Two-stage surgical treatment of infected pacemaker leads and tricuspid valve endocarditis occurring 20 years after implantation

Takıldıktan 20 yıl sonra meydana gelen, kalp pili tellerindeki enfeksiyonun ve triküspid kapak endokarditinin iki aşamalı cerrahi tedavisi

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Infective endocarditis associated with permanent transvenous pacing is a rare but serious complication. A 64-year-old man was referred to our hospital with fever of unknown origin. Despite repeated antibiotic therapies, he sustained fever for a year without any documented infectious foci, and all blood cultures were negative. He had a history of permanent transvenous pacemaker (PM) implantation 20 years before, followed by two subsequent reimplantation procedures due to lead detachment. After unsuccessful efforts of percutaneous removal, all PM leads and wires were left in place. On admission, he was in sinus rhythm and the PM leads were completely dysfunctional. His temperature was above 38.5 °C. Transthoracic echocardiography findings were normal except for mild to moderate tricuspid insufficiency. Transesophageal echocardiography revealed a large vegetation, 19x13 mm in size, attached to the pacemaker leads, and multiple tiny vegetations over the anterior and septal leaflets. There was also moderate tricuspid insufficiency. Under cardiopulmonary bypass and aortic cross-clamping, infected pacemaker wires were removed and infected anterior and septal leaflets of the tricuspid valve were excised. Cultures from the PM wires and leaflets revealed methicillin-resistant *Staphylococcus epidermidis*. After 10 days of specific antibiotic therapy, tricuspid valve replacement was performed. During a follow-up of 17 months, the patient remained free of any cardiac events or fever.

Key words: Echocardiography, transesophageal; endocarditis, bacterial/surgery; equipment contamination; pacemaker, artificial/adverse effects; staphylococcal infections/surgery.

İnfektif endokardit, kalıcı transvenöz kalp pili olan hastalarda görülen nadir fakat ciddi bir komplikasyondur. Altmış dört yaşında bir erkek hasta merkezimize nedeni bilinmeyen ateş nedeniyle gönderildi. Tekrarlayan antibiyotik tedavilerine rağmen hastanın ateşi bir yıldır geçmemişti; herhangi bir infeksiyon odağı bulunamamıştı ve kan kültürleri negatif idi. Hastaya 20 yıl önce kalıcı transvenöz kalp pili takılmış, sonrasında da lead bağlantısızlığı nedeniyle iki kez girişimde bulunulmuş ve sonuçta perkütan çıkarma işlemleri başarısız olunca tüm leadler ve teller yerinde bırakılmıştı. Yatırıldığında hasta sinus ritmindeydi ve tüm leadler fonksiyon dışıydı. Ateşi 38.5 °C'nin üzerindeydi. Transtorasik ekokardiyografi bulguları, hafif-orta derecede triküspid yetersizlik dışında normaldi. Transözafajiyal ekokardiyografide kalp pili leadlerine yapışmış, 19x13 mm boyutlarında bir vejetasyon ve anterior ve septal yaprakçıklarda çok sayıda küçük vejetasyon görüldü. Ayrıca, orta derecede triküspid yetersizliği vardı. Kardiyopulmoner baypas ve aortik kros-klemp altında infekte kalp pili leadleri çıkartıldı ve yaygın olarak infekte olan triküspid kapak anterior ve septal yaprakçıkları için valvulektomi uygulandı. Kalp pili tellerinden ve yaprakçıklardan elde edilen kültürlerde metisiline dirençli *Staphylococcus epidermidis* üredi. On günlük spesifik antibiyotik tedavisi sonrasında hastanın triküspid kapağı değiştirildi. On yedi aylık takip sırasında hastada herhangi bir kardiyak olay ya da ateş görülmedi.

Anahtar sözcükler: Ekokardiyografi, transözofajiyal; endokardit, bakteriyel/cerrahi; ekipman kontaminasyonu; kalp pili/yan etki; stafilokok infeksiyonu.

Pacemaker (PM)-lead infection is a rare but serious complication of permanent transvenous pacing with a reported incidence of 0.3% to 12.6%.[1] Predisposing factors include contamination during insertion, pocket hemorrhage and infection, repeated surgical procedures on the pacemaker system, use of corticosteroids,

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diabetes mellitus, immunosuppressive therapy, and malignancies.[2]

It has an insidious onset and is often difficult to diagnose. The spectrum of clinical presentation varies from fever and chills to severe vascular embolic phenomena.[2,3] It has a high mortality rate; thus, early diagnosis is important.

In this report, we presented a case of chronic PM-lead infection and related tricuspid valve endocarditis that developed 20 years after implantation and was treated with a two-stage surgical treatment.

