**Pasteurella** species peritoneal dialysis-associated peritonitis: Household pets as a risk factor

Philippe Guillaume Poliquin MD FRCP(C), Philippe Lagacé-Wiens MD FRCP(C),*, 1,2 Mauro Verrelli MD FRCP(C), 3 David W Allen MD, 4 John M Embil MD FRCP(C) 2,6

BACKGROUND: *Pasteurella* species are Gram-negative coccobacilli that are part of the normal oropharyngeal flora of numerous domestic animals. They have been recognized as a rare but significant cause of peritonitis in patients undergoing peritoneal dialysis (PD). A consensus about management strategies for PD-associated peritonitis caused by *Pasteurella* species currently does not exist.

METHODS: The microbiological database serving the Manitoba Renal Program was searched from 1997 to 2013 for cases of *Pasteurella* species PD-associated peritonitis, and charts were reviewed. PubMed was searched for case reports and data were abstracted.

RESULTS: Seven new local cases and 30 previously reported cases were analyzed. This infection is clinically similar to other forms of PD peritonitis, with household pet exposure appearing to be the strongest risk factor. Cats are the most commonly implicated pet. Direct contact between the pet and the equipment was commonly reported (25 of 37 patients) but was not necessary for infection to develop. The mean duration of treatment was 15 days. Complication rates were low, with only 11% of patients requiring PD catheter removal. There was no mortality reported.

CONCLUSION: *Pasteurella* species are a rare cause of PD-associated peritonitis that can be successfully treated with a 2-week course of intraperitoneal antibiotics with a high likelihood of catheter salvage.

Key Words: Cat; *Pasteurella* multocida; *Pasteurella* species; Peritoneal dialysis; Peritonitis

*Pasteurella multocida* is a Gram-negative coccobacillus first identified in 1878 in diseased birds (1). Since then, *P. multocida* has become associated primarily with skin and soft tissue infections following animal bites. The organism is known to colonize the upper respiratory tract of 90% of cats and 66% of dogs (2). Contamination with *P. multocida* may result in a wide range of infections including pneumonia, endocarditis and meningitis (1).

Among more unusual sites, *P. multocida* has been found to cause peritonitis in individuals undergoing peritoneal dialysis (PD) for renal replacement (3). Patients undergoing PD consider it to be a convenient alternative to hemodialysis that is associated with a reduced impact on their quality of life (4). One of the major drawbacks of PD, however, is the risk for peritonitis due to frequent manipulation of the catheter and PD equipment (5). Despite improvement in infection rates due to better equipment and a focus on hand hygiene, an event rate of 0.5 episodes/patient/year is average (6).

Over the past 15 years, eight cases of *P. multocida* PD peritonitis have been observed within the Manitoba Renal Program (Winnipeg, Manitoba), which currently provides care to 280 PD patients. In the present article, we briefly describe seven of these cases; the eighth case was previously reported in the *Canadian Journal of Infectious Diseases & Medical Microbiology* (7) due to its unique features as a polymicrobial zoonosis. In addition, we reviewed and analyzed the available published case reports of *Pasteurella* species PD-associated peritonitis (2,3,7-30). While the burden of such infections is small in comparison with the usual microbiology, both the prevalence of chronic renal disease (31) and pet ownership are increasing (32). As a result, we anticipate that there will be an increase in cases of PD peritonitis caused by *Pasteurella* species, and new strategies may be needed for improved management.
of therapy. IP antibiotics were discontinued and patient completed 14 days of amoxicillin-clavulanic acid orally.

Case 5: A 37-year-old woman who had been on CAPD for 11 years for ESRD secondary to chronic interstitial nephropathy sought medical attention for a 10 h history of abdominal pain, chills and diarrhea. She had regular contact with a domestic cat but not in the vicinity of her PD equipment. She was treated with IP ceftazolin and ceftazidime for five days but had ongoing cloudy dialysate and abdominal pain. The PD catheter was removed, and she completed her therapy with three days of ceftriaxone and one week of oral amoxicillin.

Case 6: A 59-year-old woman who had been on CAPD for the past three years for ESRD secondary to diabetic nephropathy sought medical attention for a four-day history of nausea and vomiting and a one-day history of abdominal pain. The woman had regular contact with a domestic cat in her home, but no documented contact with PD equipment or tubing. She received a five-day course of IP ceftazolin and tobramycin followed by IP ceftazidime for 14 days with complete recovery.

