

Case Report

Granulicatella adiacens infective endocarditis

Arun Kumar Alagesan*, Tirumalasetty Sriharsha, Raghav J., Vikranth V.,
Kannan R., Meenakshi K.

Department of General Medicine and Cardiology, Saveetha Medical College and Hospital, Tamil Nadu, India

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*Correspondence:

Dr. Arun Kumar Alagesan,

E-mail: arunronin9@gmail.com

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ABSTRACT

Infective endocarditis is an unconventional infectious disease nonetheless life-threatening. A roundabout of 3% to 5% cases of *Streptococcal* infective endocarditis is caused by nutritionally variant *Streptococci* (NVS). *Granulicatella* species is one of the atypical causes of infective endocarditis. In this context, the authors are disclosing a case of infective endocarditis in an underlying rheumatic heart disease patient, caused by *Granulicatella adiacens*. The patient had breathlessness for the past four months, on and off fever for two months anew and mid-diastolic murmur with vegetation in aortic valve as appeared by echocardiogram. The blood cultures were tested positive for *Granulicatella adiacens*. The patient was successfully treated with intravenous vancomycin for a period of six weeks.

Keywords: *Granulicatella adiacens*, Rare organism, Life threatening

INTRODUCTION

Infective endocarditis (IE) consorts with high morbidity and mortality. Diagnosis of infective endocarditis can be gruelling as symptoms can be nonspecific and equivocal. So, echocardiogram is routinely necessary to attain an absolute diagnosis. The well recognized nutritionally variant *Streptococci* (NVS) and fastidious micro-organisms, although an uncommon cause of Infective Endocarditis totals for 5% of infective endocarditis cases.¹⁻³ The part of NVS, *Granulicatella* is rare but an absolute fatal cause of infective endocarditis. On account of the fastidious nature of the organism and indistinct symptoms, the diagnosis of infective endocarditis may be possibly delayed. It further triggers the formation of large, bulky vegetations and consequent embolic lesions to the brain and other organs.⁴ We report a case of infective endocarditis due to *Granulicatella adiacens* in a patient with prior rheumatic heart disease. Timely recovery of organisms from the blood cultures encouraged successful treatment with antimicrobial therapy.

CASE REPORT

A 47-year-old male, who is a known case of rheumatic heart disease presented with breathlessness on exertion for four months. He also had fever associated with chills and rigor for the past two months. In the immediate two months, he reported a weight loss of about 8 kilograms. During his childhood, between 10 to 20 years of age, he developed 3 to 4 occurrences of migratory joint pain and swelling each year. At the age of 35, he developed breathlessness and was diagnosed with rheumatic heart disease. Shortly after that, he was put on medication. The patient did not indicate any significant travel history and the patient did not delineate any recent dental procedures. The patient was attentive, alert, and oriented to time, place and person, on conventional examination. Vital signs divulged a temperature of 101.3°F, blood pressure of 120/80 mmHg, pulse rate-92 beats per minute and SpO₂-98%. General physical examination revealed pallor and grade 3 pan digital clubbing (Figure 1).



Figure 1: Grade 3 pan digital clubbing.

The left index finger showed irregular, erythematous flat and painless macule suggestive of Janeway lesion (Figure 2).



Figure 2: Janeway lesion on left index finger.

Janeway lesions were also seen over soles (Figure 3). Auscultation of the chest revealed loud S1 and mid-diastolic murmur over the mitral area. Dilated fundus examination revealed the presence of Roth's spot (Figure 4). Periodic blood investigations were done and reports are as follows: Hb-9 gm/dl, platelet-90000 cells/microlitre, total leukocyte count-5500 cells/microlitre, absolute neutrophil count-3920 cells/microlitre, ESR-82 mm/hr, CRP- 118.05 mg/l. Blood sugar, RFT, LFT, electrolytes and urine routine were in the range of normal limits. An echocardiogram with parasternal long axis view shows echogenic vegetation of size 1.5x0.8 cm attached to the right coronary cusp of aortic valve (Figure 5). There was moderate aortic stenosis (peak gradient 45 mmHg) and mild aortic regurgitation. There was associated moderate mitral stenosis (Mitral valve area 1.3 sqcm) and mild mitral regurgitation. In addition, there is also mild tricuspid regurgitation and mild pulmonary artery hypertension. The global LV systolic function was normal (EF-60%) and there was no pericardial effusion. Three sets of blood cultures drawn from three different

sites were sent to a microbiological laboratory before antibiotic therapy.



