the patient with an implanted cardiac device was febrile and had elevated markers of systemic inflammation, the diagnosis was further delayed because of the atypical pattern of lung involvement assessed by CT. The observed pulmonary lesion was solitary without cavitary changes and the presence of a feeding vessel was not observed.

Current recommendations for managing patients with pacemaker endocarditis include the removal of the entire pacemaker system followed by long term, appropriate antibiotic therapy targeting the isolated organisms. [10] Conservative treatment alone is rarely successful and is associated with a high risk of recurrence. The reinfection rate has been reported to be 0.8% when the device is removed and 50% if it is not removed. When antibiotic administration is the only therapeutic intervention, reported mortality rates range from 31-66%, while mortality is 18% when extraction of the device is accompanied by medical treatment. [2, 4] There are two surgical options for removing the pacemaker leads: the percutaneous or the open surgical techniques. The decision on which technique to use should be based on vegetation size, duration of implantation, the age of the patient and coexisting conditions. [11]

Percutaneous lead extraction is the preferred method for removal of CDIE hardware, although this method carries risks of arrhythmias, tricuspid valve tear or right ventricle damage especially in patients who have pacemakers for a prolonged length of time. Over time, the intravascular pacemaker leads can be encapsulated deeply into right ventricular tissue, making extraction difficult. There are many techniques for percutaneous lead extraction. The simplest method is direct, gentle manual traction. An intravascular approach through the transvenous removal of the endocardial leads using wire loop snares, hook-tipped wires, grasping forceps, basket retrievers or locking stylets is an alternative. [12] The risk of embolic events in the presence of

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large (>20 mm) vegetations is considered a relative contraindication to transvenous removal. Another feared complication of the transvenous lead extraction technique, is cardiac tamponade (0–3.3%). According to the current literature, percutaneous lead removal is feasible and safe even when vegetation size is up to 40 mm, but a high level of experience is required. [13] Surgical extraction should be considered when any of the following are present: percutaneous extraction is incomplete or impossible, a large vegetation is present or there is an associated destruction of the tricuspid valve. [2, 4] The presence of long term leads (more than 12 months after implantation) is also a strong indication for surgical intervention under cardiopulmonary bypass. [3] Immediate reimplantation should be delayed. If a PM is necessary, implantation of a PM system with epicardial leads is advised. We decided pacemaker lead removal by surgical treatment in our patient. The main reasons for this were the long period that the pacemaker was in place and the vegetation size (> 10mm).

Since the number of implanted cardiac devices has significantly increased, the incidence of CDRIE has concomitantly increased. PM endocarditis is associated with substantial morbidity, mortality and increase in hospital costs. There is a need for the earlier suspicion and recognition of the clinical signs of CDRIE and the proper management of this condition. The clinical presentation may be atypical and the presenting symptoms may appear years after PM implantation. Septic pulmonary emboli may be the key presenting feature of CDRIE. Although imaging plays an important role in identifying septic pulmonary emboli, atypical lung involvement must also be considered when making a correct diagnosis.

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FIGURE LEGENDS

Figure 1. CT scan images from the lung showing a solitary pleural – based lesion in the right lower lobe.

Figure 2. Transesophageal echocardiogram: view of the right atrium. There is a round vegetation (1.18x0.87 cm) attached to the pacemaker lead.

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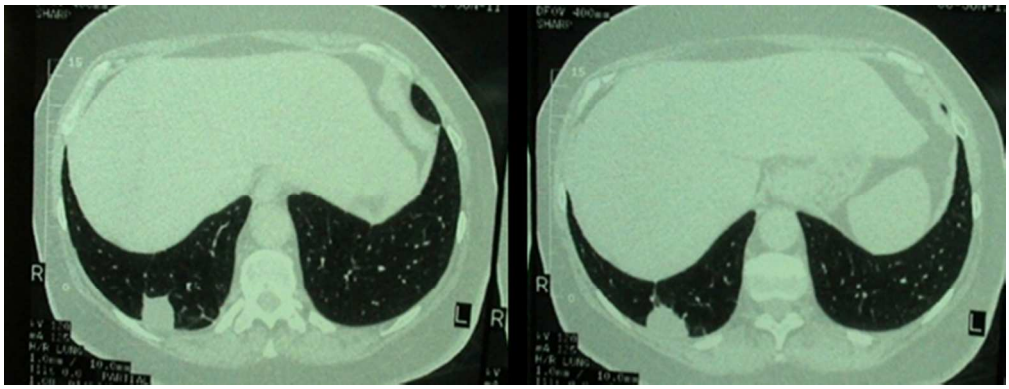

CT scan images from the lung showing a solitary pleural – based lesion in the right lower lobe.

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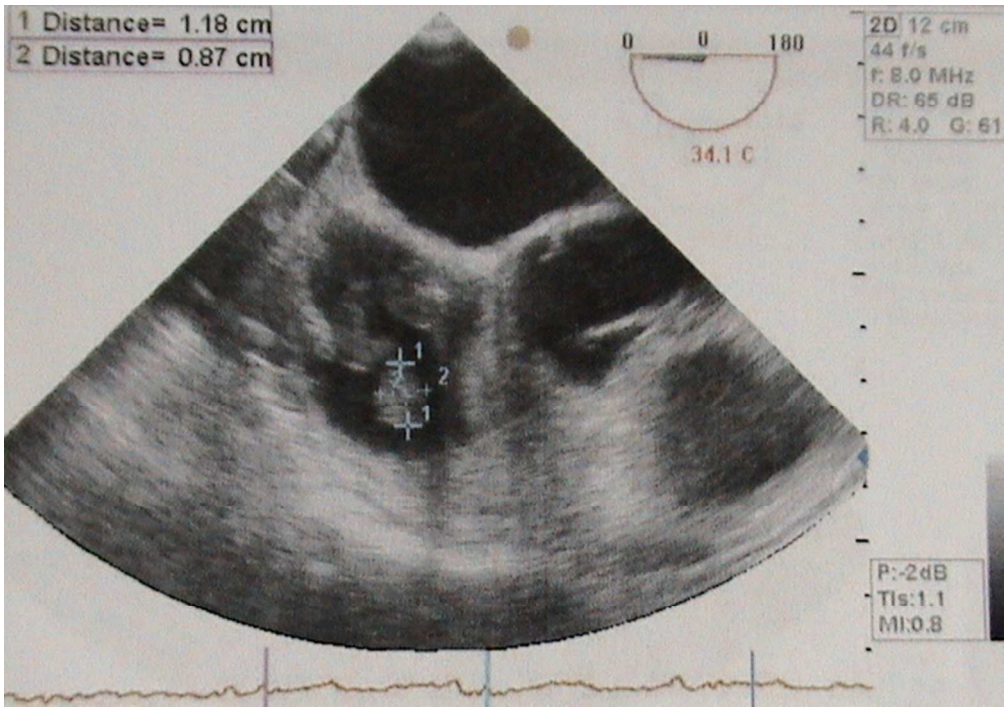

Transesophageal echocardiogram: view of the right atrium. There is a round vegetation (1.18x0.87 cm) attached to the pacemaker lead.