Significant advancements in the care of children with cardiac valve disease over the past 15 years have led to the increasingly common use of percutaneous transcatheter valve implantation as an alternative to surgical replacement in selected patient populations. Although the transcatheter approach has several advantages, this approach and the valves used are not without complications. Bacterial endocarditis is a known and concerning complication after transcatheter pulmonary valve replacement (TPVR). Most reported cases have involved organisms that are common etiologic agents of bacterial endocarditis and are readily identified via blood culture. However, culture-negative endocarditis in the setting of TPVR has not been well described. We present our experience with one afebrile teenager with culture-negative, serology-positive Bartonella henselae endocarditis of a Melody valve 18 months after TPVR for management of tetralogy of Fallot. The teen was successfully managed with long-term antibiotic therapy followed by surgical replacement of the valve. To our knowledge, this is the first reported case of culture-negative endocarditis of a Melody TPVR in the absence of fever. This report discusses the importance of considering culture-negative endocarditis in the differential diagnosis of an afebrile patient with TPVR presenting with constitutional symptoms and valve dysfunction, particularly in the primary care setting. It is anticipated that with an increase in the successfully aging population of children who have undergone cardiac repair, the evaluation of these patients will become an increasingly important and common task for the community pediatrician.

CASE REPORT

A 14-year-old boy with a history of tetralogy of Fallot and a complete atrioventricular septal defect was initially palliated with a modified Blalock-Taussig shunt and subsequently received an abstract

Transcatheter pulmonary valve replacement (TPVR) represents an important advancement in the management of right ventricular outflow tract (RVOT) disease, as it allows for avoidance of an open surgical repair. Infective endocarditis (IE) is a known complication after TPVR; thus far, there have been fewer than 50 reported cases with very few reported in pediatric patients. The causative organism is typically easily isolated via blood culture.1 To our knowledge, there have been 2 documented cases of febrile patients with culture-negative endocarditis in the setting of TPVR; in both cases, the causative organism was Bartonella henselae.2–3 This is the first documented case of culture-negative endocarditis in an afebrile patient.

aortic homograft right ventricle to pulmonary artery conduit. He underwent Melody TPVR at age 12 due to conduit stenosis and regurgitation, and was clinically well with stable echocardiograms for ~18 months. He then presented to outpatient cardiology clinic with a 5-month history of fatigue, shortness of breath, light-headedness, intermittent perioral cyanosis with exertion, and a 7-pound weight loss. He was afebrile during this time period. He had 3 domestic cats from which he frequently sustained scratches and bites. His physical examination did not reveal any stigmata of endocarditis. Laboratory studies were significant for a mild microcytic anemia, mild thrombocytopenia, markedly elevated C-reactive protein and erythrocyte sedimentation rate, and a normal procalcitonin. Transthoracic echocardiography (TTE) and transesophageal echocardiography demonstrated a markedly increased gradient across the Melody valve (Medtronic Inc, Minneapolis, MN) with thickening of the valve leaflets without visualization of a discrete vegetation. A peripheral blood culture was obtained and he was hospitalized for further evaluation and management.

An extensive laboratory evaluation was significant for elevated lactate dehydrogenase and rheumatoid factor with low C3 and C4 levels. Multiple antibody studies to evaluate for autoimmune disease were negative. Immunoglobulin levels were significant for elevated immunoglobulin (Ig)G and IgM. A urinalysis was normal with the exception of elevated urine protein in the setting of normal renal function. Serial peripheral blood cultures were obtained and were held for 14 days to evaluate for fastidious organisms; all remained negative. Given the presence of cats in the patient’s home, B henselae antibody titers were sent. The patient met 2 minor modified Duke criteria for IE (predisposing heart condition and elevated rheumatoid factor). As an alternative diagnosis could not be identified, empirical treatment of culture-negative endocarditis was initiated on hospital day 4 with a regimen of ceftriaxone, doxycycline, and synergistic gentamicin. On hospital day 5, the B henselae serologies returned highly positive, with an IgM titer of 1:32 (reference < 1:16) and an IgG titer of >1:1024 (reference <1:64). A peripherally inserted central catheter was placed for intravenous antibiotic therapy and the patient was discharged on hospital day 6. A repeat TTE before discharge was unchanged.

An improvement in exercise tolerance, shortness of breath, appetite, and energy level was noted <1 week after initiating antibiotic therapy; however, this did not recover to his previous baseline. C-reactive protein and erythrocyte sedimentation rate demonstrated a downward trend. Repeat TTE 3 weeks after discharge revealed an unchanged degree of RVOT obstruction and Melody valve appearance. The patient and family agreed with the recommendation for surgical valve replacement. He completed a total of 2 weeks of gentamicin, 6 weeks of ceftriaxone, and 8 weeks of doxycycline before surgical repair.

After uncomplicated removal of the Melody valve (Fig 1), a 23-mm right ventricle to pulmonary artery pulmonary homograft was placed. Cultures obtained from the surgical specimen demonstrated no organisms on Gram stain; anaerobic, fungal, and acid-fast bacteria cultures were negative. Pathology of the Melody valve demonstrated dystrophic calcification and suppurative inflammation with degeneration of the surrounding vessel wall. B henselae was subsequently detected in the excised specimen via 16S rRNA and ribC polymerase chain reaction (PCR). The discharge TTE demonstrated a mild RVOT gradient with normal right-sided cardiac function. His doxycycline course was continued on discharge for an additional 6 months of therapy with serial Bartonella titers followed as an outpatient.

