KOCURIA SPECIES PERITONITIS: ALTHOUGH RARE, WE HAVE TO CARE

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***Kocuria* species are found in the environment and on human skin. These micro-organisms are generally considered to be nonpathogenic saprophytes, rarely causing infection. However, the peritoneum has been reported to be a site of *Kocuria* infection. We reviewed all cases of peritonitis in peritoneal dialysis (PD) patients caused by *Kocuria* species that were reported in the worldwide literature. In total, 12 episodes of *Kocuria* species peritonitis have been reported in 9 PD patients. The median age of the patients was 62 years (range: 8 – 78 years). In the reported episodes, 4 different *Kocuria* species were isolated, with *K. varians* being the predominant species (41.7%). The most common initial symptom was abdominal pain (83.3%), followed by turbid effluent (75%) and fever (33.3%). Intraperitoneal first-generation cephalosporins and glycopeptides were the most-used antibiotics, with first-generation cephalosporins being more often preferred as first-line therapy. The median duration of treatment was 14 days, and in 2 episodes, the Tenckhoff catheter was removed. Although *Kocuria* peritonitis in PD patients is rare, it should be promptly treated because relapses can occur, especially with *K. varians* episodes.**

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***Kocuria* species are gram-positive, coagulase-negative, coccoid Actinobacteria that belong to the family Micrococcaceae (1). Organisms of the genus *Kocuria* can be found as part of the normal skin and oral flora of humans, but are ubiquitous in the environment, inhabiting soil and several other ecologic niches (2). Only sporadic reports about *Kocuria* species are found in the literature dealing with infections. In most of them,**

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patients were compromised because of serious underlying conditions, including hematologic malignancies, solid tumors, or metabolic disorders (3). Bacteremia, cholecystitis, and peritonitis are some of the infections that can be caused by these rare pathogens (3,4). The isolation and identification of *Kocuria* species by standard microbiologic methods has been problematic because of the similarity of this organism to other commonly reported pathogens (2).

We recently treated an 8-year-old immunocompetent girl who experienced peritonitis attributable to *K. rosea* while receiving automated peritoneal dialysis (PD) treatment because of dysplastic kidneys, and who experienced a favorable outcome (5). Here, we review all cases recorded in the worldwide literature of peritonitis attributable to *Kocuria* species in PD patients.

METHODS

The Medline and Google Scholar databases were searched using the keywords “peritonitis,” “peritoneal dialysis,” and “*Kocuria*” in any available language. All articles found were reviewed, and a master spreadsheet was constructed. In addition, the reference list for each article was examined to verify that all published cases had been collected for the review.

A predefined set of criteria, based on the definition of peritonitis in PD patients, were used to screen the publications for eligibility for the review. Specifically, cloudy effluent in conjunction with laboratory confirmation of an increased effluent cell count exceeding 100/mm³, with at least half being polymorphonuclear neutrophils, and a positive culture are the criteria establishing a diagnosis of bacterial peritonitis in PD patients (6,7).

When a peritonitis episode occurs within 4 weeks of completion of therapy for a prior episode, but involving a different organism, that episode can be characterized as recurrent peritonitis. When an episode occurs within 4 weeks of completion of therapy for a prior

episode and involves the same organism or is classified as sterile, that episode is called relapsing peritonitis. In addition, “repeat peritonitis” is characterized as an episode that occurs more than 4 weeks after completion of therapy for an earlier episode with the same organism. Finally, refractory peritonitis is the failure of the effluent to clear after 5 days of appropriate antibiotic treatment (6,7).

RESULTS

In PD patients, 12 cases of peritonitis attributable to *Kocuria* species have been recorded in the Medline and Google Scholar databases to date (Tables 1 and 2). One patient experienced 3 episodes of relapsing peritonitis attributable to *K. varians*; another had 2 episodes of relapsing peritonitis attributable to the same *Kocuria* species. In total, 9 PD patients with end-stage renal disease were reported to experience peritonitis caused by *Kocuria* species (4,5,8–13). In all the *Kocuria* peritonitis episodes, no ultrafiltration problems were reported.

