Case Report

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Infectious Endocarditis Caused by *Abiotrophia Defectiva* in an Adult CHD Patient with a Transcatheter Pulmonary Valve

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ABSTRACT

Abiotrophia defectiva, a potentially pathogen bacterium, may cause endocarditis presenting with atypical symptoms causing valvular destruction, pneumonia, or mycotic aneurysms. In most incidents those bacteria do not get detected and present as culture negative endocarditis due to specific growth patterns. Few cases have been reported, mostly in children with no underlying conditions. In this case, a 22-year-old male patient with a Melody® Valve in position of the pulmonary valve presented with intermittent fever, excessive fatigue, weight loss and mild anemia for 4 weeks. Unconventional diagnostic workup including endovascular biopsy of the thickened Melody® valve and rRNA gene amplification of the biopsy specimen revealed an endocarditis caused by *Abiotrophia defectiva*. In conclusion, *Abiotrophia defectiva* may play a significant role in patients with atypical symptoms suggestive for subacute endocarditis, and especially those with a transcatheter pulmonary valve or negative blood cultures. In addition, direct endovascular biopsy and subsequent genetic workup may help in differentiating causative organisms.

KEYWORDS: Abiotrophia defectiva; Endocarditis; Transcatheter pulmonary valve

ABBREVIATIONS: CHD: Congenital Heart Disease; FISH: Fluorescence in Situ Hybridization; CRP: C-Reactive Protein

INTRODUCTION

Abiotrophia defectiva, a gram-positive bacterium of the family of Nutrition Variant *Streptococci*, causes a variety of invasive bacterial infections both in children as well as in adults. It is part of the normal flora of the oropharynx, the intestine as well as the urinary tract; it forms satellite colonies around other bacterial colorizations and may commonly cause bacterial endocarditis [1]. Survival and growth of the bacterium is dependent on the availability of pyridoxine (Vitamin B6) and cysteine; thus, colonies need to grow in close position to *streptococci* [1,2]. Consequently, it may be missed when using standard culture media and present as false negative, culture negative endocarditis. Therefore, additive screening with special culture growth media, direct biopsy of the vegetations using Fluorescence in situ hybridization analysis of the specimen and rRNA gene amplification may be necessary to detect unusual pathogens.

CASE PRESENTATION

A 22-year-old male patient presented with typical signs of endocarditis such as intermittent fever, weight loss, excessive fatigue, splenomegaly as well as relative anemia with a hemoglobin decrease of 2 g/dl (from 14 to 12 g/dl) without any obvious blood loss. Further tests revealed systemic inflammation (C-reactive protein (CRP) 11.6mg/dl, Interleukin-6 242pg/ml), an elevated Troponin T (0.031 ng/ml) as well as slightly elevated transaminases (AST 54 U/l, ALT 50 U/l). Several blood cultures taken before admission were culture negative. The patient had been treated by percutaneous pulmonary valve implantation (22mm Melody®

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Transcatheter Pulmonary valve, Medtronic inc., MI, USA) for severe pulmonary valve regurgitation after a Fallot repair. Regular follow-ups demonstrated normal function of the valve without stenosis or regurgitation. On admission transthoracic as well as transesophageal echocardiography revealed a new pronounced stenosis of the Melody® Valve (6mm lumen) as well as vegetations on the cusps (Figure 1). Invasive measurements showed an elevated pressure in the right ventricle of 85 mmHg and a gradient of 50 mmHg over the valve thereby reaching 2/3 of the patient's systemic blood pressure. Angiography confirmed a severe stenosis of the valve ring with a lumen of 6mm. To clarify the possible cause, four transcatheter biopsies of the vegetations were taken (Figure 1).

