DOI: 10.7860/JCDR/2025/79202.22132

Case Series

Microbiology Section

Emerging and Unusual Gram-positive Coccal Infections: A Case Series

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ABSTRACT

Gram-Positive Cocci (GPC), like coagulase-negative staphylococci and a few beta-haemolytic streptococci, are usually found as a part of the normal flora of the human body. Opportunistic infections, caused by these cocci, are increasingly being reported. Worldwide, there are a few reports of infections caused by these commensal GPC in immunocompetent patients, too. *Kocuria kristinae* is a coagulase-negative coccus. *K. kristinae* has been isolated in paired blood culture of a 54-year-old patient on haemodialysis, who presented with fever. His Echocardiography (ECHO) revealed endocarditis with vegetations on the mitral and pulmonary valves. *Staphylococcus warneri* is also a coagulase-negative Staphylococcus. *S. warneri* was reported as a pathogen in paired blood culture of a three-year-old kid with fever who was being investigated for pyrexia of unknown origin. *Gemella sanguinis* and *Globicatella sanguinis* are beta-haemolytic streptococci. *G. sanguinis* was isolated from a 46-year-old man with recurrent sebaceous cyst on the left lumbar region and *G. sanguinis* from the sputum of a 54-year-old lady with fever and cough with expectoration. All four isolates are commensals of the human body. In this case series, they have been reported as pathogens due to standard techniques of sample collection and processing, growth of no other pathogen in the culture and clinical evidence.

Keywords: Clinical correlation, Normal flora, Vitek 2 compact

INTRODUCTION

Normal microflora is a group of various microorganisms that reside in the bodies of all humans or animals. These organisms consistently exist and are relatively stable, with specific genera populating various body regions during periods in an individual's life, from shortly after birth until death. The indigenous normal microbiota provides a first line of defence against microbial pathogens, assists in digestion, and contributes to maturation of the immune system and in general is able to assist the anatomy, physiology, susceptibility to pathogens, and even morbidity of the host [1].

Coagulase-negative Staphylococci (CoNS) are opportunistic pathogens that can cause a range of infections, including bloodstream infections, endocarditis, and infections associated with medical devices. CoNS are among the most frequently isolated bacteria in the clinical microbiology laboratory. To distinguish clinically significant CoNS from contaminant strains is one of the major challenges of daily diagnostic work [2]. *Kocuria kristinae*, formerly referred to as *Micrococcus kristinae*, is an aerobic gram-positive bacterium believed to be pan-sensitive to most antimicrobials. It is part of the normal flora of human skin and mucosa and is not a common cause of infection. Although the disease caused by this organism is extremely uncommon, recent data have shown that it is on the rise, even in relatively healthy individuals, and poses a major public health problem. Occasionally, it is reported as a pathogen in blood, urine, sputum and drainage fluids. Its presence is often misinterpreted in microbiological laboratories as CoNS. However, most laboratories are equipped with molecular and advanced laboratory techniques that aid in accurate identification, which we believe occurred in our case [3,4]. Similarly, it has also been reported that there is a scaling-up axis for infections due to commensal beta-haemolytic streptococci. These Streptococci are other than the usual beta-haemolytic Streptococcal pathogens like *Streptococcus pyogenes* and *Streptococcus agalactiae* [5]. Overall, in recent decades, infections due to commensal flora of healthy human skin and mucosa have been increasingly reported. Hence, it is always a diagnostic challenge to report them as pathogens [6].

Four cases from a multi-specialty tertiary care hospital are reported here. In these patients, infection was due to commensal GPC.

