CASE REPORT

EDWARDSIELLA TARDA BACTEREMIA AND SEPTIC ARTHRITIS IN A PATIENT WITH DIABETES MELLITUS

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Abstract. *Edwardsiella tarda* is an uncommon pathogen in the family Enterobacteriaceae which usually infects patients with underlying diseases. Its habitats include fresh water, a variety of animals and human feces. We report a case of *E. tarda* bacteremia and septic arthritis with underlying diabetes mellitus, the first found in Thailand.

The genus *Edwardsiella* belongs to the family Enterobacteriaceae (Jordan and Hadley, 1969; Farmer and McWhorter, 1984). The organism was first recognized by Ewing *et al* in 1965 (Jordan and Hadley, 1969; Farmer and McWhorter, 1984; Michael Janda and Abbott, 1993). It was named after the American bacteriologist PR Edwards (Michael Janda and Abbott, 1993). Currently, three species in the genus *Edwardsiella* have been identified. However, only *Edwardsiella tarda* has been demonstrated to be pathogenic for humans. In human infections, *E. tarda* has been suspected as a potential cause of gastroenteritis since its identification (Michael Janda and Abbott, 1993). *E. tarda*-associated diarrhea appears to be more common in tropical and subtropical regions (Kourany *et al*, 1977; Sakazaki and Murata, 1962), in persons with a history of exposure to aquatic environments or exotic animals (Michael Janda and Abbott, 1993). In rarer extraintestinal disease, *E. tarda* may cause serious infections (*eg* septicemia, meningitis or liver abscess) in individuals with underlying illnesses, particularly chronic liver disease (Clarridge *et al*, 1980; Wilson *et al*, 1989; Zighelboim *et al*, 1992).

We report a case with poorly controlled diabetes mellitus who developed *E. tarda* septic arthritis after a brief episode of self-limited gastroenteritis. To our knowledge, this is the first reported case of *E. tarda* bacteremia and septic arthritis.

A 72-year-old poorly controlled diabetic female from the northeastern part of Thailand was admitted to Chulalongkorn University Hospital with a 2-day history of acute onset of pain in her right knee, hip and shoulder. Seven days earlier, after having beef soup, the patient developed watery diarrhea more than 10 times a day with a low-grade fever. The diarrhea improved spontaneously. Four days before being admitted to the hospital, she had a high-grade fever without chill or diarrhea, followed the next 2 days by pain in the right shoulder, hip and knee. Physical examination revealed a distressed elderly woman with temperature of 38°C, pulse 110/minute and blood pressure 160/100 mmHg. Her right knee was swollen, warm and tender on palpation. The knee movements were limited with moderate amount of joint effusion. The rest of the physical examination was unremarkable. The initial complete blood count showed Hb 13.8 g/dl, Hct 41.7%, white cell count 8,890/mm^3 with 70% neutrophils, 16% lymphocytes, 11% monocytes, 2% eosinophils and 1% basophils. Platelet count was 105,000/mm^3. Urinalysis showed 1+ protein and 2+ glucose without active sediments. Random plasma glucose was 498 mg/dl, BUN was 22 mg/dl and creatinine was 1.0 mg/dl. The liver function test revealed hypoalbuminemia (2.8 g/dl). The roentgenograms of the patient's knees showed mild osteoarthritic change without lytic lesion. The chest X-ray was within normal limits for age. The synovial fluid obtained from the patient's right knee was turbid and yellow in color. White cell count in the fluid was 112,000/mm^3 with 95% neutrophils. Gram stain revealed intra- and extracellular gram negative bacilli. On the first day of admission, the patient was initially treated with intravenous ceftazidime 2 g every 8 hours to cover Enterobacteriaceae and *Burkholderia pseudomallei*. All blood cultures and 2 consecutive synovial fluid cultures grew *Edwardsiella tarda*. Stool culture was negative. The organism was susceptible to

ampicillin, co-trimoxazole, amoxy-cillin-clavulanic acid, gentamicin, ciprofloxacin, third generation cephalosporins and imipenem. Antibiotic treatment was changed to ampicillin 1 g intravenously every 6 hours for a duration of 6 weeks. Repeated joint aspirations were performed daily. The clinical course was unevenly improved. Fortunately, no osteomyelitis complicated the disease.

Edwardsiella tarda, the only species implicated in human disease and the most commonly isolated member of this genus (Farmer and McWhorter, 1984; Michael Janda and Abbott, 1993; Wilson *et al*, 1989), is a motile, lactose-nonfermenting gram negative bacillus (Farmer and McWhorter, 1984; Michael Janda and Abbott, 1993). Sometimes it is misidentified as *Salmonella* because of biochemical similarity (Jordan and Hadley, 1969; Farmer and McWhorter, 1984; Michael Janda and Abbott, 1993). More than 105 serotypes are currently identified, using somatic (O) and flagellar (H) antigens (Michael Janda and Abbott, 1993).

E. tarda has been isolated from fresh water with and without overt sewage contamination and many kinds of animal such as fish, snakes, toads, lizards, turtles, monkeys, sea mammals, cattle, swine, opossums and birds (Michael Janda and Abbott, 1993; Kourany *et al*, 1977; Rao *et al*, 1981; Vandepitte *et al*, 1983). It has also been isolated from stools of asymptomatic humans (Michael Janda and Abbott, 1993, Wilson *et al*, 1989; Rao *et al*, 1981). Only the wild-type (or classical biotype) strains cause infections in humans and animals, while biotype 1 isolates have been found in snakes and water (Michael Janda and Abbott, 1993).

