

A Common Defect With a Not So Common Complication: *Abiotrophia Defectiva* Endocarditis in a Child With Unrepaired Ventricular Septal Defect



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INTRODUCTION

The frequency of infective endocarditis (IE) in children has been increasing over the last decade, predominantly among patients with congenital heart disease (CHD). This trend has been seen among those with repaired and unrepaired CHD in the developed world as these patients are surviving longer.¹ Viridans group streptococci are the most frequently isolated organisms in this patient population, closely followed by *Staphylococcus* species, which have a more acute and fulminant presentation.¹ *Abiotrophia defectiva* is a rare cause for IE in children, present in about 5% of streptococcal cases, and only a handful of pediatric cases have been described in the literature.² This organism was initially identified as a nutritionally variant streptococcus from 1961 until 1995, when it became its own genus, *Abiotrophia*. It is a gram-positive coccobacillus in chains and requires pyridoxine or L-cysteine-rich media to grow.³ It is part of the normal oral, intestinal, and genital flora.^{3,4} However, it causes severe disease and is difficult to isolate given its growth media requirements, leading to delay in treatment and misdiagnosis as culture-negative IE.^{2,3,5}

CASE PRESENTATION

We present the case of a 3-year-old boy from Nicaragua with a diagnosis of unrepaired ventricular septal defect (VSD) who presented to the pediatric emergency department with 3 months of daily fever up to 103 °F, worsening fatigue, decreased appetite, and 4-pound weight loss since symptom onset. There were also reports of left knee pain but no signs of swelling or erythema. While undergoing medical evaluation in Nicaragua, the patient completed treatment for pharyngitis and elevated cytomegalovirus (CMV) titers; however the fevers persisted despite treatment, at which point the family came to the United States to seek further evaluation.

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Illness Course in Nicaragua

The fevers began in January 2022, and the patient was treated for pharyngitis with a 7-day course of amoxicillin-clavulanic acid. Because of a murmur on cardiac examination, the patient was referred to 2 different pediatric cardiologists. Transthoracic echocardiography (TTE) showed a 7-mm perimembranous VSD, an ejection fraction of 75%, and no description of intracardiac findings suggestive of endocarditis. The fevers persisted into the second month, recurring every 6 hours, and they were referred to an infectious disease (ID) specialist for evaluation. Infectious workup revealed hepatomegaly with perihepatic lymphadenopathy on ultrasound and elevated IgM and IgG titers for CMV, which were treated with a 14-day course of valganciclovir. The fevers persisted into the third month, and when ID recommended a second course of valganciclovir the mother sought out a second opinion.

Evaluation at Our Institution

On presentation, the patient was noted to be febrile, tachycardic, and with increased work of breathing. Physical examination revealed mild tachypnea, clear lungs, an active precordium, and holosystolic murmur graded 5/6 best heard at the left lower sternal border. Examination was also remarkable for jugular venous distention, hepatomegaly 4 cm below the right costal border, and splenomegaly. The patient was well perfused peripherally and irritable with the examiners. Chest x-ray showed cardiomegaly and an interstitial pulmonary pattern. Laboratory findings were remarkable for a hemoglobin of 6.8 g/dL consistent with anemia of chronic disease, normal white blood cell count with monocyte predominance, and elevated erythrocyte sedimentation rate (70 mm/hour), C-reactive protein (5.9 mg/dL), lactate dehydrogenase (367 unit/L), and N-terminal pro-brain natriuretic peptide (650 pg/mL). A TTE was obtained given the physical exam findings that was consistent with heart failure, cardiomegaly, and suspected endocarditis with large left-to-right shunting.

