

Review

Weissella Infections in Varied Clinical Contexts: Three Case Reports and A Literature Review

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Abstract Purpose: Weissella species represent a noteworthy group of opportunistic pathogens, yet investigative efforts into their connection with human infections are relatively limited. Improving the documentation, compilation, and evaluation of infections caused by Weissella will contribute to the advancement of diagnostic techniques, therapeutic interventions, and preventative measures against these infections.

Methods: Three case reports and a systematic literature review were conducted to investigate the risk population, clinical manifestations, treatment options and prognosis of Weissella infection.

Results: Three patients exhibited unique clinical presentations of Weissella infection, manifesting as biliary tract infection, heat stroke complicated by polymicrobial infections, and an esophagopleural fistula. A systematic review of the literature revealed the infrequency of Weissella-related infections, common sites of infection, identified populations at elevated risk, and highlighted efficacious therapeutic strategies. Notably, the present study constitutes the first documented instance of a human infection caused by Weissella viridescens, thereby expanding the current understanding on the pathogenic potential of this bacterial genus.

Conclusions: Weissella genus are considered important opportunistic pathogens, particularly among individuals with compromised immune function. Prompt identification and the administration of effective anti-infective treatments are crucial for enhancing patient outcomes. Future research endeavors should aim to elucidate the pathogenic mechanism and epidemiological characteristics of Weissella spp., as well as to develop standardized protocols for its management, thereby facilitating a more profound comprehension of this emergent pathogen.

Keywords: Weissella infections; Opportunistic pathogens; Compromised immune function

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Introduction

Weissella spp. is a group of Gram-positive, non-spore-producing, acidophilic bacteria under the order Lactobacillales. It is widely distributed in nature, especially in naturally fermented foods, and can be present in the digestive system of humans. To date, the Weissella genus has been delineated to encompass approximately thirty distinct species, including Weissella confusa, Weissella cibaria, Weissella paramesenteroides, Weissella viridescens, Weissella halotolerans, Weissella minor, etc.. While the majority of Weissella species are considered innocuous to

the human host, and may even confer health benefits, particularly in the context of probiotic applications, the pathogenic potential of these bacteria has been increasingly acknowledged over recent decades[1,2]. Notably, they have been implicated in a spectrum of pathological conditions, predominantly in individuals with compromised immune systems, with potential manifestations ranging from severe infections such as sepsis and endocarditis[3,4].

The objective of this research was to explore the population at risk, clinical manifestations, diagnostic strategies, therapeutic interventions, and prognostic

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outcomes of *Weissella* infection, by analyzing three clinical case reports and conducting a literature review. The goal was to enhance understanding of this uncommon pathogen and provide recommendations for future clinical practice based on the findings.

Methods

2.1. Methods of Case Selection and Analysis

2.1.1 Case Selection Process

Data Source: This study conducted a retrospective analysis of cases identified from May 11, 2018, to January 31, 2024, utilizing the electronic medical records system of our institution.

Inclusion Criteria: The research encompassed patients from whom *Weissella* spp. was isolated in cultures derived from blood, bodily fluids, tissues, or internal catheters. Only subjects with comprehensive clinical documentation, including medical history, clinical presentations, results of laboratory and imaging evaluations, treatment modalities, and follow-up outcomes were considered.

Exclusion Criteria: Any cases presenting with ambiguous diagnoses or lacking integral data were systematically excluded from the study.

2.1.2 Methods of Case Analysis

Data Collection: Patient information, including age and gender, as well as clinical data, such as medical history, clinical presentation, auxiliary examination result, treatment, and prognosis, were collected for each selected case.

Data Analysis: A descriptive analysis was performed on the history, clinical manifestation, treatment, and prognosis of the cases, and the characteristics of *Weissella* infection were summarized.

2.2. Methods of Literature Review

2.2.1 Search Strategy: The keywords "Weissella" and "Weissella infection" were defined, and the Boolean operation "AND" and "OR" combined with keywords were used to conduct literature search in PubMed, Web of Science and Scopus databases. No time limit was set for this search to ensure inclusion of all relevant literature. The deadline for the last search was January 31, 2024.

2.2.2 Data Collection and Analysis: The fundamental information and clinical data of the chosen cases were gathered and subjected to a descriptive analysis in order to elucidate the characteristics of *Weissella* infection.

2.2.3 Criteria for Inclusion and Exclusion

The Inclusion Criteria: Eligibility for this investigation was confined to case reports, case series analyses, and both retrospective and prospective studies specifically addressing infections, pathogenic mechanisms, and therapeutic responses associated with *Weissella* spp..