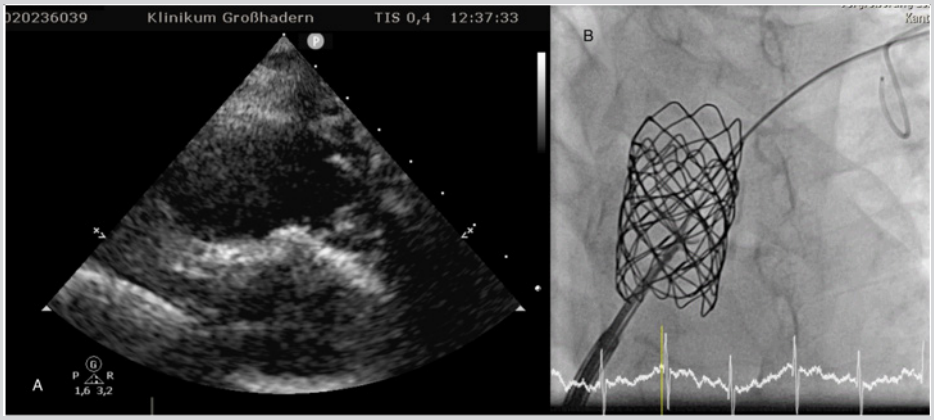

Figure 1: A. Echocardiographic picture with the thickened and obstructed Melody® valve and a gradient of > 50mmHg.

B. Angiographic documentation of the endovascular biopsy of the Melody® valve using an 8 french guiding sheath.

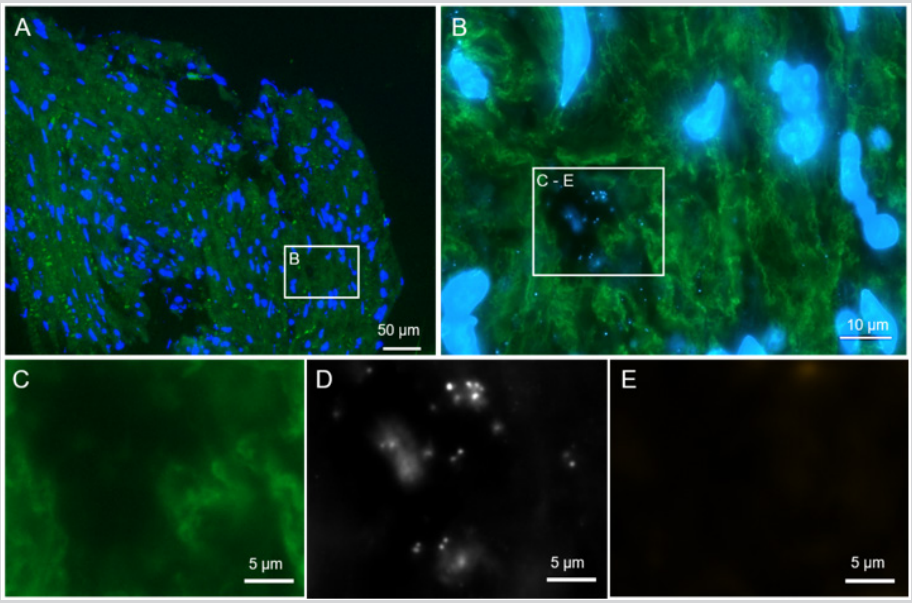

Figure 2: Sequencing result of the16S rRNA-gene: 99.8% identity over 439 bp to Abiotrophia defectiva

A: Overview

B: Higher resolution shows a tissue defect (green: tissue background, blue: nucleic acid stain DAPI)

C-E: High resolution of insert, single channels

C: Tissue background (green)

D: DAPI shows cocci (black and white for better contrast)

E: No signal with the pan-bacterial FISH-Probe as well with the specific FISH probe (data do not show).

In addition, balloon valvuloplasty with a 24mm high pressure balloon was performed to improve cardiac output reducing the gradient to 26 mmHg, followed by blood cultures taken directly from the pulmonary artery. The biopsy specimens underwent fluorescent in situ hybridization analysis detecting severely degraded microorganisms using the nucleic acid-specific dye - 4',6-diamidino-2-phenylindole (DAPI). The following rRNA gene amplification identified the bacterium *Abiotrophia defectiva* (99.8% identity over 439 base pairs) (Figure 2). Repeated blood cultures finally confirmed a bacteremia with Abiotrophia defectiva. The patient received an antibiotic therapy with ampicillin and gentamicin for the first 3 days. According to the resistogram the therapy was changed to a combination of gentamicin and penicillin. The clinical condition improved within a few days following the

balloon-valvuloplasty and the beginning of the antibiotic therapy. Dental examination showed carious destructions of multiple teeth as a potential source for the bacterial endocarditis. The patient underwent a dental restoration and removal of four teeth. Moreover, elevated laboratory values (hemoglobin, CRP, interleucin-6, troponin, transaminases) normalized until discharge on day 47. Gentamicin was administered for three weeks, penicillin for six weeks. By the time of discharge, the echocardiographic findings showed a normal biventricular function. The tricuspid valve showed a mild regurgitation with a maximum gradient of 40mmHg. The transcatheter pulmonary valve still showed echo-dense vegetations, no regurgitation, a maximal gradient of 40mmHg, a mean gradient of 18mmHg and an internal diameter of 21mm.

