Emerging Bacterial Infection: Identification and Clinical Significance of Kocuria Species

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Abstract

Recently there have been reports of gram-positive cocci which are morphologically similar to both Staphylococci and the Micrococos. These bacteria have been identified as Kocuria species with the help of automated identification system and other molecular methods including 16S rRNA (ribosomal ribonucleic acid) evaluation. Kocuria belongs to the family Micrococcaceae which also includes Staphylococcus species and Micrococos species. Isolation and clinical significance of these bacteria from human specimens warrant great caution as it does not necessarily confirm infection due to their ubiquitous presence, and as a normal flora of skin and mucous membranes in human and animals. Most clinical microbiology laboratories ignore such bacteria as laboratory and specimen contaminants. With increasing reports of infections associated with these bacteria, it is now important for clinical microbiologists to identify and enumerate the virulence and antibiotic susceptibility patterns of such bacteria and assist clinicians in improving the patient care and management. We review the occurrence and clinical significance of Kocuria species.

Introduction And Background

Actinobacteria are a unique and large group of bacterial species containing five classes, nineteen orders, 50 families and around 220 genera as revealed by the 16S rRNA studies. They have a rigid cell wall and appear Gram-positive or Gram-variable in Gram’s staining. These bacteria are aerobic/facultatively anaerobic and grow better at neutral pH. Many species of Actinobacteria are saprophytic and are present in the environment growing under varied conditions as acidophiles, alkaliphiles, halophiles, and thermophiles. Several other actinobacterial species infect plants and animals. Morphologically Actinobacteria show different shapes ranging from cocci, coccobacilli, bacilli, and long filamentous bacteria.

Kocuria is a Gram-positive cocci arranged in pairs, short chains, tetrads, cubical packets of eight and irregular clusters. Kocuria belongs to the phylum Actinobacteria, class Actinomycetales, order Actinomycetales, sub order Micrococinae and family Micrococcaceae. This bacterium was first identified and described by Miroslav Kosur, a Slovakian microbiologist. Currently, there are more than 18 species of Kocuria identified based on the 16S rRNA phylogenetic studies. The species of Kocuria identified thus far include Kocuria assamensis, Kocuria aegyptia, Kocuria gwangalliensis, Kocuria atrinae, Kocuria carniphila, Kocuria flava, Kocuria palustris, Kocuria halotolerans, Kocuria himalakensis, Kocuria koreensis, Kocuria kristinae, Kocuria marina, Kocuria polysars, Kocuria rhiophila, Kocuria rosea, Kocuria salicina, Kocuria sediminis, Kocuria turfanensis, and Kocuria varians. Kocuria species (Kocuria spp) inhabit the normal skin and mucous membrane of human and animals [1]. Kocuria was also isolated from various environmental and ecological niches [2]. These are usually considered as non-pathogenic bacteria which are rarely associated with human infections. Recently there has been a rise in the incidence of infections caused by Kocuria spp causing both superficial infections and deep-seat/invasive infections. The cause of concern is that this bacterium appears to have a broad host range involving both immunocompromised as well as immunocompetent individuals. This review attempts to update the morphology, cultural characteristics, pathophysiological properties, and laboratory diagnosis of Kocuria spp.

Review

Cultural characteristics of Kocuria

Kocuria spp do not produce hemolysis on blood agar, unlike most clinical isolates of Staphylococci. They usually form 2-3 mm whitish, small, round, raised, convex colonies on initial isolation and might develop non-diffusible yellowish pigmentation after prolonged incubation, as shown in Figure 1.
These bacteria appear large and show both tetrads (Micrococci) and irregular clusters. An interesting observation in Gram’s stained smear includes the presence of darkly stained and abnormally large clones of cocci, which are not observed in the case of Staphylococci and Micrococci as shown in Figure 2.

Biochemically these bacteria show great variability by reacting differently towards conventional laboratory identification tests including the catalase, urease, and citrate utilization test. These bacteria are normally negative for mannitol fermentation and coagulase enzyme (both bound and free coagulase).

Susceptibility towards bacitracin and lysozyme and resistance to nitrofurantoin, furazolidone and lysostaphin can be used to separate this bacterium from Staphylococci. Modified oxidase test results differentiate between Kocuria spp (negative) and Micrococci.

Clinical profile of Kocuria spp

Kocuria spp have been reported to be normal flora of human skin and oral cavity and are usually regarded as laboratory contaminants and ignored when isolated in the clinical specimens undermining its pathogenic potential.
potential. Kocuria was first identified as a causative agent of urinary tract infection way back in 1974, and it was named as Micrococcus kristinae [3]. Reports of infection with Kocuria species have gained prominence in the late twentieth century and are showing an increased trend, signifying its pathogenic potential. Infections associated with isolation of Kocuria include urinary tract infections, cholecystitis, catheter-associated bacteremia, dacyrocystitis, canaliculitis, keratitis, native valve endocarditis, peritonitis, descending necrotizing mediastinitis, brain abscess and meningitis [4–15]. The predisposing factors associated with infections related to Kocuria spp include congenital deformities (short bowel syndrome), chronic catheterization (in cases of total parenteral nutrition), malignancies (ovarian cancer, gastric cancer, myelodysplastic syndrome, acute myelogenous leukemia, non-Hodgkin’s disease) and patients with end-stage renal disease undergoing continuous ambulatory peritoneal dialysis. Other underlying conditions associated with Kocuria infection include diabetes mellitus, tuberculosis, stem cell transplant patients, patients suffering from galstones, methylnalonic aciduria and pancreatic pseudocyst [16–21].

