

Granulicatella adiacens: A Rare Cause of Infective Endocarditis: A Case Report

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Abstract

Granulicatella adiacens (*G. adiacens*), formerly classified as a nutritionally variant streptococci (NVS), is a commensal organism in the mouth. It is known to be a rare cause of infective endocarditis (IE). This case report presents a case of IE caused by *G. adiacens* in a 63-year-old man with mitral valve prolapse (MVP), severe mitral regurgitation (MR), and dual vessel disease (DVD). *G. adiacens* was isolated from two of three blood cultures, and the organism was sensitive to penicillin, vancomycin, cefotaxime, and gentamicin. He was successfully treated with a combination of ceftriaxone and gentamicin. Prompt identification of the organism and determination of antibiotic sensitivity pattern led to successful treatment. This case report showcases the challenges in diagnosis, and treatment, giving insight to healthcare providers on a rare entity.

Keywords

Granulicatella adiacens, Infective Endocarditis, Nutritionally Variant Streptococci, Antibiotic Sensitivity Pattern, Mitral Valve Disease

1. Introduction

A rare, yet potentially fatal condition of the endocardium, is infective endocarditis [1]. Streptococci account for 60% - 80%, with viridans streptococci contributing 30% - 40%, enterococci 5% - 18%, and other streptococci 15% - 25% [2]. Infective endocarditis in both native and prosthetic valves can be caused by *G. adiacens*, a natural microbiota found in the oral cavity, digestive system, and urogenital tract. A tiny, facultatively anaerobic streptococcus-like bacterium, *G. adiacens* is Gram-positive, non-motile, non-spore-forming, oxidase- and catalase-negative [3] [4]. NVS, which includes both *G. adiacens* and *Abiotrophia* species [4], is the etiological agent of IE in 5% - 6% of cases [4] and can also cause ocular, pulmonary, and

CNS infections [5]. Furthermore, higher rates of morbidity, bacteriologic failure, and mortality are linked to NVS [4]. Despite its clinical significance, only a few case reports of *G. adiacens* exist in the literature. Amongst others, these include cases with no pre-existing cardiac abnormalities [4] [6], one involving a patient with severe diverticulosis [7], another with rheumatic valvular disease and who underwent a ventriculoperitoneal shunt for cerebellar infarct with subsequent hydrocephalus [2], and a patient with prostate cancer and chronic moderate mitral valve regurgitation [8]. This case report describes a 63-year-old patient with a significant predisposing cardiac condition who was diagnosed with IE caused by *G. adiacens*, emphasizing the diagnostic challenges posed by this rare pathogen.

2. Case Report

A 63-year-old retired police officer presented with a two-month history of high-grade intermittent fever, nocturnal sweating, and loss of appetite (LOA). He was a non-smoker, and a social drinker and denied any intravenous (IV) drug use. He had no chest pain, palpitations, urinary symptoms, or recent travel history.

His past medical history includes ischemic heart disease (IHD) with complications, three years ago. Due to persistent poor exercise tolerance, a transthoracic echocardiogram (TTE) at that time revealed, a mitral valve prolapse with partial posterior chordal rupture causing severe pulmonary hypertension (PHTN), with preserved biventricular function. Cardiothoracic surgery was then consulted for mitral valve replacement. His coronary angiography divulged dual vessel disease (DVD) involving the left main coronary artery (LMCA) and left anterior descending artery (LAD), with a maximum of 60% and 80% stenosis, respectively. Although surgical revascularization and mitral valve replacement (MVR) were recommended, the patient had poor follow-up.

On examination, he had a temperature of 101°F, blood pressure of 110/60 mmHg, pulse rate of 96 beats/min, and respiratory rate of 24 breaths/min. His dental examination showed no active caries or periodontal disease. Cardiac examination was notable for a prominent grade three pansystolic murmur, best heard over the mitral area with radiation to the axilla and a loud second heart sound. No peripheral stigmata of IE were observed. Hepatosplenomegaly was also noted.

