Bacteremia Due to *Clostridium hathewayi* in a Patient with Acute Appendicitis

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**CASE REPORT**

A 39-year-old Indonesian woman was admitted to the hospital because of fever, chills, and rigor for 1 day. She also complained of lower abdominal pain which radiated to the right loin. There were no urinary or bowel symptoms. Her past medical history was unremarkable. On admission, her oral temperature was 39°C. The physical examination revealed tenderness, guarding, and rebound tenderness over the right loin and suprapubic areas. Bowel sounds were active. Her total leukocyte count was 10.2 × 10^9/liter (neutrophils, 9.5 × 10^9/liter; and lymphocytes, 0.6 × 10^9/liter), a hemoglobin level of 13.7 g/dl, and a platelet count of 272 × 10^9/liter. Her renal and liver function tests were within normal limits. An abdominal radiograph was unremarkable. Blood culture was performed. She went into septic shock with metabolic acidosis soon after admission. Fluid resuscitation was administered, and empirical intravenous cefuroxime and metronidazole were commenced. Contrast-computed tomography of the abdomen showed a swollen appendix with fecalith and free fluid in the pouch of Douglas. An emergency appendectomy was performed. Intraoperatively, an acutely inflamed and gangrenous appendix pending perforation was found. Culture of the peritoneal swab grew only scanty *Escherichia coli*. The patient recovered uneventfully after the operation and was discharged after 4 days of hospitalization.

*Clostridium* is a heterogeneous genus that consists of over 150 species. Besides *Clostridium perfringens*, *C. difficile*, *C. tetani*, and *C. botulinum*, of which the epidemiology and clinical disease spectra are better defined, studies of the pathogenic potential and disease association of the other *Clostridium* species have been hampered by difficulties in accurately identifying these bacteria. Since the recognition of the 16S rRNA gene as a new standard for classification and identification of bacteria (12, 13), most *Clostridium* species have been subjected to 16S rRNA gene sequence analysis, with revisions being made in their classifications and with new species being identified (3, 4, 14, 15, 17). Recently, the use of this technique for identifying and defining the clinical significance of anaerobic gram-positive bacilli, including the identification of a strain of *Lactobacillus salivarius* isolated from a patient with cholecystitis (19) and a strain of *Actinomyces odontolyticus* from a patient with pelvic inflammatory disease (20) and the discovery of a novel *Actinomyces* species (21) and two novel *Eggerthella* species (7), has been reported.

*Clostridium hathewayi* is a newly discovered *Clostridium* species isolated from stool samples of healthy human subjects. Although the phenotypic characteristics of the two strains isolated were consistent with the genus *Clostridium*, their species identification was determined only after 16S rRNA gene sequencing, which showed that they represent a new species within the *Clostridium coccoides* rRNA complex (16). Since this first report, there has been no additional information on the bacterium in the literature and the clinical significance of the bacterium has been unknown. In this article, we describe a case of *C. hathewayi* bacteremia in a patient with acute appendicitis complicated by septic shock.

**Clinical and microbiological data.** All clinical data were collected prospectively as described previously (8). The isolates were identified by standard conventional biochemical methods (10), the VITEK system (ANI) (bioMérieux Vitek, Hazelwood, Mo.), the API system (20A) (bioMérieux Vitek), and the ATB Expression system (rapid ID32A) (bioMérieux Vitek). Antimicrobial susceptibility was tested by E-test (AB Biodisk, Solna, Sweden) on brucella blood agar plates, and the results were interpreted according to the NCCLS criteria for anaerobic bacteria (11). All tests were performed in triplicate with freshly prepared media on separate occasions.
On day 2 postincubation, the anaerobic blood culture bottle turned positive, with a straight or slightly curved bacillus which stained gram negative (strain HKU18). It grows on sheep blood agar as nonhemolytic, gray colonies of 1 mm in diameter with a slightly irregular margin after 48 h of incubation at 37°C in an anaerobic environment. It does not grow in ambient air, or microaerophilic in an anaerobic environment. It does not grow in ambient air, with a slightly irregular margin after 48 h of incubation at 37°C. Blood agar as nonhemolytic, gray colonies of 1 mm in diameter stained gram negative (strain HKU18). It grows on sheep blood agar as nonhemolytic, gray colonies of 1 mm in diameter stained gram negative. HKU18 and one of the strains previously described were motile, while the other previous strain was motile. However, the two previous isolates fermented melezitose while HKU18 did not. The identification of more strains of \textit{C. hathewayi} would be helpful in delineating its key phenotypic profile to be differentiated from closely related species.

The phenotypic characteristics of HKU18 closely resembled those of the two previously described isolates of \textit{C. hathewayi} (Table 1). All three isolates were strictly anaerobic gram-positive rods but stained gram negative. HKU18 and one of the strains previously described were nonmotile, while the other previous strain was motile. However, the two previous isolates fermented melezitose while HKU18 did not. The identification of more strains of \textit{C. hathewayi} would be helpful in delineating its key phenotypic profile to be differentiated from closely related species.

The clinical significance of \textit{C. hathewayi} in the present patient is evident by its pure growth in the blood culture of an
immunocompetent patient before the administration of antibiotics, which was associated with the development of fever, neutrophilia, and septic shock. The source of the bacteremia is most likely the inflamed appendix. Since C. hathewayi has been isolated from the stool of healthy individuals, it is likely a normal gut commensal in humans. We speculate that the bacterium may have been in the gut flora of our patient and may have translocated through the inflamed intestinal mucosa to the bloodstream. Although other anaerobic bacteria, such as the Bacteroides fragilis group and C. perfringens, have been associated with or implicated in the pathogenesis of acute appendicitis (2, 9), the role of C. hathewayi in the development of the acute appendicitis in the present patient cannot be determined. The failure to isolate the bacterium from her peritoneal swab could be due to its stringent transport and growth requirements and the overgrowth of the less fastidious E. coli. Further studies are required to investigate the pathogenic potential of C. hathewayi in humans.

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