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**Case Series** **Open Access**

# Bloodstream infection caused by *Kocuria* species in a tertiary hospital in Lagos, Nigeria: A case series

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## Abstract

*Kocuria* species are emerging opportunistic pathogens commonly misidentified as coagulase-negative staphylococcus. Improvement in laboratory diagnostic techniques and the expansion in the number of patients with immunocompromised diseases has led to the rising number of *Kocuria* infections being reported. We report cases of *Kocuria* bacteraemia in three immunocompromised patients. The first case was an 11-year-old with metastatic nasopharyngeal carcinoma and *Kocuria kristinae* isolated from the second blood culture, but due to discharge of the patient against medical advice, the role of *K. kristinae* and outcome of the case could not be ascertained. The second case was a 30-year-old with acute lymphoblastic leukaemia, with fever and diarrhoea, and *Kocuria* species isolated from the second blood culture, but despite treatment with antibiotic with *invitro* activity against the organism, the outcome was fatal. The third case was a very low birth weight premature male neonate who was delivered by emergency cesarean at 31 weeks gestation, due to maternal chronic hypertension and superimposed preeclampsia. Although, *Kocuria rosea* was isolated from the third blood culture of the case, it was most likely a colonizer, as the clinical condition of the patient had improved before isolating the organism. This report may be the first case of bacteraemia caused by *Kocuria* from Nigeria, indicating that this organism should not ignored as a possible cause of bacteraemia because advancement in laboratory diagnostics will aid correct identification.

**Keywords:** *Kocuria* species; bloodstream infection; opportunistic pathogen; immunocompromised

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# Infection sanguine à *Kocuria* spp dans un hôpital universitaire de Lagos, au Nigéria: une série de cas

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## Résumé:

Les espèces de *Kocuria* sont des pathogènes opportunistes émergents souvent confondus avec des staphylocoques à coagulase négative. L'amélioration des techniques de diagnostic en laboratoire et l'augmentation du nombre de patients immunodéprimés ont entraîné une hausse des infections à *Kocuria* rapportées. Nous présentons ici trois cas de bactériémie à *Kocuria* chez des patients immunodéprimés. Le premier cas concernait un enfant de 11 ans atteint d'un carcinome nasopharyngé métastatique chez lequel *Kocuria kristinae* a été isolée lors de la seconde hémoculture. Cependant, en raison de sa sortie contre avis médical, le rôle de *K. kristinae* et l'évolution de la maladie n'ont pu être déterminés. Le deuxième cas concernait un homme de 30 ans atteint de

leucémie lymphoblastique aiguë, présentant fièvre et diarrhée. Une espèce de *Kocuria* a été isolée lors de la seconde hémoculture. Malgré un traitement antibiotique actif in vitro contre cette bactérie, l'issue a été fatale. Le troisième cas était celui d'un nouveau-né prématuré de sexe masculin, de très faible poids de naissance, né par césarienne en urgence à 31 semaines d'aménorrhée en raison d'une hypertension artérielle chronique maternelle et d'une prééclampsie surajoutée. Bien que *Kocuria rosea* ait été isolée lors de la troisième hémoculture de ce patient, il s'agissait très probablement d'une bactérie colonisatrice, l'état clinique du patient s'étant amélioré avant l'isolement de cet organisme. Ce cas pourrait être le premier cas de bactériémie à *Kocuria* rapporté au Nigéria, ce qui souligne l'importance de ne pas négliger cet organisme comme cause possible de bactériémie, les progrès des techniques de diagnostic en laboratoire facilitant son identification.

**Mots-clés:** *Kocuria* spp; infection sanguine; pathogène opportuniste; immunodéprimé

## Introduction:

*Kocuria* species are opportunistic pathogens that affect mostly the immune compromised (1). Phylogenetic and chemotaxonomic analyses have reclassified *Kocuria* species from the family Micrococcacae to the family Kocuria (2). They are normal flora of skin and mucus membrane, strict aerobes except for *Kocuria kristinae,* that is a facultative anaerobe (3). They are catalase-positive, coagulase-negative Gram-positive cocci arranged in tetrads, which often to misidentification and misinterpretation as coagulase-negative staphylococci in the clinical laboratory (3).

Five *Kocuria* species namely *K. Kristinae, K. rosea, K. varians, K. marinia*, and *K. rhizophila* (*4*) are reported to cause a wide range of infections in the immunocompromised and immunocompetent host (3) worldwide and have been described to cause bacteraemia, septicaemia, urosepsis (5), endocarditis (6), cholecystitis (7), peritonitis (8), and arthritis (5). However, the risk of infection increases with indwelling medical devices (central venous catheter, ventilator, urethral catheterization, total parenteral nutrition), haemodialysis or peritoneal dialysis (8), and malignancy.

