

CASE REPORT

Granulicatella adiacens, the Elusive Endocarditis Causative Agent: Highlighting the Challenges Faced by Microbiology Laboratory

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ABSTRACT

A 58-year-old man with history of mitral valve prolapse and previous motor vehicle accident presented with one week history of lower back pain and fever. He was initially treated for pyelonephritis and given ceftriaxone. Blood culture grew *Granulicatella adiacens* after 7 days of incubation. The laboratory then referred the case to infectious disease team in view of possible infective endocarditis. Urgent echocardiogram was done and confirmed the diagnosis. His antibiotic was changed to intravenous benzylpenicillin and gentamicin. *Granulicatella adiacens* are difficult to be isolated in the laboratory hence they imposed certain challenges in laboratory identification. Most patients with *Granulicatella adiacens* infective endocarditis present with non-specific symptoms, imposing further challenge in recognizing the condition. These factors posed significant challenges in diagnosing *Granulicatella adiacens* endocarditis. This case highlighted challenges faced by the laboratories and the need of high index of clinical suspicion and prompt communication to ensure optimum patient care and management.

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INTRODUCTION

First described by Frenkel & Hirsch in the 1960s, nutritionally variant streptococci (NVS) requires pyridoxal or cysteine for growth on blood agar. These bacteria can also grow as satellite colonies around colonies of staphylococcus. *Granulicatella* and *Abiotrophia* are the genera under the group NVS. Because of its fastidious nature, currently laboratory identification of these bacteria posed certain challenges. It can be extremely difficult to isolate and identify these organisms in the laboratory.

Three species of *Granulicatella* have been described: *G. adiacens*, *G. elegans* and *G. balaenopterae* (1). *Granulicatella* species are part of the dental flora, however they can rarely cause bacteremia and endocarditis. Main risk factor that predisposes a person to infective endocarditis include congenital heart defects, rheumatic valvular disease, bicuspid aortic valves, and mitral valve prolapse.

Currently infective endocarditis caused by *G. adiacens* are rare and together with *Abiotrophia*, it has been estimated that they account for approximately 1.5% (2) of bacterial infective endocarditis. *G. adiacens* also known to cause postinstrumentation meningitis, infections of breast implants, and peritoneal dialysis-related peritonitis (3)

We present a case of infective endocarditis caused by *G. adiacens* that were nearly missed attributed to certain challenges in their diagnosis due to vague clinical presentation and challenges in laboratory detection of the organism.

CASE REPORT

A 58-year-old man with a history of mitral valve prolapse presented to our health care facility with back pain high-grade fever of two weeks duration. On further questioning, he denied any other significant symptoms. He was diagnosed with mitral valve prolapse years ago, however, due to unknown reasons he defaulted treatment and follow-up. In 2015, he was involved in a motor vehicle accident, following which he required facial reconstruction and multiple titanium implants on the face. On examination, he was alert and not septic

looking. Oral examination revealed poor dental hygiene and exposed mandibular plate with calculus overlying the plate can be seen. The recorded temperature was 37°C with his SPO₂ 97% at room air, blood pressure, respiratory rate was all within normal range. Systemic examination revealed pansystolic murmur loudest heard at the mitral area. His lung was clear bilaterally and per abdomen examination was not significant with negative renal punch bilaterally. His blood parameters during admission were high WCC- 15.6 with neutrophils predominant (85%) and high CRP (35.4). At this point in time, given his presenting symptoms, the presumptive diagnosis was pyelonephritis, and he was treated with ceftriaxone.

On day one of admission, a set of blood culture samples was collected for laboratory investigations. The aerobic bottle was positive within twenty-four hour and the direct Gram smear showed Gram-positive cocci arranged in chain (figure 1). As the impression for this patient at this point of time is suspected pyelonephritis, subcultures were done on our centre standard culture media; on blood agar (BA), chocolate agar (CA) and Mac-Conkey's agar (MAC). After overnight incubation, no colony growth observed on all cultured agar and all culture medias were reincubated. Minute, semi-translucent, moist colonies appeared on BA (figure 2), and CA after four days of incubation with no growth observed on MAC agar. The colonies were alpha-hemolytic. The identity of the isolate was confirmed as *Granulicatella adiacens* using Vitek 2 automated bacterial identification system (Bio Merieux) and it was found to be sensitive to both penicillin, and vancomycin, and resistant to ceftazidime by MIC method. The anaerobic bottle took four days to become positive. The colony were observed on cultured media BA (figure 3) and CA also after four days of incubation. The isolate was then identified using Vitek 2 automated bacterial identification system (Bio Merieux). The sensitivity pattern was similar to the isolate from aerobic bottle.

