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# *Vibrio parahaemolyticus* infection caused by market sewage: A case report and literature review

Weixian Xu<sup>a</sup>, Miaozhen Chen<sup>b</sup>, Xinxi Chen<sup>a</sup>, Yi Su<sup>a</sup>, Liqun Tang<sup>a</sup>, Yunhai Zhang<sup>a,\*</sup>

<sup>a</sup> The Eighth Clinical Medical College of Guangzhou University of Chinese Medicine, 6 Qinren Road, Chancheng District, Foshan City, Guangdong Province, 528000, China

<sup>b</sup> Foshan Clinical Medical School of Guangzhou University of Chinese Medicine, 3 Sanyou South Road, Chancheng District, Foshan City, Guangdong Province, 528000, China

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#### ABSTRACT

*Vibrio parahaemolyticus* is distributed worldwide in seafood such as fish, shrimp, and shellfish and is a major cause of seafood-borne diarrhoeal disease. Previous studies have reported infections contacting with contaminated seafood seawater. So far, 11 cases reported of skin and soft tissue infections (SSTIs) caused by *V. parahaemolyticus*, which 5 patients died and 6 survived. We found that transmission through contact with contaminated water also causes infection. We report a 46-year-old male contracted *V. parahaemolyticus* after being splashed with market sewage. His condition deteriorated rapidly and he died eventually, suggesting that more atypical modes of *V. parahaemolyticus* are rare, so, detailed questioning of the patient's exposure history can help with empirical drug administration early. Patients with immunodeficiency disease and progressive blistering need mandatory debridement urgently. If fascial necrosis is found during debridement, early amputation may save the patient's life.

#### 1. Introduction

*Vibrio parahaemolyticus*, a Gram-negative, salt-loving bacterium distributed worldwide, is the most common food poisoning bacterium associated with seafood consumption and causes self-limiting gastroenteritis usually. Sepsis following gastroenteritis and wound infection can lead to death [1]. *V. parahaemolyticus* was first identified in tropical oceans and coastal waters, and its endemic area is expanding globally as sea surface temperatures rise due to climate warming [2]. The increase in seafood aquaculture and global trade has also increased the chances of *V. parahaemolyticus* infection and transmission [3]. Therefore, exposure risk reduction, early diagnosis, and multidisciplinary treatment are particularly important.

### 2. Case report

A 46-year-old man presented to Foshan Hospital of Traditional Chinese Medicine on 2022-8-17 with calf ulcers for 3 months, fever, swelling, and pain for 1 day. He had a previous history of hypertension, IgA nephropathy, diabetes mellitus, and chronic viral hepatitis B. The patient had been pricked by a tree branch on the posterior aspect of his left calf three months previously and an ulcer had

\* Corresponding author. *E-mail address:* fsszyyicu@163.com (Y. Zhang).

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developed, with recurrent oozing but no pain. Born and lived in Foshan, he and his wife worked in a printing factory and commuted to work together usually, denying exposure to seafood and seawater. One day before admission, he went to the market after work to buy vegetables and the market sewage splashed on his foot, including the wound, then that evening he developed a high fever, swelling, and pain in his left calf. At the first visit, he had a temperature of 39 °C, heart rate of 130 bpm, respiratory rate of 22 bpm, blood pressure of 64/46 mmHg, and a 2 cm  $\times$  2 cm ulcer visible on the posterior side of his calf (Fig. 1A). On the second day, we found blister formation on the left lower limb, spreading from the left inner ankle to the entire dorsum of the foot. The skin under the blister was purple and dark, while the left toe was ruddy with good blood flow (Fig. 1BC). We took blister fluid and blood for bacterial culture. After centrifugation, the blister fluid was inoculated on blood culture medium, MacConkey agar medium, chocolate agar medium and nutrient broth, which was cultured in a 5 % CO2 incubator at 35 °C for 24h. The suspected colonies were selected and identified as nonresistant V. parahaemolyticus (Figs. 2-3) by VITEK ® MS Mass Spectrometry Identification System. There are no reference strains of V. parahaemolyticus in our lab. But we also sent the specimen to Agene® for metagenomic Next Generation Sequencing (mNGS). The results showed that the number of V. parahaemolyticus sequences was 110,457 in the blister fluid and 18 in the blood (Fig. 4). We used Imipenem cilastatin sodium (0.5g/q6h for 3 days, since the second hours after admission) empirically for anti-infection, and then adjusted to ceftazidime avibactam sodium (2.5g/q8h for 14 days), moxifloxacin (0.4g/qd for 6 days), and doxycycline (0.2g/qd for 6 days) based on culture results. The patient was in septic shock and had multiple organ dysfunction. We treated with fluid resuscitation, pressure elevation, blood transfusions, mechanical assisted ventilation, and continuous blood purification. The surgeon refused our requests for debridement as the terminal toe had good blood flow and no pus cavity had formed.

