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CASE REPORT

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Peritoneal dialysis-associated peritonitis presenting with *Ralstonia pickettii* infection: A novel series of three cases during the COVID-19 pandemic

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Abstract

Peritoneal dialysis (PD)-associated peritonitis secondary to *Ralstonia* infection is very rare. *Ralstonia pickettii* is an organism that can grow in contaminated saline, water, chlorhexidine, and other medical products used in laboratories and the clinical setting. Infective endocarditis, prosthetic joint, and severe chest infections are previously reported with *R. pickettii* infection. We report a novel series of three cases diagnosed with PD-associated peritonitis caused by *R. pickettii*, where the cases appeared consecutively to our unit during a span of 4 weeks. During the COVID-19 pandemic, there were increased uses of non-sterile gloves by clinical staff as a form of personal protective equipment throughout patient interaction and PD exchange, as recommended by local hospital policy for all staff attending to patient care. A multidisciplinary team root cause analysis of our cases suggested non-sterile gloves being the likely source of environmental contamination, leading to PD-associated peritonitis caused by *R. pickettii* in this scenario.

1 | CASE REPORT

We report a case series of three patients diagnosed with *Ralstonia pickettii* peritoneal dialysis (PD)-associated peritonitis presenting in our unit within a span of 4 weeks (Table 1). A dendrogram of the pulsed-field gel electrophoresis of *Ralstonia pickettii* isolates from peritoneal fluid culture in our three reported cases is presented in Figure 1. Our unit is a tertiary nephrology center in north-west UK catering for an adult population of 1.5 million people, with approximately 100 patients receiving PD under outpatient follow-up currently.

The first case was a 52-year-old Caucasian female patient with previous history of kidney transplantation, who had been receiving automated PD during the past 17 months. Her primary kidney disease was immunoglobulin A nephropathy, and she was taking regular oral prednisolone 5 mg tablet daily as part of her post-transplant immunosuppression regime. The patient had two previous episodes of PD-associated peritonitis—growing *Staphylococcus aureus* 5 months ago and *Streptococcus gordonii* and *Micrococcus luteus* 12 months ago in peritoneal fluid culture. She did not have any issues in relation to her PD exit site. The patient initially presented with abdominal pain and appearances of cloudy effluent, and initial peritoneal fluid white

TABLE 1 Characteristics of the three patients presenting with PD-associated peritonitis by *Ralstonia pickettii* infection

	First case	Second case	Third case
Age (years)	52	82	64
Gender	Female	Female	Male
Ethnicity	Caucasian	Asian	Caucasian
Primary kidney disease	IgA nephropathy	Unknown	Diabetic nephropathy
Diabetes mellitus	No	No	Yes
Immunosuppression medications	Yes - Prednisolone 5 mg daily as part of post-transplant immunosuppression	No	None
Time since PD catheter insertion (months)	17	34	7
Mode of PD received	APD	CAPD	APD
History of Exit site issues	No	No	No
Previous PD peritonitis	Yes *Staphylococcus Aureus* (5 months ago) *Streptococcus Gordonii* and *Micrococcus Luteus* (12 months ago)	No	No
Clinical presentation	Mild abdominal pain, Cloudy PD fluid	Mild abdominal pain, Cloudy PD fluid	Pink colored fluid. Patient asymptomatic
Peritoneal fluid white cell count (count/μL)	140	1,520	11
Concurrent organisms in peritoneal fluid culture	*Corynebacterium Propinquum*	*Micrococcus Luteus*	Nil
Antibiotic treatment received	Intraperitoneal vancomycin for two doses and oral ciprofloxacin for 21 days	Intraperitoneal gentamicin for one dose, Intraperitoneal vancomycin for two doses and oral ciprofloxacin for 21 days	None
Clinical outcome	Organisms cleared following antibiotic treatment. Patient clinically improved	Organisms cleared following antibiotic treatment. Patient clinically improved	Organism cleared without antibiotic treatment

Abbreviations: APD, automated peritoneal dialysis; CAPD, continuous ambulatory peritoneal dialysis; IgA Nephropathy, Immunoglobulin A nephropathy; PD, peritoneal dialysis.

