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SUCCESSFUL TREATMENT OF ENDOCARDITIS WITH NONSPECIFIC PRESENTATION IN A KIDNEY TRANSPLANT PATIENT- CASE REPORT

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Abstract

Infective endocarditis (IE) is a serious complication in patients with transplanted kidney, leading to graft loss and a high mortality rate. We present a case of native valve endocarditis in a 51-year-old male with transplanted kidney that had atypical clinical course.

The patient experienced prolonged subfebrile temperature with paroxysmal arrhythmia and development of cardio-pulmonary insufficiency. Transthoracic echocardiography (TTE) set the diagnosis of aortic valve vegetation with severe aortic regurgitation and pulmonary edema. We failed to isolate a microbiological agent, but all blood cultures were taken under antibiotic therapy.

The patient was treated with surgical replacement of the native aortic valve with mechanical heart valve with significant clinical improvement. Ten days after the intervention, he was discharged with reduced markers of inflammation and proper function of the kidney graft. Immunosuppressive therapy was gradually reinstated.

One year later, the patient was clinically stable and with proper graft function. Early diagnostic and therapeutic intervention, particularly intensive antibiotic therapy and surgical management can preserve the patient and the kidney allograft.

Keywords: kidney transplantation, endocarditis, cardiac surgery.

Introduction

With the progress of transplantation and the increase in the number of transplanted patients, the complications, including infections, have also increased.

The usage of potent immunosuppressive therapy, diabetes mellitus, fibrotic changes of the native and mechanical heart valves as well as the previous use of A-VF or another vascular access for hemodialysis are among the risk factors for the occurrence of infections and endocarditis. Infective endocarditis (IE) is a serious complication that compromises the graft function and is a life-threatening condition [1].

It is substantially more common in renal transplant patients than in general population [2]. A high index of suspicion must be maintained for diagnosis of Infective endocarditis (IE) due to different clinical features, especially in patients with immunosuppressive therapy.

Case Report

We present a case of native valve endocarditis with unusual presentation in a 51-year-old male with transplanted kidney. The patient developed kidney failure due to autosomal dominant polycystic kidney disease and was on maintenance hemodialysis for 4 years with vascular access arteriovenous

fistula. A bilateral nephrectomy of the native kidneys was performed, followed by a kidney transplant from a living unrelated donor - his wife.

During the follow-up period, the patient had stable graft function, under standard triple immunosuppressive therapy with prednisolone, mycophenolate mofetil (MMF) and tacrolimus.

Shortly after transplantation, the patient developed drug-induced diabetes mellitus. Later he was diagnosed with benign prostatic hyperplasia and anxious-depressive syndrome. On one occasion he was treated for an abscess of the auricle.

Two months before admission to the hospital, the patient had a headache, malaise, neck pain, dizziness and occasionally fever. He was examined in a local hospital and treated with oral antibiotic therapy.

Due to the present symptoms, examinations and treatment were performed by an orthopedist, with mobilization of the neck. An infectious agent was not isolated.

One week prior to admission, the patient had tooth extraction and took prophylactic antibiotic therapy.

In spite of that, symptoms like malaise, neck pain, dizziness, and febrility were intensified. A CT scan of the head had been made, with a finding of thickening of the sinuses; chest X- ray showed paracardial reticulonodular shadowing on the right lobe with an increase in leukocytes and C-reactive protein (CRP) in the blood. At that point, he was hospitalized at the Department of Nephrology.

During hospitalization, he was afebrile, mildly hypotensive and without need for oxygen in the first six days. From the laboratory investigations, an increase in serum creatinine and CRP was observed (Table 1). No microbiological agents from urine and blood were isolated.

Serological tests for cytomegalovirus (CMV) and Epstein-Barr virus (EBV) were negative, and anti-HLA antibodies were not detected. Computed tomography scan of the brain was normal. On two occasions, paroxysmal atrial fibrillation was registered on the electrocardiogram (ECG).

The treatment included parenteral antibiotics with cephalosporin and quinolone, partial reduction of the immunosuppressive therapy, as well as therapy by a cardiologist.

On the seventh day, the condition worsened with shortness of breath, a drop in oxygen saturation and the appearance of left-bundle branch block (LBBB). The patient was transferred to the University Clinic for Cardiology.

