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Case Report

A Survived Case of *Vibrio Vulnificus* Infection with Multiple Endocrine Neoplasia Type I

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Abstract A 35-year-old female with malabsorption syndrome who underwent a pancreatoduodenectomy for multiple endocrine adenomatosis 13 years prior was admitted to our hospital with diarrhea, general fatigue, high fever, and eruption in the lower legs. The patient had consumed raw shrimp a few days before onset and presented systemic inflammatory response syndrome at the time of hospitalization. *Vibrio vulnificus* was isolated from a blood culture performed before admission to the intensive care unit. We excised necrotizing tissue in the legs after improvement of her general condition. During the treatment process, glucose, catecholamine, and appropriate antibiotics were administered for hypoglycemia, hypotension, and high fever, respectively. The patient was discharged 107 days after contracting the disease. Of 18 septic patients with *V. vulnificus* infection admitted to our hospital, this was the first to develop septicemia in the absence of a previous liver dysfunction. In order to prevent this type of fatal infection, public education for immuno-compromised individuals as well as those with liver disease is essential. For early diagnosis and appropriate treatment, more effective strategies are required, such as the establishment of a network system where family physicians and emergency hospital staff could discuss information regarding high-risk patients.

Key words : *Vibrio vulnificus*, multiple endocrine neoplasia type I, malabsorption syndrome

Introduction

Vibrio vulnificus infection comes from eating contaminated raw seafood during the summer season or exposure of a wound to seawater, and occurs mainly in patients with severe liver dysfunction such as cirrhosis of the liver. The disease has a poor prognosis, as septic shock and necrotizing fasciitis can develop within a few days. In Japan, most case reports are from western Japan and particularly numerous from the

northern Kyushu region surrounding the Ariake Sea¹⁾. We treated a case of *V. vulnificus* infection with septicemia and necrotizing fasciitis that had a good outcome. Prior to infection, the patient had multiple endocrine neoplasia type I (MEN-I), instead of the usual severe liver dysfunction, with underlying malabsorption syndrome that had developed following a previous pancreatoduodenectomy.

Case Report

The patient was a 35-year-old female with the chief complaint of marked generalized malaise and fever. Her past medical history included surgical procedures for MEN-I performed at our hospital (extirpation of a parathyroid tumor at 21 years of age and a pancreatoduodenectomy for a vasoactive intestinal polypeptide producing tumor at 22 years old). There was no history of blood transfusion. The patient had been taking oral calcium, thyroid hormone, and iron preparations, though no steroids were administered. In addition, there were no indications of liver dysfunction.

The history of the present illness included malabsorption after the pancreatoduodenectomy and hypoproteinemia, which were being followed by a nearby physician. After eating raw shrimp in early July 2005, the patient experienced generalized malaise, then developed a fever of approximately 39°C, diarrhea, and erythema in the bilateral lower limbs with pain. However, she did not seek medical treatment at that time. Three days after onset, the pain became intense and the patient visited her nearby physician, who suspected enteritis and sent her to our hospital by emergency transport.

Her physical findings at admission to our hospital were as follows: height 158.5 cm, body weight 30.5 kg, temperature 39.2°C, blood pressure 116/67 mmHg, pulse 157 bpm regular, respiratory rate 18/minutes, and percutaneous oxygen saturation (SpO₂) 99%. The patient was alert, and there was no cutaneous or superficial lymph node enlargement. Although anemia was indicated by bulbar conjunctiva, there was no jaundice. Her abdominal area was flat and soft without tenderness, and there were normal bowel sounds. In the left thigh, we

Table 1 Laboratory findings at admission

Blood count			Biochemical parameters		
WBC	30200	/μl	TP	3.9	g/dl
RBC	272 x 10 ⁴	/μl	Alb	1.8	g/dl
Hb	8.3	g/dl	AST	145	IU/l
Ht	24.7	%	ALT	71	IU/l
Plt	19.1 x 10 ⁴	/μl	T-bil	1.6	mg/dl
			γ-GTP	485	IU/l
Coagulation			ALP	410	IU/l
PT	19.1	sec	ChE	40	IU/l
	29.9	%	BUN	12.5	mg/dl
APTT	43.8	sec	Cre	1.9	mg/dl
	58	%	CPK	805	IU/l
TIBC	63	μg/dl	Na	130	mEq/l
			K	4.1	mEq/l
Blood gas			Cl	93	mEq/l
PH	7.461		Ca	7.1	mg/dl
PCO ₂	20.4	mmHg	CRP	20.6	mg/dl
PO ₂	103.7	mmHg			
HCO ₃	14.3	mmol/l			
ABE	15	mmol/l			
SpO ₂	99.3	%			

observed purpura and erythema with, in part, a black necrotic area, as well as tenderness (Fig. 1).

Laboratory findings at admission are shown in Table 1. The patient had systemic inflammatory response syndrome (SIRS). The blood test results showed a marked increase in white blood cell count with a left shift and a marked increase in CRP level. An abdominal CT examination showed marked intestinal edema.