CASE REPORT

A 64-year-old male patient was admitted with a diagnosis of fever of unknown origin. He had a history of permanent transvenous PM implantation 20 years before due to second-degree heart block and bradycardia. In addition, he underwent two subsequent reimplantation procedures due to lead detachment within two years after the first one. All pacemaker leads and wires were left in place after previous unsuccessful efforts of percutaneous removal. Within the last year before admission, he was hospitalized two times in different centers because of persistent fever. First, he was treated with antibiotics with a diagnosis of right lower lobe pneumonia. Then, three months after this, he was re-hospitalized due to recurrent fever of unknown origin, at which time evaluation of all systems was normal and he had the following transthoracic echocardiography (TTE) findings: normal right and left heart functions, normal pulmonary artery pressures, trivial tricuspid valve insufficiency, and no evidence for endocarditis over the heart surfaces, valves, or the PM wires.

Finally, he was referred to our hospital with a diagnosis of fever of unknown origin. On admission, he was in sinus rhythm and the PM leads were completely dysfunctional. His body temperature was above 38.5 °C. All previous prophylactic antibiotics were stopped and repeated blood cultures were taken during bouts of fever. On physical examination, there were no sings of infection in the PM pockets or on subcutaneous parts of the leads. His chest roentgenogram showed bilateral subclavian transvenous PM wires without any apparent infectious foci or infiltration into the lungs (Fig. 1). He had leukocytosis (34,000/µl) with a shift to the left and elevated ESR (42 mm/hr) and C-protein (104 mg/l) levels. Serologically, serum levels of complement 3 and 4 were decreased (0.185 mg/dl and 0.0136 mg/dl, respectively) while the level of rheumatoid factor was increased (219 IU/ml). Serum creatinine was on the incline during the evaluation (from 0.8 to 3.8 mg/dl) and urinalysis revealed microscopic hematuria. Neither sputum culture nor repeated blood cultures (aerobes and anaerobes) taken during the periods of fever revealed any microbial yield. Computed tomography of the thorax revealed a small area of consoli-

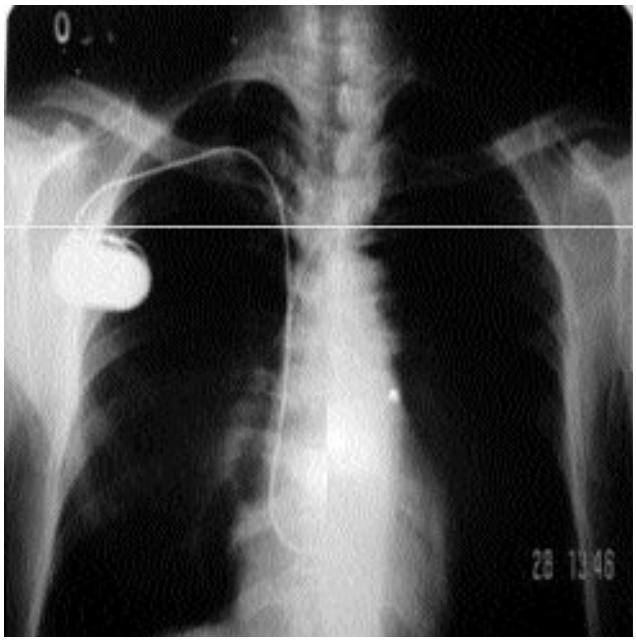

Figure 1. Chest roentgenogram showing bilateral subclavian transvenous pacemaker wires and a subcutaneous pacemaker.

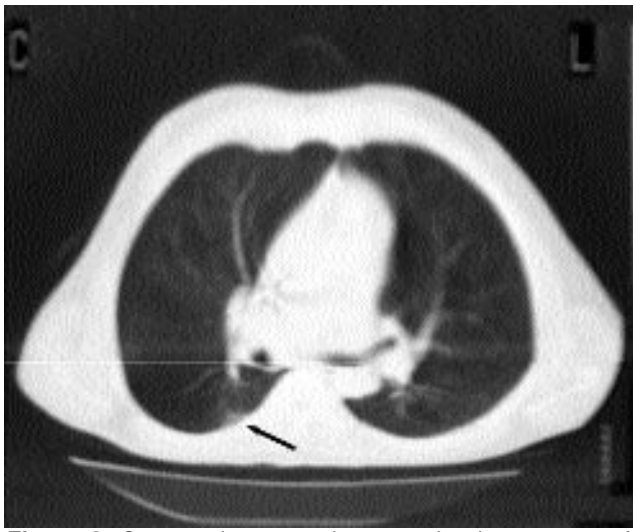

Figure 2. Computed tomography scan showing an area of consolidation (arrow) confined to the superior segment of the right lower lobe.

