Staphylococcus intermedius infections: case report and literature review

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Abstract

Staphylococcus intermedius is part of the normal skin and oral flora of dogs. Case reports of human infections are rare, but the true incidence is unknown because the pathogen is frequently misidentified as *Staphylococcus aureus*. Reported cases range from soft tissue infections to brain abscess. Most reported cases in humans have been related to dog exposure. We report a case of a 73 year old female with *S. intermedius* surgical wound infection one month following a left elbow total arthroplasty. This is the first reported human case of *S. intermedius* infection of a mechanical prosthesis. The presumed source of infection was the patient's dog. The patient was treated with vancomycin, then switched to cefazolin and rifampin once susceptibilities were known. Case reports suggest that patients generally respond well to tailored antibiotics with complete or near-complete recovery. *S. intermedius* should be included in the differential diagnosis of invasive infection amongst patients with close contact with dogs.

Introduction

Staphylococcus intermedius was first described in 1976 as a coagulase-positive Staphylococcus. It has since been identified as part of normal skin and mucosal flora in a variety of animals, including dogs, cats, pigeons, minks, horses, foxes, raccoons, goats, and gray squirrels.[1] It is the predominant cause of skin and soft tissue infection in dogs,[2-6] but has only rarely been isolated from humans. However, there are an increasing number of case reports documenting serious invasive infections with *S. intermedius* in humans including infected dog bite wounds,[4,7-11] bacteremia,[1] pneumonia,[12] sinusitis,[13] otitis externa,[14] nail bed infection,[15] mastoiditis,[16] brain abscess,[17] skin abscess,[18] and bacteremia complicated by septic arthritis and iliacus abscess.[19] There has also been one reported outbreak of *S. intermedius* related food intoxication involving over 265 cases in the western United States in 1991.[20] More recently, the discovery of *Staphylococcus pseudintermedius* in 2005 has led to the reclassification of isolates formerly identified as *S. intermedius* based on molecular techniques.[21] The *S. intermedius* group (SIG) was divided *into S. intermedius*, *S. pseudintermedius*, and *Staphylococcus delphini*.[22] According to this new grouping, *S. pseudintermedius*, and not *S. intermedius*, is the species that colonizes and causes infections in dogs and cats, and *S. intermedius* mainly colonizes pigeons.[22,23] Thus, older reports of *S. intermedius*, particularly in animal bites, are often now viewed as *S. pseudintermedius*.[24]

Because human infection with coagulase positive Staphylococci other than *S. aureus* is rare, pitfalls in identification of SIG organisms abound. The true incidence of SIG infections is unknown but likely higher than reported since laboratories tend to presumptively identify coagulase-positive Staphylococci as *S. aureus*.[1] Additionally, *S. intermedius* has been falsely identified as MRSA on the basis of the phenotypic PB2 latex agglutination test which has otherwise good performance for detection of methicillin resistant *S. aureus* and coagulase negative Staphylococci.[15] Talan *et al*. found that 100% of *S. aureus* isolates were coagulase positive at 4 hours compared to only 26% of *S. intermedius* isolates.[4] Thus, microbiology personnel should suspect SIG when coagulase tests proceed more slowly than normal and there is high clinical suspicion, such as history of an animal bite. The presence of SIG can then be confirmed through additional biochemical tests: SIG is pyrrolidonyl arylamidase and β-galactosidase positive in contrast to *S.aureus*.[4,25] More recently, Sasaki *et al.* found that *S. intermedius* can be chemically distinguished from *S. pseudintermedius* by positive arginine dihydrolase and acid production from beta-gentiobiose and D-mannitol.[22] The two species can also be distinguished using molecular and genetic testing, as well as MALDI-TOF mass spectrometry, although this is not commonly done.[24,26]

Case Report

A 73 year old Caucasian female with a history of severe osteoarthritis developed fever, pain, redness, and swelling of her left elbow one month following a revision left elbow total arthroplasty. The original arthroplasty 10 years earlier had been complicated by infection that was successfully treated with several weeks of intravenous antibiotics according to the patient; the details of this remote infection and treatment were unattainable. She was subsequently well for many years without antibiotics until about 2 years prior to presentation when she began to develop gradually progressive joint instability and pain. She was admitted for elective total arthroplasty of the left elbow. Following surgery, she noted continuous serosanguinous drainage. Her orthopedist aspirated the joint on post-operative day 22. The joint fluid was described as cloudy with 26,000 red blood cells, 1300 white blood cells and 31% neutrophils. No organisms were seen on Gram stain, and bacterial cultures were negative. Patient was not started on antibiotics at this time. A few days later (post-operative day 25) she developed progressive elbow pain and fever and was admitted to the hospital. On admission, her temperature was 102.2°F and her white blood cell count was 11,000 cells/mm^3.

