**Abstract**

**Background:** Ochrobactrum spp. are non-fermenting, Gram-negative bacilli that are regarded as emerging human pathogens of low virulence that can cause infections. The first identified case of *Ochrobactrum intermedium* was reported in 1998 in a liver transplantation patient with liver abcess. There are no reports of infections in pediatric patients. Here, we report the first case of *O. intermedium* bacteremia in a pediatric patient.

**Case presentation:** A two and a half years old male was admitted with fever, chills and nausea. He had been diagnosed as pineoblastoma and underwent surgical resection and chemotherapy. *O. intermedium* was isolated from his blood cultures and identified by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS), however, the Vitek II automated system failed to identify the organism. Then the pathogen was confirmed by 16S rDNA sequencing and average nucleotide identity result (ANI) confirmed the precise identification of *O. intermedium* at genomic level. In addition, the patient recovered well after antibiotic combined therapy.

**Conclusions:** This, to our knowledge, is the first case of *O. intermedium* bacteremia in a pediatric patient with malignant tumor. Traditional biochemical identification methods such as API 20NE or VITEK2 system cannot differentiate *O. anthropi* and *O. intermedium*. MALDI-TOF may be a promising tool for rapid identification of microorganisms such as *O. intermedium*.

**Keywords:** Ochrobactrum, Ochrobactrum intermedium, Bacteremia, Pediatric patient

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**Background**

*Ochrobactrum* spp. belongs to the family *Brucellaceae* and it is widely distributed in the environment and clinical unit, such as soil, plant, water and indwelling catheters [1]. To date, there are 18 *Ochrobactrum* species with validly published names but only five of them, *O. anthropi*, *O. intermedium*, *O. haematophilum*, *O. pseudodogriignonense* and *O. pseudointermedium*, were isolated from clinical specimens [2]. *O. anthropi* is the most common species recovered from clinical samples, and a variety of infections, such as catheter-related bloodstream infection, peritonitis or endophthalmitis, could be caused by this pathogen [3]. Unlike *O. anthropi*, *O. intermedium* infections were rare and up to now, only nine cases of *O. intermedium* infection were reported, and they usually cause infections in adult patients with bacteremia, prostatic abscess, endophthalmitis and infective endocarditis [2]. Here, we report the first case of *O. intermedium* bacteremia in a pediatric patient with malignant tumor.

**Case presentation**

A two and a half years old male with fever was admitted to our hospital on August 2019. He had been diagnosed as pineoblastoma 7 months ago and underwent surgical...
resection and chemotherapy. He received a ventriculoperitoneal shunt for obstructive hydrocephalus 4 months ago. He presented with fever (up to 40.4 °C), chills and nausea 2 days before hospital admission. Physical examination did not reveal any significant findings except pharyngeal hyperemia and swollen tonsils. His breath and heart sounds were normal. No redness or swelling occurred at the peripherally inserted central catheter (PICC) site, which had been in indwelled for 6 months, and the catheter was flushed. Computed tomography, urine examination and cerebrospinal fluid were normal. His white blood cell count and C-reactive protein concentration were $17.6 \times 10^9/L$ (96.3% neutrophils) and 130.5 mg/L (Fig. 1). Three sets of blood cultures were collected from peripheral venipuncture at the beginning of the febrile period, then he was treated with cefoperazone/sulbactam. Two of the blood cultures were positive and the pathogens were identified as *Stenotrophomonas maltophilia* by MALDI-TOF MS (bioMérieux, Marcy-l’Étoile, France). Susceptibility testing showed the organism was susceptible to sulfamethoxazole-trimethoprim, minocycline, ceftazidime, levofloxacin, chloramphenicol, and ticarcillin/clavulanate. The antibiotic treatment was changed to the combination of cefoperazone/sulbactam and sulfamethoxazole—trimethoprim. Then the boy remitted and the body temperature dropped to normal range within 3 days since the treatment was adjusted. The white blood cell counts also returned to normal level and repeated blood cultures (collected from peripheral vein) were negative. However, on the 13th day, his temperature increased again with the highest point of 39.1 °C, and blood specimens were collected from two peripheral

