

Pasteurella multocida non-native joint infection after a dog lick: A case report describing a complicated two-stage revision and a comprehensive review of the literature

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Prosthetic joint infections (PJIs) are commonly caused by pathogens such as *Staphylococcus aureus* and coagulase-negative staphylococci; however, other microbial etiologies and specific risk factors are increasingly recognized. *Pasteurella multocida* is a Gram-negative coccobacillus that is part of the normal oral flora in many animals, and is particularly common in dogs and cats. PJIs caused by *P multocida* have been reported only rarely in the literature and typically occur in the context of an animal bite or scratch. The present article describes a *P multocida* joint infection that occurred after a dog lick and complicated a two-stage revision arthroplasty. A comprehensive review of the literature regarding *P multocida* PJIs follows.

Key Words: Dog bite; Dog lick; *Pasteurella multocida*, Prosthetic joint infection

Prosthetic joint infections (PJIs) are common, occurring in approximately 1% to 2% of all joint replacements (1). Bacterial seeding of the prosthetic joint can occur during surgery or afterward via hematogenous spread. Pathogens such as *Staphylococcus aureus* and coagulase-negative staphylococci account for the majority of PJIs; however, other factors, such as the joint involved, timing of infection postoperatively, and comorbidities, can influence the microbiology (1). Risk factors for PJIs include older age, diabetes, rheumatoid arthritis, immunosuppressive medications, malignancy and history of arthroplasty revision (1). Perioperative factors, such as hematoma formation, superficial surgical site infection, wound drainage and wound dehiscence, have also been identified as risk factors (1).

In the present report, we describe a two-stage revision arthroplasty that was complicated by a *Pasteurella multocida* joint infection following a dog lick, and present a comprehensive review of the literature surrounding *P multocida* PJIs.

CASE PRESENTATION

A 55-year-old woman presented to the emergency department with a five-day history of chills, progressive right hip pain and difficulty ambulating. Her medical history was significant for a right total hip arthroplasty eight years previously due to osteoarthritis and severe obesity. She experienced an acute postoperative wound infection requiring irrigation and debridement and a second infection two years later requiring a staged revision. One year before presentation, she began to experience a series of monomicrobial PJIs that were treated with a combination of surgery and antimicrobial therapy as follows: *Staphylococcus lugdunensis* (two-stage revision, ceftriaxone), *Klebsiella*

L'infection à *Pasteurella multocida* non indigène d'une articulation léchée par un chien : rapport de cas d'une révision compliquée en deux étapes et analyse bibliographique approfondie

Les infections sur prothèse articulaire (IPA) sont souvent causées par des pathogènes comme le *Staphylococcus aureus* et les staphylocoques à coagulase négative. Cependant, on constate de plus en plus d'autres étiologies microbiennes et de facteurs de risque particuliers. Le *Pasteurella multocida*, un coccobacille à Gram négatif qui fait partie de la flore orale normale de nombreux animaux, est particulièrement courant chez les chiens et les chats. Peu d'IPA causées par le *P multocida* sont signalées dans les publications scientifiques, mais elles se produisent surtout après une morsure ou une griffure d'animal. Le présent article décrit une infection à *P multocida* qui s'est manifestée après que l'articulation a été léchée par un chien et une arthroplastie de révision compliquée en deux étapes. Une analyse bibliographique approfondie de l'IPA à *P multocida* suit.

pneumoniae (irrigation and debridement with liner exchange, ciprofloxacin), coagulase-negative *Staphylococcus* (first stage of a planned two-stage revision with cement spacer, vancomycin) and *Candida albicans* (cement spacer exchange, fluconazole). Two months before presentation, she underwent excision of all hardware in the hip as part of a planned two-stage joint revision given recurrent infections with the cement spacer in situ. At that time, she received a six-week course of ertapenem for a joint infection with class A extended-spectrum beta-lactamase (ESBL)-producing *Escherichia coli*, with a vacuum-assisted wound dressing of the surgical site.

At presentation, she was afebrile, but examination of the right hip revealed a nonhealing, erythematous wound with purulent discharge. She had leukocytosis (13,320 cells/ μ L) and elevated inflammatory markers (erythrocyte sedimentation rate 68 mm/s, C-reactive protein 132 mg/L), and was immediately taken to the operating room for irrigation and debridement.