With a transthoracic echocardiography (TTE), a hyperechoic mobile formation of 0.6 x 0.8 cm size was confirmed, indicating aortic valve vegetation (Fig.1). CT scan of the lungs showed pulmonary edema.

Further deterioration of the situation was noted, followed by bradycardia, somnolence, cardiopulmonary resuscitation and occasional need for mechanical ventilation. In the next few days and after stabilization of the condition, he was transferred to the UC for Cardiac Surgery.

A surgical replacement of the native aortic valve with mechanical heart valve (St. Jude size 19 mm) was performed. Intraoperative transesophageal ultrasonography confirmed normal flow through a surgically implanted mechanical aortic prosthesis.

The patient was treated with antibiotics and other supportive therapy and after 10 days he was discharged with reduced markers of inflammation and proper function of the kidney graft. Immunosuppressive therapy was gradually reinstated. One year later, the patient was clinically stable and with proper graft function.

Table 1. Chronological display of laboratory parameters during hospital treatment.

	nephrology	22.sep	26.sep	27.sep	cardiology	27.sep	29 sep	30 sep	Cardiosurgery	03.oct	05.oct	05.oct	06.oct	07.oct	08.oct	11.oct
Hgb		110 g/L	104 g/L	104 g/L		117 g/L	118 g/L	120 g/L		122 g/L	100 g/L	86 g/L	**77 g/L**	89 g/L	132 g/L	79 g/L
Rbc		4.7 10^12/L	4.5 10^12/L	4.4 10^12/L		5.1 10^12/L	5.2 10^12/L	5.2		5.4 10^12/L	4.3 10^12/L	3.2 10^12/L	**2.9 10^12/L**	3.3 10^12/L	5.0 10^12/L	2.9 10^12/L
Wbc		14 10^9/L	13 10^9/L	15 10^9/L		**20 10^9/L**	**27 10^9/L**	**21 10^9/L**		13 10^9/L	10 10^9/L	27 10^9/L	7.8 10^9/L	11 10^9/L	9.9 10^9/L	7 10^9/L
Urea		5.4 mmol/L	7.8 mmol/L	**12 mmol/L**		**12.2 mmol/L**	16.6 mmol/L	12.9 mmol/L		10 mmol/L	8 mmol/L	7 mmol/L	5.8 mmol/L	4.5 mmol/L	4 mmol/L	2 mmol/L
Creatinine		72 umol/L	92 umol/L	**139 umol/L**		**139 umol/L**	102 umol/L	70 umol/L		96 umol/L	88 umol/L	77 umol/L	85 umol/L	79 umol/L	75 umol/L	59 umol/L
Uric acid				**515 umol/L**												
Glucose			12 mmol/L	6.7 mmol/L		9.8 mmol/L						5.5 mmol/L		3.5 mmol/L		5.2 mmol/L
K		4.2 mmol/L	4.3 mmol/L	4.3 mmol/L		4.8 mmol/L	4.1 mmol/L	3.8 mmol/L		3.9 mmol/L	4.3 mmol/L	4.2 mmol/L	3.9 mmol/L	3.9 mmol/L	4.1 mmol/L	3.8 mmol/L
Na		136 mmol	137 mmol	135 mmol		137 mmol/L	140 mmol	139 mmol		131 mmol	134 mmol	139 mmol	140 mmol	142 mmol	142 mmol	138 mmol

		/L	/L	/L			/L	/L		/L	/L	/L	/L	/L	/L	/L
CRP		**77 mg/L**	**119 mg/L**	**89 mg/L**		**99 mg/L**	**53 mg/L**	**63 mg/L**		**67 mg/L**	**59 mg/L**	**31 mg/L**	**83 mg/L**	**170 mg/L**	**176 mg/L**	**47 mg/L**
Albumins				35 g/L						26 g/L	24 g/L	22 g/L	25 g/L	24 g/L	24 g/L	22 g/L
Total proteins				65 g/L						56 g/L	51 g/L	**41 g/L**	43 g/L	50 g/L	54 g/L	52 g/L
CK-MB				13 U/L												
CK				48 U/L						127 U/L			216 U/L			
LDH				208 U/L						303 U/L	299 U/L	**440 U/L**	289 U/L	288 U/L	275 U/L	246 U/L
Troponin				797 ng/L		705 ng/L	627 ng/L			326 ng/L			**1375 ng/L**			
Procalcitonin										**1.38 ng/ml**						0.22 ng/ml

