Case Report

Infective endocarditis due to *Granulicatella adiacens*: a case report and review

Kanne Padmaja[1], Vemu Lakshmi[1], Sreevidya Subramanian[1], Mamidi Neeraja[1], Siva Rama Krishna[2], O. Sai Satish[2]

[1] *Department of Microbiology, Nizam's Institute of Medical Sciences, Hyderabad, Andhra Pradesh, India*
[2] *Department of Cardiology, Nizam's Institute of Medical Sciences Hyderabad, Andhra Pradesh, India*

Abstract

Infective endocarditis (IE) caused by nutritionally variant *Streptococci* (NVS) is associated with high bacteriologic and treatment failure and mortality rates compared to endocarditis caused by other *Streptococci*. With automated blood culture systems, the rates of NVS-associated IE accounts for 5%-6% cases. We report a case of IE caused by NVS in an elderly female patient with no risk factors. The patient was successfully treated with combination antimicrobial therapy.

Key words: Gram-positive cocci; fastidious pathogen; sepsis; satellitism

J Infect Dev Ctries 2014; 8(4):548-550. doi:10.3855/jidc.3689

(Received 18 April 2013 – Accepted 27 September 2013)

Introduction

Nutritionally variant S*treptococci* (NVS) are fastidious,pleomorphicGram-positivecocci belonging to the viridans group that grow as satellite colonies around other helper bacteria [1]. They are the normal flora of oral cavity and are considered to be agents of endocarditis involving both native and prosthetic valves [2]. NVS are the etiological agents of infective endocarditis (IE) in 5%-6% of cases [3]. The two genera that are categorized under NVS are *Granulicatella* and *Abiotrophia.* We report a case of IE due to *Granulicatella adiacens* with no pre-existing abnormalities. An early recovery of the organism from blood cultures facilitated successful treatment with combination antimicrobial therapy.

Case Report

A 48-year-old female with no pre-existing cardiac abnormalities developed progressive dyspnoea with fever, chills, and rigors. On evaluation, a pan-systolic murmur was heard in the mitral area. A 2D echo showed vegetations in the mitral valve leaflet. Other systems were found to be normal. Clinical impression was that of infective endocarditis.

Three sets of blood cultures, BacT/Alert FAN aerobic and standard aerobic bottle per set (bioMerieux, Marcy l'Etoile, France) were submitted to the microbiology lab within 24 hours of admission and before antibiotic therapy with intravenous amikacin of 1 mg/kg body weight was initiated. The bottles were incubated at 37°C in the BacT/Alert incubator. All the three sets flagged positive with a mean time to detection of 18.0 hours. Gram smear of the broth from all the three sets of positive blood culture bottles showed Gram-positive cocci arranged in chains. The blood culture broths were subcultured on 5% sheep blood agar (COS) and chromogenic agar (CPS, bioMerieux, Marcy l'Etoile, France) and incubated at 37°C aerobically. After 72 hours, colonies appeared on the blood agar plates. They were 0.2-0.5 mm, smooth, white, non-hemolytic, and satelliting around colonies of *Diphtheroids* (Figure 1). The property of satelletism of the isolate was confirmed by performing a satellitism test using ATCC *Staphylococcus aureus* 43300 (Figure 2). The isolate was identified as *G. adiacens* by the Vitek 2 Advanced Expert System (bioMerieux, Marcy l'Etoile, France) using ID GP panel. Antibiotic susceptibility testing was performed with the mini API (bioMerieux, Marcy l'Etoile, France) using ATB strep panel. The isolate was susceptible to penicillin, cefotaxime, gentamicin, levofloxacin, and vancomycin and was resistant to erythromycin, clindamycin, chloramphenicol, and co-trimoxazole.

