

Native Valve Endocarditis Caused by Coagulase Negative Staphylococci; an Appeal to Start Outpatient Antimicrobial Therapy: An Unusual Case Report

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Abstract

Coagulase negative staphylococci (CNS) were a rare cause of native valve endocarditis. However, they are emerging as an important cause of native valve endocarditis (NVE) in both community and healthcare settings. We describe a 64 yrs. old male who developed mitral valve endocarditis caused by coagulase negative staphylococci. There were no predisposing conditions or underlying cardiac disease that could have been the risk factor for the development of native valve infection. The patient had good recovery after six weeks of treatment with anti-staphylococcal antibiotics.

Keywords: Coagulase negative staphylococcus; CoNS; Native valve endocarditis; NVE; Outpatient antimicrobial therapy; OPAT.

Case Report

This is a report of a 64 year old man with ethanol related liver cirrhosis and portal hypertension. He had past history of cervical spine fixation with a titanium plate. The patient presented with one year history of neck pain radiating to the right shoulder. The symptoms worsened in the 4 weeks prior to hospitalization. He also gave history of feeling cold.

On admission, he was having low grade fever of 37.6°C and there was an ejection systolic murmur at the aortic area. His leukocyte count was $16 \times 10^9/L$, Neutrophil count was $4.0 \times 10^9/L$ and C-reactive protein was 62.8 mg/L. Blood culture grew Gram positive cocci after ten hours of incubation in the automated BACTEC 9240 machine. Then, the patient blood was sub-cultured in four different microbiological culture media that were incubated aerobically and anaerobically for approximately 18 to 24 hours, resulted in the growth of gram positive cocci in all inoculated media. The growth then evaluated by biochemical tests that revealed a preliminary identification of coagulase

negative staphylococci i.e. catalase-positive, tube coagulase-negative and latex agglutination (Staphaurex)-negative. After that, staphylococcus was identified to species level by further biochemical testing including the API staph and automated system (Phoenix 100- BD).

The final identification of the isolate revealed *Staphylococcus epidermidis*, which was differentiated from *Staphylococcus lugdenensis* (organism which is most commonly associated with severe CoNS native valve endocarditis) by the PYR test which turned out negative (*S. lugdenensis* is PYR positive). The organism was sensitive to cloxacillin and ceftiofuran. The susceptibility testing was performed by Disc diffusion method using Ceftiofuran and Oxacillin discs and Broth dilution method through the automated system (Phoenix-BD) that calculated the minimal inhibitory concentration (MIC), based on the CDC- CLSI 2010 guidelines. The MIC for Oxacillin was <0.25 microgram/ml. Ceftiofuran susceptibility was identified by Ceftiofuran 30 microgram Disc-zone diameter of >25 mm.

Trans-thoracic echocardiography (TTE) showed a mobile structure attached to the base of posterior mitral leaflet (PML), probably vegetation. Trans-esophageal echocardiography (TEE) confirmed the finding of PML vegetation with size of 8x5 mm. Magnetic resonant imaging (MRI) of the cervical spine and right shoulder joint were both inconclusive for any evidence of infection.

The patient was started on a combination of teicoplanin and rifampicin for a total duration of six weeks. He also received gentamycin for the first five days of antimicrobial therapy. His C-reactive protein on discharge was 48.9 mg/L. He was discharged after one week of starting antibiotic therapy and continued for 5 weeks on teicoplanin as outpatient antimicrobial therapy (OPAT) introduced through PICC line. At the end of the six weeks of antimicrobial therapy, he was asymptomatic, the neck pain has disappeared and inflammatory markers normalized. Blood culture was repeated at 48 hours after initiation of antibiotics, at 2, 4 and 6 weeks of therapy and was sterile. TTE done at week 2 of treatment and at the end of antimicrobial therapy showed complete disappearance of the mitral valve vegetation.

