Staphylococcous epidermidis, Staphylococcous schleiferi Infections: Are CoNS Cons?

Betsy Abraham1, Antara U Gokhale2, Jalila Mohsin3, Sadanandan Prakash4

ABSTRACT
Coagulate-negative Staphylococcus (CoNS) represents one of the major nosocomial pathogen in multimorbid, immunosuppressed patients, especially with device-associated infections, often presenting with a diagnostic dilemma and aggressive antibiotic resistance. We report a case of a healthy young man with no comorbidities who succumbed to an extensive abdominal infection with Staphylococcus epidermidis and Staphylococcus schleiferi after an uneventful diagnostic procedure, despite aggressive antibiotic therapy and surgical source control. Early identification, diagnosis, and aggressive management of CoNS species is warranted depending on clinical scenario and should not be viewed as mere skin contaminants or physiological colonization.

Keywords: Coagulate-negative Staphylococcal species, Intra-abdominal infection, Postprocedure.

Indian Journal of Critical Care Medicine (2020): 10.5005/jp-journals-10071-23523

Introduction
With improved microbiological techniques, identification and differentiation of Staphylococcus species is feasible. Increasing resistance to methicillin and glycopeptides, coagulate-negative Staphylococcus (CoNS) represents one of the major nosocomial pathogen, especially in elderly, multimorbid, immunocompromised patients with device-associated health care-associated infections causing a subtle subacute or chronic course with rare aggressiveness, more frequently than earlier thought. A PubMed search on CoNS culminates in more than 15,000 references, revealing the spiraling medical influence of these bacteria.1 We present a case report of a young, healthy man who developed fatal intra-abdominal infection with Staphylococcus schleiferi and Staphylococcus epidermidis.

Case Description
A 36-year-old, diabetic man presented with obstructive jaundice. Computed tomography (CT) scan of the abdomen showed a mass at the head of pancreas. He underwent an uneventful diagnostic laparotomy for biopsy, which revealed features suggestive of chronic pancreatitis on histopathology and no bacterial growth. Ten days post surgery, he presented with fever, abdominal pain, and shortness of breath and discharge from skin wound. Pus microscopy from surgical site showed gram-positive cocci with high probability of CoNS. CT showed necrotic pancreatic duct leak and infected large loculated peripancreatic collection extending to the paracolic, subdiaphragmatic spaces and anterior abdominal wall. Collection was drained under ultrasound guidance and cultured. Patient was started on meropenum, vancomycin, and anidulafungin. Culture grew Staphylococcus epidermidis sensitive to vancomycin (MIC-2 μg/mL; Central laboratory standard institute (CLSI)-standard <4 μg/mL) and cotrimoxazole (MIC-1/19 μg/mL, CLSI-2/28 μg/mL), clindamycin (MIC<0.5 μg/mL; CLSI <0.5 μg/mL), and linezolid but resistant to oxacillin. Post procedure, he was electively intubated for worsening type I respiratory failure, requiring dialysis, and progressive increase in oxygen to maintain PaO2/FiO2 ratios; he finally succumbed.

Discussion
Infections with CoNS can be grueling to treat due to diverse vulnerabilities among strains and multidrug resistance.1,2

© The Author(s), 2020 Open Access This article is distributed under the terms of the Creative Commons Attribution 4.0 International License (https://creativecommons.org/licenses/by-nc/4.0/), which permits unrestricted use, distribution, and non-commercial reproduction in any medium, provided you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made. The Creative Commons Public Domain Dedication waiver (http://creativecommons.org/publicdomain/zero/1.0/) applies to the data made available in this article, unless otherwise stated.
Each time CONS is isolated, like wolves in sheep's clothing, it often fires a dilemma whether it constitutes an authentic infection or a mere contaminant or just a physiological colonization, often getting overlooked as an etiology for serious infection. Clinical symptoms of foreign body-related infections can be vague, initially leading to infection resulting in metastatic seeding, embolic complications, and septic thrombophlebitis.