Figure 1. Colonies of *Granulicatella adiacens* on 5%sheep blood agar (0.2-0.5mm), satelliting around opaque, white, large colonies of *Diphtheroids* after subculture from BacT/Alert blood culture bottles

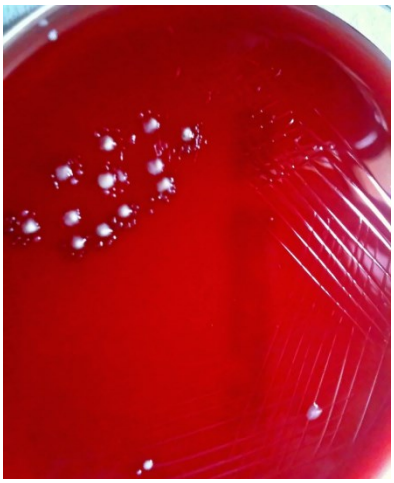

Figure 2. Colony morphology of *Granulicatella adiacens* on 5% sheep blood agar 0.2-0.5 mm, white, non-hemolytic satellite colonies (lateral streak line) supported by colonies of *Staphylococcus aureus* (centre streakline)

Based on blood cultures, antimicrobial therapy was initiated with intravenous ceftriaxone (1 gm) and gentamicin (80 mg) twice daily for four weeks. The patient made an uneventful recovery by the fourth week.

Discussion

Frenkle and Hirsch in 1961 discovered a new type of viridans group *Streptococci* based on characteristic growth requirement, prolonged incubation period, and satellite promoting phenomenon around colonies of other bacteria and variable Gram stain findings and termed them as NVS[4I]. Bouvet *etal.* in 1989 demonstrated two species within the NVS: *Streptococcus adjacens* and *Streptococcus defectiva.* In 1995, using the 16S rRNA gene, Kawamura *et al.* proposed a new genus, *Abiotrophia*, for the NVS and included four species: *Abiotrophia defectiva, adjacens, elegans,* and *balanopterae.* In 2000, Collins and Lawson proposed a new genus, *Granulicatella,* and the latter three species have been reclassified as *Granulicatella adiacens*, *elegans,* and *balaenopterae*. The genus *Abiotrophia* consists of only one species – *A. defectiva* [4]. NVS are members of the normal flora of the oral cavity and the urogenital and gastrointestinal tracts. *G. adiacens* is more frequent in the oral cavity [5].

Satelliting colonies are usually supported by Gram-positive bacteria such as *Diphtheroids, Staphylococci, Streptococci*, Gram-negative bacteria, and yeasts. While satellite growth can be observed after 24 hours of incubation, colonies at the outer edge of the zone become enlarged after 48 hours, presumably because of the abundance of nutrients in the surrounding medium (Figure 1).

Infections due to NVS, though unusual, are usually associated with significant morbidity and mortality [6]. Besides endocarditis (5%-6%), NVS has been implicated in a variety of other infections such as bacteremia,septicemia,centralnervoussystem infections,ocularinfections,andrespiratory infections [7]. The clinical course is more severe than other viridans group *Streptococci*. Nutrition limitation within vegetation, slow growth rate, and production of exopolysaccharide contribute to a longer course of endocarditis and require a longer duration of effective antibacterial coverage [8].

NVS are usually very fastidious; the routinely used blood culture media are incapable of supporting the growth of NVS unless supplemented with pyridoxal, a rare nutritional requirement. In the present case, the NVS was successfully recovered from the blood of the patient, as culture medium of the BacT/Alert standard aerobic and FAN aerobic (bioMerieux, l'Etoile, France) bottlescontains pyridoxal with a concentration of 0.001%, which supports and promotes growth.

Simone *et al.* reported NVS in a patient with IE with no risk factors, similar to our case [1]. Analysis of literature revealed a high prevalence (61%) of valvular heart disease associated with endocarditis caused by NVS, such as congenital valvular heart disease or heart valve prosthesis [1]. Vandana *et al.* also reported *G. adiacens* from a patient of native valve endocarditis and femoral embolism [2]. Yuko

Ohara-Nemoto *et al.* also reported IE caused by *G. adiacens* originating from the oral cavity [7].

