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Staphylococcus hyicus Bacteremia in a Farmer▽

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Bacteria known in animal infectious diseases can cause challenges in human diagnostic laboratories. We present pitfalls in the identification and susceptibility testing of *Staphylococcus hyicus*, a pathogen that typically causes exudative epidermitis in pigs. In this case, the coagulase-positive staphylococcus isolated from a septic patient was misidentified as *Staphylococcus aureus*.

CASE REPORT

A 49-year-old man was admitted to our hospital because of sepsis and cellulitis of the left foot. His history included destruction of the left middle foot due to osteomyelitis caused by *Campylobacter fetus.* After prolonged antimicrobial treatment, an ankle arthrodesis with external fixation was performed.

At admission, clinical examination of the extremity revealed edematous erythema with pus discharging along the pin tracks. The external fixator was removed and thorough debridement performed. Biopsy specimens taken from the pinhole and blood cultures were sent for microbiological analysis, and antimicrobial treatment with ceftriaxone was initiated. The patient's clinical condition improved rapidly within 1 day.

After 24 h of incubation (35°C, 5% CO_2-enriched atmosphere, Columbia sheep blood agar), white, nonhemolytic colonies grew from both the biopsy specimens and blood cultures. The isolates were positive for catalase and tube coagulase and showed DNase activity. According to the routine identification algorithm, the pathogen was identified as *Staphylococcus aureus*. Susceptibility testing (disc diffusion, Clinical and Laboratory Standards Institute [CLSI] interpretation criteria) revealed that the isolates were susceptible to penicillin, oxacillin, gentamicin, trimethoprim-sulfamethoxazole, tetracycline, clindamycin, erythromycin, vancomycin, ciprofloxacin, fusidic acid, and rifampin (2). No β-lactamase production could be detected with BBL Cefinase paper discs (BD, Sparks, MD).

From a clinical perspective, however, the rapid clinical improvement was unusual for an *S. aureus* bacteremia. Similarly, from a microbiological perspective, the isolates displayed several microbiological features that were not typical for *S. aureus*. The colonies displayed no beta-hemolysis and were nonpigmented. The tube coagulase test required more than 4 h to become positive, and the test for clumping factor was negative. Consideration of all these factors together indicated the necessity of further testing. An *S. aureus*-specific DNA probe targeting the rRNA (AccuProbe *Staphylococcus aureus* culture identification test; Gen-Probe Inc., San Diego, CA) was performed, and the result was negative. Finally, sequence analysis of the first 500 bp of the 16S rRNA gene identified the isolates as *Staphylococcus hyicus* (100% sequence identity with strain ATCC 11249, GenBank accession number D83368).

The patient, a farmer, was requestioned, and he confirmed that he had been in close contact with his piglets while wearing the external fixator. Antimicrobial treatment was switched to penicillin, and the clinical outcome was favorable.

S. hyicus is a coagulase-variable species comprising both coagulase-positive and coagulase-negative isolates. To date, eight species of coagulase-positive staphylococci have been described. In addition to the well-established pathogen *S. aureus*, these include species that are known primarily in veterinary medicine. *Staphylococcus intermedius*, *Staphylococcus pseudintermedius*, and *Staphylococcus delphini* have been isolated from the commensal flora of skin and nasopharynx, as well as from infection sites of dogs, cats, horses, birds, and various other animals (3, 12). Reported human infections are mainly wound infections and cellulitis following dog bites. *Staphylococcus schleiferi* subsp. *coagulans* was originally isolated from dogs with pyoderma and otitis externa (5). *Staphylococcus lutrae* has been isolated from otters, and *Staphylococcus agnetis*, which also comprises coagulase-positive and coagulase-negative isolates, has been detected in the milk of bovines with mastitis (16).

S. hyicus is part of the commensal flora of various animals and is primarily known as the causative agent of exudative epidermitis in pigs (4). The disease is characterized by exfoliation and the formation of a thick, greasy, brown exudate. Its acute form can rapidly lead to the dehydration and death of suckling pigs (6). Furthermore, *S. hyicus* has been isolated from animals with septic polyarthritis and bovine mastitis (9, 10). To the best of our knowledge, only one case of human infection has been published, namely, a wound infection after a donkey bite (7). In this case, the patient's close contact with his piglets was the presumed source of infection.

Our case emphasizes the following important points for clinical practice and diagnostic laboratories. First, *S. hyicus* can cause sepsis in immunocompetent humans. This Gram-positive coccus expresses various virulence factors, such as coagulase, lipase, and a homolog of the immunoglobulin G-binding protein (synonym, staphylococcal protein A) (11). Moreover, it produces exfoliative toxins causing loss of cell adhesion in the

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epidermis by cleaving desmoglein-1. However, human desmoglein-1 is likely resistant to *S. hyicus* exfoliative toxins (4).

Second, in routine diagnostic laboratories, *S. hyicus* can be misidentified as *S. aureus* or coagulase-negative staphylococci. On the one hand, like coagulase-negative staphylococci, *S. hyicus* colonies are nonhemolytic and nonpigmented. On the other hand, like *S. aureus*, *S. hyicus* is often coagulase positive. In order to avoid diagnostic pitfalls, close collaboration between clinicians and microbiologists is essential (e.g., clinicians should obtain the patient's medical history and determine any exposure to animals).

Third, if neither clinical nor laboratory findings are typical for *S. aureus*, further investigations are indicated. *S. hyicus* is distinguished from other coagulase-positive staphylococci by analysis of the 16S rRNA genes or the thermonuclease *nuc* gene (13, 15).

Fourth, correct species identification of coagulase-positive staphylococci in zoonotic infection is important because the CLSI interpretive criteria for the methicillin susceptibility of *S. aureus* are not applicable to all other coagulase-positive staphylococci. Studies of *S. pseudintermedius* from dogs revealed that the oxacillin breakpoint for *S. aureus* and the cefoxitin disc test in particular cannot reliably identify isolates that carry the *mecA* gene, which determines resistance mediated by PBP2a (1, 14). Thus, in cases of coagulase-positive staphylococci causing zoonotic infection, it is reasonable to apply oxacillin breakpoints recommended for coagulase-negative staphylococci in human infections (MIC $\leq$ 0.25 μg/ml [using broth dilution] and/or $\geq$18-mm zone diameter [using the disc diffusion test]). Furthermore, the cefoxitin disc test should be avoided (8). However, to the best of our knowledge, there are no data on the performance of tests for the detection of methicillin resistance in coagulase-variable species such as *S. hyicus*. Likewise, there are no recommendations for oxacillin breakpoints for coagulase-positive staphylococci other than *S. aureus* causing human infections. The *S. hyicus* isolate in this report was oxacillin susceptible (the MIC was 0.25 μg/ml using Etest [AB Biodisk, Solna, Sweden], and the zone diameter was 20 mm using disc diffusion).

In conclusion, this case demonstrates that *S. hyicus* can cause sepsis in humans. It also highlights the fact that in zoonotic staphylococcal infection, close collaboration between clinicians and microbiologists is required to ensure correct species identification and optimized susceptibility testing.

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