DISCUSSION

The epidemiology of *Abiotrophia defectiva* as a pathogenic microorganism of an infectious endocarditis has been poorly investigated up to this date. Previous studies reported that *Abiotrophia* species may be responsible for 4.3-6% of all cases of streptococcal endocarditis [3]. Because of the unique growth conditions of this bacterium many infections may be missed or misdiagnosed as culture negative endocarditis therefor mistreated leading to significant complications. It may well be speculated that a lot of additional cases diagnosed as culture-negative endocarditis lack the identification of *Abiotrophia defectiva* due to a lack of the adequate supplements in the medium of the blood culture. Its detection can be difficult due to an inadequate composition of the culture medium, which requires an additional L-cysteine- or pyridoxal-supplementation to support its growth [3,4]. One may therefore estimate that an unknown number of blood cultures may bring false negative results for *Abiotrophia defective* and in this respect, a relevant number of undetected cases must be assumed. In adults, *Abiotrophia defectiva* may also induce an infectious endocarditis, presenting clinically in most cases as subacute endocarditis. The most common symptoms seem to be fever, arthralgia, and splenomegaly. Most of these infections seem to be community acquired and they mainly affect the left sided heart valves [5]. The most frequent complications are a moderate to severe aortic/mitral valve regurgitation as well as a new on-set heart failure. Less frequent complications include valve perforations, abscess formation, pseudoaneurysms as well as affections of the central nervous system – that is emboli, mycotic aneurisms, and hemorrhage [5].

The few cases reported in children and adults with CHD indicate that most of the patients were previously healthy or had no knowledge of a pre-existing congenital heart defect. The right heart valves seemed to be affected slightly more often in this group of patients, the symptoms being similar to the adults with the exception of abdominal pain. Almost 90% of the patients had complications - all patients with affection of the right heart valves developed a septic pneumonia [3,4]. Two patients with vegetations on the mitral valve developed both cerebral mycotic aneurysm as well as splenic infarction, while two others acquired moderate to severe heart failure and emboli in the extremities [3,4]. Furthermore, 66.7% of the patients developed valvular dysfunction. Surgery had to be performed in 66.7% of the cases due to recurrent embolic events, persistent large vegetation or increasing valvular dysfunction [6]. The risk of a bacterial endocarditis after a percutaneous pulmonary valve implantation seems substantially higher when using Melody® valves as compared to the implantation of Sapien™ valves [7]; additional studies confirmed that a substantial number (9%) of bacterial endocarditis affecting Melody® valves remains culture-negative or unknown [8].

The present case as well as the previous studies demonstrate the importance of rapid diagnosis and treatment of *Abiotrophia defectiva* by the administration of adequate intravenous antibiotics. In general, infections with *Abiotrophia defectiva* are treated with ß-lactam-antibiotics or vancomycin augmented by gentamicin [9]. A combination of penicillin and gentamicin has been shown to be effective in just 10% of the cases, whereas a recent study indicates that *Abiotrophia defectiva* is highly susceptible (95-100%) to 3. Generation cephalosporins, suggesting those as the most appropriate treatment while the antibiotic resistogram is pending [10]. Direct catheter assisted biopsies of right valvular vegetations have been recently proven to enable FISH detection of microorganisms causing bacterial endocarditis [11]. These methods may identify and visualize bacteria even when they are severely degraded [11-13].

CONCLUSION

In conclusion, endocarditis caused by *Abiotrophia defectiva* has a high complication rate in pediatric and adult patients, especially those with congenital heart disease. Due to specific growth patterns, this bacterium may be missed leading to the incorrect diagnosis of a culture negative bacterial endocarditis. Using a culture medium supplemented with adequate nutrients (L-cysteine- or pyridoxal) is pivotal for the diagnosis in order to ensure rapid and efficient treatment. In addition, direct endovascular biopsy and bacterial detection with FISH-analysis may improve the detection of the causative pathogen. In this respect, *Abiotrophia defectiva* should be considered as a possible cause when pediatric patients present with infectious endocarditis, especially with a subacute course, atypical symptoms, and a culture-negative microbiology.

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CONFLICT OF INTEREST

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