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Kocuria Rhizophila peritonitis in peritoneal dialysis: About 2 cases and review of the literature)

(Péritonite à Kocuria Rhizophila en dialyse péritonéale : A propos de 2 cas et revue de la littérature)

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Summary

The authors report two clinical cases of peritonitis caused by *Kocuria rhizophila*, an uncommon but pathogenic bacterium, that occurred in a dialysis center over a three-month period in 2022. These cases required removal of the peritoneal dialysis catheter, illustrating the potential severity of these infections. The authors describe the clinicobiologic features of these peritonitis and highlight the difficulty in distinguishing Kocuria from other gram-positive cocci, such as staphylococci, due to their morphologic similarity and the need for accurate identification for appropriate treatment.

The discussion focuses on the incidence and management of *Kocuria* peritonitis in France, based on an observational cohort study using data from the Registre de Dialyse Péritonéale de Langue Française (RDPLF) between January 2018 and May 2023. The study found that *Kocuria* peritonitis accounted for 3.5% of documented peritonitis, with *Kocuria rhizophila* being the most commonly identified. The study highlights a high recurrence rate and the frequent need for catheter removal, underscoring the severity of these infections.

Conclusion: The authors suggest that rapid catheter removal and replacement should be considered in cases of *Kocuria rhizophila* peritonitis, given the high rate of relapse. They also call for increased vigilance and close follow-up of patients treated conservatively with antibiotics to minimize the risk of relpase and technical failure, suggesting the need for therapeutic strategies tailored to this specific pathogen.

Keywords: peritoneal dialysis, peritonitis, relapse, kocuria, catheter

Résumé

Les auteurs rapportent deux cas cliniques de péritonite à *Kocuria rhizophila*, un germe peu fréquent mais pathogène, survenus dans un centre de dialyse sur une période de trois mois en 2022. Ces cas ont nécessité la dépose du cathéter de dialyse péritonéale, illustrant la gravité potentielle de ces infections. Les auteurs décrivent les caractéristiques clinico-biologiques de ces péritonites et soulignent la difficulté de distinguer Kocuria des autres cocci Gram positif, comme les staphylocoques, en raison de leur ressemblance morphologique, et la nécessité d'une identification précise pour un traitement approprié.

La discussion aborde la fréquence et la gestion des péritonites à *Kocuria* en France, basée sur une étude observationnelle de cohorte utilisant les données du Registre de Dialyse Péritonéale de Langue Française (RDPLF) entre janvier 2018 et mai 2023. Cette étude a révélé que les péritonites à *Kocuria* représentaient 3,5% des péritonites documentées, *Kocuria rhizophila* étant le plus fréquemment identifié. L'étude met en évidence un taux important de récidives et la nécessité fréquente de retirer le cathéter, soulignant la gravité de ces infections.

Conclusion : Les auteurs suggèrent qu'en cas de péritonite à *Kocuria rhizophila*, une dépose-repose rapide du cathéter pourrait être envisagée en raison du taux élevé de récidives. Ils appellent également à une vigilance accrue et à un suivi rapproché des patients traités conservativement par antibiothérapie pour minimiser le risque de récidive et d'échecs techniques, indiquant un besoin de stratégies thérapeutiques adaptées face à ce pathogène spécifique.

Mots-clés : Dialyse péritonéale, péritonite, kocuria, récidive, cathéter

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Introduction

LIST OF ABBREVIATIONS	
GPC:	Gram-Positive Cocci
AOMI:	Obliterative Arteriopathy of the Lower Limbs
CAPD:	Continuous Ambulatory Peritoneal Dialysis
APD:	Automated Peritoneal Dialysis
IP:	Intraperitoneal
NPC:	Non-Polymorphonuclear Cells
CRP:	C-Reactive Protein

Peritonitis currently represents 14% of the cases necessitating a transition from peritoneal dialysis to hemodialysis in France and accounts for 3% of all mortality rates associated with dialysis [1]. Innovations in both the technical and medical spheres, including the implementation of the «flush before fill» technique, enhanced antisepsis protocols, and the application of mupirocin, in conjunction with the establishment of therapeutic patient education initiatives, have contributed to a decrease in the incidence of peritonitis. This reduction is particularly notable in the case of gram-positive cocci (GPC) infections, which are prevalent among diabetic individuals.

