PACE MAKER RELATED INFECTION WITH ENDOCARDITIS CAUSED BY SMALL COLONY VARIANTS OF STAPHYLOCOCCUS AUREUS – A CASE REPORT

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ABSTRACT
Small colony variants (SCVs) of Staphylococcus aureus often cause persistent and recurrent infections. SCVs are characterized by a very slow metabolic rate, atypical colony morphology and unusual biochemical properties. Here we describe a case of pacemaker related blood stream infection and endocarditis caused by Staphylococcus aureus small colony variants.

KEY WORDS: Small colony variants, Staphylococcus aureus, pacemaker related infection.

INTRODUCTION
Staphylococcus aureus small colony variants (SCVs) have been associated with relapsing infection in bone, heart valves and soft tissues.[1] S.aureus SCVs are characterized as electron deficient bacteria because of their auxotrophism to hemin and menadione or are recognized as thymidine dependant.[2] These variants produce small, nonpigmented and non hemolytic colonies. They also demonstrated various other features like decreased coagulase production,
failure to ferment mannitol and increased resistance to cell wall active antibiotics.\[3\] Because of their atypical characteristic SCVs present a challenge both to the microbiologists and clinicians, often resulting in misidentification and misinterpretation. Here we report a case of pacemaker related blood stream infection and endocarditis caused by SCVs of *S.aureus* in a tertiary care hospital.

**CASE REPORT**

A 53 year old man was transferred to our tertiary care hospital with the presumptive diagnosis of endocarditis related to a pacemaker lead infection. Patient was hypertensive and having coronary artery disease. Six years prior he had suffered an extensive myocardial infarction resulting in ischemic cardiomyopathy. Because of this necessitated placement of a pacemaker biventricular defibrillator. Four weeks before admission, this device had been removed because of a pocket of infection after road traffic accident with dislocation of device and perforation of the skin. The pacemaker leads were left in the place, a gentamicin containing sponge was placed to the infection site and a new pacemaker was implanted on the opposite side of the chest. Two weeks later the patient sought treatment at the local health care facility for high fever, chills and a subcutaneous abscess with oxacillin- susceptible *S.aureus* at the primary site. Antimicrobial therapy was started with intravenous (I/V) cloxacillin and the fever subsided. Ten days later again the patient developed high fever with chill and rigor. That time I/V vancomycin was tried. After initial improvement there was recurrence of fever. The patient was transferred to our tertiary care set up for pacemaker ablation. Trans-esophageal echocardiography (TEE) done after antimicrobial therapy showed vegetation on the pacemaker leads. Laboratory investigation showed rise in C Reactive protein level (CRP) 50mg/L, Erythrocytic sedimentation rate (ESR) 66mm/1st hr and moderate neutrophilia. Other laboratory parameters were within normal range. Four sets of blood culture obtained on four consecutive days yielded nonhemolytic colony with .1mm diameter. The isolated strain was tube coagulase test negative and catalase positive. Antibiotic susceptibility test result showed the isolated strain was susceptible to vancomycin, cloxacillin, linezolid, and resistant to azithromycin, co-trimoxazole, cefpodoxime, rifampicin. A lawn culture was put on nutrient agar plate along with 20ug and 40ug menadione impregnated discs over it. The colonies around menadione discs grew as large colonies thereby confirming menadione auxotrophy. Subsequent subculture from this colony revealed yellow pigmented normal *S.aureus* colony. (Fig-1)
These large colonies were catalase, coagulase (slide and tube) test positive and oxidase negative. According to susceptibility test result the patient was treated with I/V vancomycin and cloxacillin. The patient became afebrile and his CRP and ESR levels returned to normal. Two weeks later the patient readmitted with recurrent high fever. Three blood culture taken on readmission were again positive with *S.aureus* SCVs. A TEE showed the remaining tip of the pacemaker lead fixed in myocardium along with few vegetations. The remaining device was finally removed by open heart surgery with use of cardiopulmonary bypass. Microbiologic culture of the pacemaker electrode yielded menadione auxotrophic small colony variants of *S.aureus*. The patient recovered completely and was discharged on the 12th postoperative days.

**DISCUSSION**

SCVs of *S.aureus* cause persistent long-term infection in patients with long standing predisposing conditions like cystic fibrosis and osteomyelitis and often give a poor clinical and bacteriologic response to standard antimicrobial therapy in patients with abscess, chronic osteomyelitis, and bronchopulmonary infection especially after prolonged exposure to antimicrobials.\(^4\) SCVs have very slow growth rate, atypical colony morphology and unusual biochemical characteristics. They are usually auxotrophic for vitamin K, thymine, and hemin and lacking in essential component of electron transport chain. Because of this they are resistant to aminoglycosides and other cell wall antimicrobials.\(^3\) SCVs of *S.aureus* are able to persist intracellularly in unprofessional phagocytes.\(^5\) The intracellular position shield SCVs from defenses and reduce exposure to antibiotics. Diagnosis usually achieved by...
reversal to wild type *S. aureus* colonies in presence of menadione, resistance to co-trimoxazole (auxotrophocity for thymidine) and increased size and growth around haemin containing discs.

There are a few reports of isolates of SCVs from clinical specimens. One report mentions isolation of SCVs from pacemaker related endocarditis from Germany.\(^6\) Baddour LM et al also describe a pacemaker related endocarditis caused by SCVs of *S. aureus*.\(^7\) Von Eiff and colleagues recently reported few cases of osteomyelitis due to SCVs of *S. aureus*.\(^8\) But to our best knowledge there is no such reported case of device related endocarditis in eastern part of India. Also in our case findings suggests that SCVs might have been selected from the parent strain population with normal phenotype after exposure to locally applied aminoglycosides or to the prolonged exposure to the antimicrobials particularly vancomycin. Repeated positive blood culture by same strains and presumable persistence of these organisms on pacemaker lead tip may explained the poor efficacy of vancomycin and cloxacillin against these slow growing organisms that were adherent to the remaining foreign body and ability of these variants to persist intracellularly. Our finding illustrates that complete removal of any foreign body is essential for the complete cure of prosthetic intravascular device related *S.aureus* infection. Laboratories should particularly cautious for *S.aureus* small colony variants when samples are submitted when samples are submitted from patients who have received long term antimicrobial therapy, especially if the infection is persistent or recurrent.

**REFERENCES**