dation confined to the superior segment of the right lower lobe (Fig. 2). Transthoracic echocardiography demonstrated normal left ventricular functions, normal pulmonary artery pressures, and mild to moderate tricuspid insufficiency without any evidence for infection. Upon suspicion of a PM-lead infection or related endocarditis, transesophageal echocardiography (TEE) was performed, which revealed a large vegetation, 19x13 mm in size, attached to the PM wires and multiple tiny vegetations over the ventricular surface of the anterior and septal leaflets. There was also moderate tricuspid insufficiency. On the basis of the modified Duke criteria,[4] the diagnosis was made as chronic PM-lead infection and related tricuspid valve endocarditis. Renal alterations were accepted as glomerulonephritis secondary to the immunologic reaction induced by the infection. Consolidation was considered to be septic pulmonary embolism of the infectious material covering the PM leads. Prophylactic intravenous antibiotic therapy (cefazolin + rifampin) was started immediately and a decision for surgery was made.

A standard median sternotomy was performed. After opening the pericardium and systemic heparinization, cardiopulmonary bypass was established with aortobicaval cannulation. Cardiac arrest was induced by antegrade tepid blood cardioplegia following aortic cross-clamping. The PM leads within the right heart were inspected through a right atriotomy. A layer of multiple vegetations covering the surface of the PM wires and a single free-floating vegetation attached to the right ventricular part of the wires were detected. The leaflets seemed to be of normal morphology, but there were multiple tiny vegetations attached to the ventricular side of the anterior and septal leaflets. During right atriotomy, infected PM leads were removed from the wall of the right ventricle by resection of the fibrotic tissue covering the leads. Then, infected anterior and septal leaflets were resected whereas the posterior leaflet was preserved. Annular tissue of the anterior and septal leaflets was very fragile due to the active infective process. Tricuspid valve replacement (TVR) was deferred pending specific antibiotic treatment. Then, the right atrium was closed, the patient was weaned off cardiopulmonary bypass and the rest of the operation was completed in a standard fashion.

The patient was extubated at the sixth postoperative hour and central venous pressure values were between 14 and 20 mmHg during the early postoperative period. He was in sinus rhythm with 70 to 80 beats per minute. Cultures from the PM wires and leaflets of the tricuspid valve revealed methicillin-resistant *Staphylococcus epidermidis*. Antibiotic therapy was switched to intravenous vancomycin on the second postoperative day and its dose was adjusted according to creatinine clearance. On the tenth postoperative day, the patient was reoperated for TVR. A mechanical bileaflet mitral valve (CarboMedics, no: 33, Austin, TX, USA) was placed in the tricuspid position with separate pledgeted mattress sutures. The rest of the operation was completed in a standard fashion. The patient had no fever and intravenous vancomycin therapy was continued for six weeks postoperatively. He was anticoagulated and discharged from the hospital uneventfully. During a follow-up period of 17 months, he remained free of any cardiac events or fever.

DISCUSSION

The chronic form of PM-lead infection has been one of the most challenging problems in current clinical practice, with a mortality rate being 30% to 35% and delay in diagnosis even worsens the situation.[4]

Diagnosis of acute PM-lead infection is relatively more straightforward than that of the chronic one because of the short period elapsed after implantation and more obvious acute clinical findings. Common symptoms of chronic PM-lead infection in order of frequency are fever, local symptoms at the pouch of the pacemaker, pneumonia, pulmonary embolism, arthralgia, and spondylitis.[2,4] The mean time between implantation and appearance of the first symptoms ranges from 25 to 33 months.[2,4,5] In our case, the absence of local symptoms and an unproblematic gap of 20 years after implantation diverted the attention from the possibility of a PM-lead infection in the differential diagnosis.

Staphylococcus aureus (in acute cases) and S. epidermidis (in chronic cases) are the most common pathogens in PM-lead infection and the etiology is multiple in 25% of the cases.[5,6] Septicemia is rare in these patients and blood cultures alone are not always sensitive for PM-lead infection.[5] Negative blood cultures are thought to result from the production of an amorphous material or slime in colonies of Staphylococcus species, which isolates the pathogen

growing on the leads from the blood.[7] It has also been proposed that this slimy material is responsible for the persistence of colonization and antibiotic resistance to infection.[4,6]

In chronic cases, common causes of delay between the onset of symptoms and the diagnosis include misinterpretation of *S. epidermidis* isolation in blood cultures as contamination, failure to regard local signs at the site of implantation as a systemic infection, and exclusion of the diagnosis of PM-lead infection depending on false negative TTE results.[4] Klug et al.[6] found that local infective findings at the site of implantation were a strong predictor of intravascular PM-lead infection even in the absence of systemic findings. Involvement of the extravascular and intravascular parts of the leads may be due to extension of local infection into the vascular system.

