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First reported human isolation of *Staphylococcus delphini*

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ABSTRACT

The *Staphylococcus intermedius* group is a collection of coagulase-positive staphylococci composed of 5 members, including *Staphylococcus pseudintermedius*, a zoonotic pathogen often associated with exposure to dogs, and *Staphylococcus delphini*, which has not previously been recovered from humans. Here, we describe the first human case of *S. delphini* infection.

1. Introduction

Coagulase-positive staphylococci, the archetype species being *Staphylococcus aureus*, are pathogens of medical and veterinary importance (Becker et al., 2014; Becker et al., 2015). The *Staphylococcus intermedius* group (SIG) is a collection of coagulase-positive staphylococci that comprises *Staphylococcus delphini*, which is divided into 2 phylogenetically distinct clades (groups A and B), *Staphylococcus intermedius sensu stricto*, *Staphylococcus pseudintermedius*, and the recently described *Staphylococcus cornubiensis* that was isolated from a human skin infection ([Fig. 1]; Fitzgerald, 2009; Ben Zakour et al., 2012; Murray et al., 2018). *Staphylococcus pseudintermedius* is a zoonotic pathogen where dogs are the presumed source of infection, and has been isolated from a variety of human specimens, including blood, respiratory specimens, and wounds (notably those associated with dog bites) (Börjesson et al., 2015; Kuan et al., 2016; Somayaji et al., 2016; Yarbrough et al., 2018). In contrast, *S. delphini*, which was first described in 1988 after recovery from 2 dolphins suffering from suppurative skin lesions (Varaldo et al., 1988), is typically associated with horses, pigeons, and mustelids (badgers, ferrets, and mink) (Bannoehr et al., 2007; Guardabassi et al., 2012; Sasaki et al., 2007). To the best of our knowledge, *S. delphini* has not been previously reported as an agent of human infection or colonization. Herein, we present the first human case of *S. delphini* infection.

2. Case

A 57-year-old woman with a past medical history of depression and chronic alcoholism developed an open wound following partial gastrectomy for the management of a chronic gastric ulcer. The procedure was uncomplicated, and the patient reported progressive wound healing.

Three months following surgery, she presented to an outside hospital emergency department for treatment of alcohol withdrawal and was transferred to an inpatient psychiatry ward at our institution for substance abuse rehabilitation. At that time, a small 0.5×0.5-cm open skin defect at the inferior aspect of her abdominal incision was noted. The patient denied pain, tenderness, or drainage from the site but reported she had exposed the defect after unroofing a small pruritic eschar at the inferior aspect of her surgical wound several days prior to presentation. She denied fevers, chills, nausea, vomiting, abdominal pain, and other areas of skin breakdown. She resided in a private residence prior to presentation where she was caring for a dying cat.

The patient was afebrile without symptoms of systemic infection. The physical examination was notable for the above-mentioned defect of an otherwise well-healing abdominal surgical wound. There was no erythema or tenderness to palpation, and only scant serous drainage was noted. Imaging was not performed, but the wound was swabbed using a single swab for bacterial culture. The specimen Gram stain was

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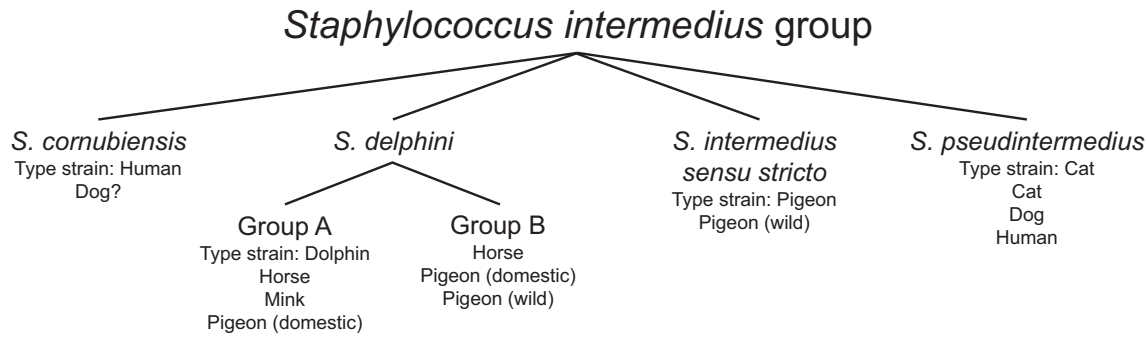