On the seventh day of admission, his dorsal foot skin had turned black, multiple existing blisters had ruptured and there were new petechiae and blisters on the lateral aspect of the left knee. Ultrasound showed abscess formation on the posterior lateral gastrocnemius muscle, fluid was seen in the left knee joint cavity and the subcutaneous tissue on the lateral left thigh was swollen. An amputation of the left thigh was performed on the seventh night. Postoperatively, the patient's blood pressure gradually stabilized, lactate gradually decreased and the antihypertensive medication was stopped. However, the patient's coagulation failure led to systemic hemorrhage on the 14th day and cardiac arrest after a clot obstructed the airway. After resuscitation, the patient regained sinus rhythm but was diagnosed as brain dead because of deep coma and brain tissue swelling.



**Fig. 1.** (A) Wound on the patient's posterior calf on the first day of admission. (B–C) blister formation on the left lower limb, spreading from the left inner ankle to the entire dorsum of the foot.



Fig. 2. Left: Culture results of V. parahaemolyticus. Right: Electron microscope image of V. parahaemolyticus.

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姓名:		重症医学科住院	LIF.	样本类型: 分泌物	样本来源: 左足						
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一般细菌培养及鉴定+参 培养结果:副溶血弧											
抗菌药物	结果	解释	折点	方法	抗菌药物	结果	解释	折点	方法		
阿莫西林/克拉维酸(AMC)	<=2	S		MIC	哌拉西林/他唑巴坦(TZP)	<=4	S		MIC		
头孢呋辛 (CXM)	16	I		MIC	头孢他啶 (CAZ)	0.5	S		MIC		
头孢哌酮/舒巴坦 (SCF)	<=8	S		MIC	头孢吡肟 (FEP)	<=0.12	S		MIC		
头孢西丁 (FOX)	<=4	S		MIC	亚胺培南 (IPM)	<=0. 25	S		MIC		
阿米卡星 (AK)	<=2	S		MIC	替加环素 (TGC)	<=0.5	S		MIC		
复方新诺明(SXT)	<=20	S		MIC	左氧氟沙星(LEV)	<=0.12	S		MIC		
注:R-而	药; I-	·中介;	SDD-剂里依赖敏	感; S-每	g感; MIC法、稀释法结果单	位- µg	/ml; K-1	8法结果单位	Ž−mm. ∘		
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【结果仅供临床参考,本 签收时间:2022-08-1 主检岗位:微生物鉴定岗	820:3		<b>&amp;告时间: 2022-</b>	08-20	<u>于当天反馈。检验咨询电话:0</u> 10:46 报告者:黄注 :: 佛山市禅城区亲仁路6号 佛山	吉雯	审核人:	1727-1 24			

Fig. 3. Drug sensitivity test results

The result of bacterial culture was "副溶血弧菌" means V. parahaemolyticus.

#### 3. Discussion and literature review

*V.* parahaemolyticus grows preferentially in warm (>15  $^{\circ}$ C), low-salinity marine water (<25 ppt NaCl) [4]. In coastal areas of southeastern China, the warm climate is sufficient for the growth and reproduction of *V. parahaemolyticus* [5]. V. parahaemolyticus densities in seafood were positively correlated with water temperature [6]. July–August is the hottest month in the Northern Hemisphere, when the abundance of *V. parahaemolyticus* in seafood is the highest [7]. The trade and transport of seafood extend its growth range. *V. parahaemolyticus* population exhibited a high detection rate with 131 samples (71.6 %) tested positive in seafood, in Nanjing, China [8]. *V. parahaemolyticus* is transported to the market along with seawater or seafood. When the vendors process the seafood, they rinse it with tap water and rush it to the ground or ditch the market. When we walk across these wet surfaces, the splashing water picks up *V. parahaemolyticus*.

The market sewage is interspersed with seawater and freshwater, and this light saline environment [9] allow *V. parahaemolyticus* to survive. This patient had no direct contact with seafood or seawater, but developed the disease the same night after the market sewage contaminated the wound, suggesting that this is a lethal vector of transmission for immunocompromised patients with wounds.

