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Infective endocarditis caused by *Gemella haemolysans* in a patient with bicuspid aortic valve: A case report

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Abstract

Gemella haemolysans is a gram-positive coccus, and commensal of the upper respiratory tract and oral mucosa. In rare cases, it has been identified as an opportunistic pathogen in the development of endocarditis. Here, we describe a case of *Gemella haemolysans* endocarditis in a patient with bicuspid aortic valve. A 14-year-old male presented to our hospital with a 1-month history of intermittent fever. *Gemella haemolysans* was isolated from the patient's blood cultures. Transesophageal echocardiography revealed severe aortic stenosis and a pseudoaneurysm of the mitral–aortic intervalvular fibrosa. The patient underwent aortic valve replacement with pseudoaneurysm of the mitral–aortic intervalvular fibrosa repair and remained symptom-free during follow-up. This case highlights the importance of considering atypical pathogens as causative agents of infective endocarditis.

Keywords

Gemella haemolysans, infective endocarditis, pediatrics, antimicrobial therapy

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Introduction

Infective endocarditis (IE) is a life-threatening disease still associated with a high mortality rate.[1–3] The vast majority of IE cases stem from streptococci, staphylococci, and enterococci infection, with *Staphylococcus aureus* specifically responsible for around 30% of cases in the developed world.[4] Changes in the causative organisms have been noted in recent years with emerging species that are often difficult to grow.[5,6] *Gemella haemolysans* is a facultative anaerobic gram-positive coccus that normally resides in the upper respiratory tract and oral cavity of humans.[7] *Gemella haemolysans* is able to cause severe and generalized infections as opportunistic pathogens, and it has become an emerging bacterial etiology in IE.[8] Most documented cases of *Gemella haemolysans* endocarditis occur in patients with underlying mitral or aortic valve disease (including prosthetic valves) and/or poor dentition or dental manipulation.[9] We present a case of IE caused by *Gemella haemolysans* in a pediatric patient with bicuspid aortic valve.

Case presentation

A 14-year-old male was referred to our hospital with intermittent fever of 1-month duration. The patient had a medical history of congenital aortic stenosis due to bicuspid aortic valve, and underwent balloon valvuloplasty after birth.

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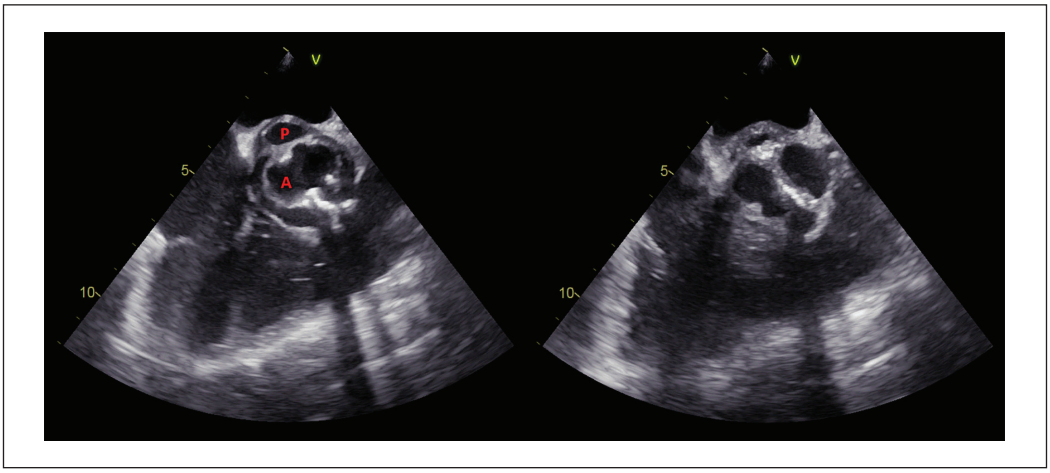

Figure 1. Transesophageal echocardiography showing bicuspid aortic valve (A) and the pseudoaneurysm of the mitral–aortic intervalvular fibrosa (P) in systole (left) and diastole (right).

Investigations

Upon admission, a physical examination revealed the patient to be in good general condition. Vital signs were as follows: body temperature of 38.8°C, respiratory rate of 19 breaths/min, heart rate of 114 bpm, and blood pressure of 110/70 mmHg. Oxygen saturation was 99% while breathing room air. The cardiovascular examination showed no jugular venous distension, pitting edema, or systolic murmurs. There were no mucocutaneous lesions, petechiae, Osler nodes, Janeway lesions or subungual hemorrhages. Ophthalmoscopy and examination of the mouth, ears, nose, throat, and nervous system were normal. Laboratory tests revealed moderate normocytic-normochromic anemia, an increased C-reactive protein level (13.1 mg/dL), a white blood cell count of 9.130/μL with 75.7% neutrophils, and a hemoglobin level of 9.8 g/dL. Hepatic and renal functions were within the normal range. The serum immunoglobulin A level was elevated (437 mg/dL; normal values 70–400). Serum C3 level, titers for antistreptolysin O, and anti-deoxyribonuclease B were within normal limits, and searches for rheumatoid factor, antinuclear antibodies, antineutrophil cytoplasmic antibodies, and cryoglobulins were negative. The chest radiograph was unremarkable, and abdominal ultrasound revealed no hepatic, renal, or splenic abscesses. Serological testing for Toxoplasma, human immunodeficiency virus, and Cytomegalovirus were negative.