The capacity to identify causative germs is not consistently achievable, with the prevalence of culture-negative peritonitis exhibiting significant variation, ranging from 10% to 50% across different facilities [2]. The process for germ identification necessitates a prompt analysis of the effluent dialysate, which is incubated in blood culture bottles (e.g., BACTEC, Kent, UK) following a minimum dwell time of two hours. Employing an optimal dialysate culture methodology involving centrifugation of the dialysate followed by resuspension of the supernatant in a culture medium should curtail the incidence of undocumented peritonitis to below 10%. Typically, a phenotypic analysis utilizing mass spectrometry (bioMérieux VITEK MS) is conducted initially, with subsequent identification of bacteria through automated biochemical galleries (bioMérieux VITEK 2) in cases where spectrometry is inconclusive.

Staphylococci, encompassing both coagulase-positive staphylococci, such as Staphylococcus aureus, and coagulase-negative *staphylococci*, predominantly account for GPC-related peritonitis cases. In both micro and macroscopic evaluations of cultures, it is common to encounter difficulties in distinguishing coagulase-negative *staphylococci* from other GPC species, such as *Kocuria*.

Species within the *Micrococcus* and *Kocuria* genera, members of the *Micrococcaceae* family, are characterized as cluster- or tetrad-forming GPCs. These species are distinguishable from staphylococci by their larger size and more pronounced yellow pigmentation under light microscopy. Although typically saprophytic on human skin, mucous membranes, and oropharynx, they can become pathogenic in the context of immunodepression. In relation to peritoneal dialysis, these bacteria have been implicated in cases of peritonitis.

The International Society for Peritoneal Dialysis has issued guidelines for the probabilistic antibiotic treatment of peritonitis, which were recently summarized by Taghavi and Dratwa [3]. These guidelines primarily focus on GPCs and gram-negative bacilli; however, they do not

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explicitly address peritonitis caused by *Micrococcus* and *Kocuria* species.

In this report, we present two instances of *Kocuria rhizophila* peritonitis identified at our facility within a span of 3 months in 2022, both of which necessitated the removal of the peritoneal dialysis catheter. The objective of this study is to delineate the clinico-biological profiles and outcomes of these *K. rhizophila* peritonitis cases and compare the findings with data recorded in the French Language Peritoneal Dialysis Registry (RDPLF) as well as existing literature on the subject.

Clinical Cases

Case 1

Case 1 involves Mr. L, a 70-year-old male, presenting with chronic renal failure attributed to probable nephroangiosclerosis. His medical history included active smoking, exogenous factors, and endovascular revascularization for stage 3 obliterative arteriopathy of the lower limbs (AOMI). He had been undergoing continuous ambulatory peritoneal dialysis (CAPD) for 5 years, with three daily exchanges. Two years prior, he experienced *Streptococcus salivarius* and *Streptococcus vestibularis* peritonitis, which responded favorably to intraperitoneal (IP) cefazolin.

Upon first evaluation, the patient presented with a compromised infusion line, necessitating its replacement, yet there were no clinical or biological indicators initially suggesting peritonitis. Subsequent routine analysis of his dialysate identified the presence of *Micrococcus luteus*. This bacterium was interpreted as a contaminant due to its non-pathogenic nature and the absence of increased cellularity in the dialysate, indicating a lack of inflammatory response typically associated with infection.

Despite developing severe abdominal pain, widespread defensiveness, and functional ileus 3 weeks later, the patient remained apyretic and showed no signs of hemodynamic compromise. The effluent appeared turbid, and analysis confirmed peritonitis with a dialysate hypercellularity of 9440 elements/mm3, of which 80% were non-polymorphonuclear cells (NPCs).