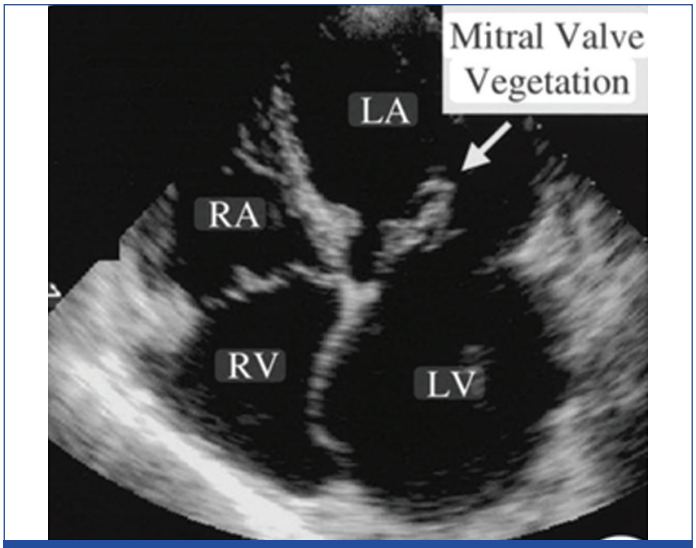
The first case was of infective endocarditis, wherein *K. kristinae* was the etiological agent. The second case was a paediatric patient with fever, wherein *Staphylococcus warneri* was the culprit. The third case presented with an infected recurrent sebaceous cyst on the left lumbar region, where *Globicatella sanguinis* was isolated in a postoperative culture sample. The fourth patient had fever and cough and *Gemella sanguinis* was the pathogen. Detailed findings and observations have been discussed ahead.

CASE SERIES

Case 1

A 54-year-old gentleman, a known case of diabetes mellitus, hypertension and chronic kidney disease stage V, was on Maintenance Haemodialysis (MHD). He was admitted with a history of high-grade fever with chills for two weeks. The patient also complained of lumbar pain, breathlessness with dry cough, oliguria and abdominal distension. On examination, his general condition was poor. Blood pressure was 114/60, pulse was 98 per minute and oxygen saturation was 96%. Laboratory investigations like total leucocyte count (15,500/µL), serum creatinine (7.1), serum urea (59), urine routine (normal), rapid malaria antigen (negative), dengue antigen/antibody test (negative), and rapid typhi IgM (negative) were done. X-ray chest and ECHO were also performed.

ECHO report impression revealed hypertensive heart disease. Concentric left ventricular hypertrophy. No Left Ventricular Regional Wall Motion Abnormality (LV RWMA). Grade II diastolic dysfunction. Moderate Mitral Regurgitation (MR) moderate to severe Pulmonary Stenosis (PS), moderate Tricuspid Regurgitation (TR). Moderate Pulmonary Hypertension (PH), good left ventricular and right ventricular systolic function. Possible infective endocarditis of the mitral and pulmonary valve. Vegetations in mitral and pulmonary valves are depicted in [Table/Fig-1]. Such patients are quite prone



[Table/Fig-1]: Echocardiography (ECHO) image of mitral valve vegetation.

to fungal infections due to decreased immunity. The patient in this reported case had a poor general condition.

For isolating the causative agent of endocarditis, paired blood samples were collected for blood culture. The first set of samples was collected from the left femoral vein and the second set of blood samples from the left cubital vein before dialysis. After dialysis, one more set of blood culture was collected from the right femoral vein and another set from the right cubital vein. Paired samples were collected before and after dialysis in BACTEC PLUS Aerobic/F, BACTEC PLUS Anaerobic/F and BD BACTEC Mycosis-I/F vials. Then empirical antimicrobials (Vancomycin, Imipenem-Cilastin and Caspofungin) were started along with other supportive treatment.

