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CASE REPORT

A Case of *Weissella confusa* Isolated from Blood of a Patient with Coronary Heart Disease Complicated with Gastrointestinal Bleeding

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Introduction: *W. confusa* has been known to cause various human infections. It is naturally resistant to vancomycin and is difficult to identify using traditional methods, which may lead to misidentification and delay treatment.

Case Presentation: We present a case of a 42-year-old male patient with gastrointestinal bleeding and coronary heart disease who developed sepsis caused by *Weissella confusa*. The patient's blood cultures showed the presence of gram-positive coccobacilli, later identified as *W. confusa* through matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS). Antimicrobial susceptibility testing revealed that *W. confusa* had low minimum inhibitory concentrations (MICs) for some drugs (eg, ampicillin) and higher MICs for others (eg, cefotaxime). Empirical treatment with vancomycin was initially started, but after obtaining the identification and susceptibility results, the treatment was switched to meropenem combined with daptomycin, resulting in a successful outcome.

Conclusion: *Weissella confusa* bacteremia is relatively rare, and accurate pathogenic diagnosis is essential for effective clinical treatment.

Keywords: *Weissella confusa*, bacterial identification, 16S rRNA, matrix-assisted laser desorption/ionization time-of-flight mass spectrometry

Introduction

Weissella, a bacterial genus established in 1993 through 16S rRNA sequence analysis by Collins et al,[1] encompasses nearly 20 species. However, only three species, namely *Weissella confusa, Weissella cibaria, and Weissella viridescens*, have been isolated from humans.[2] Among these species, *Weissella confusa* is commonly found in fermented foods[3–7] and healthy animal feces,[8] and has been associated with various human infections such as bacteremia,[9,10] endocarditis,[11–13] and meningitis.[14] There is currently limited information that exists regarding *W. confusa* infections.

Therefore, in this report, we present a case of *W. confusa* bacteremia in a patient with gastrointestinal bleeding and coronary heart disease in China. By shedding light on this clinical case, we aim to enhance our understanding of the pathogenic potential of *W. confusa* and its implications for human health.

Case Presentation

A 42-year-old male patient with a history of hypertension for over 10 years and diabetes for more than a year was admitted to our hospital after experiencing tarry stools. Two weeks prior, he had been diagnosed with "coronary heart disease and acute exacerbation of chronic heart failure" at an external hospital due to dyspnea after activity. On admission, his vital signs were stable with a blood pressure of 124/65 mm Hg, pulse rate of 112/min, respiratory rate of 18/min, and a body temperature of 36.5°C. Further investigation revealed approximately 60% stenosis in the proximal

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segment of the left anterior descending artery, 80–90% stenosis in the middle segment, occlusion in the proximal segment of the circumflex artery, as determined by coronary angiography. Electrocardiogram (ECG) showed ST-T changes. Gastroscopy showed large duodenal bulb ulcer with bleeding and chronic non-atrophic gastritis.

On admission, laboratory tests indicated dark red stool color, positive fecal occult blood, peripheral blood white blood cell count of 12.35 × 10^9/L (Reference range: 3.5~9.5×10^9/L), neutrophil ratio of 70.20% (Reference range: 40~75%), hemoglobin level of 78 g/L (Reference range: 130~175g/L), hematocrit of 23.9% (Reference range: 40~55%), red blood cell count of 2.63 × 10^{12}/L (Reference range: 3.9~5.8× 10^{12}/L), glycosylated hemoglobin level of 6.36% (Reference range: 4~6%), blood troponin T level of 50 ng/L (Reference range: 0~14ng/L), N-terminal pro-brain natriuretic peptide level of 2251pg/mL (Reference range: 0~125pg/mL), high-sensitivity C-reactive protein level of 3.37 mg/L (Reference range: 0~3mg/L), calcitonin level of 0.07 ng/mL (Reference range: 0~0.046ng/mL), and interleukin-6 level of 18.3 pg/mL (Reference range: 0~7pg/mL). Around 24 hours after admission, the patient started to develop a fever. Within the past four hours, the body temperature increased from 37.7°C to 39.7°C. The procalcitonin level rose to 2.55 ng/mL, and interleukin-6 increased to 1462 pg/mL. The patient was diagnosed with sepsis. Blood samples were collected and inoculated into two sets of Bact/ALERT FA-Plus and FN-Plus bottles (bioMérieux Inc.) for culture. Gram-positive coccobacilli were isolated from 3 bottles (1 pair of FA-Plus and FN-Plus bottles and another FN-Plus bottle) within 48 hours of incubation at 35°C with 7% CO_2 (Figure 1). Gray-white and small-sized α-hemolytic colonies were observed on sheep blood agar (Figure 2). It was identified as "Unidentified organism" based on the gram-positive identification card of the Vitek 2 Compact systems (bioMérieux Inc.). The biochemical reaction profile is shown in the following figure (Figure 3). Then, the organism was identified as *Weissella confusa* through matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS, VITEK MS system, bioMérieux Inc.), with a coincidence rate of 99.9% (Figure 4). We conducted in vitro drug susceptibility experiments using both the disk diffusion method (using sheep blood Mueller–Hinton agar plates) and the microbroth dilution method. The disk diffusion method identified 11 antimicrobial drugs, such as ampicillin, with an inhibitory zone diameter of ≥20.0 mm, indicating potential higher sensitivity. On the other hand, 12 antimicrobial drugs, including cefazolin, showed inhibitory zone diameters ranging from 7.0 to 19.0 mm, suggesting relatively lower sensitivity. Additionally, 5 antimicrobial drugs, like cefoxitin, showed an inhibitory zone diameter of 6.0 mm, indicating potential lack of antibacterial activity. The results from the microbroth dilution method revealed that 7 antimicrobial drugs, including ampicillin, had lower MICs (<2μg/mL), while 8 antimicrobial drugs, such as cefotaxime, had higher MICs (≥2μg/mL) (Table 1).