The Exclusion Criteria: Literature not written in English, conference abstracts, and duplicate studies.

Case Reports

Case 1

A 25-year-old woman was admitted to the hospital with a history of intermittent epigastric pain and fever that had persisted for over 20 days, with an absence of notable medical history prior to admission. Upon admission, her vital signs remained stable, and abdominal palpation disclosed neither significant or rebound tenderness. Diagnostic imaging, including abdominal ultrasonography and MRI, identified intrahepatic bile duct calculi, cholelithiasis, and dilation of the proximal common bile duct containing multiple calculi. Consequently, the patient was diagnosed with hepatolithiasis and cholelithiasis. On

the second day of her hospital stay, the patient underwent Oddi sphincterotomy, endoscopic retrograde cholangiopancreatography (ERCP), balloon dilatation with lithotomy, and endoscopic nasobiliary drainage (ENBD). Subsequent bile culture post-operation showed *Weissella confusa* infection, achieving a colony count of +++ level, but no antimicrobial susceptibility test was conducted. The therapeutic regimen included administration of latamoxef sodium, dosed at 2 grams BID. Following the administration of anti-infective therapy, a laparoscopic cholecystectomy was performed on the fourth day of admission. The anti-infective treatment extended over a five-day period, and then the patient recovered and subsequently discharged from the hospital.

Case 2

A 45-year-old man with no prior medical history was urgently admitted to the hospital following a loss of consciousness and collapsed, accompanied by dyspnea and excessive perspiration, after completing a 6-kilometer segment of a marathon. Upon presentation, the patient exhibited a temperature of 38.1°C, tachycardia with a heart rate of 135 beats per minute, a respiratory rate of 23 breaths per minute, an oxygen saturation of 98%, and a blood pressure reading of 112/57 mmHg. He was in an unconscious state, with bilateral pupils measured at 3.5 mm exhibiting diminished light reflexes. Cardiac and pulmonary auscultation disclosed no remarkable abnormalities and the abdomen was found to be soft and non-tender upon palpation, and no lower limb edema was noted. Routine hematological assessment revealed an elevated white blood cell count of $11.45 \times 10^9/L$, and the proportion of neutrophils was 39.0%. Biochemical tests indicated abnormal levels, including troponin I at 0.0560

ng/mL, myoglobin at 361.20 ng/mL, and lactic acid at 16.50 mmol/L. Additional parameters demonstrated serum creatinine at 149.34 $\mu\text{mol/L}$, aspartate aminotransferase at 51.62 U/L, alanine aminotransferase at 65.40 U/L, and plasma osmolality recorded at 317 mmol/L. Microbiological investigations confirmed the presence of *Weissella viridescens* and *Staphylococcus hominis* in blood cultures. Next-Generation Sequencing (NGS) analysis of bronchoalveolar lavage fluid revealed a microbial spectrum consisting of *Enterococcus faecalis*, *Staphylococcus epidermidis*, *Staphylococcus hominis*, *Enterobacter cloacae* complex, *Haemophilus influenzae*, *Klebsiella pneumoniae*, *Candida albicans*, and *Candida albicans*. CT imaging of the cranial, thoracic, and abdominal regions, showed that hypostatic pneumonitis within the dorsal inferior lobes of both lungs and no significant abnormalities were identified in other examined areas. Considering the patient's etiological evidence and clinical manifestations, a diagnosis was established of heat stroke with concurrent polymicrobial infections.

Initially, the patient received empiric antimicrobial therapy with piperacillin-tazobactam and vancomycin. Based on subsequent bacteriological findings indicative of *Weissella viridescens* infection, the antimicrobial strategy was revised to include meropenem, teicoplanin, and caspofungin. Concomitantly, the patient was provided with comprehensive supportive care encompassing respiratory and circulatory stabilization, thermoregulation, cerebral protection, anticonvulsant treatment, continuous renal replacement therapy (CRRT), hepatic support, reduction of serum ammonia levels, suppression of gastric acid and enzymatic secretion, and transfusion of blood components. Following the intervention, there was a gradual amelioration of the patient's infectious condition, with

subsequent restoration of normal organ functions and he was successfully discharged after 20 days of treatment.

