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CASE REPORT

Emergence of a CTX-M-14- ESBL-Producing Multidrug-Resistant *Pasteurella multocida* from Human Bacteremia in China: A Case Report and Literature Review

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Abstract: *Pasteurella multocida* (*P. multocida*) bloodstream infections in humans without a history of animal bites are commonly associated with immunocompromise. Empirical therapy typically involves a β-lactam/β-lactamase inhibitor combination (eg, amoxicillin-clavulanate), but a small number of amoxicillin-clavulanate–resistant strains have been reported. Herein, we report a rare case of human *P. multocida* bacteremia in a patient with no history of animal bites. Antibacterial susceptibility testing showed the strain was sensitive to trimethoprim-sulfamethoxazole; resistant to erythromycin; and non-susceptible to azithromycin, levofloxacin, tetracycline, penicillin, ampicillin, amoxicillin-clavulanate and ceftriaxone. Whole-genome sequencing (WGS) confirmed the presence of CTX-M-14-type extended-spectrum β-lactamases (ESBLs). The potential emergence of multidrug-resistant (MDR) *P. multocida* may challenge the empirical treatment of the strain. This case highlights the necessity of studying the antibiotic susceptibility patterns of *P. multocida* in humans and animals, as well as the need for a One Health approach.

Keywords: *Pasteurella multocida*, extended-spectrum β-lactamases, ESBLs, multidrug-resistant, whole-genome sequencing, one health

Introduction

P. multocida is a small, gram-negative, facultative anaerobic coccobacillus that is highly prevalent in the digestive tract and oral cavity of many animal species.[1,2] The bacterium harbors various potential virulence factors, such as toxins, lipopolysaccharides, fimbriae, adhesins, iron-regulated acquisition proteins, hyaluronidase, and sialic acid metabolism pathways.[3] These factors can cause infections in diverse hosts, including livestock, wildlife, and humans.[4] Of the reported human cases of *P. multocida* infection, approximately 43% had no history of animal bites. Although many infections associated with animal bites are limited to soft tissues, the isolation of *P. multocida* from respiratory tract and bloodstream is more often associated with no animal bite.[5–7]

Most *P. multocida* infections can be traced to cat and dog bites. As previously documented, infections unrelated to animal bites are typically associated with bacteremia, severe comorbidities, advanced age, or immunocompromised states.[5] Most *P. multocida* isolates from humans are susceptible to penicillin and other antibiotics such as macrolides fluoroquinolones and tetracyclines.[2,6,8] Approximately 13% of strains are β-lactamase–positive, but the specific types of enzyme have been little studied.[5] Resistance to amoxicillin/clavulanate is extremely rare in human infections caused by *P. multocida*.[9,10] MDR *P. multocida* isolated from animals has been reported, but primarily involving resistance to ampicillin, macrolides, aminoglycosides, fluoroquinolones, and/or tetracyclines.[11–13] Here, we present a case of human bacteremia caused by *P. multocida* whose isolate was resistant or non-susceptible to penicillin, ampicillin, amoxicillin/clavulanate, and ceftriaxone. WGS revealed a chromosomally located $bla_{\text{CTX-M-14}}$. The strain was also resistant or non-susceptible to macrolides, quinolones, and tetracyclines.