Figure 3: Janeway lesions on sole of right foot.



Figure 4: Right eye fundus showing Roth's spot in the infero nasal quadrant.

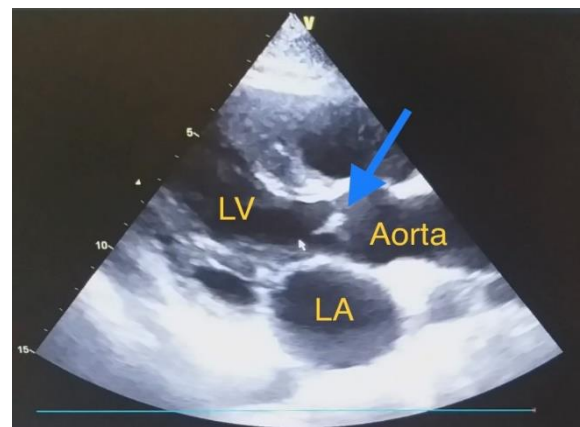


Figure 5: Echocardiogram with parasternal long axis view shows echogenic vegetation of size 1.5x0.8 cm (arrow) attached to the right coronary cusp of aortic valve. LA, left atrium; LV, left ventricle.

The patient was empirically put on an antibiotic regimen (Inj. ceftriaxone IV 2-gram OD) for aortic valve IE, with unresolved susceptibility data. After 48 hours, these cultures grew gram-positive cocci, mimicking the nature of *Streptococcus*, which was eventually pinned down as

Granulicatella adiacens. The isolate was directed for susceptibility testing and has been unveiled to be sensitive to Clindamycin, erythromycin, gentamicin, linezolid, and vancomycin.



Figure 6: Right eye fundus showing resolving Roth's spot post treatment.

The isolate has apparently shown resistance to ampicillin, cotrimoxazole, and penicillin. The patient was promptly subjected to Inj. vancomycin 1gram IV BD and Inj. gentamicin 80 mg IV BD. The blood cultures tested after 72 hours post treatment have been negative. The patient showed a satisfactory response to the treatment and was symptomatically better. Repeat fundus on day 5 post treatment showed resolving Roth's spot (Figure 6). The treatment prevailed for six weeks (vancomycin over a period of six weeks and gentamicin over a period of two weeks). The rest of the hospital stay was found insipid. Both the blood counts and ESR came down progressively. After six complete weeks of admission, the patient was discharged. After one month, the patient was doing significantly better on proper evaluation and his blood parameters were found to be within normal limits. At three month follow up visit, the patient had no symptoms of fever and breathlessness. Along with that, the echocardiogram showed normal ejection fraction (60%) with reduction in the size of vegetation of about 2 mm.

DISCUSSION

Though infective endocarditis is an uncommon infectious disease, it is fatal with an annual incidence of 3-7 persons per 1 lakh persons each year.⁵ The major risk factors of infective endocarditis encompass cardiac valvular abnormalities, congenital heart diseases, prosthetic valves, and drug abusers.⁶ *Streptococcus viridans*, *Streptococcus gallolyticus* (*S. bovis*), HACEK group, *Staphylococcus aureus*, and *Enterococci* are the typical organisms causing infective endocarditis.⁷ Just about 3-5% of cases of *Streptococcal* infective endocarditis is caused by nutritionally variant *Streptococci* (NVS), also known under the name of thiol dependent or symbiotic *Streptococci*.⁸ The rate of complications is apparently shown to be more for Infective Endocarditis caused by NVS rather than *Streptococci*.⁹ NVS was first and

foremost described in 1961 by Frenkel and Hirsch as fastidious gram-positive cocci that solely depend on pyridoxal or cysteine for its growth in standard blood culture media. NVS has been categorically divided into two different genera- *Abiotrophia* and *Granulicatella*. NVS has been reported to be the cause of 5%-6% of all cases of *Streptococcal* endocarditis.

