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***Staphylococcus intermedius* is not only a zoonotic pathogen, but may also cause skin abscesses in humans after exposure to saliva**

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SUMMARY

Background: *Staphylococcus intermedius* is a very rare human pathogen. There are only 16 cases in the literature that have described *S. intermedius* as a cause of infection in humans. Most of these cases have been described in association with exposure to animals, mostly dogs. However, this pathogen can cause infection in healthy individuals even without exposure to animals.

Methods: All previous cases of *S. intermedius* infection included in our literature review were found using a PubMed search (1960–November 2009) of the English-language medical literature applying the terms '*Staphylococcus intermedius*', 'abscess', 'infection', 'humans'. The references cited in these articles were examined to identify additional reports.

Results: We describe the first case of skin abscesses caused by *S. intermedius* in an immunocompetent patient who used intravenous cocaine after coating his syringes with his saliva. We also summarize the literature regarding infections caused by *S. intermedius* in humans.

Conclusions: This case illustrates for the first time that *S. intermedius* can cause skin abscesses in humans after direct inoculation of this pathogen into the skin and soft tissues. Clinicians should be aware of the fact that although the vast majority of infections from coagulase-positive *Staphylococcus* infections are secondary to *Staphylococcus aureus*, *S. intermedius* is also a potential pathogen in humans.

Keywords

Staphylococcus intermedius; Skin abscess; Saliva; Intravenous drug use

1. Introduction

Staphylococcus intermedius is a coagulase-positive *Staphylococcus* that is a very rare cause of infection in humans, despite being pathogenic in animals.¹ We describe, for the first time,

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Conflict of interest

The authors have no conflict of interest to declare.

a case of skin abscesses that were caused by *S. intermedius* in an intravenous drug user and we summarize the available literature on infections caused by *S. intermedius* in humans.

2. Case report

A 43-year-old male with a history of chronic hepatitis C infection and opioid dependence presented with chills after developing two skin abscesses in the right forearm two days after injecting intravenous cocaine. The patient denied any exposure to animals. He had the habit of licking the syringes prior to injecting cocaine 'to prevent clotting'. He was afebrile with a temperature of 36.5 °C, hemodynamically stable, and he had two abscesses in the forearm, one 2 × 3 cm and the other 2 × 2 cm (Figure 1). Pertinent laboratory investigations revealed a white blood cell count of $5.1 \times 10^9/l$ with 70% polymorphonuclear cells. The patient underwent incision and drainage of the two abscesses. Gram staining of the pus revealed Gram-positive cocci in clusters, and vancomycin 1 g intravenously every 12 h was administered empirically. Coagulase-positive staphylococci grew in the culture of the pus and further testing identified the organism as *S. intermedius*. More specifically, white glistening microbial colonies were isolated on blood and MacConkey agar. The colonies were coagulase-, pyrrolidonyl arylamidase-, and *o*-nitrophenyl-β-D-galactopyranoside-positive. The isolate was identified correctly as *S. intermedius* after analysis with the ID32 Staph system using the API database. 16S rRNA gene sequence analysis confirmed the presence of this rare human pathogen. Sensitivity testing revealed that the isolate was susceptible to oxacillin, ampicillin/sulbactam, cefazolin, levofloxacin, clindamycin, doxycycline, gentamicin, trimethoprim–sulfamethoxazole, and vancomycin. The patient was further treated with 875 mg of oral amoxicillin–clavulanic acid twice daily for a total of two weeks with resolution of the abscesses. Unfortunately, cultures of saliva and nasal/oropharyngeal cultures were not performed in our case, since the patient was discharged prior to final identification of the pathogen.

3. Discussion

Staphylococcus intermedius is a coagulase-positive Staphylococcus and a zoonotic organism that can be isolated from dogs, pigeons, minks, cats, horses, foxes, raccoons, goats, and gray squirrels.¹ Talan et al. calculated the prevalence of this microorganism in dogs as 39%.² Although this bacterium is pathogenic in animals, it has been identified very rarely as a cause of infection in humans. Human carriage of *S. intermedius* is uncommon (less than 20%), based on culture of saliva and *S. intermedius* anti-DNAse antibodies.^{3–7} Previous isolations of *S. intermedius* from humans have been described in either case reports^{1,8,9} or in the context of studies on populations with an increased risk of acquiring *S. intermedius* infections (veterinarians and patients bitten by dogs).^{2,5,8,10} In the latter population, a higher prevalence of this species may be assumed, since risk factors for acquiring or harboring *S. intermedius* are occupational exposure to pets (e.g., veterinarians) and bites from certain animals, including dogs.^{2,5,8,10} However *S. intermedius* can also be a pathogen in humans, as our case indicates. Thus, we summarize the available scientific evidence regarding the role of *S. intermedius* as a pathogen in humans.

