Case Report

Kytococcus schroeteri: An Emerging Pathogen on the Horizon

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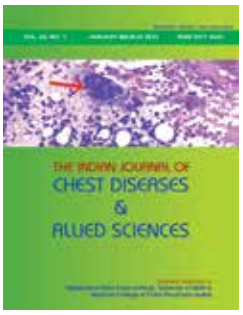

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ABBREVIATIONS USED IN THIS ARTICLE

IE = Infective endocarditis

VP = Ventriculoperitoneal

CL= Central line

ASD = Atrial septal defect

RHD = Rheumatic heart disease

PTMC = Percutaneous transvenous mitral commissurotomy

CVA = Cerebrovascular accidents

TEE = Transthoracic echocardiography

rRT-PCR = Real-time reverse transcriptase-polymerase chain reaction

MALDI-TOF MS = Matrix assisted laser desorption ionisation-time of flight mass spectrometry

AST = Antimicrobial-susceptibility testing

MIC = Minimum inhibitory concentration

Abstract

Kytococcus has long been considered to be a skin commensal or environmental contaminant. However, it has emerged as an aetiological agent of prosthetic valve infective endocarditis, pneumonia, bacteremia, osteoarticular, and implant/device infections, especially in patients with immunocompromised conditions, such as haematological malignancies, febrile neutropaenia and in patients on immunosuppressant therapy. We report a case of prosthetic valve endocarditis associated with *Kytococcus schroeteri* in a patient with rheumatic heart disease and mitral valve replacement. Special efforts to reach correct identification have to be made as Kytococcusis, commonly resistant to penicillins and oxacillins; and often needs prolonged treatment with glycopeptides containing combination antimicrobial therapy.

Introduction

Kytococcus is a gram-positive cocci, earlier included in the genus *Micrococcus*. However, based on phylogenetic and chemotaxonomic analysis, the genus *Kytococcus* has been separated from genus *Micrococcus* and assigned separate status along with other genera, *viz* genus *Kocuria*, genus *Nesterenkonia*, and genus *Dermacoccus*.[1] Earlier, *Kytococcus* has been postulated to be a skin commensal flora or an environmental contaminant. Recently, it has been isolated from various biological samples in specific clinical situations, like foreign implants/devices[2-5], immunocompromised conditions such as haematological malignancies[6-9], febrile neutropaenia[8,9], cancer chemotherapy[7-9], patients on immunosuppressant therapy[5,10] as well as in cardiac conditions, *viz* infective endocarditis (IE), especially in patients with prosthetic valves and associated heart diseases/conditions.[11,13-19] The common clinical presentation include pneumonia[6-10], bacteremia[7,8,10,20], IE and implants/device infections, like ventriculo peritoneal (VP) shunt infections[2,3], central line (CL) infections[8], septic arthritis, osteomyelitis and surgical site infections.[4,5,21]

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Case Report

A 45-year-old male came to a tertiary care hospital in South India with chief complaints of intermittent high-grade fever, more at night, associated with chills and rigors for one month. He also had non-productive cough for one month with shortness of breath for the same duration. There was no history of associated haemoptysis, chest pain, palpitations, syncope, swelling of legs, bleeding manifestations, skin rashes, headache, and seizures. He had no recent history of undergoing any dental or diagnostic procedures or intravenous drug abuse. He was a known case of atrial septal defect (ASD) since birth with spontaneous closure, and diagnosed with rheumatic heart disease (RHD) at the age of 10 years, pulmonary hypertension, with severe mitral stenosis for which he underwent percutaneous transvenous mitral commissurotomy (PTMC) eight years back and mitral valve replacement surgery three years after PTMC. He also had a history of cerebrovascular accidents (CVA) with right-sided haemiplegia five years ago. He was non-diabetic, reformed alcoholic and a reformed smoker for the last five years.

