Discussion on *Staphylococcus schleiferi*

Taxonomy

The *Staphylococcus* genus is comprised of 49 species, including 25 subspecies, classified in the family Staphylococcaceae, order Bacillales, and phylum Firmicutes.[1] Coagulase detection has long been used to separate the more virulent *Staphylococcus aureus* group from species that are coagulase negative. Moreover, some zoonotic species have also been identified as coagulase-positive or variable such as *Staphylococcus schleiferi*. *Staphylococcus schleiferi* can be further divided into two subspspecies, the coagulase-negative *S. schleiferi* subsp. *schleiferi* and coagulase-positive *S. schleiferi* subsp. *coagulans.* [2]

Identification

Staphylococci are gram-positive cocci measuring 0.5 to 1.5 microns in diameter that appear as single cells, pairs, irregular clusters and sometimes short chains. The majority are facultatively anaerobic, non-motile and non-spore-forming as well as catalase-positive and able to grow in 10% NaCl.[2] Most *Staphylococcus* spp. will grow within 18 to 24 hours of incubation on routine media such as sheep blood agar under aerobic conditions. Colonies of *S. schleiferi* are medium to large in size, round, non-pigmented and are beta-hemolytic on blood agar. Several biochemical reactions can be used to differentiate *S. schleiferi* from other *Staphylococcus* species that cause human infections. *Staphylococcus schleiferi* is characteristically pyrrolidonyl arylamidase (PYR) positive, alkaline phosphatase positive, ornithine decarboxylase negative, and susceptible to novobiocin.[1] The two subspecies can be differentiated by the slide coagulase (clumping factor), tube coagulase (free coagulase) and urease reactions. *S. schleiferi* subsp. *schleiferi* is clumping factor positive, tube coagulase negative and urease negative whereas, *S. schleiferi* subsp. *coagulans* is clumping factor negative, tube coagulase positive and urease positive.[2] An international, multicenter study found that 25-75% of *S. schleiferi* can give false-positive latex agglutination tests used for the identification of *S. aureus*.[3] Due to β-hemolysis on blood agar and positivity by coagulase tests (eg, slide, tube and latex agglutination methods), misidentification of *S. schleiferi* as *S. aureus* can occur. A PYR test could be performed and if positive should raise suspicion that an isolate is not *S. aureus*. *S. schleiferi* subsp. *coagulans* or *Staphylococcus intermedius* group organisms fit the description of a coagulase-positive staphylococci that are PYR positive. These species can be differentiated based on sugar fermentation patterns.[1]

Scarce data are available on the performance of commercially available biochemical identification systems to identify *S. schleiferi*. Additional testing, such as sugar fermentation, for confirmation of identification is often required with commercial biochemical systems.[2] Matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) systems have been demonstrated to reliably identify *S. schleiferi* to the species level but is unable to differentiate the subspecies.[4,5] Increasing reports of *S. schleiferi* correlate with the widespread implementation of MALDI-TOF MS that has allowed clinical microbiology laboratories to better identify staphylococci species, including *S. schleiferi*.

Clinical Significance

Staphylococcus schleiferi is an increasingly reported zoonotic pathogen that can cause opportunistic infections in humans. It colonizes the skin and mucosal surfaces of small animals, including dogs, cats, parrots and pigs.[1,2,6] In dogs, *S. schleiferi* causes canine otitis media, otitis externa and pyoderma.[2] As in this case, *S. schleiferi* infections in humans are often associated with wound infections from dog bites. Of the subspecies, *S. schleiferi* subsp. *schleiferi* is more commonly associated with human infections, including skin and soft tissue infections, device infections, osteomyelitis, and bacteremia. Few cases of human infection caused by *S. schleiferi* subsp. *coagulans* have been documented, although wound infections, endocarditis, and device infections have been reported.[2,6] Risk factors associated with infection include immunosuppression, malignancies, and recent surgical procedures suggesting nosocomial acquisition. However, the association of *S. schleiferi* with small animals and human infections supports the possibility that close contacts with these animals (pets or livestock) can result in transmission from animals to humans.[1,2]

Antimicrobial Resistance and Therapy Considerations

From 39-73% of veterinary *S. schleiferi* isolates have been reported as oxacillin resistant.[6] Similar to other staphylococci, oxacillin resistance infers resistance to all beta-lactam antibiotics except for new anti-methicillin-resistant *S. aureus* cephalosporins (eg, ceftaroline). Beta-lactam resistance, is mediated by *mecA* (PBP2a) and has been associated with the staphylococcal cassette chromosome *mec* types I and IV in *S. schleiferi*.[2,6] In addition to oxacillin resistance, reduced susceptibility to erythromycin, clindamycin and fluoroquinolones has been reported.[6]

Antimicrobial Susceptibility Testing

Guidance for testing clinical isolates of *S. schleiferi* are found in the Clinical and Laboratory Standards Institute (CLSI) M100 document and by the European Committee on Antimicrobial Susceptibility Testing (EUCAST).[7,9] Breakpoints are available for disk diffusion and dilution methods.[7,9] A CLSI working group evaluated phenotypic methods and breakpoints to determine *mecA*-mediated oxacillin resistance in a set of human and veterinary *S. schleiferi* isolates.[6] The authors showed that the best methods to determine the presence of *mecA*-mediated resistance in *S. schleiferi* was to use oxacillin disk diffusion or minimal inhibitory concentration (MIC) testing applying the *S. pseudintermedius* M100-S28 interpretations.[6,8] Cefoxitin disk diffusion and MIC testing are unreliable for detection of *mecA*-mediated resistance in *S. schleiferi* and should not be used clinically due to high numbers of false-susceptible results.[6,7] EUCAST recommends the use of an oxacillin screen performed by disk diffusion (1µg oxacillin disk) to detect *mecA*-mediated resistance in *S. schleiferi*.[9]

Key Points

- *Staphylococcus schleiferi* is an increasingly encountered zoonotic pathogen that colonizes the skin and mucosal membranes of small animals, including dogs.
- Due to β-hemolysis on blood agar and variable positivity by coagulase tests (eg, slide, tube and latex agglutination methods), misidentification of *S. schleiferi* as *S. aureus* or other *Staphylococcus* species can occur.
- MALDI-TOF MS is a reliable method to identify and differentiate *S. schleiferi* from other *Staphylococcus* species. Differentiation of staphylococci to the species level is growing increasingly important due to differences in methods and breakpoints applied to detect *mecA*-mediated oxacillin resistance among staphylococci, including *S. schleifer*i.

References

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