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CASE REPORT

# The first imported human case of *Yersinia pseudotuberculosis* serotype O1 septicemia presents with acute appendicitis-like syndrome in Taiwan

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Human nonplague yersiniosis occurs more commonly in temperate regions than in tropical or subtropical regions. In Taiwan, which is located in a subtropical region of Southeast Asia, only environmental isolates and human infection of *Yersinia enterocolitica* were reported, but a human case of *Y. pseudotuberculosis* infection had not been identified. We report the first person with *Y. pseudotuberculosis* serotype O1 septicemia who presented with acute appendicitis-like syndrome and who was probably contracted the infection via ingestion of raw foods in a barbecue restaurant in Japan.


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## Introduction

Human nonplague yersiniosis, mainly caused by the infection of *Yersinia enterocolitica* and *Y. pseudotuberculosis*, occurs more commonly in temperate regions than in tropical or subtropical regions.[1] Outbreaks of *Y. pseudotuberculosis* have been reported in Finland,[2,3] France,[4] and Japan.[5,6] In Taiwan, which is located in a subtropical region of Southeast Asia, only a few isolates of *Y. enterocolitica* from swine[7–9] and human[10,11] have reported. Neither human infection nor nonhuman isolate of *Y. pseudotuberculosis* had been identified in Taiwan. Herein, we report the first human case of *Y. pseudotuberculosis* septicemia in Taiwan, which was probably imported from Japan.

## Case report

A Taiwanese businessman who was 33 years of age and who had resided in Osaka, Japan, for more than 6 months, presented to our emergency department with chief complaints of intermittent fever, abdominal pain, diarrhea, and progressive jaundice for 5 days at the end of May 2010. He recalled that he had eaten at a barbecue restaurant with friends 2 days before the illness occurred. In addition to barbecue, he also ate raw cattle liver (liver sashimi), fish sashimi, raw Tako (octopus), and semi-boiled pig's ear. Abdominal pain and mild diarrhea occurred in the first 2 days, and vomiting, fever, and progressive jaundice developed in the following 3 days. His friends also experienced mild gastrointestinal upset, but neither of them had abdominal pain, diarrhea, or fever. He sought medical help in Japan, but the symptoms persisted despite the prescribed medication. He came back to Taiwan and visited our emergency department immediately. Clinically, he had a high fever with a body temperature of 40°C, icteric sclera, and tenderness over the right lower abdomen. The blood examination revealed a white cell count of 12,760/mm$^3$, a hemoglobin level of 13.5 g/dl, and a platelet count of 193,000/mm$^3$. The biochemical tests showed the following: blood urea nitrogen level of 24.3 mg/dL, serum creatinine level of 1.7 mg/dL, alanine transaminase level of 62 U/L, aspartate transaminase level of 52 U/L, total bilirubin level of 6.85 mg/dL, alkaline phosphatase level of 820 U/L, C-reactive protein level of 148 mg/L, and glucose level of 121 mg/dL. Electrolytes, amylase, and lipase were within normal limits. The findings of chest X-ray, abdominal plain view, and abdominal ultrasonography were unremarkable. The stool examination was positive for occult blood test, but no inflammatory cells, pus, parasites, or ova were found. The abdominal computed tomography revealed segmental wall thickening over the terminal ileum with regional lymphadenopathy; terminal ileitis was considered by the radiologist (Fig. 1A). However, shock developed a few hours later. The patient was admitted under the tentative diagnosis of infectious diarrhea and septic shock