	结果列表						结果列表	ŧ			
			细菌						细菌		
	属			种				属		种	
地型	名称	序列数	相对丰度	名称	序列数	类型	名称	序列数	相对丰度	名称	序列
-	弧菌属 Vibrio	18	47,37%	副溶血弧菌 Vibrio parahaemolylicus	18	G-	弧菌属 Vibrio	112,580	99,97%	副溶血弧菌 Vibrio parahaemolyticus	110,4
型	名称	病毒 序列数 相对丰度		名称	序列数	G-	埃希氏菌属 Escherichia	11	<0,01%	大肠埃希菌 Escherichia coli	10
IA	巨细胞病毒属	12	80.0%	CMV	12			病毒			
~	Cytomegalo	16	80,0%	Human betaherpesvirus 5	12	类型	名称	序列数	相对丰度	名称	序列
IA	正嗜肝DNA病毒属 hepadnavividae	1	6,67%	乙型肝炎病毒 Hepatitis B virus	1	-	-	-	-	=	-
IA	多瘤病毒属 Betapolyomavirus	1	6,67%	人类多瘤病毒2型 (JC病毒) Human polyomavirus 2	1				真菌		
			真菌				名称	序列数	相对丰度	名称	序列
名称    序		序列数 相对丰度		名称	序列数		-	-	-	-1	
	-	-	-	-	-				寄生虫		
			寄生虫				名称	序列数	相对丰度	名称	序列
	名称	序列数	相对丰度	名称	序列数		-	-		-	-
	-	-	-	-				特殊病原体	(包括分枝杆菌、	支原体/衣原体等)	
	特殊	病原体(包	括分枝杆菌、	支原体/衣原体等)		类型	名称	序列数	相对丰度	名称	序列
型	名称	序列数	相对丰度	名称	序列数		-	-	-	-	-
		-	-	-	-						

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Fig. 4. Left: mNGS results of blood. Right: mNGS result of blister fluid.

The results showed that the number of V. parahaemolyticus sequences was 110,457 in the blister fluid and 18 in the blood.

He had a previous history of IgA nephropathy, diabetes mellitus, chronic viral hepatitis B, and left calf ulcer, all of which are highrisk factors for *V. parahaemolyticus* infection. Microbial adhesion to host tissues is the initial event during the process of infection. *V. parahaemolyticus* infects the human body through ulcers. *V. parahaemolyticus* is able to attach different types of host cells by hemagglutinin, enolase, type VI secretion system and multivalent adhesion molecules [10,11]. Iron is an indispensable element in the growth and metabolism of *V. parahaemolyticus* [12]. Hepatitis B virus affects iron metabolism in the body [13], and iron overload provides sufficient raw materials for *V. parahaemolyticus* growth. *V. parahaemolyticus* uses the Type III and VI secretion system to inject toxins into host cells like syringes [14]. TDH and TRH are considered to be the main pathogenic factors. TDH is a pore-forming toxin makes colloidal osmotic lysis [15]. In diabetes, levels of branched-chain amino acids and related metabolites rise significantly, which promotes the production of TDH [16]. IgA nephropathy weakens the immune function, which makes *V. parahaemolyticus* avoid being killed by Type III secretion system [17]. So *V. parahaemolyticus* proliferates in this patient and releases a lot of toxins, which accelerates the disease and leads to death.

A total of 47 native English language articles were searched in PubMed, Web of Science, Embase, and Cochrane using the search terms: *V. parahaemolyticus* and soft tissue skin infections, cellulitis, necrotizing fasciitis, sepsis, and multiorgan dysfunction, in order to investigate the pathogenesis of patients with this disease. After reviewing the titles and abstracts, 15 irrelevant articles were excluded. Additionally, 7 articles that could not be downloaded in full text were also excluded. By reading the full text, we further excluded 14 articles that did not provide the required data. Consequently, 11 articles were selected for analysis (Fig. 5). The data extracted from these selected articles included information on age, sex, underlying disease, location, trigger, time of onset, initial presentation, skin condition, drug sensitivity, drug regimen, surgical regimen, intraoperative fascia, and outcome. These data were tabulated for further analysis (Table 1). Our article only included articles in PubMed, Web of Science, Embase, and the Cochrane in native English, and did not search for articles in other countries and languages that may not have been comprehensively searched and collected.

