

## Polymicrobial Bacteremia Caused by *Escherichia coli*, *Edwardsiella tarda*, and *Shewanella putrefaciens*

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*Edwardsiella tarda*, a member of Enterobacteriaceae, is found in freshwater and marine environments and in animals living in these environments. This bacterium is primarily associated with gastrointestinal diseases, and has been isolated from stool specimens obtained from persons with or without clinical infectious diseases. *Shewanella putrefaciens*, a saprophytic gram-negative rod, is rarely responsible for clinical syndromes in humans. Debilitated status and exposure to aquatic environments are the major predisposing factors for *E. tarda* or *S. putrefaciens* infection. A 61-year-old woman was febrile with diarrhea 8 hours after ingesting shark meat, and two sets of blood cultures grew *Escherichia coli*, *E. tarda* and *S. putrefaciens* at the same time. She was successfully treated with antibiotics. We present this rare case of polymicrobial bacteremia caused by *E. coli*, *E. tarda* and *S. putrefaciens* without underlying disease, which is the first found in Taiwan. This rare case of febrile diarrhea with consequent polymicrobial bacteremia emphasizes that attention should always be extended to these unusual pathogens. (*Chang Gung Med J* 2004;27:701-5)

**Key words:** bacteremia, *Edwardsiella tarda*, *Shewanella putrefaciens*.

*Edwardsiella tarda*, a member of the Enterobacteriaceae family, is a rare human pathogen that is primarily associated with gastrointestinal disease.<sup>(1-8)</sup> Extraintestinal infections, including soft-tissue infection, bacteremia, meningitis, cholecystitis, osteomyelitis, salpingitis and endocarditis, have rarely been reported.<sup>(1-8)</sup> Risk factors for *E. tarda* infections include exposure to aquatic environments or exposure to exotic animals (e.g. reptiles or amphibians), preexisting liver disease, conditions leading to iron overload, and dietary habits (e.g. ingestion of raw fish).<sup>(4)</sup>

*Shewanella putrefaciens*, a saprophytic gram-negative rod, is rarely isolated from clinical specimens.<sup>(9-13)</sup> *S. putrefaciens* is widely distributed in nature, and its natural habitat includes all forms of water, fish, oily food, and soil.<sup>(9,10)</sup> Both *E. tarda* and

*S. putrefaciens* are uncommon as isolates in clinical settings. *S. putrefaciens* bacteremia had been reported in premature and neonates, traumatic cases with ulceration and cellulitis of the lower extremities and hepatobiliary disease.<sup>(9-11)</sup> Herein, we report 61-year-old otherwise healthy female with febrile diarrhea and polymicrobial bacteremia of *Escherichia coli*, *E. tarda*, and *S. putrefaciens* that occurred 8 hours after ingesting shark meat. According to the database of Medline, this is the first reported case of polymicrobial bacteremia caused by *E. coli*, *E. tarda*, and *S. putrefaciens* in a patient with previous cholecystectomy in Taiwan.

### CASE REPORT

A 61-year-old woman was admitted to our hos-

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Received: Oct. 1, 2003; Accepted: Dec. 16, 2003

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pital because of epigastric pain, fever, and chills for several hours on September 29, 2000. The day before admission, she had ingested shark meat for lunch, and then persistent epigastric pain developed 8 hours after lunch, accompanied by nausea and mild diarrhea.

She was in a good state of health except for a cholecystectomy for gallbladder stones 13 years prior to this admission. On examination her height was 152 cm, weight was 57 kg, and temperature was 38°C, with a pulse rate of 80/min and blood pressure of 120/80 mmHg. There was a little tenderness over the epigastric area. Neither rebounding pain nor costovertebral tenderness was noted.

Laboratory test results showed a white blood cell count at 10,600/mm<sup>3</sup> with 82% segments, 6% bands, 7% lymphocytes, and 4% monocytes; hemoglobin at 13.1 g/dL; serum aspartate aminotransferase at 50 U/L; total bilirubin at 1.5 mg/dL; alkaline phosphatase at 91 U/L; and serum creatinine at 0.8 mg/dL. Her stool analysis was strongly positive for occult blood without pus cells. Her abdominal radiograph was unremarkable. Colonofibroscope showed internal hemorrhoids only. Renal sonography revealed a 5.3-cm cyst at the left kidney without parenchymal changes.