On surgical exploration, a large fluid collection was found in the elbow. The joint capsule appeared intact, however both wound and joint fluid cultures grew *S. intermedius*, as identified by the Vitek II automated microbiology system without further subspeciation. The wound was irrigated but the elbow prosthesis was not removed. Blood cultures were negative. In accordance with CLSI standards, the elbow isolates were determined to be resistant to penicillin and tetracycline but susceptible to oxacillin, erythromycin, clindamycin, chloram-

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Table 1. Staphylococcus intermedius group infections in humans.

Author, year	Infection site	Age sex	Presentation	Predisposing factors	Pet exposure	Treatment‡	Resistance	Sensitivity	Initially misidentified?	Recovery
Atalay, 2005	Brain abscess	4M	Fever, nausea, vomiting, headache, lethargic, R hemiparesis	None	Unknown	IV vancomycin x8wks	PCN, MET, CLI, SAM	NR	N	Partial (minimal residual hemiparesis)
Barnham,1992	Hand wound	78M	Pain, discharge, inflammation	None	Y (dog bite)	Amoxicillin-clavulanate	PCN, TET	AMC, FUS, ERY, FLU, GEN	N	Complete
Chuang, 2010*	Catheter-related bacteremia	6M	Erythema, catheter site tenderness, fever	Hemophilia B	Y (dog owner)	Oxacillin 100 mg/kg/day x18d	PCN, COL	VAN, OXA, CIP	Y (*S. aureus*, then *S. intermedius*)	Complete
Gerstadt, 1999	Pneumonia	73M	POD5 s/p CABG, fever, increased secretions	NIDDM	N	Vancomycin	PCN, OXA, CFZ, CTX, CLI, ERY, OFX	SXT, GEN, VAN	N	Complete
Hatch, 2012	Bacteremia, septic arthritis, iliacus abscess	76M	Fever, rash	NIDDM, MDS	Y (dog owner)	Vancomycin x52d	NR	VAN	N	NR
Kelesidis, 2010	Forearm abscesses	43M	Chills	HCV, intravenous drug use	N	Amoxicillin-clavulanate PO x2wks	NR	OXA, SAM, CFZ, LVX CLI, DOX, GEN, SXT, VAN	N	Complete
Kempker, 2009	Sinusitis	28F	Foul-smelling nasal discharge, mild headache	8 mo s/p transphenoidal resection of pituitary adenoma, CSF leak, diabetes insipidus, anemia	Y (dog with recent pyoderma licked face)	Bilateral sphenoidotomy, IV vancomycin, then PO linezolid to complete 6wk course	CFZ, LVX, OXA, SXT, TET	NR	Y (CoNS, then MRSA)	Complete
Kikuchi, 2004	Mastoiditis	51F	Irritation, otorrhea	Chronic otitis media with cholesteatoma, 7 yrs s/p mastoidectomy	Y (dog licked ear)	Ofloxacin ear drops	NR	PCN, OXA, CFZ, GEN, ERY, CLI, MIN, VAN, LVX, SXT	Y (*S. aureus*)	Complete
Lee, 1994		NR	NR	NR	Y (dog bite)	NR	NR	NR	N	NR
		NR	NR	NR	Y (dog bite)	NR	NR	NR	N	NR
		NR	NR	NR	Y (dog bite)	NR	NR	NR	N	NR
		NR	NR	NR	Y (dog bite)	NR	NR	NR	N	NR
		NR	NR	NR	Y (dog bite)	NR	NR	NR	N	NR
		NR	NR	NR	Y (dog bite)	NR	NR	NR	N	NR
	Leg ulcer	NR	NR	Varicose ulcer	Y (dog owner)	NR	NR	NR	N	NR
	Leg ulcer	NR	NR	Varicose ulcer	Y (dog owner)	NR	NR	NR	N	NR
	Infected suture line	13	NR	NR	Y (dog contact)	NR	NR	NR	N	NR
Pottumarthy, 2004	Nail bed infection	60F	Inflamed nail bed, greenish discoloration	Breast cancer undergoing chemotherapy	Unknown	NR	PCN	OXA, SAM, AMC, CFZ, CIP, LVX, ERY, CLI, GEN, NIT, TET, SXT, VAN	Y (MRSA)	NR
	Leg laceration	37M	Cellulites, non-healing wound with foul discharge	None	Unknown	NR	PCN, TET	OXA, SAM, AMC, CFZ, CIP, LVX, ERY, CLI, GEN, NIT, SXT, VAN	Y (MRSA)	NR
Riegel, 2011*	ICD-related endocarditis	70F	Purulent drainage, fever	None	Y (dog exposure)	Cloxacillin 2g Q4hrs 6wks, gentamicin 240 mg Qday x5d	ERY, AMK	MET, GEN, CIP, RIF, VAN	Y (*S. intermedius*)	Complete

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Table 1. Continued from previous page.

