Multidrug-Resistant Salmonella Associated with AmpC Hyperproduction

We report identification of the first multidrug-resistant strain of Salmonella harboring a plasmid-mediated AmpC β-lactamase in the United States.

An 18-year-old pregnant woman (32 w) was transferred to our facility for percutaneous drainage of an infected choledochocholangitis cyst. Despite empirical antibiotic therapy with ampicillin and gentamicin, on arrival at the hospital the patient became tachycardic and hypotensive and was taken to the operating room for an emergency cesarean section followed by surgical drainage of the cyst.

Blood and bile cultures yielded Salmonella enterica subspecies enterica serovar heidelberg, which was resistant to tobramycin, gentamicin, ampicillin/sulbactam, trimethoprim-sulfamethoxazole, piperacillin, tetracycline, cefazidime, and cefotaxime. Resistance to ticarcillin/clavulanate was reported as intermediate. The patient was discharged; medications at the time of discharge were ciprofloxacin and intravenous cefepime. Six months later, she was readmitted to our center for definitive resection of the choledochal cyst with choledochojejunostomy. Repeated cultures of bile and a cyst wall specimen were negative. She recovered uneventfully, and her child is doing well.

The patient lives in a small town in North Carolina and has no unusual travel history or animal exposure. The local health department reported no additional cases of infection due to multidrug-resistant Salmonella in the town.

Resistance of Salmonella due to an AmpC β-lactamase has been described in one strain in the Middle East [1,2] but, to our knowledge, has not been previously described in the United States. Bacterial strains producing AmpC β-lactamases and extended-spectrum β-lactamases (ESBLs) are frequently resistant to cephalosporins, thereby causing many clinical laboratories to confuse these two types of enzymes. The clinical interpretation of results of in vitro susceptibility testing differs for strains harboring these β-lactamases. Strains of Klebsiella pneumoniae and Escherichia coli producing ESBLs are reported by laboratories as resistant to aztreonam and all cephalosporins [3], regardless of their in vitro susceptibility to these agents; cephamycins like cefoxitin usually remain active. By comparison, the actual results of susceptibility testing are reported for organisms producing AmpC-type β-lactamases. Because the isolate recovered from this patient was resistant to both gentamicin and trimethoprim-sulfamethoxazole (a pattern frequently observed for ESBL-producing organisms), it might have been incorrectly identified as an ESBL producer. The Salmonella isolate from this patient also produced the TEM-1 β-lactamase almost ubiquitous in gram-negative enteric bacteria.

In summary, this report of an AmpC β-lactamase-producing Salmonella in the United States is of concern because of the degree of resistance and has significant public health implications.

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Polymerase Chain Reaction Analysis for Diagnosis of Tropheryma whipplei Infective Endocarditis in Two Patients with No Previous Evidence of Whipple’s Disease

Blood culture–negative infective endocarditis (IE) is often caused by fastidious organisms that grow poorly or not at all on acellular media, such as Coxiella burnetii, Bartonella species, or Chlamydia [1]. Despite the use of appropriate diagnostic techniques (i.e., serology and cell culture), no microbial agents are identified in a number of definite cases of IE. Polymerase chain reaction (PCR) analysis with primers targeting the eubacterial 16S rRNA gene provide powerful etiologic tools in such cases [2]. We report two cases of IE caused by Tropheryma whippelii, the causative agent of Whipple’s disease, that were diagnosed by means of PCR analysis of resected heart valve specimens.

A 40-year-old man (patient 1) with a 5-year history of ankylosing spondylitis (HLA B27) who was receiving immuno-
suppressive therapy was admitted to the hospital in June 1995 with a tentative diagnosis of blood culture–negative IE. Severe hemodynamic failure necessitated emergency valve replacement, and an abscess of the aortic ring was found during surgery. Despite 6 weeks of postoperative antibiotic therapy (ofloxacin, 400 mg/d; doxycycline, 200 mg/d), his condition deteriorated again 6 months later, necessitating replacement of both the prosthetic aortic valve (because of paraprosthetic leakage) and the mitral valve (marked mitral insufficiency). He died suddenly the day after surgery. Histological features of the valve specimens removed during the two operations were very similar, with proliferation of fibrous tissue, focal calcification mixed with a few microabscesses containing polymorphonuclear (PMN) cells, and voluminous macrophages (all of which were consistent with the diagnosis of IE).

A 55-year-old man (patient 2) was admitted to the hospital in October 1998 for blood culture–negative IE associated with hemiparesis and severe mitral insufficiency. He had a 5-year history of arthralgia of the shoulders and fingers. He underwent surgical quadrangular resection of the posterior leaflet, during which vegetations were removed, and annuloplasty by means of a Carpentier ring. Histological examination revealed lesions typical of acute IE, with numerous PMN cells and voluminous macrophages. He was treated with ceftriaxone (2 g/d) for 1 month followed by co-trimoxazole (400 mg/d). He was well during co-trimoxazole treatment 5 months after surgery.

In a retrospective study of blood culture–negative IE conducted in our hospital in November 1998, PCR amplification was applied to DNA extracted from the two patients’ valves (which were kept frozen) and from blood from patient 2 that was obtained 7 days before surgery; primers targeting T. whippelii 16S rDNA were used in this procedure [3]. A 284-bp amplicon was obtained from the two valves but not from blood, and the DNA sequences showed significant alignments (98% homology for patient 1; 99% homology for patient 2) with the previously reported T. whippelii 16S rRNA gene sequence (accession number X99636; GenBank, Bethesda, MD). In addition, periodic acid–Schiff (PAS) staining revealed macrophages containing PAS-positive intracytoplasmic rods and granules in both cases, thus establishing the diagnosis of T. whippelii IE.

Endocardial involvement is relatively frequent during the course of Whipple’s disease, presenting as valvulitis or IE that usually involves the mitral or aortic valve [4–7]. However, in many cases, these lesions are preceded by or associated with involvement of one or several other organs, producing gastrointestinal disorders, weight loss, polyarthralgia, or neurological symptoms [7]. In our two patients, the articular symptoms could have been related to Whipple’s disease (although patient 1 was diagnosed with ankylosing spondylitis), but neither patient had significant weight loss or gastrointestinal disorders. In patient 2, the lack of gastrointestinal involvement was confirmed by histological examination of a jejunal biopsy specimen obtained 4 weeks after surgery.

Our findings confirm previous reports that cardiac symptoms may occur several years before gastrointestinal manifestations, which may thus appear as late complications of the disease [6]. Our two cases emphasize the need to consider T. whippelii as a potential cause of blood culture–negative IE. In cases of blood culture–negative IE, resected heart tissue specimens should be routinely studied by PAS staining and PCR analysis for evidence of T. whippelii infection.

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