Diagnosis

Three of three operative cultures of synovial tissue and fluid were positive for *P multocida* (susceptible to ceftriaxone, imipenem, levofloxacin, meropenem, penicillin and trimethoprim/sulfamethoxazole) (Table 1) and *Corynebacterium striatum* (susceptible to vancomycin and gentamicin, resistant to erythromycin and penicillin) (Table 2). Bacterial identification was confirmed using fatty acid methyl ester analysis with gas chromatography, and susceptibilities were determined using Sensititre Susceptibility MIC Plates (TREK Diagnostic Systems, USA). Of note, she was also confirmed to be colonized with ESBL-producing organisms based on rectal swabs obtained as part of routine infection control screening practices then in place. On further

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TABLE 1
In vitro susceptibility profile of *Pasteurella multocida* isolate

Antimicrobial agent	Susceptibility	MIC, µg/mL
Ceftriaxone	Susceptible	≤0.03
Imipenem	Susceptible	≤0.5
Levofloxacin	Susceptible	≤0.03
Meropenem	Susceptible	≤0.06
Penicillin	Susceptible	0.12
Trimethoprim/sulfamethoxazole	Susceptible	≤0.06

MIC Minimum inhibitory concentration

questioning, she was found to live with five dogs and two cats, and reported allowing her dogs to lick a superficial laceration on her right lower leg that she had sustained in a fall just before symptom onset; she denied allowing her pets to lick her surgical wound site. On the basis of her most recent culture results and known ESBL colonization, she was treated with intravenous vancomycin and ertapenem for six weeks. One month following admission, she was discharged to a rehabilitation facility with instructions to avoid close pet contact with any unhealed or open wounds. She responded well to antimicrobial therapy and a vacuum-assisted dressing. Two months later, the patient underwent the second stage of her planned two-stage revision, with hip prosthesis re-implantation without complications. She remains free of infection after 10 months of follow-up.

DISCUSSION

P. multocida is a Gram-negative coccobacillus that is part of the normal oral flora in many animals, including domestic dogs and cats (2,3). Infections caused by *P. multocida* may follow an animal bite or scratch, and range from cellulitis to septic arthritis and osteomyelitis (4). Respiratory infections can also occur, especially in patients with a history of pulmonary disease or immune suppression (4). Other less common infections include bacteremia, endocarditis, meningitis and intra-abdominal infections (4).

Although our case is unique in that infection occurred after excision arthroplasty in the midst of a two-stage revision, PJIs caused by *P. multocida* have been reported in the literature and typically occur in the context of an animal bite or scratch. A comprehensive literature review revealed 32 documented cases of *P. multocida* PJIs, all of which involved either the hip or knee joint (Table 3) (5-35).

Of the 32 documented cases, almost all patients had a history of animal contact, with 26 cases of soft tissue injury as a result. Twenty-two of the cases involved cats, while 10 cases involved dogs. Women have been shown to experience cat bites more frequently compared with men (36), and this may explain why 26 of the 32 reported cases of *P. multocida* PJIs involved women. Known risk factors for PJIs that were also present in patients with *P. multocida* PJIs included older age (mean 66.7 years), rheumatoid arthritis (11 of 32 patients [34.4%]), corticosteroid use (10 of 32 patients [31.3%]), other immunosuppressive therapy (two of 32 patients [6.3%]) and malignancy (one of 32 patients [3.1%]).

The presumed pathogenesis of *P. multocida* PJIs following animal contact involves the inoculation of bacteria into soft tissues causing bacteremia and subsequent hematogenous seeding of prosthetic material. This is supported by the fact that most documented cases of *P. multocida* PJI occur remote from prosthesis implantation (months to years) and shortly after animal contact (days to weeks) (Table 3). Only two cases documented animal contact >1 month before onset of clinical signs or symptoms (16,31).

Despite the importance of biofilm formation in the pathogenesis of typical PJIs, the characteristics of *P. multocida* biofilm formation have not been well studied. Animal strains of *P. multocida* have been shown to produce biofilms in vitro (37); however, in vivo evidence is lacking. Romanò et al (31) performed an in vitro spectrophotometric screening with positive control testing in their reported case of *P. multocida* PJI but found no biofilm production in their isolate.

TABLE 2
In vitro susceptibility profile of *Corynebacterium striatum* isolate

Antimicrobial agent	Susceptibility	MIC, µg/mL
Erythromycin	Resistant	≥4
Gentamicin	Susceptible	≤2
Penicillin	Resistant	8
Vancomycin	Susceptible	0.5

MIC Minimum inhibitory concentration

The case we presented represents only the sixth documented report of *P. multocida* non-native joint infection following a dog lick, and the first to occur after excision arthroplasty. Our patient's extensive history of PJIs requiring multiple surgical revisions likely contributed to the increased risk for subsequent infections. Although the patient's hardware was surgically removed two months before presentation, underlying joint damage likely facilitated bacterial adhesion and infection. We suspect the patient's superficial laceration on the lower leg served as a portal of entry for bacteria from the dog's saliva, facilitating hematogenous spread and seeding of the damaged hip joint. Although direct inoculation of the surgical wound by a dog lick was possible, both the history and the presence of a vacuum dressing made this less likely.

