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Case Report

Ochrobactrum intermedium septicemia

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Abstract

Ochrobactrum species are emerging Gram-negative, non-fermenting bacteria with low virulence. Infection with the *Ochrobactrum* species is commonly nosocomial and has been reported in patients with indwelling medical devices and implants. Among the species of *Ochrobactrum* infecting humans, *Ochrobactrum anthropic* and *Ochrobactrum intermedium* are the commonest ones. We present a case of septicemia caused by *Ochrobactrum intermedium* in a 75-year-old patient with lower limb cellulitis. This report describes the epidemiology, clinical manifestations, laboratory diagnosis, antibiotic susceptibility pattern, and treatment of *Ochrobactrum* infections.

Key words: *Ochrobactrum intermedium*, *Ochrobactrum*, septicemia, cellulitis.

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Introduction

The genus *Ochrobactrum* belongs to the Brucellaceae family and is an emerging opportunistic pathogen [1]. *Ochrobactrum* was formerly called CDC group Vd [2]. It closely resembles *Brucella* species phenotypically and laboratory misidentification is not uncommon [3,4]. It is an aerobic, motile non-fermenting Gram-negative bacillus that is oxidase and catalase-positive. *Ochrobactrum* species have been isolated from several environmental sources such as plants, rhizosphere, soil, and water. Nosocomial infections are associated with indwelling medical devices and contaminated infusate [5]. Though bacteria belonging to this genus are of low virulence, infections in morbid and immunocompromised patients can be serious [6,7]. *Ochrobactrum anthropi* is the most common species of the genus *Ochrobactrum*. *Ochrobactrum intermedium* is an emerging multidrug resistant pathogen whose clinical features are poorly characterised. To the best of our knowledge this is the first case of septicemia caused by *Ochrobactrum intermedium* to be reported from India. This case report describes a fatal case of septicemia caused by *Ochrobactrum intermedium* in a 75-year-old diabetic and hypertensive man.

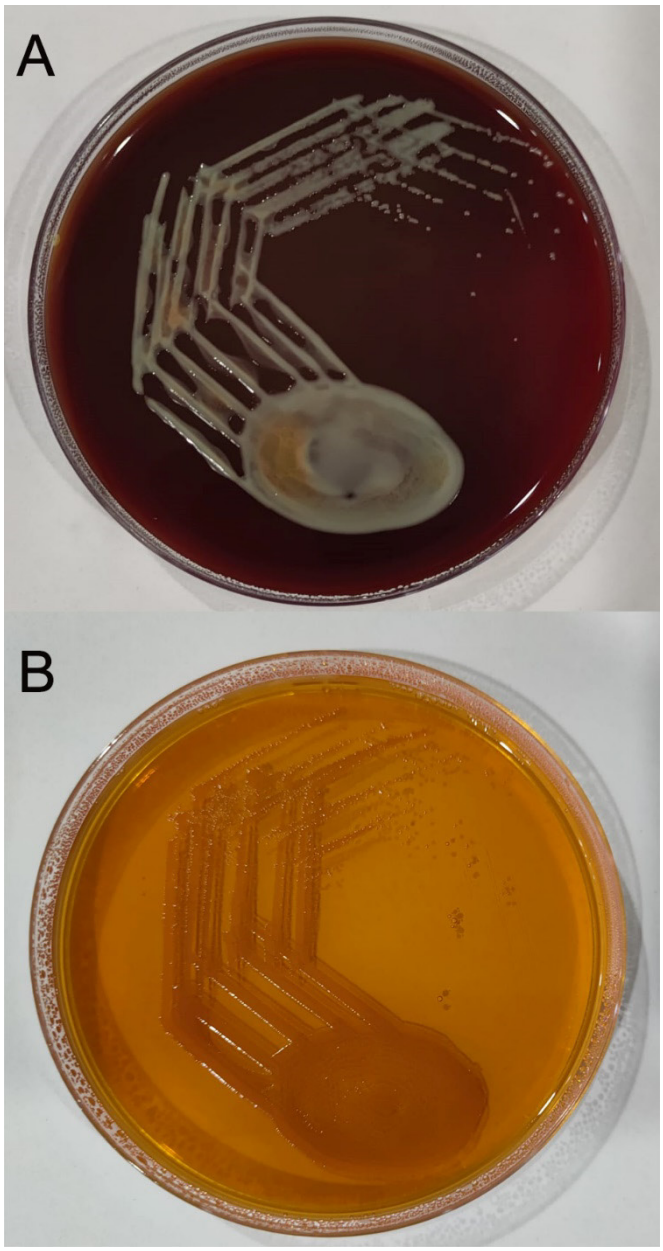
Case report

A 75-year-old diabetic and hypertensive man presented to the emergency department of our hospital with complaints of fever, throbbing pain, swelling in the lower limb, and decreased urine output for the past two days. The patient had chronic kidney disease and was on medical management for the past two years. The patient underwent coronary artery bypass surgery 15 years ago and laparoscopic cholecystectomy two years ago. On presentation, the patient was conscious-oriented and afebrile. His pulse rate was 110 per minute, and his blood pressure was 110/80 mmHG. Local examination revealed left lower limb swelling and tenderness. Lower limb doppler ultrasound showed diffuse subcutaneous edema, suggestive of cellulitis. Routine laboratory investigations revealed leucopenia (2400 cells per µL), thrombocytopenia (80,000 cells per µL) and deranged renal parameters {urea: 83 mg/dL (normal range :15-45mg/dl), creatinine: 2.74 mg/dL (normal range: 0.6-1.2 mg/dL)}. Two sets of blood cultures were collected from the patient during the

febrile episode. He was started on amoxicillin and clavulanate (1.2 mg, IV stat dose), and other supportive medications.