The patient's blood analysis indicated a biological inflammatory syndrome with a C-reactive protein (CRP) level of 125 mg/L, notably without hyperleukocytosis. Plasma albumin concentration was measured at 30 g/L. In accordance with local protocols and International Society for Peritoneal Dialysis recommendations, empiric treatment commenced with IP cefazolin and ceftazidime. Subsequent direct examination detected the presence of GPCs, leading to the discontinuation of ceftazidime and the continuation of cefazolin as monotherapy.

The patient's condition rapidly improved, as evidenced by diminished pain following lavage and the placement of a nasogastric tube for functional ileus. However, cultures of the dialysate remained positive for *K. rhizophila* over a period of 6 days, prompting the substitution of cefazolin with IP vancomycin, pending the results of susceptibility testing. The susceptibility testing revealed a strain responsive to multiple antibiotics. Cultures became sterile after 48 hours of vancomycin therapy, which was extended for a total duration of 21 days. At the conclusion of treatment, the dialysate analysis showed no microbial growth and a normalization of peritoneal

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cellularity to 17 elements/mm3, albeit with a predominance of 68% NPCs. The CRP level remained mildly elevated at 40 mg/L.

Ten days post-antibiotic therapy, the patient experienced severe abdominal pain and diffuse tenderness. The dialysate appeared cloudy, and analysis confirmed a recurrence of peritonitis, with 5760 nucleated cells/mm3, including 89% NPCs. Blood tests indicated an elevated inflammatory response, with a CRP level of 80 mg/L; however, no hyperleukocytosis was observed. Treatment was reinitiated with IP vancomycin, ceftazidime, and amikacin.

Cultures of the dialysate once again isolated *K. rhizophila*, without detection of mycelial filaments. Considering the recurrence of *K. rhizophila* peritonitis, potentially due to catheter colonization, the management strategy included a one-stage catheter removal and replacement under vancomycin coverage, which resulted in an improvement in the infection.

This case highlights the unique pathogenic potential of *K. rhizophila*, an organism typically considered low-virulence, and its ability to form a biofilm on the catheter, necessitating its removal. Notably, catheter cultures remained sterile, likely due to the antibiotic regimen.

The case study underscores the necessity of recognizing *Kocuria* and *M. luteus* not merely as contaminants but as potential pathogens in dialysate cultures, emphasizing their clinical significance in the context of peritoneal dialysis-associated peritonitis.

Case 2

Case 2 involves Mrs. L, a 77-year-old female with chronic renal failure secondary to acute tubular necrosis during hemorrhagic shock. Her medical history includes endovascularly revascularized AOMI, arterial hypertension, and an anaphylactic reaction to cephalosporins. Notably, the patient had experienced 12 prior episodes of peritonitis, attributed to exposure to cats at home, leading to multiple instances of *Pasteurella*-induced peritonitis.

Following a failed kidney transplant, she had been receiving automated peritoneal dialysis (APD) for 7 years. The patient was admitted to the hospital presenting with cloudy dialysate but no abdominal pain or fever. Dialysate analysis confirmed peritonitis, with 800 nucleated elements/mm3, 80% of which were NPCs. The biological workup did not indicate an inflammatory syndrome. Due to a documented allergy to ceftazidime and cefazolin, probabilistic treatment was initiated with aztreonam IV and vancomycin IP. Subsequent direct examination revealed GPCs, leading to the discontinuation of aztreonam. Culture results yielded a multi-susceptible *K. rhizophila* strain. The patient responded well to IP vancomycin therapy, and after 4 weeks of treatment, a one-stage catheter removal and reinstallation were performed due to recurrent peritonitis.

This second case, occurring 3 months after the first, prompts consideration of the transmission mode and the potential for nosocomial transmission of *Kocuria*. In both instances, the *Kocuria* strains were multi-susceptible, with phenotypic analysis alone not providing sufficient evidence to conclude the identity between the strains. Pulsed-field gel electrophoresis is currently being conducted at Nantes University Hospital to compare the strains and investigate the possibility of nosocomial transmission.

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Discussion

1 - *Kocuria rhizophila*

K. rhizophila is an environmental commensal GPC. It is a member of the *Micrococcaceae* family, comparable to *staphylococci* and *Micrococcus*, characterized by the formation of tetrads and being catalase positive as well as coagulase negative (Figure 1).

