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Transcatheter Closure Combined with Antibiotic Therapies for Patients with Infective Endocarditis and Congenital Heart Disease

Boli Ran, Minfeng Li, Yeqing Li, Yang Lin, Weimin Liu, Qiulin Luo, Yongxin Fu, Qianmei Tang, Ya Yang and Yunfei Pu*

Department of Cardiology, Third People's Hospital of Chongqing, China

*Corresponding author: *Yunfei Pu, Department of Cardiology, Third People's Hospital of Chongqing, Chongqing 400014, P. R. China, Tel: +86-023-63539259, E-mail: 12944048@qq.com*

Abstract

Objective: To explore a new therapy for patients with certain subtypes of infective endocarditis.

Methods: The experience of transcatheter closure combined with antibiotic therapies at our cardiovascular center was retrospectively analyzed in 5 cases of infective endocarditis with congenital heart disease. Transcatheter closure was performed at least 7 to 10 days after the patient's body temperature had recovered normal following effective antibiotic therapies, and after cardiac vegetations were not detected by echocardiography.

Results: Patients' age ranged from 8 to 24 years, with a median age of 14.4 years. All 5 patients had an insidious onset of mild to moderate fever and malaise with mild anemia. Blood culture of bacteria was positive for Gram-positive cocci (staphylococcus and streptococcus) in 4 patients. All 5 patients had confirmed underlying heart disease: 4 patients with patent ductus arteriosus (PDA) and 1 with peri-membranous ventricular septal defect (VSD). Vegetations were detected in tunica intima of the main pulmonary arteries of the two patients with PDA, and on the ventricular aspect of tricuspid valve (3 mm × 4 mm in size) of another patient with VSD. All defects were successfully occluded without causing any complications. During the follow-up period (19.6 ± 14.4 months), no residual shunt or no device embolization or recurrence of cardiac vegetation was observed in any of the patients.

Conclusions: Transcatheter interventional therapy may be a useful method for certain patients with infective endocarditis and congenital heart disease following intravenous application of effective antibiotics.

Keywords

Infective endocarditis, Congenital heart disease, Transcatheter closure, Antibiotic therapy, Interventional therapy

Introduction

Infective endocarditis is one of the most dreadful complications of uncorrected congenital heart disease [1]. It occurs less frequently in children, adolescents and adults, but has a mortality of 11%~20% [2-4]. The classic therapeutic regimen for infective endocarditis includes large doses of effective antibiotics combined with curative or palliative cardiovascular surgery [3,5]. Transcatheter closure is now considered by most cardiologists to be a treatment of choice for patients with indicated cardiac defects or abnormal communications [2-4]. However, it is still unknown whether transcatheter closure is applicable to patients with infective endocarditis and congenital defects or abnormal communications. Here we reported the therapeutic experience of combining antibiotic therapies with transcatheter closure at our cardiovascular center in treating 5 patients with infective endocarditis and congenital ventricular septal defect or patent ductus arteriosus, and analyzed the clinical features and therapeutic outcomes of the patients retrospectively.

Materials and Methods

Clinical data of patients with infective endocarditis and uncorrected congenital heart disease treated from November 2004 to August 2007 were analyzed retrospectively. Five patients (3 males, 2 females) aged from 8 to 24 years (mean age, 14.4 ± 6.4 years) were involved in the present study.

Infective endocarditis was diagnosed according to the Duke criteria [6]. According to the Duke criteria, typical microorganisms for infective endocarditis must be detected upon at least two separate blood cultures, or be detected persistently upon all blood cultures; body temperature must be ≥ 38.0 °C; vascular and immunologic findings should support endocardial involvement. Culture positivity was detected in recurrent samples. A definite clinical diagnosis of infective endocarditis requires 2 major criteria, 1 major and 3 minor criteria, or 5 minor criteria. All 5 patients were accorded with the to the Duke criteria and confirmed to have congenital heart disease. Two-dimensional and color Doppler echocardiography revealed patent ductus arteriosus in 4 cases and ventricular septal defect in 1 case. According to aortography or ventriculography, the size of patent ductus arteriosus was estimated to be 6~18 (14.0 ± 5.6) mm and that of ventricular septal defect to be 4 mm.