P. multocida infections following close pet contact have also occurred with other foreign materials including breast prostheses (38,39), vascular stent graft (40), peritoneal dialysis catheters (41) and hemodialysis lines (42). However, foreign material is not a prerequisite for infection, as illustrated by the present case (postexcision arthroplasty), as well as in three cases of respiratory pasteurellosis, which developed in patients providing palliative care to their pets (43). These cases demonstrate the importance of counselling patients about the risk for zoonotic infection and the steps that can be taken to potentially reduce this risk, including good hand hygiene after pet contact and before dressing changes, covering the wound at all times, avoiding direct pet contact with the surgical site or other wounds, and reporting any animal-induced wounds to a physician. Moreover, facilities that use animal-assisted interventions (also known as pet therapy) should ensure that institution-specific infection control policies are consistent with published guidelines (44) to minimize the risk for zoonotic infection.

Isolates of *P. multocida* from human infections continue to be susceptible to most antibiotics including penicillin, amoxicillin-clavulanate, doxycycline, third-generation cephalosporins, fluoroquinolones and carbapenems (45-47). Infections caused by beta-lactamase producing *P. multocida* have been reported in respiratory infections but remain uncommon (48,49). It is important to note that while most human isolates remain susceptible to beta-lactams, strains isolated from animals have demonstrated marked resistance to a variety of antibiotics (50). Furthermore, empirical treatment of a PJI in the context of a recent animal bite should be directed against a polymicrobial microbiota including Gram-positive and Gram-negative aerobes, and anaerobes, consistent with the expected oral flora of the animal.

Early cases of *P. multocida* PJIs were treated with penicillin alone (6-9,11). Although there were more cases of treatment failure in this group, these patients were also less likely to be treated surgically (Table 3). More recent reports have successfully used a third-generation cephalosporin, beta-lactam/beta-lactamase inhibitor combination or fluoroquinolone in addition to surgical intervention. Interestingly, linezolid, an oxazolidinone with Gram-positive activity has been shown to demonstrate in vitro activity against *P. multocida* (51). Ferguson et al (33) successfully treated a penicillin-allergic patient with *P. multocida* PJI using a combination of linezolid and ciprofloxacin in conjunction with surgical debridement, joint lavage and replacement of the joint liner. It is unclear whether combination therapy is more effective than monotherapy for the treatment of *P. multocida* PJIs, despite several case reports describing the successful use of dual antibiotics (13,20,22,25,26,30,31,33,35). Current guidelines recommend treating

TABLE 3
Literature review of documented *Pasteurella multocida* prosthetic joint infections