Case 7: A 69-year-old woman with an underlying history of diabetes mellitus, hypertension, thalassemia and diabetic nephropathy was started on CAPD. She presented three days later with cloudy dialysate and subjective fever. She reported abdominal pain with her latest fluid exchange. Concern was raised that her cat may have bitten the cycler line. She was discharged from the emergency department with reassurance but was asked to return because P. multocida was recovered in the PD fluid culture. She was successfully treated as an outpatient with two days of IP ceftazolin and tobramycin followed by seven days of IP ceftazidime and seven days of oral amoxicillin-clavulanic acid.

RESULTS

The local database search revealed the seven cases described above. An additional published case from our centre (7) was added to 29 published cases identified using the search strategy described above. This resulted in a total of 37 cases for analysis. The vast majority (33 of 37) of cases were secondary to P. multocida, with one each of P. aerogenes, P. canis, P. dagmatis and P. multomuris accounting for the remainder.

Demographics

The mean (± SD) patient age was 44±17.6 years (range eight to 75 years), with a male-to-female ratio of 1:1. There were three pediatric patients. Cases were heterogeneous regarding the underlying reason for renal failure, including both congenital as well as acquired causes. PD modality varied, with 43% using continuous cycling PD, 41% using CAPD and 16% being unspecified. The mean length of time on PD was 24.1 months, with a wide range (three days to 11 years).

Clinical and laboratory features at presentation

The median time to presentation was 18.5 h (range 1 h to 168 h). Information on clinical presentation was available for 34 of 37 patients. Abdominal pain was most commonly reported (91%). Other signs and symptoms were as follows: fever (91%), nausea (78%), vomiting (78%), diarrhea (68%) and chills (65%). Serum creatinine increased in 91% of cases. The mean (± SD) length of hospital stay was 24.1±10.9 days (range 3 to 90 days; median 14 days). The presenting organism was determined in 26 cases (71%). P. multocida was the most common cause (54%), followed by P. canis (19%), P. dagmatis (9%) and P. multomuris (9%). Of patients, 51% had evidence of systemic involvement on presentation in the form of positive blood cultures or elevated inflammatory markers.

Local case series

All of the cases included in the present series ultimately yielded P. multocida from culture of the PD fluid obtained at the time of presentation. None of these local patients experienced a relapse of PD peritonitis caused by P. multocida. All patients were initially treated using the PD program's standing protocol for the empirical treatment of PD peritonitis—specifically, once-daily intraperitoneal (IP) cefazolin (or vancomycin for beta-lactam allergic patients) and tobramycin. Table 1 demonstrates dosing guidelines used at the authors' institution.

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Dose</th>
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<tbody>
<tr>
<td>Cefazolin</td>
<td>1.5 g intraperitoneal once daily if ≥50 kg</td>
</tr>
<tr>
<td></td>
<td>1 g intraperitoneal once daily if &lt;50 kg</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>1.5 g intraperitoneal once daily</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>If no residual renal function:</td>
</tr>
<tr>
<td></td>
<td>2 g intraperitoneal every 7 days if ≥50 kg</td>
</tr>
<tr>
<td></td>
<td>1 g intraperitoneal every 7 days if &lt;50 kg</td>
</tr>
<tr>
<td></td>
<td>If patient has residual renal function with urine output &gt;100 mL/day</td>
</tr>
<tr>
<td></td>
<td>Same empirical doses as above; however, dosing is adjusted after vancomycin level is obtained four to five days after initial dose</td>
</tr>
<tr>
<td>Tobramycin</td>
<td>60 mg intraperitoneal once daily if ≥50 kg</td>
</tr>
<tr>
<td></td>
<td>40 mg intraperitoneal once daily if &lt;50 kg</td>
</tr>
</tbody>
</table>

TABLE 1

Intraperitoneal antibiotic dosing

Pasteurella peritoneal dialysis peritonitis

METHODS

Identification of local cases

The electronic microbiology laboratory database that serves the Manitoba Renal Program was searched for P. multocida or Pasteurella species isolated from peritoneal fluid from January 1, 1997 to June 30, 2013. Patient charts were abstracted for the following: age, sex, comorbidities, PD history, animal exposure and symptoms. Laboratory data, including white blood cell (WBC) counts from peripheral blood and peritoneal fluid as well as Gram stain and culture results, were collected.