The clinical course after admission (Fig. 2) included preservation of peristalsis and no abdominal tenderness, thus bacterial translocation was suspected. After collecting blood for culture testing, an administra-



Fig. 1 Lower leg skin lesion at admission. Purpura, erythema, and necrotic area were observed.

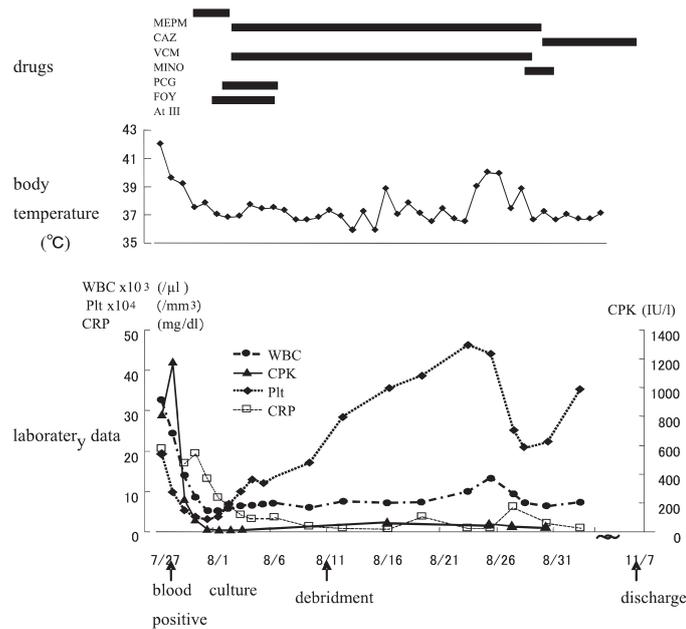


Fig. 2 Clinical course and administrated drugs

tion of the antibiotic Meropenem was started. Since tachycardia due to severe dehydration, hypotension, and hypoglycemia due to poor food intake were observed, systemic management including fluid transfusion and sugar supplementation were performed. On the second day of hospitalization, Gram-negative bacilli were detected in the blood culture. Further, bullae had formed on the right lower thigh and a septic rash was suspected, thus a skin biopsy was performed. On the third day of hospitalization, the laboratory reported findings suspicious of *V. vulnificus*, though there was no tendency for the rash to expand. We considered that indications for surgical treatment were not present and made a plan to follow the patient closely.

Following the results of a drug sensitivity test, the antibiotic agent was changed to ceftazidime and minocycline. In blood test findings, WBC and CPK improved, however, disseminated intravascular coagulation (DIC) progressed and the patient was transferred to the intensive care unit (ICU) for systemic management. After being placed

in the ICU, 1500 units of dried antithrombin III were repeatedly administered for 1 week. On the sixth day of hospitalization, DIC showed a tendency toward improvement, tenderness of the lower limbs had improved, and her complexion showed a tendency toward improvement. Thereafter, the vital signs also became stabilized and she was moved out of the ICU. On the fourteenth day of hospitalization, the margins of the rash on the lower limbs had become well defined. Further, ulcers were observed in the right heel, right lower thigh, and left thigh regions, with plastic surgery treatment for the right heel thought to be necessary, though the area that needed treatment was extensive. It was decided that such treatment would be performed after improvement of her overall condition and the patient continued to be followed closely.

On the eighteenth day of hospitalization, redness and warmth were observed surrounding the necrotic tissue in the medial area of the right ankle. The condition worsened rapidly from white to black necrosis, and infection in the necrotic lower

layer was suspected. Therefore, an emergency debridement procedure was performed. Postoperatively, the patient suffered hypoglycemic episodes, hypotension, and fever, and was treated with intravenous glucose, an administration of catecholamine, and a change in antibiotics. Skin treatment was continued during this time. On the 57th day of hospitalization, an arterial flap of the right lower thigh and skin graft of the right lower thigh were performed, after which the postoperative clinical course was good. There was no infection in the wound site and the skin graft survival was good. Therefore, on the 65th day of hospitalization, rehabilitation was started. On the 107th day, the condition of the patient had improved sufficiently and she was discharged from the hospital.

Discussion

The clinical forms of *V. vulnificus* infection are (1) primary septicemia due to oral transmission of infection, (2) wound infection, and (3) gastroenteritis²⁾, with more than half of the cases in the form of primary septicemia, for which the rate of mortality is overwhelmingly high. The present patient ingested raw shrimp prior to the occurrence of symptoms, thus we speculated oral transmission. Typical clinical symptoms of *V. vulnificus* infection include sudden chills and fever, shock, and DIC accompanied with necrotizing fasciitis, cellulitis, and cutaneous bullae, which were all present in our patient. A report from the United States indicated that the fatality rate was 33% for patients whose treatment was started within 24 hours. However, when begun 72 hours or later, the fatality rate was 100%³⁾, indicating that fatalities increased with time before starting treatment. The present patient did not seek

medical care soon, thus treatment was started 3 days after onset. Thereafter, she received intensive care and treatment such as debridement, and her life was saved. This good outcome was thought to have resulted from a lack of severe liver dysfunction as an underlying disease, as well as prompt and effective treatment, during which the antibiotics were appropriately changed, based on the results of a blood culture drug sensitivity test that was conducted soon after admission.