Echocardiogram Findings

The TTE showed a perimembranous VSD that measured 7 to 10 mm in different planes with left-to-right shunting and a peak gradient of 50 mm Hg (Figure 1, Video 1). There was presence of a double-chambered right ventricle causing mild restriction to flow below the pulmonary valve (Figure 2, Video 2). There were multiple structures attached to the tricuspid valve subvalvular apparatus and the transformational tissue that was partially occluding the VSD, with echogenicity and nodularity suggestive of multiple vegetations (Figure 3, Videos 3 and 4). There were also findings consistent with long-standing over-circulation from the VSD including main pulmonary artery dilatation (2.4 cm; Z score, 5.9), dilated left atrium (40 mL/m²), and dilated left

VIDEO HIGHLIGHTS

Video 1: Two-dimensional TTE, subcostal long-axis view without (*left*) and with (*right*) color Doppler demonstrates small echogenicities on the transformational tissue from the tricuspid subvalvular apparatus concerning for vegetations. This transformational tissue partially restricts flow across the VSD. A small noncircumferential pericardial effusion is seen inferior to the right ventricle.

Video 2: Two-dimensional TTE, subcostal short-axis view without (*left*) and with (*right*) color Doppler demonstrates a region of flow turbulence within the right ventricle caused by the formation of a double-chambered right ventricle.

Video 3: Two-dimensional TTE, parasternal short-axis view demonstrates vegetations along the tricuspid valve chordae and attached to the outlet septum.

Video 4: Two-dimensional TTE, apical 4-chamber view focusing on the right ventricle and tricuspid subvalvular apparatus demonstrates prominent echogenicities attached to the chordae consistent with vegetations. The tricuspid valve leaflets appear normal and free of vegetations.

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ventricle (left ventricular internal diameter in diastole [LVIDd] in M mode, 4.2 cm; Z score, 3.7).

Blood cultures were obtained 3 times, per endocarditis guidelines, and empiric treatment for endocarditis was started with vancomycin and gentamycin largely based on clinical and TTE findings. The 3

blood cultures were all positive at 21 hours for gram-positive cocci in chains, which was identified at 64 hours as penicillin-sensitive *A. defectiva*. The patient was transitioned to ampicillin to complete 6 weeks of antibiotics, including gentamicin for 14 days per ID recommendations. Diuresis with furosemide 10 mg 3 times a day was temporarily administered to treat fluid overload. Of note, the patient had no history of dental procedures and underwent dental evaluation at our institution, which revealed no dental caries. A TTE repeated on day 11 from admission due to fever recurrence was largely unchanged. A TTE 5 weeks later did show decrease in left ventricle dilatation; the LVIDd in M mode was 4.0 cm with a Z score of 2.5. The patient was discharged on ceftriaxone and oral rifampin to complete 6 weeks with plan for surgical repair after completion of treatment.

DISCUSSION

We describe the case of a child from a developing country with IE secondary to *A. defectiva* in the presence of an unrepaired perimembranous VSD. While this organism is an uncommon cause of IE, especially in children, a case series demonstrated that its complications tend to be more serious in the pediatric population, with some patients requiring surgical intervention due to recurrent embolism or persistence of vegetation.² Complications included cerebral mycotic aneurysms, septic pneumonia, and splenic infarction, and their development was in part due to delay in treatment given the organism's growth media requirements. The fastidious nature of *A. defectiva* led to an increase in patients being diagnosed as having culture-negative endocarditis and therefore receiving nonspecific and ineffective treatment. *A. defectiva* has a high binding capacity to endothelial cells through secretion of exopolysaccharide and fibronectin, giving it an affinity for endovascular structures, which can cause valve destruction and congestive heart failure.⁶ Our patient did not present obvious vegetations attached to the atrioventricular or