Advancement in laboratory diagnostics has made possible the accurate diagnoses of infection caused by this pathogen as we reported in these case series from a tertiary hospital in Lagos, Nigeria. To the best of our knowledge, this is the first report of *Kocuria* bloodstream infections from Nigeria.

## Case Series:

### Case 1:

An 11-year-old boy with metastatic nasopharyngeal carcinoma was referred to the Lagos University Teaching Hospital (LUTH) on 3rd of June 2021, with a history of progressive swelling on the back of the head of 2 months duration, high-grade fever, and pain in the right hip of 3 weeks duration. There was associated generalized recurrent throbbing headache with blurring of vision, but no associated vomiting, cough, trauma or loss of consciousness, memory, seizure, or sphincteric control. Because his condition persisted, he was admitted to a private facility for 2 weeks, where he received analgesics to relieve pain and transfused with 2 units of blood on account of anaemia. Brain and cervical computerized tomography (CT) scans were suggestive of metastatic lesions to the scalp, occipital bone and lobe. Abdominopelvic ultrasound scan showed liver metastasis. Because the mother declined further treatment at the private facility, the patient was referred to LUTH. Two years prior to the present admission of the patient, he was diagnosed with nasopharyngeal carcinoma and had undergone chemotherapy, with a course of radiotherapy, but defaulted from the paediatric oncology clinic and taken to his hometown for an undisclosed reason.

Physical examination on admission revealed a young boy that was febrile (temperature: 38°C), mildly pale, acyanosed, anicteric, not in obvious respiratory distress, not dehydrated, and no pedal oedema. There was an occipital swelling that measured 10cm by 10cm, firm and non-tender. He was conscious, and oriented in time, place, and person, with no other craniofacial abnormalities. Systemic examinations revealed no significant findings. He was commenced empirically on intravenous (IV) ceftriaxone 500 mg daily in line with the oncology department protocol of placing immunocompromised patients with recent hospitalisation on empirical antibiotic with or without evidence of infection.

Blood culture, serology for viral markers (hepatitis B, hepatitis C, and human immunodeficiency virus) and blood film for malaria parasites, were all negative. Full blood count (FBC) showed a white cell count (WBC) of 8,260/$mm^3$ (neutrophil 78%, lymphocyte 12%), packed cell volume (PCV) 38.2%, and platelet count of 547,000/$mm^3$. Erythrocyte sedimentation rate (ESR) was elevated (85 mm/hour). Electrolyte analysis (E, U, Cr) showed hyponatraemia with metabolic acidosis ($Na^+$ 130m mol/l, $K^+$ 3.18 mmol/l, $HCO_3^-$ 17 (22-30mmol/l) that was appropriately corrected.

On day 15 of admission, a mini craniectomy was performed, and a biopsy of the sub-galeal mass and extradural tumor was taken for histology, the result of which was suggestive of metastatic adenocarcinoma a

week later. Patient then developed fever and non-productive cough two weeks after craniectomy, necessitating an increase in the dose of empirical IV ceftriaxone to 1 g 12 hourly. Despite this, fever persisted, and the antibiotic was changed to meropenem. A repeat blood culture and FBC analysis were performed with FBC result showing neutropenic leukocytosis (WBC 12,600/mm$^3$, neutrophil 11%), anaemia (PCV 28%) but normal platelet counts of 539,000/mm$^3$. The patient was optimized with blood products. The repeat blood culture incubated in Bact/Alert (BioMérieux) equipment flagged positive on day 3 of incubation, with Gram smear showing Gram-positive cocci that was identified by Vitek 2 version 8.0 as *Kocuria kristinae*, sensitive to linezolid, erythromycin, clindamycin, minocycline, levofloxacin, ciprofloxacin, and sulfamethoxazole.

Fever subsided upon commencement of meropenem and before the result of blood culture positive for *K. kristinae* was available. His craniectomy wound healing was favorable, and anti-cancer chemotherapy was commenced, for which the patient received a dose before the mother declined further chemotherapy, and requested for the patient discharge against medical advice (DAMA). Further clinical condition of the patient remained unknown to us after DAMA.