Before the bacterial identification results were available, empirical treatment with vancomycin was initiated based on Gram staining results. The patient's temperature remained between 38.4~40°C, and procalcitonin increased to 8.7 ng/mL. Based on the identification results and drug susceptibility test results provided by the laboratory, the treatment was switched to meropenem combined with daptomycin. Two days later, the patient's temperature gradually decreased to

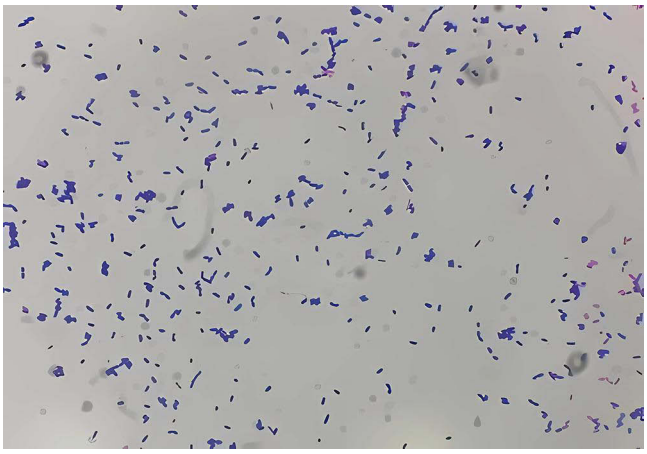

Figure 1 *Weissella confusa* Gram stain morphology from a sheep blood agar plate (×1000).

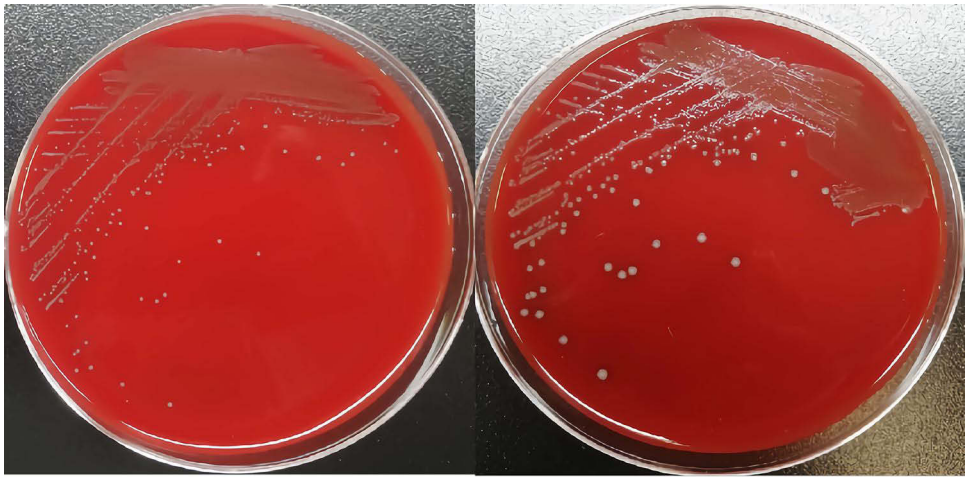

Figure 2 Colonies of *Weissella confusa* on a sheep blood agar plate grown at 35°C with 7% CO2 after 24hr (left) and 48hr (right) of incubation.