Positive predictive value of TTE in the diagnosis of right heart endocarditis ranges from 30% to 80% and the presence of sleeve-like growth of the infection around PM leads and normal function of the tricuspid valve have been associated with false negative results on TTE. In contrast, TEE is more helpful in the diagnosis with a sensitivity of approximately 95%.[4,7,8] Therefore, TEE is indispensable in the initial evaluation of patients with a suspicion of PM-lead infection whatever the results of previous blood cultures or TTE are.

Victor et al.[8] proposed that diagnosis of PM-lead infection could be made with even one major criterion, namely, a positive TEE result for endocarditis. In our case, the diagnosis of PM-lead infection was made on the basis of one major criterion (positive TEE) supported by two minor criteria (fever >38 °C and glomerulonephritis). It has been suggested that acceptance of local or pulmonary symptoms as a major criterion increases the predictability of the diagnosis by clinical findings.[4]

Immediate removal of the entire pacing system was planned in our case when the diagnosis was made by TEE. Surgical removal of infected leads is preferred when the size of vegetation is greater than 10 mm and the risk for septic pulmonary embolism is higher.[4]

In our patient, a two-stage surgical treatment was performed for concomitant tricuspid valve endocarditis. First, the infected leaflets were resected and specific antibiotic therapy was instituted for eradication of the infection. Ten days after the initial operation, TVR was performed. Dehiscence and infection of the prosthesis due to the fragility of the annulus surrounding the anterior and septal leaflets would have been inevitable if we had performed TVR in the same session. A two-stage surgical approach is recommended in patients with tricuspid valve endocarditis due to drug addiction or ongoing severe active infection unless there are no clinically evident pulmonary hypertension and right heart failure.[9] Arbulu et al.[10] reported or 55 patients with intractable right-sided endocarditis, of whom 53 patients were treated by tricuspid valvulectomy without replacement. Only six patients (11%) required prosthetic heart valve insertion following valvulectomy to control medically refractory right-sided heart failure.

In conclusion, a two-stage surgical approach may be a reasonable alternative in the treatment of tricuspid endocarditis especially in patients with severe infection of the valvular apparatus.

REFERENCES

1. Voet JG, Vandekerckhove YR, Muyldermans LL, Missault LH, Matthys LJ. Pacemaker lead infection: report of three cases and review of the literature. Heart 1999;81:88-91.
2. Arber N, Pras E, Copperman Y, Schapiro JM, Meiner V, Lossos IS, et al. Pacemaker endocarditis. Report of 44 cases and review of the literature. Medicine 1994;73:299-305.
3. Anderson JL, Sande MA, Kartalija M, Muhlestein JB. Infective endocarditis. In: Fuster V, Alexander RW, O'Rourke RA, Roberts R, King SB III, Nash I, et al. editors. Hurst's the heart. 11th ed. Philadelphia: McGraw-Hill; 2005. p. 2001-34.
4. Klug D, Lacroix D, Savoye C, Goullard L, Grandmougin D, Hennequin JL, et al. Systemic infection related to endocarditis on pacemaker leads: clinical presentation and management. Circulation 1997;95:2098-107.
5. Klug D, Wallet F, Kacet S, Courcol RJ. Detailed bacteriologic tests to identify the origin of transvenous pacing system infections indicate a high prevalence of multiple organisms. Am Heart J 2005;149:322-8.
6. Klug D, Wallet F, Lacroix D, Marquie C, Kouakam C, Kacet S, et al. Local symptoms at the site of pacemaker implantation indicate latent systemic infection. Heart 2004;90:882-6.
7. Vilacosta I, Sarria C, San Roman JA, Jimenez J, Castillo JA, Iturralde E, et al. Usefulness of transesophageal echocardiography for diagnosis of infected transvenous permanent pacemakers. Circulation 1994; 89:2684-7.
8. Victor F, De Place C, Camus C, Le Breton H, Leclercq C, Pavin D, et al. Pacemaker lead infection: echocar-

diographic features, management, and outcome. Heart 1999;81:82-7.
9. Shemin RJ. Tricuspid valve disease. In: Cohn LH, Edmunds LH Jr, editors. Cardiac surgery in the adult. 2nd ed. New York: McGraw-Hill; 2003. p. 1001-15.
10. Arbulu A, Holmes RJ, Asfaw I. Tricuspid valvulectomy without replacement. Twenty years' experience. J Thorac Cardiovasc Surg 1991;102:917-22.