On presentation, he was conscious, oriented, febrile, had grade 1 clubbing with a pulse rate of 130/min, irregularly irregular in rhythm, normal blood pressure and maintaining oxygen saturation at room air. There were few petechial spots observed in the palpebral conjunctiva of the eyes. There were no Roth's spots, Osler nodes, Janeway lesions, or splinter haemorrhages. Electrocardiography showed atrial fibrillation with rapid ventricular response. Chest radiograph revealed mitral valve prosthesis with normal lung fields. On transthoracic echocardiography (TEE), left ventricle ejection fraction was 50%, sclerosed aortic valve, normally functioning mitral prosthetic valve with no appreciated vegetations or pericardial effusion or cardiac abscess. In view of the long history of fever and no obvious aetiology (fever of unknown origin), a provisional clinical diagnosis of prosthetic valve IE was made.

Incidentally, he was found to be positive for Coronavirus disease 2019 (COVID-19) by real-time reverse transcriptase-polymerase chain reaction (rRT-PCR). Sputum examination by Ziehl-Neelsen staining for acid-fast bacilli was negative.

Three pairs of blood culture samples (six bottles) from three different venipuncture sites were collected serially at 0 hour, 4.5 hours, and 9.5 hours were sent to Microbiology laboratory for culture. All six samples were incubated using new advanced automated BacT/Alert Virtuo Microbial Detection System (bioMérieux, Marcy l'Etoile, France) with a preset incubation period of 10 days, as IE was suspected. All blood culture bottles flagged positive with an average time-to-positivity of 17 hours, 53 hours, 58 hours, 68 hours, 73 hours, and 76 hours. Gram stain from the bottle flagged earliest with TTP of 17 showed gram-positive bacilli and grew aerobic spore bearer as contaminant. Gram stain from rest of the five bottles showed gram-positive cocci in tetrads and small clusters. The pathogen was fastidious, required 48 hours of incubation at 37 °Cunder aerobic conditions to obtain full plate growth. Colonies on blood agar were small circular, dry, and non-haemolytic (Figure 1). It was found to be catalase-positive, modified oxidase-negative, and gram-positive cocci in tetrads. Latex agglutination test for *Staphylococcus aureus* performed from colony was negative.

Figure 1. Growth of *Kytococcus schroeteri* on 5% sheep blood agar after 48 hours of aerobic incubation at 37 °C.

The colony was subjected to Matrix Assisted Laser Desorption Ionisation-Time of Flight Mass Spectrometry (MALDI-TOF MS) automated identification method, which identified isolates from all the five bottles as *Kytococcus schroeteri*. Antimicrobial susceptibility testing (AST) was performed on Mueller-Hinton agar with 5% sheep blood for gentamicin, erythromycin, tetracycline, and linezolid by Kirby-Bauer's disk diffusion method, along with the minimum inhibitory concentration (MIC) determination by Epsilometer test for vancomycin, as the isolate was growing very poorly on usual Mueller-Hinton agar (Figure 2). MIC by broth microdilution was determined using an automated Vitek-2 (bioMérieux, Marcy l'Etoile, France) platform. The interpretation of AST was performed using clinical breakpoints for *Staphylococcus* species given by Clinical Laboratory Standards Institute,[22] as clinical breakpoints for *Kytococcus* were not available. The isolate was susceptible to gentamicin, erythromycin, tetracycline, linezolid, and vancomycin.

