

# First report of *Kocuria marina* bloodstream infection unrelated to a central venous catheter: a mini-review on an emerging and under-recognized opportunistic pathogen

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## SUMMARY

We report a case of sepsis by *Kocuria marina* in a 45 year-old woman carrying a midline venous catheter to provide total parenteral nutrition. Despite the finding of *K. Marina* bacteraemia, no bacteria grew from the culture of the catheter tip. As the patient was affected with severe leg ulcers, *K. marina* bloodstream infection from a skin breakage other than CVC was supposed. *K. marina* is an

emerging opportunistic agent deserving attention and probably under-recognized, as it can be misdiagnosed as *Staphylococcus* if only conventional microbiological analyses are performed for bacterial identification.

**Keywords:** *Kocuria marina*, bloodstream infection, venous leg ulcers.

## INTRODUCTION

The genus *Kocuria* was introduced in 1995 in order to categorize (inside the family *Micrococcaceae*) a group of Gram-positive, aerobic, non-encapsulated and non-endospore-forming cocci, which emerged as being phylogenetically different from other actinobacteria, such as *Micrococcus*, *Arthrobacter* and *Rothia*. Members of genus *Kocuria* have been found ubiquitously in soil, fresh water and mammalian skin, too. To date, more than 20 species have been classified in the genus *Kocuria*, but others are currently under microbiological and genotypic typing [1, 2].

Interestingly, some species resulted to behave as human opportunistic pathogens, as those are able to cause infections in (immunologically) compromised hosts [3]. Currently, very few reports concerning human infectious diseases caused by *Kocuria* members have been published: here, we report a clinical case of sepsis by *Kocuria marina* in a patient showing several comorbidities, including severe malnutrition [4].

## CASE REPORT

A 45-year-old woman was admitted to the general medicine ward at the hospital of Vizzolo Predabissi (Milano, Italy) in January 2016, because of a severe asthmatic attack during acute bronchitis. She was known in the local clinic because of her compromised nutritional status

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with chronic and severe thinness (weight=31 kg, height=157 cm, body mass index [BMI]=12.6), which had required a midline venous catheter to provide total parenteral nutrition (TPN), placed around 2 weeks before the hospitalization. Her malnutrition resulted to be multifactorial: indeed, some years before, the patient developed chronic esophagitis complicated with Barrett's esophagus and also underwent total gastrectomy (because of a complicated aneurism of the right gastric artery); additionally, the patient showed tobacco dependence (at least 15 cigarettes/day) and was affected with anxious depressive syndrome treated with carbamazepine and pregabalin. Moreover, the patient suffered from venous insufficiency ulcerations on the legs, requiring careful and daily skin care. Thus, when the patient was admitted to the hospital, she showed quite compromised clinical conditions. As regards laboratory tests, the blood cell count showed moderate anemia (WBC =8,800/mm<sup>3</sup>; RBC =2,830,000/mm<sup>3</sup>; Hb =8.4 g/dl; MCV =89 fl; PLT =244,000/mm<sup>3</sup>) and the biochemistry was actually fine, except for hypokaliemia (K<sup>+</sup> =2,7 meq/l). Therefore, she received an adequate electrolyte correction and potassium canreonate, in addition to TPN, the appropriate management of ulcerative skin lesions and, of course, the therapy for asthma (inhaled budesonide/formoterol combination and ipratropium bromide). On the 8<sup>th</sup> day (d-8) after the admission, the patient devel-

oped intermittent fever with daily isolate spikes for 7 days (d-9: 38°C; d-10: 37.5°C; d-12: 37.6°C; d-13: 37.2°C; d-15: 37.7°C), in absence of any new and localized clinical manifestation. Blood tests were repeated in the first 24 hours after the febrile onset: briefly, the main laboratory findings were mild leukopenia (WBC=3,700/mm<sup>3</sup>; neutrophils=2,200/mm<sup>3</sup>; lymphocytes=1,000/mm<sup>3</sup>; Hb=9.2 g/dl; MCV=92 fl; PLT=242,000/mm<sup>3</sup>; and moderate C-reactive protein increase (CRP=25 mg/l, n.v. <5 mg/l). Concomitantly, two blood cultures were obtained, from a peripheral vein and from the midline catheter: both resulted to be positive for Gram-positive cocci, which were identified as *K. marina*, through MALDI-TOF MS analysis (Figure 1). Antibiotic susceptibility testing (performed through BD Phoenix™ Automated Microbiology System) showed bacterial resistance to clindamycin, macrolides and penicillin, whereas this bacterial strain resulted to be sensitive to fluoroquinolones, gentamicin, co-trimoxazole, tetracyclin, vancomycin and teicoplanin. Based upon these microbiological results, the midline catheter was removed and antibiotic therapy with levofloxacin (500 mg q.d. for 10 days) was started, leading to clinical (resolution of fever) and microbiological (sterilization of blood culture) improvement by 48-72 hours. Of course, the tip of the removed catheter was sent for microbiological culture and, unexpectedly, there was no bacterial growth. After the