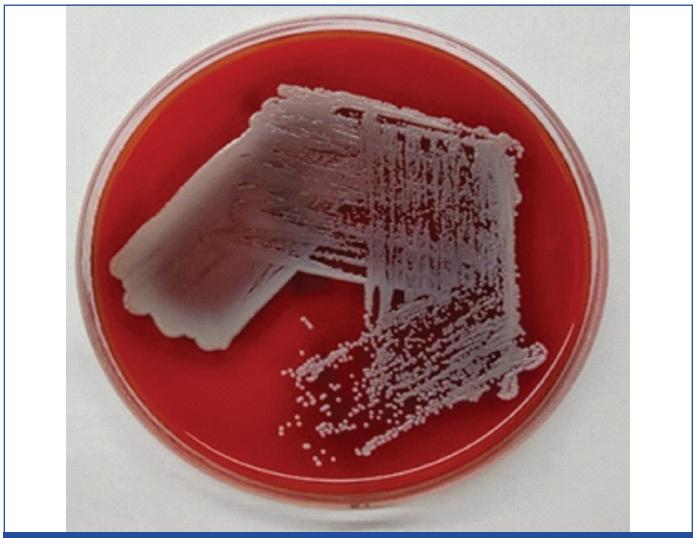
All blood culture bottles were incubated in the Becton Dickinson (BD) BACTEC automated blood culture system [7]. All BACTEC PLUS Aerobic/F bacterial blood culture bottles flagged positive in 48 hours. GPC were seen in the Gram stain of smears of the broth from all positive blood culture bottles. Subcultures from these bottles were done on Blood Agar (BA) & Mac Conkey's Agar (MA). After aerobic incubation at 37°C, small, cream-coloured, non-haemolytic, opaque colonies were grown in all subcultures on BA. There was no growth on MA. GPC were seen in the Gram stain of all smears of subcultures. Identification was done using GP ID on Vitek 2 Compact [8]. The organism in all samples was identified as *K. kristinae* on Biomerieux Vitek 2 Compact. Being a rare isolate, antibiotic susceptibility was not reported by Vitek 2 Compact. Hence, the conventional method was used here for Antibiotic Susceptibility Testing (AST). The isolate was catalase-positive and coagulase-negative. Antibiotic susceptibility was performed by the conventional method (modified Kirby-Bauer method) [8,9] on Muller-Hinton Agar (MHA). The isolated *K. kristinae* was susceptible to Penicillin, Ceftriaxone, Vancomycin, Linezolid, Trimethoprim-Sulphamethoxazole, Cefoxitin, Doxycycline and Gentamycin. It was resistant to Erythromycin, Clindamycin and Ciprofloxacin. Negative signals flagged in all BACTEC PLUS Anaerobic/F & BD BACTEC Mycosis-I/F vials, after incubation as per standard guidelines.

After the culture and sensitivity report, de-escalation of antimicrobials was done. Caspofungin and Imipenem-Cilastin were discontinued. The patient was successfully treated with a combination of Vancomycin and Trimethoprim-Sulfamethoxazole for 14 days and was later hemodynamically stable. Patient came for follow-up two months later and was found to be symptom-free.

Case 2

A three-year-old female was admitted with a history of high-grade fever for four days. On examination, the patient was drowsy. There were no other associated symptoms. Neutrophil count was 16,000/microliter, which was higher than the reference range of 5000 to 15,000/microliter. Urine routine was normal. Rapid malaria antigen test, dengue antigen/antibody detection test were negative. The x-ray chest was normal. The patient was not catheterised. No significant past medical history was present. Paired blood culture was collected from right and left cubital veins in BD BACTEC Peds Plus blood culture vials before starting antibiotics. After blood collection, Ceftriaxone was started (60 mg/kg/day) in two divided doses intravenously.

Blood culture vials were processed in the BD BACTEC automated blood culture system [7]. A positive signal was flagged within 36 hours of incubation in both of the blood culture vials. Gram-Positive Cocci (GPC) were detected in the Gram stain of the smear of the blood culture broth. Subcultures from the blood culture bottle were performed on BA and MA. White, opaque, tiny, non-haemolytic colonies were seen on BA [Table/Fig-2].



[Table/Fig-2]: *S. warneri* on Blood Agar (BA).

Whereas on MA, tiny lactose fermenting colonies (pink) with diameter 1 millimeter, were seen [Table/Fig-3].