The patient was empirically started on intravenous gentamicin. Based on the literature review, a combination of gentamicin, vancomycin, and rifampicin for *Kytococcus* IE, intraversion vancomycin was added to the regimen when the aetiological diagnosis arrived. The patient developed drug-induced acute kidney injury and gentamicin was stopped at two weeks. Rifampicin was

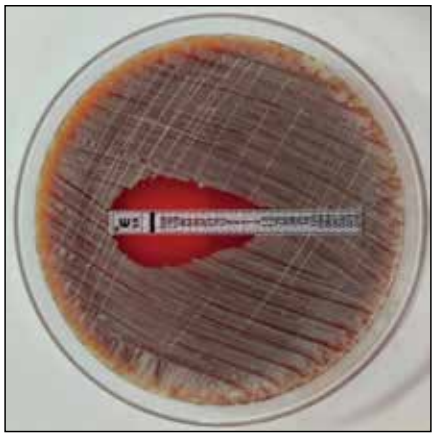

Figure 2. Antimicrobial susceptibility testing of *Kytococcus schroeteri* on Mueller-Hinton agar with 5% sheep blood for vancomycin minimum inhibitory concentration by epsilometer strip (e-strip) gradient diffusion method.

added. Patient recovered symptomatically and becomes afebrile, cough subsided, with normal breathing. After 11 days, RT-PCR was negative for COVID-19. Patient discharged on intraversion vancomycin and rifampicin for six weeks.

Discussion

The diagnosis of IE can be arrived at using revised/ modified Duke's clinical diagnostic criteria.[23,24] It includes two major criteria—one being the evidence of endocardial involvement using echocardiography in terms of oscillating intracardiac mass, cardiac abscess, new partial dehiscence of prosthetic valve, or new valvular regurgitation; whereas the second one is the microbiological criterion using blood culture. Minor criteria include (i) predisposing heart condition or injection drug use, (ii) fever, (iii) vascular phenomena, (iv) immunologic phenomena and microbiological minor criteria, such as positive blood culture that does not meet a major criterion or serological evidence of active infection with organism consistent with IE.[23,24]

Positive blood culture criteria for IE includes (1) isolation of typical organisms causing IE [Viridans streptococci, *Streptococcus gallolyticus, Haemophilus* (except *H. influenzae*), *Aggregatibacter, Cardiobacterium, Eikenella,* and *Kingella* (HACEK) group, community-acquired *Staphylococcus aureus or Enterococcus* species, in the absence of a primary focus] from two separate blood cultures, (2) isolation of microorganism consistent with IE from persistently positive blood culture, defined as: (i) two blood cultures drawn >12 hours apart, or (ii) all of three, or a majority of four or more separate blood cultures, with first and last sample drawn should be at least one hour apart or more.[23, 24]

Meeting two major criteria, or one major and three minor criteria, or five minor criteria is termed as 'Definite IE'. Meeting one major criterion and one minor criterion, or three minor criteria is termed as 'Possible IE'.[23,24] So, even if either of the microbiological positive blood culture criteria (termed as culture-negative IE) or criteria for endocardial involvement is not met, it can still be classified as IE by clinical criteria when more than three minor criteria are met.

In the present case, five out of six serial blood cultures collected over >1 hour flagged positive for *Kytococcus schroeteri*, which satisfied one major criterion. There was no obvious evidence of endocardial involvement on transthoracic echocardiography. Among minor criteria of IE, patient had met three criteria, *i.e.* high-grade fever, predisposing heart condition (RHD, ASD), and vascular phenomena in the form of arterial embolisation and episodes of CVA. There were no appreciable immunologic phenomena. So, on the basis of one major criterion and three minor criteria, it was diagnosed to be a case of definite IE.

When conjunctival petechiae are present, clinicians should consider IE as a possible differential diagnosis and never overlook it. In a recent large case series, conjunctival petechiae are reported in 5% of cases.[1] This ratio is almost the same as that of splinter haemorrhages, Janeway's lesions, and Roth's spots, known as characteristic findings of IE.[25]

On PubMed search data-base and Google Scholar data-base with the search term "*Kytococcus schroeteri*",to date, there are 20 reported cases of *Kytococcus schroeteri*, 15 had some type of foreign implants/devices or post-operative cases, and five with immunosuppressive conditions. Out of 20 cases, there are nine cases of IE due to *Kytococcus schroeteri*,[11-19] all of them with prosthetic valve IE. Aortic valve (8 out of 9 reports) is the most commonly affected valve with only one mitral valve involvement case.[13] In the present study, mitral prosthetic valve was involved. Among these nine reports, one patient had predisposing heart condition in the form of RHD[13], and one patient had a history of CVA.[18] Development of IE after the prosthetic valve replacement ranged from 3 to 12 years in the literature, which in our case was five years.

