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Case report

Vibrio vulnificus infection from tilapia sting wounds in an inland city: A case report

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ABSTRACT

Vibrio vulnificus is a pathogen that can cause serious and fatal infections, primarily associated with a history of contact with the sea or aquatic organisms or products. However, with global climate change and increased global seafood trade, *V. vulnificus* infections are also occurring in non-coastal areas. In this report, we present the successful diagnosis and treatment of a case of necrotizing wound caused by *V. vulnificus* infection in an inland city in southwest China. In addition, we review the epidemiology and distribution of *V. vulnificus* in China and related vaccine research, which may provide a reference for the clinical diagnosis and treatment of *V. vulnificus* infection.

1. Introduction

Vibrio vulnificus (*V. vulnificus*), a gram-negative, opportunistic pathogen belonging to the genus *Vibrio* and family *Vibrionaceae* [1], can cause wound infections, gastroenteritis, septicemia, and potentially fatal infections. In susceptible individuals, *V. vulnificus* infection can be fatal [2], with reported case-fatality rates of up to 50% for primary septicemia [3]. In most such cases, patients die within 72 hours of admission [4].

In this report, we present the successful diagnosis and treatment of a case of necrotizing wound caused by *V. vulnificus* infection in an inland city in southwest China. We also review the epidemiology and distribution of *Vibrio* infections in China and related vaccine research. Our case indicates that environments in which *V. vulnificus* can survive are not limited only to coastal areas. Greater attention should thus be paid to *V. vulnificus* infections in more areas.

2. Case presentation

On October 2, 2022, a 76-year-old man was admitted to hand microsurgery with a painful stab wound to his left index finger from a knife used to handle tilapia. Ten hours before admission, the patient complained of increased pain at the top of the left index finger, as

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well as elevated temperature, swelling, and significant limitation of movement of the left hand. Based on the above, the surgeon diagnosed an infection with necrosis of the left index finger. Vital signs at the time of presentation were as follows: temperature 36.5 °C, heart rate 78/min, respiration 20/min, and blood pressure 94/55 mmHg. An auxiliary examination at the time of admission yielded the following findings: white blood cell count, 18.47 × 10^9/L; neutrophil percentage, 91%; platelet count, 103 × 10^9/L; C-reactive protein, 111.98 mg/L; serum lactate, 185 U/L; alanine amino-transferase, 15 U/L; aspartate, 24U/L; gamma-glutamyltranspeptidase, 29 U/L; total bilirubin, 18.8 μmol/L; international normalized ratio, 1.18; plasma albumin, 36 g/L; plasma creatinine, 96 μmol/L; and fasting blood glucose, 7.6 mmol/L. He hadn't any co-morbid condition and wasn't immunocompromised. On October 3, 2022, the patient underwent debridement. On October 4, 2022, the patient's blood culture results revealed bacterial infection, which cultured on Vibro Chromogenic Agar Plate showed blue-green colonies (Fig. 1) and was confirmed as *V. vulnificus* (identified by matrix-assisted laser desorption ionization-time-of-flight mass spectrometry [MALDI-TOF-MS], Supplementary material 1). Meanwhile, Antibiotic susceptibility was determined with broth microdilution (BMD) by BioMerieux automatic microbial identification and drug sensitivity analysis system. The results are shown in Table 1. Unfortunately, the patient's distal left upper arm had become more swollen. As a result, amputation of his left index finger was performed on the same day (Fig. 1).

On the day that the infectious agent was identified, treatment was initiated with intravenous ceftazidime and levofloxacin for 9 days. The wound healed significantly, and physical indicators of infection gradually improved (Table 2). On October 24, 2022, the patient underwent reconstruction of the left first webbing, partial resection of the second metacarpal, trimming of the stump, and debridement and suturing. On the 29th day after admission, the patient had recovered and was discharged from the hospital, with follow-up visits every 2 weeks for a total of 7 months. The patient recovered well (Fig. 1).

Early precise diagnosis and timely treatment are critical for the treatment of *V. vulnificus* infection. The Sanford Guide to Antimicrobial Therapy (48th edition) guidelines [5] recommend doxycycline and ceftriaxone as first-line therapeutic agents and levofloxacin as second-line therapeutic agents. Some researchers have noted that treatment with third-generation cephalosporins in combination with quinolones for 7–10 days is more effective [3,5,6]. However, recent evidence suggests that *Vibrio* species isolated from different seas around the world are resistant to multiple antibiotics [7]. Therefore, the drug susceptibility of strains must be determined before individual drug administration. In addition to antibiotic treatment, aggressive and timely wound care is critical. Surgical exploration, surgical debridement, and even timely amputation if necessary are recommended for patients with *Vibrio* infections, as these steps can shorten the length of hospitalization and reduce mortality [8].