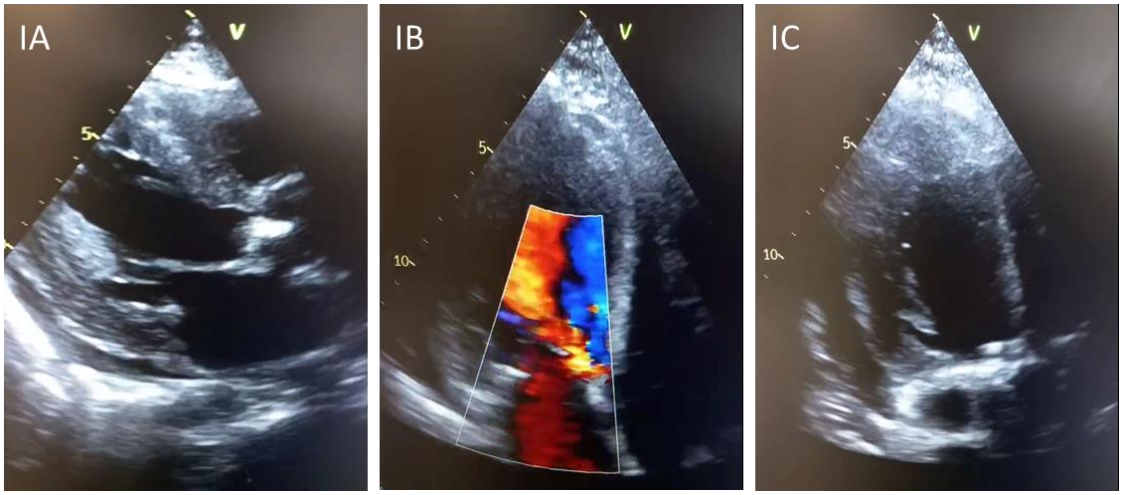

Figure 1. IA: Parasternal long axis showing thickened aortic valve cusps with dense hyperechoic structures protruding on both aortic and ventricular side of the valve. IB: 3-chamber view with Color Doppler showing severe aortic regurgitation. IC: 3-chamber long axis view showing dense hyperechoic mass on ventricular side of aortic valve.

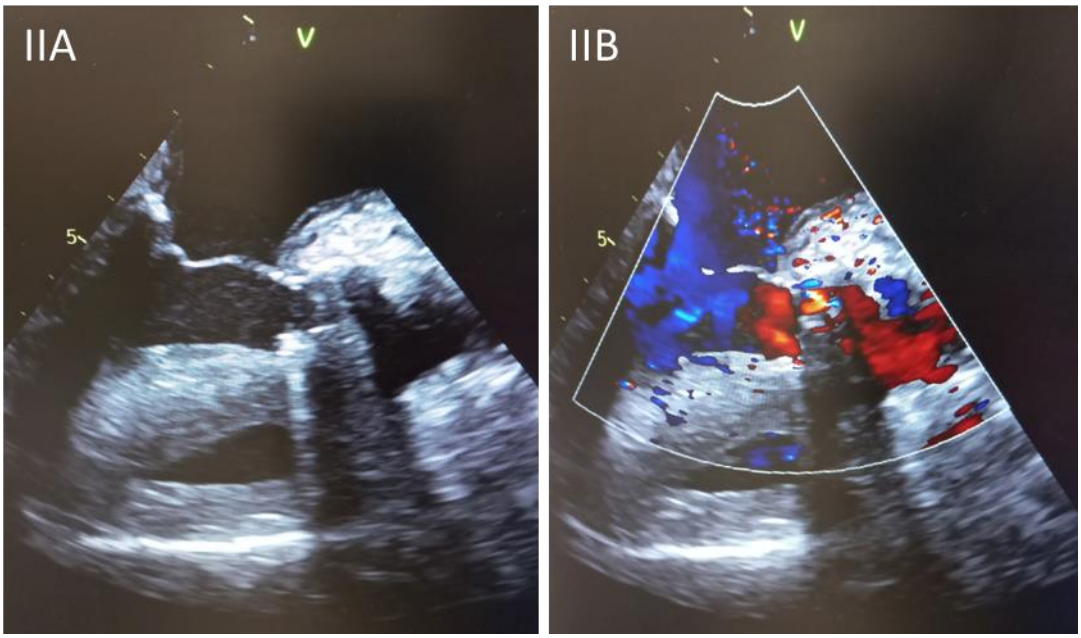

Figure 2. IIA: Intraoperative transesophageal view at 120 degree showing well seated aortic medical prosthesis. IIB: Intraoperative transesophageal view at 120 degree with superimposed Color Doppler showing normal flow through a surgically implanted mechanical aortic prosthesis.

