Case Report

Fulminant necrotizing fasciitis due to *Vibrio parahaemolyticus*

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Necrotizing soft-tissue infection due to *Vibrio parahaemolyticus* is unusual. We report a case of necrotizing fasciitis due to *V. parahaemolyticus* in a 92-year-old woman with a history of chronic renal failure, diabetes mellitus and malnutrition. Clinical evolution was fulminant and the patient died 6 h after admission. A review of all cases previously reported showed that the infection occurred in patients with underlying diseases through ingestion of raw oysters or inoculation via traumatic injury in marine environments. The mortality rate of all reviewed cases was 42.8 %. In conclusion, *V. parahaemolyticus* should be considered a possible causative agent of necrotizing fasciitis, especially in patients with underlying disease. Early diagnosis and prompt aggressive debridement associated with antibiotic therapy are essential in order to save the patient's life, because clinical evolution can be fulminant and mortality rates are high.

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Introduction

Vibrio parahaemolyticus is a Gram-negative, halophilic bacterium that inhabits marine and estuarine environments, and causes three major syndromes of clinical illness: gastroenteritis (the most common syndrome), wound infections and septicemia (Nair *et al.*, 2007). Isolates from ill persons have traditionally been differentiated from (presumed non-pathogenic) isolates from environmental sources on the basis of haemolytic activity seen when these isolates are grown on special medium (Wagatsuma agar) (Morris, 2003). Infection is generally acquired through consumption of contaminated food or water or by direct invasion through wounds. There has been an increase in the incidence of *V. parahaemolyticus* infections since the mid-1990s. This increase has been noted in multiple countries and appears to be associated with the appearance of a new clonal group with pandemic potential (Daniels *et al.*, 2000).

Wound infections due to *V. parahaemolyticus* are usually minor infections. However, necrotizing soft-tissue infections are unusual and other members of the family *Vibrionaceae* have been more frequently implicated. These infections can be life-threatening because of rapid invasion and destruction of the fascial planes accompanied by release of several cytotoxins (Chiang & Chuang, 2003). We report a case of necrotizing fasciitis due to *V. parahaemolyticus* which had a fulminant course and review the literature.

Case report

A 92-year-old woman with a history of chronic renal failure, diabetes mellitus and malnutrition was admitted to

the hospital with a 24 h history of vomiting, food intolerance and diarrhoea. There was no history of trauma or exposure to seawater. No information about previously consumed food could be obtained. On admission, the patient appeared conscious with a bad general aspect. Physical findings included a body temperature of 35.8 °C, pulse rate of 115 min⁻¹ and blood pressure of 82/53 mmHg. Examination of the patient's right ankle revealed marked oedema with a large blister. The skin appeared painful, cold, erythematous and smelly. Pulses were weak and no open wounds were observed. The rest of the physical examination was unremarkable. Blood parameters revealed the following values: haemoglobin 11.6 g dl⁻¹, haematocrit 33.5 %, white blood cells 16 300 mm⁻³ (neutrophils 93.9 %, lymphocytes 1.9 %, monocytes 4.2 %), platelets 221 000 mm⁻³, creatinine 2.87 mg dl⁻¹ and creatine kinase 1140 IU l⁻¹. Aspartate aminotransferase level, prothrombin and partial thromboplastin times were within normal limits. A sample from the blister and blood samples were taken for culture. Stool culture was not performed. Aggressive management with intravenous fluids and empiric treatment with ceftriaxone (2 g intravenously every 24 h) and clindamycin (600 mg intravenously every 8 h) was initiated. Gram stain of the blister aspirate demonstrated Gram-negative bacilli. The blister aspirate and blood cultures were found to be positive for a Gram-negative, oxidase-positive organism. Urease and indole reaction were positive. The strain was susceptible to O/129 agent (Oxoid). Initial identification with the Vitek II automated system (bioMérieux) and the API 20 NE system (bioMérieux; profile 7477445) yielded *V. parahaemolyticus*. The isolate was sent to the National

Reference Laboratory, where identification was further confirmed. An antibiotic susceptibility study was done using the N058 susceptibility card by Vitek (bioMérieux) according to CLSI recommendations (NCCLS, 2008). The strain was susceptible to amoxicillin/clavulanic acid ($\text{MIC} \leq 2 \mu\text{g ml}^{-1}$), cefotaxime ($\leq 1 \mu\text{g ml}^{-1}$), imipenem ($\leq 1 \mu\text{g ml}^{-1}$), ciprofloxacin ($\leq 0.25 \mu\text{g ml}^{-1}$), trimethoprim/sulfamethoxazole ($\leq 20 \mu\text{g ml}^{-1}$) and gentamicin ($\leq 1 \mu\text{g ml}^{-1}$), and resistant to ampicillin ($32 \mu\text{g ml}^{-1}$). Skin lesions rapidly extended from the right ankle to the groin and also appeared on the left leg. Small vesicles developed on both legs progressing to necrosis. The patient suffered acute clinical deterioration that resulted in her death 6 h after admission. Her demise occurred very quickly and surgical treatment could not be performed.