3. Discussion

V. vulnificus is a halophilic and thermophilic bacterium and a global concern for seafood safety [9,10]. Ecological factors such as climate change and geographic distribution can affect *V. vulnificus* infections. Some environmental parameters affect the virulence and abundance of *V. vulnificus*, including ocean temperature, turbidity, conductivity, sea level, sea ice, winds, salinity, and wavelength and velocity of propagation [11]. In recent years, climate warming has led to an increased risk of *V. vulnificus* infections [12,13]. When the water temperature *exceeds* 18 °C, bacterial growth is increased, with an optimal growth temperature of 26 °C [2]. Infection with *V. vulnificus* is considered one of the most dangerous bacterial diseases in the southeastern coastal region of China [14]. In this study, we present a case of *V. vulnificus* infection in an inland city in Sichuan Province of southwest China. Panzhihua City has a subtropical climate characteristic of the southern subtropics, and this region has the highest annual calorific value in Sichuan Province, with an average annual temperature of 20 °C. Higher temperatures throughout the year may be a high-risk factor for *Vibrio* infections in area residents.

We searched PubMed and the China Knowledge Initiative for reported cases in China from 2013 to 2023 using the keyword "*V. infections*". According to current statistics, the reporting rates are higher in China's coastal provinces of Zhejiang and Guangdong, but

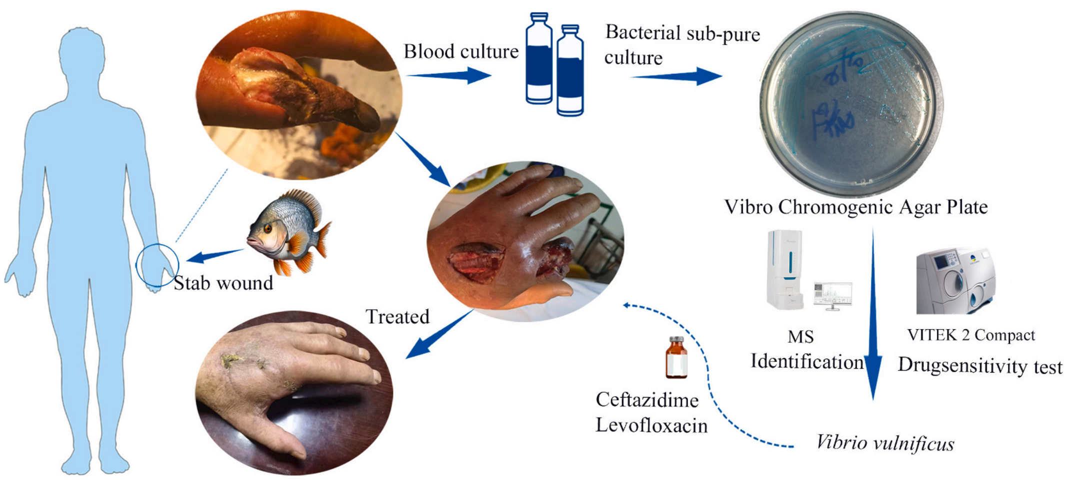

Fig. 1. *V. vulnificus* direct diagnosis and treatment workflow.

Table 1
Antimicrobial agents and MIC breakpoints for *V. vulnificus*.

	MIC (μg/mL) for category			Result
	Susceptible (S)	Intermediate (I)	Resistant (R)	
Ampicillin	≤8	16	≥32	≤2 (S)
Ampicillin-sulbactam	≤8/4	16/8	≥32/16	≤2 (S)
Piperacillin-tazobactam	≤16/4	32/4–64/4	≥128/4	≤4 (S)
Cefazolin	≤2	4	≥8	16 (R)
Ceftazidime	≤4	8	≥16	≤1 (S)
Cefepime	≤2	4–8	≥16	≤1 (S)
Imipenem	≤1	2	≥4	≤1 (S)
Amikacin	≤16	32	≥64	8 (S)
Gentamicin	≤4	8	≥16	≤1 (S)
Ciprofloxacin	≤1	2	≥4	≤0.25(S)
Levofloxacin	≤2	4	≥8	≤0.25(S)
Trimethoprim-sulfamethoxazole	2/38	–	≥4/76	≤1/19 (S)

Table 2
Biochemical parameters at critical times.