On day 2 of admission to the medicine ward, the patient had an episode of hypoglycaemia followed by an episode of seizure. These events lead to hypotension (blood pressure not recordable) and desaturation (SpO_2: 40%). The patient was shifted to the intensive care unit and started on O_2 support and inotropic support. Since he had hypoxemia, the patient was electively intubated.

Figure 1. Colony morphology of the isolate identified as Ochrobactrum intermedium on culture media.

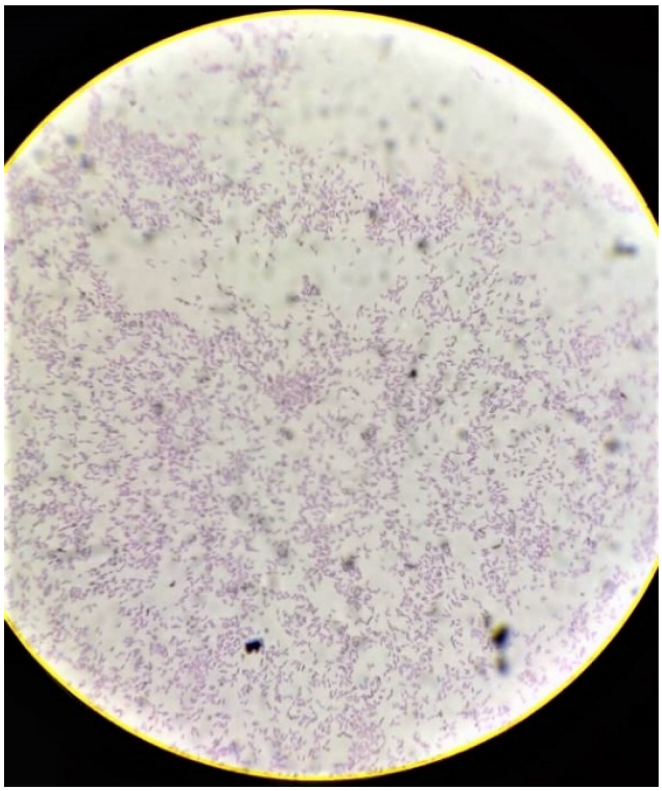


A: Subculture on blood agar after 24 hours shows confluent, mucoid, grey-moist, non-hemolytic growth; **B:** Subculture on MacConkey agar after 24 hours shows mucoid, non-lactose fermenting colonies.

The patient had recurrent episodes of hypoglycaemia for which 25% dextrose was administered 6th hourly. Antibiotics were escalated up to meropenem and clindamycin. The patient then developed metabolic acidosis, and a bicarbonate infusion was started. A bedside echocardiogram revealed severe left ventricular dysfunction (ejection fraction: 15%). His condition continued to worsen due to persistent hypotension, and despite all resuscitative measures, the patient expired on day 2 of hospital admission.

Among the four, two aerobic blood cultures were flagged positively by the BacT/ALERT 3D machine (BioMérieux, Durham, USA) after 48 hrs of incubation. BacT/ALERT broth Gram stain revealed small, uniformly stained, Gram-negative bacilli. Subculture on blood agar revealed confluent, grey moist, mucoid, non-hemolytic growth and mucoid, non-lactose fermenting colonies on Mac Conkey agar (Figure 1). Microscopic examination of Gram stain performed on the colony smear from blood agar showed small Gram-negative bacilli (Figure 2). The organism was identified by the VITEK 2 system (BioMérieux, Durham, USA) as *Ochrobactrum anthropi*. VITEK 2 systems (BioMérieux, Durham, USA) automated minimum inhibitory concentration (MIC) testing by micro broth

Figure 2. Microscopic examination of Gram-stained colony smear of the isolate identified as Ochrobactrum intermedium. Magnification × 1000.



dilution was performed, and the result was interpreted using CLSI M100 (2021) [8]. Our isolate was sensitive to ciprofloxacin, trimethoprim/sulfamethoxazole, meropenem, and imipenem; intermediate sensitive to amikacin and gentamicin; resistant to ceftazidime, cefepime, cefoperazone-sulbactam, piperacillin-tazobactam, ticarcillin-clavulanic acid and colistin (Table 1). Though our isolate showed relatively swift growth on MacConkey agar which is rather inconsistent with the identification of *Brucella*, we performed a few more differential tests to rule it out. Phenotypic tests such as motility testing by hanging drop, and utilization of mannitol, sorbitol, and d-arabitol were performed to rule out the possibility of *Brucella*. Our isolate was motile and utilised mannitol, sorbitol and d-arabitol. The isolate was submitted for gene sequencing for confirming its identification. Based on 16S rRNA gene sequence alignment analysis over the NCBI BLAST server, the test isolate was identified as *Ochrobactrum intermedium* (GenBank accession number: OM302143) with a sequence similarity of > 98.65%.