Immediate blood (two sets each in aerobic and anaerobic bottles) (Becton Dickinson, BACTEC 9240), urine, and stool cultures were collected and empirical intravenous antibiotics with cefazolin and gentamicin were initiated after obtaining blood cultures. Subcultured blood specimens were plated onto traditional blood agar, eosin-methylene blue agar, and chocolate agar, the first two were incubated both in air and anaerobically at 37°C. Small colonies of variant morphology became evident within 36 hours. On a Gram stain, the isolates were found to be gram-negative rods. Identification was initially performed using conventional biochemical tests, including hydrogen sulfide in triple-sugar-iron agar, citrate, urease, sulfide-indole-motility, Voges-Proskauer, ornithine, and oxidase. The semiautomated ATB ID 32 GN method (bioMérieux), which is based on 32 assimilation tests, was used for further confirmation of *S. putrefaciens*. The semiautomated API 20 E system (bioMérieux) which is based on 21 assimilation tests, was used for further confirmation of *E. tarda*. The Kirby-Bauer agar diffusion method was used for antimicrobial susceptibility determination.

Her fever subsided on the second day of hospitalization. At the same time, a remarkable improvement of her clinical status was observed. On the fourth day of hospitalization, both sets of blood cultures grew *E. coli*, *E. tarda*, and *S. putrefaciens*. Susceptibility testing showed that both of the *E. coli* and *E. tarda* isolates were susceptible to amikacin, aztreonam, ceftazidime, ciprofloxacin, ceftriaxone, cefuroxime, cefazolin, gentamicin, imipenem, piperacillin, and sulfamethazole-trimethoprim. The *E. tarda* isolate was also susceptible to ampicillin. The *S. putrefaciens* isolate was susceptible to amikacin, ceftazidime, ciprofloxacin, ceftriaxone, gentamicin, imipenem, piperacillin, and sulfamethazole-trimethoprim. The urine culture was negative and the stool culture specimen was not obtained before the start of antibiotics. The patient was discharged in a stable condition on the eighth day of hospitalization, and was on treatment with cefixime and doxycycline for another seven days. Outpatient clinic follow-up visits were uneventful. She visited our clinic twice within 2 weeks after discharge and did not come back thereafter.

## DISCUSSION

*E. tarda* has been isolated from both freshwater and marine environments and many animals, including turtles, water tortoises, fish, pelicans, alligators, seals, penguins, toads, snakes, swine, cattle, and lizards.<sup>(1,3,4)</sup> The main types of infections associated with this species include bacterial gastroenteritis, wound infections with cellulitis or gas gangrene due to trauma to mucosal surfaces, and systemic diseases such as septicemia, meningitis, cholecystitis, and osteomyelitis.<sup>(1-8)</sup> Although studies indicate that this bacterium is susceptible to most commonly prescribed antibiotics,<sup>(1,4)</sup> fatal gastrointestinal and extraintestinal infections have been reported.<sup>(8)</sup> Gastroenteritis caused by *E. tarda* appears to be more common in tropical and subtropical regions where raw fish known to carry Edwardsiellae is a dietary staple.<sup>(4)</sup>

Extraintestinal isolates of this species have been discovered in blood, urine, bile, cerebrospinal fluid (CSF), peritoneal fluid, synovial fluid and wounds.<sup>(1-8)</sup> *E. tarda* bacteremia has a mortality rate about 50%,<sup>(4)</sup> and 75% of *E. tarda* bacteremia has been described in patients with underlying conditions such as hepa-

tobiliary disease or iron overload states.<sup>(1,3,4)</sup> Approximately 12% of *E. tarda* bacteremia is polymicrobial.<sup>(1,3,4)</sup> Most researchers failed to document the specific type of exposure (e.g. to reptiles) or food causing the *E. tarda* infection, although two patients in previous reports had occupations (a gardener and a farmer) that may have led to environmental exposure to *E. tarda*.<sup>(4)</sup> *E. tarda* wound infections have been commonly mixed infections resulting from lacerations or penetrating injuries to limbs via aquatic injuries.<sup>(1,4-6)</sup>

*E. tarda* appears to be susceptible to most agents that target gram-negative bacteria; these include  $\beta$ -lactam antibiotics, aminoglycosides, chloramphenicol, imipenem, and fluoroquinolone.<sup>(1,3,4)</sup> Major resistance has only been reported with colistin and polymyxin B.<sup>(1,3,4)</sup> Treatment for gastrointestinal infection is not usually required as the illness resolves spontaneously without antibiotic therapy. For extraintestinal disease, most infections, particularly septicemia, are treated with a combination of antibiotics, including a cephalosporin and an aminoglycoside.<sup>(4)</sup>