**Fig. 1** Temperature, white blood cell count and the therapeutic schedule of the patient.
strain 045999 was susceptible to sulfamethoxazole–trimethoprim (bioMérieux) and interpreted according to the guidelines for other non-Enterobacterales in CLSI M100 (2019). The broth microdilution with the Vitek II automated system (bioMérieux) failed to identify strain 045999. Genomic DNA of strain 045999 was prepared using the QIAamp DNA mini kit (Qiagen; Hilden, Germany) and were subjected to whole genome sequencing using the HiSeq X10 Sequencer (Illumina; San Diego, CA, USA). For the whole genome sequence of strain 045999, 5,619,077 reads and 1.69 GB bases were generated (coverage, ×400), which were assembled into a 4.9 Mb draft genome contains 82 contigs ≥ 200 bp in length (N50, 454,256 bp) with a 57.71 mol% GC content. ANI between strain 045999 and the type strain LMG 3301T of O. intermedium (ACQA00000000) was determined using the JSpecies [4]. The ANI value was 97.57%, which was above the cutoff (≥ 95–96% ANI) defining the boundaries of bacterial species [5], confirming that the identification was precise. The same organisms were isolated from the other blood culture collected from right foot after 4 days incubation. Antimicrobial susceptibility testing was performed using broth microdilution with the Vitek II automated system (bioMérieux) and interpreted according to the guidelines for other non-Enterobacterales in CLSI M100 (2019). The strain 045999 was susceptible to sulfamethoxazole–trimethoprim, minocycline, tigecycline, cefepime, levofloxacin, meropenem, imipenem (Table 1). The strain 045999 formed beige, translucent, shiny and mucoid colonies on blood agar within 24 h of incubation and gram-staining indicated gram-negative, rod-shaped bacteria without spores. The antimicrobial susceptibility of the S. maltophilia was consistent with previous results. According to the results of susceptibility test, the S. maltophilia was susceptible to levofloxacin and ceftazidime, and strain 045999 was also susceptible to sulfamethoxazole–trimethoprim and levofloxacin. Therefore, cefoperazone/sulbactam was replaced with levofloxacin and ceftazidime, and sulfamethoxazole–trimethoprim was continued as before. One week after the treatment, blood cultures were obtained from both peripheral venipuncture and PICC. The blood culture obtained from PICC was positive with the growth of S. maltophilia and O. intermedium whereas the blood obtained from peripheral venipuncture was negative. Meanwhile, the PICC was removed and the culture was negative. Therefore, the therapy mentioned above was continued for 10 days, and the patient discharged after recovery.

**Discussion and conclusion**

Ochrobactrum spp. non-fermenting, Gram-negative bacilli are regarded as emerging human pathogens of low virulence that can cause infections not only in immunocompromised patients but also in human without underlying diseases [6]. Unlike O. anthropi, infection caused by O. intermedium is relatively rare. The first identified case of O. intermedium was reported in 1998 in a post-liver transplantation patient with a liver abscess, however, the microorganism was wrongly identified as O. anthropi by biochemical testing, and it was confirmed to be O. intermedium by PCR amplification of 16S rDNA gene [7]. But up to now, there were few reports about the O. intermedium infection. Based on our literature search in PubMed, only nine cases of O. intermedium infection were reported (Table 2). In the reported cases, O. intermedium causes various infections in immunocompromised patients, such as liver abscess, prostatic abscess, and infective endocarditis [7–9]. Moreover, there were two cases reporting that O. intermedium were responsible for causing endophthalmitis and pelvic abscess in immunocompetent hosts [10, 11]. In two cases, O. intermedium was isolated from fecal in patients suffering from either bacteremia or bacteremia associated

**Table 1** Antimicrobial susceptibility of the strain 045999

| Antimicrobial                  | MIC (mg/L) | Category | Antimicrobial                  | MIC (mg/L) | Category |
|-------------------------------|------------|----------|-------------------------------|------------|----------|
| Amikacin                      | 64         | R        | Imipenem                      | 1          | S        |
| Aztreonam                     | ≥ 64       | R        | Levofloxacin                  | 0.25       | S        |
| Cefepime                      | 4          | S        | Meropenem                     | ≤ 0.25     | S        |
| Cefoperazone/sulbactam<sup>a</sup> | 32        | I        | Minocycline                   | 1          | S        |
| Ceftazidime                   | 32         | R        | Piperacillin/tazobactam       | ≥ 128      | R        |
| Ciprofloxacin                 | ≤ 0.25     | S        | Tigecycline                   | 0.5        | S        |
| Colistin                      | 64         | R        | Tobramycin                    | ≥ 16       | R        |
| Gentamicin                    | 8          | I        | Sulfamethoxazole–trimethoprim | ≤ 1/19     | S        |

*S* susceptible, *I* intermediate, *R* resistant

<sup>a</sup> The breakpoint of cefoperazone instead of cefoperazone/sulbactam
with liver abscess, indicating that the gastrointestinal tract was possibly the source of infection [7, 12]. Of the nine cases, seven patients male (so do our case), five patients had bacteremia, two of whom were associated with catheters [2, 13]. O. anthropi infection is usually seen in immunocompromised patients with indwelling catheters, and catheter-related bacteremia is also most reported in immunocompromised children, especially among boys under 10 years old with malignancies [6, 14]. In the present case, similar to the O. anthropi bacteremia, O. intermedium bacteremia occurred in pediatric patient with PICC, who underwent chemotherapy and was immunocompromised. Compared to O. anthropi, O. intermedium infection is rare, and it is likely that some infections thought to be caused by O. anthropi may be actually caused by O. intermedium, since these species cannot be differentiated by traditional biochemical identification methods such as API 20NE or VITEK2 system leading to misidentification. Thus, the incidence of O. intermedium infection in human may be underestimated [6, 15]. In addition, O. intermedium may undergo an ecological niche specialization and some lineages may shift toward an adaption to the human host based on a phylogenomic approach [16]. In order to accurately identify O. anthropi and O. intermedium, molecular typing was recommended, however, it was more time-consuming and complicated compared with MALDI-TOF. In this case, the pathogen was initially identified as O. intermedium by MALDI-TOF, which was consistent with previous study [8, 13, 17]. ANI result confirmed the precise identification of O. intermedium at genomic level, indicating MALDI-TOF is a promising tool for rapid identification of O. intermedium in clinical situations, though more studies are required.