Discussion

Ochrobactrum species commonly associated with human infections are *O. anthropi*, *O. intermedium*, *O. pseudintermedium*, *O. haematophilum*, and *O. pseudogrignonense*. *O. anthropi* and *O. intermedium* are most commonly associated with human infections among the *Ochrobactrum* species. *O. intermedium* has been associated with various human infections such as liver abscess, pelvic abscess, prostatic abscess, endophthalmitis, bacteremia, and infective endocarditis [9]. *Ochrobactrum* species are non-fastidious bacteria that produce indole and hydrolyse urea [10]. The genus *Ochrobactrum* differs from the genus *Brucella* by utilizing glycine, succinate, rhamnose, mannitol, sorbitol, d- arabitol, and by producing acid from glucose, xylose, and fructose [11]. It is clinically significant to differentiate between species of *Ochrobactrum* as the rate of mortality and drug resistance differs among the species [10,12]. Our literature search on PubMed revealed only 6 cases of bacteremia caused by *Ochrobactrum intermedium* documented to date [9,13–16]. *Ochrobactrum* species mainly cause indwelling device-associated nosocomial infections in the immunocompromised and are considered less virulent. Cases of severe infections by *Ochrobactrum anthropic* in immunocompetent individuals such as sepsis, septic shock, meningitis, and endocarditis have been increasingly reported [6,7,17–22]. Since the blood sample was collected on the day of admission and the patient did not give any history of hospitalization in the recent past, nosocomial origin is ruled out. *Ochrobactrum intermedium* is not included in the Gram-negative database of VITEK 2 systems, which leads to the isolate's misidentification as *Ochrobactrum anthropi*. Because of the inability of commercial identification systems such as API 20NE or VITEK2 system to differentiate the *Ochrobactrum* species, there is a low possibility that the currently reported incidence of *Ochrobactrum intermedium* might be false. 16S rRNA gene sequence analysis and matrix-assisted laser desorption ionization–time of flight mass spectrometry (MALDI ToF MS) accurately identify the species of *Ochrobactrum* [23]. *Ochrobactrum* species are resistant to all the beta-lactams except carbapenems due to presence of AmpC beta-lactamases. They are usually susceptible to aminoglycosides, trimethoprim-sulfamethoxazole, rifampicin, and fluoroquinolones [9,10,24]. The antibiotic sensitivity of our isolate was in concordance with the susceptibility pattern of the previously reported *Ochrobactrum* isolates from human infections, except that the aminoglycosides (amikacin and gentamicin) showed intermediate sensitivity [9,10,25]. *Ochrobactrum intermedium* demonstrates resistance to a wide range of antibiotics (beta-lactams, aminoglycosides, colistin) compared to *Ochrobactrum*

Table 1. Antibiotic susceptibility of the isolate.

Name of antibiotic	MIC (µg/mL)	Interpretation
Ticarcillin/Clavulanic acid	≥ 128	Resistant
Piperacillin/Tazobactum	≥ 128	Resistant
Ceftazidime	≥ 64	Resistant
Cefaperazone/Sulbactum	≥ 64	Resistant
Cefepime	≥ 64	Resistant
Imipenem	0.5	Sensitive
Meropenem	1	Sensitive
Amikacin	32	Intermediate
Gentamicin	8	Intermediate
Ciprofloxacin	≤ 0.25	Sensitive
Colistin	≥ 16	Resistant
Trimethoprim/Sulfamethoxazole	≤ 20	Sensitive

anthropi. Colistin resistance, negative urease test, and mucoid growth on culture media are necessary phenotypic tests to differentiate *O. intermedium* from *O. anthropi*. [10]. Late presentation, presence of multiple co-morbidities, resistance to antibiotics, and age of the patient are the factors that could have possibly led to the fatal outcome in our case.

Conclusions

To our knowledge, this is the first reported case of septicemia caused by *Ochrobactrum intermedium*. This case highlights the importance of having high clinical suspicion and early identification of such drug-resistant organisms. Lack of clinical suspicion, laboratory misidentification, drug resistance, and underlying diseases can lead to fatal infections by this organism with low virulence. Phenotypic tests in combination with commercial identification tests can be used for species differentiation in places where molecular identification is not feasible.

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Data availability

Data used to support the findings of this study are included in the article. The sequence of our isolate has been deposited in GenBank (https://blast.ncbi.nlm.nih.gov/Blast.cgi) with GenBank accession number OM302143

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