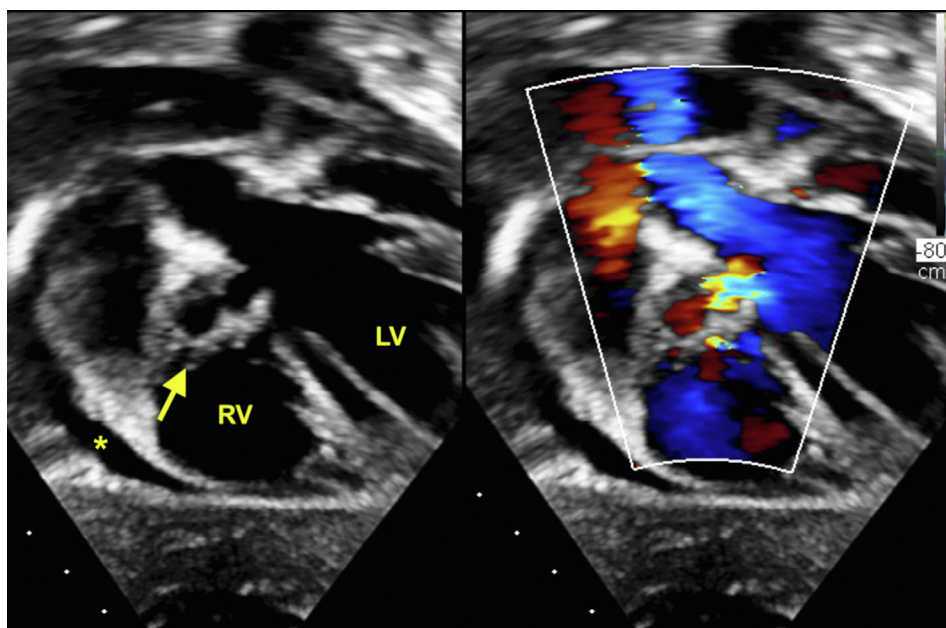


Figure 1 Two-dimensional TTE, subcostal long-axis view without (*left*) and with (*right*) color Doppler demonstrates transformational tissue from the tricuspid subvalvular apparatus partially restricting flow across the ventricular septal defect (*arrow*). A small noncircumferential pericardial effusion is depicted by the *asterisk*. LV, Left ventricle; RV, right ventricle.

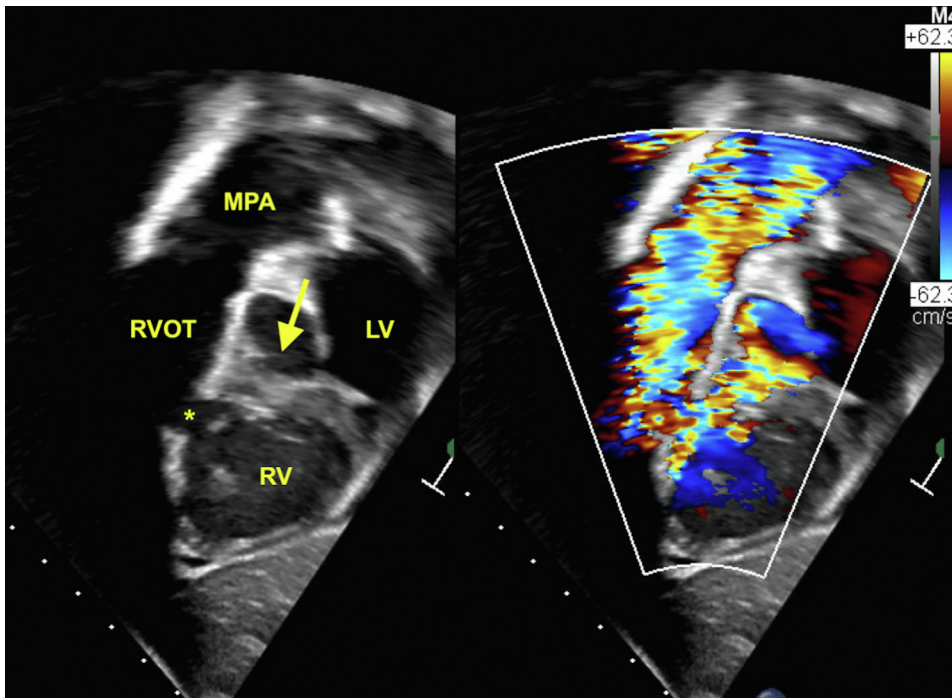


Figure 2 Two-dimensional TTE, subcostal short-axis view without (*left*) and with (*right*) color Doppler demonstrates flow turbulence created within the right ventricle by the development of a double-chambered right ventricle (*asterisk*). Transformational tissue from the tricuspid subvalvular apparatus with echogenicity consistent with vegetations was noted (*arrow*). LV, Left ventricle; MPA, main pulmonary artery; RV, right ventricle; RVOT, right ventricular outflow tract.

