

Fatal *Aeromonas hydrophila* Infection of Soft Tissue after Endoscopic Injection Sclerotherapy for Gastric Variceal Bleeding

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Aeromonas hydrophila, an anaerobic gram-negative bacillus, can cause severe infections in immune-compromised patients. We present a 45-year-old cirrhotic man who suffered from hematemesis and received emergency endoscopic injection sclerotherapy (EIS) for gastric variceal bleeding. Twenty-one hours after EIS, painful swelling of the bilateral lower extremities and fever occurred. Severe soft-tissue infections with emergence of hemorrhagic bullae over the bilateral lower extremities followed. Even under aggressive treatment, the patient died of overwhelming sepsis 42 hours after EIS. Cultures of the blood and serosanguineous fluid from the hemorrhagic bullae revealed *Aeromonas hydrophila*. To the best of our knowledge, this is the first case of fatal *Aeromonas hydrophila* infection after emergency EIS for gastric variceal bleeding reported in the English literature. It is worth emphasizing that physicians should consider *Aeromonas hydrophila* infection in cirrhotic patients who develop soft-tissue infections after variceal bleeding whether emergency EIS has been performed or not. (*Chang Gung Med J* 2004;27:766-9)

Key words: emergency endoscopic injection sclerotherapy, soft-tissue infections, *Aeromonas hydrophila*.

Major varices hemorrhage is a life-threatening complication of liver cirrhosis. Endoscopic injection sclerotherapy (EIS) is the treatment of choice for controlling active varices hemorrhage. It has a high success rate and reduces the frequency and severity of recurrent bleeding.⁽¹⁾ However, it may also be associated with systemic and local complications. Transient bacteremia can occur after EIS with the mean rate around 15.4%, but septicemia tends to be relatively infrequent.^(2,3) Herein, we presented a fatal *Aeromonas hydrophila* (*A. hydrophila*) sepsis in a cirrhotic patient after emergency EIS for cardiac variceal bleeding.

CASE REPORT

A 45-year-old man with a history of hepatitis B-related liver cirrhosis for 4 years had two episodes of hematemesis. He had no fever, diarrhea, abdominal pain, or lower extremity pain before the hematemesis. He also denied any history of trauma or consumption of raw seafood.

His vital signs were temperature 36.8°C, heart rate 118 beats/min, blood pressure (BP) 105/64 mmHg, and respiratory rate 19 breaths/min. Physical examination revealed a normal heart and chest, spider angioma on the upper chest wall, and mild

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Received: Sep. 18, 2003; Accepted: Dec. 29, 2003

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abdominal distension with shifting dullness. There was no sign of infection or trauma on the skin of the extremities. Laboratory data revealed white blood count (WBC) 8,900/ μ l without left shift, hemoglobin 7.2 g/dl, hematocrit 19.4%, platelets 85,000/ μ l, total bilirubin 2.2 mg/dl, and prothrombin time 14.3 seconds (international ratio 1.32). The reserved hepatic function was grade B by modified Child's criteria. Under the impression of variceal bleeding, supportive treatment was given including intravenous somatostatin infusion. Six hours after his arrival, an upper gastrointestinal endoscopy revealed oozing moderate-sized cardia varices (Form 2) as well as moderate esophageal varices (Form 2). There was no specific finding over the fundus or high body of the stomach and duodenum. Emergency EIS with 1.5 ml of Histoacryl[®] mixed with 2.0 ml of Ethiodized oil (38% w/w) was done in 3 sessions for cardia variceal bleeding. No hematemesis was noted after EIS and his hypovolemic condition became stable.

Twenty-one hours after EIS, he began to suffer from progressive pain in the bilateral lower extremities. Subsequently, fever up to 39.2°C occurred 23 hours after EIS, and his BP dropped to 85/55 mmHg with a pulse rate of 128/min. Progressive dusky blue discoloration of the skin and edematous soft tissue over the bilateral legs were also noted. Twenty-six hours after EIS, hemorrhagic bullae emerged, initially over the bilateral legs, and then expanded rapidly to both thighs (Figure). Repeated studies of the urine, ascites and chest radiography were normal. Cultures of the blood, ascites and serosanguineous fluid from the hemorrhagic bullae were collected. Laboratory data showed (WBC 4,500/ μ l with 10% of band form, hemoglobin 6.2 g/dl, hematocrit 16.4%, platelets 45,000/ μ l) and the coagulation studies revealed a pattern consistent with disseminated intravascular coagulation (DIC). Under the impression of septic shock with DIC, the patient was transferred to the intensive care unit and antibiotics including cef-tazidime, amikacin and doxycycline were given. Owing to recurrent hematemesis, upper gastrointestinal endoscopy was performed and moderate esophageal varices (Form 2) with a positive red color sign were found. Endoscopic variceal ligation for esophageal varices was done. In addition, surgical intervention was suggested under the impression of severe soft-tissue infections or purpura fulminans, but his family refused. Even after aggressive treat-



Fig. Emergence of hemorrhagic bullae on the right thigh and soft-tissue infection on the right leg are seen. Eschar developed at the site of bullae rupture on the left thigh.

ment, the patient died of overwhelming sepsis 42 hours after emergency EIS. Cultures of blood and serosanguineous fluid from the hemorrhagic bullae grew gram-negative bacilli, which were identified as *A. hydrophila* with resistance to cefazolin, ampicillin and amoxicillin-clavulanic acid on susceptibility testing.