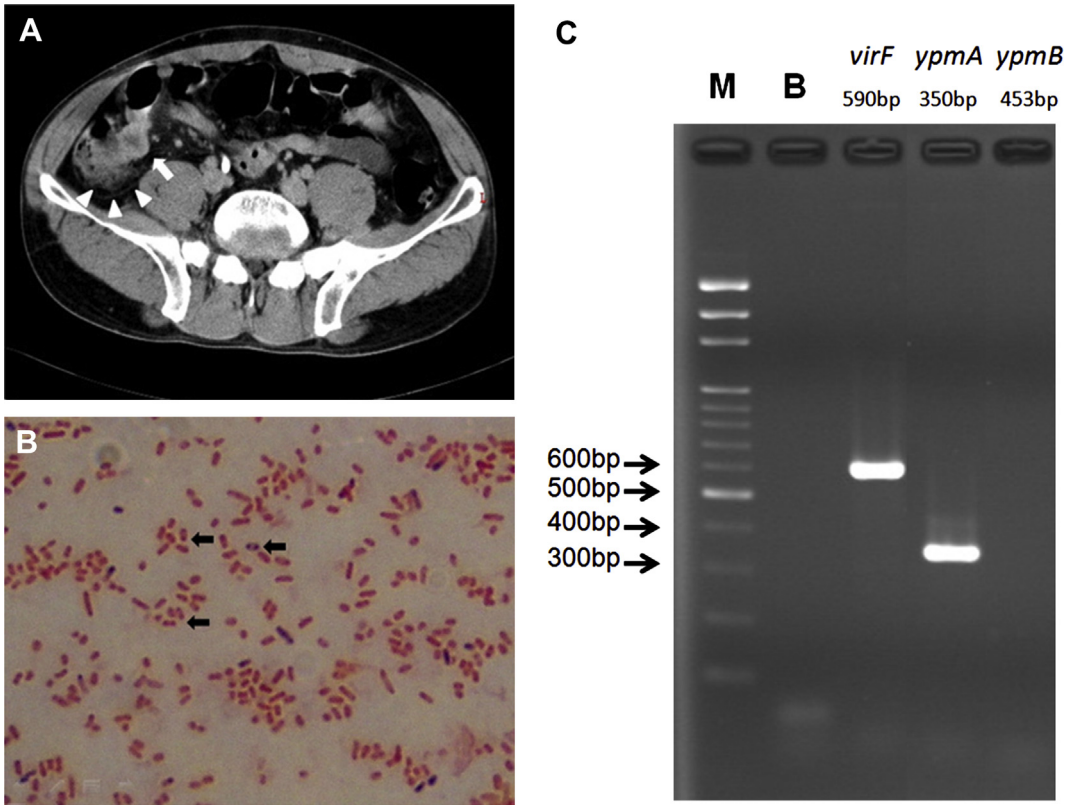


**Figure 1** (A) Abdominal computed tomography disclosed a bowel wall thickening over the terminal ileum (white arrow) and inflammatory change over the local mesentery (white arrowheads), indicating terminal ileitis; (B) Gram stain of the isolated microorganism showed Gram-negative bacilli with the characteristic of bipolar stain (black arrows); (C) electrophoresis of polymerase chain reaction products of *virF*, *ypmA*, and *ypmB* genes, indicating that the isolated strain has presence of *virF* (pYV) and *ypmA* (YPMa), but an absence of *ypmB* (YPMb). B = blank; M = marker.

and empiric antibiotic with moxifloxacin was administered. The results of serum anti-hepatitis A virus (HAV) IgM, HBs Ag, anti-HBc IgM, anti-Hepatitis C virus, amebiasis antibody, anti-HIV, and venereal disease research laboratory (VDRL) tests were all negative. The blood culture yielded a growth of Gram-negative bacilli with the characteristic of bipolar-stain 2 days later (Fig. 1B). The bacterium was identified as *Y. pseudotuberculosis* later by API 20E (bio-Me'rieux, Marcy l'Etoile, France) and VITEK 2 Automated Microbiology System GN (Ref. 21341/AST-N081) (bio-Mérieux, Marcy l'Etoile, France), and BD Phoenix Automated Microbiology System (Becton Dickinson, Sparks, MD, USA) with panel NMIC/ID-4 and NMIC/ID-32. The antibiotic was changed to a combination of ciprofloxacin and gentamicin according to the results of antimicrobial susceptibility tests (Table 1).[12] No pathogenic bacterium was isolated from stool culture. The fever, abdominal pain, diarrhea, and hyperbilirubinemia resolved and the patient recovered uneventfully after a 10-day course of intravenous antibiotic therapy.

### Molecular identification, serotyping, and virulence genes detection

The 16S ribosomal DNA of the isolate was obtained by polymerase chain reaction and its sequence was > 99% identical to the 16S rDNA of the *Y. pseudotuberculosis* (ATCC 29833, GenBank accession no. AF366375) using NCBI BLAST. *Y. pseudotuberculosis* serotype O1 was identified using the commercial available antisera (Denka Seiken, Tokyo, Japan). Detection of virulence genes was performed as described previously.[13] The isolated strain showed presence of pYV (70-kb virulence plasmid) for *virF*, and one variant of *Y. pseudotuberculosis*—derived mitogen (YPM), YPMa, for *ypmA*, but the absence of YPMb, YPMc (Fig. 1C), and high pathogenicity island (HPI). Combined with the results of serotype O1 and associated genetic detection, the isolated *Y. pseudotuberculosis* belonged to a genetic group 3 ($YPMa^+$, $HPI^-$), indicating a Far East systemic pathogenicity type.[13]

## Discussion

*Y. pseudotuberculosis*, secondary to *Y. enterocolitica*, is one of the two most common yersinia species causing human nonplague yersiniosis. It can be recovered from the natural environment or animal reservoirs, including rodents, rabbits, domestic animals (particularly pigs), and birds.[1] Human infection occurs via ingestion of food or water contaminated with the organism. Common manifestations of *Y. pseudotuberculosis* infection include gastroenterocolitis, acute mesenteric adenitis, and terminal ileitis, which is also known as acute appendicitis-like syndrome.[1]