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Case Presentation

An 88-year-old woman was admitted to a local hospital on October 25, 2024, following 7 days of dizziness, blurred vision, facial drooping, generalized weakness, and persistent abdominal distension and pain. Her medical history included hypertension, heart disease, cerebral infarction, and rheumatic diseases. On admission, a physical examination revealed bilateral crackles in the lungs. She had no cough, sputum, or fever (36.5°C), and no evidence of scratches or bite marks. The patient's cranial CT showed multiple lacunar infarcts in the bilateral basal ganglia, the left corona radiata, and the brainstem (some lesions are considered old). Laboratory tests showed leukocytosis (35.40×10^9/L), markedly elevated C-reactive protein (CRP; 315.2 mg/L; normal < 5 mg/L), anemia (hemoglobin 92 g/L; normal 110–150 g/L), and an increased erythrocyte sedimentation rate (116 mm/h; normal 0–15 mm/h). One set of blood cultures (aerobic and anaerobic) was obtained. An empirical treatment with intravenous cefoperazone-sulbactam was initiated. On the third day of hospitalization, small gram-negative coccobacilli were detected in both the aerobic and anaerobic blood culture bottles. The isolate was subcultured on blood and chocolate agar plates at 37°C and 5% CO_2. Small, non-hemolytic, gray colonies grew on both media. The bacterial strain was identified as *P. multocida* by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS1000, Antu). By the sixth day of hospitalization, the patient's leukocyte was 8.52×10^9/L and CRP level was 81.76 mg/L, indicating a favorable response to treatment, which was continued for 2 weeks. On the 14th day, her leukocyte count of 5.47×10^9/L and CRP < 5.0 mg/L. She was conscious with no other discomfort and was discharged.

Antibiotic Sensitivity Testing

Following the CLSI M45-Ed3 protocol,[14] broth microdilution and disk diffusion methods were used for antimicrobial susceptibility testing. Blood Mueller–Hinton agar plates supplemented with 5% sheep blood were used for disk diffusion, whereas a commercial susceptibility testing kit (Bio-Mérieux, France) was used for the broth microdilution method. All the plates were incubated at 35°C in ambient air. Each antibiotic susceptibility test was performed in duplicate. *Streptococcus pneumoniae* (ATCC 49619), *Escherichia coli* (ATCC 35218), and *Staphylococcus aureus* (ATCC 25923) were used as the quality control strains. Inhibition zones were measured after 18 hours. Inhibition zones of the strain were showed in Figure 1A–C. The results showed that the isolate was sensitive to trimethoprim–sulfamethoxazole (SXT), resistant to erythromycin (E), and non-susceptible to azithromycin (AZM), levofloxacin (LEV), tetracycline (TE), amoxicillin, amoxicillin/clavulanate (AMC), ceftriaxone (CRO), penicillin (P), and ampicillin (AMP; Table 1). Presently, no CLSI breakpoints are available for ceftazidime (CAZ), cefepime, piperacillin/tazobactam, Cefoperazone-sulbactam, meropenem (MEM), and imipenem (IPM); however, their MIC values are markedly low, suggesting good in vitro activity against the isolates.

ESBL Test

The ESBL test was performed in accordance with the CLSI M100.[15] The ceftazidime (CAZ) zone measured 29 mm, and the ceftazidime–clavulanate (CCV) zone measured 29 mm. The cefotaxime (CTX) zone measured 24 mm, while the cefotaxime–clavulanate (CTC) zone measured 31 mm. The 7 mm increase in the CTC zone in combination with CTC (Figure 1D) indicated that the strain was a CTX-M-type ESBL producer.[14]

Genome Sequencing and Analysis

Whole genome sequencing (WGS) was performed using the Illumina HiSeq 2500 and PacBio platforms. Raw reads were filtered using Skewer and Porechop (https://github.com/rrwick/Porechop) to remove low-quality sequences and adaptors, respectively. De novo assembly was performed using the SPAdes Genome Assembler v3.13.1 and Unicycler. Antimicrobial resistance genes were identified using the CGE server (https://cge.food.dtu.dk/services/) and Comprehensive Antibiotic Resistance Database (CARD).

The strain carried 13 antibiotic resistance genes (ARGs), including those conferring resistance to β-lactam drugs such as *Haemophilus influenzae (H. influenzae)* PBP3, $bla_{\text{CTX-M-14}}$ (located at positions 2,166,705–2,167,580; Figure 2), and $bla_{\text{OXA-1}}$. Additional resistance genes included *catP* (chloramphenicol acetyltransferase), *tetB, tetR, FosA3* (fosfomycin thiol transferase), e*rmT* (erm 23S rRNA methyltransferase), and aminoglycoside antibiotic inactivation genes, such as