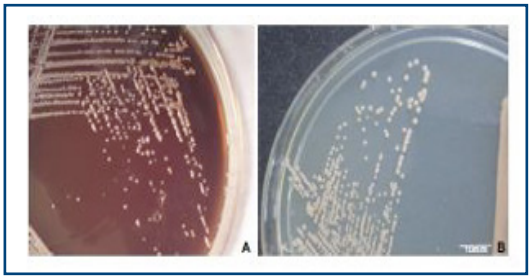

Figure 1. Macroscopic appearance of Kocuria colonies on solid culture medium [6]

Distinguishing between *Staphylococcus* and *Kocuria* based on direct, micro, and macroscopic examination of cultures presents challenges due to the similar appearance of their colonies. Nonetheless, spectrometric analysis of the bacterial proteins facilitates the identification of the species with notable specificity. This method is employed at our center for the accurate identification of *K. rhizophila*. To date, 19 species of *Kocuria* have been identified (Figure 2), with five species, including *K. kristinae*, *K. varians*, *K. marina*, *K. rosea*, and *K. rhizophila*, being documented as pathogens in human infections.

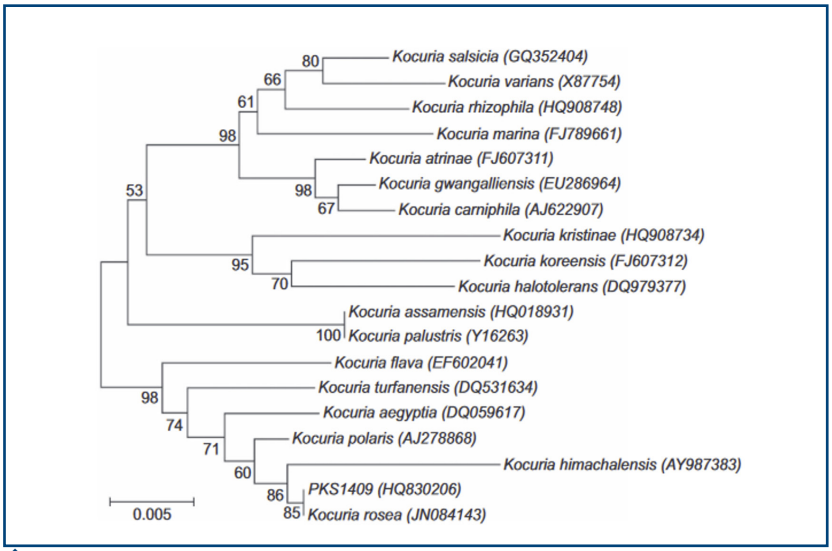

Figure 2. Phylogenetic analysis by 16S rRNA sequencing of different species of the Kocuria genus [6]

K. rhizophila is ubiquitously found in soil, dust, water, and air, forming part of the natural flora on mammalian skin. This bacterium is also capable of colonizing the oral cavity and mucous membranes, particularly within the oropharynx and upper respiratory tract in humans. Transmission can occur through contact with contaminated objects or surfaces or through droplet transmission and inhalation of contaminated aerosols. Moreover, *K. rhizophila* has been isolated

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from oxalic acid-treated chicken, indicating that contact with contaminated meat could serve as a potential source of exposure. A recent study has underscored the bacterium's propensity for adhering to silicone tubing, which may contribute to failures in antibiotic treatments. While biofilm production has been posited for *Kocuria* species, it has not been conclusively demonstrated across all strains [7].

Given the diverse environments *K. rhizophila* inhabits and its potential for biofilm formation, managing infections poses unique challenges, particularly in the context of antibiotic treatment. In the absence of species-specific guidelines, the antibiotic susceptibility thresholds applied to *Kocuria* are aligned with those established for staphylococci. To our knowledge, there has been no documented antibiotic resistance profile specific to *K. rhizophila* in the existing literature.

2 - *Kocuria* Peritonitis in Mainland France

2 - 1 Materials and Methods

We conducted an observational cohort study to document instances of *Kocuria* peritonitis occurring within metropolitan France, utilizing data from the RDPLF spanning from January 1, 2018, to May 15, 2023.

