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Letter to the Editor

Antitoxin treatment for liver abscess caused by *Clostridium perfringens*

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To the Editor,

We read with great interest the article 'A case of emphysematous hepatitis with spontaneous pneumoperitoneum in a patient with hilar cholangiocarcinoma' by Jung Ho Kim et al.[1]

The authors described fatal case of emphysematous hepatitis caused by *C. perfringens*, but did not mention the hemolysis or disseminated intravascular coagulopathy (DIC) during hospital course. Laboratory data on admission revealed anemia (hemoglobin 9.3 mg/dL), severely elevated aspartate transaminase (AST) level (882 IU/L), and high total bilirubin level (17.9 mg/dL), but alanine transaminase (ALT) level was elevated moderately (257 IU/L). Although clinical data was limited, this disproportion between AST and ALT may suggest the intravascular haemolysis caused by *C. perfringens*.

Van Bunderen et al retrospectively reviewed 40 cases of *C. perfringens* septicaemia that rapidly progressed to intravascular haemolysis and metabolic acidosis and led to death within a few hours after admission.[2] The mortality rate was >80% despite treatments with high-dose intravenous penicillin and surgical debridement to eliminate the focus of infection. Therefore, we must redefine conventional treatments by reexamining the pathophysiology of such infections.

Alpha toxin secreted by *C. perfringens* is responsible for intravascular haemolysis followed by severe anemia, acute renal failure, DIC and multi-organ failure. Therefore, specific antitoxic globulins (antitoxin) should be administered with antibiotics as early as possible to neutralise the toxin. In fact, the antitoxin against the alpha toxin of *C. perfringens* has been used for decades for the treatment for gas gangrene (myonecrosis) caused by *C. perfringens*.[3] However, this product is no longer available in the United States because of poor efficacy and severe allergic reactions.[4] Aggressive surgery, including amputation and repeated debridement, constitute the mainstay of treatment of myonecrosis caused by *C. perfringens*.

On the other hand, the efficacy of antitoxin treatment for liver abscess caused by *C. perfringens* has not been evaluated. Unlike gas gangrene, *C. perfringens* septicaemia rapidly causes haemolysis followed by multi-organ failure; therefore, surgical intervention is not attempted in many cases. We recently introduced the use of the antitoxin against the *C. perfringens* alpha toxin to cease haemolysis and prevent multi-organ failure.[5] Here we confirmed that the antitoxin effectively neutralises the alpha toxin secreted by *C. perfringens*; however, it does not possess antibacterial activity or the capacity to prevent bacterial growth and cannot restore organ function. Therefore, we propose that the optimal treatment for *C. perfringens* septicaemia should combine the antitoxin, antibiotics and surgical intervention.

Conflicts of Interest

The authors have no conflicts to disclose.

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Author's Response to Letter to the Editor

We thank Dr Toru Hifumi et al for their comments on our article. We completely agree that alpha-toxin, which is produced in large amounts by type A strain of Clostridium perfringens, is likely to be the major factor responsible for the tissue pathology in myonecrosis (gas gangrene) and intravascular hemolysis leading to multiorgan failure and even death.[1] Patients with liver cirrhosis, gastrointestinal tract malignancy, poorly controlled diabetic mellitus, and the elderly are known to be high risk groups for Clostridium septicemia. Though it is rare, liver abscess caused by Clostridium perfringens leads to rapidly deteriorating condition with a high mortality rate ranging from 70 to 100%.[2] Early recognition and aggressive treatment with a multidisciplinary team approach is critical for the treatment of this catastrophic condition.

Recently , Law et al reported the mortality of a middle-aged woman caused by *C. perfringens* associated liver abscess[3] based on a review of 20 cases of *C. perfringens* associated pyogenic liver abscess published in the English literature since 1990. To date, high dose penicillin (10-24 million units daily) with surgical debridement of all involved gangrenous tissue are the treatment of choice for *C. perfringens* septicemia. When surgical debridement is difficult, hyperbaric oxygen therapy is worth considering as it can decrease the toxin production rate and make the environment less anaerobic. The less anaerobic environment hinders the growth of *C. perfringens* because they lack superoxide dismutase, which makes them incapable of surviving in the oxygen-rich environment created within a hyperoxic tissue.[4] However, in patients with *C. perfringens* associated liver abscess, surgical debridement of the infected liver tissue seems almost impossible in clinical practice and the role of percutaneous drainage for prevention of further production of toxin is usually limited. Accordingly, the antitoxin treatment for *C. perfringens* associated liver abscess suggested by Dr Hifumi et al is a fascinating treatment option. However, the data regarding the efficacy of antitoxin treatment for *C. perfringens* associated liver abscess is currently very limited and it seems premature for antitoxin therapy to be used for clinical practice. Moreover, antitoxin for *C. perfringens* has not yet been released on the market in Korea. Nevertheless, we hope that the antitoxin therapy for this fatal disease proposed by Dr Hifumi and colleagues is shown to be successful in the near future.

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