Realising the possibility of *Granulicatella adiacens* as an important pathogen causing infective endocarditis, the laboratory promptly conveyed the culture result to the infectious disease team at our centre. Following this, an urgent cardiac echogram was performed on the patient. An echocardiogram revealed a large vegetation measuring 2.3x0.5 cm at the posterior mitral valve with mitral regurgitation. The antibiotic was then changed to intravenous benzylpenicillin and gentamicin, in accordance with treatment guidelines for infective endocarditis. Two set blood cultures taken after one week and one month of antibiotic therapy respectively were all negative. An echocardiogram done after a month of antibiotic therapy showed the vegetation has shrunken to a smaller size; 0.2x0.5 cm. A mitral valve replacement was planned after completion of a six-week duration of antibiotic therapy. At the point of writing, the patient is fine and stable, waiting for the scheduled

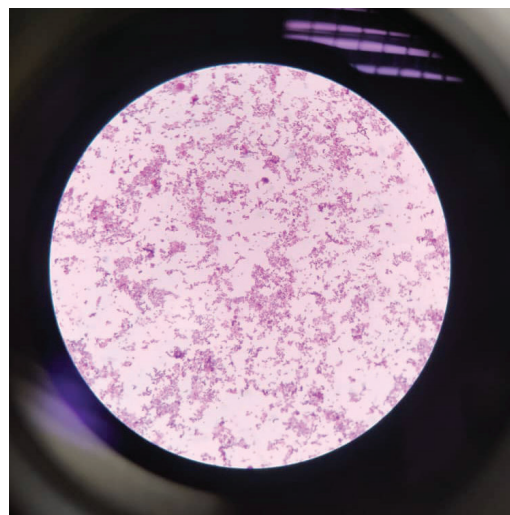


Figure 1: Photomicrograph of the gram stained smear from the blood bottle

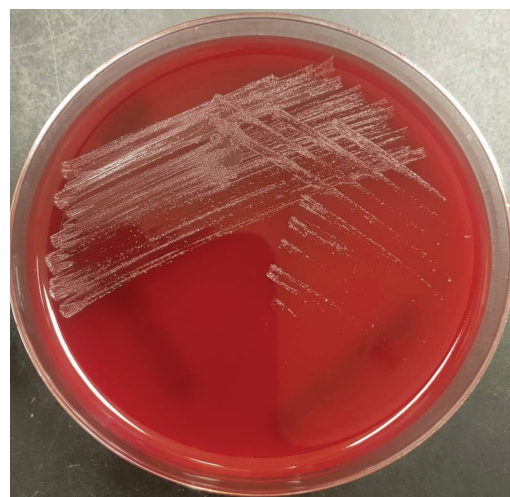


Figure 2: Photograph of the colonies cultured on the blood agar from the aerobic bottle at 4 days of incubation

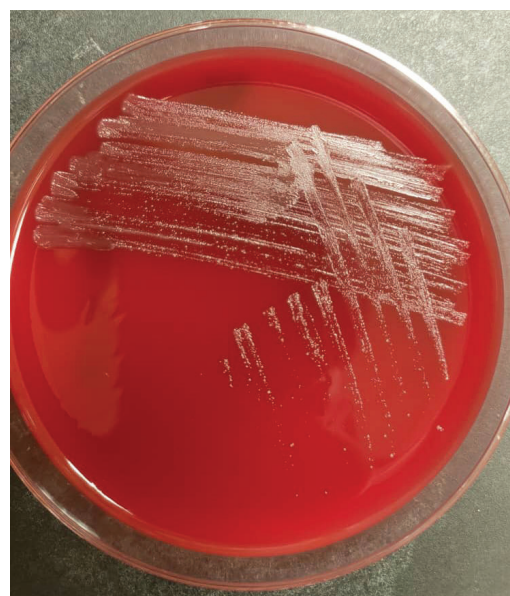


Figure 3: Photograph of the colonies cultured on the blood agar from the anaerobic bottle at 4 days of incubation

mitral valve replacement.

DISCUSSION

Infective endocarditis caused by the *G* species is rare and they usually do not present clinically as classic infective endocarditis. The classic endocarditis signs such as digital clubbing, petechiae, and Osler nodes are rare, and patients usually presented with general and unspecified signs and symptoms (4). This is also true in our patient who presented with fever and back pain. These unspecified signs and symptoms can mimic other conditions like pyelonephritis, as illustrated in this case. However, this patient has history of mitral valve prolapse which put him at risk for infective endocarditis.