Fig. 1. Members of the *Staphylococcus intermedius* group and typical host affiliations of isolates based upon data presented in Sasaki et al., 2007 and Murray et al., 2018. The animal sources of the type strains (*S. cornubiensis* NW1^T, *S. delphini* DSM 20771^T, *S. intermedius sensu stricto* DSM 20373^T, and *S. pseudintermedius* DSM 21284^T) are shown. With respect to *S. pseudintermedius*, the human isolates likely represent zoonotic transmission from dogs. While *S. cornubiensis* was isolated from a human, a related isolate (2008-01-1056-2) was recovered from a dog (Slettemeås et al., 2010), suggestive of a canine link.

negative for organisms and white blood cells, but due to suboptimal collection with a single swab, this was not unexpected.

Abundant (4+) β-hemolytic Gram-positive cocci in clusters were recovered in pure culture. The organism tested catalase positive and Staphaurex Plus (Remel, Lenexa, KS) negative, suggestive of a coagulase-negative *Staphylococcus* species. In our laboratory, Gram-positive cocci in clusters that test catalase positive and Staphaurex negative isolated from wounds are screened for *Staphylococcus lugdunensis*, which has proclivity for skin and soft tissue infections and is pyrrolidonyl arylamidase (PYR) positive (Frank et al., 2008), using the PYR Test Kit (Remel). The isolate tested positive with the PYR Test Kit and was identified to the species level using matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF MS; Bruker Daltonics, Inc., Billerica, MA). Ultimately, the isolate was identified as *Staphylococcus delphini* (MALDI-TOF MS-based identification log [score] value, >2.00; database, 7311 MSP), which is clumping factor (bound/slide coagulase) negative, and free (tube) coagulase and PYR positive (Becker et al., 2015; Compton et al., 2017). The identity of the isolate (denoted MI 18-1587) was confirmed as *S. delphini* belonging to group A using a thermonuclease gene (*nuc*) PCR test (Sasaki et al., 2010). Furthermore, the resultant MI 18-1587 *nuc* PCR product was sequenced (GenBank [https://www.ncbi.nlm.nih.gov/genbank/] sequence identification: MK124609.1) and using the program lalign (https://embnet.vital-it.ch/software/LALIGN_form.html, accessed December 25, 2018) compared to the sequence of the *nuc* PCR product amplified from the type strain: *S. delphini* DSM 20771^T. The identity between the 2 sequences was 98.9%. Susceptibility testing was performed using reference broth microdilution testing (Clinical and Laboratory Standards Institute [CLSI], 2015). Minimum inhibitory concentration (MIC) values for all antibiotics tested were low (Table 1), including oxacillin, implying β-lactam susceptibility (CLSI, 2018). The patient was treated with topical bacitracin and discharged home and lost to follow-up.

3. Discussion

Prior to this report, *S. delphini* had not been reported as an agent of human infection. Furthermore, with the recent documentation of *S. cornubiensis* as a cause of human infection (Murray et al., 2018), this is only the second documented recovery of a non–*S. pseudintermedius* SIG member from a human infection.

Typically, SIG members have a relatively narrow host range (Fig. 1); however, the source of our patient's infection remains mysterious as no contact with host animals allied with *S. delphini* was noted, rather only her cat. To the best of our knowledge, *Staphylococcus delphini* has no known associations with felines, although this case suggests the possibility of a connection that warrants further investigation.