Review of published reports

The PubMed database was searched from 1966 to June 1, 2013 using the MeSH terms (“Pasteurella”[Mesh] OR “Pasteurella pneumotropica”[Mesh] OR “Pasteurella multocida”[Mesh] OR “Pasteurella Infections”[Mesh]) AND (“Peritoneal Dialysis”[Mesh] OR “Peritoneal Dialysis, Continuous Ambulatory”[Mesh] OR “Peritonitis”[Mesh]). This search returned 64 citations. Cases describing a PD-associated episode of peritonitis caused by Pasteurella species were included. Bibliographies were reviewed for additional cases. Individual reports were abstracted for the same information as the local cases.

Local case series

All of the cases included in the present series ultimately yielded P. multocida from culture of the PD fluid obtained at the time of presentation. None of these local patients experienced a relapse of PD peritonitis caused by Pasteurella species. All patients were initially treated using the PD program's standing protocol for the empirical treatment of PD peritonitis—specifically, once-daily intraperitoneal (IP) cefazolin (or vancomycin for beta-lactam allergic patients) and tobramycin. Table 1 demonstrates dosing guidelines used at the authors' institution.

Case 1: A 28-year-old woman with a history of tetralogy of Fallot, hypertension and congenital solitary kidney developed end-stage renal disease (ESRD) managed by continuous ambulatory peritoneal dialysis (CAPD). She had been on CAPD for one month and presented with a 5 h history of severe abdominal pain and chills. Her cat had chewed on her dialysate line earlier that day. She was started on IP cefazolin and tobramycin for 48 h. Treatment was tailored to IP ceftazidime for an additional 12 days, with clinical improvement within 24 h.

Case 2: A 37-year-old man who had been on CAPD for 15 months for ESRD secondary to diabetic nephropathy sought medical attention for a one-day history of abdominal pain, fever and chills. His cat had bitten the dialysate line the day before, although a puncture was not observed. He was started on IP cefazolin and tobramycin, and experienced prompt recovery. The tobramycin was discontinued after five days and he completed 14 total days of IP cefazolin.

Case 3: A 41-year-old man who had been on CAPD for ESRD secondary to diabetic and hypertensive nephropathy for the past 18 months sought medical attention for a 4 h history of abdominal pain, fever, chills, nausea, vomiting and diarrhea. The patient noted that his dialysate fluid had been cloudy that morning. He was the owner of three cats that were allowed into the PD area, and reported that one may have bitten the tubing. He demonstrated rapid improvement after initiation of IP cefazolin and tobramycin. Tobramycin was discontinued on day 5 and he completed 14 days of IP cefazolin.

Case 4: A 51-year-old woman who had been on CAPD for the past seven months for ESRD secondary to hypertension sought medical attention for a 5 h history of abdominal pain, fever, nausea and vomiting. She indicated that her dialysate fluid was cloudy during her most recent session. Although she owned a cat, she reported that it was not permitted within the PD area. The patient was treated with three days of IP cefazolin and tobramycin, with marked improvement within 24 h.
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Numerically, the WBC was abnormal in only 54% of cases (as per the
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**TABLE 2** Management approaches for patients with *Pasteurella*
peritoneal dialysis-associated peritonitis

<table>
<thead>
<tr>
<th>Proportion of patients receiving specific treatment</th>
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<tbody>
<tr>
<td><strong>Initial management</strong></td>
</tr>
<tr>
<td>Intraperitoneal antibiotics only</td>
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<tr>
<td>Intravenous antibiotics only</td>
</tr>
<tr>
<td>Combination intravenous/intraperitoneal/oral</td>
</tr>
<tr>
<td>No therapy</td>
</tr>
<tr>
<td><strong>Definitive therapy</strong></td>
</tr>
<tr>
<td>Intraperitoneal antibiotics only</td>
</tr>
<tr>
<td>Intravenous antibiotics only</td>
</tr>
<tr>
<td>Combination intraperitoneal/oral</td>
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<tr>
<td>Oral antibiotics only</td>
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<tr>
<td>Duration of therapy, days, mean ± SD (range)</td>
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<td>Duration of therapy, days, median</td>
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</table>