[Table/Fig-3]: *S. warneri* on MacConkey agar.

GPC was detected in the smear of colonies on BA and MA. Identification and antibiotic susceptibility of these GPC were performed on Vitek 2 Compact [8]. The isolate was identified as *S. warneri*. It was susceptible to Gentamycin, Ciprofloxacin, Levofloxacin, Clindamycin, Teicoplanin, Vancomycin, Linezolid and Trimethoprim-sulphamethoxazole. As Tetracycline and Tigecycline are contraindicated in pediatric age group, they were not reported though the isolate was susceptible to them. The isolated *S. warneri* was resistant to Benzylpenicillin, Oxacillin and Erythromycin. Cefoxitin screen was positive. Hence, Penicillin and Cephalosporin groups of antibiotics were not recommended for treatment. After susceptibility report, patient was shifted from Ceftriaxone to Trimethoprim-sulphamethoxazole.

Patient was afebrile after 10 days of treatment with Trimethoprim-Sulphamethoxazole (Concentration: 16 mg/mL Trimethoprim and 80 mg/mL Sulphamethoxazole and dose as per Trimethoprim concentration: 15 mg Trimethoprim/kg/day divided every 8 hours).

Case 3

A 46-year-old gentlemen had infected recurrent sebaceous cyst on left lumbar region. There was no history of diabetes, hypertension or any other co-morbidities. Patient was non-reactive for Human Immunideficiency Virus (HIV) 1/2 and Hepatitis C Virus (HCV) antibodies. HBsAg was not detected. Neutrophil count was slightly raised (12,700/microliter).

The cyst was surgically removed after giving a dose of Amoxycillin-Clavulanic acid pre-operatively. Amoxycillin-Clavulanic acid was continued post-operative till the culture and susceptibility report. The infected cyst was sent for culture in a sterile container. Moderate number of pus cells and a few GPC were seen on the Gram stain of primary smear of the infected cyst. Tiny transparent beta-haemolytic colonies grew on BA after 24 hours of aerobic incubation at 37°C [Table/Fig-4].

[Table/Fig-4]: *Globicatella sanguinis* on Blood Agar (BA).

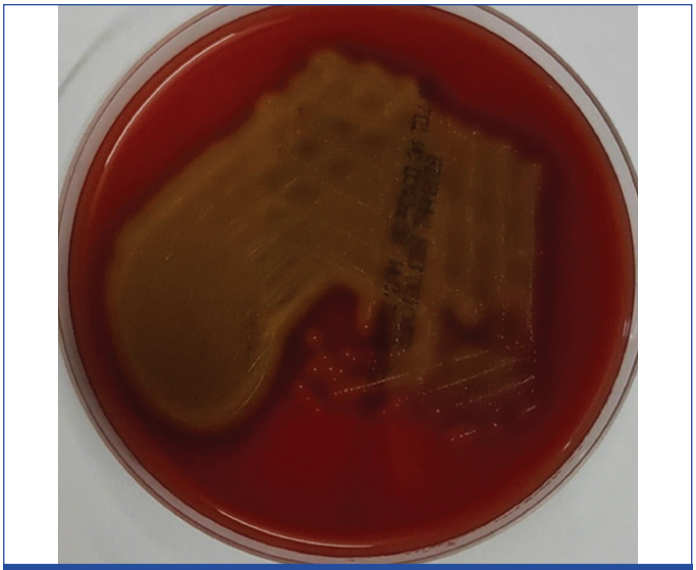
There was no growth on MA. The isolate was catalase-negative. Identification was done on Vitek 2 Compact. The isolate was identified as *G. sanguinis* by Vitek 2 Compact. As antibiotic susceptibility was not reported by Vitek 2 Compact, it was performed by the conventional method (modified Kirby-Bauer method) [9]. The isolate was susceptible to Penicillin, Vancomycin, Ceftriaxone, Linezolid and Ofloxacin. It was resistant to erythromycin, Clindamycin and Chloramphenicol. As the isolate was susceptible to Amoxicillin-Clavulanic acid and it was already given to the patient for three days post-operatively, it was continued to complete seven days course. There was no recurrence of sebaceous cyst after one month's follow-up.