Author (reference), year	Age, years/ sex	Risk factors	Site	Time from prosthesis	Animal contact	Time to symptoms	Surgical intervention	Antibiotic treatment*	Outcome
Griffin et al (5), 1975	64/F	RA, CS	TKA	6 months	Cat scratch	2 days	None	Ampicillin	Cure
Maurer et al (6), 1975	55/F	RA, CS	TKA	Years	Dog lick	–	None	Penicillin ×2 weeks	Cure
Sugarman et al (7), 1975	33/F	RA, CS	TKA	5 weeks	Dog lick	–	None	Penicillin ×60 weeks	Failure, revision
Arvan and Goldberg (8), 1978	72/F	NR	TKA	4 months	Cat bite	1 week	Debridement, joint lavage and irrigation/suction drainage (2 weeks)	Penicillin ×55 weeks	Cure
Spagnuolo (9), 1978	72/F	NR	TKA	4 months	Cat bite	5 days	None	Penicillin ×6 weeks	Cure
Gomez-Reino et al (10), 1980	64/F	NR	TKA	3 years	Cat bite	1 day	None	Cephalothin ×6 weeks, cephalexin ×2 weeks	Failure, revision
Mellors and Schoen (11), 1984	68/F	RA, CS	B/L TKA	NR	Cat scratch	4 days	Joint lavage	Penicillin ×6 weeks	Cure
Orton and Fulcher (12), 1984	74/F	NR	B/L TKA	3 years	Cat bite	12 h	None	Ampicillin ×17 days, penicillin + tetracycline ×12 weeks	Failure, revision
Braithwaite and Giddins (13), 1992	48/F	Diabetes	THA	14 years	Cat bite	NR	Single stage revision	Penicillin + flucloxacillin ×6 weeks	Cure
Gabuzda and Barnett (14), 1992	88/F	NR	TKA	10 months	Cat bite	Days	Debridement, removal of prosthesis, placement of cement spacer	Ampicillin/sulbactam ×3 weeks, penicillin ×3 weeks	Cure
Guion and Sculco (15), 1992	45/F	RA, CS	TKA	2 years	Dog scratch	Days	Two-stage revision	Cefotaxime ×6 weeks	Cure
Antuna et al (16), 1997	73/F	RA	TKA	1 year	Dog bite	2 months	Single-stage revision	Ciprofloxacin ×10 weeks	Cure
Maradona et al (17), 1997	73/F	Diabetes	TKA	6 months	Dog bite	45 days	Debridement, joint lavage	Penicillin ×3 weeks, ciprofloxacin ×3 weeks	Cure
Takwale et al (18), 1997	57/F	RA, MTX, CS	THA	12 years	Cat scratch	1 day	Two-stage revision	Benzyl penicillin ×4 weeks, ciprofloxacin ×8 weeks	Cure
Chikwe et al (19), 2000	69/M	NR	THA	4 years	Dog contact	–	Two-stage revision	Unknown	Cure
Ciampolini et al (20), 2004	73/F	NR	TKA	14 months	Cat scratch	2 weeks	Two-stage revision	Benzyl penicillin + ciprofloxacin, amoxicillin + ciprofloxacin ×6 weeks	Cure
Mehta and Mackie (21), 2004	84/F	RA, CS	THA	15 years	Cat scratch	1 month	Single-stage revision	Benzyl penicillin ×1 week, ciprofloxacin ×7 weeks	Cure
Mehta and Mackie (21), 2004	57/F	RA, MTX, CS	THA	10 years	Cat scratch	NR	Two-stage revision	Benzyl penicillin ×4 weeks, ciprofloxacin ×8 weeks	Cure
Polzhofer et al (22), 2004	73/F	NR	TKA	6 months	Cat bite	Days	Arthroscopic debridement, synovectomy, irrigation/suction drainage (6 days)	Ampicillin/sulbactam + clindamycin ×3 weeks	Cure
Stiehl et al (23), 2004	63/M	NR	TKA	12 days	Dog contact, horse injury	–	Two-stage revision	Ciprofloxacin and piperacillin/tazobactam	Cure
Zebeede et al (24) 2004	41/F	SLE, APS, CS	TKA	2 years	Cat scratch	2 weeks	None	Ciprofloxacin ×12 weeks	Cure
Heym et al (25), 2006	72/F	NR	TKA	1 year	Dog lick	3 weeks	Synovectomy, removal with reimplantation	Doxycycline + amoxicillin ×8 weeks	Failure, revision
Serrano et al (26), 2007	79/M	NR	TKA	6 years	Cat scratch	NR	Joint lavage	Amoxicillin/clavulanate ×3 weeks, ciprofloxacin ×4 weeks + TMP/SMX ×12 weeks	Cure
Kadakia and Langkamer (27), 2008	80/F	Breast carcinoma	TKA	9 months	Cat bite	8–10 days	Arthroscopic joint lavage	Cefuroxime ×2 weeks, ciprofloxacin ×8 weeks	Cure

Continued on next page

TABLE 3 – CONTINUED
Literature review of documented *Pasteurella multocida* prosthetic joint infections

Author (reference), year	Age, years/ sex	Risk factors	Site	Time from prosthesis	Animal contact	Time to symptoms	Surgical intervention	Antibiotic treatment*	Outcome
Miranda et al (30), 2013	64/M	NR	TKA	1 year	Cat scratch/ bite	9 days	Joint lavage, debridement, replacement of spacer	Amoxicillin/clavulanate + levofloxacin ×6 weeks	Cure
Romanò et al (31), 2013	82/F	RA	TKA	10 years	Cat scratch	5 months	Debridement and replacement of tibial tray	Amoxicillin/clavulanate ×34 days + ciprofloxacin ×6 weeks	Cure
Subramanian et al (32), 2013	47/M	NR	TKA	23 days	Probable dog lick	–	Debridement, joint lavage and replacement of liner	Cefuroxime ×2 weeks, doxycycline ×6 weeks	Cure
Ferguson et al (33), 2014	67/F	NR	TKA	13 weeks	Dog lick	–	Debridement, joint lavage and replacement of insert	Linezolid ×4 weeks + ciprofloxacin ×8 weeks	Cure
Vélez et al (34), 2014	75/M	NR	TKA	16 months	Cat bite	2 days	Debridement, and replacement of spacer	Ampicillin/sulbactam ×4 weeks, amoxicillin/clavulanate ×24 weeks	Cure
Alsaffar and Gaur (35), 2014	74/F	NR	THA	26 years	Cat bite	4 days	Joint lavage	Amoxicillin + ciprofloxacin ×8 weeks	Cure