Discussion

Endocarditis is a life -threatening inflammation of the inner lining of the heart's chambers and valves. Symptoms of endocarditis can vary from person to person. Typical clinical presentation goes with: aching joints and muscles, chest pain when you breathe, fatigue, flu-like symptoms, such as fever and chills, night sweats, shortness of breath, swelling in the feet, legs or belly, a new or changed whooshing sound in the heart.

Patients with a transplanted kidney are more susceptible to any kind of infections and to the development of IE, compared to the general population [3,4].

Continuous immunosuppressive therapy, which modulates the immune response in order to avoid rejection of the organ, is indicated as the greatest risk factor for the development of IE. Hemodialysis treatment before transplantation, as well as the presence of A-VF or the use of catheters as vascular accesses for hemodialysis, due to frequent cannulations can be a source of bacteria and a risk factor for Infective endocarditis (IE). The presence of concomitant disease such as diabetes mellitus also increases the risk and factors such as poor dental hygiene and tooth decay, which are valid for the general population, but are also valid for kidney transplant patients [5,6,7].

In the case we have presented, four risk factors for Infective endocarditis (IE) were present.

The development of the clinical presentation can often be slow and nonspecific, resembling any other type of infection and making the diagnosis difficult in kidney transplant patients. The classic signs and symptoms of Infective endocarditis (IE) may be absent, which was the reason for doubting Infective endocarditis (IE) even more in the case that we have presented [8,9].

The most common microbiological causative agent is *Staphylococcus*. In the population with a transplanted kidney, *Enterococcus* was also isolated quite often, which is explained by the disruption of the normal intestinal flora due to the immunosuppressive therapy and the frequent use of antibiotics. However, in 2.5-31% of cases with Infective endocarditis (IE) in the general population, the

microbiological causative agent cannot be isolated, which is explained by the fact that blood for blood cultures is taken with already started antibiotic therapy [10,11,12]. In our case, we failed to isolate a microbiological agent because all blood cultures were taken under antibiotic therapy.

The presence of vegetations or abscesses on the native heart valves, but also on the artificial valves, is one of the major criteria for the diagnosis of Infective endocarditis (IE) according to Duke's criteria. Vegetations of the aortic valve are more often described.

The gold standard for detecting changes such as vegetations or abscesses in patients with high suspicion for Infective endocarditis (IE) is transesophageal echocardiography (TEE) with a sensitivity of 85-95% in cases highly suspicious for Infective endocarditis (IE), with a negative finding on TTE. But in cases where the vegetation is confirmed with TTE it may be sufficient for to suspect Infective endocarditis (IE) as a possible diagnosis [13].

The severe general condition of our patient, complicated by heart rhythm disturbance, cardiac decompensation, drop in oxygen saturation and need for occasional mechanical ventilation and TTE and detection of vegetation on aortic valves were sufficient for establishing the diagnosis.

In kidney transplant patients, it is sometimes necessary to modify Duke's criteria for IE, with the aim of faster diagnosis and rapid treatment, which is the basis for the survival of the graft and the patient [14].

The treatment of Infective endocarditis (IE) consists in reducing or stopping part of the immunosuppressive therapy and including an appropriate antibiotic according to an antibiogram or an antimycotic, depending on the causative agent. In certain patients, there is an indication for treatment with surgical replacement of the valves [15].

With the development of cardiac surgery, not only the treatment and recovery of the patient but also the survival of the graft were achieved [16].

The same principles of treatment were applied to our patient. Due to the characteristics of the vegetation as well as the severe clinical picture, an indication for surgical treatment was established. The patient was cured, but also the function of the graft was restored.

Conclusion

The presentation of infective endocarditis in patients with immunosuppressive therapy may also have a delayed development of the clinical picture. This condition not only compromises graft function, but is also a life-threatening condition. With the development of cardiac surgery, there is an excellent opportunity to quickly and effectively treat Infective endocarditis (IE) and restore the normal function of the graft.

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