**Case 2:**

A 30-year-old woman known acute lymphoblastic leukaemia (ALL) BCR-ABL positive was admitted on 23rd March 2022 with elevated white cell counts of 458,000/mm$^3$ and associated history of blurred vision, vomiting, and difficulty in swallowing and walking of 2 days duration. There was an associated history of recurrent headaches, difficulty in urinating, and deviation of the mouth to the left. There was no fever, night sweats, neck pain, eye pain, loss of consciousness, or seizure. She was treated for COVID-19 in 2020 and diagnosed with adult-onset ALL in October 2021. She had haematological remission, and subsequently discharged home for follow-up in the outpatient clinic. However, the patient defaulted only to present with the present complaints. She was not a known hypertensive or diabetic, and does not smoke or take alcohol.

On examination at admission, she was chronically ill-looking, pale, conscious and afebrile (temperature: 36.9°C). There was bilateral ptosis, ophthalmoplegia, bilateral cranial nerve (CN) 6, right CN 7, and CN 12 palsies. There was also a deviation of the mouth to the left, however, she had no neck stiffness, and the muscle tones were normotonic globally. Abdominal examination showed that liver was about 10 cm below the right coastal margin, non-tender, with a smooth surface, while the chest and cardiovascular examinations were essentially normal. A diagnosis of relapsed adult ALL with possible metastatic lesions to the CNS was made. Exchange blood transfusion (EBT) and pre-induction chemotherapy with oral prednisolone (60 mg daily) and intravenous vincristine (2 mg) were administered, in addition to prophylactic antibacterial (trimethoprim-sulfamethoxazole 960 mg daily), antivirals (acyclovir 400 mg and itraconazole 200 mg daily) and antimalarial (proguanil/ paludrine 100 mg daily).

Baseline investigations consisting of FBC showed anaemia (PCV 28%), leucocytosis (WBC 309,013/mm$^3$ and absolute neutrophil count 13,850/mm$^{3)}$), and thrombocytopaenia (platelets 52,000/mm$^3$). Electrolytes were deranged ($Na^+$ 147 mmol/l, $K^+$ 2.47 mmol/ l, $Cl^-$ 109 mmol/l, bicarbonate 28 mmol/l, blood urea nitrogen 7.5 mmol/l, creatinine 55 µmol/ l) and hypokalaemia was appropriately corrected. The clotting profile was normal (prothrombin time PT 11.6 seconds, PT control 12.5 seconds, INR 1.00, partial thromboplastin time in kaolin (PTTK) 29.6 seconds, PTTK control 27.6 seconds) and optimization with 2 units of packed cells and 3 units of platelet concentrates were done. On day 3, brain MRI revealed no intracranial extensions, and induction chemotherapy with hypercvad-methcytarabine was commenced.

There was a gradual clinical improvement until patient complained of a productive cough with non-radiating chest pain, sore throat, orthopnoea and diarrhoea on day 13. On chest auscultation, bi-basal crepitations were heard. Consequently, urine and blood cultures, urinalysis, and FBC investigations were ordered. The results of FBC showed pancytopaenia (Hb 9.8 g/dl, PCV 27%, WBC 0.1 x $10^9$/L with ANC of 0.06, and platelets 31,000/ mm$^3$), but urine culture and urinalysis results were negative. Blood culture incubated in Bact/Alert machine grew *Enterobacter cloacae* sensitive to ciprofloxacin, ertapenem, imipenem, levofloxacin, cefoxitin, cefepime, but resistant to meropenem, amikacin, gentamicin, trimethoprim-sulfamethoxazole, and tobramycin, necessitating antibiotic change from trimethoprim-sulfamethoxazole to levofloxacin 500 mg daily, with optimization of her blood level. By day 22, patient was able to swallow food and saliva, ambulating slowly, and fever had subsided. However, by day 29, patient developed fever associated with diarrhoea, and fluconazole (200 mg), vancomycin (500 mg), metronidazole (500 mg 8 hourly), and subcutaneous filgrastim (neupogen) 300 µg daily were added to the treatment.

The patient's condition however continued to deteriorate, and a repeat blood culture in BACTEC equipment, which flagged po-

sitive after 48 hours of incubation showed Gram-positive cocci on direct Gram stain, and was identified as *Kocuria* species using Vitek 2 version 8.0 system, sensitive to linezolid, clindamycin, ciprofloxacin, levofloxacin, and moxi floxacin. Despite continuous treatment with levofloxacin, patient had cardiopulmonary arrest, and after unsuccessful active resuscitation, was certified dead by 2.10 a.m. on May 2022 (day 41 of admission).