The most common clinical syndrome reported with *E. tarda* is gastroenteritis from ingesting contaminated food, although it has been difficult to implicate *E. tarda* as a true pathogen because of spontaneous resolution or the presence of other enteric pathogens (Michael Janda and Abbott, 1993). In most studies (Jordan and Hadley, 1969; Michael Janda and Abbott, 1993; Ovartlarnporn *et al*, 1986; Bockemuhl *et al*, 1971), asymptomatic colonization or convalescent state for *E. tarda* is extremely low, however, a published report indicates at least a 3 : 1 ratio of infected to colonized persons harboring *E. tarda* (Michael Janda and Abbott, 1993). So it may be regarded at times as an enteropathogen capable of producing disease similar to *Salmonella* gastroenteritis (Farmer and McWhorter, 1984; Michael Janda and Abbott, 1993; Clarridge *et al*, 1980). Although gastrointestinal infection is the most common feature in humans, the more serious forms are the extraintestinal infections (Clarridge *et al*, 1980; Wilson *et al*, 1989; Le Frock *et al*, 1970). The hallmark of extraintestinal disease caused by *E. tarda* is bacteremia in all ages with a high mortality rate. Most bacteremias are thought to arise endogenously by prior colonization and infection of gastrointestinal tract. The other route of infection is inoculation of wounds (Farmer and McWhorter, 1984; Michael Janda and Abbott, 1993; Clarridge *et al*, 1980; Rao *et al*, 1981). The majority of patients previously reported with bacteremia due to *E. tarda* have had gastroenteritis or localized wound infections. As in the literature, the preceding episode of self-limited gastroenteritis in our patient was the most likely cause of bacteremia and septic arthritis. Unfortunately, stool culture after admission failed to confirm *E. tarda* gastroenteritis. Our patient was also unable to document specific exposure to a known reservoir of *E. tarda*. Interestingly, there is only one report of *E. tarda* causing primary bacteremia in an elderly patient (Le Frock *et al*, 1970).

Septic arthritis in our case was a result of hematogenous spreading from the source in the bowel, which has not been reported elsewhere. However, there has been evidence of high prevalence of nongonococcal septic arthritis in elders, especially with underlying joint diseases (Vincent and Amirault, 1990). Our elderly patient might have had preexisting degenerative joint disease of the knees which can predispose bacterial lodging, although the X-ray appearance was within normal limits for age.

To our knowledge, the first case of osteroarticular edwardsiellosis ever reported was a man with sickle cell hemoglobinopathy who developed a puncture wound of his right foot after stepping on the remains of a snake. Right hip septic arthritis and osteomyelitis of femoral head complicated the disease. The bone fragment culture, obtained from open biopsy, yielded *E. tarda* and *Staphylococcus aureus* (Rao *et al*, 1981). The source of *E. tarda* infection in this case was assumed to be the snake skeleton but the mechanism of bacterial extension into the joint was not mentioned. This was different from our patient in the route of infection.

Previous reports of other extraintestinal edwardsiellosis included an enteric-like syndrome (Clarridge *et al*, 1980), wound infection/cellulitis (Jordan and Hadley, 1969; Clarridge *et al*, 1980),

liver abscess (Jordan and Hadley, 1969; Zighelboim *et al*, 1992), cholecystitis (Ovartlarnporn *et al*, 1986), cholangitis (Kourany *et al*, 1977), peritonitis (Clarridge *et al*, 1980), meningitis (Sonnenwirth and Kallus, 1968), salpingitis (Sechter *et al*, 1983), subacute bacterial endocarditis (Le Frock *et al*, 1976) and infected abdominal aortic prosthesis (Coutl'ee *et al*, 1992).

The majority of patients with serious extraintestinal infections had preexisting chronic liver disease or iron overload conditions. There were also reports of patients with other medical illnesses including SLE with steroid therapy, hepatocellular carcinoma, hematologic malignancy, rheumatic heart disease and diabetes mellitus (Clarridge *et al*, 1980; Wilson *et al*, 1989; Michael Janda and Abbott, 1993; Rao *et al*, 1981; Kourany *et al*, 1977; Le Frock *et al*, 1976; Sonnenwirth and Kallus, 1968; Barett-Connor, 1971). Our patient, a poorly controlled diabetic, was the second reported case to have this underlying disease.

E. tarda is susceptible to most antibiotics that target Enterobacteriaceae, based on *in vitro* susceptibility testing, including β-lactam antibiotics, cephalosporins, aminoglycosides and quinolones (Clarridge *et al*, 1980; Wilson *et al*, 1989; Michael Janda and Abbott, 1993). Although there is evidence of β-lactamase production by all strains of *E. tarda*, the minimal inhibitory concentrations (MIC) of this organism to all mentioned antibiotics are very low (Wilson *et al*, 1989; Michael Janda and Abbott, 1993). Gastrointestinal infections usually resolve spontaneously without antibiotic therapy, but in some cases with severe infections can be successfully treated with ampicillin, co-trimoxazole, third generation cephalosporins or quinolones (Jordan and Hadley, 1969; Clarridge *et al*, 1980; Wilson *et al*, 1989; Ovartlarnporn *et al*, 1986). In our patient, the susceptibility test of *E. tarda* isolates was similar to previous reports, but the clinical course was not an even one. This is compatible to other reports, in which *in vitro* susceptibility tests showed sensitivity of the organism to all antibiotics but the patients with extraintestinal diseases, especially bacteremia, still sustained high morbidity and mortality rates (Carridge *et al*, 1980; Wilson *et al*, 1989; Michael Janda and Abbott, 1993; Rao *et al*, 1981; Zighelboim *et al*, 1992). This might be due to defects of host immunity or organism virulence (Michael Janda and Abbott, 1993). Combination of antibiotics, such as a cephalosporin and an aminoglycoside was proposed in the treatment of extraintestinal edwardsiellosis, particularly bacteremia, to improve the outcome (Janda and Abbott, 1993).

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