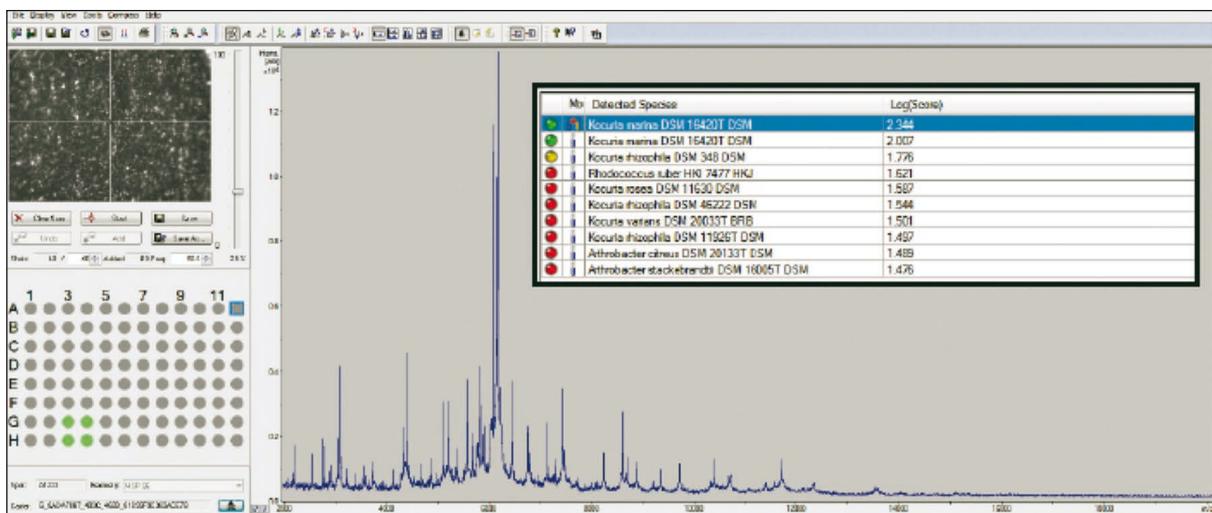


Figure 1 - Output of MALDI-TOF MS analysis of blood culture isolate confirming its identification as *K. marina*.

complete resolution of the febrile episode and the asthmatic condition, the patient was moved to a suitable clinic to take care of her comorbidities and nutritional issues.

## ■ DISCUSSION

As for our knowledge, only two cases of catheter-related sepsis caused by the species *Kocuria marina* have been described to date. In 2014, Mi-Na L et al. reported a case of central venous catheter-related *K. marina* bloodstream infection in a patient affected with multiple myeloma [5]. Later, in 2015, Horiuki A et al. described a pediatric patient with a history of inguinal hernia and complex congenital cardiac disease, treated with intra-cardiac reparative surgery. However, because of the development of pulmonary arterial hypertension requiring continuous intravenous epoprostenol, a broviac-type central venous catheter (CVC) was placed. During the hospitalization for intermittent fever since several weeks, the authors isolated *K. marina* from blood cultures [6].

Those two cases ruled out, all CVC-related cases of bacteraemia reported in the medical literature so far have been caused by *Kocuria* species other than *spp. Marina*, mainly *K. kristinae* [4]. Lai CC et al. published the greatest case series of *Kocuria*-related bloodstream infections from a single hospital, which was collected in a 3 year-period. All their 5 patients were carriers of a Port A catheter, as they were affected with gastrointestinal diseases and/or cancer, and all the microbiological isolates were identified as being *K. kristinae*. Actually, only 4 of them received antibiotic therapy, because of bacteraemia or infective endocarditis, as one isolate resulted to be a contamination only. Interestingly, all patients, excluding the case of contamination, had received TPN [1, 3, 7].