Biochemical parameters	White blood cell count (×109/L)	Hemoglobin (g/L)	Neutrophil percentage (%)	Platelet count (×109/L)	C-reactive protein (mg/L)	Fibrinogen (g/L)	Fasting blood glucose (mmol/L)
Initial admission	18.47	130	91.3	103	111.98	3.68	7.6
Pre-amputation	14.12	126	93	92	187.15	/	/
Post-amputation	6.1	126	63.7	196	28.45	5.67	/

Normal reference range: White blood cell count (× 109/L): 4.0–10.0; Hemoglobin (g/L):120–160; Neutrophil percentage (%): 39.8–70.5; Platelet count (× 109/L): 100–300; C-reactive protein (mg/L): 0.0–5.0; Fibrinogen (g/L): 2.38–4.98; Fasting blood glucose (mmol/L): 3.5–11.1.

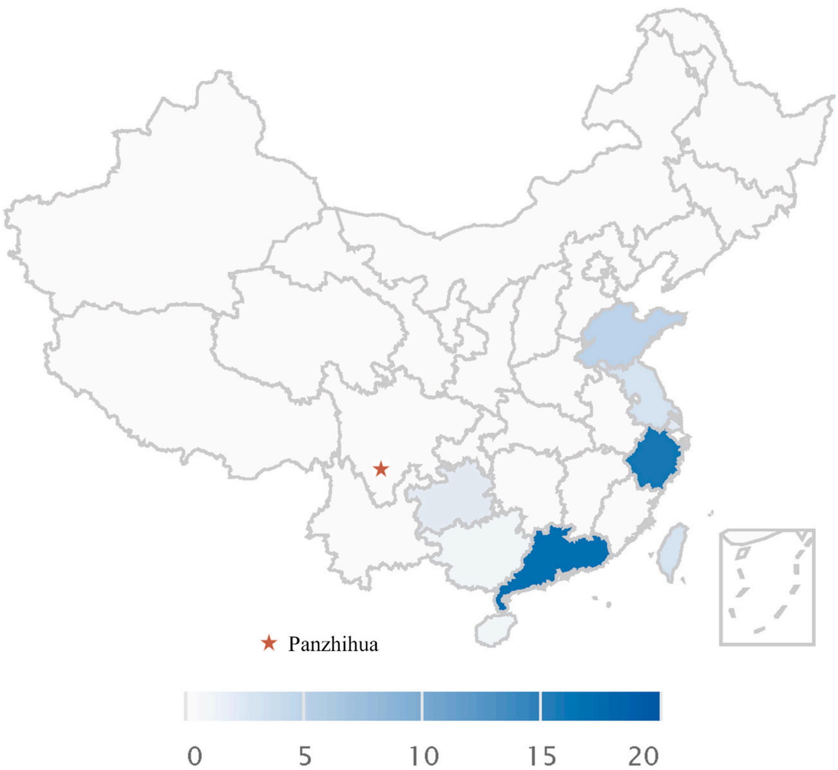

Fig. 2. Distribution of *V. vulnificus* in China, 2013–2023.

infections have also been reported in the remaining coastal provinces. In our survey, we found that two cases of *V. vulnificus* infection also occurred in the inland province of Guizhou. This inland infection could have been related to increased seafood aquaculture and global seafood trade, which has resulted in increasing reports of *V. vulnificus* in freshwater environments [2,15]. However, there were no cases reported in Fujian Province (Fig. 2, Supplementary material 2, Supplementary material 3).

Domestic studies [16] have shown that *V. vulnificus* transmission may occur in inland freshwater aquaculture, marketing, and catering and that freshwater shrimp stings can also lead to *V. vulnificus* infection. In our case, the tilapia associated with the patient was bought from the largest local seafood market in Panzhihua. We speculate that the source of infection may have been contaminated water. The gradual expansion of *V. vulnificus* infections is further illustrated by the discovery of more cases of *V. vulnificus* infections in inland cities. Freshwater areas of these cities may have been colonized by *V. vulnificus*, indicating that the situation may be far more serious than expected.