The RDPLF database is officially registered with the National Commission on Informatics and Liberty under the registration number 11950164795. The data were exported to a separate file following complete and irreversible anonymization. Given the retrospective nature of register-based data, obtaining written consent from patients was not deemed necessary for this study. The structure and functionality of the RDPLF are elaborated upon in further detail in previous literature [8].

During the specified period, a total of 4,655 cases of peritonitis were reported to the RDPLF registry. Bacteriological verification was provided by 23 of the participating centers, accounting for 1,144 episodes of peritonitis. Among these, 40 cases were identified as *Kocuria* peritonitis, constituting 3.5% of the bacteriologically documented instances of peritonitis.

2 - 2 Results

General Characteristics

Among the 40 cases of *Kocuria* peritonitis documented, 26 were attributed to *K. rhizophila*, representing 65% of all Kocuria peritonitis episodes. This includes a single case each of *K. kristinae*, *K. marina*, and *K. varians*, alongside 8 cases of unidentified *Kocuria* species, collectively accounting for 2.27% of all bacteriologically documented peritonitis incidents.

The 26 episodes of *K. rhizophila* peritonitis were identified in 18 patients. The general characteristics of these patients are delineated in Table 1.

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Table I. General characteristics of patients with K. rhizophila peritonitis

Characteristic	Value
Number of Patients	18
Sex (Female)	7 (38.8%)
Average Age (Years)	50.6 (36–83.5)
Diabetes Requiring Insulin Therapy	3 (16.6%)
autosomal dominant polycystic kidney disease	2 (11%)
Diabetic Nephropathy/Nephroangiosclerosis	8 (44.5%)
Other Glomerulopathies	4 (22.25%)
Etiology Unknown	4 (22.25%)
Continuous Ambulatory Peritoneal Dialysis	12 (66.6%)
Automated Peritoneal Dialysis	6 (33.3%)

The cohort of 18 patients diagnosed with *K. rhizophila* peritonitis exhibited an average age lower than that reported for the broader population of peritoneal dialysis patients, as indicated in the RDPLF annual report of 2022, where the average ages were 58 years for APD patients and 70 years for CAPD patients [9]. Additionally, this cohort had a marginally lower incidence of insulin-requiring diabetes (16.6% versus 23% within the general peritoneal dialysis population). The prevalence of various nephropathies among these patients mirrored the distribution observed within the overall peritoneal dialysis patient population.

Recurrence Rates and Catheter Management

Within this specific cohort, a notably high recurrence rate of peritonitis was observed. Recurrence was defined as the manifestation of peritonitis caused by the identical microorganism within 4 weeks following the conclusion of the treatment regimen. Given the absence of specific data regarding the treatment duration for each patient, recurrences were identified in all instances of peritonitis that arose within a 2-month period, predicated on the assumption that the initial course of antibiotic therapy ranged from 14 to 28 days.

The evolutionary characteristics of *K. rhizophila* peritonitis are delineated in Table 2.

Only seven centers contributed to the registry's catheter module, providing data on catheter removal due to peritonitis for nine patients. However, we attributed all catheter removals reported within 3 months—lacking alternative explanations—to peritonitis.

Patient 14 experienced two distinct episodes of *K. rhizophila* peritonitis, occurring 9 months apart. These episodes were considered separate instances of peritonitis rather than recurrences. Within this cohort, a notable proportion of patients, 5 out of 18 (26.3%), encountered recurrences. Dotis et al. observed a 22% recurrence rate for *K. varians* peritonitis in their series, including one case of refractory peritonitis, without any reported instances of *K. rhizophila* peritonitis [10].

Of the 18 patients, accounting for 19 episodes of peritonitis (including two separate episodes in Patient 14), seven (36%) necessitated catheter removal within 3 months. The registry documented a direct association between peritonitis and the need for catheter removal in four cases.