In this case the portal of entry of NVS into the bloodstream was not known. These organisms are assumed to have originated from the oral cavity, as the patient had bad oral hygiene, for which she had undergone dental manipulations several times, before the episode of IE.

Isolates of NVS are frequently resistant to penicillin, extended-spectrum cephalosporins, and fluoroquinolones. The recommended regime is usually along-termcombinationofantimicrobial chemotherapy with penicillin or ceftriaxone (2 gm twice daily) and gentamicin (80 mg twice daily) for four weeks [9].

Conclusions

As NVS are associated with high rates of treatment failure and relapse and mortality in patients with IE, communication between the microbiologist and the clinician is of crucial importance for identification of these microorganisms early during the course of the infection before complications such as embolization or valvular failure occur. NVS should also be considered 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 fail or are very slow to grow on blood agar should alert the microbiologist to the possibility of NVS. Frequent subculture of the positive blood culture bottles followed by prolonged incubation (> 72 hours) of the subculture plates, incubation under carbon dioxide, and use of appropriate media with nutritional supplementation with pyridoxal to promote growth are very essential for a successful recovery of these fastidious organisms.

Endocarditis caused by NVS is often difficult to eradicate; a combination of penicillin or ceftriaxone and an aminoglycoside for prolonged periods are recommended for treatment. Since IE due to NVS is associated with higher morbidity and mortality, rapid identification with automated systems and prompt treatment are essential for a successful clinical outcome.

References

1. Giuliano S, Caccese R, Carfagna P, Vena A, Falcone M, Venditti M (2012) Endocarditis caused by nutritionally variant streptococci: a case report and literature review. Infez Med 20: 67-74.
2. Vandana KE, Mukhopadhyay C, Rau NR, Ajith V, Rajath P (2010) Native valve endocarditis and femoral embolism due to *Granulicatella adiacens*: a rare case report. Braz J Infect Dis 14: 634-636.
3. Lin CH, Hsu RB (2007) Infective Endocarditis caused by Nutritionally Variant Streptococci. Am J Med Sci 334: 235-239.
4. Liao CH, Teng LJ, Hsueh PR, Chen YC, Huang LM, Chang SC, Ho SW (2004) Nutritionally Variant Streptococcal Infections at a University Hospital in Taiwan: Disease Emergence and High Prevalence of b-Lactam and Macrolide Resistance. Clin Infect Dis 38: 452-455.
5. Christensen JJ, Facklam RR (2001) *Granulicatella* and *Abiotrophia* Species from Human Clinical Specimens. J Cli Microbiol 39: 3520-3523.
6. Ruoff KL (1991) Nutritionally Variant Streptococci. Clin Microbiol Rev 4: 184-190. 7.
7. Ohara-Nemoto Y, Kishi K, Satho M, Tajika S, Sasaki M, Namioka A, Kimura S (2005) Infective Endocarditis Caused by *Granulicatella elegans o*riginating in the Oral cavity. J Clin Microbiol 43: 1405.
8. Baddour LM and Wilson WR (2006) Infections of prosthetic valves and other cardiovascular devices. In Mandell GL, Bennett JE, Dolin R, editors. Mandell, Douglas and Bennett's Principles and Practice of Infectious Diseases. United States: Churchill Livingstone Elseiver. 2440-2441.
9. Kathryn LR (2011) *Aerococcus, Abiotrophia* and other Aerobic Catalase Negative, Gram-positive cocci. In Versalovic.J, Carrol KC, Funke G, Jorgensen JH, editors. Manual of clinical Microbiology. Washington DC: ASM Press. 365-376.

Corresponding author
Dr. Vemu Lakshmi
Department of Microbiology, Nizam's Institute of Medical Sciences
Punjagutta, Hyderabad
500082, Andhra Pradesh, India
Phone: 91 40 66618773, 91 40 23489290
Fax: 040 23310076
Email: lakshmi57vemu@gmail.com

Conflict of interests: No conflict of interests is declared.