G. adiacens requires pyridoxal and L-cysteine as growth factors which are not present in most standard media and most of the time it is extremely difficult to grow them on standard media. In this case, we were able to isolate the organism on our standard media albeit at a longer time. The standard turns around time for culture results is two to three days, whereas in our patient culture result was only available after seven days. Even though we manage to isolate minute colonies on day four of incubation, the colonies were not sufficient for identification and antimicrobial sensitivity testing. These agars were then reincubated until day seven when we finally managed to get sufficient colonies and identification of the organism colonies was achieved with Vitek 2 automated bacterial identification system. Ways to increase the yield of this organism in a laboratory setting include supplementing the media with 0.001% pyridoxal or 0.01% L-cysteine.

This highlights the importance of having high index of suspicion in identifying fastidious gram positive cocci that grow on chocolate agar, but do not grow or grow minimally on blood agar. Cross streaking a suspicious Gram positive cocci colonies that grow only on chocolate agar with *Staphylococcus aureus* will enable the laboratory to identify *G. adiacens*, growing as satellite colonies. The availability of relevant clinical information such as the diagnosis of infective endocarditis would help the laboratory tremendously in identifying the causative agent and in providing guidance in the choice of antibiotic therapy.

One critical factor in the diagnosis of infective endocarditis is the demonstration of persistent bacteremia typical of an endovascular infection. A minimum of three sets of blood culture with 10 mls of blood for each bottle is usually required. In this patient the diagnosis of infective endocarditis was not initially suspected. Nevertheless, at least two sets of blood cultures should be taken, as adequate volume of blood sent for culture is the most important factor for the recovery of pathogen.

According to European Society of Cardiology 2009 guidelines, treatment of infective endocarditis caused

by NVS should include penicillin G, ceftriaxone, or vancomycin for six weeks, combined with an aminoglycoside for at least the in first two weeks of treatment. Our patient was initially treated for pyelonephritis and was given intravenous ceftriaxone. Upon communication with the laboratory regarding the isolation of *G. adiacens*, a possible causative agent for infective endocarditis, an urgent echo was done. The presence of large vegetation confirmed the diagnosis of infective endocarditis. The antibiotic was then changed to intravenous benzylpenicillin and gentamicin. The changed regime of antibiotics proved to be effective as evidenced by the improvement of patient condition and the shrinkage of the vegetation size.

Literatures report that outcome with infective endocarditis caused *G* species had been associated with adverse consequences (5). Our patient is fortunate enough to survive the condition and now currently stable while waiting for mitral valve replacement surgery.

As isolation of these fastidious organisms often requires additional measures and the standard culture practice are often not sufficient. Laboratories are very much reliant on their clinical counterpart to provide relevant clinical information. More often than not, little communication between the clinician and the laboratories occurs. Scarce clinical information was shared between clinician with their laboratories counterpart when sending clinical specimens for their patients. Often, minimal information was written down in the laboratory request form. There is a need to encourage the clinicians to share more relevant information of their patients when requesting laboratory test.

CONCLUSION

This case highlighted the challenges faced by the microbiology laboratory in identifying *G. adiacens* as a cause of infective endocarditis. High index of suspicion, prompt conveyance of relevant clinical information, and close communication between the treating clinicians and the microbiology laboratory, would enable the early recognition and effective treatment of this elusive pathogen.

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REFERENCES

1. Collins MD, Lawson PA. The genus *Abiotrophia* (Kawamura et al.) is not monophyletic: proposal of *Granulicatella* gen. nov., *Granulicatella adiacens*

- comb. nov., *Granulicatella elegans* comb. nov. and *Granulicatella balaenopterae* comb. nov. *Int J Syst Evol Microbiol.* 2000; 50: 365–9. doi: 10.1099/00207713-50-1-365
2. Téllez A, Ambrosioni J, Llopis J, et al. Epidemiology, Clinical Features, and Outcome of Infective Endocarditis due to *Abiotrophia* Species and *Granulicatella* Species: Report of 76 Cases, 2000-2015. *Clin Infect Dis.* 2018;66(1):104-111. doi: 10.1093/cid/cix752.
 3. Christensen JJ, Facklam RR. *Granulicatella* and *Abiotrophia* species from human clinical specimens. *J Clin Microbiol.* 2001;39(10):3520–3. doi: 10.1128/JCM.39.10.3520-3523.2001
 4. Adam EL, Siciliano RF, Gualandro DM, Calderaro D, Issa VS, Rossi F, et al. Case series of infective endocarditis caused by *Granulicatella* species. *Int J Infect Dis.* 2015;31:56–8. doi: 10.1016/j.ijid.2014.10.023
 5. Quiroga B, Arroyo D, Verde E, Eworo A, Luco J. Infective endocarditis on a percutaneous prosthetic aortic valve with associated glomerulopathy due to *Granulicatella adjacens*. *Braz J Infect Dis.* 2012;16(6):601–2. doi:10.1016/j.bjid.2012.07.011