**Table 1** Results of antimicrobial susceptibility tests of the isolated *Y. pseudotuberculosis* serotype O1.

| Antimicrobial agents | BD Phoenix | | VITEK 2 | |
|---|---|---|---|---|
| | MIC (ug/ml) | Susceptibility | MIC (ug/ml) | Susceptibility |
| Amikacin | ≤8 | S | ≤2 | S |
| Amoxicillin/clavulanate | ≤4/2 | S | NA | NA |
| Ampicillin | ≤4 | S | ≤2 | S |
| Ampicillin/sulbactam | ≤4/2 | S | ≤2 | S |
| Aztreonam | > 16 | R | NA | NA |
| Cefazolin | ≤4 | S | ≤4 | S |
| Cefepime | ≤2 | S | ≤1 | S |
| Cefotaxime | ≤4 | S | NA | NA |
| Cefoxitin | ≤4 | S | NA | NA |
| Ceftazidime | ≤0.5 | S | ≤1 | S |
| Ceftriaxone | 8 | S | ≤1 | S |
| Cefuroxime | ≤4 | S | NA | NA |
| Chloramphenicol | ≤4 | S | NA | NA |
| Ciprofloxacin | ≤0.5 | S | ≤0.25 | S |
| Colistin | > 2 | ND | NA | NA |
| Ertapenem | NA | NA | ≤0.5 | S |
| Gentamicin | ≤2 | S | ≤1 | S |
| Imipenem | ≤1 | S | NA | NA |
| Levofloxacin | ≤1 | S | ≤0.12 | S |
| Meropenem | ≤1 | S | ≤0.25 | S |
| Moxifloxacin | ≤1 | ND | NA | NA |
| Nitrofurantoin | 32 | S | NA | NA |
| Piperacillin | ≤4 | S | ≤4 | S |
| Piperacillin/tazobactam | ≤4/4 | S | ≤4 | S |
| Tetracycline | ≤2 | S | ≤2 | S |
| Tigecycline | NA | NA | ≤0.5 | ND |
| Trimethoprim/sulfamethoxazole | ≤0.5/9.5 | S | ≤20 | S |

MIC = minimal inhibitory concentration; NA = not available; ND = no interpretative data based on Clinical and Laboratory Standards Institute (CLSI) Antimicrobial Susceptibility Testing[12]; S = susceptible; I = intermediate; R = resistant.

Several outbreaks of *Y. pseudotuberculosis* have been reported.[2–6] In Finland, the contaminated source was traced to iceberg lettuce[2] and raw carrots.[3] An increased *Y. pseudotuberculosis* in human was supposed to be related to increased prevalence of the pathogen in rodent reservoirs in France.[4] In the two reports from Japan, contaminated vegetable juice might be responsible for a community outbreak,[5] and two groups of people acquired infection after eating meat products, vegetables, and rice at the same barbecue restaurant sequentially.[6] The incubation period of intestinal yersiniosis is about 3 to 7 days[1] and the patient recalled the illness developed few days after the meal at the barbecue; we supposed that the patient was infected via ingestion of contaminated raw or incompletely broiled foods at the barbecue restaurant in Osaka, Japan. However, it was impossible to trace the exact foods he had eaten at that time.

Our report is different from previous reports indicating that septicemic cases of *Y. pseudotuberculosis* commonly occur in patients with underlying diseases of diabetes mellitus, liver cirrhosis, malignancy, thalassemia, iron-overload disorders, and immunocompromised status such as postorgan transplantation and HIV infection,[14–16] since none of these was found in this patient. This might suggest an ingestion of large bacterial load, an infection with more virulent strain, or a failure to identify possible predisposing diseases in this case.

Except for aztreonam and colistin, the isolated *Y. pseudotuberculosis* serotype O1 are susceptible to most antimicrobial agents tested, including the newer ones of ertapenem, levofloxacin, moxifloxacin, and tigecycline (Table 1). *In vitro*, *Y. pseudotuberculosis* was reported to be susceptible to ampicillin, tetracycline, chloramphenicol, cephalosporins, and aminoglycosides. Among these, ampicillin is the recommended antibiotic to treat severe infection. However, the mortality rate of septicemia is as high as 75% despite antibiotic therapy.[16] Because of this high mortality rate and initial presentation of septic shock in this patient, a combination of ciprofloxacin and gentamicin rather than ampicillin was administered following the moxifloxacin. Fortunately, the patient responded well and survived. The excellent outcome of this case might due to no other underlying diseases and receiving newer antibiotic therapy. In conclusion, this report not only describes the first human *Y. pseudotuberculosis* infection in Taiwan, but it also suggests that this organism may be transported between countries and from temperate regions to tropical or subtropical regions via human infection.

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