Ochrobactrum isolates were highly resistant to β-lactams, due to expression of AmpC β-lactamase, but they were mostly susceptible to levofloxacin, imipenem, ciprofloxacin, TMP-SMX and meropenem [6]. Susceptibility to colistin seems to be a potential marker for distinguishing between O. anthropi and O. intermedium, as O. anthropi is usually sensitive, whereas O. intermedium is usually resistant to this class of drugs [6]. In present case, S. maltophilia was isolated along with O. intermedium, indicating that it can cause polymicrobial infections in bloodstream infection (BSI), but O. anthropi seldom cause polymicrobial infections with other bacteria in BSI. Thus, the difficulty of treatment was increased. Catheter-related BSI was highly suspected in this case, but it was denied, because the blood culture obtained from PICC was positive, however, blood culture obtained from peripheral venipuncture and catheter culture were both negative. This is likely due to the use of antibiotics, therefore, the correct collection location, timing or times of blood sample play important roles in diagnosis of BSI infections [18]. Although both the two isolates were susceptible to sulfamethoxazole–trimethoprim, the combination treatment (levofloxacin, ceftazidime and sulfamethoxazole–trimethoprim) was used in our case and showed a good response.

In conclusion, here we reported the first case of O. intermedium bacteremia in a pediatric patient with malignant tumor. Infection caused by O. intermedium is uncommon, however, the incidence is probably being underestimated due to the difficult identification, and the clinical significance of O. intermedium remains unclear. Currently, the identification of O. intermedium is confirmed by molecular biological technique, however, this method may not be available in many clinical

Table 2 Case reports of O. intermedium infection

| Author/Year       | Age (year)/sex | Diagnose          | Underlying disease | Antibiotic regimen          | Prognosis | References |
|-------------------|---------------|-------------------|--------------------|-----------------------------|-----------|------------|
| Moller et al.1999 | 45/F          | Liver abscess     | Liver transplant   | CIP/metronidazole           | Improved  | [7]        |
| Apisarnthanarak et al./2005 | 74/M     | Bacteraemia       | Bladder cancer     | IPM/CIP                     | Improved  | [12]       |
| Vaidya et al./2006 | 49/M     | Pelvic abscess    | Non                | LVX/metronidazole           | Improved  | [11]       |
| Dharne et al./2008 | 26/M     | Non- ulcer dispepsia | Unknown         | Unknown                     | Improved  | [19]       |
| Jacobs et al./2013 | 34/M     | Endophthalmitis   | Vitrectomy, lensectomy, removal of intraocular foreign body | Intravitreal MOX | Improved  | [10]       |
| Rodriguez-Villores et al./2016 | 70/M    | Prostatic abscess | Bladder cancer     | CIP/cotrimoxazole           | Improved  | [8]        |
| Bharucha et al./2016 | 23/M    | Infective endocarditis | Renal failure     | MEM/MIN                     | Improved  | [9]        |
| Hirai et al./2016  | 86/M     | Bacteraemia       | Cerebral infarction | MEM                        | Improved  | [17]       |
| Kassab et al./2021 | 84/F     | Bacteraemia       | Primary sclerosing cholangitis | MIN           | Improved  | [13]       |
| Present case       | 2/M      | Bacteraemia       | Pineoblastoma      | LVX/CAZ/SXT                 | Improved  | –          |

*Abbreviations: CIP, ciprofloxacin; IPM, imipenem; LVX, levofloxacin; MOX, moxifloxacin; MEM, meropenem; MIN, minocycline; CAZ, ceftazidime; SXT, sulfamethoxazole–trimethoprim.*
laboratories. Instead, MALDI-TOF MS could be helpful in identifying O. intermedium.

Abbreviations
MALDI-TOF MS: Matrix-assisted laser desorption/ionization time-of-flight mass spectrometry; ANI: Average nucleotide identity result; CLSI: Clinical Laboratory Standards Institute; PICC: Peripherally inserted central catheter; BSI: Bloodstream infection.

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Authors’ contributions
WJW and LHK designed the study, analyzed the data, and wrote the manuscript. WZ, XXL and YMJ analyzed the data and reviewed the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials
The draft genome sequence of strain 045999 has been deposited into GenBank/DDBJ/EMBL under Accession number JABXOG00000000.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Written informed consent was obtained from the child’s parent for publication of this report and any accompanying images.

Competing interests
The authors declare no conflicts of interests.

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