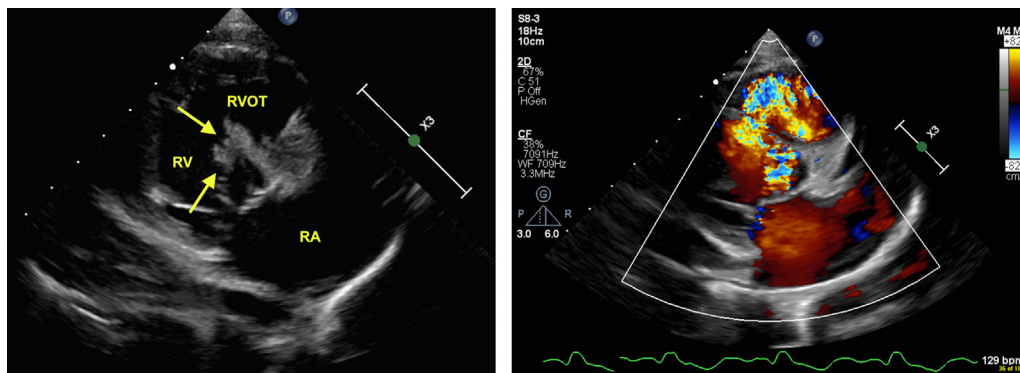


Figure 3 Two-dimensional TTE, parasternal short-axis view without (*left*) and with (*right*) color Doppler demonstrates vegetations along the tricuspid valve chordae and attached to the outlet septum as depicted by the *arrows*. The *right panel* demonstrates flow turbulence along the chordal tissue and in the double-chambered right ventricle. RA, Right atrium; RV, right ventricle; RVOT, right ventricular outflow tract.

semilunar valves but rather multiple small vegetations attached to the subvalvular apparatus of the tricuspid valve. A high index of suspicion based on the clinical history led to close examination of the subvalvular apparatus by TTE.

Children with *A. defectiva* IE tend to have subacute, atypical presentations such as months of fever, arthralgias, and weight loss, similar to our patient. This oftentimes leads to alternate differential diagnoses and workup for other diseases such as malignancy, septic arthritis, or treatment of incidental and unrelated illnesses, further delaying appropriate IE treatment.² At this point it becomes useful to know the diagnosis of CHD as it can help include workup for IE early in

presentation. The TTE findings in our patient allowed for prompt initiation of antimicrobial therapy while we waited for blood culture results, which became particularly useful in this case given the fastidious nature of *A. defectiva*.

This case highlights the importance, as previously shown in the literature, that unrepaired VSD, especially that with high-velocity jets hitting the endocardium, remains a leading risk factor for the development of IE.¹ Prompt diagnosis of CHD, close follow-up, and surgical repair will significantly reduce the risk of acquiring IE as early as 6 months following intervention, thereby preventing significant morbidity.¹

CONCLUSION

Abiotrophia defectiva is an organism that is difficult to isolate, leading to its initial association with culture-negative endocarditis. It has proven to cause very serious morbidities and has been seen predominantly in patients with CHD. This emphasizes the importance of early diagnosis of CHD with appropriate follow-up and surgical correction. The echocardiographer should always maintain a high index of suspicion when clinically indicated and thoroughly evaluate the subvalvular apparatus for multiple small vegetations in the absence of obvious large valvular vegetations. We believe TTE made a difference in diagnosing endocarditis in our patient. *A. defectiva* should be considered as a possible organism when evaluating IE as a cause of fever of unknown origin in children, particularly those with CHD. This will allow for timely and appropriate management and prevention of complications.

SUPPLEMENTARY DATA

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.case.2022.08.005>.

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