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Multidrug-Resistant *Escherichia fergusonii*: a Case of Acute Cystitis▽

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We report a case in which *Escherichia fergusonii*, an emerging pathogen in various types of infections, was associated with cystitis in a 52-year-old woman. The offending strain was found to be multidrug resistant. Despite in vitro activity, beta-lactam treatment failed because of a lack of patient compliance with therapy. The work confirms the pathogenic potential of *E. fergusonii*.

CASE REPORT

A 52-year-old female presented on 16 May 2006 at our department with clinical signs of acute cystitis. Her temperature was elevated (37.8°C). A urine sample was taken, and antibiotic treatment was started empirically with oral cefixime (400 mg every 24 h). After 24 h, *Escherichia fergusonii* was grown (10^6 CFU/ml) as a single organism from the urine.

Bacterial identification was performed using the Vitek2 ID-GN system (bioMérieux). The identification test was repeated three times by three different operators and generated the following result: *E. fergusonii*, 99%, excellent identification. The isolate was found to be motile at 36°C.

Vitek2 AST-N021 and AST-N041 cards were used to determine susceptibilities to antibiotics. The organism was found to be susceptible to amoxicillin-clavulanic acid (MIC, 4 mg/liter), ampicillin/sulbactam (MIC, 8 mg/liter), piperacillin-tazobactam (MIC ≤ 4 mg/liter), cefoxitin (MIC ≤ 4 mg/liter), cefixime (MIC ≤ 0.25 mg/liter), cefotaxime (MIC ≤ 1 mg/liter), ceftazidime (MIC ≤ 1 mg/liter), imipenem (MIC, 2 mg/liter), meropenem (MIC ≤ 0.25 mg/liter), nitrofurantoin (MIC ≤ 16 mg/liter), and tetracycline (MIC, 4 mg/liter) but resistant to ampicillin (MIC ≥ 32 mg/liter), piperacillin (MIC ≥ 256 mg/liter), ciprofloxacin (MIC ≥ 4 mg/liter), levofloxacin (MIC ≥ 8 mg/liter), gentamicin (MIC ≥ 16 mg/liter), netilmicin (MIC ≥ 32 mg/liter), tobramicin (MIC ≥ 16 mg/liter), and cotrimoxazole (MIC ≥ 320 mg/liter). The susceptibility test was repeated three times by three different operators (a summary of the MIC for each drug is shown in Table 1). There are no published guidelines for the detection of extended-spectrum beta-lactamases (ESBLs) in organisms other than *Escherichia coli* and *Klebsiella* spp.; therefore, the Vitek2 ESBL card failed to detect potential *E. fergusonii* ESBL production.

Notwithstanding documented cefixime in vitro activity, the patient returned 1 week later with worsening symptoms. Cefixime was discontinued, a second urine sample was taken, and cefotaxime was started (1,000 mg, every 12 h, intramuscularly).

After 24 h, *E. fergusonii* was grown (10^6 CFU/ml) as a single organism from the second urine sample, as well. We thought that the organism could be a potential ESBL producer.

A modified version of the Jarlier et al. double-disk synergy method (7) for detecting clavulanic acid synergy was used. Cefotaxime (30-μg) and ceftazidime (30-μg) disks (Oxoid) were placed around an amoxicillin (20-μg)-clavulanic acid (10-μg) disk at a distance of 20 mm center to center and incubated at 37°C overnight (aerobic atmosphere), but no clavulanate synergy was detected. Etest with ceftazidime plus ceftazidime/clavulanate and cefotaxime plus cefotaxime/clavulanate (AB Biodisk) confirmed the absence of synergy. Hence, the isolate was labeled as non-ESBL phenotype.

The patient returned 7 days later with unchanged symptoms, so cefotaxime was discontinued and oral nitrofurantoin was started (50 mg every 4 h), with relief of symptoms within 36 h of starting therapy. Two urine samples were taken after 1 week and 2 weeks from the end of antibiotic therapy, respectively, but we were not able to isolate *E. fergusonii* again.