GP

2	+	AMY	4	-	PIPLC	5	+	dXYL	8	-	ADH1
9	-	BGAL	11	-	AGLU	13	-	APPA	14	-	CDEX
15	-	AspA	16	+	BGAR	17	-	AMAN	19	-	PHOS
20	-	LeuA	23	-	ProA	24	-	BGURr	25	-	AGAL
26	-	PyrA	27	-	BGUR	28	-	AlaA	29	-	TyrA
30	-	dSOR	31	-	URE	32	+	POLYB	37	+	dGAL
38	+	dRIB	39	-	ILATk	42	+	LAC	44	+	NAG
45	+	dMAL	46	+	BACI	47	+	NOVO	50	+	NC6.5
52	-	dMAN	53	+	dMNE	54	+	MBdG	56	-	PUL
57	+	dRAF	58	+	O129R	59	+	SAL	60	+	SAC
62	-	dTRE	63	+	ADH2s	64	+	OPTO			

Figure 3 Biochemical reaction spectrum of *Weissella confusa*.

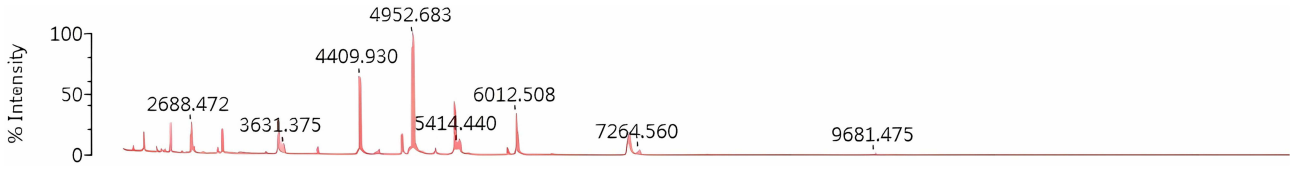

Figure 4 Mass spectrogram of *Weissella confusa*.

below 37°C, and procalcitonin decreased to 0.67 ng/mL. Additionally, the blood culture turned negative after 5 days of treatment.

Discussion and Conclusion

Weissella confusa is a gram-positive, facultative anaerobic, catalase-negative, α-hemolytic bacterium that can grow at temperatures ranging from 25°C to 45°C.[1,9,15] However, identification of this bacterium can be challenging using traditional phenotypic methods, which are known to yield inaccurate results.[16,17] In our laboratory, we also experienced difficulty in identifying *Weissella confusa* using biochemical methods. Molecular DNA sequencing methods, such as 16S rRNA sequence analysis, have been shown to be highly accurate for identifying *Weissella confusa* to the species level.[17] Apart from DNA sequencing technology, a study from Lebanon reported the use of PCR technology targeting the 16S rRNA gene to co-identify *Campylobacter jejuni* and *Campylobacter coli*. By amplifying the hippuricase gene specific to *C. jejuni* and the aspartokinase gene specific to *C. coli* using specific primers, and observing the PCR products on agarose gel, the identification of *Campylobacter* species was achieved.[18] This provides a promising approach for differentiating *Weissella confusa*, which can be further explored and validated for molecular identification of *Weissella confusa* using

Table 1 Antimicrobial Susceptibilities of *Weissella confusa*

Antibiotic	Diameter of Inhibition Zone (mm)	MIC (ug/mL)
Imipenem	30	/
Piperacillin/Tazobactam	26	/
Meropenem	25	/
Erythromycin	24	≤0.25
Ampicillin	24	≤0.25
Linezolid	23	2.0
Clindamycin	23	≤0.12
Cefoperazone/sulbactam	21	/
Cefuroxime	21	/
Ampicillin/sulbactam	20	/
Tetracycline	20	4
Cefepime	19	/
Amikacin	19	/
Minocycline	19	/
Chloramphenicol	19	4
Penicillin	18	1.0
Ceftriaxone	17	/
Cefazolin	16	/
Cefotaxime	16	2
Ciprofloxacin	16	/
Gentamicin	16	≤0.5
Levofloxacin	15	2
Moxifloxacin	/	0.5
Ceftazidime	9	/
Oxacillin	6	/
Vancomycin	6	≥256
Sulfamethoxazole/trimethoprim	6	≥2/38
Cefoxitin	6	/
Teicoplanin	6	≥32
Rifampicin	/	≥32

Note: "/" was not tested.

