DOI: 10.7860/JCDR/2023/62482.18085

Case Series

Microbiology Section

Obstructive Uropathy Caused by *Chryseobacterium indologenes*: A Case Series from University Hospital, Uttar Pradesh, India

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ABSTRACT

Chryseobacterium spp., is non motile, non fermenter, Gram Negative Bacillus (GNB) showing enzymatic activity of catalase, oxidase, and indole production. *Chryseobacterium* spp. are found widely in the soil and aquatic milieu. It is also capable of surviving in chlorinated water, which can be attributed to the spread of infection in hospital settings hosting profusely immunosuppressed individuals. Newer diagnostic modalities like Matrix-Assisted Laser Desorption Ionisation-Time Of Flight-Mass Spectrometry (MALDI-TOF-MS) and Vitek-2 facilitate early identification and treatment can alleviate the infections caused by them. Present series discusses three cases of *Chryseobacterium indologenes* (*C. indologenes*) Urinary Tract Infection (UTI) Case 1- was a 61-year-old hypertensive and diabetic male patient diagnosed with renal failure with pyelonephritis. Case 2- was a female patient of 64-year-old with left upper ureteric calculus. Case 3- was a 31-year-old male patient having left mid ureteric calculus. All the patients were catheterised with a urinary catheter and developed UTI by *C. indologenes*. *C. indologenes* infection in UTI patients is uncommon but these cases of complicated UTIs demonstrate *C. indologenes* as a potential cause of UTI in hospitalised patients using invasive equipment like urinary catheters. As the organism was Multidrug-Resistant (MDR), appropriate antibiotic treatment and accurate identification can alleviate infection by this organism.

Keywords: Gram negative bacillus, Immunosuppressed individuals, Multidrug resistance, Urinary catheterisation, Urinary tract infection

INTRODUCTION

Chryseobacterium indologenes comes under the genus *Chryseobacterium* (it was previously categorised as *Flavobacterium* CDC group IIb). It is a non motile and non fermenting bacterium, showing enzymatic activity of catalase, oxidase, and indole production [1]. This organism is widely distributed on plants, soil, and water but human infections are very rare [1]. The organism can colonise water supplies because of its ability to survive in chlorine-treated waters; thus the hospital water supply can act as the reservoir for these infections [2]. Although generally found in soil, plants, and water bodies it does not exist as a commensal on human body [3].

Liquid medium supports the growth of the microorganism, so it can grow well in hospital settings, particularly from sinks, feeding tubes, vials, indwelling vascular catheters, and equipment that are in contact with fluids, water, and even liquid disinfectants which act as a supporting niche for the growth of *C. indologenes* [4]. Human diseases are uncommon with *C. indologenes*. Immunocompromised patients are at a higher risk rather than immunocompetent individuals for *C. indologenes* infections. Hospital stay for longer duration with indwelling devices, and antibiotics therapy for prolonged durations is also risk factors that can contribute to its infection [5].

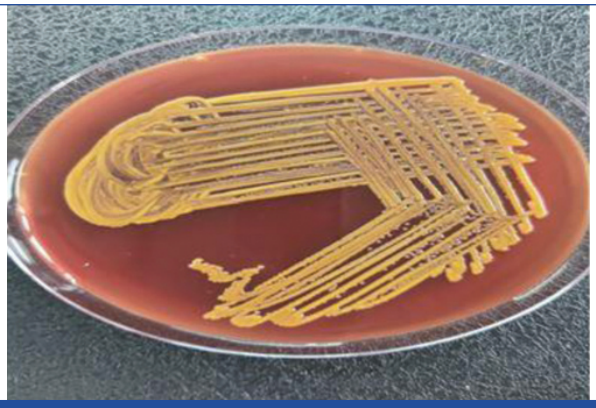
As *Chryseobacterium* is a rare pathogen that can cause infection, very few cases have been reported of urine infections caused by *Chryseobacterium spp.* Here, three cases are reported who had obstructive uropathy admitted to the hospital, as during the stay they developed complicated UTIs caused by *C. indologenes*.