Author, year	Infection site	Age sex	Presentation	Predisposing factors	Pet exposure	Treatment°	Resistance	Sensitivity	Initially misidentified?	Recovery
Stegmann, 2010*	Surgical wound	NR, M	Purulent drainage	5wks s/p sinus surgery for R frontal sinus mucocele, h/o recurrent sinusitis	Y (dog, cat, horse owner)	Fusidic acid gauze + 2% mupirocin ointment QID x3d, topical packing (0.5 mg/g fluocinonide, 2.5 mg/g neomycin, 0.25 mg/g gramicidin, 100,000 IU/g nystatin) x4d	AMC, CEF, CLI, ENR, ERY, GEN, KAN, MUP, OXA, PCN, STR, TET, SXT	AMK, CHL, FUS, LZD, NIT, RIF, VAN, QDA	N	Complete
Talan, 1989	Hand wound	45M	Pain, swelling, erythema	None	Y (dog bite)	Amoxicillin-clavulanate 500mg PO TID x10d	PCN	OXA, SAM, AMC, CFZ, CIP, LVX, ERY, CLI, GEN, NIT, TET, SXT, VAN	Y (*S. aureus*)	Complete
	Hand, thigh, forearm wounds	20M	Pain, swelling, erythema	None	Y (dog bite)	Penicillin V 500 mg PO QID x5d	NR	PCN	Y (*S. aureus*)	Complete
	Forearm wound	34F	Pain, erythema, exudate	None	Y (dog bite)	Penicillin V 250 mg PO QID x5d	NR	PCN	Y (*S. aureus*)	Complete
Talan, 1999	Wound	NR	NR	NR	Y (dog bite)	NR	NR	NR	Y (*S. aureus*)	NR
	Wound	NR	NR	NR	Y (cat bite)	NR	NR	NR	N	NR
Tanner, 2000	Otitis externa	38F	NR	None	Y (dog owner)	Topical neomycin, polymyxin B	NR	NR	N	Complete
Vandenesch, 1995	Bacteremia	63M	Inflammation at line site, fever	Metastatic NSC lung carcinoma s/p splenectomy, chemotherapy	Y (cat owner)	Amoxicillin-clavulanate 1gm PO Q8hrs, ciprofloxacin 200mg PO Q12hrs x10d	DOX	PCN, OXA, GEN, KAN, CHL ERY, LCM, PRI, RIF, SXT, PEF, FOF, VAN, TEC	N	Complete
Van Hoovels*	ICD pocket infection	60M	Pocket perforation	Ischemic cardiomyopathy, prostate cancer	Unknown	Flucloxacillin 500 mg PO QID x1wk	PCN, CLI, ERY	OXA	Y (*S. aureus*)	NR
This report	Elbow wound	73F	Pain, erythema, swelling, fever	1 mo s/p revision L elbow arthroplasty	Y (dog owner)	Cefazolin 2gm IV Q24hrs, rifampin 300mg PO Q12hrs x4wks	PCN, TET	OXA, ERY, CLI, CHL, GEN, RIF, LVX, LZD, VAN	N	Complete

NR, not reported; PCN, penicillin; MET, methicillin; CLI, clindamycin; SAM, ampicillin sulbactam; AMC, amoxicillin clavulanate; TET, tetracycline; FUS, fusidic acid; ERY, erythromycin; FLU, flucloxacillin; GEN, gentamicin; COL, colistin; OXA, oxacillin; CFZ, cefazolin; CTX, cefotaxime; OFX, ofloxacin; LVX, levofloxacin; DOX, doxycycline; SXT, trimethroprim-sulfamethoxazole; VAN, vancomycin; MIN, minocycline; CIP, ciprofloxacin; NIT, nitrofurantoin; DOX, doxycycline; AMK, amikacin; KAN, kanamycin; LCM, lincomycin; PRI, pristinamycin; PEF, pefloxacin; FOF, fosfomycin; TEC, teicoplanin; CHL, chloramphenicol; RIF, rifampin; LZD, linezolid; CEF, cefalotin; ENR, enrofloxacin; MUP, mupirocin; STR, streptomycin; QDA, quinupristin/daltopristin; MVA, motor vehicle accident; HIV, human immunodeficiency virus; POD, postoperative day; CABG, coronary artery bypass graft; s/p, status post; NIDDM, non-insulin dependent diabetes mellitus; HCV, Hepatitis C virus; MDS, myelodysplastic syndrome; CoNS, coagulase negative Staphylococcus; MRSA, methicillin resistant *Staphylococcus aureus*; NSC, non small cell, *Staphylococcus pseudintermedius* infection. °Duration not specified unless otherwise noted. See reference list.