The historic paucity of biochemical methods for reliably differentiating members of the SIG from *Staphylococcus aureus* has led to their misidentification as *S. aureus* (Börjesson et al., 2015). All members of the SIG, including *S. cornubiensis*, elaborate PYR, while *S. aureus* is PYR negative (Becker et al., 2015; Compton et al., 2017; Murray et al., 2018). Therefore, this simple, rapid biochemical test can be used in all clinical and veterinary microbiology laboratories for rapid discrimination between *S. aureus* and SIG members, followed by species-level identification using MALDI-TOF MS (Dubois et al., 2010; Murugaiyan et al., 2014), which is readily available in many laboratories, or various nucleic acid–based methods (Ben Zakour et al., 2012; Blaiotta et al., 2010; Sasaki et al., 2007; Sasaki et al., 2010). Indeed, accurate differentiation between members of the SIG and *S. aureus* has important treatment implications as methods and interpretative criteria for detecting *mecA*-mediated β-lactam resistance differ between *S. aureus* and *S. pseudintermedius* (Wu et al., 2016) and may exist for other members.

Our isolate exhibited low MIC values to all antimicrobials assayed, including oxacillin (Table 1), suggestive of methicillin (β-lactam) susceptibility. A study of 55 *S. delphini* isolates recovered from mink in Denmark revealed that 51%, 47%, and 20% of isolates were resistant to tetracycline, penicillin, and erythromycin, respectively, while all isolates tested susceptible to the vast majority of antimicrobials assayed, including cefoxitin, thus implying methicillin (β-lactam) susceptibility (Nikolaisen et al., 2017). However, cefoxitin-based methods are known to perform

Table 1
Reference broth microdilution antimicrobial susceptibility testing data for the *S. delphini* isolate described in this case report.

Antibiotic	MIC value (μg/mL)	Interpretation[a]
Oxacillin	0.12	S
Daptomycin	0.25	S
Erythromycin	0.25	S
Clindamycin	0.12	S
Gentamicin	≤1	S
Levofloxacin	0.25	S
Moxifloxacin	≤0.06	S
Delafloxacin	0.004	N/A
Linezolid	1	S
Minocycline	0.06	S
Tetracycline	≤0.5	S
Doxycycline	≤0.06	S
Tigecycline	0.06	N/A
Trimethoprim-Sulfamethoxazole	≤0.5	S
Vancomycin	1	S
Teicoplanin	0.25	S
Dalbavancin	0.03	S

Abbreviations: S = susceptible; N/A = categorical interpretation not available; R = resistant.

[a] Antibiotic susceptibility data were interpreted using the Clinical and Laboratories Standards Institute M100-S28 recommendations for *Staphylococcus* species (CLSI, 2018).

poorly for detection of *mecA*-mediated β-lactam resistance in *S. pseudintermedius* (Bemis et al., 2009; Wu et al., 2016) and may also be inadequate for *S. delphini*. In contrast, methicillin (β-lactam) resistance in *S. pseudintermedius* has increased dramatically in canine isolates from less than 5% in 2001 to near 30% in 2007 (Bemis et al., 2009), and many methicillin-resistant *S. pseudintermedius* isolates are also resistant to ciprofloxacin, clindamycin, doxycycline, erythromycin, and trimethoprim-sulfamethoxazole (Humphries et al., 2016). Therefore, members of the SIG clearly have the ability to acquire resistance to antimicrobials of medical and veterinary importance.

In conclusion, we describe a case of *S. delphini* soft tissue infection in a human possibly transmitted from the patient's cat. The organism was identified using MALDI-TOF MS, and the MIC values of all tested antibiotics were low. Together with the recent description of human *S. cornubiensis* infection, a novel member of the SIG, this report clearly demonstrates that non–*S. pseudintermedius* SIG members possess the ability to infect humans; however, to what extent remains unknown. Non–*S. aureus* staphylococcal species isolated from wound infections should be screened for PYR activity to ensure species with known, and emerging, associations with human infection are recognized and subsequently identified to the species or group level using higher-resolution methods such as MALDI-TOF MS.

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