*Data presented as n/total n (%) unless otherwise indicated.*

symptoms included: nausea and vomiting (65%), cloudy dialysate fluid
(50%), fever (38%), chills (29%) and diarrhea (12%). No patients were
asymptomatic. A tunnel site infection was diagnosed in one of 37 patients.
The peripheral WBC count was available for 26 of 36 patients, with an
average WBC count of 10.8×10⁹/L (3.7×10⁹/L to 20.7×10⁹/L).
Numerically, the WBC was abnormal in only 54% of cases (as per the
reported normal range for individual institutions). The peritoneal fluid
cell count was universally abnormal, with an average of 6621×10⁶/L
(range 210×10⁶/L to 25,879×10⁶/L; normal <100×10⁶/L). The Gram
stain was not reliably helpful, demonstrating Gram-negative rods in
only six of 33 cases. Blood cultures were not routinely drawn; two
patients had *P. multocida* bacteremia, one asymptptomatically and one
with a shock-like syndrome.

Animal type and degree of contact

Cats were the most commonly implicated animal, accounting for 83%
(31 of 37) of cases. Exposure to animals other than cats occurred
conclusively in four cases. This appeared to be more common in the few
pediatric patients (two of three nonline exposure) and resulted in
non-*P. multocida* infections. Direct contact between the animal and the
equipment was documented in 25 of 37 cases, of which 10 of 25
confirmed a puncture of the line or fluid bags. An additional 10 cases
reported no contact between the animal and PD equipment or treat-
ment area. There was no association between type of exposure and PD
modality (P=0.304). There was a significant difference in time from
symptom onset to presentation between patients with a bite or punctu-
ure of the PD catheter tubing compared with patients with non-
specific contact (15 h versus 44 h; P=0.04).

Management and outcomes

The approach to management of these infections was highly variable
within the reported literature in terms of both route of delivery and
length of therapy (Table 2). Outcomes were generally favourable. Two
patients experienced a septic shock-like syndrome requiring admission
to the intensive care unit. One patient experienced a recurrence four
weeks after discontinuation of therapy. The PD catheter was removed
in 11% (four of 37) of patients. There was no discernable association
between a particular therapeutic regimen and a poor outcome. No mortality was reported.

**DISCUSSION**

Since the first case of *P. multocida* peritonitis was described in 1987,
this organism has become recognized as an infrequent but clinically
significant cause of PD-associated peritonitis (3). The seven cases from
our centre represent the largest series reported to date. Together with
the existing 30 published reports, important trends emerge (2,3,7-30).

Overall, patients with *Pasteurella* species PD-associated peritonitis
have a very similar symptom constellation to other forms of infectious
peritonitis. When our patients were compared with patients from a
recent case series of PD-associated peritonitis (5), rates of abdominal
pain (91% versus 88%), nausea and vomiting (65% versus 51%) and
fever (38% versus 29%) were similar. Observation of a cloudy effluent
was less common in infections caused by *Pasteurella* species (50%)
compared with other organisms (84%). This may be due to the rela-
tively rapid median time to presentation for care of 18.5 h. Given that
cases occurred in PD recipients with both lengthy (11 years) and
limited (third day of PD) experience, it is evident that ongoing education
regarding the risk of PD-associated peritonitis in the presence of
household pets is critical.

Exposure to a colonized animal is a prerequisite of infection; how-
ever, the degree of contact necessary for infection appeared to be lim-
ited. Direct contact between the animal and the equipment was
documented in 25 of 37 cases, of which 10 of 25 confirmed a puncture
of the line or fluid bags. More intriguing were the 10 cases that
reported only casual contact between the owner and the animal. While
a surreptitious contact event cannot be excluded, the observa-
tion that animal breeders can acquire oropharyngeal colonization with
*Pasteurella* species raises the possibility that self-inoculation from the
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Furthermore, it has been demonstrated using pulsed-field electrophor-
esis that *Pasteurella* species oropharyngeal colonization with the same
organism can occur in both patient and pet (24).