**Case 3:**

This case was a preterm very low birth weight male neonate delivered on 15th March 2022 via an emergency cesarean section at 31 weeks gestation on the indication of superimposed preeclampsia secondary to chronic hypertension. Examinations revealed a conscious neonate with a birth weight of 1260g, occipitofrontal circumference of 28.4cm and length of 39cm, in obvious respiratory distress evidenced by respiratory rate of 50 cycles per minute. Other examinations were essentially normal. He was commenced on continuous positive airway pressure (CPAP) at 3L oxygen flow from the theatre with $SPO_2$ of 98% and was admitted directly to the neonatal intensive care unit (NICU) on account of prematurity.

Baseline laboratory investigations at NICU consisting of FBC, ESR, serum bilirubin, and random plasma glucose (RPG) were essentially within reference intervals except for the low random plasma glucose (32.4 mg/dl) that was corrected. In addition, a blood culture sample was collected and incubated in Bact/Alert (BioMérieux) equipment in the Medical Microbiology laboratory before commencing empirical antimicrobials which included cefotaxime 50 mg/kg and fluconazole 5 mg/kg stat, then 3 mg/kg every 72 hours.

He was also placed on therapeutic phototherapy at 21 hours of age and became warm to touch (temperature: 36.3-37.7°C), cyanosed, icteric, dyspneic with subcoastal resection (RR-64cpm) at 48 hours of age. The abdomen also becomes scaphoid with bronchovesicular sound and crepitations on chest auscultation. Amikacin 5 mg/kg/day was added to the treatment and CPAP was increased to 8L oxygen flow/minute. Serum bilirubin was elevated (total bilirubin was 100.2 µmol/l, conjugated bilirubin 13.7 µmol/l, unconjugated bilirubin 86.50 µmol/l). Electrolytes result suggested metabolic acidosis with hyponatremia ($Na^+$ 131 mmol/l (135-145 mmol/l), $K^+$ 5.19 mmol/l (3.5-5.1 mmol/l), $Cl^-$ 98 mmol/l (98-110 mmol/l), $HCO_3^-$ 17 (22-30mmol/l)), which was appropriately corrected.

At 96 hours of age, the patient condition began to deteriorate with development of generalised sclerema, with FBC result showing thrombocytopaenia (which was optimized) and serum procalcitonin of 7.77 ng/dl. Blood culture result showed no bacteria growth on day 5. Despite changing the empirical antibiotics from cefotaxime to levofloxacin, the patient developed abdominal distension on day 9, with periumbilical erythema and scrotal oedema, prompting insertion of a nasogastric tube for abdominal decompression. A second blood culture sample was collected. Babygram showed dilated bowel loops with no intraluminal and extraluminal gas, suggestive of necrotizing enterocolitis. The electrolytes were essentially within the reference interval.

On 13th day of life, the second blood culture grew extended-spectrum β-lactamase (ESBL) producing *Klebsiella pneumoniae* sensitive to amikacin, ertapenem, imipenem, and levofloxacin with intermediate sensitivity to cefotaxime and meropenem. Transfontanelle ultrasound scan (USS) and Chest x-ray findings were normal. Levofloxacin was discontinued, and tigecycline commenced on day 15 of life. The fever and abdominal distension however persisted, and by day 23, the patient developed respiratory distress (RR: 48 cycle per minute) and right upper limb swelling. There was laboratory evidence of hypokalemia ($K^+$ 3.13 mmol/l), anaemia with thrombocytopaenia (PCV 25.8%, WBC 8000/$mm^3$, ANC 1,920/$mm^3$, and platelets 6,000/$mm^3$), which were appropriately corrected.

A third blood culture collected on day 25 flagged positive and Gram stain of the culture showed Gram-positive cocci that was identified by Vitek 2 version 8.0 as *Kocuria rosea*, sensitive to clindamycin, moxifloxacin, gentamicin, erythromycin, and ciprofloxacin. By the time of isolation of *K. rosea* from the blood, the clinical condition of the patient had improved significantly and was continued on tigecycline until day 43, with serum procalcitonin level dropping to <0.5 ng/ml. Patient was discharged home alive on day 46 of life.

## Discussion:

*Kocuria* species are now regarded as potential true pathogen because infections caused by them in transplant recipients, premature infants, patients with malignancy, diabetes mellitus, sickle cell and chronic renal diseases, pregnant women, and immunocompetent hosts, have been well-documented in the literature (1,7,9,10,11). Interestingly, the changes in climatic conditions and lifestyles have altered the evolution of microorganisms in a way that new pathogens are emerging (12).