Repeated segregation of same strain over the sequence of the infection and from pure culture of infected tissue increases the prediction of a true infection. At least two positive blood cultures of CoNS within 5 days or clinical evidence of infection with one positive blood culture, presence of central venous catheter, neutropenic patients, time to positivity \( \leq 16 \text{ hours} \), a Charlson score \( \geq 3 \) or a Pitt score \( \geq 1 \) increases the predicament of CoNS blood stream infections. True repercussions of less frequently isolated species may be underrepresented due to difficulties in delineation of CoNS in the premolecular/mass spectrometry era. With matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF MS) and whole-genome sequencing methods, more of these species are being diagnosed.\(^6,7\)

*Staphylococcus epidermidis* comprises of 65–90% of all staphylococci forming the most rampant and tenacious species isolated on the human skin and mucous membranes.\(^1,5\) *Staphylococcus epidermidis* activates human monocytes to release cytokines like TNF-α, IL-1, and IL-6 mimicking symptoms of toxic shock syndrome. About 37–47% of early cases and about 25% of late cases of prosthetic valve infective endocarditis (PVIE) are caused by *S. epidermidis*. They commonly cause infections of prosthetic devices, stents, and catheters by means of biofilm production mainly by small colony variants. Infections are rarely seen in a healthy person due to low virulence of these bacteria. However, impaired or inappropriate host immune responses may cause infection. Ability of the organism to evade the host immune innate response may contribute to infections in the absence of foreign body. Treatment with specific antibiotics may thus yield frustrating results, as they internalize into nonprofessional phagocytes evading natural immune defense.\(^1\)

*Staphylococcus schleiferi*, a coagulase-negative anaerobic *Staphylococcus* species, was primarily delineated as a zoonotic pathogen in dogs. The sparse existence of *S. schleiferi* in human flora could explain the low incidence of infections. *Staphylococcus schleiferi* is commonly misrepresented as *Staphylococcus aureus*, as both manifest clumping factor, and heat-stable DNase but can be differentiated by its production of heat-stable nuclease, free coagulase, protein A, and Q-ribitol teichoic acid. Both *S. schleiferi* strains (schleifen and coagulans) express esterase, lipase, and \( \beta \)-hemolysin as ostensible virulence factors and are often incriminated in infections in elderly men, immunosuppressed, and cancer patients producing toxin genes such as staphylococcal enterotoxins and toxic shock syndrome toxin. They have been isolated from surgical site, body fluids, wound, and, in some cases, gastrointestinal and respiratory infections. Co-colonization by coagulase-negative and -positive species increases the propensity for horizontal gene transfer.\(^5,7\)

MecA-positive CoNS like *S. epidermis* and *S. Schleferri* horizontally relay their genes within the *Staphylococcus* genus with the propensity to give rise to new methicillin-resistant strains with the potential to induce superantigens and cytotoxins increasing their virulence. The biofilm production and tissue invasion by CONS are aided by quorum sensing system and production of extracellular proteins, hemolysins, and enzymes.

Both clindamycin and co-trimoxazole are considered class A drugs in terms of *in vitro* sensitivity for *Staphylococcus* species.\(^8,9\) When faced with multi-drug resistant *Staphylococcus*, including vancomycin resistance or in species sensitive to vancomycin but with inadequate clinical response dual antibiotics have been used. Increasing resistance for *S. aureus* to vancomycin has been reported when \( \text{MICs} \geq 2 \mu g/mL \).\(^10\) Whether this can be extrapolated to CONs in near not clear. Cotrimoxazole has been added among other antibiotics.\(^9\) Clindamycin although a bacteriostatic agent has been shown to have a synergic effect. It also demonstrates antistaphylococcal toxic effect.\(^10\) Besides, clindamycin has excellent tissue penetration compared to vancomycin for intra-abdominal sepsis.\(^11\) Faced with a difficult situation with inadequate vancomycin levels and clinically worsening patient, a combination of cotrimoxazole and clindamycin along with source control with repeated debridement was used.

Our patient developed infection in the postoperative period. Initial cultures were negative. Screening is not routinely carried out for CoNS as they represent skin flora. Bacteria can colonize and tract from skin colonization. The abdomen was closed primarily during the first surgery with no drains. The cause of surgical site infection could not be ascertained and possibility of perioperative contamination cannot be ruled out. Treatment of infection with severe clinical manifestations often warrants use of multiple antibiotics to improve synergism along with aggressive source control.

**Conclusion**

Early identification, diagnosis, and aggressive management of CoNS species is warranted and should not be dismissed as mere skin contaminants or physiological colonization.

**References**