All previous cases included in our literature review were found using a PubMed search (1960–November 2009) of the English-language medical literature applying the terms ‘*Staphylococcus intermedius*’, ‘abscess’, ‘infection’, ‘humans’. The references cited in these articles were examined to identify additional reports.

S. intermedius has been described as a human pathogen in 16 cases in the literature.^{1,8,9,11–18} One case of infectious endocarditis caused by *S. intermedius* in a patient with HIV infection was reported in the Spanish literature and was not included in our analysis.⁹ Thus, we summarize the data from 15 cases of *S. intermedius* infections in humans (Table 1).^{1,8,11–18} The most frequent clinical presentations are wound infections.^{8,11,12,15} In 1989, Talan et al. described *S. intermedius* as a human pathogen for the first time in three cases of dog-bite-induced soft tissue infection, which were treated with penicillin and amoxicillin–clavulanate. In humans, it is recognized as an invasive zoonotic pathogen and has been isolated from 18% of canine-inflicted wounds.⁸ Cellulitis and a malodorous discharge are common, while regional adenopathy, fever, and lymphangitis occur in only 20% of cases.¹⁰ The true incidence of *S. intermedius* in human wound infections is probably underestimated, because coagulase-positive staphylococci are often misclassified as *Staphylococcus aureus*.¹

In addition, single cases of endocarditis,⁹ catheter-related bacteremia,¹ pneumonia,¹³ ear infection,¹⁴ mastoiditis,¹⁷ sinusitis,¹⁸ nail bed infection,¹⁵ and brain abscess¹⁶ have been reported. Because *S. intermedius* may also possess enterotoxins,^{19–21} this species has been considered in addition to *S. aureus* as the etiologic agent of staphylococcal food poisoning.^{20,22,23}

S. intermedius infections have been described in both immunosuppressed (3/15 cases, 20%)^{1,13,15} and immunocompetent patients (12/15, 80%).^{8,11,12,14–18} Based on 13 cases with available data, the average age of patients was 44 years (range 4–78 years), and 7/12 (58.3%) were males and 5/12 (41.7%) were females.

From 11 cases with available data on antimicrobial susceptibility of human isolates of *S. intermedius*,^{1,11–13,15–18} penicillin resistance was documented in seven cases (63.6%),^{11–13,15,16,18} methicillin resistance in three cases (27.3%),^{13,16,18} cefazolin resistance in three cases (27.3%),^{13,16,18} resistance to doxycycline in five cases (45.5%),^{1,12,13,15,18} and resistance to clindamycin in two cases (18.2%).^{13,16} Resistance to levofloxacin and cotrimoxazole and intermediate susceptibility to gentamicin have also been reported in one case.¹⁸ While *S. intermedius* appears to be more susceptible to penicillin than *S. aureus*, it may also be resistant to penicillin. Hoskins et al. found that β -lactamase was produced in as many as 55% of *S. intermedius* isolates.²⁴

From 10 cases with available data on treatment,^{1,11–14,16–18} antibiotics that have been used for the treatment of *S. intermedius* infection, based on susceptibility results and site of infection, include topical antibiotics (polymyxin, neomycin, ofloxacin), penicillin, amoxicillin–clavulanic acid, vancomycin, and linezolid (Table 1). The duration of treatment varied from five days for wound infections¹¹ to eight weeks in a case of brain abscess.¹⁶ Of cases with data available on outcome, a complete recovery was observed in nine cases^{1,11–14,17,18} and partial recovery in one case¹⁶ of *S. intermedius* infection.^{1,11–14,16–18}

Identification of *S. intermedius* is difficult, since *S. intermedius* may be misclassified as *S. aureus* unless specific biochemical tests are done.¹⁴ To clearly distinguish between *S. intermedius* and *S. aureus*, differences in biochemical reactions must be used. The API database is a system that uses specific biochemical reactions to differentiate between the various coagulase-positive staphylococci and is the primary method used in routine medical practice for this purpose. In a comparison of the two organisms, Talan et al. found that in contrast to *S. aureus* isolates, none of the *S. intermedius* isolates had a positive acetoin reaction and all *S. intermedius* isolates, but no *S. aureus* isolates, had a positive β -galactosidase reaction.² *S. intermedius* is coagulase-, pyrrolidonyl arylamidase-, and *o*-nitrophenyl- β -D-galactopyranoside-positive and hydrolyses urea.¹⁵ It grows well on blood and MacConkey agars incubated under aerobic conditions at 35 °C.¹⁵ Exact molecular identification is performed by 16S rRNA gene sequencing PCR analysis.¹⁵ The very low frequency of coagulase-positive staphylococci other than *S. aureus* in human specimens does not justify the efficient but expensive identification of all coagulase-positive staphylococci using commercially available galleries. However, specific biochemical tests and PCR of the 16S rDNA gene could be an effective alternative in detecting *S. intermedius* in human infections where zoonosis is suspected.¹⁴

