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Kocuria Kristinae-The Emerging Pathogen

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Case report

A 52 year old female with history of Type II diabetes mellitus,Systemic hypertension on oral medications,developed gradually progressive defective vision (loss of peripheral vision) on both eyes (left>right) since 2 years.When it affected her daily chores,she finally sought medical help.She was diagnosed with Bitemporal Hemianopia.CT brain revealed a well-defined hyperdense lesion (28*29*29 mm) in sellar and suprasellar region abutting and displacing optic chiasma posteroinferiorly and extending upto internal carotid artery ,likely to be a Pituitary macroadenoma.

She was admitted under neurosurgery and was takenup for Endoscopic Transnasal Transsphenoidal excision of Pituitary macroadenoma under neuronavigation; Extraventricular drain (EVD) was inserted.Patient was on Inj.Ceftriaxone and Inj.Augmentin.Postoperative period were uneventful until day 6 when patient developed mild fever spikes.Total WBC count was 13,70.EVD was removed after collecting CSF for further investigation.The CSF collected and the EVD tip were sent to our lab for Culture and sensitivity;CSF was also sent for biochemical analysis.Antibiotics was changed to Inj.Cefoperazone -sulbactam.

CSF received was Turbid,gram stain showed 0-1 pus cells along with gram positive cocci /OIF .CSF biochemical analysis : elevated protein,sugar:152,cells:30,occasional lymphocytes.clinician was informed about the same and was adviced to provide gram positive coverage too.The sample was inoculated onto blood agar,chocolate agar,macconkey agar,glucose broth,Anaerobic blood agar,direct ST was also putup (on blood agar) .After 24 hours of incubation,blood agar and chocolate agar had heavy growth of minute white opaque non-lytic colonies,small lactose fermenting colonies on MacConkey agar,glucose broth was turbid.EVD tip also grew same type of colonies.Gram stain from the colony confirmed gram positive cocci.It was catalase positive,slide coagulase

negative.The organism was identified as Kocuria kristinae using VITEK2 System sensitive to Gentamicin,Vancomycin and Linezolid;resistant to nitrofurantoin and furazolidone .Clinical correlation was adviced considering chances of EVD contaminantion.

Patient clinically improved on starting Inj. Vancomycin.A repeat CSF sample from new EVD inserted was sent for culture as the patient developed altered sensorium diagnosed to be due to increased hydrocephalus and Intraparenchymal hemorrhage.Scanty growth of the same organism was obtained with same antibiotic sensitivity pattern.Patient clinically improved from features of bacterial meningitis with Inj.Vancomycin and was discharged.

Introduction

Bacteriae of the *Kocuria* genus are microorganisms that belong to *Actinobacteria* class, *Actinomycetes* order, *Micrococcaceae* family. *Kocuria* was described for the first time in 1974 by the Slovak microbiologist Miroslav Kocur as gram-positive aerobic and facultatively anaerobic cocci, which grow on sheep

blood agar cultures. There are 18 species of *Kocuria*, most of them considered commensal bacteria, and only some are potential pathogens *(K. kristinae, K. varians, K. rhizophila, K. rosea,* and *K. marina)*. In humans, *Kocuria* can be found on the skin and oral cavity and is usually nonpathogenic. In immunocompromised patients, it can become pathogenic, causing cholecystitis, peritonitis, catheter-associated bacteremia, dacryocystitis, endocarditis, or meningitis [1]

Recently there have been reports of gram-positive cocci which are morphologically similar to both *Staphylococci* and the *Micrococci*. 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 *Micrococcus* 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. [2]

Cultural characteristics

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.

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* .

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.

Laboratory identification

This bacterium is normally misidentified in the clinical microbiology laboratories as coagulase-negative Staphylococci (CoNS) based on its gram reaction, catalase positive and coagulase negative properties. Other physiological and biochemical properties of Kocuria are the formations of non-hemolytic colonies on blood agar, non-capsulated, non-spore forming, non-motile, 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 inulin, 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 (BioMe´rieux Inc., Durham, NC, USA), VITEK 2 (BioMe´rieux Inc., Durham, NC, USA), API (BioMe´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 . 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 Micrococci using

morphological, cultural characteristics and differential antibiotic discs. Kocuria spp are sensitive to bacitracin, lysozyme and resistant to nitrofurantoin, furazolidone and lysostaphin .

Antimicrobial susceptibility profile

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 . 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, amikacin, linezolid, teicoplanin, vancomycin, imipenem, quinupristin, dalfopristin, rifampicin and was found to be moderately sensitive to ceftazidime. 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 . 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 intermediately sensitive to cefotaxime . 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 . 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) .

Recent advances

A recent research report has highlighted the significance of Kocuria in causing hospital-acquired infections . 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 . 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 . 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. Evaluation of biofilm production by Kocuria spp isolated from a case of peritonitis showed that the strain was negative for biofilm production .[2]

Treatment and Outcomes of Kocuria spp. Infections in General

The most commonly used antimicrobials for the treatment of Kocuria spp. infections were vancomycin in 47%, cephalosporins in 39.6%, quinolones in 36.6%, linezolid in 17%, aminoglycosides in 14%, penicillin in 7.9%, aminopenicillin in 6.9%, clindamycin in 5.9%, carbapenems in 5%, and daptomycin in 2%. Surgery was performed along with antimicrobials in 36.6%. Overall mortality was 5.9%, and mortality that was attributed directly to the infection was 4.9%.[3]

Conclusion

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.[2]

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