Large doses of penicillin were administered intravenously in patients suspected of infective endocarditis immediately after blood examples for bacterial culture had been collected at least 3 times. Initial antibiotics were replaced with norvancomycin or a combination of 2 antibiotics according to the susceptibility of the isolated bacterial strain and the change of body temperature.

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Table 1: Demographic and clinical features of patients with endocarditis and congenital heart diseases.

Patients	1	2	3	4	5
Sex/Age (years)	M/8	M/9	M/24	F/16	F/15
Underlying disease	PDA	VSD	PDA	PDA	PDA
Organisms	*Staphlycoccus epidermidis*	-	*Streptococcus viridans*	*Staphylococcus aureus*	*Staphylococcus aureus*
Site of vegetation on TTE	MPA	TV	-	MPA	-
Initial antibiotics	Penicillin	Penicillin	Penicillin	Penicillin	Penicillin
Alternative antibiotics	Norvancomycin	Penicillin + aminoglycosides	Penicillin	Penicillin + cefotaxime	Norvancomycin
Duration of antibiotics (days)	43	36	52	44	45
PAP mmHg	30/8(20)	35/11(23)	49/11(30)	38/10(25)	40/13(26)
Size of occluder	8/6	6	14/16	16/18	18/20
Complications	-	Tricuspid regurgitation	-	-	-
Time of follow-up (months)	45	16	15	12	10

PDA: Patent Ductus Arteriosus; VSD: Ventricular Septal Defect; TV: Tricuspid Valve; MPA: Main Pulmonary Artery; TTE: Transthoratic Echocardiography; PAP: Pulmonary Arterial Pressure.

After body temperature had turned normal for at least 7 to 10 days, blood cultures of bacteria were negative for at least 3 times and after echocardiography did not reveal cardiac vegetations, transcatheter closure was performed under local or combined anesthesia. After the establishment of the arteriovenous wire loop, a patent ductus arteriosus or ventricular septal defect occluder was deployed carefully via the antegrade venous approach in all patients. Antibiotics were intravenously administered continuously after intervention for 4 to 6 weeks, or until blood cultures of bacteria were negative for at least 3 times.

Follow-up visits were carried out regularly. An ultrasonic doctor performed transesophageal ultrasonic inspections, and another physician observed the patients' symptoms and physical signs. Both of them did not know the clinical outcomes of the patients.

Results

Clinical and laboratory findings

The demographic and clinical features of the 5 cases of infective endocarditis and congenital heart disease are shown in table 1. Patients' age ranged from 8 to 24 years, with a median age of 14.4 years. Four patients aged < 16 years. The male/female ratio was 3/2.

The time from the onset of symptoms to the diagnosis of infective endocarditis was 97 ± 32 (63-132) days. All 5 patients had an insidious onset of mild to moderate fever and malaise with mild anemia. Other symptoms included anorexia in 3 cases, weight loss in 2 cases, night sweats in 3 cases, and skin rash in 1 case. Heart failure was not observed in the 5 cases. Other clinical findings included splenomegaly in 3 cases and elevated erythrocyte sedimentation rates (> 60 mm/h) in all 5 cases. Upon admission, two patients had haematuria and one patient presented with subungual hemorrhage. In addition, rheumatoid factor was found positive in 4 patients.

All 5 patients had confirmed underlying heart disease upon admission, but without significant clinical manifestations related to heart abnormalities. Four patients had patent ductus arteriosus and one patient had peri-membranous ventricular septal defect. Intra- or extracardiac vegetations were detected in 3 patients by transthoracic echocardiography. Vegetations were seen in tunica intima of the main pulmonary artery of the two patients with patent ductus arteriosus, and the other was found to be 3 mm × 4 mm on the ventricular aspect of tricuspid valve of the patient with ventricular septal defect. Meanwhile, severe tricuspid regurgitation was seen in the patient with infective endocarditis and ventricular septal defect. Blood cultures of bacteria were positive in 4 patients, and staphylococcus aureus (1 case), staphylococcus epidermidis (2 cases) and streptococcus viridans (1 case) were isolated. None of the 5 patients had heart failure, or cardiac arrhythmia.