phenicol, gentamicin, rifampin, levofloxacin, linezolid, and vancomycin. The patient was treated with intravenous cefazolin and rifampin for six weeks and then transitioned to oral levofloxacin and rifampin with plan for a prolonged course given retention of infected prosthesis. She has not had any recrudescence of disease after 10 months on this regimen and will be reevaluated for possible cessation of therapy at one year's time.

The patient was an avid dog lover. Although she did not recall her dog licking or biting her elbow after surgery, she did report that her dog frequently licked her face. She admitted to frequent close contact with her dog including sharing her bed at night. She denied any recent illness or skin lesions in her dog.

Discussion

Human SIG infections are rarely reported. We conducted a literature review by searching PubMed using the terms *Staphylococcus intermedius*, *S. intermedius*, *Staphylococcus delphini, Staphylococcus pseudintermedius*, *infection* and *human*. References cited in these articles were also examined. Only articles published in English were reviewed, and only invasive infections were included in this discussion. The documented outbreak of *S. intermedius* related food-borne illness was excluded as additional clinical information on the individual cases was not available.

We found 17 published articles documenting 29 SIG infections in humans, 25 with *S. intermedius* and 4 with *S. pseudintermedius*. There were no published cases of *S. delphini* in humans. All 29 cases are outlined in Table 1, with asterisks marking cases of *S. pseudintermedius*. Notably, *S. intermedius* and *S. pseudintermedius* were initially misidentified as *S. aureus* in 34% of 29 cases. Seven of 29 cases (24%) were reported to be polymicrobial by Gram stain, culture, or PCR restriction fragment length polymorphism. Four of the seven polymicrobial cases occurred in dog bite wounds, and one occurred in a patient with known dog exposure.

S. intermedius was first described as a human pathogen in dog bite wounds by Talan in 1989.[4] Overall, 23 of the 29 (79%) of reported cases involved dog bites (11 cases), cat bites (one case), or dog or cat exposure without documented bites (11 cases).[8-11,19,27-29] The rate of *S. intermedius* infection in dog bite infection case series ranged from two to 21%.[10,11] Three of the 11 cases in patients without documented bites but with dog or cat exposure were delayed surgical site infections: one case of sinusitis eight months after a transsphenoidal resection of a pituitary adenoma, one case of mastoiditis seven years after a mastoidectomy, and one case of a surgical wound infection five weeks after sinus surgery.[13,16,27] These cases suggest that alteration of local host defenses may be a risk factor for inoculation without a bite.

Six of the 29 cases (21%) in this series occurred in patients without known animal exposures suggesting that humans can carry this organism in the absence of animal pressure.[12,15,17,18,30] In one case, an intravenous cocaine user accustomed to licking his syringe prior to injection developed skin abscesses.[18] Notably, screening series have variously found *S. intermedius* in five of 56 (9%) human subjects' oral flora, and five of 17 (29%) subjects' skin flora.[31,32] Nonetheless, other staphylococcal species are much more common: *S. intermedius* constituted only 23 of 375 staphylococcal isolates from the skin of 17 individuals.[32]

Interestingly, regular contact with animals in and of itself does not appear to increase the rate of colonization. Talan *et al*. only found *S. intermedius* in the nasopharyngeal flora of one out of 144 healthy veterinary workers.[33] Similar studies on *S. pseudintermedius* have detected the methicillin-resistant strain of the organism

Table 2. Antibiotic susceptibilities across cases reviewed.