*Antibiotics separated by commas denote subsequent change in antibiotics, antibiotics separated by plus sign denote concurrent use. APS Antiphospholipid antibody syndrome; B/L Bilateral; CS Corticosteroids; F Female; M Male; MTX Methotrexate; NR Not reported; RA Rheumatoid arthritis; SLE Systemic lupus erythematosus; THA Total hip arthroplasty; TKA Total knee arthroplasty

nonstaphylococcal PJIs with four to six weeks of antimicrobial therapy (52). Of the 29 case reports with documented duration of therapy, 27 were treated with at least four weeks of antibiotics and 16 were treated with >6 weeks of antibiotics (Table 3).

The present report represents the first case of *P. multocida* joint infection successfully treated with ertapenem. The decision to treat with ertapenem was based on its documented efficacy in vitro against *P. multocida* (45), the patient’s positive ESBL screening swabs and history of PJI caused by ESBL-producing organisms and the ease of outpatient dosing. The presence of *C. striatum* in all operative cultures also prompted treatment with vancomycin. In one study of the microbiology of infections after animal-induced injuries, *Corynebacterium* species accounted for 12% of aerobic bacteria isolated from infected dog bite wounds (53). However, *Corynebacterium* species are part of normal human skin flora and, therefore, may have entered the wound from the patient’s skin postoperatively during prolonged wound healing.

The optimal surgical management of PJIs should be individualized. Our literature review demonstrated a wide spectrum of surgical interventions, including no intervention (seven of 32 patients [21.9%]), lavage only (four of 32 patients [12.5%]), debridement and lavage (four of 32 patients [12.5%]), debridement with replacement of exchangeable components (six of 32 patients [18.8%]), single-stage revision (four of 32 patients [12.5%]) and two-stage revision (six of 32 patients [18.8%]). Earlier case reports of *P. multocida* PJIs were more likely to be treated nonoperatively. Of the seven patients treated nonoperatively, three (42.9%) failed antimicrobial therapy alone (7,10,12). The benefits of less-invasive interventions must be balanced with the risk of treatment failure. Algorithms have been developed by expert panels to identify patients with PJIs suitable for less-invasive interventions (52,54). Factors in the algorithm include duration of illness, extent of soft tissue infection, presence of coexisting illness, surgical risk, stability of implant and bacterial susceptibility to antibiotics (52,54). However, these algorithms do not specifically address PJIs associated with zoonotic pathogens. Our patient underwent irrigation and debridement because there was no prosthetic material present at the time of infection.

Several authors of previous case reports have advocated for the use of prophylactic antibiotics in all individuals with a prosthetic joint

who have sustained an animal bite, especially if other risk factors are present (such as rheumatoid arthritis or corticosteroid use). Proposed antibiotics include penicillin (9), oxacillin (12), amoxicillin (18), cefuroxime (18) and amoxicillin/clavulanate (20). Recent guidelines have recommended antibiotic prophylaxis in all individuals with bite wounds at high risk for developing infection, such as those with significant immunocompromise (diabetes, steroid use, HIV, peripheral vascular disease), advanced liver disease, edema of the affected area and wounds involving deeper structures (55). To our knowledge, the use of prophylactic antibiotics following an animal bite or scratch in individuals with a prosthetic joint has not been directly addressed.

CONCLUSION

The present report represents the sixth documented case of *P. multocida* non-native joint infection following a dog lick, and the first to occur in the midst of a two-stage revision. The accompanying literature review of PJIs caused by *P. multocida* is the most comprehensive performed to date and includes all 32 cases reported in the literature. While PJIs due to *P. multocida* classically occur following an animal bite or scratch, our review highlights the fact that penetrating trauma is not a prerequisite for infection. It is important for clinicians to ask about animal exposure when evaluating a patient with a PJI, particularly if the infection has occurred remote from the surgery, so that the appropriate empirical therapy can be chosen. Our literature review also documented other risk factors that may increase the risk for *P. multocida* PJI following an animal-induced wound, including rheumatoid arthritis, corticosteroids, other immunosuppressive therapy and malignancy. In light of the case presented here, it is reasonable to counsel patients about the risk for zoonotic infections of surgical wounds and the steps that can be taken to potentially reduce this risk, such as maintaining good hand hygiene after pet contact, keeping wounds covered, avoiding direct pet contact with any unhealed, uncovered or open wounds, and reporting all significant animal-induced wounds to a physician.

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