Successful long-term antibiotic suppressive therapy in a case of prosthetic valve endocarditis and a case of extensive aortic and subclavian graft infection

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Abstract

Introduction The indication for surgical valve replacement in cases of infective endocarditis is well defined in current guidelines. However, some patients are not fit or willing to undergo major surgical procedures. Interestingly, to the best of our knowledge, there is scarce information in the literature on how to deal with such cases and what might be the outcome.

Case report We present two complicated cases of prosthetic infective endocarditis with definite indication for replacement of involved foreign material, who were treated successfully with long-term suppressive antibiotic therapy.

Conclusion These two cases demonstrate that individualized long-term antibiotic suppressive therapy might be effective in selected patients with complicated PVE unfit or unwilling to undergo high-risk cardiothoracic surgical interventions.

Keywords Prosthetic valve endocarditis · Antibiotic long term suppression

Introduction

The indication for surgical valve replacement in current guidelines is well defined, in general, in cases of acute aortic or mitral native or prosthetic valve endocarditis with severe regurgitation or obstruction causing symptoms of heart failure or echocardiographic signs of poor hemodynamic tolerance, uncontrolled infection or to prevent embolism [1, 2]. However, there is plenty of circumstances, that surgical valve replacement is not feasible, sometimes due to contraindications or serious comorbidities and also, when the patient is not willing to undergo major surgery. There

are reports, that in such cases only 50% of patients undergo surgical repair [3–5]. Interestingly, to the best of our knowledge, there is scarce information in the literature, how to deal with such cases and what might be the outcome.

Case 1

A 58-year old patient was admitted to intensive care unit under emergency conditions due to septic shock that developed within few hours. He was hyperpyretic, strongly catecholamine dependent and non-invasive ventilation as well as hemofiltration were implemented. The patient's history included replacement of aorta ascendens and the aortic valve in 2013 due to 5.7 cm measuring aneurysma of aorta ascendens and severe insufficiency of the aortic valve. In addition, comorbidities included severe obesity with a body mass index of 49.4 (height 184 cm, body weight 167 kg), obesity hypoventilation syndrome (daytime hypercapnia and sleep disordered breathing), chronic renal failure (GFR 47 ml/min/1.73 m²), arterial hypertension and type II diabetes mellitus. A transesophageal echocardiography (TEE) on admittance revealed a 10 mm measuring structure on the anterior medial leaflet of the insufficient mitral valve, highly suspicious for endocarditic vegetation, and a 17 mm paraprosthetic abscess at the base of the aorta ascendens

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Fig. 1 Mid-esophageal long axis view, with vegetation at the anterior mitral leaflet (blue arrow) and paraprosthesis abscess in the aortic root (red arrow)

prosthesis (Fig. 1). After 2 days, three blood cultures were positive for methicillin-susceptible *Staphylococcus aureus*, therefore, initial empiric antibiotic therapy consisting of vancomycin, rifampin and piperacillin/tazobactam was deescalated to flucloxacillin and clindamycin. The patient's condition improved within the first few days and his case was discussed in the weekly organized heart team. Considering the diagnosis of two-valve-endocarditis including the prosthesis of the aorta ascendens and the high risk profile of his comorbidities and accepting the definitive decision of the patient not to undergo surgery, it was decided to treat the patient with appropriate antibiotics and supportive care. After 2 weeks of antibiotic therapy consisting of flucloxacillin and rifampin, the follow up blood cultures were sterile, however, fever and elevation of inflammatory parameters continued. There was no sign of major embolization or satellite abscess forming, that could explain prolongation of infection signs. Daptomycin was added to the previous regimen expecting synergistic effect of oxacillin and daptomycin based on experimental data [6]. This regimen was continued for 6 weeks and then switched to oral suppressive therapy including trimethoprim/sulfamethoxazole (TMP/SMX) 160 mg/800 mg tid combined with rifampin 450 mg bid. This regimen was chosen considering the need for biofilm activity of rifampin and data on long term tolerance of TMP/SMX in clinical practice [7]. 18 months later, the patient is still adherent on this antibiotic regimen without signs of the most serious notorious sideeffects of TMP/SMX and rifampin. During this period, there was no new episode of bacteremia due to *S. aureus*. A transthoracic echocardiography performed 16 months later showed a normal dimensioned left ventricle and sustained left ventricular function. In addition, the mobile structure at the anteromedial leaflet of the mitral valve was intense echogenic and unchanged in comparison to previous examinations. The patient reduced

Fig. 2 PET CT-scan with intense tracer activity along the right-sided subclavian graft and a part of arcus aortae

his body weight by 30 kg, is home mobile and is able to care for himself.