The median age of the patients (6 male, 3 female) when their first episode of *Kocuria* peritonitis occurred was 62 years (range: 8 – 78 years; Table 1). In the reported episodes, 4 different *Kocuria* species were found, including *K. varians* in 5 of the 12 episodes (41.7%) and *K. rosea*, *K. marina*, and *K. kristinae* in 2 episodes each (16.7%). In 1 episode, the *Kocuria* species was unspecified. The preferred identification method was the Vitek 2 system [bioMérieux, Marcy l’Etoile, France (4 of 12 episodes, 33.3%)], followed by the 16S rRNA gene sequencing method (25%) and the API Staph system [bioMérieux (16.7%)]. In 1 case, the Vitek 2 system and 16S rRNA gene sequencing were both used to identify a *K. varians* peritonitis.

In patients in whom the cause of end-stage renal disease was available, diabetic nephropathy was found to be the most common reason for renal replacement therapy being started. Except for the pediatric patient (who was receiving automated PD), all the other patients were being preferentially treated with continuous ambulatory PD (median dialysis vintage: 2 years; range: 1 – 10 years).

TABLE 1
Characteristics of Peritoneal Dialysis (PD) Patients and *Kocuria* Species Peritonitis Episodes

Reference	Ep ID	Language	Sex	Age (years)	<i>Kocuria</i> species	Identification method	Cause of ESRD	Dialysis vintage (years)	PD modality
Kaya <i>et al.</i> , 2009 (8)	1	Turkish	Female	56	<i>K. rosea</i>	API Staph ^a	NA	1.5	CAPD
Lee <i>et al.</i> , 2009 (4)	2	English	Male	57	<i>K. marina</i>	16S rRNA gene sequencing	DM nephropathy	6	CAPD
	3		Male	73	<i>K. marina</i>		DM nephropathy	4	CAPD
Rou <i>et al.</i> , 2010 (9)	4 ^b	Korean	Female	62	<i>K. varians</i>	Vitek 2 ^a and 16S rRNA gene sequencing	DM nephropathy	10	CAPD
	5 ^b				<i>K. varians</i>			NA	
	6 ^b				<i>K. varians</i>			NA	
Carlini <i>et al.</i> , 2011 (10)	7	English	Male	78	<i>K. kristinae</i>	Vitek 2	NA	2	CAPD
Cheung <i>et al.</i> , 2011 (11)	8	English	Male	69	<i>K. kristinae</i>	Vitek 2	NA	2	CAPD
Dotis <i>et al.</i> , 2012 (5)	9	English	Female	8	<i>K. rosea</i>	API Staph	Dysplastic kidney	1	APD
Meletis <i>et al.</i> , 2012 (12)	10 ^c	English	Male	70	<i>K. varians</i>	Vitek 2	NA	NA	CAPD
	11 ^c				<i>K. varians</i>			1.5	
Kao <i>et al.</i> , 2012 (13)	12	English	Male	54	Unspecified	NA	Chronic GN	NA	CAPD

Ep = episode; ESRD = end stage renal disease; NA = not available; CAPD = continuous ambulatory PD; DM = diabetes mellitus; APD = automated PD; GN = glomerulonephritis.

^a BioMérieux, Marcy l’Etoile, France.

^b Patient relapsed twice with *K. varians*.

^c Patient relapsed once with *K. varians*.

TABLE 2
Clinical, Laboratory, and Therapeutic Characteristics of *Kocuria* Species Peritonitis Episodes