The most recent recommendations of the International Society for
Peritoneal Dialysis recommend a three-week course of antimicrobial ther-
apy for Gram-negative peritonitis (34). Based on previously published
reports and our case series, it appears that, when compared with infection
cause by other Gram-negative microorganisms, patients with
PD-associated peritonitis caused by *Pasteurella* species experienced fewer
recurrences and catheter loss events. The vast majority of these patients
were successfully treated with a 14-day course of antimicrobial therapy,
primarily delivered intraperitoneally. The one recurrence occurred in
a patient treated for three weeks (11). Shorter courses of therapy (as short as
seven days) have provided equivalent outcomes but the data are insuffi-
cient to allow definitive conclusions about shorter duration of therapy.
Catheter loss was uncommon (four of 37). This compared favourably with
a previously reported rate of 23% in non-*Enterobacteriaceae* Gram-
negative-induced peritonitis (5). As such, a 14-day course of IP antibiotic
therapy aimed at catheter salvage appears to be warranted for PD-associated
peritonitis caused by *Pasteurella* species. On average, substantial clinical
improvement occurred within 48 h to 72 h of initiation of therapy. The
lack of mortality is reassuring, especially given that *P. multocida* bacteremia
typically carries a 30% mortality rate (22).

Given the heterogeneity of antibiotic choices, it is difficult to draw
definitive conclusions about optimal antimicrobial choice. In general,
however, penicillin- or ampicillin-based regimens are preferred for
non-β-lactamase-producing isolates (1). Third-generation cephalo-
sporins are believed to have equivalent activity to penicillin and
ampicillin. Oral fluorquinolone monotherapy was successfully used in
five of 33 patients. Aminoglycoside IP monotherapy was used in three
patients (3,11,17), one of whom (11) experienced the only recurrence
following three weeks of therapy. This event, together with the unreli-
able activity of aminoglycosides against *Pasteurella* species described in
the literature (35), suggests that aminoglycoside monotherapy in
*Pasteurella* species peritonitis should be avoided.

There are several limitations inherent to retrospective review of
isolated case reports. Those most pertinent to the present report
include: patient recall bias, specifically with regard to animal exposure;
insufficient reporting/documentation of risk factors (such as type and
extent of animal exposure) leading to infection; publication bias; dif-
ferences in practice patterns within and between centres; and reliable
laboratory identification of rare microorganisms. Recognizing the
limits of this type of study, we believe that sufficient points of com-
monality have emerged to allow these trends to be reported.
CONCLUSION

The present case series and review of published reports is the largest and most complete to date, and provides a clear picture of PD-associated peritonitis caused by Pasteurella species. This infection is indistinguishable from other forms of PD peritonitis except for a tendency toward rapid (<24 h of symptoms) presentation for care. These organisms should be suspected as an etiological agent if there is a pet at home, even if direct contact between the pet and the equipment was not observed. Moreover, a history of a puncturing animal bite to PD tubing or fluid bags should raise the index of suspicion. Gram stain and WBC counts from both peripheral blood and peritoneal fluid are not helpful to differentiate Pasteurella from other forms of PD peritonitis except for a tendency toward rapid presentation for care. These organisms should be suspected as an etiological agent if there is a pet at home, even if direct contact between the pet and the equipment was not observed. Moreover, a history of a puncturing animal bite to PD tubing or fluid bags should raise the index of suspicion. Gram stain and WBC counts from both peripheral blood and peritoneal fluid are not helpful to differentiate Pasteurella from other forms of PD peritonitis except for a tendency toward rapid (<24 h of symptoms) presentation for care. These organisms should be suspected as an etiological agent if there is a pet at home, even if direct contact between the pet and the equipment was not observed. Moreover, a history of a puncturing animal bite to PD tubing or fluid bags should raise the index of suspicion. Gram stain and WBC counts from both peripheral blood and peritoneal fluid are not helpful.

REFERENCES


The suggestion in the International Society for Peritoneal Dialysis guideline of empirical Gram-positive and Gram-negative therapy for PD-associated peritonitis is appropriate even if Pasteurella species are suspected (34). If Pasteurella species are recovered from PD fluid culture, we suggest a 14-day course of IP therapy guided by antimicrobial susceptibilities; aminoglycoside monotherapy should be avoided. Antibiotic-based PD catheter salvage therapy is an appropriate goal given that this approach was successful in 90% of published cases.

DISCLOSURES: The authors have no conflicts of interest to declare.

ACKNOWLEDGEMENTS: There were no study sponsors or funding sources.

ETHICS APPROVAL: Ethics approval was not required for this study.