**DISCUSSION**

The published data on IE after TPVR are limited, and the data on pediatric cases are even more scant. In the 1- to 4-year postoperative period, IE after TPVR has been documented in <3% of patients; however, this may be a significant underestimation given the lack of long-term follow-up.
data in this population. In one recent prospective study, 5 (6%) of 86 patients who underwent Melody TPVR from 2009 to 2012 developed IE after 2.6 to 28.0 months of follow-up. All cases had a history of fever and demonstrated a sudden increase in RVOT gradient on echocardiogram. The same authors published a review of TPVR-associated IE in which they proposed that a sudden increase in RVOT gradient should be included as a major criterion in the modified Duke criteria in this setting. Another study raised concern for a potential increased risk of IE in the bovine jugular vein graft population, as it demonstrated a 98.7% IE-free survival rate in a surgical homograft cohort compared with 84.9% in a Melody valve cohort and 87.8% in a surgical Contegra (Medtronic Inc) cohort over a 5-year period.

In a 2014 review of Melody valve IE, most reported cases of IE in this population involved *Staphylococcus* and *Streptococcus* species. More than half of the patients were managed via bioprosthesis explantation in addition to antibiotic therapy.

Culture-negative endocarditis has been reported only twice previously in the setting of a Melody valve; both cases were due to *B henselae*. *B henselae* is most commonly known as the etiologic agent of "cat scratch disease," which involves fever and lymphadenitis. *Bartonella* endocarditis was first described in 1993 and has since been recognized as a significant cause of culture-negative endocarditis; however, <10 pediatric cases have been reported. Patients typically present with subacute and nonspecific symptoms, including fever, fatigue, and weight loss. *Bartonella* species are fastidious gram-negative bacteria requiring specific laboratory conditions for optimal growth, often involving specialized agar with cultures held for a minimum of 21 days. The most effective diagnostic strategy has been a combination of serology and direct PCR from valve specimens when available. One study demonstrated that PCR testing for *Bartonella* on cardiac valve tissue was positive in >95% of patients with *Bartonella* endocarditis, despite the fact that 60% of patients were already treated with antibiotics. Recommended therapy for suspected *Bartonella* endocarditis varies, but typically includes ceftriaxone plus gentamicin with or without doxycycline.

The first case of *Bartonella* endocarditis in the setting of TPVR was reported by Atamanyuk et al. They reported a 15-year-old boy with a repaired truncus arteriosus who developed fever, abdominal pain, splenomegaly, anemia, and increased echogenicity of the valve leaflets on TTE, suggestive of vegetations. Blood cultures were negative and serology was positive for *Bartonella quinata* and *B henselae*. He underwent successful RVOT reconstruction with a pulmonary homograft, and *B henselae* was subsequently identified via PCR of the excised valve tissue. The second case of *Bartonella* endocarditis after TPVR was reported by Georgievskaya et al. They reported a 21-year-old male veterinary technician with a history of complex congenital heart disease status post repair and previous streptococcal endocarditis of the RVOT who presented with a history of fever, weight loss, and abdominal pain. An increased gradient across the Melody valve was noted without evidence of vegetations. Blood cultures were negative and serologies for *Bartonella* were positive. After management with antibiotics and surgical removal of the valve, *B henselae* was identified on Warthin-Starry silver stain and *B henselae* immunostain. Diagnostic evaluation of IE after TPVR may be aided by additional advanced imaging techniques. The use of intracardiac echocardiography (ICE) to further define vegetations not easily seen on transesophageal echocardiogram may assist in determining if surgical explantation is warranted. In our case, similar to other cases in the literature, surgical explantation was deemed to be necessary due to the persistent symptoms and TPVR dysfunction despite antibiotic therapy. ICE may add to the sensitivity of cardiac imaging in cases in which IE is suspected with fewer signs and symptoms present or when competing diagnoses, including TPVR-associated pulmonary embolus, are present. Computed tomography scan of the chest also may be considered to evaluate for septic thromboembolism, especially in the setting of an abnormal chest radiograph. However, similar to ICE, such a scan would not have altered the course of management in our case and was considered of limited benefit.

Our experience represents an important clinical lesson for physicians caring for patients after TPVR. Although 2 previous cases of *Bartonella* endocarditis have been reported, it is of significant clinical value to recognize that our patient was afebrile, blood culture negative, and without echocardiographic evidence of vegetations. It is anticipated that as a result of technological advancements in the management of congenital heart disease and the successfully aging population of children who have undergone cardiac repair, TPVR will become more prevalent in the community pediatrician setting. As a consequence, it is critical to maintain a low threshold to recommend that patients post-TPVR are evaluated by their cardiologist even when the classic signs and symptoms of endocarditis are absent. We are in agreement with those who suggest that new RVOT dysfunction in the absence of a structural complications (including stent fracture or...
compression) should be considered as a criterion for the diagnosis of IE in the setting of TPVR.\textsuperscript{10,11}

**ABBREVIATIONS**

ICE: intracardiac echocardiography
IE: infective endocarditis
PCR: polymerase chain reaction
RVOT: right ventricular outflow tract
TPVR: transcatheter pulmonary valve replacement
TTE: transthoracic echocardiogram

**REFERENCES**

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