In China, the mortality rate for *V. vulnificus* infections ranges from 18% to 56% and is higher in patients with chronic liver disease, malignant tumors, or hematological disorders [17]. Furthermore, high concentrations of glucose may favor the growth of *V. vulnificus*, *V. vulnificus* infections are more severe in diabetics than in healthy individuals. Without prompt and effective treatment, *V. vulnificus* infections can cause severe bacteremia and sepsis [18]. We found that patients with *Vibrio* infections are predominantly male, which may be related to the fact that more men are engaged in seafood-related work. Moreover, estrogen is reportedly protective [19]. Patients are typically infected with *V. vulnificus* through seafood-related injuries and contaminated seafood, indicating that the spread of *V. vulnificus* is still mainly through seafood organisms. However, some patients have been infected with *V. vulnificus* through insect bites and other forms of injury, it has also been reported that *V. vulnificus* septicemia in a cirrhotic patient with no history of contact with seawater or consumption of seafood [20], which also indicates that the modes of *V. vulnificus* transmission are gradually diversifying and that more attention should be paid to other infection pathways. According to our case statistics, among all 50 affected patients, 22 exhibited bacteremia. Seven patients had no identifiable history of contact with contaminated seafood or water. Among the 22 bacteremia patients, the mortality rate was 31.9%. Previous studies have reported that *V. vulnificus* infections are easy to acquire and exhibit seasonality [2], with *V. vulnificus* infections more common in warmer climates during the summer months (Supplementary material 2). Furthermore, *V. vulnificus* infections were generally concentrated between May and October, but cases have also been reported in colder climates; therefore, it is important to be aware of this disease even in the winter months [21].

At present, no effective *V. vulnificus* vaccine is available for use in humans, but a variety of proteins have been established as targets in vaccine research. Studies have shown that *V. vulnificus* expresses a wide array of virulence factors, including capsular polysaccharide, siderophores, cytolytic hemolysin, protease phospholipase A, and repeats-in-toxin (RtxA1) [22,23]. These factors are closely related to the pathogenicity of *V. vulnificus* [24] and also provide the basis for research into the development of a *V. vulnificus* vaccine.

In preliminary studies using *Scophthalmus maximus* models of vibriosis resulting from *V. vulnificus* infection, *V. vulnificus* formalin-killed vaccine and ghost vaccine (VVGs) have shown promising results. Further findings showed that the VVGs vaccine induces stronger innate and acquired immune responses [25]. Studies using experimental mouse models found that immunization with *V. vulnificus* metalloprotease (VvpE) [26] induces a high antibody response and confers 75% protection against lethal challenge with *V. vulnificus* [27], Thus, VvpE may be a potential candidate for development of a vaccine against *V. vulnificus*.

RtxA1 plays an important role in *V. vulnificus* cytotoxicity and causes programmed necrotic cell death by inducing calcium-mediated mitochondrial dysfunction [28]. RtxA1 may therefore be a useful target for the development of specific preventive and therapeutic measures targeting the cytotoxicity of *V. vulnificus* [24,28,29]. Other studies have reported that the live attenuated vaccine strain CMM781 (with deletions in three genes encoding major virulence factors: *rtxA1*, *vvhA*, and *vvpE*) appears to be a safe and effective vaccine candidate [30], exhibiting significant protective efficacy against fatal *V. vulnificus* septicemia.

4. Conclusion

Vibrio vulnificus infection can result in acute gastrointestinal symptoms or serious and fatal complications either through wound infections or primary septicemia. When *V. vulnificus* infection is suspected, early diagnosis, timely treatment, and appropriate antibiotics should be administered to reduce the risk of mortality and disability. As the geographic distribution of *V. vulnificus* infections continues to expand, clinicians must be aware of the risk of *Vibrio* infections in non-coastal areas. To reduce mortality from *V. vulnificus* infections in at-risk populations, effective vaccines, and more appropriate preventive measures are needed.

Ethical declarations

All participants/patients provided informed consent to participate in the study.

Consent for publication

The patient consented to publication of potentially identifying information.

Data availability statement

Data included in article/supp. material/referenced in article.

CRediT authorship contribution statement

Taigui Chen: Writing – review & editing, Writing – original draft, Supervision, Investigation, Data curation. **Jun Wang:** Writing – review & editing, Writing – original draft, Investigation, Data curation. **Shijie Peng:** Supervision, Software, Methodology. **Lianbao Li:** Writing – review & editing, Writing – original draft. **Changxue An:** Supervision, Software, Methodology. **Jun Li:** Supervision, Project administration. **Wei He:** Supervision, Data curation.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e28012.

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