DISCUSSION

The pathogenic mechanism for increased risk of infection in cirrhotic patients has been suggested to be depressed cell-mediated immunity, reduced serum levels of complements, and shunting of the portal-systemic circulation.^(4,5) In cirrhotic patients with gastrointestinal bleeding, prospective studies have shown that up to 22% of cases develop bacterial infection,⁽⁶⁾ about 20% within the first 48 hours.^(4,6) The increased risk of bacterial infection is generally considered due to invasive procedures, increased intestinal translocation and greater suppression of the reticuloendothelial system.⁽⁶⁾ EIS is widely used for the treatment of variceal bleeding in cirrhotic patients and may also be associated with systemic and local complications. Many infectious complications have been reported including brain abscess, meningitis, bacterial peritonitis, perinephric abscess, meningococemia, and candida sepsis.⁽²⁾ The bacterial species in septicemia are usually oropharyngeal flora.^(7,8) To the best of our knowledge, this is the first

case in the English literature of fatal septicemia after emergency EIS caused by *A. hydrophila* that presented with severe soft-tissue infections and emergence of hemorrhagic bullae over the bilateral lower extremities.

A. hydrophila is an anaerobic gram-negative bacillus with positive catalase and oxidase reactions. It is recovered widely from soil, sewage, and fresh or brackish water and from clinical specimens such as feces, blood, ascites, wound discharge, sputum, and cerebrospinal fluid.⁽⁹⁾ In immunocompromised patients, *A. hydrophila* can cause infectious diarrhea, soft-tissue infections, meningitis, endocarditis, peritonitis, cholecystitis, and septicemia.⁽⁹⁾ Two mechanisms for soft-tissue infections caused by *A. hydrophila* have been proposed. First, the organism invades through trauma and causes primary infection of the soft tissue. Second, sepsis is first induced by the pathogen and then metastatic lesions develop in the soft tissue.⁽¹⁰⁾ Due to shunting of the portal-systemic circulation in cirrhotic patients; *A. hydrophila* can establish bacteremia by gaining access to the systemic vein from the gastrointestinal tract to escape phagocytosis by the Kupffer cells of the hepatic reticuloendothelial system. Our patient had neither infectious signs nor a history of gastroenteritis or trauma over legs before EIS. Possibly, the infection was caused by introducing *A. hydrophila* into the bloodstream via the EIS procedure or the puncture wound. The pathogen then caused septicemia and severe soft-tissue infections. However, we did not have a direct evidence that *A. hydrophila* septicemia was induced by EIS. The hemorrhagic bullae developed 21 hours after EIS, it is possible that septicemia was presented before EIS.

In immunocompromised patients, the fatality rate of *A. hydrophila* septicemia with soft-tissue infections is high.⁽¹⁰⁾ In this setting, early recognition of the surgical conditions and adequate antimicrobial therapy are very important. However, an increasing number of clinical studies have pointed out that the organism has become resistant to antibiotics resulting from inducible β -lactamases, and that first-generation cephalosporins, penicillin, semi-synthetic penicillin and their combinations with β -lactamase inhibitors are not recommended for empiric thera-

py.⁽⁹⁾ Despite aggressive treatment with empiric antibiotics, our patient expired 42 hours after EIS due to overwhelming sepsis.

In conclusion, fatal septicemia can occur after emergency EIS for varices bleeding. Our patient expired due to *A. hydrophila* sepsis and severe soft-tissue infections after EIS. Lacking direct evidence, we could not prove that EIS caused *A. hydrophila* sepsis. It is still worth emphasizing that physicians should consider *A. hydrophila* infection in cirrhotic patients who develop soft-tissue infections after variceal bleeding whether emergency EIS has been performed or not. Appropriate empiric antimicrobial therapy and prompt surgical evaluation are recommended.

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胃靜脈曲張出血經內視鏡注射硬化治療後發生致命性親水性 產氣單胞菌的軟組織感染：三病例報告

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親水性產氣單胞菌 (*Aeromonas hydrophila*) 為厭氧革蘭氏陰性菌，常會造成免疫不全患者嚴重的感染。在此報告一位45歲有肝硬化病史的男性因胃靜脈曲張出血而接受緊急內視鏡注射硬化治療。在硬化治療21小時後，發生雙下肢疼痛腫脹及發燒，進而發展成雙下肢的嚴重軟組織發炎合併出現出血性水泡。雖然給予積極的內科治療，病患於內視鏡硬化治療42小時後死於嚴重的敗血症。血液及水泡液培養長出親水性產氣單胞菌。就目前所知在英文文獻中本病例為第一個在實行內視鏡硬化治療後而發生感染親水性產氣單胞菌的報告。在此提醒臨床醫師，肝硬化病患在靜脈曲張出血後無論是否接受內視鏡硬化治療，若發生軟組織發炎應及早考慮親水性產氣單胞菌感染的可能性。(長庚醫誌2004;27:766-9)

關鍵字：緊急內視鏡注射硬化治療，軟組織發炎，親水性產氣單胞菌。

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受文日期：民國92年9月18日；接受刊載：民國92年12月29日。

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