Case 3

A 69-year-old man with a medical history notable for type 2 diabetes mellitus (T2DM), depression, and Parkinson's disease, was admitted to the hospital due to acute respiratory distress that emerged approximately 12 hours earlier. It was reported that preceding the dyspnea, the patient experienced an episode of vomiting, which contained coffee-ground-like material, and had one instance of passing black stools. Upon admission, the patient exhibited a temperature of 37.8°C, tachycardia with a heart rate of 165 beats per minute, hypotension with blood pressure recorded at 80/59 mmHg, a respiratory rate of 30 breaths per minute, and an oxygen saturation level of 88%. The patient was clinically diagnosed with severe pneumonia, respiratory failure, and acute gastrointestinal hemorrhage. Endotracheal intubation was performed, followed by the initiation of mechanical ventilation support. An indwelling nasogastric tube facilitated the extraction of a substantial volume of coffee-brown fluid. Thoracic CT imaging showed a substantial fluid pneumothorax on the left side and extensive bilateral pulmonary inflammatory changes. Subsequent to emergent thoracentesis and catheter insertion, a copious volume of coffee-colored fluid was evacuated. Analysis of the pleural effusion identified polymicrobial infections, including *Weissella confusa*, *Limosilactobacillus fermentum*, *Candida albicans*, and *Acinetobacter baumannii* complex. In light of the severe polymicrobial infections identified, a therapeutic regimen comprising meropenem and caspofungin was initiated for anti-infective management. Due to the identification of *Weissella confusa* in the pleural effusion, which frequently

encountered in fermented food or the human gastrointestinal tract, and the presence of a diverse bacterial flora within the pleural fluid, coupled with the patient's potential for gastrointestinal hemorrhage, further gastroscopy was undertaken, revealing an esophagopleural fistula. Subsequent interventions included video-assisted thoracoscopic surgery for drainage of the empyema, insertion of a drainage tube, and daily pleural lavage. Concurrently, therapeutic management continued with meropenem and caspofungin. After a ten-day treatment period, the patient demonstrated clinical improvement, the continuation of meropenem as monotherapy was continued for an additional seven days, and the extension of piperacillin sodium tazobactam was continued for fourteen days. Subsequent to these interventions, the patient's condition ameliorated significantly, leading to a successful discharge from the hospital.

Literature Review

In this systematic literature review, a total of seventeen published articles were identified and analyzed, encompassing a cohort of twenty-seven patients diagnosed with *Weissella* spp. infection. (Table 1)

Table 1. Literature reports on *Weissella* infections

First author publication year	Sex, age (years)	Underlying condition	TPN	CVC	Infection type	Species	Co-infection	outcome
Lee 1997-2007[3]	F, 58	NHL	U	Yes	Bacteremia	confusa	Yes	Died
	M, 68	COPD, Pneumonia	Yes	Yes	Bacteremia	confusa	No	Died
	F, 62	B-cell Lymphoma	U	Yes	Bacteremia	confusa	Yes	Died
	F, 92	CRF, Vascular dementia	U	U	Bacteremia	confusa	No	Died
	F, 27	Goiter, Ankylosing spondylitis	U	U	Bacteremia	confusa	Yes	Survived
	F, 62	CRF, NSTEMI, ISBODI	Yes	Yes	Bacteremia	confusa	No	Died
	M, 73	Malignant peritonitis, Asphyxia	Yes	Yes	Bacteremia	confusa	Yes	Died
	M, 52	Esophageal cancer	U	Yes	Bacteremia	confusa	No	Survived
	F, 8	Intestinal obstruction	Yes	U	Bacteremia	confusa	No	Survived
M, 64	SAH	U	U	Bacteremia	confusa	Yes	Survived	
Flaherty 2003 [4]	M, 49	TM, Alcoholism, Drink lots of milk	U	U	Endocarditis, Bacteremia	confusa	No	Died
Medford 2014[5]	F, 94	Osteoarthritis	U	U	Knee prosthesis infection	confusa	Yes	U

Cheatio2020[6]	M, 78	Stroke, AD, T2DM, CAD, Pneumococcal meningitis, Bile duct stones, Intrahepatic bile duct stent insertion and cholecystectomy	U	U	Meningitis	confusa	No	Survived
Wang2023[7]	M, 42	CAD, CHF, GIB, Hypertension, DM	U	U	Bacteremia	confusa	No	Survived
Hunt2021[8]	M, 63	T2DM, Hypertension, Hypercholesterolemia, CMVD	U	U	Endocarditis	confusa	No	Survived
Azim2023[9]	M, 11	AP, ARDS	U	U	Bacteremia	confusa	Yes	Survived
Spiegelhaer2020[10]	M, 25	Crohn's disease, Short bowel	Yes	Yes	Bacteremia	confusa	Yes	Survived
Shin2007[11]	M, 65	Aortic valve insufficiency, Angina pectoris	U	U	Endocarditis	confusa	No	Survived
Harlan2011[12]	M, 54	HCC, HAT, Fatty liver	U	U	Bacteremia	confusa	No	Survived
Olano2001[13]	M, 46	Abdominal aortic dissection surgery, Short bowel	Yes	Yes	Bacteremia	confusa	Yes	Survived
Wijampreecha2022[14]	M, 65	Alcoholic cirrhosis	U	U	Endocarditis, Bacteremia	confusa	No	Died