CASE SERIES

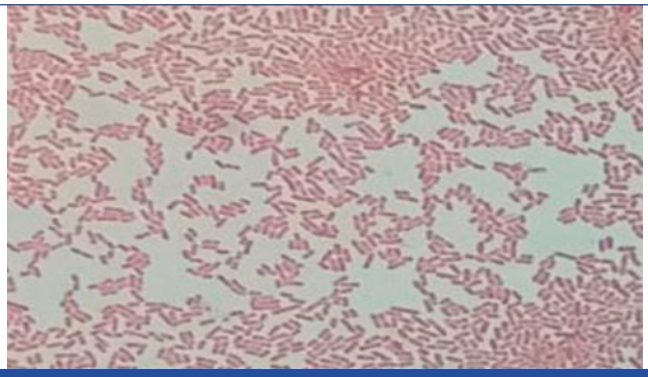
Case 1

A 61-year-old male patient, follow-up case of advanced renal failure with type 2 diabetes mellitus and systemic hypertension presented to the medicine outpatient department with chief complaints of high-grade fever and chills, vomiting, and progressive leg swelling for two months and diagnosed as an advanced renal failure with acute pyelonephritis. He had a previous history of admission and haemodialysis in the hospital seven days earlier, his blood investigations reported haemoglobin of 8.4 mg/dL, Total Leukocyte Count (TLC) 17400 cells/ cubic mm with 90% polymorphs and 10% lymphocytes, serum creatinine 8.36 mg/dL, uric acid 8.6 mg/dL.

Urine routine microscopy showed 11-12 pus cells/HPF and a few RBC/high power fields with bacteriuria. A urine sample was sent to the bacteriology section, Department of Microbiology, for culture and sensitivity. The sample was inoculated on Blood agar and MacConkey agar and subjected to overnight incubation at 37°C. After complete incubation, colonies observed only on blood agar were dark yellow in colour, 1-2 mm in diameter and non haemolytic, [Table/Fig-1]. From the blood agar colony, a Gram-stained smear was prepared which showed gram-negative bacilli [Table/Fig-2]. After performing the motility and biochemical characteristics test, the following results were observed: non motile bacilli, catalase-positive, oxidase-positive, and indole were produced in tryptophan broth, urease was not produced and citrate not utilised. Finally, for confirmation and identification of bacteria, the flexirubin type of pigment was confirmed by adding 1 drop of 10% KOH solution to colonies giving a red to pink colour [Table/Fig-3] and MALDI-TOF-MS were performed and the organism was identified as *C. indologenes* by both routine method and proteomics. Antibiotic Sensitivity Test (AST) was performed by the Kirby-Bauer disc diffusion method on Muller-Hinton Agar (MHA) according to the CLSI guidelines [6] and the organism was sensitive to doxycycline, minocycline, cotrimoxazole, levofloxacin and it was resistant to piperacillintazobactam, and ciprofloxacin. Based on the culture and sensitivity report, patient was given intravenous (i.v.) levofloxacin.



[Table/Fig-1]: Yellow-golden, non haemolytic, low convex, circular colonies with regular margins of *Chryseobacterium indologenes* on blood agar.



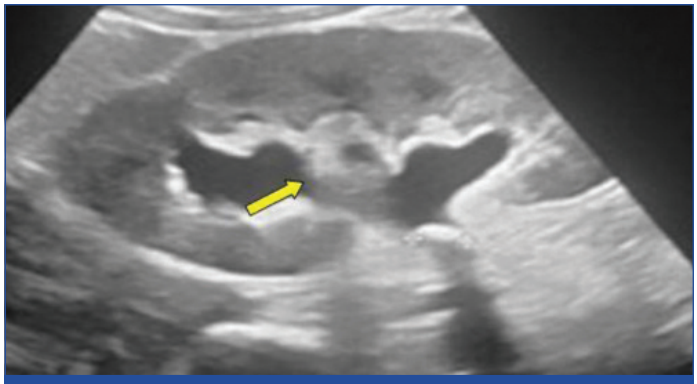
[Table/Fig-2]: Gram-stained smear from culture on blood agar showing gram negative bacilli when examined under 100X magnification of the microscope.

[Table/Fig-3]: Red colour produced by action of potassium hydroxide on flexirubin from colonies of *Chryseobacterium indologenes* on Muller Hinton Agar (MHA).

The patient was earlier administered i.v. meropenem by the clinician, but was started on i.v. levofloxacin after antibiotic susceptibility testing and the same continued for five days. His fever subsided within two days, sugar was controlled with insulin according to a sliding scale. His urine output was 2.5 liters/day and after 5 days of i.v. treatment with levofloxacin, he was discharged on oral levofloxacin 400 mg BD. After 14 days, the patient presented to the nephrology outpatient department for routine follow-up and due to persisting high creatinine levels of 7.4 mg/dL was advised to undergo Continuous Ambulatory Peritoneal Dialysis (CAPD).

