Necrotizing Duodenitis Caused by Clostridium perfringens Type A in a Japanese Young Man

Hideharu Hagiya, Hiromichi Naito, Junichi Sugiyama, Hiroyoshi Nojima, Shingo Hagioka and Naoki Morimoto

Abstract

A 21-year-old Japanese man with a history of marked body weight loss over a short period of time died of necrotizing duodenitis caused by Clostridium perfringens (C. perfringens) type A. C. perfringens type A is considered to usually cause self-limiting gastroenteritis. Necrotizing enteritis sometimes occurs due to C. perfringens in developing countries; however, it is primarily caused by the type C strain and its site of onset is typically the jejunum or ileum. This is a rare case of necrotizing duodenitis caused by C. perfringens type A in a Japanese young man. Physicians need to be more aware of this emerging fatal disease in developed countries.

Key words: necrotizing enteritis, Clostridium perfringens, type A, pigbel, duodenitis

Introduction

Clostridium perfringens (C. perfringens) is a large gram-positive rod that is ubiquitously distributed in the soil and the intestines of various animals, including humans (1). C. perfringens is classified into five types (A-E) depending on the pattern of the toxin (α, β, ε and ι) it produces: type A produces only the α toxin; type B produces the α, β and ε toxins; type C produces the α and β toxins; type D produces the α and ε toxins; and type E produces the α and ι toxins.

Type A organisms cause food poisoning and gas gangrene throughout the world. Food poisoning is a self-limiting disease and gas gangrene usually occurs in the soft tissue after trauma or surgery. Type B and D organisms are considered to be nonpathogenic to humans. Meanwhile, type C organisms are known as the pathogenic organisms of enteritis necroticans (pigbel or clostridial necrotizing enteritis: CNE), a type of hemorrhagic necrosis of the jejunum and ileum. CNE is a health problem in developing countries where people are in a chronic state of malnutrition, especially protein deficiency, and sweet potatoes, which contain trypsin inhibitors that prevent the intestinal degradation of the toxin, are ingested as a staple food (2, 3). As a result, several factors are generally required for CNE to occur.

We herein describe a fatal case of necrotizing duodenitis caused by C. perfringens type A in a Japanese young man.

Case Report

A 21-year-old man was transported in a state of cardiopulmonary arrest to Tsuyama Central Hospital. The patient had no particular past medical history and had been healthy 10 months previously. His height was 170 cm and his body weight was approximately 70 kg. However, he had experienced marked body weight loss of approximately 15 kg over 10 months after he began living alone upon becoming a university student. The reason for his profound weight loss was unclear. His family was not aware of any possible underlying diseases such as anorexia nervosa.

Two days previously, he had attended an all-you-can-eat restaurant where he ate plenty of curry with rice, a Japanese-style cooked meat soup, and began vomiting a few times. He then lost consciousness and was transported to Tsuyama Central Hospital.

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C. perfringens was detected in a blood culture after the patient’s death. Polymerase chain reaction genotyping showed that this pathogen possessed the α-toxin gene only (4), indicating that it was C. perfringens type A (Fig. 2). Additionally, it was also proven that the pathogen had the toxigenicity to produce the α toxin in a culture test using a Western blot analysis and the activation of phospholipase C. Test for enterotoxin and the TpeL toxin, a newly discovered virulence factor (5), were negative.

**Discussion**

CNE is a fatal disease of the intestines that causes hemorrhage, necrosis and perforation primarily in the jejunum or ileum. It is usually caused by C. perfringens type C, which produces the β toxin, the direct mediator of vascular endothelial cells in the intestines (1, 6). Healthy young adults seldom contract CNE since unconventional conditions are required in the host. From this point of view, this case is worth being reported. There are three notable points in the present case: namely, the causative organism, the infected site, and the geographical distribution.

First, we refer to the virulence factor. Among five different types of C. perfringens, type A produces the α toxin only and is considered to be the common cause of enterotoxin-mediated self-limiting food poisoning or gas gangrene in soft tissue (7). In general, type A does not cause CNE since it does not produce the β toxin that is considered the main causative factor of necrotic lesions. However, although its pathogenicity and pathophysiological mechanisms have not yet been identified, C. perfringens type A has been reported to be a cause of CNE, and the number of CNE cases caused by type A organisms is reported to be increasing (2, 8). The present case indicates

<table>
<thead>
<tr>
<th>Table</th>
<th>Clinical Data on Arrival</th>
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<tr>
<td>WBC</td>
<td>2,800 /mm³</td>
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<tr>
<td>LDH</td>
<td>688 IU/L</td>
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<tr>
<td>PT-INR</td>
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<td>Neutrocyte</td>
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<tr>
<td>AST</td>
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<tr>
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<tr>
<td>Monocyte</td>
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<tr>
<td>γGTP</td>
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<tr>
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<tr>
<td>Amylase</td>
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<tr>
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<tr>
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<tr>
<td>Mb</td>
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<tr>
<td>Free T3</td>
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<tr>
<td>Platelet</td>
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<td>T-bil</td>
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<td>IgA</td>
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<tr>
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<tr>
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<tr>
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<tr>
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that the α toxin can be related to the occurrence of CNE since test for the other known virulence factors, including the TpeL toxin, were negative.