Massasati 2023[15]	F, 92	Heart valve replacement, HF, AF, CKD, Hypothyroidism, Lumbar fusion	U	U	Prosthetic bioinfectious	confusa	No	Survived
Fairfax 2014[16]	M, 34	ALL, Allo-HSCT	U	Yes	Bacteremia	confusa	No	Survived
	M, 58	Second to third-degree burning	U	Yes	Bacteremia	confusa	Yes	Survived
Kumar2011[17]	M, 48	AEG, Esophago-gastric resection	Yes	U	Bacteremia	confusa	No	Survived
Lee2013[18]	F, 60	Hypertension, Thoracic and abdominal aortic subintimal hematoma	U	U	Bacteremia	confusa	No	Survived
Sevc2007[19]	M, 4	Peritoneal neuroblastoma, Chemotherapy, Intestinal obstruction	U	U	Bacteremia	confusa	No	Survived

M: male; F: female; U: unknown; TPN: total parenteral nutrition; CVC: central venous catheter; NHL: non-Hodgkin's Lymphoma; COPD: chronic obstructive pulmonary disease; CRF: chronic renal failure; NSTEMI: non-ST-segment elevation myocardial infarction; ISBODI: ischemic bowel disease; SAH: subarachnoid hemorrhage; TM: transverse myelitis; AD: Alzheimer's disease; CAD: coronary artery disease; CHF: chronic heart failure; GIB: gastrointestinal bleeding; DM: diabetes mellitus; CMVD: congenital mitral valve disease; AP: acute pancreatitis; ARDS: acute respiratory distress syndrome; HCC: hepatocellular carcinoma; HAT: hepatic artery thrombosis; HF: heart failure; AF: atrial fibrillation; CKD: chronic kidney disease; ALL: acute lymphoblastic leukemia; Allo-HSCT: allogeneic hematopoietic stem cell transplantation; AEG: adenocarcinoma of the esophago-gastric junction.

In this review, the age range of patients infected with *Weissella* ranged from 4 to 94 years, with 48.15% (n=13) aged above 60 years old. The demographic distribution demonstrated a predominance of male patients, accounting for 66.67% (n=18), compared to the female patients. Predominantly, the infections manifested as bacteremia, accounting for 74.07% (n=20) of instances, succeeded by endocarditis at 18.52% (n=5), with isolated occurrences of osteoarthritis and meningitis each representing 3.70% (n=1). Notably, up to 81.48% of the patients (n=22) were immunocompromised, including malignant tumors (29.63%, n=8), prolonged corticosteroid usage, chronic renal failure, diabetes mellitus (each 14.81%, n=4), as well as liver cirrhosis and burns (each n=1). In the case report presented, infections of the biliary tract and thorax were not documented in prior literature. Patients who had

undergone central venous catheter implantation and receiving prolonged total parenteral nutrition represented 37.04% (n=10) and 25.93% (n=7) of the cohort, respectively. It is suggested that individuals with compromised immune function, those with central venous catheters, or those undergoing total parenteral nutrition may exhibit an elevated risk of infection. Co-infection with additional microorganisms was prevalent, accounting for approximately one-third of the patients (n=9), involving a variety of microorganisms, such as *Acinetobacter baumannii*, *Enterobacter cloacae*, and *Candida albicans*. This suggests that *Weissella* infection may frequently occur in conjunction with multiple microorganisms. Two case reports from our series were accompanied by multiple microbial infections, thereby reinforcing this concept. Except for three individuals who declined intervention, the others received antimicrobial therapy, including agents such as cephalosporin, meropenem, teicoplanin, peracillin-tazobactam, amoxicillin, clavulanate potassium, and daptomycin. Post-therapeutic outcomes were favorable for the majority of the patients, nonetheless, a mortality rate approaching 30% (n=8) was observed. Furthermore, several case reports highlighted that patients had ingested readily fermented food items, such as pickled vegetables and dairy products, before the onset of the disease.