	Isolates tested	Isolates susceptible (%)
Aminoglycosides	23	18 (78%)
Amikacin	1	0 (0%)
Erythromycin	10	7 (70%)
Gentamicin	10	10 (100%)
Kanamycin	1	1 (100%)
Streptomycin	1	0 (0%)
Cephalosporins	8	5 (63%)
Cefazolin	7	5 (71%)
Cefotaxime	1	0 (0%)
Glycopeptides	12	12 (100%)
Teicoplanin	1	1 (100%)
Vancomycin	11	11 (100%)
Lincosamides	10	7 (70%)
Clindamycin	9	6 (66%)
Lincomycin	1	1 (100%)
Penicillins	35	22 (63%)
Amoxicillin-clavulanate	4	4 (100%)
Ampicillin-sulbactam	5	4 (80%)
Flucloxacillin	1	1 (100%)
Methicillin	2	1 (50%)
Oxacillin	10	8 (80%)
Penicillin	13	4 (31%)
Quinolones	14	12 (86%)
Ciprofloxacin	5	5 (100%)
Levofloxacin	7	6 (86%)
Ofloxacin	1	0 (0%)
Pefloxacin	1	1 (100%)
Streptogramins	2	1 (50%)
Pristinamycin	1	1 (100%)
Quinupristin/dalfopristin	1	0 (0%)
Tetracyclines	9	4 (44%)
Doxycycline	2	1 (50%)
Minocycline	1	1 (100%)
Tetracycline	6	2 (33%)
Other		
Chloramphenicol	2	2 (100%)
Colistin	1	0 (0%)
Fosfomycin	1	1 (100%)
Fusidic acid	1	1 (100%)
Linezolid	1	1 (100%)
Mupirocin	1	1 (100%)
Nitrofurantoin	3	3 (100%)
Rifampin	3	3 (100%)
Trimethoprim-sulfamathoxazole	8	7 (88%)

Method of susceptibility testing was not reported in 11 of 17 articles reviewed. Reported methods included the automated Vitek system, Phoenix automated system, disc diffusion testing, manual dilution testing. Only two published reports referenced CLSI guidelines.

in 3-5% of samples from owners of pets with recent *S. intermedius* clinical infection and seven of 128 (5%) veterinarians.[34-36] There are data, however, to suggest that transient increases in dogs' bacterial load may increase the risk of transmission to humans. Guardabassi *et al.* found antimicrobial-resistant *S. intermedius* strains in six of 13 dog owners whose pets were being treated for pyoderma.[37] The owners' strains were mostly identical to those found in their dogs. However, *S. intermedius* was no longer present in these same dog owners two months later, suggesting that human acquisition might be transiently related to increased colonization pressure or antibiotic exposure when their pets are acutely ill.

Only three pet-related cases confirmed matching *S. intermedius* strains between patient and dog via pulse field gel electropheresis and PCR restriction fragment length polymorphism. In two of the cases, the patient reported a history of dog licks at the site of infection. Our patient did not recall any episodes of her dog licking her wound, but transmission could have occurred through direct inoculation of the wound from contact with her dog's skin or indirectly through colonization of the patient followed by invasion of the wound.[3]

Treatment of SIG infections in humans has been largely directed by the site of infection and antibiotic susceptibilities. In the cases reviewed, treatment courses ranged from four days of topical antibiotics for otitis externa to eight weeks of intravenous antibiotics for brain abscess.[14,17] Susceptibility patterns are documented in Table 2. Three reports performed testing for the mecA gene, with three of four cases being negative.[15,27,30] Guardabassi *et al*. suggest that pets may facilitate the spread of resistance genes, serving as reservoirs, and resistance patterns in human infections may reflect increasing use of antibiotics in pets.[37] In all except one case, patients had complete recovery after treatment: one individual with a *S. intermedius* brain abscess reported minor residual hemiparesis following antibiotic treatment but no recrudescent infection.[17] Our patient is the first reported case of mechanical prosthesis infection. Despite retention of prosthesis, our patient has been clinically well thus far following six weeks of induction therapy with cefazolin and rifampin followed by 10 months of oral levofloxacin and rifampin to date.

Conclusions

To the best of our knowledge, this is the first reported human case of mechanical prosthesis infection with a SIG organism, the second reported case of infection in the immediate post-operative period, and only the fourth case of a SIG post-surgical wound infection. The actual incidence may be higher due to misidentification of *S. intermedius* and *S. pseudintermedius* as *S. aureus*. Immune status does not appear to be a factor in SIG infection, and infections can be monomicrobial or polymicrobial. Overall, infections seem to respond well to therapy guided by susceptibility tests. The possibility of direct transmission of a pathogenic organism from a pet to a post-surgical wound suggests that surgical patients may need to be warned to limit direct contact with pets, particularly dogs, during recovery. However, more studies confirming matching strains between pets and owners are needed to establish direct transmission in the setting of human infection.

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