Recently, Purty S et al. reported a case of peritonitis caused by *K. rosea* in a patient with diabetic nephropathy treated by peritoneal dialysis and they reviewed all reported cases of significant *Kocuria* infections. Based upon this study, most infections were confirmed to be due to the species *K. kristinae* and 11 cases out of the total (n=20) were bloodstream infections. The remaining cases recognized other *Kocuria* species as etiologic agents: *K. varians* (n=3), *K. rosea* (n=2), *K. rhizo-*

*phila* (n=2), *K. marina* (n=2). In addition to bacteraemic infections, also localized diseases, involving peritoneum (n=6), kidney (n=1), gallbladder (n=1) and brain (n=1), were described. All cases of *Kocuria*-related peritonitis occurred in patients undergoing continuous ambulatory peritoneal dialysis (CAPD) and two of these were caused by *K. marina*.<sup>4</sup> Both cases were reported by Lee JY et al. in 2009: they were old men (57- and 73 year-old, respectively) with end-stage kidney disease and were investigated because of the recovering of turbid dialysis effluent [8]. Recently, another case of peritonitis caused by *K. marina* in a child with no risk factors was described in 2014 by Brandle G. et al.: indeed, this 2 year-old infant had no history of previous invasive procedure and showed no immunodeficiency; interestingly, the episodes of vomiting appeared shortly after his return from a holiday in Crete, where he ate seafood every day [9].

As regards *Kocuria* bloodstream infections specifically, almost all cases were associated with the presence of a factor compromising the skin barrier, namely CVC, and/or the immunological status, such as cancer diseases. CVC was present also in both aforementioned cases of bacteraemia sustained by *K. marina*, as it was in our clinical description [5, 6]. However, the culture of the catheter tip removed from our patient resulted negative for any bacterial growth, despite the isolates of *K. marina* obtained from blood cultures, both from peripheral venous puncture and from midline blood sample. The mild to moderate and intermittent febrile illness (being similar to other reported cases of CVC-related *Kocuria* infection), the laboratory panel characterized with CRP increase and leukopenia, and the positivity of both blood cultures obtained from different venous entries clearly supported the diagnosis of bloodstream infection due to *K. marina*. Indeed, the patient recovered from fever after 48-72 hours since starting the antibiotic therapy with levofloxacin that was confirmed to be efficacious against this bacterial strain by the antibiotic sensitivity test. Moreover, considering the association of *Kocuria spp.* bacteraemia to the presence of a permanent venous access, the midline catheter was removed, but surprisingly the microbiological culture from the tip resulted to be negative for any bacterial growth. This finding significantly seemed to reduce the probability that the starting point of the

ascertained *K. marina* bloodstream infection was the midline catheter used to provide TPN, in our clinical case. Thus, alternative modes of entry into the bloodstream could be plausible in our patient, as she was affected with severe leg ulcers being difficult to be managed, also considering her co-morbidity and malnutrition. Indeed, *K. marina* is known to colonize the skin and, thus, bacterial entry from skin ulcers can be likely. This hypothesis could be supported by a previous case of *K. kristinae* endocarditis associated with diabetic foot infection a 74 year-old man who did not carry a CVC [10].

However, the real prevalence of infections sustained by *Kocuria* species, including *K. marina*, might be under-estimated, as these bacteria have been demonstrated to be misdiagnosed as coagulase-negative *Staphylococci*, if only conventional phenotypic microbiological assays are used to achieve the bacterial identification. In these cases, the introduction of Matrix-assisted Laser Desorption/Ionization Time of Flight (MALDI-TOF) Mass Spectrometric Analysis (MALDI-TOF MS analysis) can lead to the certain identification of bacteria or fungi, as obtained mass spectra can be analyzed by dedicated software and compared with stored microbiological profiles [4, 11].

In conclusion, we are very likely to report the first case of bloodstream infection caused by the species *K. marina* being unrelated to the presence of a permanent venous catheter; actually, the infection could have started from an alternative skin breakage, represented by extensive and severe venous leg ulcers.

**Conflict of interest.** The authors have no conflicts of interest to disclose.

The authors are responsible for the content and writing of this article.

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