Transthoracic echocardiography (TTE) revealed severe aortic stenosis, but no vegetation was seen. Due to a strong suspicion of IE, TEE was performed. TEE did not reveal any vegetation on the cardiac valves but did identify a pulsatile echo-free cavity, posterior and underneath the aortic valve, measuring approximately 7 mm × 13 mm (Figures 1 and 2). The cavity was recognized as a pseudoaneurysm of the mitral–aortic intervalvular fibrosa (P-MAIVF). Concurrently,

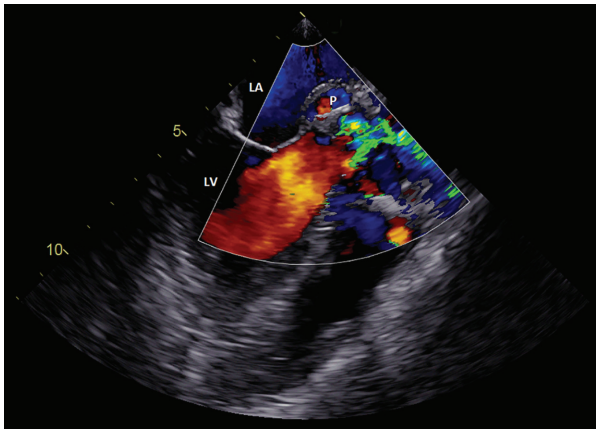

Figure 2. TEE with color Doppler demonstrating the blood flow into the pseudoaneurysm during systole.
P: pseudoaneurysm, LA: left atrium, LV: left ventricle, TTE, transthoracic echocardiography.

one out of two sets of blood cultures obtained upon admission grew *G. haemolysans*. The isolate was sensitive to penicillin G (0.250 mg/L), ceftriaxone (⩽0.500 mg/L), meropenem (⩽0.5 mg/L), and vancomycin (2 mg/L; Table 1).

Treatment and outcome

The patient was treated with broad-spectrum antibiotics, including intravenous (IV) ceftriaxone (2 g daily) and gentamicin (1 mg/kg IV every 8 h). A cardiovascular surgeon was consulted and the patient was transferred to a children's hospital to undergo aortic valve replacement with P-MAIVF repair. The postoperative course was uneventful, and the patient has remained symptom-free during follow-up. A

Table 1. Antimicrobial susceptibility testing results for *Gemella haemolysans* isolated from our patient.

Antimicrobial agent	MIC (μg/ml)	Susceptibility
Piperacillin/tazobactam	⩽0.06	S
Metronidazole	>8	R
Clindamycin	⩽0.06	S
Penicillin G	0.250	S
Vancomycin	2	S
Ertapenem	⩽0.125	S
Doxycycline	⩽0.125	S
Ampicillin	0.250	S
Amoxicillin/clavulanic acid	<0.5	S
Meropenem	⩽0.5	S
Cefotaxime	0.500	S
Ceftriaxone	0.500	S

MIC: minimum inhibitory concentration; S: susceptible; R: resistant.

The antimicrobial susceptibility testing was performed by broth microdilution method (MERLIN Diagnostika GmbH, Bornheim, Germany). Interpretative MIC breakpoints were based on the European Committee on Antimicrobial Susceptibility Testing criteria.