Case 4

A 58-year-old lady with no past significant contributory medical history, presented with moderate fever and cough with expectorations for eight days. There was no history of loss of weight/appetite. Neutrophil count was raised (17,000/microliter). Urine routine, peripheral smear, liver function tests was normal. Azithromycin was started to the patient after sending sputum sample for culture.

Acid fast bacilli were not detected in Ziehl-Neelsen stain of sputum sample. Numerous pus cells and GPC were detected in the Gram stain of primary smear of sputum (Barlett score 3) [10]. Tiny beta hemolytic transparent colonies grew on BA after 24 hours of aerobic incubation at 37°C [Table/Fig-5].

There was no growth on MA. GPC in chains were seen in the smear of the colonies. Vitek 2 identified the isolate as *G. sanguinis*. As antibiotic susceptibility was not analysed by Vitek 2, it was performed by conventional method (Modified Kirby-Bauer method) [9].



[Table/Fig-5]: *Gemella sanguinis* on Blood Agar (BA).

The isolate was sensitive to Erythromycin, Clindamycin, Azithromycin and Linezolid. It was resistant to Penicillin, Ceftriaxone and Ciprofloxacin. Azithromycin was started to the patient after giving sputum sample for culture. The isolate was susceptible to Azithromycin. Also, patient was responding clinically to Azithromycin. Hence, Azithromycin was continued for five days. Patient was completely recovered at seven days follow-up.

DISCUSSION

There was a wide range of age distribution (3 years to 81 years). There was no foreign body (catheter/intra-venous line) present in the patients. All samples were collected under all aseptic precautions and before administration of antibiotics.

GPC were isolated from samples collected from these patients. All these GPCs are known to be commensals. In this study, they are reported as pathogens because no other pathogen has grown in the culture. There was a clinical correlation in each case.

These isolates were identified on the Vitek 2 Compact automated system. A susceptibility report was given by Vitek 2 for the two *S. warneri* isolates. For organisms isolated rarely, antibiotic susceptibility is not reported by Vitek 2. This is due to the unavailability of the respective susceptibility data for comparison in the system. Hence, in this study, there is no susceptibility report by Vitek 2 for *K. kristinae*, *Gemella sanguinis* and *G. sanguinis*. Antibiotic susceptibility was done by the modified Kirby-Bauer method on MHA for *Kocuria* and on BA for *Gemella* and *Globicatella*, as per the standard guidelines [8,9]. No Clinical and Laboratory Standard Institute (CLSI) guidelines are available for the interpretation of antibiotic susceptibility for *Kocuria*, *Gemella* and *Globicatella*. *Kocuria* is a catalase-positive, coagulase-negative GPC. Hence, CLSI disk diffusion susceptibility criteria of CoNS for *K. kristinae* are used as a reference for reporting antibiotic susceptibility. Both *Gemella* and *Globicatella* had beta-haemolytic, tiny, transparent colonies on BA. The catalase test was negative. Hence, CLSI disk diffusion susceptibility criteria are used for Streptococcus species beta-haemolytic group (conventional method) as a reference for reporting antibiotic susceptibility of *Gemella* and *Globicatella* [9].

Kocuria is a commensal of human skin and mucosa. The diseases caused by this Genus are extremely uncommon. But recent data have shown that infection due to *Kocuria* is on the rise, even in relatively healthy individuals. *K. kristinae* is one of the potential pathogenic species [3]. Napolitani M et al., carried out a systematic search of various studies reporting cases of human infections due to *K. kristinae*. The latter was reported in bacteraemia, endocarditis,

peritonitis, abdominal abscess, umbilical sepsis, acute cholecystitis and urinary tract infection across the globe [4]. Some studies isolating *K. kristinae* have been shown in [Table/Fig-6] [3,11].