Given the history of prolonged fever and a cardiac murmur, a provisional diagnosis of IE was made. After obtaining three blood cultures, IV ceftriaxone 2g daily and IV gentamicin 1 mg/kg every 12 hours were initiated. Laboratory studies showed leukocytes at 9030/ μ L, hemoglobin at 12.8 g/dL, platelets at 151,000/ μ L, erythrocyte sedimentation rate (ESR) at 32 mm/hour, c-reactive protein (CRP) level at 70.0 mg/L, and normal liver enzymes and renal function. Urine analysis was unremarkable, but the rheumatoid factor (RF) level was elevated at 24 IU/mL (Table 1).

On the second day of admission, TTE revealed no evidence of infective endocarditis. However, two blood cultures yielded Gram-positive cocci (GPC) in chains, initially identified as viridans streptococci. Despite the fever subsiding, a

Table 1. Summary of investigations across three days with the normal range.

Investigation	18/06	28/06	08/07	Normal range
C-reactive protein (CRP) mg/L	70	28	4	0 - 5 mg/L
White blood cell (WBC) $\times 10^9$ /L	9.03	5.82	5.39	4.0 - 11.0 $\times 10^9$ /L
Hemoglobin (Hg) g/dL	12.8	11.9	12.3	13 - 18 g/dL
Platelet (PLT) $\times 10^9$ /L	151	162	183	150 - 400 $\times 10^9$ /L
ESR mm/hour	32	-	28	0 - 20 mm/hour
Creatinine μ mol/L	66	88	88	74 - 110 μ mol/L
Sodium (Na) mmol/L	138	138	138	136 - 145 mmol/L
Potassium (K) mmol/L	4.3	4.0	4.0	3.5 - 5.2 mmol/L
Chloride (Cl) mmol/L	107	102	102	95 - 110 mmol/L
Aspartate transaminase (AST) U/L	35	18	29	0 - 35 U/L
Alanine transaminase (ALT) U/L	24	22	21	0 - 45 U/L
Total bilirubin μ mol/L	5	-	-	5 - 21 μ mol/L
Direct bilirubin μ mol/L	2	-	-	0 - 3.4 μ mol/L
Hs-c troponin I ng/L (High-sensitivity cardiac)	4.6	-	-	<12 ng/L
UFR: Protein	Not detected	-	-	
UFR: Glucose	Not detected	-	-	
UFR: Red Blood Cell (RBC)	Not seen	-	-	
Rheumatoid Factor (RF) IU/ml	24 IU/ml	-	-	<18 IU/ml

trans-esophageal echocardiogram (TOE) was planned given the patients' preexisting cardiac condition and positive blood cultures. Using the Modified Duke Criteria [6], the patient was diagnosed with definitive IE based on one major criterion (positive blood culture) and three minor criteria (fever, elevated RF, and a predisposing condition).

Five days after admission, two of the three blood cultures grew *G. adiacens*, which were susceptible to vancomycin, penicillin, cefotaxime, and gentamicin. On the eighth day of antibiotic therapy, TOE showed multiple vegetations on the anterior and posterior mitral valve leaflets, with the largest measuring 16 mm. No abscess or valve perforation was detected.

By day 22 of ceftriaxone, TTE revealed a notable reduction in vegetation size to 6 \times 5 mm, demonstrating effective treatment. The patient showed significant clinical improvement and a reduction in inflammatory markers.

Following the latest guidelines, the patient received 22 days of IV ceftriaxone, with plans to continue up to six weeks, and gentamicin for the first two weeks [6]. He was later transferred to a local hospital for continuation of antibiotic therapy, closer to his residence, and was discharged home after completion. He awaited outpatient follow-up in view of valve replacement surgery.