Over 75% of patients with *V. vulnificus* infection have chronic liver diseases, such as cirrhosis of the liver, hepatocellular carcinoma, and hemochromatosis, as the underlying disease⁴⁾. A reduction in filter function, such as lowered number of phagocytes, is thought to have an important involvement in onset. Our patient had MEN-I and previously underwent 2 surgical procedures; extirpation of a parathyroid tumor and a pancreatoduodenectomy. In approximately half of the patients with MEN-I, hyperparathyroidism occurs by age 20 and most patients have onset by age 40. Our patient was a typical case with onset at age 19. In an approximately 15-year period, her body weight had decreased from 50 to 30 kg due to malabsorption syndrome following the pancreatoduodenectomy. In particular, in the half year prior to *V. vulnificus* infection, her weight loss totalled approximately 10 kg. As a result, the patient was considered to be immunodeficient and in a compromised condition due to extremely severe malnutrition, dehydration, and low body weight for an extended period of time. Sun et al. reported long-term laboratory test results of malabsorption syndrome after a pancreatoduodenectomy⁵⁾, and indicated that conditions such as anemia, hypocholesterolemia, and liver dysfunction gradually pro-

gressed.

Our patient also had anemia and hypocholesterolemia, which were being monitored. She was found to not have liver dysfunction prior to admission to our hospital and that lack was thought to be one of the factors that led to her survival. Pancreatic diabetes developed after the pancreatoduodenectomy⁵⁾ and her HbA1c level was approximately 6%, which is not severe. However, it was difficult to control the blood sugar level during the treatment process and she had frequent hypoglycemic episodes. It had been approximately 10 years since the patient had contracted postoperative pancreatic diabetes, which is the time frame in which complications appear. Since diabetes is considered to be one of the risk factors of *V. vulnificus* infection, it was thought that these factors overlapped and led to its onset.

An increase in free iron is a condition important for *V. vulnificus* proliferation *in vivo* in humans. The bacterial iron-acquisition mechanism involves a system of effective absorption of even minute amounts of iron by producing chelating agent siderophores. The presence of siderophores has also been reported in *V. vulnificus* infections⁶⁾. The present patient was taking an oral iron preparation for chronic anemia, which was speculated to have allowed *V. vulnificus* to proliferate.

Many reports have indicated that early surgical treatment is effective for soft tissue infections and removal of all macroscopic necrotic areas is said to be necessary at the time of surgery⁷⁾. In our patient, the symptoms of necrotizing fasciitis were not initially remarkable and the condition was determined to be septic rash, which was monitored. First, DIC treatment was performed, followed by treatment for the skin

condition on the lower thigh. However, until her overall condition stabilized following the extreme malnutrition and poor control of pancreatic diabetes, we decided to merely clean and disinfect the necrotic areas on the lower thigh, and debridement could not be performed at the acute stage. As a result, the necrotic area became enlarged and an emergency debridement procedure was performed on the eighteenth day of hospitalization. Thereafter, the overall condition of the patient became stabilized, and on the 57th day of hospitalization an arterial flap and skin graft were performed. These results confirmed that treatment of the wound area together with improvement of overall condition were important for the good outcome of this patient.

We have treated 18 patients with *V. vulnificus* infection at our hospital⁸⁾, all of whom, until the present patient, clearly had liver dysfunction. We think that there is a need for education to restrict compromised patients from consuming raw seafood during the summer, not only those with liver dysfunction, but also immunodeficient and malnourished patients. If *V. vulnificus* infection occurs, prompt treatment at an early stage is extremely important for survival. Further, it is essential to establish a system of prompt communication of information between medical personnel providing the initial care and higher level medical institutions.

Conclusion

We treat a patient with MEN type I who survived *V. vulnificus* infection after developing septicemia and necrotizing fasciitis. We found that it was important to select suitable antibiotics in addition to intensive systemic management at an early stage. Further, the need for education regarding *V.*

vulnificus infection for patients other than those with liver dysfunction, such as immunodeficient and compromised patients, was recognized.

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(和文抄録)

多発内分泌腫瘍 I 型患者に 合併した *Vibrio vulnificus* 感染症の 1 救命例

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多発性内分泌腫瘍術後の吸収不良症候群の 35 歳女性が、下痢、全身倦怠感、発熱及び両下肢の疼痛を伴う皮膚病変のため当院へ入院となった。患者は発症前に海老を生食していた。入院時は Systemic Inflammatory Response Syndrome の状態で、血液培養より *Vibrio vulnificus* が同定され ICU 入室となった。下肢の壊死組織部分に関しては、全身状態の改善を待ちデブリドマンを施行した。経過中に、低血糖発作や血圧低下、発熱を起こしたが、ブドウ糖静注やカテコラミン投与、抗生剤の変更等で対処し、入院 107 日目に軽快退院となった。当院での *Vibrio vulnificus* 感染症患者は、本症例以外はすべて明らかな肝機能障害を認めていたが、今後は免疫不全や低栄養状態の患者など、易感染性の状態である患者に対しても、本症の予防に関する啓発活動が重要であり周辺医療機関との相互の情報交換が必要である。