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 clindamycin, and ceftazolin 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,2,4 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,3-11 bacteremia,1 pneumonitis,12 sinusitis,13 otitis externa,14 nail bed infection,15 mastoiditis,16 brain abscess,17 skin abscesses,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 pseudointermedius 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. pseudointermedius, and Staphylococcus delphini.22 According to this new grouping, S. pseudointermedius, 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. pseudointermedius.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 28% 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.16 More recently, Sasaki et al. found that S. intermedius can be chemically distinguished from S. pseudointermedius by positive arginine dihydrolase and acid production from beta-gentiobiose and D-mannitol.25 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.21,26

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 aspired 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/mm3.

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-
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  | M   | Fever, nausea, vomiting, headache, lethargic | None | Unknown | IV vancomycin x 8wks | PCN, MET, CLI, SAM | NR | No | Partial (minimal residual hemiparesis) |
| Barnham, 1992 | Hand wound | 78M | M   | Pain, discharge, inflammation | None | Unknown | Y (dog bite) | Amoxicillin-clavulanate | PCN, TET | AMC, FUS, ERY, FLU, GEN | N | Complete |
| Chuang, 2010* | Catheter-related bacteremia | 6M  | M   | Erythema, catheter site tenderness, fever | Hemophilia B | Y (dog owner) | Oxacillin 100 mg/kg/day x 18d | PCN, COL | VAN, OXA, CIP | Y (S. aureus, then S. intermedius) | Complete |
| Gerstadt, 1999 | Pneumonia | 73M | M   | Pneumonia | NIDDM | N | Vancomycin | PCN, OXA, CFZ, CTX, CLI, ERY, OFX | SXT, GEN, VAN | N | Complete |
| Hatch, 2012 | Bacteremia, septic arthritis, iliacus abscesses | 76M | M | Fever, rash | NIDDM, MDS | Y (dog owner) | Vancomycin x 52d | NR | VAN | N | NR |
| Kelesidis, 2010* | Forearm abscesses | 43M | M | Chills, HCV, intravenous drug use | N | Unknown | Amoxicillin-clavulanate PO x 2wks | CFZ, LVX, OXA, SXT, TET | NR | Y (CoNS, then MRSA) | Complete |
| Kempker, 2009 | Sinusitis | 28F | F   | Foul-smelling nasal discharge, mild headache | 8 mo s/p transphenoidal resection of pituitary adenoma, CSF leak, diabetes insipidus, anemia | Y (dog with recent proderma licked face) | Bilateral sphenoidotomy, IV vancomycin, then PO linezolid to complete 6wk course | CFZ, LVX, OXA, SXT, TET | NR | Y (S. intermedius) | Complete |
| Kikuchi, 2004 | Mastoiditis | 51F | F   | Irritation, otorhea | Chronic otitis media with cholesteatoma, 7 yrs s/p mastoidectomy | Y (dog licked ear) | Ofloxacin ear drops | | | | Complete |
| Lee, 1994 | NR | NR | NR | NR | Y (dog bite) | NR | NR | NR | NR | NR | NR |
| Leg ulcer | NR | NR | NR | NR | Y (dog bite) | NR | NR | NR | NR | NR | NR |
| Leg ulcer | NR | NR | NR | NR | Y (dog bite) | NR | NR | NR | NR | NR | NR |
| Infected suture line | 13 | NR | NR | NR | Y (dog contact) | NR | NR | NR | NR | NR | NR |
| Potmumarthy, 2004 | Nail bed infection | 60F | F   | Inflamed nail bed, greenish discoloration | Breast cancer undergoing chemotherapy | Unknown | PCN, OXA, CFZ, GEN, ERY, CLI, MIN, VAN, LVX, SXT | Y (MRSA) | NR | | |
| Leg laceration | 37M | M | M | Cellulitis, non-healing wound with foul discharge | None | Unknown | PCN, TET | OXA, SAM, AMC, CFZ, CIP, LVX, ERY, CLI, GEN, NIT, TET, SXT, VAN | Y (MRSA) | NR | |
| Riegel, 2011* | ICD-related endocarditis | 70F | M | Purulent drainage, fever | None | Y (dog exposure) | Cloxacillin 2g Q8hrs x 6wks, gentamicin 240 mg Qday x 5d | ERY, AMK | MET, GEN, CIP, RIF, VAN | Y (S. intermedius) | Complete |

To be continued on next page
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, b/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 QID x10d | PCN | OXA, SAM, AMC, CFZ, CIP, LIX, ERY, CLI, GEN, NIT, TET, SXT, VAN | Y (S. aureus) | Complete |
| Hand, thigh, forearm wounds | | | | | | | | | | |
| Vanhooves* | ICD pocket infection | 60M | Pocket perforation | Ischemic Unknown | Flucloxacillin 500 mg PO QID x1wk | PCN, CLI, ERY | OXA | Y (S. aureus) | N | Complete |
| 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 | CLA, CHL, ERY, RIF, LIX, LZD, VAN | N | Complete |

NR, not reported; PCN, penicillin; MET, methicillin; CLI, clindamycin; AMS, ampicillin-sulbactam; AMC, amoxicillin-clavulanate; TET, tetracycline; RUS, fosfomycin; ERY, erythromycin; FLU, fluconazol; GEN, gentamicin; CXL, colistin; OXA, oxacillin; CFZ, cefazolin; CTX, cefotaxime; OFX, ofloxacin; LFX, levofloxacin; DOX, doxycycline; SXT, trimethoprim-sulfamethoxazole; VAN, vancomycin; MIN, minocycline; CIP, ciprofloxacin; NIT, nitrofurazone; DOX, doxycycline; AMK, amikacin; KAN, kanamycin; LCM, lincomycin; PRI, pristinamycin; PEF, pefloxacin; FOF, fosfomycin; TEC, teicoplanin; CHL, chloramphenicol; RIF, rifampin; LZD, linezolid; CEF, cephalosporin; ENR, enrofloxacin; MUE, mupirocin; STR, streptomycin; QDA, quinupristin/dalfopristin; 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; HOC, Hepatitis C virus; MDS, myelodysplastic syndrome; GAGS, coagulase negative Staphylococcus; MRSA, methicillin resistant Staphylococcus aureus; NSC, non small cell. *Staphylococcus pseudintermedius infection. °Duration not specified unless otherwise noted. See reference list.
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 pseudointermedius, 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. pseudointermedius. There were no published cases of S. delphini in humans. All 29 cases are outlined in Table 1, with asterisks marking cases of S. pseudointermedius. 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).4,11,15,17,27,29 The rate of S. intermedius infection in dog bite infection case series ranged from two to 21%.11,15 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.11,15-27 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 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.

| Antibiotic Group | 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%)                  |
| Ceftaxime        | 1               | 0 (0%)                   |
| Glycopeptides    | 12              | 12 (100%)                |
| Teicoplanin      | 1               | 1 (100%)                 |
| Vancomycin       | 11              | 11 (100%)                |
| Lincomamides     | 10              | 7 (70%)                  |
| Clindamycin      | 9               | 6 (66%)                  |
| Lincomycin       | 1               | 1 (100%)                 |
| Penicillins      | 35              | 22 (63%)                 |
| Amoxicillin-clavulanate | 4  | 4 (100%)           |
| Amoxicillin-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. 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. 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 electrophoresis 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.

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.1,14,17 Susceptibility patterns are documented in Table 2. 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.27 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 recrudescence infection.27 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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