16S rRNA gene PCR technology. Additionally, matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) can also accurately identify *Weissella confusa*.[5,10] In our laboratory, we were able to identify *Weissella confusa* using the VITEK MS v2.0 database, which includes this species and provides reliable identification results. In conclusion, *Weissella confusa* is often difficult to accurately identify using traditional phenotypic methods. Molecular DNA sequencing and MALDI-TOF MS are more reliable methods for identifying this bacterium.

Weissella confusa is considered an opportunistic pathogen and a normal inhabitant of the human gastrointestinal tract.[16] Reports of human infections caused by *Weissella confusa* have primarily involved immunocompromised patients, such as those undergoing liver transplantation, joint replacement, hematopoietic stem cell transplantation, or suffering from multisystem diseases and multiple bacterial infections.[9,17,19] Risk factors for *Weissella confusa* infection include chemotherapy, organ transplantation, burns, chronic alcoholism, long-term use of corticosteroids, chronic kidney disease, and diabetes. Studies have suggested that surgical-induced gastrointestinal barrier damage may also be a susceptible factor for *Weissella confusa* infections, leading to sepsis and endocarditis.[12,13] Our laboratory isolated *Weissella confusa* from the peripheral blood of patients with coronary heart disease complicated with gastrointestinal bleeding, the patient had chronic heart failure, diabetes, which can cause immunocompromise, who also had duodenal bulb ulcer and bleeding, chronic non-atrophic gastritis, which can cause damage to the gastrointestinal barrier, these factors may be the cause of *Weissella confusa* bacteremia in the patient. While *Weissella confusa* has been identified as an opportunistic

pathogen in immunocompromised patients and those with certain underlying conditions, further research is needed to better understand the risk factors and potential routes of infection for this bacterium. The findings of our laboratory suggest that *Weissella confusa* may be a potential pathogen in patients with compromised immune function and gastrointestinal barrier damage, who may be at a higher risk for developing bacteremia. Therefore, clinicians should consider the possibility of *Weissella confusa* infection in these patients and use appropriate diagnostic methods for accurate identification and timely treatment.

It is known that the *Weissella* genus is naturally resistant to vancomycin, but its sensitivity to other antibiotics is not fully understood, and there is currently no standardized method and breakpoints for drug susceptibility testing. Kamboj et al[2] summarized the drug susceptibility results of previous reports using broth dilution, agar dilution, and E-test methods, which showed that this bacterium has low MICs for most antibiotics such as penicillin and ampicillin, but high resistance levels to cefotaxime, levofloxacin, metronidazole, teicoplanin, and imipenem/meropenem. Currently, there are no relevant reports on disk diffusion method for drug susceptibility testing of this bacterium. In this study, we attempted to utilize the disk diffusion method and microbroth dilution method for conducting drug susceptibility testing on isolated strains. We discovered that this particular strain exhibited antibacterial activity against a majority of antibiotics, such as ampicillin, in vitro. However, it demonstrated resistance to five antibiotics, including teicoplanin. However, it should be noted that this bacterium does not grow on ordinary Mueller–Hinton agar plates. When we used Mueller–Hinton agar plates for disk diffusion method drug susceptibility testing, no bacterial growth was observed on the agar plates after 24 hours and even after 48 and 72 hours of incubation, suggesting that further exploration and standardization of drug susceptibility testing methods for this bacterium are needed.

The importance of accurate identification of *Weissella confusa* cannot be overstated, as it is often misidentified using traditional methods, leading to delay in appropriate treatment. In this study, mass spectrometry was used for accurate identification of the isolated strain, which can serve as a reference for other laboratories. Furthermore, it is essential to note that empirical treatment with vancomycin based on Gram staining results was ineffective, and a switch to meropenem combined with daptomycin was successful in eliminating the bacteremia.

In conclusion, this study provides useful insights into the identification and drug susceptibility testing of *Weissella confusa*. The findings highlight the need for a standardized method for drug susceptibility testing and caution against the use of vancomycin in empirical treatment of suspected *Weissella* infections. The results of this study can be used to guide appropriate treatment of *Weissella* infections and contribute to the development of standardized diagnostic and treatment protocols.

Data Sharing Statement

All data and materials used in this study are provided within the manuscript. No additional data or materials are available.

Ethics Approval and Consent to Participate

This study was approved by the ethical review committee of the Wuhan Asia General Hospital Affiliated to Wuhan University of Science and Technology. Written informed consent was obtained from patients in accordance with the Declaration of Helsinki.

Consent for Publication

The patient of this report had already agreed and signed the consent form.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically

reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that the research was conducted in the absence of any commercial relations or financial relationships of interest that might be a constant of interest.

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