E. fergusonii is an infrequent but emerging human pathogen whose name was coined in honor to the American microbiologist William H. Ferguson. It was formerly known as enteric group 10, and this vernacular name was used until the species could be studied further and proposed by Farmer et al. (2, 3) in 1985 as a new species in the family *Enterobacteriaceae*.

E. fergusonii strains are gram-negative rods, oxidase negative, catalase positive, and generally motile. They are positive for in-

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TABLE 1. Summary of MICs for drugs

Antibiotic	MIC (mg/liter)[a]
Ampicillin	≥32 (R)
Ampicillin/sulbactam	8 (S)
Amoxicillin-clavulanic acid	4 (S)
Piperacillin	≥256 (R)
Piperacillin-tazobactam	≤4 (S)
Cefoxitin	≤4 (S)
Cefixime	≤0.25 (S)
Cefotaxime	≤1 (S)
Ceftazidime	≤1 (S)
Imipenem	2 (S)
Meropenem	≤0.25 (S)
Ciprofloxacin	≥4 (R)
Levofloxacin	≥8 (R)
Tobramicin	≥16 (R)
Gentamicin	≥16 (R)
Netilmicin	≥32 (R)
Cotrimoxazole	≥320 (R)
Tetracycline	4 (S)
Nitrofurantoin	≤16 (S)

[a] S, susceptible; R, resistant.

dole production, lysine decarboxylase, ornithine decarboxylase, and methyl red. They ferment adonitol, L-arabinose, L-rhamnose, maltose, trehalose, cellobiose, D-xylose, and D-arabitol and ferment D-glucose with gas production. They are negative for growth in KCN, Voges-Proskauer reaction, citrate utilization (17% positive), phenylalanine deamination, urea hydrolysis, arginine dihydrolase, and fermentation of lactose, sucrose, D-sorbitol, raffinose, *myo*-inositol, and alpha-methyl-D-glucoside. The results of DNA hybridization experiments showed that the closest relatives to this new species were *E. coli-Shigella* spp., which are up to 64% related. Other genera in the family *Enterobacteriaceae* are more distantly related (2, 3).

E. fergusonii has recently been known to be responsible for wound infections, urinary tract infections, bacteremia, diarrhea, and pleural infections. Furthermore, it has been isolated from the intestinal contents of warm-blooded animals (5, 8) and from beef during routine screening procedures (4). Funke et al. (6) isolated *E. fergusonii* from a stool sample taken 1 week after an episode of cholangiosepsis in a patient with pancreatic carcinoma and proposed that the intestinal flora could have been the source of a retrograde colonization of the gall bladder, resulting in cholangiosepsis. In any case, little is known about the natural habitat of the organism.

To determine the mechanism of enteropathogenicity of *E. fergusonii*, clinical isolates from diarrheal stools have been studied and have produced significant fluid accumulation in rat ileal loops, by both live cells and their culture filtrates. Thus, it can be inferred that this species is diarrheagenic (1), but its pathogenic potential is unclear.

In 1993, Funke et al. (6) described the presence of a beta-lactamase in *E. fergusonii* strains they studied. In 2002, Naas et al. cloned and sequenced the AmpC-type enzyme of *E. fergusonii* (9). In the case we reported, we first thought of potential ESBL production as a reason for cefixime and cefotaxime failure despite the in vitro activities of both. Actually, after obtaining complete disappearance of symptoms with nitrofurantoin therapy, the patient said she was not compliant with the previous beta-lactam treatment she had received; in particular, she consumed only a few cefixime doses because of an outbreak of abdominal pain and received only a few cefotaxime administrations because intramuscular treatment was too painful. This could be the reason why beta-lactam therapy failed despite in vitro activity. Beta-lactam action is time dependent, and drugs should be consumed regularly to maintain therapeutic blood levels.

This case further confirms that lack of patient compliance with therapy makes it difficult to diagnose and treat infectious diseases. However, most importantly, the case report we presented provides further evidence for the pathogenic potential of *E. fergusonii*, although much is still unclear about its habitat, pathogenicity, and drug resistance.

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