We assume that the patient in our case was a healthy carrier of *S. intermedius* in his saliva, and as a result of coating the syringes with saliva prior to injection of cocaine, development of abscesses secondary to *S. intermedius* occurred. Only one case of brain abscess caused by this pathogen has been described in humans.¹⁶ This is the first case of a skin abscess caused by *S. intermedius* in humans. Ways of transmission other than bites have been described. Clinicians should be aware of the potential risk of the development of infections from unusual pathogens isolated in human saliva,⁷ as we have shown in this case. *S. intermedius* is a coagulase-positive Staphylococcus that can cause similar infections to *S. aureus*, and astute acumen and detailed history are paramount to diagnose infections caused by this pathogen.

4. Conclusions

In summary, this case illustrates for the first time that *S. intermedius* can cause skin abscesses in humans after direct inoculation of the pathogen into the skin and soft tissues. Clinicians should be aware of the fact that although the vast majority of infections from coagulase-positive Staphylococcus infections are secondary to *S. aureus*, *S. intermedius* can also be a potential pathogen in humans. Infections from this pathogen can occur both in immunocompetent and immunocompromised patients and thus a detailed history to identify risk factors for this infection (dog exposure, veterinary occupation, exposure to saliva) is important.

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Figure 1.
Two abscesses in the forearm (one 2 × 3 cm and the other 2 × 2 cm) that developed two days after intravenous cocaine use.

Table 1
Staphylococcus intermedius infections in humans (described in the English-language literature^a)

Author, year [Ref.]	Age, years	Sex	Underlying conditions	Type of infection	Treatment	Outcome
Kempker, 2009 [18]	28	F	Had trans-sphenoidal endoscopic tumor removal 5 weeks prior complicated by a CSF leak. Canine exposure	Sinusitis	Bilateral sphenoidotomy with the removal of infected fat grafts, vancomycin and then linezolid for a total of 6 weeks	Complete recovery
Atalay, 2005 [16]	4	M	None	Brain abscess	Stereoactac drainage of abscess, vancomycin 40 mg/kg/day for 8 weeks	Partial recovery
Kikuchi, 2004 [17]	51	F	Had radical mastoidectomy for chronic otitis media with cholesteatoma. Canine exposure	Mastoiditis	Local cleaning with saline washes, ofloxacin ear drops	Complete recovery
Pottumarthy, 2004 [15]	60	F	Breast cancer under chemotherapy	Nail bed infection	NR	NR
Pottumarthy, 2004 [15]	37	M	None	Leg wound infection	NR	NR
Tanner, 2000 [14]	38	F	Canine exposure	Otitis	Topical antibiotics neomycin and polymyxin B	Complete recovery (approximately 4 days)
Gerstadt, 1999 [13]	73	M	Diabetes mellitus type II	Hospital- acquired pneumonia	Vancomycin	Complete recovery
Vandenesch, 1995 [1]	63	M	Metastatic non-small cell lung carcinoma, splenectomy. Pet exposure (cat)	Catheter-related bacteremia	Amoxicillin-clavulanate and ciprofloxacin for 10 days	Complete recovery
Lee, 1994 [8]	NR	NR	Pet exposure (dogs)	Wound infections	NR	NR
Bamham, 1992 [12]	78	M	Pet exposure (dog)	Wound infection	Hydrogen peroxide lavage and a course of amoxicillin-clavulanate	Complete recovery
Talan, 1989 [11]	45	M	Pet exposure	Wound infection	Amoxicillin-clavulanate (for 10 days)	Complete recovery
Talan, 1989 [11]	20	M	Pet exposure	Cellulitis	Penicillin (5 days)	Complete recovery
Talan, 1989 [11]	34	F	Pet exposure	Wound infection	Penicillin (5 days)	Complete recovery

M, male; F, female; NR, Not reported; CSF, cerebrospinal fluid.

^a A case of endocarditis caused by Staphylococcus intermedius (Llorca et al, 1992) described in the Spanish literature is not included in the table.