Combination therapy with intravenous vancomycin, gentamicin, and rifampicin for a mean duration of six weeks seems to be the preferred choice in most of the studies, except in one, where daptomycin was used.[19] Apart from cases of IE, there are five reported cases of *Kytococcus schroeteri* pneumonia,[6-10] out of which three had associated bacteremia[7,8,10], one was associated with skin eruptions[9], and one had only respiratory presentation.[6] Associated risk factors include haematological malignancies, like acute myeloid leukaemia[7,9], hairy cell leukaemia[8], induction chemotherapy[7-9], febrile neutropaenia[8,9], uncontrolled diabetes mellitus[14,21], and

chronic corticosteroid therapy.[5,10] Ventriculo-peritoneal shunt infections were reported in two cases in the pediatric age group.[2,3] Osteo-articular involvement was the next common presentation, like spondylodiscitis[21], septic arthritis, osteomyelitis.[4,5] The patients with osteo-articular involvement were post-operative and associated with implants/foreign devices.

In conclusion, microbiological diagnosis of *Kytococcus* is very challenging in the absence of advanced automated identification methods, like MALDI-TOF MS and Vitekc. A high index of suspicion is essential to suspect this diagnosis in the relevant clinical setting. However, advanced technology may be a challenge in a resource-limited setting, like our country to establish the diagnosis.