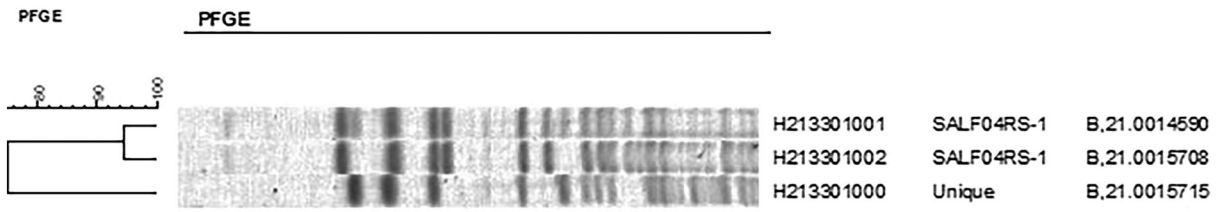

FIGURE 1 Dendrogram of the pulsed-field gel electrophoresis of *Ralstonia pickettii* isolates from peritoneal fluid culture in our three reported cases

cell count (WCC) was 140/μl. No features of contamination were identified within the peritoneal fluid sample. The patient received an initial dose of intraperitoneal vancomycin and intraperitoneal gentamicin and continued oral ciprofloxacin as per our local microbiology policy. The peritoneal fluid culture initially grew *Cornybacterium propinaquim*, a gram-positive organism. Oral ciprofloxacin was stopped, and the patient received three further doses of intraperitoneal vancomycin over a 2-week period. Peritoneal fluid sample extracted following the three doses of intraperitoneal vancomycin showed a decline in peritoneal fluid WCC to 14/μl, however, the peritoneal fluid culture was reported to have grown a new gram-negative organism subsequently identified as *Ralstonia pickettii*. A repeat

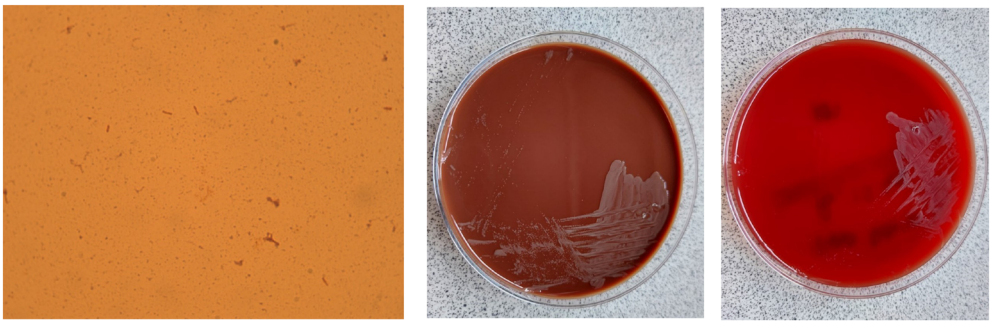

FIGURE 2 (A) *Ralstonia pickettii* in gram stain; (B) *Ralstonia pickettii* culture in chocolate agar; (C) *Ralstonia pickettii* culture in blood agar

peritoneal fluid sample was sent confirming the growth of *Ralstonia pickettii*, with peritoneal fluid WCC rising back to 142/μl (Figure 2). Following multidisciplinary discussion and input from the local microbiology services, this was managed as a new case of PD-associated peritonitis. The patient was commenced on a 3-week course of oral ciprofloxacin. She remained clinically well and asymptomatic throughout this episode.

The second case was an 82-year-old Asian female patient with an unknown primary cause for his kidney failure. She was receiving continuous ambulatory PD over the previous 34 months prior to presentation. The patient presented acutely with abdominal pain. Cloudy effluent was detected, and peritoneal fluid WCC was 1,520/μl on admission. Peritoneal fluid culture grew gram-positive and negative organisms (*Micrococcus leutus* and *Ralstonia pickettii*) concurrently. He received an initial dose of intraperitoneal vancomycin and gentamicin followed by three more doses of vancomycin over 2 weeks and a 3-week course of oral ciprofloxacin as guided by our microbiology services. Following completion of this antibiotic regime, the patient was clinically well and repeat peritoneal fluid culture was negative.

Our third case in the series relates to a 64-year-old Caucasian gentleman with a background of diabetic nephropathy who was receiving automated PD for 7 months prior to presentation. There was no previous history of peritonitis or PD exit site issues. He presented to the unit with pink-colored effluent. Initial peritoneal fluid sampling revealed peritoneal fluid WCC to be 11/μl and the peritoneal fluid culture grew *Ralstonia pickettii*. The patient did not complain of any symptoms and appeared clinically well. The repeat peritoneal fluid culture was negative for any microbiological organisms, suggesting that the infection may have cleared spontaneously given no antibiotic treatment was administered to the patient.

Following the presentation of these three cases, a multidisciplinary root cause analysis was conducted involving the nephrologists and PD specialist nurses attending to the care of these patients, and the microbiology department. Factors analyzed include each patient's PD exchange technique, the performance of staff members involved in supporting patient PD exchanges, and the process of peritoneal fluid sample collection. There were no common links found between the PD fluid or normal saline used for PD exit site care across these three cases.

The recommended practice in our unit for infection control is for the staff to wash their hands with soap and alcohol gel use prior to performing PD exchanges. During the COVID-19 pandemic, an additional measure to staff practices during the preparation, procedural, and post-procedural phases of PD exchange was the use of non-sterile gloves and alcohol gel over non-sterile gloves as a form of personal protective equipment throughout patient interaction and PD exchange. From the multidisciplinary root cause analysis, environmental bacterial contamination due to non-sterile glove use was considered a key factor of PD-associated peritonitis in our reported cases.

