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First Case of Invasive Human Infection Caused by *Cupriavidus metallidurans*▽

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We describe the first case of invasive human infection (a nosocomial septicemia) caused by *Cupriavidus metallidurans*. This metal-resistant bacterium has not been reported to be pathogenic in humans or animals.

CASE REPORT

A 74-year-old Caucasian man, known to have type 2 diabetes, arteriosclerotic heart disease, dyslipidemia, arterial hypertension, and obesity (113 kg), underwent a radical cystoprostatectomy with ileal duct and ileostomy for a vesical high-grade carcinoma with four pelvic lymph nodes positive for neoplasia. A subtotal pancreatectomy and splenectomy were performed simultaneously for a pancreatic neuroendocrine tumor. The patient suffered two episodes of bacteremia with a pancreatic collection caused by *Enterococcus faecalis* 1 week after the operation and by an ESBL (extended-spectrum-β-lactamase)-producing *Klebsiella oxytoca* isolate 6 weeks later. In each instance, the patient was treated with antimicrobial agents and drainage. Ten weeks after the initial operation, the patient presented with a fever with leukocytosis. At this time, the patient had necrotic abdominal wounds and two abdominal drains. The site of the left subclavian central catheter was normal. The chest X-ray films showed stable bilateral atelectasis and small bilateral pleural effusion. On the abdominopelvic computed tomography scan, a reduced pancreatic collection (from 5.5 by 4.1 cm to 2.6 by 1.5 cm), normal bilateral kidneys, and a new voluminous subcutaneous collection (10.4 by 6.6 cm) near the ileostomy were found. Four out of five blood culture sets (BD-Bactec, Franklin Lakes, NJ) were positive for a Gram-negative rod. Urine, pancreatic fluid, bronchial secretions, and central catheter cultures were not performed at that time. The abdominal wound culture was positive for *Enterococcus faecium*. The subcutaneous collection and the abdominal wounds were surgically debrided, but, unfortunately, no specimen was cultured. After 2 days of piperacillin-tazobactam, the fever resolved. One week later, two blood culture sets were negative. The patient's condition deteriorated with refractory renal insufficiency, and he died 6 weeks after the last septicemia.

During a 6-day period, after 3 to 4 days, four aerobic blood culture bottles showed growth of a Gram-negative rod. The five anaerobic and one aerobic blood culture bottles remained negative after 5 days of incubation. After 48 h, the blood agar (Oxoid, Basingstoke, United Kingdom) and chocolate agar (Oxoid) plates revealed greyish small colonies with only a few lactose-negative colonies on the MacConkey plates (Oxoid). This bacterium was oxydase and catalase positive, motile, susceptible to polymyxin B, and a nonfermenter on TSI (triple sugar iron). The API 20 NE (bioMérieux, Marcy l'Etoile, France) gave the profile 1000477 and therefore was positive for Simmons citrate, for reduction of NO_3 in NO_2, and for gluconate, caprate, adipate, malate, and phenyl-acetate assimilation with 59.3% identity to *Alcaligenes faecalis* 2 and 30.5% identity to *Achromobacter denitrificans*. Two different isolates of this bacterium were identified by nearly full 16S rRNA gene sequencing (1). DNA sequences were determined with an ABI 3100 sequencer using a BigDye sequencing kit (Applied Biosystems). The strains were found to be 99.1% identical to the *Cupriavidus metallidurans* type strain ATCC 43123 and 99.7% and 100% identical to two other strains isolated from patients with cystic fibrosis (4). Antimicrobial susceptibility testing of two different isolates to eight agents was performed by the agar dilution method as standardized by the Clinical and Laboratory Standards Institute for *Pseudomonas aeruginosa* (3). The MIC ranges tested included breakpoints for resistant and susceptible categories. The MICs of the two isolates were identical and are reported in Table 1.

Cupriavidus metallidurans, once known as *Ralstonia metallidurans*, is able to survive to high concentrations of over 20 different heavy metals (5, 6, 9, 10). When documented in bronchial secretions of two patients with cystic fibrosis, its pathogenic or colonizing role could not be determined, as clinical data were unavailable (4). This bacterium has not been isolated in animals (5, 6, 9, 10). Our patient suffered a significant nosocomial septicemia, since he had signs of sepsis, and *C. metallidurans* was recovered repeatedly from blood culture sets over a period of 6 days. The source of infection was probably the new subcutaneous collection near the ileostomy, but, unfortunately, no culture was available to confirm this. Other possible sources for this infection include the abdominal wounds, central catheter, pancreatic collection, lower respiratory tract, and urinary tract. However, the patient had not

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TABLE 1. Antimicrobial susceptibility of *Cupriavidus metallidurans* to eight agents

Antimicrobial agent	MIC (mg/liter)	Interpretation[a]
Piperacillin	8	S
Ceftazidime	16	I
Meropenem	≤1	S
Gentamicin	>8	R
Tobramycin	>8	R
Ciprofloxacin	0.5	S
Piperacillin-tazobactam	≤16/4	S

[a] S, susceptible; R:, resistant; I, intermediate. The susceptibility and resistance breakpoints were those for *Pseudomonas aeruginosa* (3), since breakpoints for *C. metallidurans* are not available.

shown clinical or radiological signs to support these hypotheses and previous and subsequent cultures of these sites failed to find this bacterium. No environmental cultures were performed, and the means of transmission is unknown. The only environmental sources recorded so far in the literature are metal-contaminated soils or sediments (5, 6, 9, 10).

Although other *Cupriavidus* species such as *C. pauculus*, *C. gilardii*, and a new *Cupriavidus* species have been described as causes of human infections (2, 7, 8), to our knowledge, this is the first reported case of proven human invasive infection with *C. metallidurans*, a nosocomial septicemia, revealing a pathogenic potential for this bacterium. The identification is reliable only through 16S rRNA gene sequencing. Consequently, this infection may be underdiagnosed. More cases will be required to identify risk factors and sources of infection and to fine-tune diagnostic modalities.

Nucleotide sequence accession number. The 16S rRNA gene sequence obtained for our isolate was submitted to GenBank, and the obtained accession number is GU230889.

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