*S. putrefaciens*, a saprophytic gram-negative rod, is widely distributed in nature, and its natural habitats include water and soil. It has been discovered in all forms of water (fresh, sea, river, and sewage), as well as in oysters, frogs, milk, butter, eggs, fish, meat, natural gas, petroleum brines, and it is one of the primary spoilage organisms of chilled protein-rich food.<sup>(9,10)</sup> *S. putrefaciens* has been occasionally isolated from various clinical specimens, including ear discharge, sputum, skin wounds, feces, conjunctiva, urine, CSF, bile, ascitic fluid, pleural fluid, and stored blood.<sup>(9-13)</sup> Three clinical syndromes are associated with *S. putrefaciens* bacteremia including (1) a fulminant disease resembling gram-negative septicemia seen in patients with liver disease, malignancy, or other severe debilities, (2) a relatively benign disease associated with chronic ulcers of the lower extremities, and (3) a syndrome associated with prematurity.<sup>(9-11)</sup> The incidence of polymicrobial bacteremia combined with *S. putrefaciens* is over 50%.<sup>(9-11)</sup> The mortality rate of *S. putrefaciens* bacteremia ranges from 22% to 43%.<sup>(9,10)</sup>

*S. putrefaciens* is susceptible to a wide variety of common antibiotics that target gram-negative bacteria.<sup>(9,10)</sup> Two multiple drug-resistant isolates have been previously reported,<sup>(9)</sup> and empirical therapy

using a combination of piperacillin and amikacin or gentamicin is suggested.<sup>(9)</sup>

This patient was in her usual state of health and had no specific underlying disease. She experienced febrile diarrhea several hours after eating lunch, which included some shark meat. Poorly cooked fish may have led to the concurrent infection with *E. coli*, *E. tarda*, and *S. putrefaciens* in her blood. Since two sets of blood cultures yielded *E. coli*, *E. tarda* and *S. putrefaciens*, the possibility of contamination can be excluded. Both *E. tarda* and *S. putrefaciens* are rare human pathogens. Their importance in human pathology has become increasingly evident during the last few years, however, mixed bacteremia caused by *E. tarda* and *S. putrefaciens* has not been reported in the literature.

In our opinion, this rare case of febrile diarrhea with consequent polymicrobial bacteremia emphasizes the hypothesis that attention should always be extended to unusual pathogens, especially under particular circumstance. This case demonstrated the occurrence of mixed bacteremia of *E. coli*, *E. tarda*, and *S. putrefaciens* after the consumption of poorly cooked shark meat. Both *E. tarda* and *S. putrefaciens* may be regarded as opportunistic pathogens in some immunocompromised patients with specific predisposing factors.

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# 大腸桿菌、遲鈍艾德氏菌和 *Shewanella putrefaciens* 混合： 一菌血症病例報告

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遲鈍艾德氏菌是一種可從淡水和海水以及許多水生動物分離出來的細菌。其歸屬於腸細菌科。此細菌主要和胃腸道疾病有關，而且可從有無臨床感染症狀人的糞便所分離出來。*Shewanella putrefaciens* 是一種腐生性的格蘭氏陰性桿菌，而且很少導致人類疾病。病患本身的慢性疾病和暴露於水生的環境是造成遲鈍艾德氏菌和 *S. putrefaciens* 感染的主要危險因子。一位61歲的女性吃鯊魚8小時後而有上腹疼痛、發燒、畏寒、輕微腹瀉的症狀。血液培養產生大腸桿菌、遲鈍艾德氏菌和 *S. putrefaciens*。此病患成功地接受抗生素治療。我們報告台灣第一個大腸桿菌、遲鈍艾德氏菌和 *S. putrefaciens* 等菌血症發生在沒有潛在疾病患者的罕見病例。此少見的腹瀉病例併發發燒和多種菌血症，提醒醫界必須注意這些罕見的病原菌。(長庚醫誌 2004;27:701-5)

**關鍵字：**菌血症，遲鈍艾德氏菌，*Shewanella putrefaciens*。

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受文日期：民國92年10月1日；接受刊載：民國92年12月16日

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