Laboratory identification of Kocuria spp

This bacterium is normally misidentified in the clinical microbiology laboratories as coagulate-negative Staphylococci (CoNS) based on its gram reaction, catalase positive and coagulate negative properties. Other physiological and biochemical properties of Kocuria are the formations of non-hemolytic colonies on blood agar, non-capsulated, non-saprophyte forming, non-motive, non-acid fast and positive for Voges-Proskauer test (VP). It has also been observed that various species of Kocuria react differently to routine biochemical tests like the oxidase, amylase, urease, citrate utilization test, gelatinase, phosphatase tests, utilization of insulin, arabinose, N-acetyl-L-glutamic acid, and nitrate reduction tests [22]. This could be attributed to the reason behind the inaccurate identification by both conventional and an automated bacterial identification systems.

The major drawback faced by many laboratories in accurately identifying this bacterium is the need for advanced techniques like 16S rRNA and Matrix-Assisted Laser Desorption/Ionization Time-Of-Flight Mass Spectrometry (MALDI-TOF–MS). Although many clinical microbiology laboratories are now equipped with automated identification systems that include VITEK (BioM’rieux Inc., Durham, NC, USA), VITEK 2 (BioM ‘rieux Inc., Durham, NC, USA), API (BioM’rieux Inc., Durham, NC, USA) and the BD Phoenix™ Automated Microbiology System (BD Diagnostic Systems, Sparks, MD) identification systems, there are studies that have noted false identification of CoNS as Kocuria spp and its limitations to identify all the species of Kocuria [23]. Previous research has highlighted that in the case of non-availability of molecular and advanced laboratory methods, Kocuria can still be identified and differentiated from Staphylococci and Micrococcus using morphological, cultural characteristics and differential antibiotic discs. Kocuria spp are sensitive to bacitracin, lysozyme and resistant to nitrofurantoin, furazolidone and lysostaphin [18, 24].

Antimicrobial susceptibility profile of Kocuria spp

Currently, there are only a few studies that have evaluated the susceptibility profile of Kocuria spp. Antimicrobial susceptibility testing results of random case reports are available, although they are still insufficient to establish the exact susceptibility results of Kocuria [25]. Kocuria spp isolated from a case of peritonitis in a 57-year-old patient suffering from end-stage renal disease revealed sensitivity to ampicillin, cloxacillin, cefotaxime, ciprofloxacin, ofloxacin, levofloxacin, gentamicin, erythromycin, clindamycin, tetracycline, azamin, linosolid, troleandomycin, vancomycin, imipenem, quinupristin, dalofpristin, rifampicin and was found to be moderately sensitive to cefazidime [11]. Becker et al. have reported that the Kocuria rhizophila isolated in blood from a case of sepsis in pediatric age patient revealed resistance only to norfloxacin [21]. Studies by Lee et al., who reported multiple cases involving both extreme age groups noted that Kocuria marina isolated from peritoneal fluid was resistant only to tetracycline. Other observations by the same authors showed that K. kristinae isolated from bacteremia cases revealed resistance to oxacillin, cefazolin and intermediate sensitive to cefotaxime [11]. Resistance to ciprofloxacin and erythromycin was observed in K. rhizophila isolated from blood of a 3-year-old catheterized patient as reported by Moissenet et al. [26]. K varians isolated in peritoneal fluid resistant only to levofloxacin was reported by Meletis et al in a patient undergoing continuous ambulatory peritoneal dialysis (CAPD) [27].

Recent advances

A recent research report has highlighted the significance of Kocuria in causing hospital-acquired infections [13]. The same study has also noted that although Kocuria spp are commensals of humans, animals and are present in the environment, they should be considered as potential pathogens in patients who are immunocompromised, undergoing critical care treatment and neonates. A study which included 12 pediatric age patients suffering from underlying debilitating conditions like premature birth and cancer had noted that more than 50% of patients suffered from invasive infections with Kocuria spp [28]. Reports of infections caused by Kocuria spp among previously healthy and immunocompetent individuals are showing an increased trend. Kocuria rosea was isolated from a case of descending necrotizing mediastinitis in a 58-year-old woman who was taking medications for gout and hypertension [13]. Another very recent report has observed endocarditis caused by Kocuria rosea in a 10-year-old female patient. Although the patient was healthy before suffering from the infection, a history of surgery to correct congenital heart disease was present [9]. Evaluation of biofilm production by Kocuria spp isolated from a case of peritonitis showed that the strain was negative for biofilm production [18]. Isolation of K. marina showing tolerance to severe alkaline conditions in a 7-year-old patient receiving epoprostenol therapy should be considered as an
Conclusions

Identification of *Kocuria* spp remains elusive because most clinical microbiology laboratories have limited or no access to advanced molecular techniques. Laboratory identification of *Kocuria* spp can be made conventionally only after high laboratory suspicion. Properties such as morphological variability between these bacteria and other similar gram-positive cocci, as well as biochemical properties including the antimicrobial susceptibility patterns against selective antibiotics could be used to presumptively identify *Kocuria* spp. Infections of *Kocuria* spp normally involve patients with various debilitated conditions. In the era of drug resistance, and prevalence of multi-drug resistant bacteria, occurrence of *Kocuria* spp in hospitalized patients should not always be ignored as contaminants. Further studies emphasizing the determination of the virulence, pathogenic potential, predisposing factors and antimicrobial susceptibility patterns of *Kocuria* spp are warranted.

Additional Information

Disclosures

Conflicts of interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following: Payment/services info: All authors have declared that no financial support was received from any organization for the submitted work. Financial relationships: All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. Other relationships: All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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