References

1. Stackebrandt E, Koch C, Gvozdiak O, Schumann P. Taxonomic dissection of the genus Micrococcus: *Kocuria gen. nov., Nesterenkonia gen. nov., Kytococcus gen. nov., Dermacoccus gen. nov., and Micrococcus Cohn 1872 gen. emend. Int J Syst Bacteriol* 1995;45:682–92. *Erratum in: Int J Syst Bacteriol* 1996;46:366.
2. Jourdain S, Miendje Deyi VY, Musampa K, Wauters G, Denis O, Lepage P, *et al*. Kytococcusschroeteri infection of a ventriculoperitoneal shunt in a child. *Int J Infect Dis* 2009;13:e153–5.
3. Schaumburg F, Schmalstieg C, Fiedler B, Brentrup A, Omran H, Becker K. A bumpy road to the diagnosis of a *Kytococcus schroeteri* shunt infection. *J Med Microbiol* 2013;62:165–8.
4. Chan JF, Wong SS, Leung SS, Fan RY, Ngan AH, To KK, *et al*. First report of chronic implant-related septic arthritis and osteomyelitis due to *Kytococcus schroeteri* and a review of human K. schroeteri infections. *Infection* 2012;40:567–73.
5. Shah AS, Vijayvargiya P, Jung S, Wilson JW. Postoperative hardware-related infection from *Kytococcus schroeteri*: its association with prosthetic material and hematological malignancies: a report of a case and review of existing literature. *Case Rep Infect Dis* 2019:6936472.
6. Hodiamont CJ, Huisman C, Spanjaard L, van Ketel RJ. *Kytococcus schroeteri* pneumonia in two patients with a hematological malignancy. *Infection* 2010;38:138–40.
7. Blennow O, Westling K, Fröding I, Ozenci V. Pneumonia and bacteremia due to *Kytococcus schroeteri. J Clin Microbiol* 2012;50:522–4.
8. Amaraneni A, Malik D, Jasra S, Chandana SR, Garg D. *Kytococcus schroeteri* bacteremia in a patient with hairy cell leukemia: a case report and review of the literature. *Case Rep Infect Dis* 2015;2015:2173–07.
9. Nagler AR, Wanat KA, Bachman MA, Elder D, Edelstein PH, Schuster MG, *et al*. Fatal *Kytococcus schroeteri* infection with crusted papules and distinctive histologic plump tetrads. *Arch Dermatol* 2011;147:1119–21.
10. Mohammedi I, Berchiche C, Becker K, Belkhouja K, Robert D, von Eiff C, *et al*. Fatal *Kytococcus schroeteri* bacteremic pneumonia. *J Infect* 2005;51:E11–3.
11. Becker K, Wüllenweber J, Odenthal HJ, Moeller M, Shumann P, Peters G, *et al*. Prosthetic valve endocarditis due to *Kytococcus schroeteri. Emerg Infect Dis* 2003;9:1493–5.
12. Le Brun C, Bouet J, Gautier P, Avril JL, Gaillot O. *Kytococcus schroeteri* endocarditis. *Emerg Infect Dis* 2005;11:179–80.
13. Mnif B, Boujelbène I, Mahjoubi F, Gdoura R, Trabelsi I, Moalla S, *et al*. Endocarditis due to *Kytococcus schroeteri*: case report and review of the literature. *J Clin Microbiol* 2006;44:1187–9.
14. Aepinus C, Adolph E, von Eiff C, Podbielski A, Petzsch M. *Kytococcus schroeteri*: a probably underdiagnosed pathogen involved in prosthetic valve endocarditis. *Wien Klin Wochenschr* 2008;120:46–9.
15. Renvoise A, Roux V, Casalta JP, Thuny F, Riberi A. *Kytococcus schroeteri*, a rare agent of endocarditis. *Int J Infect Dis* 2008;12:223–7.
16. D'Andria A, Avallone L, Cinquanta L, Greco L, Marino S. Involvement of *Kytococcus schroeteri* in a case of prosthetic valve endocarditis. *Microbiologia Medica* 2008;23. doi:10.4081/mm.2008.2601
17. Yousri T, Hawari M, Saad R, Langley S. *Kytococcus schroeteri* prosthetic valve endocarditis. *BMJ Case Rep* 2010:bcr0620103064.
18. Poyet R, Martinaud C, Pons F, Brisou P, Carlioz R. Endocarditeinfectieuseà *Kytococcus schroeteri* [*Kytococcus schroeteri* infectious endocarditis]. *Med Mal Infect* 2010;40:51–3.
19. Liu JC, Jenkins DR, Malnick H, Kovac J, Szostek J. *Kytococcus schroeteri* endocarditis successfully managed with daptomycin: a case report and review of the literature. *J Med Microbiol* 2012;61750–3.
20. Bayraktar B, Dalgic N, Duman N, Petmezci E. First case of bacteremia caused by *Kytococcus schroeteri* in a child with congenital adrenal hyperplasia. *Pediatr Infect Dis J* 2018;37:e304–e305.
21. Jacquier H, Allard A, Richette P, Ea HK, Sanson-Le Pors MJ, Berçot B. Postoperative spondylodiscitis due to *Kytococcus schroeteri* in a diabetic woman. *J Med Microbiol* 2010;59:127–9.
22. CLSI. Performance Standards for Antimicrobial Susceptibility Testing. 30th edition. *CLSI Supplement M100*. Wayne, PA: Clinical Laboratory Standards Institute; 2020.
23. Durack DT, Lukes AS, Bright DK. New criteria for diagnosis of infective endocarditis: utilization of specific echocardiographic findings; Duke Endocarditis Service. *Am J Med* 1994;96:200–9.
24. Li JS, Sexton DJ, Mick N, Nettles R, Fowler VG Jr, Ryan T, *et al*. Proposed modifications to the Duke criteria for the diagnosis of infective endocarditis. *Clin Infect Dis* 2000;30:633–8.
25. Matsuura H, Uegami M, Matsuo N. Conjunctival petechiae and infective endocarditis. *QJM: An Int J Med* 2018;6:423.