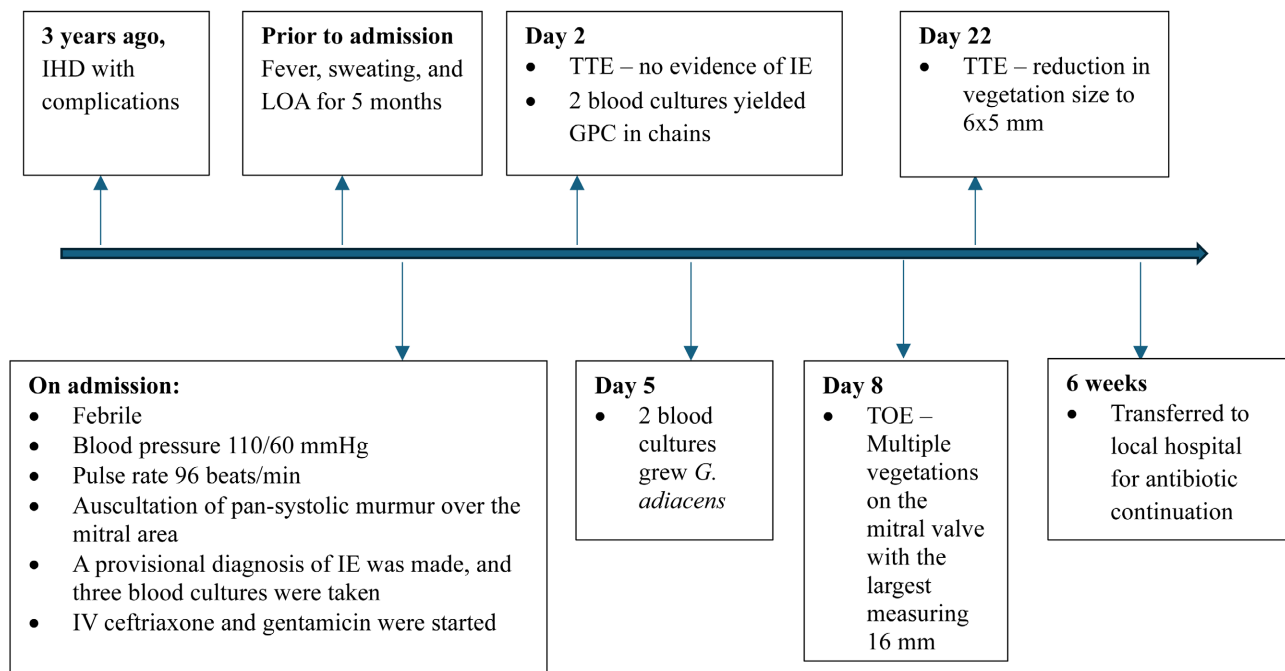


Figure 1. Timeline of events.

Patient Perspective

The patient was immensely grateful during the treatment for the significant clinical improvement he experienced and the ability to resume his daily and extended living activities with ease. **Figure 1** provides an overview of the chronology of the events mentioned above.

3. Discussion

Frenkel and Hirsch first described NVS in 1961, noting its satellite formation around other bacterial colonies, unique growth requirement, prolonged incubation, and variable gram stain findings [4] [9]. *Abiotrophia* is a novel genus that was established in 1995 by Kawamura *et al.* using 16s RNA sequencing [10]. Based on the amplification and sequencing of the 16sRNA, Collins and Lawson later proposed in 2000 that the three species members of the genus *Abiotrophia* be reclassified the species into a new genus *Granulicatella*, as *Granulicatella adiacens*, *balaenopterae*, *elegans*, and *G. para adiacens* [5] [11] [12], based on the amplification and sequencing of the 16sRNA [12]. In Taiwan region, the first case of human NVS infection occurred in 1996 [1].

Although infections due to NVS are less recognized, they are associated with higher morbidity and mortality compared to viridans streptococci and enterococci [1]-[4]. Factors contributing to this include nutritional limitation within vegetation, a slow growth rate that may attenuate the effect of beta-lactam antibiotics, and the production of exopolysaccharides with high binding capacity for fibronectin and extracellular matrix [1] [4]. These characteristics contribute to the distinct features of NVS causing endocarditis, necessitating a longer duration of

effective antibiotic coverage.