Case 2

A 64-year-old female patient was admitted to the Department of Emergency medicine with a chief complaint of bilateral flank pain for the past six months, which was associated with nausea but not associated with any lower urinary tract symptoms, haematuria, turbiduria, or urinary retention. In the course of her hospital stay, she was diagnosed with Pelvic Ureteric Junction (PUJ) calculus with left upper ureteric calculus on ultrasound of the kidney and urinary bladder region [Table/Fig-4]. Bilateral Percutaneous Nephrostomy (PCN) insertion was done under interventional radiology on day of admission. The daily output was from the right PCN 1400 mL and the left PCN 800 mL; bilateral PCN culture sensitivity was done and it was sterile.

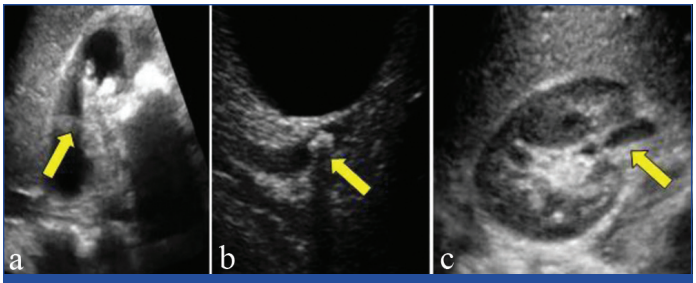


[Table/Fig-4]: Ultrasound image showing Pelvic Ureteric Junction (PUJ) calculus (marked by yellow arrow) with left upper ureteric calculus on ultrasound of the kidney and urinary bladder region seen in case 2.

But after seven days of admission, the patient developed a high-grade fever with decreased output from the right PCN and his TLC was 18800 cells/mm^3 with increased polymorphs. On examination, there was a right, the PCN per catheter leak. PCN urine sample was sent to the bacteriology section, Department of Microbiology and was inoculated in routine culture media. A Gram-stained smear was prepared from the colonies on blood agar which were 1-2 mm in diameter accompanied by production of yellow to orange pigmentation on blood agar and were gram-negative bacilli; further motility test was performed to observe non motile bacterium and routine biochemical identification was performed along with MALDI-TOF-MS and the organism was identified as *C. indologenes* both routine method and proteomics. Using AST and Kirby-Bauer disc diffusion method, the organism was sensitive to doxycycline, minocycline, and cotrimoxazole, and levofloxacin and ciprofloxacin and it was resistant to piperacillin and tazobactam and cefoperazone-sulbactam. Based on the AST, i.v. of ciprofloxacin 400 mg for every 12 hours, prescribed for five days and the patient improved symptomatically after this particular treatment. Interventional radiology was used to reposition the right nephrostomy tube. Urine output increased after repositioning of the PCN. On repeat, bilateral PCN culture and sensitivity, urine was sterile. She underwent antegrade urolithotripsy and left mini Percutaneous Nephrolithotomy (PCNL) under general anaesthesia after 15 days of PCN insertion. Bilateral PCN was clamped on the 4th postoperative day and bilateral PCN removed on the 7th day postsurgery. The patient was afebrile and discharged in a stable condition with advice to follow-up in seven days. After 21 days, the patient came back to the urology outpatient department for a routine check-up and his urine output was 3 L/day along with no pain in the flanks with no sign of infection. It was observed on routine blood investigations and urine culture results were also sterile.

Case 3

A 31-year-old male patient presented to our hospital with chief complaints of bilateral flank pain, dysuria, vomiting, and haematuria for the last 15 days. The patient had a history of a renal stone disease diagnosed two years back and was on homeopathic treatment. On evaluation by ultrasound of the kidney and urinary bladder region, the patient had bilateral renal stone disease with left hydroureteronephrosis, left mid-ureteric calculi with multiple bilateral cysts [Table/Fig-5] along with anaemia and advanced renal failure. On examination he was afebrile with a pulse rate of 98/minutes and blood pressure 160/100 mmHg. Laboratory investigations revealed haemoglobin as 8.2 mg/dL, total lymphocyte count 13,500 cells/mm^3, blood urea 45 mg/dL and serum creatinine elevated level of 4.7 mg/dL. The patient developed fever chills and rigors and back pain after four days of admission. Urine routine microscopy showed 11-12 pus cells/HPF and a few RBC under high power magnification, with bacteriuria. A urine sample was sent to the bacteriology section, Department of Microbiology, for culture