Case 2

A 71-year old female patient was admitted in August 2017 for suspected infected extraanatomical graft of the right arteria subclavia, that was implanted in 2007 after dissection of the native vessel. Her previous history included cardiothoracic surgery in 2003 with implantation of a valve-bearing aortic conduit due to aneurysm of the aorta ascendens and high grade insufficiency of the aortic valve. This implant was replaced in 2006 after development of aneurysms of the descending aorta including implantation of two stent grafts. In addition, a 2-chamber pacemaker was implanted in 2008 due to sick sinus syndrome and sinoatrial arrest.

On admission, the patient was febrile and laboratory tests showed highly elevated inflammatory parameters. *Streptococcus salivarius* was grown in two blood culture sets and additional imaging studies were performed. In transesophageal echo strands were found on the mechanical aortic prosthesis and the native mitral valve. No signs of abscess formation or severe valve dysfunction were detected. A positron-emission-tomography showed inflammatory signals surrounding the aortic valve prosthesis, intense tracer activity all along the right subclavian graft (Fig. 2), the

arcus aortae and the stents in the descending aorta. The patient denied the projected surgical procedure aiming to replace the aortic valve prosthesis, the foreign material of aorta ascendens, arcus aortae and the thoracic section of aorta descendens. Antibiotic treatment included ceftriaxone in combination with gentamicin, followed by vancomycin (30 mg/kg daily in 2 divided doses) and gentamicin because of ceftriaxon resistance of the pathogen (MIC 1 µg/ml). Penicillin G was not considered in this case based on a study, that 70.2% out of 52 clinical isolates of *S. salivarius* were intermediate susceptible to penicillin, but 89.5% susceptible to ceftriaxone [8]. Due to worsening renal function and considering the option of out-patient-parenteral-therapy, teicoplanin and clindamycin were used instead of vancomycin and gentamicin for 10 weeks. Both glycopeptides were monitored carefully by measuring their through levels, which were mostly in the non-toxic, therapeutic range. During this period, the renal function normalized, inflammatory parameter improved and there was no new episode of bacteremia. Considering the large volume of foreign material being involved in the infectious process and the denial of the patient for surgical replacement of the infected grafts, long term antibiotic suppression therapy was recommended. The patient was treated then with clindamycin 600 mg tid that was reduced to 600 mg bid due to elevation of transaminases. This therapy was continued for additional 5 months and was stopped unreflected by the patient after she was lost to follow up. 6 months later, the patient and her primary care physician could be interviewed. There were no clinical or laboratory signs of infection (blood cell count, C-reactive protein), which were taken three times, each 2 months apart.

Discussion

In these two reports we present a case of complicated endocarditis and a case of extensive aortic and subclavian graft infection involving large prosthetic material with clear indication for mayor surgery including replacement of all infected parts if feasible. In both cases, the extent of involved foreign material and comorbidities added to a high risk profile for surgery, so that both patients denied surgical intervention despite clear information about possible deleterious consequences. However, in both cases we noticed effective long term antibiotic suppression and acceptable tolerance of the antibiotic regimens. TMP/SMZ was chosen in the first patient for long term suppression, because its use is recommended in recent guidelines albeit in cases of uncomplicated right sided endocarditis [1] and a previous preliminary study using TMP/SMX in combination with clindamycin in 31 patients [9]. Moreover, a body of experience with long term use of TMP/SMX is available in other indications like nocardiosis and Whipple's disease or secondary prophylaxis after

Pneumocystis jiroveci pneumonia in HIV- patients. Rifampin was chosen in the first patient because of its biofilm activity in staphylococcal foreign body infections and plenty of data on long term treatment in patients with tuberculosis. Prolonged administration of clindamycin in the second case was chosen, because it was the only option left for oral antibiotic treatment and its tolerance in reduced dose. There is scarce information in the literature about duration of antibiotic therapy in cases of serious infections due to *S. salivarius*. A literature review published in 2011 reported durations between 14 days and 18 months in patients with intracerebral abscesses due to this microorganism [10]. To the best of our knowledge, there is no report on this topic in comparable cases of complicated PVE.

In conclusion, these two cases demonstrate, that individualized long term antibiotic suppressive therapy might be effective in selected patients with complicated PVE unfit or unwilling to undergo high-risk cardiothoracic surgical interventions.

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Compliance with ethical standards

Conflict of interest All authors state, that for this work, there was no funding and there is no conflict of interest.

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