Our case series were diagnosed clinically as sepsis and microbiologically confirmed as bacteraemia from blood culture specimens. Identifications were carried out with Vitek 2

automated system, thus avoiding issues of misidentification. Although the three cases had different clinical presentations and differing co-morbid conditions, fever unresponsive to empirical antibiotics was common to all. Cases 1 and 2 were patients with background malignancies who received cancer chemotherapy on admission, while case 3 was a premature, very low birth weight neonate who had the propensity to develop sepsis because of the immature immune cells (3,18). Isolating *Kocuria* species from the blood cultures of these patients was not surprising as invasive devices used, broad-spectrum antibiotics administered and potential immunosuppression in the neonate were predisposing risks for *Kocuria* infections. *Kocuria* species are normal flora of the skin and mucous membrane, and may have gained entry into the bloodstream during the insertion of the invasive devices.

All the three cases were on admission for more than 72 hours before *Kocuria* species were isolated. Also, the first blood culture was negative for cases 1 and 3, while *Enterobacter cloacae* was isolated in the first blood culture in case 2. This case 2 did not respond to the various antibiotics administered, which warranted a repeat blood culture that grew *Kocuria* species. This *Kocuria* may be a true pathogen contributing to the patient's clinical illness, but despite the use of antibiotic (levofloxacin) that showed good *invitro* activity against the organism, the clinical outcome was poor. However, *K. rosea* isolated in case 3 may be a coloniser that contaminated the sample during collection while the role of *K. kristinae* in case 1 remains uncertain because the patient voluntarily discharged self against medical advice and failed to return for further follow-up.

Recently, there have been growing reports of infections caused by *Kocuria* species in the literature, with some patients recovering with antibiotic treatment or the removal of the invasive devices. In Italy, a woman with ovarian cancer recovered from recurrent *K. Kristinae* catheter-associated bacteraemia when the central line was removed (4). Similarly, two paediatric patients with *K. kristinae* and *K. varians* were reported by Bhavar et al., (15), one was a 3-year-old child on chemotherapy following nephrectomy for bilateral Wilms tumour and the second was a 7-month-old child with shotgun syndrome on total parenteral nutrition, both recovered with combination of anti biotic treatment and invasive catheter removal.

*Kocuria kristinae* is a potential pathogen (13) and other rare *Kocuria* species cause infection in immunocompromised patients (14). Several cases of *K. kristinae* infections have been reported from various countries in diverse patient populations and clinical conditions (3,16,17). Siravaman et al., (18) reported a case of umbilical sepsis due to *K. kristinae* is a term male neonate. In another report from Greece, *K. rosea* peritonitis was reported in an 8-year-old girl with dysplastic kidney on peritoneal dialysis (19). The second case of *K. rosea* in paediatric was reported from Brazil in a 10-year-old with endocarditis post-surgery for congenital heart disease (20). Also, endocarditis and bacteremia due to *K. rosea* in a 10-year-old boy following heart valve replacement for ventricular septal defect and mitral valve incompetence have been reported (21). A prospective study in Iraq reported 7 *Kocuria* bacteraemia from 261 positive cultures, 5 of these patients had *K. kristinae* infection while the remaining 2 patients had *K. rosea* and *K rhizophilia* infections respectively (22). However, in case 3 of our report, *K. rosea* was recovered from the blood culture, but may have been a colonizer because the patient's condition had improved before it was isolated from the third blood culture, rather the ESBL-producing *K. pneumoniae* isolated from the second blood culture was likely the pathogen responsible for sepsis in this patient, and which was responsive to empirical tigecycline administered.

All the patients in this case series were exposed to various antibiotics. The use of antibiotics promotes resistance development, leading to treatment failure. Despite the patients' prior antibiotic exposure, all *Kocuria* species isolated in our cases were sensitive to fluoroquinolones, lincosamides, and macrolides. This agrees with what has been reported in the literature, in which *Kocuria* species are sensitive to a broad spectrum of antibiotics (17,18), but contrast the case described by Siravaman, in which the isolated *Kocuria* was resistant to multiple antibiotics (18).

## Conclusion:

Uncommon pathogens such as *Kocuria* species that rarely cause human infection are emerging and increasingly recognized worldwide because of the introduction of better identification techniques. Therefore, their isolation in the laboratory should not be considered as laboratory contaminants in all cases but must be correlated with clinical findings to guide proper treatment of bloodstream infections and good clinical outcomes.

## Contributions of authors:

OCS conceptualized the study, participated in the literature review and writing of the manuscript; DAI was involved in reviewing

the literature and writing the manuscript; ROO participated in the literature review and performed a critical review of the manuscript. All the authors reviewed and accepted the final version of the manuscript submitted for publication.

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## Conflicts of interest:

Authors declare no conflict of interest.

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