Discussion

Necrotizing fasciitis is an uncommon soft tissue infection manifesting with a rapid course of inflammation and necrosis of skin, subcutaneous fat and fascia. The incidence has been reported to be 0.40 cases per 100 000 of the population (File *et al.*, 1998). Necrotizing fasciitis has been divided into distinct groups on the basis of microbiological cultures (Elliott *et al.*, 2000; Fontes *et al.*, 2000). Type-I infections are polymicrobial infections that usually are caused by non-group-A streptococci, and other aerobic and anaerobic micro-organisms. Type-II infections are usually caused by *Streptococcus pyogenes* alone or with staphylococci. *Vibrio* species are a rare cause of necrotizing soft-tissue infections and the most common species implicated is *Vibrio vulnificus* (Tsai *et al.*, 2009; Kuo *et al.*, 2007). However, necrotizing fasciitis due to *V. parahaemolyticus* is unusual. To our knowledge, only seven cases have been previously reported (Roland, 1970; Howard *et al.*, 1985; Howard & Lieb, 1988; Lim & Stebbings, 1999; Tsai *et al.*, 2004; Ralph & Currie, 2007; Payinda, 2008). The characteristics of the patients in these cases and of our patient are summarized in Table 1. Sporadic cases caused by other species such as *Vibrio damsela*, *Vibrio alginolyticus* and *Vibrio cholerae* non-O1 have also been reported (Yuen *et al.*, 1993; Gómez *et al.*, 2003; Chang-Chien, 2006; Tsai *et al.*, 2009).

In our study, seven of the eight patients (87.5%) had underlying diseases and risk factors, including cirrhosis, haemochromatosis, diabetes, hepatitis C, treatment with prednisone and chronic renal failure. These have been associated with primary *Vibrio* wound infections (Howard *et al.*, 1985; Howard & Lieb, 1988; Chiang & Chuang, 2003; Tsai *et al.*, 2004; Kuo *et al.*, 2007). The clinical course was fulminant in two patients. Several studies of severe infections caused by other vibrios such as *V. vulnificus* suggest that host factors play a large role in the fulminant nature of the disease (Borenstein & Kerdel, 2003; Gulig *et al.*, 2005). In the other reported cases reviewed, the infection occurred through ingestion of raw oysters or inoculation via traumatic injury in marine environments.

The source of infection was unknown in our case. Since our patient showed no open wounds, it is possible that ingestion of seafood served as a vehicle for the entry of the micro-organism with a subsequent extraintestinal spread causing necrotizing fasciitis. Unfortunately, information about food that she had eaten was unknown and stool samples were not taken for culture.

The mechanisms predisposing *V. parahaemolyticus* to cause necrotizing infections are unknown. These mechanisms have been studied in severe soft-tissue infections caused by other members of the family *Vibrionaceae*. *V. vulnificus* can produce many extracellular toxic factors that contribute to its virulence, including haemolysin, protease, lipase, cytotoxin, hyaluronidase, mucinase, DNase and sulfatase (Zhang & Austin, 2005). *V. vulnificus* haemolysin disrupts erythrocytes and proteases enhance vascular permeability, which can result in haemorrhagic lesions that can eventually cause severe skin necrosis. In addition, proteases can facilitate oedema formation and bacterial invasion (Chakraborty *et al.*, 1997). *V. cholerae* non-O1 produces many toxins such as El-Tor (HlyA) haemolysin which may contribute to the disease process (Tsai *et al.*, 2009).

In our review, *V. parahaemolyticus* necrotizing fasciitis did not differ clinically from necrotizing soft-tissue infections caused by other members of the family *Vibrionaceae*. Symptoms typically begin anywhere from hours to several days later, consisting of swelling, erythema and often intense pain. The presence of oedema and bullae formation is another important diagnostic clue. However, bullae formation, fever and hypotension are late signs of infection (Kuo *et al.*, 2007). Early diagnosis of necrotizing fasciitis is difficult and the disease can be mistakenly diagnosed as cellulitis, resulting in delayed management.