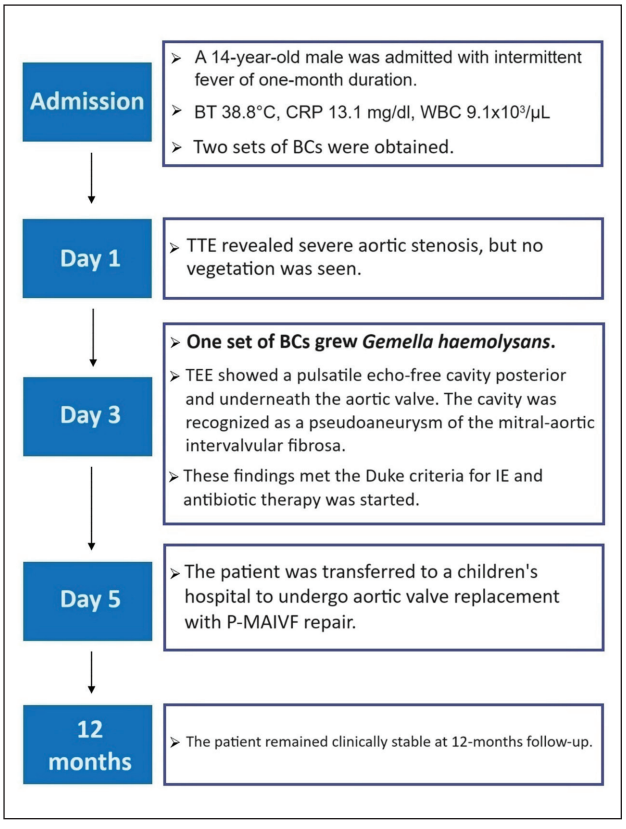

Figure 3. The timeline of the case presentation.
BCs: blood cultures; BT: body temperature; CRP: C-reactive protein; IE: infective endocarditis; P-MAIVF: pseudoaneurysm of the mitral–aortic intervalvular fibrosa.

detailed timeline of the case presentation is provided in Figure 3.

Discussion

The epidemiology of IE in children has changed in recent years, with congenital heart disease becoming the main predisposing factor in the developed world, while rheumatic heart disease has become less frequent.[10,11] *Staphylococcus aureus* is now the most prevalent cause of IE in most studies, accounting for approximately 26.6% of all cases, followed by viridans group streptococci at 18.7%, other streptococci at 17.5%, and enterococci at 10.5%.[5,11] These organisms together account for 80%–90% of all cases of endocarditis. *Gemella haemolysans* often colonizes the upper respiratory, gastrointestinal, and genitourinary tract as a commensal organism and occasionally causes localized and/or disseminated infections. Most cases of *Gemella haemolysans* endocarditis involve either the mitral or aortic valve and are found in patients with previous valve damage or those in an immunocompromised state[12] (Table 2). Patients with bicuspid aortic valves not only have a higher risk of IE, but they also face an increased likelihood of developing periannular complications, such as abscess and pseudoaneurysm.[13]

IE remains a clinical challenge, even though there have been strides in the diagnostic techniques and management approaches over the past few decades.[10] In cases of prolonged fever, especially in patients with a history of heart disease, IE should be considered as one of the potential causes. The first step in the diagnosis of IE is to identify risk factors, including prosthetic heart valves, structural cardiac anomalies, intravenous drug use, and recent invasive procedures. Echocardiography continues to be the primary imaging modality for detecting anatomical evidence of IE. According to the modified Duke criteria,[33] our patient fulfilled one major criterion (echocardiography finding of pseudoaneurysm) and three minor criteria (fever of at least 38°C, valvular heart disease as a predisposing heart condition, and positive blood culture for *G. haemolysans*). *Gemella* isolates have shown susceptibility to β-lactams. In almost all published cases, patients were successfully treated with antibiotics alone or in combination with cardiac valvular replacement.

TTE is recommended as the first-line imaging modality in suspected IE.[34] TEE must be performed in case of negative TTE, but high clinical suspicion of IE. TEE has a sensitivity of 90%–100% and a specificity of 90% for detection of vegetations, and it is superior to TTE for detection of complications, such as abscess, leaflet perforation, and pseudoaneurysm.[35,36]

P-MAIVF can be a catastrophic sequela of untreated active IE.[37,38] If there is a delay in diagnosis or treatment, the bacteria may invade into the fibrous tissue between the mitral and aortic valves, leading to the development of P-MAIVF. A total of 89 cases were reported in the literature from 1966 to 2009.[38] P-MAIVF appears as a pulsatile echo-free pouch that expands during systole and collapses during diastole. Sudhakar et al.[38] observed that the most common clinical presentations of P-MAIVF were symptoms and/or signs of active endocarditis (39%), followed by dyspnea and heart

Table 2. Summary of documented cases of infective endocarditis caused by *Gemella haemolysans*.