Therapeutic outcomes

In the present study, the treatment with large doses of penicillin or penicillin and aminoglycosides and/or cefotaxime was effective in 3 patients, and the treatment with norvancomycin was effective in the other 2 patients. Intravenous administration of antibiotics lasted about 44 (36-52) days. All defects were occluded successfully without causing any complications. 14-20 mm patent ductus arteriosus occluders were used in the 4 patients with infective endocarditis and patent ductus arteriosus, and an 8 mm ventricular septal defect occluder was used in the patient with infective endocarditis and ventricular septal defect. Two patients developed mild fever (< 38.5 °C) within the first 2 days after procedure, without increases in white blood cells and neutrophils and their body temperature turned normal on the third day without administering special therapy.

The patients were followed up for 10 to 45 months, with a median duration of 19.6 ± 14.4 months. During the follow-up period, echocardiography showed neither residual shunt nor aortic regurgitation, and there was also no device embolization, or recurrence of cardiac vegetation in these patients. In the patients with infective endocarditis and ventricular septal defect, severe tricuspid regurgitation turned moderate 1 month after transcatheter closure and the condition kept stable for at least 16 months.

Discussion

Infective endocarditis occurs less frequently in children, adolescents and adults. Despite major advances in treating valvular heart disease, the in-hospital mortality (15-20%) and 1-year mortality (≃ 40%) for infective endocarditis (IE) has not improved even with modern antibiotics and surgical therapy [2]. Staphylococci (30%~50%) or streptococci (20%~35%) were the most common pathogenic microorganisms for infective endocarditis. Fungi account for up to 10% of infections in drug addicts. Rarely, coxiella burnettii and chlamydia are pathogens [7]. In the present study, staphylococcus or streptococcus was isolated from four patients, which is in agreement the literature. The spectrum of infective endocarditis depends on the infective organism, and it is challenging to identify and manage infective endocarditis clinically. However, insights into relevant pathologic features can be useful. The risk factors for in-hospital mortality during infective endocarditis in patients with congenital heart disease were analyzed by stepwise logistic regression in Japan [8]. In the present study, the four patients with infective endocarditis had no such risk factors except that one of them was infected with Staphylococcus aureus. The small vegetations were found in the right heart (the tricuspid valve and main pulmonary artery) in 3 patients.

Predisposing factors of infective endocarditis differ among populations. In children, congenital heart disease is the major predisposing factor (50%~75%), which is followed by rheumatic heart disease (12%) or a structurally normal heart (14%~40%) [9]. In adolescents and adults [7], risk factors for infective endocarditis include a previous cardiovascular operation (51.9%), the use of foreign materials (38.5%), dental or other surgical procedures without recommended antibiotic prophylaxis (25.0%), or cardiac catheterization (5.8%). Infective endocarditis was also seen in those undergoing tattooing and intravenous drug abusers. Currently, patients with infective endocarditis are older and have a higher incidence of underlying heart disease, degenerative valve disease, and prosthetic valve-related infective endocarditis than before. In 2007, the AHA further listed cardiac conditions associated with the highest

risk of an adverse outcome from infective endocarditis [10]. Infective endocarditis is uncommon in patients with surgically corrected septal defects or lesions of the right heart. However, the incidence of infective endocarditis in patients with uncorrected congenital heart disease or left heart lesions is still high, even in those having undergone surgical manipulations of the aortic valve or aorta. In our study, the 5 patients had uncorrected congenital defects or abnormal communications on the left heart: 1 with peri-membranous ventricular septal defect and 4 with patent ductus arteriosus.

Patients with infective endocarditis have a broad spectrum of clinical manifestations, and the incidence of cardiac or extracardiac complications remains constantly high [7,11]. Therefore, early diagnosis and appropriate therapy has to be emphasized for infective endocarditis. The most common symptoms of infective endocarditis are fever, petechiae, malaise, embolic events, and a new or changing murmur. Fever is usually of low grade. Such classic signs as Roth spots, Osler's nodes, Janeway lesions, and splinter hemorrhages are all uncommon. There are still other symptoms or physical signs, including splenomegaly, heart failure, gastrointestinal symptoms, and arthralgia. The enlarged spleen is usually nontender. Arthralgia usually involves large joints. Additionally, laboratory findings are not very sensitive. Possible laboratory abnormalities include elevated erythrocyte sedimentation rates, anemia, and hematuria. In our study, all 5 patients had an insidious onset of mild to moderate fever and malaise with mild anemia. If patients with uncorrected or incompletely corrected cardiac anomalies developed mild fever and anemia with malaise, and had a new or changing cardiac murmur, the diagnosis of infective endocarditis should be considered, and blood cultures of bacteria and echocardiographic examination should be carried out as early as possible. Echocardiography may be valuable in assessing vegetations and complications of infective endocarditis [12].