According to the table, age and gender have no significant difference. It is associated with a history of trauma and exposure to the seashore, and it is prevalent among immunocompromised populations, including those with hepatitis, diabetes mellitus, autoimmune disorders, and hematological disorders. When classifying the literature based on the patients' local skin blisters, management, and prognosis, it was observed that patients with limited infection, insignificant swelling, and no progressive blisters can be effectively treated with medication, regardless of whether they have an underlying disease. Rapid worsening of the condition, accompanied by localized wound swelling and progressive blistering, can lead to rapid death if patients are not operated on promptly [18,19]. Patients without fascial involvement detected during debridement can be discharged after treatment [20–22]. Another patients with fascial involvement were susceptible to death [23,24]. But a patient was discharged after amputation treatment despite massive necrosis of fat and muscle tissue [25]. All patients had a rapid onset which is one day or even hours after infection. The progression of local disease and systemic inflammation requires prompt diagnosis and treatment, such as the use of appropriate antibiotics and urgent surgical debridement [26]. Skin lesions such as bullae and blisters occur when the infection is in advanced stages. Surgical debridement within 24 hours can reduce its morbidity and mortality [27]. Thorough removal of necrotic tissue is a prerequisite for effectiveness [28] and multiple debridements are required because *V. parahaemolyticus* releases factors such as hemagglutinin, enolase and multivalent adhesion molecules, which enhance its adhesion to host cells [10]. However, patients are often associated with numerous

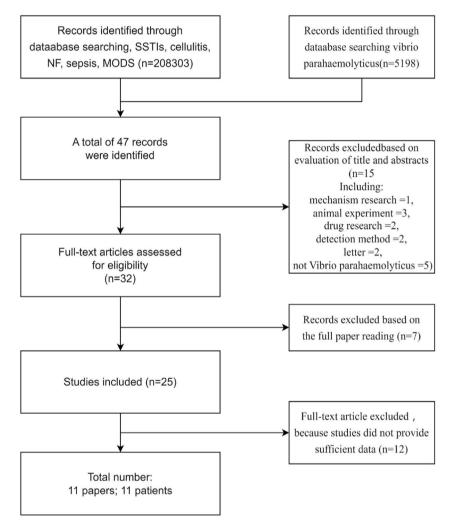


Fig. 5. Screening process.

hor	Year	ar)	ase	site	ion	ital	шо	ion	nug	nen	ery	ion	ery	me
Author	Y	Age(year) Sex	Underlyingdisease	exposuresite	Causeofinfection	Timetohospital	Symptom	Skincondition	Sensitivitydrug	Medicationregimen	surgery	Fasciacondition	Timetosurgery	Outcome
Mai, A T T [21]	2022	42—Male	None	Seaside	Right calf scratched	3h	Nausea, vomiting, diarrhea, anhelation	Black blisters, smelly	CTX, FEP, MEC, CIP, LVX, TMP- SMZ, IPM, AMP	LVX,	debridement	No necrosis fascia	Twelfth day	Recovered
Ahmad, A [30]	2013	45—Female	T2DM, morbid obesity, HCV	Seaside	Calf injury from jet skiing	24h	Leg pain , fever, chills, stiffness	Darkened and large blisters	NA	FEP, LVX, Doxy, CC	Fasciotomy	NA	First day	Death
Tena, D J [19]	2010	92—Female	CRF, T2DM, malnutrition	NA	NA	24h	Vomiting, diarrhea	Large blisters , smelly.	AMX, Clav, CTX, IPM, CIP, TMP- SMZ, GM, AMP	CRO, CC	None	None	None	Death
Payinda, G [23]	2008	79—Male	AF, PMR	Northern coast of New Zealand	Bruised right leg by anchor while fishing		Leg pain , nausea, vomiting, fever, oliguria , dizziness	Bloody blisters	NA	PIP, Tazo, CIP	Fasciotomy and debridement	Necrotizing fasciitis	NA	Death
Ralph, A [24]	2007	38—Male	T2DM, CHF, AF , CAD	Seaside	Fished in the sea	NA	Delirium, shock, myocardial ischemia, renal failure, pancytopenia, hypoglycemia, vomiting,	Calf tenderness, swelling, redness	NA	NA	Fasciotomy and debridement	Necrotizing fasciitis	NA	Death
Hally, R J [18]	1995	31—Female	HCV, liver cirrhosis, RHD , CAF	NA	Eat oysters and prawns	NA	Leg pain, diarrhea, weakness, oliguria	Bloody blisters	ATM, CTX, IPM, TE, CIP, TMP- SMZ, AG, AMP, MZ	CTX	NA	NA	NA	Death
Guillod, C [22]			HHD, CRF	Mediterranean Sea of Italy	sea.		Pain in the distal left lower extremity		Na	CIP, Doxy	debridement	fascia	NA	Recovered
Rabinowitch, B L [31]	1993	22—Male	AML	Patuxent River	Water skiing	24h	Wound pain	Swollen , painful	Na	CAZ, CIP	NA	NA	NA	Recovered
Dobroszycki, J [32]	1992	48—Male	Lymphoma	NA	Right finger torn by squid	24h	Fever, pain, swelling of the fingers	NA	TMP-SMZ, MET, CIP, ATM, Chloro, IPM, TE, CAZ.	CAZ,GM, TMP- SMZ	NA	NA	NA	Recovered
Roland, F P [25]	1970	40—Male	None	Narragansett Bay	Clamming and bathing on the beach	48h	Diarrhea , fever, papules bleeding, Vomiting	Blisters , Gangrene	AMP, Ceph, GM, PB	Na	Amputation.	Necrotizing fasciitis	NA	Recovered
Issack, M I [20]	2008	37—Male	Alcoholism	Southeast Sea of Mauritius	Stung on foot by synechia verrucosa	24h	Wound swelling	Swollen	TMP-SMZ, TE, CIP	AMP, OB, CIP	Fasciotomy and debridement	No necrosis fascia	First day	Recovered
Weixian, X	2022	Male	HTN, IgA nephropathy, T2DM, HBV	Market sewage	Market sewage splashed on foot		Fever, pain, swelling of the calf	Petechiae , blisters	AMC, TZP, CXM, CAZ, FEP, FOX, IPM, AK, TGC, SXT, LEV	MXF,	Amputation	Necrotizing fasciitis	Seventh day	Death