Discussion

Coagulase negative staphylococci are invariable constituents of the normal skin flora and they have a great propensity to colonise foreign materials in human body. These microorganisms are a major cause of prosthetic valve endocarditis. In the recent years

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significant increase in the incidence of native valve endocarditis caused by coagulase negative staphylococci has been reported.¹⁻⁴ However, it is quite unusual for this pathogen to cause endocarditis in a young, otherwise healthy person who was not an intravenous drug abuser and who had no other risk factors predisposing to infective endocarditis. Our patient had history of internal fixation of cervical spine by a titanium plate. This could be the focus for the organism to seed then to spread to the heart. He had an indolent, mild and prolonged course of symptoms which are typical presentation for endocarditis caused by this organism.⁵

The organism was isolated in four bottles of two sets of blood cultures taken in different occasions almost 24 hours apart and was showing susceptibility to cefoxitin disk. This might explain the resolution of the fever and the negativity of blood cultures taken two days later after initiation of antibiotics. The patient responded to the antibiotics and did not require any surgical intervention. Subsequent serial inflammatory markers came down and the patient condition improved dramatically with complete disappearance of the vegetation.

A prospective multicentre cohort study, conducted by a large international collaboration on endocarditis, compared cases of native valve endocarditis caused by coagulase negative staphylococci (CONS) with patients of NVE caused by *Staphylococcus aureus* and those caused by viridans group streptococci.¹ The study was conducted between June 2000 to August 2006. The study found that of 1635 patients with definite NVE and no history of injection drug use, 128 (7.8%) had NVE due to CONS. Healthcare-associated infection occurred in 63 patients (49%) with NVE caused by CONS. Medical comorbidities, long-term intravascular catheter use, and history of recent invasive procedures were similar among patients with NVE caused by CoNS and among patients with NVE caused by *S. aureus*. Surgical treatment for endocarditis occurred more frequently in patients with NVE due to CoNS (76 patients [60%]) than in patients with NVE due to *S. aureus* (150 [33%]; $p < .01$) or in patients with NVE due to viridans group streptococci (149 [44%]; $p < .01$). Despite the high rate of surgical procedures among patients with NVE due to CoNS, the mortality rates among patients with NVE due to CoNS and among patients with NVE due to *S. aureus* were similar (32 patients [25%] and 124 patients [27%], respectively); the mortality rate among patients with NVE due to CoNS was higher than that among patients with NVE due to viridans group streptococci (24 [7.0%]; $p < .01$). Persistent bacteremia, congestive heart failure, and chronic illness were independently associated with death in patients with NVE due to CoNS.

This case also shows the opportunity for the outpatient antimicrobial therapy (OPAT) and for hospitals to explore establishing daycare or home based OPAT. This is a very cost effective way tending with long courses of antibiotics. In the USA, the past three decades have seen an unprecedented increase in the delivery of these therapies in the non-inpatient setting, and outpatient parenteral antibiotic therapy (OPAT) is now an established standard of care in North America.^{6,7} However, the uptake of OPAT within Europe has been more gradual, owing to

a number of clinical, fiscal, logistical and cultural considerations. In particular, physicians who are not currently engaged in OPAT programs frequently cite concerns over patient safety as a major barrier. However, where OPAT programs have been established, high levels of satisfaction are reported by both patients and physicians, suggesting that many anxieties concerning the introduction of OPAT stem from a lack of patient and physician education regarding the key potential benefits associated with OPAT.^{6,8} Excluding Europe and North America, there is severe shortage of data, especially from the Middle East region, on the use of OPAT. As the burden of serious Gram-positive infections grows, so does the need to offer clinicians, administrators and patients alternative treatment programs that are equally effective and safe compared with inpatient treatment, while promoting optimal use of limited healthcare resources.

Conclusion

We described a case of a 64 years old man who developed mitral valve endocarditis caused by CoNS. CoNS have become increasingly recognized as agents of clinically significant nosocomial bloodstream infections. In addition native valve endocarditis due to CoNS in a previously healthy non-IVDU is an emerging disease. The number of detected cases is increasing worldwide. This necessitates the need for developing a local data to know the prevalence of such cases in Oman, and the introduction of OPAT.

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