Granulicatella and *Abiotrophia* are the normal flora of oral mucosa, urogenital and intestinal tracts in humans.¹⁰ The contemporary classification of the *Granulicatella* genus is based on 16s rRNA gene sequencing in *G. adiacens*, *G. elegans*, and *G. balaenopterae*.¹¹ *Granulicatella* species have been known to cause grievous infections in immunocompetent and immunosuppressed hosts including infective endocarditis. But due to their fastidious nature, they are often misdiagnosed as culture-negative endocarditis. Published case reports of Infective Endocarditis due to *Granulicatella* species are often affiliated with poor abysmal outcomes. A recent study described a mortality rate of 17% with embolic complications in about 30% and perivalvular abscesses in 11% of the patients with infective endocarditis due to *Granulicatella* species.¹² Typically, infective endocarditis due to NVS is habitually seen in cases with pre-existing valvular pathology.¹³ In our case, the patient had shown to have a medical history of rheumatic heart disease (RHD). The presence of pandigital clubbing, Janeway lesions, Roth's spot, and echocardiogram evidence of vegetations assisted further to the diagnosis of infective endocarditis. The most frequently infected valves with *Granulicatella* species are the aortic and mitral valves respectively. These organisms are inclined to form large and bulky vegetations. Furthermore, they are seen associated with a high risk of embolic complications. In our case, the diagnosis of *Granulicatella adiacens* was concluded based on the positive blood cultures. The challenging part is the identification of *Granulicatella adiacens* and executing antimicrobial susceptibility testing (AST) by the reason of its fastidious growth and pleomorphism. Exact and accurate identification may conceivably require a combination of special culture media with L-cysteine integrated with 16S rRNA gene sequencing. The American heart association guidelines propound combination therapy with ampicillin or penicillin G plus gentamycin for a period of 4-6 weeks or vancomycin as an alternative regimen for infective endocarditis due to *Granulicatella* species. Infective endocarditis caused by the NVS group as a whole has been delineated to produce a treatment failure rate of 41%, among which 27% may require prosthetic valve replacement.¹⁴ Prolonged antimicrobial therapy combined with valve replacement surgery is habitually needed to cure these infections. In our case, on the definite basis of antimicrobial susceptibility testing (AST), the patient was successfully treated with Inj. vancomycin 1 gram IV twice daily over a period of six weeks and Inj. gentamicin 80 mg IV twice daily over a period of two weeks. He was doing remarkably well after one month. As we now know NVS

are associated with a high risk of treatment failure, relapse, and mortality in patients with infective endocarditis, proper communication between the microbiologist and clinician is of paramount importance for identifying these microorganisms early in the course of infection before fatal complications such as embolization and valvular failure occur. NVS should also be appraised as a possible etiology in all cases of suspected endocarditis with negative blood cultures. Gram-positive pleomorphic cocci arranged in pairs and short chains in a positive blood culture that fails or in the case shown to be very slow in blood agar should alert the microbiologist about the possibility of NVS. Subsequent blood cultures of the positive blood culture bottles succeeded by prolonged incubation (>72 hours) of subculture plates, incubation under carbon dioxide, and use of pertinent media with nutritional supplementation with pyridoxal to encourage growth are indispensable for a fortunate recovery of these fastidious organisms. Endocarditis caused by NVS is often found difficult to eradicate. Timely surgical intervention may be needed in penicillin-resistant cases. In our presented case, the diagnosis was instituted within two days of admission and the patient was started on meticulous antibiotic treatment. Early prompt diagnosis and appropriate treatment thwarted alarming complications.

CONCLUSION

NVS are associated with a high risk of treatment failure, relapse, and mortality in patients with infective endocarditis. Appropriate diagnostic measures are needed in the process of identification of these fascinating microorganisms.

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