Study name	Age	Organism isolated in	Symptoms	Treatment	Recovery
This study	54 years/M	Blood culture	K/C/O Diabetes Mellitus (DM), Hypertension (HTN) and Chronic Kidney Disease (CKD) stage V, on Maintenance Haemodialysis (MHD). Admitted with history of high-grade fever with chills for 2 weeks.	Vancomycin and Trimethoprim-Sulphamethoxazole for 14 days	Later, haemodynamically stable. Symptom free at two months follow-up.
Kim KY et al., [11]	57 years/M	Blood culture	K/C/O DM, presented with dyspnoea, cough, sputum, left shoulder pain, diaphoresis, myalgia, fever, and a chilled sensation for 2 days.	Ceftriaxone, levofloxacin, and clindamycin were the initial antibiotic choices. Treatment was switched to piperacillin-tazobactam mid-course due to recurrent fevers.	The patient finally recovered after 3 weeks of therapy.
Michelle B et al., [3]	62 years/M	ETT culture	K/C/O DM, HTN, heart failure, and hypothyroidism. presented at an outside hospital with fatigue and a feeling of unwellness.	Considering the increasing evidence of multidrug resistance and the acuity of the patient's presentation, linezolid was started.	Successfully extubated

[Table/Fig-6]: Comparative analysis of different studies isolating *Kocuria kristinae* [3,11].

In this case, *K. kristinae* was reported from all four aerobic culture bottles. The positive signals were flagged within 48 hours of incubation. This indicates a high bacterial load in the blood. Also, vegetations were detected in the 2D ECHO. Thus, two major Duke's criteria for infective endocarditis were fulfilled [12]. Hence, *K. kristinae* was reported as a pathogen in this case.

S. warneri is a Gram-positive, coagulase-negative, catalase-positive, and oxidase-negative coccus [6]. Usually, it is found as a component of the healthy human and animal microbiota of the skin and mucosae. Many studies have described *S. warneri* as a pathogen causing septicaemia, endocarditis, discitis, osteomyelitis, subdural empyema, septic arthritis, ventriculo-arterial shunts and urinary tract infections [2,6,13,14]. More studies have isolated the same organism [Table/Fig-7] [15,16].

Study name	Age	Organism isolated in	Symptoms	Treatment	Recovery
This study	3 years/F	Blood culture	Fever, drowsiness	Ceftriaxone	Yes
Kini GD et al., [15]	78 years/F	Blood culture	Bilateral lower extremity oedema, Infective endocarditis	Gentamycin	Yes
Ivi´c I et al., [16]	35 years/M	Blood culture	Redness, swelling, chills, high fever, and a productive cough with thick sputum, subcutaneous abscess on the left lower leg	The patient started on vancomycin and was later switched to intravenous cloxacillin.	The patient was discharged after 4 weeks of antibiotic treatment. No symptoms seen at 2 months follow-up.

[Table/Fig-7]: Comparative analysis of different studies isolating *Staphyloccus warneri* [15,16].

The *S. warneri* isolate, in this study, was from the blood culture of a paediatric patient. The positive signals, flagged within 36 hours of incubation, confirmed high bacterial load in the blood sample.

Globicatella sanguinis is a part of normal flora of oral cavity. *G. sanguinis* is an unusual pathogenic agent. However, it is an opportunistic bacterium that can be responsible for severe infections such as gastroenteritis, osteomyelitis, endocarditis, meningitis, endodontic infections, sepsis and urinary tract infection [17,18]. Oppegaard O et al., in a retrospective study, have analysed 15 years of data about infections due to beta-haemolytic streptococci. He has mentioned many commensal streptococci-like organisms leading to opportunistic infections [5]. Many studies report isolation of *Globicatella sanguinis* from various clinical specimens [Table/Fig-8] [19,20].