Ep ID	Symptoms	Effluent TNCC (/mm ³)	Neutrophils (%)	Anti-microbial sensitivity	Treatment	PD technique problems
1	Abdominal pain, turbid effluent, nausea, mild fever	1800	NA	NA	IP teicoplanin, 14 days	No
2	Turbid effluent	780	90	P, A, Ce, E, Cl, V	IP netilmicin and ceftazidime, then IP ceftazidime and clindamycin, plus IV vancomycin for 10 days, then Tenckhoff catheter removal on day 17 and transfer to hemodialysis	Probable refractory peritonitis
3	Turbid effluent	2580	90	P, A, Ce, E, Cl, V	IP netilmicin and ceftazidime	No
4 ^a	Abdominal pain, turbid effluent	730	68	P, O, V	IP ceftazidime and cefazolin for 10 days	Relapsed after a 2-week period
5 ^a	Abdominal pain, turbid effluent	2450	41	NA	IP ceftazidime and cefazolin for 7 days	Relapsed after a 1-month period
6 ^a	Abdominal pain, fever	560	79	NA	IP ceftazidime and cefazolin for 14 days	No
7	Abdominal pain, turbid effluent, fever	9980	>90	NA	IP cefotaxime (6 days) and tobramycin (2 days), plus IV tazobactam, then IP ciprofloxacin and teicoplanin, plus IV amoxicillin and clavulanic acid for 14 days	No
8	Abdominal pain, turbid effluent	NA	NA	Clo, E, Cl	IP cefazolin and cefepime for 14 days	No
9	Abdominal pain, fever	1170	88	O, E, Cl, V, L	IP vancomycin for 10 days	No
10 ^b	Abdominal pain, turbid effluent	1200	90	E, Cl, V, L	IP vancomycin for 5 days and aztreonam for 20 days, then IP vancomycin (day 8) for 20 days	Relapsed after a 2-month period
11 ^b	Abdominal pain	550	NA	NA	IP vancomycin, plus Tenckhoff catheter revision (different position) on day 31	No
12	Abdominal pain, turbid effluent	2800	90	NA	IP vancomycin (1 dose every 3rd day) for 24 days (8 doses)	No

Ep = episode; TNCC = total nuclear cell count; PD = peritoneal dialysis; NA = not available; IP = intraperitoneal; P = penicillin; A = ampicillin; Ce = cephalothin; E = erythromycin; Cl = clindamycin; V = vancomycin; IV = intravenous; O = oxacillin; Clo = cloxacillin; L = linezolid.

^a Patient relapsed twice with *K. varians*.

^b Patient relapsed once with *K. varians*.

The most common initial symptom was abdominal pain (10 of the 12 episodes, 83.3%), followed by turbid effluent (75%) and fever (33.3%). In the publications reviewed, the mean total effluent white blood cells

was $2236 \pm 2700/\text{mm}^3$, with a neutrophil percentage of approximately 80%. In episode 7, the standard deviation for white blood cells was exceeded by a massively increased number of nuclear cells ($9980/\text{mm}^3$).

Intraperitoneal (IP) first-generation cephalosporins—including cefazolin (4 of 12 episodes, 33.3%) and ceftazidime (16.7%)—and glycopeptides—including vancomycin (41.7%) and teicoplanin (16.7%)—were the most-used antibiotics. However, first-generation cephalosporins were more often preferred as first-line IP therapy; glycopeptides were preferred as either first- or second-line IP therapy. The median duration of appropriate treatment was 14 days, ranging between 7 and 20 days, with the exception of episode 12. In that episode, the patient was treated with IP vancomycin given as a single dose every 3 days for a total of 24 days (total of 8 doses given).

In 2 episodes, the Tenckhoff catheter was removed. In one episode, caused by *K. marina*, the cause for removal was a patient response that remained unsatisfactory despite appropriate IP treatment, suggesting a probable refractory peritonitis (4). In the other episode, Tenckhoff catheter removal was a result of relapsing *K. varians* peritonitis and catheter colonization (12).

DISCUSSION

Named after a Slovakian microbiologist, Miroslav Kocur, the genus *Kocuria* was split from the genus *Micrococcus*, the members of which had been known over the years by the vernacular “micrococci,” which overlaps the genus *Arthrobacter*. In a re-evaluation of this complex cluster of *Arthrobacter* and *Micrococcus*, a new genus *Kocuria* was proposed (1). Based on phylogenetic and chemotaxonomic analysis, the genus *Micrococcus* was divided into the genera *Kocuria*, *Micrococcus*, *Kytococcus*, *Nesterenkonia*, and *Dermaococcus*. A new rearrangement separates them into two families Micrococcaceae and Dermaococcaceae, both belonging to the suborder Micrococccineae. To date, 19 *Kocuria* species have been described (1,2,14).