Vibrio necrotizing soft-tissue infections require emergency surgical care. Early recognition and prompt aggressive debridement is critical for survival and improves the rate of survival. Reported mortality rates are 25–38% in those undergoing debridement and 66–100% in those not undergoing debridement (Howard & Lieb, 1988; Howard & Bennett, 1993; Chuang *et al.*, 1992; Chiang & Chuang, 2003; Tsai *et al.*, 2004). In our review, the mortality rate in the seven cases with available information was 42.8% and the mortality rate of the surgical patients was 33.3%. These findings are consistent with previous results for *Vibrio* necrotizing infections (Howard & Lieb, 1988; Howard & Bennett, 1993; Chuang *et al.*, 1992; Chiang & Chuang, 2003; Tsai *et al.*, 2004). In addition to aggressive surgical debridement, early presurgical antimicrobial treatment with broad-spectrum antibiotics is essential. However, antibiotics alone can be ineffective against the large soft-tissue bacterial inocula resulting from the invasive nature of these infections. In this way, our patient was treated with antibiotic therapy alone and surgical treatment could not be performed because clinical evolution was fulminant. The vibrios are susceptible to a wide range of antimicrobial agents. However, *V. parahaemolyticus* may have β -lacta-

Table 1. Characteristics of patients with necrotizing fasciitis due to *Vibrio parahaemolyticus*

Case no.	Reference	Age/sex*	Underlying disease	Clinical presentation	Physical examination	Location	Mechanism of contact	Source of isolate	Antibiotic treatment†	Surgical treatment	Fulminant course	Outcome
1	Roland (1970)	40/M	None	Fever, vomiting, diarrhoea	Hypotension, papular haemorrhagic rash	Left leg	Bathing in seawater	Vesicular exudate	Gentamicin	Amputation	No	Survival
2	Howard <i>et al.</i> (1985)	43/M	Cirrhosis, alcohol abuse	Fever, chills	Massive swelling, pain, erythema, pitting oedema, necrotic ulcer	Left leg	Ate raw oysters	Blood	Ampicillin, erythromycin	Surgical debridement	No	Survival
3	Howard & Lieb (1988)	63/M	Haemochromatosis, cirrhosis, diabetes	ND	ND	Left leg, right leg	Ate raw oysters	Blood	ND	ND	ND	ND
4	Lim & Stebbings (1999)	65/M	Chronic obstructive pulmonary disease	Fever, chills	Hypotension, laceration, pain, erythema, swelling, fluctuation	Right arm	Cutting, contact with uncooked crabs	Blood	Ceftazidime + doxycycline	Surgical debridement	Yes	Survival
5	Tsai <i>et al.</i> (2004)	72/F	Diabetes mellitus, hepatitis C	Chills, general malaise	Hypotension, oedema, erythema, bullae	Left leg	Seawater	Wound	ND	Fasciotomy, above-the-knee amputation	No	Survival
6	Ralph & Currie (2007)	63/M	Diabetes, congestive cardiac failure, limb ulcer, chronic airways disease	Delirium, septic shock, acute renal failure, coffee-grounds vomitus	Pain, swelling, erythema	Left leg	Fishing in seawater	Wound aspirate, tissue specimen	Meropenem + gentamicin + doxycycline	Surgical debridement	No	Death
7	Payinda (2008)	79/M	Atrial fibrillation, polymyalgia rheumatica, prednisone	Fever, nausea, vomiting, dizziness	Hypotension, pain, tachycardia, erythema, bullae	Right leg	Fishing in seawater	Bullae aspirate	Piperacillin/tazobactam + ciprofloxacin	Surgical debridement, fasciotomy	No	Death
8	Present report	92/F	Diabetes mellitus, chronic renal failure, malnutrition	Vomiting, food intolerance, diarrhoea	Hypotension, pain, erythema, oedema, blister, vesicles	Right leg, left leg	Unknown	Blister aspirate, blood	Ceftriaxone + clindamycin	No	Yes	Death

ND, No data.

*M, Male; F, female.

†Antibiotic treatment after diagnosis of *Vibrio* infection.

mase activity (Ottaviani *et al.*, 2001). Septicaemia and soft-tissue infections caused by *V. parahaemolyticus* should be treated similarly to *V. vulnificus* infections, with ceftazidime and doxycycline or doxycycline in combination with ciprofloxacin or an aminoglycoside (Daniels *et al.*, 2000). The patients in our review were treated with a wide range of antibiotics and no conclusions could be obtained.

In conclusion, *V. parahaemolyticus* should be considered a possible causative agent of necrotizing fasciitis, especially in patients with underlying diseases. Early diagnosis and prompt aggressive debridement associated with antibiotic therapy are essential in order to save the patient's life, because clinical evolution can be fulminant and mortality rates are high.

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