Second, an unusual site was primarily impaired. Commonly, the jejunum and ileum are the primary infectious sites of CNE. In the present case, however, emphysematous changes in the intestinal wall were found in the duodenum only; therefore, we diagnosed the patient with clostridial necrotizing duodenitis. A diagnosis of emphysematous gastroduodenitis, which is also a fatal disease, could have been considered instead. However, an autopsy was not performed and it was difficult to make a conclusive diagnosis. No typical findings of emphysematous gastritis were found on CT. Although epidemiologically and pathologically rare, we considered a diagnosis of clostridial necrotizing duodenitis to be preferable. To our knowledge, there have been no reports describing a case of CNE occurring in the duodenum, and the exact etiology of this disease is understandably unknown. We cannot conclusively determine the underlying mechanisms in this case; however, the existence of unidentified virulence factors can be considered.

Finally, the geographical distribution of this disease has yet to be fully clarified. CNE is a health problem in developing countries where people are in a state of chronic malnutrition. The risk factors of CNE include prolonged protein deprivation that leads to protease depletion, consumption of sweet potatoes (which contain trypsin inhibitors, and trypsin degrades the β toxin in the intestines thereby preventing the development of CNE), ample pork consumption and ascariasis (in which the pathogen produces a potent trypsin inhibitor to prevent its own digestion) (2, 3). Pigbel is the term for necrotizing enteritis caused by C. perfringens type C in Papua New Guinea where many children die of the disease and poorly cooked pork is consumed by protein-deficient
people (9).

In developed countries, on the other hand, CNE is an infrequent disease since people tend to eat a nutritious diet, do not eat sweet potatoes as a staple food and are often not infected with ascariasis. Even though *C. perfringens* type C may be ingested, the toxin is usually degraded by digestive enzymes, such as trypsin.

Diabetes mellitus is reported to be a risk factor for CNE in developed countries (10, 11). Gui et al. reported that diabetes mellitus reduces gastrointestinal motility, which can be associated with overgrowth of clostridial bacteria and an accumulation of toxins in the gut (12). The patient in the present case had no past medical history of diabetes mellitus or its signs on admission.

One report refers to the possibility of body weight loss being a cause of CNE (2). Indeed, the patient presumably lost more than 10 kg of body weight over 10 months. His thyroid function was normal. He might have had anorexia nervosa or a malignant disease that could have been the cause of the profound body weight loss. However, even his family members were not aware of any possible underlying diseases since he lived alone for a long time. Although the cause of the patient’s body weight loss was not apparent, it is possible that the rapid and marked body weight loss was related to the infection.

It is also conceivable that the low level of immunoglobulins observed in this case was suggestive of some sort of underlying immunodeficiency disease. However, in general, serum immunoglobulins may be rapidly consumed and their levels are known to decrease in cases of severe infection, as in this case.

The source of infection should be also discussed. We assume that the curry with rice served at the all-you-can-eat restaurant is the most likely source of the infection because large amounts of food are cooked simultaneously and re-cooked repeatedly for many customers. The more food is re-cooked, the more likely it is to create an optimum environment for *C. perfringens*. Heat increases the temperature and releases dissolved oxygen inside the food. *C. perfringens* grows rapidly at relatively high temperatures (its optimum temperature is approximately 45°C) when competitive bacteria cannot grow well. Additionally *C. perfringens* can survive as spores under anaerobic conditions.

Treatment of CNE includes antibiotic therapy, surgery and hyperbaric oxygen therapy. The prognosis of patients with CNE is very poor: the mortality rate has been calculated to be 75% in the reports by Sobel et al. (2). Therefore, prevention is important. A person with severe protein deficiency, diabetes mellitus or a history of rapid emaciation should avoid consuming preserved or recooked foods that contain large amount of meat. In cases of preservation, food should be heated well for long periods and placed in the refrigerator as soon as possible after cooking to kill the spores.

This is a rare case of necrotizing enterocolitis caused by *C. perfringens* type A in a Japanese young man. The patient died soon after the onset of the disease. Physicians should be more aware of this emerging fatal disease in developed countries, and further investigation of the virulence factors of necrotizing enteritis is warranted.

The authors state that they have no Conflict of Interest (COI).

Acknowledgement

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References