Peritonitis caused by *Kocuria* species requires laboratory testing for diagnosis, and isolation of the organism from peritoneal effluent samples constitutes the confirmatory test for the disease. However, correct identification of *Kocuria* species by commercial systems is sometimes problematic, because systems such as Vitek 2 and API Staph do not include all *Kocuria* species in their database (4). For that reason, 16S rRNA gene sequencing can confirm and establish the identification of the various *Kocuria* species; unfortunately, however, this technique is not available in all microbiology laboratories. When 16S rRNA gene sequencing is unavailable, double confirmation with both Vitek 2 and API Staph can be a reasonable option.

Infections in humans caused by *Kocuria* species have included bacteremia related to a central venous catheter,

cholecystitis, brain abscess, endocarditis, synovitis, periarticular bursitis, and of course, peritonitis in PD patients. Catheter-related bacteremia and PD-related peritonitis have been hypothesized to be related to an ability of *Kocuria* to produce biofilm, but that potential was not established until recently. A study using both culture-dependent and -independent methods, including 16S rRNA gene clone libraries and pyrosequencing, recently showed that *K. varians* can be found in the flora of endotracheal tube biofilm (15). That finding accords with the known recommendation to remove venous catheters in the presence of bacteremia caused by certain *Kocuria* species (including *K. kristinae*, *K. rhizophila*, and *K. rosea*), which probably indicates biofilm formation (16–18). The ability of *K. varians* to form biofilm can partly explain the increased frequency of relapsing peritonitis in the cases involving that species compared with other *Kocuria* species. Nevertheless, further evaluation of the ability of the various *Kocuria* species to produce biofilm on certain medical devices, such as Tenckhoff catheters, is needed. A suggestion to remove the Tenckhoff catheter in peritonitis caused by *Kocuria* species cannot yet be established, but some evidence suggests removal in cases of *K. varians*. However, the ability of the other *Kocuria* species to produce biofilm is unknown, and considering the fact that the Tenckhoff catheter was removed in only 2 reported cases involving refractory and relapsing peritonitis, any recommendation for removal is currently problematic.

Current empiric regimens for peritonitis caused by gram-positive pathogens in PD patients most commonly recommend IP use of a first-generation cephalosporin, such as cefazolin or ceftazidime. However, because of a high rate of methicillin-resistant organisms, many programs often use IP glycopeptides such as vancomycin or teicoplanin for gram-positive coverage. The reported *Kocuria*-species peritonitis episodes were caused by pathogens susceptible to both first-generation cephalosporins and glycopeptides; no resistance to those antibiotic categories seems yet to have appeared. However, in the full range of infections caused by *Kocuria* species, variable susceptibility to beta-lactam drugs has been observed. Notably, no cases of resistance to glycopeptides, streptogramins, fusidic acid, rifampicin, or linezolid have been reported so far (2).

Our study found that the median duration of IP treatment was 14 days, which accords with guidelines in PD patients for the treatment of peritonitis caused by common and sensitive gram-positive pathogens (6,7). Nevertheless, the patient who experienced 3 relapsing peritonitis episodes with *K. varians* received IP cefazolin for 10 days for the first episode, IP cefazolin for 7 days

after peritonitis relapse, and IP cefazolin for 14 days after the second relapse, which is the formal suggested regimen (4). Recommendations for avoidance of *Kocuria*-species peritonitis follows the general consensus guidelines for the prevention of catheter-related infections and peritonitis in pediatric patients receiving PD (7).

This review is a first attempt to collect and review all published *Kocuria* peritonitis cases in PD patients; it could potentially be a useful tool for future studies. However, taking in account that this is a retrospective multi-source case review study, limitations in the available data might affect the ability to draw specific conclusions, a problem that is compounded by the relatively small number of reported cases.

SUMMARY

Our study addresses the demographics; frequencies and species panel; and the clinical, laboratory, and therapeutic characteristics of peritonitis caused by *Kocuria* species in PD patients. More such cases are expected to occur in upcoming years because of major advances in the diagnosis of these infections. These organisms are usually considered to be contaminants, but they can cause severe disease and symptomatic peritonitis. The effect on PD patients of peritonitis caused by *Kocuria* species seems to be minimal, but in most cases in which treatment failed, a relapsing peritonitis was caused by *K. varians*. Therefore, although *Kocuria* peritonitis in PD patients is rare, it should be promptly treated.

DISCLOSURES

The authors have no financial conflicts of interest to declare.

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