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Table II. Evolutionary characteristics of the first episode of peritonitis

	Recurrences	Number and Delay of Recurrences	Catheter Withdrawal Linked to Peritonitis	Duration of Peritoneal Dialysis After Peritonitis Episode (Months)
Patient 1	Yes	1 (2 months)	No	Ongoing
Patient 2	Yes	2 (2 and 3 months)	No	NA
Patient 3	No	0	No	Ongoing
Patient 4	No	0	No	48
Patient 5	No	0	No	6
Patient 6	Yes	1 (1.5 months)	Yes	
Patient 7	No	0	Yes	7
Patient 8	No	0	NA	2
Patient 9	Yes	1 (1.5 months)	NA	2 (due to peritonitis)
Patient 10	Yes	2 (1.5 and 3.5 months)	NA	29
Patient 11	No	0	NA	36
Patient 12	No	0	NA	11
Patient 13	No	0	Yes	12
Patient 14a	No	0	No	
Patient 14b	No	0	Yes	24
Patient 15	No	0	Yes	3
Patient 16	No	0	Yes	2
Patient 17	No	0	NA	6
Patient 18	No	0	No	Ongoing

Note: «NA» indicates data not available in the RDPLF database.

Among the 13 patients without relapse, the average peritoneal dialysis continuation duration was 17 months, with 11 out of 13 patients discontinuing the technique. This observation underscores not only the high recurrence rate but also the significant incidence of technical failures following *K. rhizophila* peritonitis.

We document two instances of *K. rhizophila* peritonitis that transpired within months of each other in our department, with ongoing comparative analysis of the strains. To date, the literature has only noted a single case of *K. rhizophila* peritonitis occurring in a pediatric patient [11]. Despite *K. rhizophila* being relatively uncommon and typically considered non-pathogenic, it presumably resulted in catheter colonization, necessitating the removal of the dialysis catheter in both cases reported here—one due to peritonitis recurrence and the other due to repeated peritonitis episodes. These cases highlight the imperative to recognize and accurately identify such underreported yet pathogenic microorganisms in individuals undergoing peritoneal dialysis rather than dismissing them as mere contaminants.

From January 1, 2018, to May 2023, in metropolitan France, *Kocuria* accounted for 3.5% of all documented peritonitis cases reported in the RDPLF, with *K. rhizophila* constituting 65% of these instances. No significant increase in prevalence was observed during this timeframe, averaging five episodes per year. Despite the limitations stemming from the incomplete nature of registry data, particularly the lack of detailed information regarding the infectious trajectory or the direct relationship between catheter removal and peritonitis, the available data appear to corroborate a notable recurrence rate of 26.3% among patients. Furthermore, the data underscore the severity

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of these infections, with 36% of the patients necessitating catheter removal within 3 months. A more detailed, center-specific analysis of these cases would facilitate a refined characterization of peritonitis incidents and allow for an assessment of the susceptibility profile of *K. rhizophila*, thereby aiding in formulating therapeutic guidelines.

Comparatively, international reports document a series of *Kocuria* peritonitis instances, with none attributed to *K. rhizophila* [10]. Within this collection, nine peritoneal dialysis patients experienced 12 episodes of *Kocuria* peritonitis. Initial treatments employed included first-generation cephalosporins intraperitoneally (C1G IP) or vancomycin IP, with a median treatment duration of 14 days (ranging from 7 to 20 days). Three out of nine patients necessitated catheter removal—two due to recurrences and one facing refractory peritonitis. While some researchers advocate for Tenckhoff catheter removal in cases of *K. varians* peritonitis, explicit recommendations for *K. rhizophila* peritonitis remain unestablished.

Conclusion

Considering the observations from our center and those reported by the RDPLF, prompt contemplation of catheter removal and replacement is advisable due to the significant recurrence rate associated with *K. rhizophila* peritonitis. The hypothesis of biofilm formation in such instances of peritonitis is strongly inferred, though not yet conclusively proven [4]. In scenarios where immediate removal and reinstallation strategies are not implemented, the application of IP urokinase treatment could be contemplated. Should conservative treatment with IP antibiotics be pursued, vigilant monitoring for recurrence and technical failure is imperative, necessitating close observation of dialysate cellularity and cultures.

Authors

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Declaration of interests

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