[Table/Fig-5]: Ultrasound of kidney and urinary bladder region, the patient had (pointed by yellow arrow): a) Bilateral renal stone disease with left hydrouretero-nephrosis; b) Left mid-ureteric calculi with; c) Multiple bilateral cysts in case 3.

and sensitivity. Routine processing of the sample was performed. The microorganism was subjected to routine biochemicals and MALDI-TOF-MS for identification. Finally, the organism was identified as *C. indologenes* by both methods. The isolate was sensitive to doxycycline, minocycline, and cotrimoxazole, and levofloxacin and resistant to ciprofloxacin and piperacillin-tazobactam. Based on AST report patient was given i.v. levofloxacin 400 mg eight hourly for five days. Double J stenting was done on the left-side to relieve urinary obstruction and the patient recovered after this treatment. On the repeat, urine sample was collected, microscopy and culture were performed. On microscopic examination, 2-3 pus cells/HPF and urine culture showed no growth. His condition improved subsequently, with adequate urine output and he was discharged on oral levofloxacin 400 mg BD and advised to follow-up after 15 days, to the outpatient department. After one month of DJ stenting, patient came to the outpatient department for follow-up and was advised to do another urine culture which showed no significant growth of microorganisms.

DISCUSSION

The genus *Chryseobacterium* consists of six species and those that are most commonly isolated from clinical samples include: *C odoratum*, *C. multivorum*, while *C. meningosepticum, C. indologenes*, and *C. gleum*, and *C. breve* comes under Group IIb *Chryseobacterium* spp. [7]. The organism can survive in the liquid medium, so through contaminated medical devices, this organism can survive in the patients' microflora and it may cause infections, fluids which are used in devices such as incubators for newborns, intubation tubes, respirators, humidifiers, syringes, ice chests, has been documented [8]. In a study conducted by Bonten MJ et al., a tracheal aspirate sample showed growth of *C. indologenes* in a ventilator-bound patient [9]. In 1996, Hsueh PR et al., studied the prevalence of other *Chryseobacterium* spp., among hospital-acquired infections, which is more common than *C. meningosepticum* (*Elizabethkingia meningoseptica*) [2]. Other reported infections include bacteraemia, pneumonia, and meningitis [10]. There are a very few cases reported from urine and [Table/Fig-6] shows all cases of *C. indologenes* UTI reported in the literature [11-17].

Three cases have been reported by Palewar MS et al., in patients with obstructive uropathy complicated UTIs developed which were caused by *C. indologenes* [18]. The clinical and demographic details of the cases included in present study are discussed in [Table/Fig-7]. The diagnostic studies performed on each case during the procedures these patients underwent in the course of the hospital stay is shown in [Table/Fig-8]. Many outbreaks of hospital-acquired infections can be attributed to MDR pathogens such as *Acinetobacter baumannii, Klebsiella pneumoniae*, *Escherichia coli*, and, *Chryseobacterium* spp., and the unregulated use of drugs of last resort like colistin and tigecycline [19].

Because of empirical therapy to Gram negative pathogens, there is antimicrobial resistance in this pathogen and it is intrinsically resistant to a variety of antibiotics like aminoglycosides, first-generation cephalosporins, aminopenicillins, aztreonam, carbapenems, and cephalosporins [19]. There are additional problems to resolve results of susceptibility testing for *Chryseobacterium* may differ when different methods are used, and one more problem is that results from Disk Diffusion (DD) methods are not reliable [3]. Infection control practices, although highly spoken of, are scarcely practiced in the Indian set-up, which becomes necessary as all the cases in literature previously suffering from, UTI gave a history of urinary catheterisation [11,14,15]. Of the three cases discussed in present case series, patients from cases 2 and 3 were managed with PCN and DJ-stenting, respectively, which could have been a reason for nosocomial colonisation of *C. indologenes*. Care bundles, strict handwashing and stringent infection control can prevent the nosocomial spread of infections caused by this rare pathogen.