Abbreviations:T2DM, Type 2 diabetes; HCV, chronic hepatitis C; CRF, Chronic renal failure; AF, Auricular fibrillation; PMR, polymyalgia rheumatica; CHF, congestive heart failure; CAD, chronic airway disease; RHD, rheumatic heart disease; HHD, hypertensive heart disease; AML, Acute myeloid leukaemia; CTX, cefotaxime; FEP, cefepime; MEC, meropenem; CIP, ciprofloxacin; LVX, levofloxacin; TMP-SMZ, trimethoprim-sulfamethoxazole; IPM, imipenem; AMP, ampicillin; VAN, vancomycin; AMX, amoxicillin; Clav, clavulanate; GM, gentamicin; ATM, aztreonam; TE, tetracycline; AG, aminoglycosides; MZ, mezlocillin; Chloro, chloramphenicol; Ceph, cephalosporins; CAZ, Ceftazidime; Doxy, doxycycline; CC, clindamycin; PIP, Piperacillin; Tazo, tazobactam; OB, cloxacillin; AMC, amoxicillin; CXM, cefuroxime; FOX, cefoxitin; AK, amikacin TGC, Tigecycline; SXT, selectrin; LEV, levofloxacin; MXF, moxifloxacin.

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Table 1

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contraindications to surgery and an optimized interim management plan recommends a small incision, drainage within 1–2 hours of diagnosis, and return to the operating room 24 hours later for complete debridement, which is more effective and feasible in patients with septic shock. Amputation is the most expeditious management when the infection in the extremity progresses or when the patient cannot tolerate surgery [29]. Nevertheless, good blood flow to the end of the limb before the patient's vasculature is involved may lead to misdiagnosis and delay the procedure easily [28]. As in our patient, the request for debridement was refused by the surgeon even though Vibrio parahaemolyticus infection had been established clearly. On the seventh day of admission, it was found that the localized lesion was still spreading. By that time, the amputation procedure was too late to minimize the damage.

#### 4. Conclusion

Markets sewage is a new vector for the transmission of *V. parahaemolyticus*. After Vibrio parahaemolyticus has caused a soft tissue skin infection, emergency debridement surgery is necessary. If fascial necrosis is found during debridement and the patient cannot tolerate multiple surgeries, early amputation is likely to save the patient's life.

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#### Ethical approval

This study adhered to the Declaration of Helsinki. Informed consent was obtained from the patient for the publication of all images, clinical data and other data included in the manuscript. At the same time, ethical approval has been obtained from Foshan Hospital of Traditional Chinese Medicine, and the approval number is KY [2023]191.

#### Data availability statement

No data was used for the research described in the article.

#### Additional information

No additional information is available for this paper.

#### CRediT authorship contribution statement

Weixian Xu: Writing - review & editing, Writing - original draft, Visualization, Validation, Supervision, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. Miaozhen Chen: Writing - review & editing, Writing - original draft, Visualization, Validation, Supervision, Software, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. Xinxi Chen: Methodology. Yi Su: Writing - review & editing, Data curation. Liqun Tang: Writing - review & editing, Formal analysis, Conceptualization. Yunhai Zhang: Visualization, Resources, Project administration, Methodology, Funding acquisition, Conceptualization.

#### Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:Yunhai Zhang reports financial support, administrative support, and article publishing charges were provided by Science and Technology Bureau of Foshan City. If there are other authors, they 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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