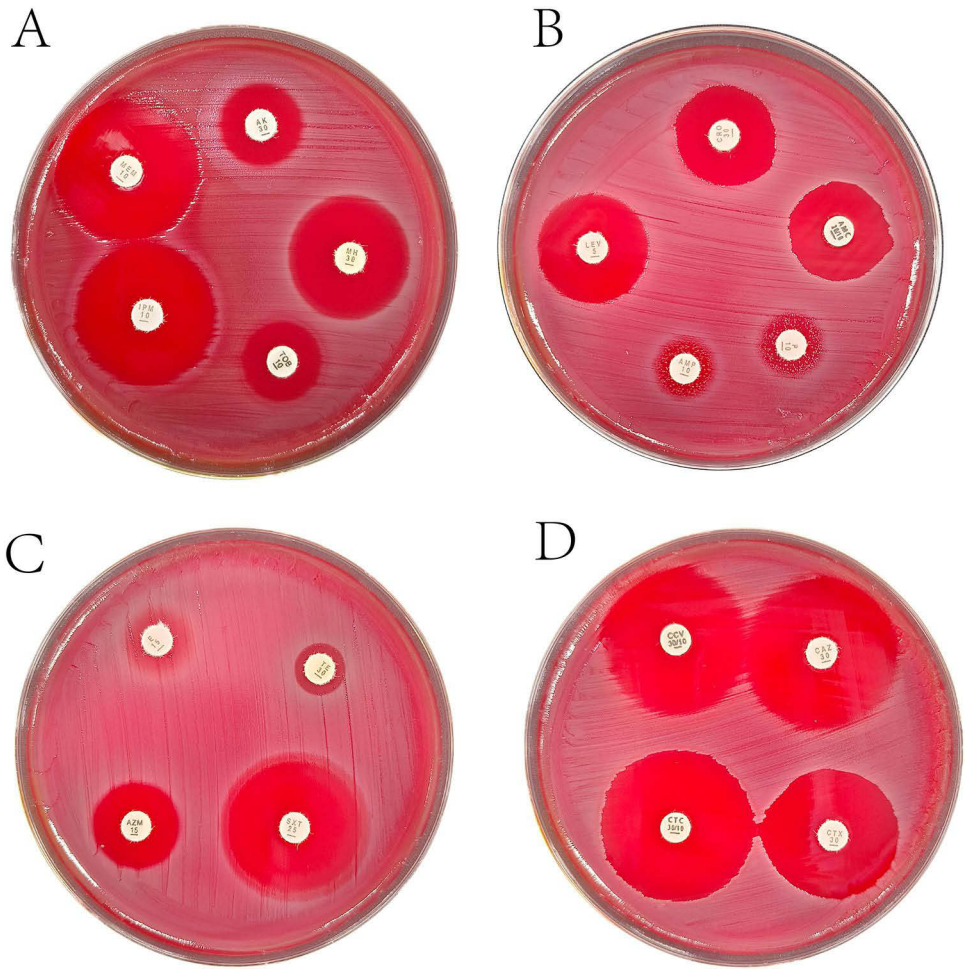

Figure 1 (**A**–**C**) Inhibition zones of *P. multocida* after incubating at 35°C for 24 hours. (**D**) Test for ESBL production.

APH(3′)-Ia, APH(3″)-Ib, APH(6)-Id, and aadA15. Mutations were also detected in *E. coli* EF-Tu (elfamycin-resistant EF-Tu). Notably, this region harbors the ESBL gene, $bla_{\text{CTX-M-14}}$.

Discussion

P. multocida is commonly found in the oropharynx and gastrointestinal tract of many animals, particularly cats and dogs, with carriage rates ranging from 70% to 90%.[5] Human infections are closely associated with exposure to animals. Rarely, *P. multocida*

Table 1 Drug Susceptibility of *P. Multocida* Determined by Broth Microdilution and Disk Diffusion Methods

Antibiotic Agent	MIC (μg/mL)	Inhibition Zone (mm)	Phenotype
Trimethoprim-sulfamethoxazole	≤ 10	28	S
Erythromycin		6	R
Azithromycin		17	NS
Levofloxacin	1	23	NS
Tetracycline		10	NS
Penicillin		6	NS
Ampicillin	≥ 32	10	NS

(*Continued*)

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Table 1 (Continued).