2 | DISCUSSION

Ralstonia species-associated PD peritonitis is extremely uncommon. The most frequent organisms encountered in PD-associated peritonitis for both adults and children are gram-positive organisms, which encompasses up to 60% of all organisms detected in PD-associated peritonitis.[1] Previously thought of as a species of minimal clinical significance, recent literature have highlighted the *Ralstonia* species as an emerging opportunistic pathogen, which can cause various infections, especially in immunosuppressed patients.[2]

Sequence analysis of the 16S ribosomal RNA (16S rRNA) sequences classifies species of the genus *Ralstonia* into two major genotypic and phenotypic lineages—the *Ralstonia eutropha* and *Ralstonia pickettii* lineages.[3] The *Ralstonia pickettii* lineage comprises of *Ralstonia insidiosa*, *Ralstonia mannitolilytica*, *Ralstonia pickettii*, *Ralstonia solanacearum*, and *Ralstonia syzygii*, of which *Ralstonia pickettii* has been the most reported organism in this species relating to human infection.[4] *Ralstonia pickettii* can grow in contaminated saline, water, chlorhexidine and other medical products used in laboratories and the clinical setting, often as a result of contamination during the manufacturing process or by extrinsic manipulation.[5] Another key source of *Ralstonia pickettii* stem from contaminated solutions used in respiratory therapies leading to airway colonization.[6]

This non-fermenting, gram-negative bacilli organism has been associated with infections of varying severity—ranging from pseudobacteremia to severe invasive sepsis. *Ralstonia picketii* cases of infective endocarditis, bone and joint (including prosthetic joint) infections, and chest infections leading to severe pneumonia (particularly in

cystic fibrosis patients who are more susceptible to opportunistic pathogens) are among those being reported.[7–9]

Like all other *Ralstonia* species, *Ralstonia pickettii* grows on routine media, although growth may be slow and require >72 h of incubation to visualize colonies. *Ralstonia pickettii*, like all *Ralstonia* species, has one or more polar flagella in motile species, produces acid from glucose and several other carbohydrates, and is resistant to colistin.[10] Identification of *Ralstonia pickettii* may be confused with other *Ralstonia* organisms and *Burkholderia cepacia* in selective media.[10] Extensive testing with 16S rRNA and Matrix Assisted Laser Desorption Ionization Time of Flight mass spectrometry is often required for clearer identification.[11,12]

Similarly to other *Ralstonia* species, *Ralstonia pickettii* produces the chromosomally encoded class D beta-lactamase OXA-22, which confers resistance or reduced susceptibility to antibiotics such as aminopenicillins, narrow-spectrum cephalosporins, and aztreonam.[13] *Ralstonia pickettii* also induces production of the chromosomal beta-lactamase OXA-60, which hydrolyzes imipenem.[13] Previous reports of *Ralstonia pickettii* isolates suggest its susceptibility towards ureidopenicillins, ciprofloxacin and trimethoprim-sulfamethoxazole, with varied susceptibility towards aminoglycosides.[10]

To our knowledge, these are the first reported cases of PD-associated peritonitis relating to *Ralstonia pickettii* infection. A case of PD-associated peritonitis relating to *Ralstonia mannitolilytica* infection has been previously reported in a pediatric patient.[14] Nevertheless, *Ralstonia pickettii* has been reported to associate with bacteremia outbreak among in-center hemodialysis. Thet et al.[15] reported a case series of *Ralstonia pickettii* and *Stenotrophomonas maltophilia* bacteremia outbreak amongst multiple patients receiving maintenance hemodialysis in the same unit. Environmental sampling of the entire hemodialysis unit suggested bacteria colonization of treated reverse osmosis water as the root cause, a result of polluted filters compounded by the usage of reprocessed dialyzers in the unit. Disinfection measures, replacement of older components in the water system, and temporary cessation of practices relating to dialyser reuse were required to halt the spread of this outbreak.

Following the escalation of the COVID-19 pandemic, several public health precautionary measures have been taken to mitigate the spread of COVID-19 infection. Use of personal protective equipment including masks, non-sterile gloves, and aprons has become a vital measure for clinical staff attending to patient care. From the investigations conducted for our three cases, the use of non-sterile gloves by clinical staff attending to patients receiving PD was identified as a likely source for the contamination of environmental pathogens like *Ralstonia picketii*, though cultures taken from used gloves for environmental sampling were not routinely collected due to COVID-19 precautions at the time. Our unit now recommends the use of sterile gloves or returning back to the essential routine practices of washing hands with soap and alcohol gel use prior to PD exchange procedures. We have not identified further cases of PD-associated peritonitis presenting with *Ralstonia pickettii* infection since.

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