In the past, *Weissella* was frequently misclassified as *Lactobacillus* spp. or lactobacillus-like organisms through conventional diagnostic approaches[1]. However, DNA sequencing technologies, notably analysis of the 16S rRNA gene sequences, can accurately identify *Weissella* at the species level, establishing this method as the gold standard for diagnosing *Weissella* infections. At present, Matrix-Assisted Laser Desorption/Ionization Time-of-Flight Mass Spectrometry (MALDI-TOF MS) has

proven to be effective in identifying *Weissella* species, albeit with certain constraints. It is necessary to enrich the database with an expanded spectrum of *Weissella* strains to enhance the precision of microbial identification[2].

The majority of patients achieve favorable prognoses after receiving aggressive treatment. Nonetheless, our collected data indicate a mortality rate associated with *Weissella* infections reaching 30%. Investigation reveals that these fatalities were attributable to the coexistence of complex, severe comorbidities and immunocompromised conditions. This indicates that the elevated mortality rate can be ascribed not solely to *Weissella* infections but to the synergistic effects of underlying health issues.

Discussion

Weissella species are widespread in the environment, yet the exploration of their role as potential pathogens in humans is a relatively novel field. In recent years, they have been identified as naturally resistant to vancomycin [2]. Our case report, complemented by a comprehensive literature review, revealed that *Weissella* spp. is capable of causing a diverse array of infections. Predominantly, the susceptible hosts are individuals with compromised immune systems, especially those suffering from diabetes or oncological conditions. Prolonged total parenteral nutrition and the presence of central venous catheters may further increase the risk of *Weissella* infection. However, it is essential to acknowledge that infections may also occur in individuals with intact immune systems. This is exemplified by Case 1 in our series, involving a previously healthy young patient who developed an infection. This underscores the necessity for vigilance regarding natural resistance to vancomycin, even among immunocompetent patients, when gram-positive cocci are identified in

cultures. Furthermore, our literature review has identified a potential association between *Weissella* infection and dietary habits. Although this relationship needs further investigation, it is suggested that dietary histories, particularly concerning the consumption of fermented foods and probiotics, be meticulously documented in patients diagnosed with *Weissella* infections. This could help identify the potential sources of infection and pathways of transmission. In terms of treatment and prognosis, the majority of individuals infected with *Weissella* exhibit favorable prognoses following appropriate antibiotics. However, it is important to note that there exists a mortality rate of up to 30% among these patients. In patients who respond favorably to therapy, the antibiotic regimen commonly comprises amoxicillin-clavulanate potassium, piperacillin-tazobactam, meropenem, daptomycin, metronidazole, cefoperazone-sulbactam sodium, gentamicin, teicoplanin, and meropenem. Conversely, for patients exhibiting treatment failure, antimicrobial strategies often incorporate vancomycin, ceftazidime, ampicillin-sulbactam, among others. In Case 2, initial antimicrobial therapy constituted piperacillin-tazobactam and vancomycin, subsequently revised to a regimen of meropenem, teicoplanin, and caspofungin, following which the patient exhibited gradual amelioration of the infection. In Case 3, the patient received antimicrobial treatment with meropenem and caspofungin, with subsequent de-escalation to piperacillin-tazobactam, achieving a good outcome. In Case 1, a young female patient with a biliary tract infection was treated surgically with a successful anti-infective regimen of ceftriaxone alone.

Prior research has predominantly focused on *Weissella confusa*, with instances of *Weissella viridescens* emerging

infrequently in clinical settings. This case report represents the initial documentation of *Weissella viridescens* infection in humans, thereby expanding our understanding of the pathogenic capabilities within the *Weissella* genus. The clinical manifestations and therapeutic responses of *Weissella viridescens* appear to be similar to those associated with *Weissella confusa*. This discovery not only enhances our understanding of the pathogenic potential of *Weissella* but also highlights the importance of advanced molecular diagnostic techniques in clinical microbiology. Conventional bacterial culture and identification may not be able to differentiate among *Weissella* species, thus precise species identification is essential for understanding the pathogenic mechanism of pathogens, formulating efficacious therapeutic strategies, and prognosticating clinical outcomes.

Conclusion

In conclusion, *Weissella* species represent a noteworthy group of opportunistic pathogens, yet academic interest and investigative efforts into their connection with human infections are relatively limited. Improving the documentation, compilation, and evaluation of infections caused by *Weissella* will contribute to the advancement of diagnostic techniques, therapeutic interventions, and preventative measures against these infections. Future research efforts ought to focus on the pathogenicity, antibiotic treatment protocols, and epidemiological trends across different demographics. By doing so, a comprehensive understanding of this emergent pathogen can be achieved.

Conflict of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Author Contributions

First author: Formal analysis, Writing – original draft;
Second author: Conceptualization, Writing – review & editing; Corresponding author: Data curation, Methodology, Writing – review & editing, Supervision.

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