Antibiotic Agent	MIC (μg/mL)	Inhibition Zone (mm)	Phenotype
Amoxicillin/clavulanate		21	NS
Ceftriaxone	≥ 64	20	NS
Piperacillin/tazobactam	≤ 4/4	29	NBP
Cefoperazone-sulbactam	0.25/0.125		NBP
Ceftazidime	≤ 1	28	NBP
Cefepime	≤ 1	25	NBP
Meropenem	≤ 0.25	28	NBP
Imipenem	≤ 1	27	NBP

Abbreviations: S, Susceptible; R, Resistant; NS, non-susceptible; NBP, NO breakpoint.

bacteremia may develop in patients with underlying liver dysfunction or immunodeficiency following its spread from a localized bite wound, pneumonia, or arthritis.[6,16] In the present case, the patient had no history of an animal bite and the definitive route of infection remained obscure. Frequent exposure to domestic animals, however, increases the potential for indirect transmission. Given her advanced age (88 years) and multiple comorbidities (hypertension, cardiovascular disease, cerebral infarction, rheumatism, and anemia), she was likely in a immunologically vulnerable state. Based on these factors and prior reports, we speculate that the patient's immune status may have predisposed her to *P. multocida* bloodstream infection. Regrettably, only one set of blood cultures was obtained; nevertheless, considering the clinical presentation, laboratory findings, and the patient's favorable response to antibiotic therapy, *P. multocida* was considered the most likely pathogen.

Most *P. multocida* isolated from animals and humans are generally susceptible to commonly used antibiotics.[5] However, *P. multocida* strains resistant to penicillin, ampicillin, and amoxicillin–clavulanic acid have been reported, albeit infrequently.[9,10,17,18] Some resistance phenotypes have been attributed to plasmid-mediated ROB-1 and TEM-1 β-lactamases in *P. multocida* isolates, theβ-lactamases may originate from drug-resistant strains in animals or human-infected *H. influenzae* or *H. parainfluenzae* strains.[17,18] In our case, the isolate was non-susceptible to penicillin, ampicillin, amoxicillin–clavulanic acid, and ceftriaxone. ESBL testing indicated a CTX-type ESBL, and WGS confirmed the presence of chromosomally located $bla_{\text{CTX-M-14}}$, which can encode a CTX-M-14 β-lactamase. β-lactam antibiotics remain the most widely used antimicrobial class globally, and β-lactamases are a major resistance mechanism among Gram-negative bacilli.[19] CTX-M-type ESBLs are highly prevalent globally, and $bla_{\text{CTX-M-14}}$ is particularly widespread in China.[20] CTX-M-type enzymes typically exhibit strong cefotaximase activity—preferentially hydrolyzing cefotaxime/ceftriaxone and some penicillins and narrow-spectrum cephalosporins—but generally have lower activity against the bulkier molecule ceftazidime.[21] Consistent with this activity profile, the *P. multocida* isolate in this report was non-susceptible to ceftriaxone and showed a low MIC for ceftazidime. Although CTX-M enzymes are most often reported in *Klebsiella pneumoniae* and *Escherichia coli*, they can also be transferred to other Enterobacterales species, and non-fermenting bacteria.[19]