Author (year)	Age/sex	Associated condition/ predisposing cause	Infected valve	Treatment	Outcome/valve replacement
Chatelain et al.[14]	62/M	Dental manipulation	Mitral	Cefamandole, gentamicin, benzylpenicillin, and amoxicillin	Cured/no
	48/M	Poor dentition and respiratory viral syndrome	Aortic	Benzylpenicillin and gentamicin	Cured/yes
	56/M	Mitral insufficiency and dental manipulation	Mitral	Benzylpenicillin and gentamicin	Cured/no
Kaufhold et al.[15]	62/F	None	Mitral	Benzylpenicillin, tobramycin, and clindamycin	Cured/no
Brack et al.[16]	74/M	Mitral prolapse	Mitral	Benzylpenicillin, gentamicin, and amoxicillin	Cured/no
Morea et al.[17]	47/M	Bioprosthetic aortic valve and periodontal disease	Aortic	Erythromycin and rifampicin	Cured/yes
Devuyst et al.[18]	53/M	Mitral regurgitation	Mitral	Benzylpenicillin and gentamicin	Cured/yes
Frésard et al.[19]	42/M	Aortic insufficiency and scalp wound	Aortic	Vancomycin, fusidic acid, amoxicillin, and gentamicin	Cured/no
Helft et al.[20]	71/M	Colonic carcinoma	Mitral	Amoxicillin + clavulanic acid and gentamicin	Cured/no
Matsis et al.[21]	20/M	None	Aortic	Benzylpenicillin, gentamicin	Cured/yes
Samuel et al.[22]	34/M	Multiple valve replacements with prosthetic valve, asymptomatic dental sepsis	Aortic	Cefuroxime, tobramycin, ciprofloxacin, and erythromycin	Cured/no
Breathnach et al.[23]	6/M	None	Pulmonary	Amoxicillin and gentamicin	Cured/no
La Scola et al.[24]	63/M	Chronic obstructive bronchitis and poor dental state	Mitral	Amoxicillin and amikacin	Kidney abscess, cured/no
Zingaro et al.[25]	49/M	Glomerulonephritis	Aortic	Piperacillin and ciprofloxacin	Cured/yes
Mosquera et al.[26]	77/M	Hemochromatosis with chronic liver disease	Aortic	Penicillin and tobramycin	Cured/no
Khan et al.[8]	80/M	Mitral prolapse with regurgitation and denture fixation	Mitral	Penicillin and gentamicin	Cured/no
Avgoustidis et al.[27]	NA	Systemic lupus erythematosus	NA	NA	NA
Liu et al.[12]	87/F	Hypertension, atrial fibrillation, diabetes mellitus type 2, COPD, and multiple myeloma	Aortic	Ampicillin and gentamicin	Cured/no
Ando et al.[28]	24/M	Dental abscess	Aortic and mitral	Clindamycin, penicillin G, vancomycin	Cured/yes
Quaesaet et al.[29]	39/M	Bioprosthetic aortic valve	Aortic	Amoxicillin, and rifampicin	Cured, splenic infarction due to septic emboli/no
Youssef et al.[9]	81/M	Coronary artery disease, hypertension, COPD, and atrial fibrillation	Mitral	Vancomycin, ceftriaxone, and gentamicin	Rupture in the mitral leaflet, died
Agrawal et al.[30]	38/M	None	Aortic	Ampicillin and gentamicin	Cured/no
Eslinger et al.[31]	63/M	Acute myeloid leukemia and poor dental hygiene	Aortic	Vancomycin, cefepime, benzylpenicillin, and gentamicin	Cured/no
Rabah et al.[32]	56/M	Dental procedure	Mitral	Vancomycin and ceftriaxone	Cured/yes

COPD: chronic obstructive pulmonary disease; NA: not available.

failure (16%), chest pain (10%), cerebrovascular accident, and systemic embolism (12%). TEE had a higher sensitivity in detecting P-MAIVF compared to TTE (90% vs 43%).[39] However, there are certain clinical scenarios where echocardiography alone may not definitively confirm or exclude the diagnosis of IE. In such cases, newer diagnostic techniques, such as cardiac computed tomography (CCT) can play a crucial role in confirming the diagnosis. In a recent meta-analysis, it was found that CCT had superior sensitivity in detecting abscess or pseudoaneurysm compared to TEE (78% vs 69%),

while TEE had significantly higher sensitivity than CCT for the detection of vegetations (94% vs 64%).[40] P-MAIVF is a rare disease in pediatric patients, with only a few case reports and case series available.[38] To the best of our knowledge, this case represents the first association of IE caused by *Gemella haemolysans* and P-MAIVF.

Conclusion

This case highlights the importance of considering atypical pathogens as causative agents of IE. *Gemella haemolysans* can cause serious infections in susceptible individuals, particularly those with underlying valvular heart disease. TEE must be performed in the majority of patients with suspected IE, because of its better sensitivity, particularly for the diagnosis of perivalvular involvement. P-MAIVF is a potentially life-threatening condition that is well described in adults but remains rare in the pediatric population.

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Author contributions

All authors contributed to this article. G.D., A.V., E.G., F.D.A., M.S., P.G., and F.A. wrote the abstract, introduction, case, discussion, and conclusion. A.V., P.G., and F.A. performed critical edits and final revision of figures. The article has been read and approved by all the named authors.

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Ethical approval

Our institution does not require ethical approval for reporting individual cases or case series.

Informed consent

Written informed consent was obtained from a legally authorized representative(s) for anonymized patient information to be published in this article.

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