G. adiacens can be challenging to grow in standard blood cultures due to its requirement for pyridoxal and L-cysteine, typically not found in standard sheep blood agar [12]. The addition of human blood to culture media enhances isolation, as human erythrocytes are rich in pyridoxal. This method is commonly used in Sri Lankan laboratories [6]. Most case reports indicate that *G. adiacens* initially appears as Gram-positive cocci in pairs or chains and grows on human blood and chocolate agars but not on MacConkey agar plates [2] [4] [6] [12]. The organism's growth on Cystine-Lactose-Electrolyte-Deficient (CLED) agar suggests it is cysteine-dependent [6]. *G. adiacens* was finally isolated by the VIETEK system [2] [4] [6]. This underscores the need for extended incubation of the initially positive culture under appropriate media and supplements, such as cysteine and pyridoxal for the effective recovery of this fastidious organism.

As seen in this case, pre-existing valvular pathology is a common predisposing factor [2], as also reported by Dao K *et al.* and Sailaja TS *et al.* [2] [12]. However, classic peripheral stigmata of IE, such as clubbing, and Osler nodes, are rare [2]. The study of the literature shows a high prevalence (61%) of valvular heart disease or prosthetic heart valves in patients with IE caused by *G. adiacens* [7]. Notably, there have been reports of *G. adiacens* infections in patients without pre-existing valvular pathologies and assumed to have originated from the oral cavity as both patients had undergone dental manipulation, including cleaning and tooth extraction prior to the presentation [4] [6].

G. adiacens exhibits a strong affinity towards aortic and mitral valves, with vegetation in about 64% of cases [2] [12], often exceeding 10 mm [6] [8], as observed in this case. In the presented case report, the initial TTE, on the second day of admission, showed no evidence of IE, which could be due to the early stage of vegetation development or other factors. This highlights the importance of serial echocardiograms in heightened clinical suspicion of IE.

G. adiacens infections are associated with higher complication rates and prolonged disease courses, likely due to delays in diagnosis and treatment [8]. In cases of NVS IE, embolization occurs in 27% of cases, relapse after therapy in 17%, and mortality in 17%. Furthermore, bacteriologic failure occurs in 41% of cases despite appropriate antibiotic therapy, and surgery is required in 27%. [1] [2] [12] [13]. Other complications include cases like that described by Dao K *et al.*, where *G. adiacens* IE was complicated by infection-related glomerulonephritis, diffuse alveolar hemorrhage, and ultimately cardiac arrest [12]. These findings underscore the need for rapid diagnosis and treatment of these fastidious organisms known to cause threatening complications.

Successful treatment of *G. adiacens* IE necessitates long-term combination therapy with beta-lactam antibiotics and aminoglycosides (gentamicin), with vancomycin advised for resistant strains [8]. However, successful treatment with double beta-lactam therapy, using IV ampicillin and ceftriaxone for six weeks, has also been reported by Khan S. *et al.* [14].

This case report highlights the importance of recognizing and diagnosing this rare organism, even without risk factors and pre-existing comorbidities. Additionally, it underscores the importance of prompt diagnosis, including the use of automated systems, and accurate treatment of the organism to prevent severe outcomes. Further research could focus on developing rapid diagnostic methods and novel treatments such as double beta-lactam therapy. This may offer a viable safe alternative to long-term aminoglycoside use while providing effective clinical outcomes.

4. Conclusion

Granulicatella adiacens, although a commensal, leads to fatal serious infections, which require prompt treatment and diagnosis. Given the elevated rates of complications, mortality, and treatment failure, it is imperative to monitor and anticipate potential outcomes closely. The case report aims to give insight to healthcare providers to lead to well-informed decisions, increase the precision of diagnosis, and optimize patient care.

Declarations

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Informed Consent

Written informed consent was obtained from the patient for publication and a copy of the consent is available for review on request.

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Conflicts of Interest

The author declares no conflicts of interest regarding the publication of this paper.

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