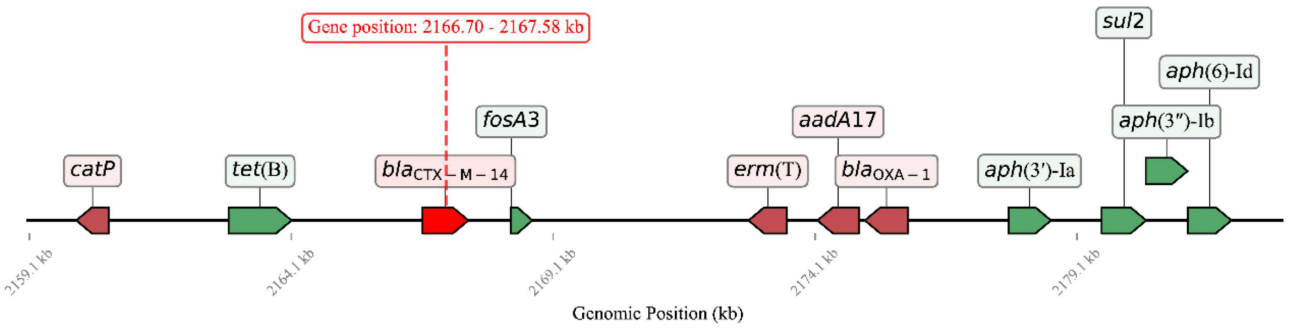

Figure 2 Linear alignment of $bla_{\text{CTX-M-14}}$ and its genomic context.

The MDR *P. multocida* isolate in this case was also resistant or non-susceptible to macrolides, fluoroquinolones, and tetracyclines. WGS identified several ARGs, including *catP, tetB, tetR, ermT*; the *tet* and *erm* genes likely explain reduced susceptibility to tetracyclines and macrolides, respectively, whereas *catP* is associated with chloramphenicol resistance. MDR *P. multocida* isolates from animals—showing phenotypic resistance to ampicillin, macrolides, aminoglycosides, fluoroquinolones, and/or tetracyclines—have been reported and are thought to result, at least in part, from the routine use of antibiotics in animal feed.[11–13,22,23] The increase in MDR microorganisms triggering infections is growing worldwide and becoming more serious in developing countries.[24,25] The emergence and dissemination of antibiotic resistance have been driven by inappropriate antibiotic use in humans, animals, and the environment. Although cross-species transmission of antibiotic resistance is relatively uncommon, it is difficult to distinguish whether a zoonotic infectious organism originated from foodborne sources or directly from humans and animals. Antibiotic resistance is therefore a key One Health issue.[26]

Human *P. multocida* infections are typically treated with penicillin; for β-lactamase–producing isolates, second- and third-generation cephalosporins, tetracyclines, and fluoroquinolones are commonly recommended.[5] Therefore, the isolation of a multidrug-resistant *P. multocida* in this case poses a significant challenge to existing empirical antimicrobial regimens and underscores the need for routine antimicrobial susceptibility surveillance of *P. multocida*. Moreover, clinical outcome from one case cannot establish treatment recommendations.

In conclusion, we report a case of *P. multocida* bacteremia in a patient without a history of animal bites. To the best of our knowledge, based on a comprehensive search of the literature and sequence databases (PubMed, Embase, Medline, Scopus, CNKI, and Wanfang) up to 13 January 2026, this is an infrequent case of a human clinical isolate of *P. multocida* in which a CTX-M-14 ESBL was identified and confirmed by WGS. The patient was successfully treated with cefoperazone-sulbactam. The limitations of this report include the use of a single set of blood cultures, the lack of source tracking for the resistant isolate, and the interpretive limitations of antimicrobial susceptibility testing for ESBLs in non-Enterobacterales organisms. Although the route of infection and the origin of the resistance gene remain unclear, this case highlights the necessity of routine antibiotic susceptibility testing of *P. multocida* isolates from humans and livestock. Because animal and human health, food/feed production systems, and the agricultural environment are all directly linked to antibiotic resistance, a multidimensional One Health approach is urgently needed to mitigate this global threat.

Data Sharing Statement

Data supporting the conclusions of this study are included in this published article.

Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of Guangzhou KingMed Diagnostics (the headquarter of Guangxi KingMed Diagnostics) (Approval No. 2025131). Institutional approval for conducting and publishing this case report was obtained from the Guangzhou KingMed Diagnostics (Approval No.KCLWFBSQ-20251020-0006), confirming that the clinical information and patient data could be disclosed in accordance with ethical standards. The studies were conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from the patient for the publication of any potentially identifiable images or data included in this article.

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Disclosure

The authors have no competing interests to declare in this work.

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