Gemella is a gram-positive, catalase-negative, facultative anaerobic coccus. It is known to be a part of the normal flora of the human oropharynx, gastrointestinal tract, and urogenital tract [21]. Gemella may be a causative agent in infections such as infective endocarditis, spondylodiscitis, brain abscess, endophthalmitis, pharyngeal abscess and empyema. Many species of Gemella have been described. These are Gemella haemolysans, *G. morbillorum*, *G. bergeri*, *G. sanguinis*, *G. asaccharolytica*, *G. taiwanensis*, *G. parahaemolysans*, *G. palaticanis* and *G. cuniculi* [22,23]. A few more studies have been included in [Table/Fig-9] [22,24].

Study name	Age	Organism isolated in	Symptoms	Treatment	Recovery
This study	46 years /M	Post-operative sebaceous cyst culture	Infected recurrent sebaceous cyst on the left lumbar region.	Amoxicillin-Clavulanic acid for 7 days.	No recurrence of sebaceous cyst after 1 month's follow-up.
Raimonda M et al., [19]	48 years/ M	Blood culture	Progressive diarrhoea and vomiting for five days. K/C/O alcoholism for 20 years	Not mentioned.	Death on the 5th day of admission
Andy MO et al., [20]	72 years/F	Intraoperative cultures of inflammatory synovial tissue	A gastric lap band and lymphoedema presented with progressive pain and dysfunction of a total hip arthroplasty.	Vancomycin	Recovered from infection but died after 3 months due to AML

[Table/Fig-8]: Comparative analysis of different studies isolating *Globicatella sanguinis* [19,20].

Study name	Age	Organism isolated in	Symptoms	Treatment	Recovery
This study	58 years/F	Sputum	Moderate fever and cough with expectorations for 8 days.	Azithromycin for 5 days	No symptoms at 7-day follow-up
Hyun JK et al., [22]	41 years/M	Blood culture	Fever	Ceftriaxone and Gentamycin	Recovered and discharged
Kim JH et al., [24]	49 years/M	Blood culture	Fever and chills, abdominal pain of 2-week duration. Previous H/O dental procedures.	Penicillin G, later switched to Amoxyclav and discharged on day 24	No complaints in further follow-up

[Table/Fig-9]: Comparative analysis of different studies isolating *Gemella sanguinis* [22,24].

Limitation(s)

There are a few limitations of these case reports. All these isolates are known to be a part of the normal flora of human skin. All these have been rarely reported as pathogens. In all patients of this case series, empirical antibiotics were immediately started

after the collection of samples. The culture and sensitivity reports were available after 48 hours. So, there were hardly any chances of isolation of these organisms from the sample after two days of antibiotic administration. Hence, a repeat sample for culture was not collected to demonstrate the same isolate in the sample.

CONCLUSION(S)

Identification of rare isolates in this study was due to the use of an automated identification system. Though these organisms are known commensals, they were reported as opportunistic pathogens due to standard techniques of sample collection, clinical correlation of infection, and isolation of only the reported organism in the culture. In two cases, de-escalation of antimicrobial treatment was done and in the other two cases, the same antibiotics were continued. This was in compliance with the antibiotic sensitivity report. Thus, Antimicrobial Stewardship (AMS) was implemented in all these cases.

Organisms that are usually commensals represent unconventional and emerging pathogens even in immunocompetent patients and they are worthy of careful attention. Reporting them as pathogens is a diagnostic challenge and it should be done with due clinical correlation.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]

- Plagiarism X-checker: Mar 28, 2025
- Manual Googling: Jul 22, 2025
- iThenticate Software: Jul 24, 2025 (10%)

ETYMOLOGY: Author Origin

EMENDATIONS: 7

AUTHOR DECLARATION:

- Financial or Other Competing Interests: None
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. Yes

Date of Submission: **Mar 20, 2025**
Date of Peer Review: **Apr 26, 2025**
Date of Acceptance: **Jul 26, 2025**
Date of Publishing: **Dec 01, 2025**