Intravenous administration of large doses of effective antibiotics combined with curative or palliative surgery acts as a standard therapeutic method for infective endocarditis. It has been emphasized that cardiovascular surgery is carried out as early as possible in recent two decades. According to a stepwise logistic regression analysis, surgical intervention is a predictive factor for lower in-hospital mortality [8]. Therefore, surgical intervention should always be considered for patients at high risk of in-hospital mortality. However, it is not clear whether surgical intervention is necessary for those low-risk patients with infective endocarditis who have no heart failure or systematic symptoms, but have only small solitary vegetations in the right heart, or ultrasonographically invisible vegetations. The combinations of noninvasive imaging, interventional catheterization techniques, and surgical therapy have brought daily miracles into the lives of most children born with cardiac anomalies. There is still much to be done and this century portends great advances for the understanding of the causation and potential prevention of certain defects as well as the possibility of targeted therapy for heart failure, pulmonary vascular disease, vessel and chamber growth, and rhythm disorders [13]. We reported the clinical outcomes of transcatheter closure used in combination with effective antibodies in the 5 cases of infective endocarditis and congenital heart disease. Transcatheter closure was performed at least 7~10 days after the patients' body temperature turned normal and after the vegetations became invisible under ultrasonography following a successful treatment with vancomycin, or penicillin or penicillin + Cefotaxime/aminoglycoside. All defects were occluded successfully by using 1 ventricular septal defect occluder and 4 patent ductus arteriosus occluders, and neither residual shunt nor aortic regurgitation was seen by echocardiography upon discharge and during the follow-up of 10 to 45 months. There was no device embolization or recurrence of cardiac vegetation in any of the patients. In the patient with infective endocarditis associated with ventricular septal defect, severe tricuspid regurgitation turned moderate at 1 month after transcatheter closure and the condition kept stable for at least 16 months. The results suggest transcatheter intervention to be suitable for patients with infective endocarditis, but without ultrasonographically visible vegetations, or for those with small solitary vegetations in the right heart.

According to the 2007 AHA guidelines [10], cardiac conditions are associated with the high risk of infective endocarditis, and incompletely corrected hemodynamics and the damaged endocardium are emphasized to be two key factors. Therefore, complete correction of haemodynamics could prevent the endocardium from damage and help improve infective endocarditis. Both cardiovascular surgery and transcatheter intervention could result in completely normal hemodynamics for certain patient subsets with ventricular septal defect, patent ductus arteriosus and pulmonary valvular stenosis [13,14]. It is well known that vegetative lesions develop along the edges of valve closure on the ventricular aspect of the aortic valve, the atrial surface of atrioventricular valves, the right ventricular endocardium and the surface of main pulmonary artery or pulmonary valves [15]. Vegetations can be friable and frequently embolize to the spleen, kidneys, and left ventricle - often before clinical recognition of the disease. In our study, transcatheter closure was performed only after the vegetations became invisible under ultrasonography (i.e., < 2 mm) in the 5 patients with infective endocarditis. It is well known that vegetations in the right heart is safer than those on the left heart, because small pulmonary emboli are easily phagocytized by mononuclear macrophages which are abundant in the lungs, and will not cause obviously abnormal haemodynamics. In our study, mild fever (< 38.5 °C) recurred in 2 patients within the first 2 days after procedure, but no other symptoms (e.g., poor appetite and malaise) or findings (increased neutrophils, hematuresis, cough, etc) were observed, suggesting the safety of transcatheter closure used in combination with sufficient antibodies.

The underlying causes of this study maybe include: 1) palliative cardiovascular surgery is often performed to correct right heart abnormalities, and a good long-term outcome can be obtained from only one normal valve, either the tricuspid or the pulmonary valve; 2) small vegetations or ultrasonographically invisible vegetations only result in mild pulmonary embolism; 3) completely corrected hemodynamics can prevent endocardial damages and thus help reduce the mortality of infective endocarditis.

The results demonstrate that transcatheter intervention may be useful in some patients with infective endocarditis and congenital heart disease after the intravenous application of effective antibiotics.

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