Publication year	Author	Country of publication	Age/Mean age of patient(s) (years)	Gender	Co-morbidities	Outcome
2012	Bhuyar G et al., [11]	Chandigarh, India	19	Female	Left renal calculus, placement of Malicot's catheter postoperatively.	Recovered
2014	Deepa R et al., [12]	Chandigarh, India	45	Male	Alcohol-induced decompensated liver disease with ascites and hepatic encephalopathy.	Dead
2014	Omar A et al., [13]	Dakar, Senegal	42	Female	Chronic myeloid leukaemia, multipara, organomegaly, portal hypertension and sepsis.	Dead
2016	Rajendran P et al., [14]	Puducherry, India	58	Male	Diabetes mellitus, cerebrovascular disease, chronic renal disease and foley's catheter in-situ.	Left against medical advice but recovery evident on medication
2016	Mukerji R et al., [15]	Michigan, USA	63	Male	Stable chronic obstructive pulmonary disease, coronary artery disease, diabetes mellitus, benign prostatic hypertrophy, atrial fibrillation, bipolar disorder and anaemia with haemoglobin of 7.7 g/dL, Foleys catheter in-situ.	Recovered
2017	Tripathi P et al., [16]	Bangalore, India	43	Female	Haemolytic anaemia, systemic lupus erythematosus and Hepatitis A.	Recovered
2017	Kaur H et al., [17]	Chandigarh, India	47.06 (A total of 16 patients)	Male: Female=9:7	Two patients had hypertension, three patients had diabetes mellitus, two patients had chronic obstructive pulmonary disease and one patient was suffering from rheumatoid arthritis.	14 patients recovered, 2 did not respond to medication

[Table/Fig-6]: Review of literature on cases of UTIs caused by *Chryseobacterium indologenes* in the past 10 years (n=7) [11-17].

S. No.	Age/Gender	Underlying disease	Invasive procedure	Infection type	Treatment	Outcome
1.	61/M	Renal failure with acute pyelonephritis	Urinary Catheter	Bacteriuria	i.v. levofloxacin	Survived
2.	64/F	Upper ureteric calculus	Urinary Catheter	Bacteriuria	i.v. ciprofloxacin	Survived
3.	31/M	Left mid ureteric calculi	Urinary Catheter	Bacteriuria	i.v. levofloxacin	Survived

[Table/Fig-7]: Demographics and clinical characteristics of patients with UTIs caused by *C. indologenes* (n=3).

Diagnostic test	Case 1			Case 2			Case 3		
Day of hospital stay	Day 0	Day 7	Day 14	Day 0	Day 7	Day 14	Day 0	Day 7	Day 14
Haemoglobin (mg/dL)	8.4	9.2	10.1	10.8	11.2	12.4	8.2	8.4	9/2
Total leukocyte count (cells/ cubic mm)	17.4	13.2	10.3	19.6	18.8	9.6	13.5	12.6	11.2
Creatinine (mg/ dL)	8.36	8.2	7.4	2.2	2.0	1.47	4.7	3.6	2.4
Uric acid (mg/dL)	8.6	7.2	6.0	8.9	8.4	7.2	5.7	5.4	4.4
Urine output (Litres/day)	2.1	2.4	2.5	2.2	2.6	3.0	2.2	2.6	3.4

[Table/Fig-8]: The diagnostic studies performed on each case during the procedures these patients underwent in course of the hospital stay (n=3).

With respect to the three cases discussed in present case series, urinary drainage of all patients was performed using a urinary catheter, with the length of catheterisation exceeding a week. The presence of indwelling catheters can be attributed to *Chryseobacterium* UTI as described in a study by Chang YC et al., [5]. What differentiates it from a colonisation include the characteristic clinical features and diagnostic parameters that were suggestive of infection. All cases included in present study are excerpts of hospital acquired infection caused by *C. indologenes*, rarely encountered. Although the source of infection cannot be recognised, but acquisition of MDR by these rare pathogens could lead to outbreaks of nosocomial infections in the respective wards. Infection control is imperative in cases of hospital acquired UTI involving strict adherence to hand hygiene protocols and routine cleaning of the patient stations along with periodic change and cleaning of objects used by patients.

CONCLUSION(S)

C. indologenes infection in UTI patients is uncommon but these cases of complicated UTIs show that *C. indologenes* is a leading cause of UTI in hospitalised patients. Thus signifies the role of *C. indologenes* in infections associated with indwelling urinary catheter. This MDR organism can be identified by MALDI-TOF-MS, administration of appropriate antibiotic treatment and following stringent infection control methods can alleviate spread of infection by this organism in susceptible patients.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]

- Plagiarism X-checker: Jan 04, 2023
- Manual Googling: Feb 15, 2023
- iThenticate Software: Mar 25, 2023 (13%)

ETYMOLOGY: Author Origin

EMENDATIONS: 6

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. No

Date of Submission: **Jan 03, 2023**
Date of Peer Review: **Feb 08, 2023**
Date of Acceptance: **Apr 05, 2023**
Date of Publishing: **Jun 01, 2023**