

## An Outbreak of *Serratia marcescens* Septicemia in Neonates

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*Serratia marcescens* is a well recognized nosocomial pathogen. We report an outbreak with this organism in 8 neonates in a neonatal intensive care unit (NICU). Seven cases were treated successfully with meropenem after the failure of imipenem treatment. Although they have similar anti-microbial effects, meropenem can effectively treat the *S. marcescens* sepsis resistant to imipenem.

**Keywords:** Imipenem, Meropenem, Newborn, Sepsis, *Serratia marcescens*.

**S***erratia marcescens* is a well-recognized pathogen of severe nosocomial infections in neonatal intensive care units (NICUs)(1-5). Sepsis caused by *S. marcescens* is difficult to treat because of the strain's resistance to antibiotics including beta-lactams and aminoglycosides(5). In the present study, we managed an outbreak of *S. marcescens* with meropenem after imipenem failure.

### METHODS

Our hospital is a 150-bed, tertiary referral care hospital. The NICU contains 17 beds: 10 level 3 NICU beds and 7 intermediate-intensive beds. In December 2006, an outbreak of systemic infections caused by *Serratia marcescens* occurred in the NICU. Clinical details were recorded. After the first case of *S. marcescens* septicemia was identified, subsequent surveillance cultures such as pharyngeal swab, rectal swab, sputum and stool cultures were obtained in all other neonates to trace reservoir/colonized neonates. Environmental cultures were taken and processed by standard laboratory methods, and susceptibility to antimicrobial agents was

performed per guidelines of the Clinical and Laboratory Standards Institute(6).

### RESULTS

Eight neonates developed clinical sepsis with positive blood cultures and one of them died. Three patients (case 1,4,8) had indwelling devices (mechanical ventilation for 11 to 23 days, central lines and total parenteral nutrition for 8-20 days). The length of stay in the NICU before *S. marcescens* varied from 4 to 72 days for infected patients. The clinical characteristics, demography and associated underlying disorders in these cases are shown in **Table I**.

The index case (case 1) of *S. marcescens* had received imipenem for seven days due to *E. coli* sepsis. The next day, three infected neonates (case 2, 3, and 4) were identified in the NICU. Standard infection control measures were reinforced. Despite efforts, four additional cases (case 5, 6, 7, and 8) of clinical septicemia in neonates occurred within ten days. Cultures were obtained weekly until sterile.

Infected neonates were treated empirically with

### WHAT THIS STUDY ADDS?

- Meropenam was successfully used for treating neonatal sepsis caused by *Serratia marcescens*.

imipenem for 5-10 days before culture results were available. Four neonates (cases 1, 5, 6 and 7) received intravenous imipenem (60 mg/kg per day divided into three doses) before *S. marcescens* sepsis occurred. After the culture results were available, gentamicin was added to the treatment regimen because of culture-antibiogram susceptibility. Lumbar puncture was not done due to severe thrombocytopenia and worsening in these babies. C-reactive protein(CRP) and blood counts were repeated frequently and cultures were repeated 72 hrs after the initiation of the treatment. As none of the neonates showed recovery signs, both clinically and with respect to the laboratory findings(CRP, thrombocyte, immature/mature ratio white blood cell and white cell count), this treatment was discontinued after 7-10 days. Case 2 died despite antibiotic therapy including imipenem and gentamicin. We ascertained that this resulted from *in vivo* resistance to imipenem, so we switched to intravenous meropenem (60 mg/kg per day divided into three doses) instead of imipenem for 3 weeks. A complete cure was obtained in seven patients with 21 days of therapy with this antibiotic regimen.

**TABLE I** CLINICAL CHARACTERISTICS OF NEONATES INFECTED WITH *S. MARCESCENS*

| Case no | Age (days) | Problem   | Therapy (drugs and days) |     |      |
|---------|------------|-----------|--------------------------|-----|------|
| 1       | 31         | CHD       | I:10                     | G:5 | M:21 |
| 2       | 16         | HIE       | I:10                     | G:6 |      |
| 3       | 44         | HIE       | I:8                      | G:5 | M:21 |
| 4       | 10         | HIE       | I:7                      | G:7 | M:21 |
| 5       | 6          | TTN       | I:3                      | G:7 | M:21 |
| 6       | 27         | Pneumonia | I:5                      | G:7 | M:21 |
| 7*      | 15         | Sepsis    | I:15                     | G:7 | M:21 |
| 8*      | 72         | RDS       | M:21                     |     |      |

*HIE*: hypoxic ischemic encephalopathy; *RDS*: respiratory distress syndrome; *CHD*: Congenital heart disease; \*Preterm low birth weight; *I*:Imipenem; *M*: Meropenem; *G*:Gentamicin; *TTN*:Transient tachypnea of newborn.

Cultures of samples from incubators, antiseptics, humidifiers, soap, distilled water, inhalation therapy equipment, hands of all healthcare workers and stethoscopes were negative for *S. marcescens*. Culture swabs from inanimate surfaces were all negative for *S. marcescens*. The *S. marcescens* isolates during the outbreak were uniformly susceptible to all of the antimicrobial agents tested, except for ampicillin, amoxicillin-clavulonate and cefazolin.

### DISCUSSION

*S. marcescens* has emerged in recent years as an opportunistic pathogen in a growing number of serious rapidly spreading nosocomial infections in NICUs, particularly as bloodstream infections(1-4). An important characteristic of *S. marcescens* is its ability to produce a beta-lactamase that confers resistance to broad-spectrum beta-lactam antibiotics, which often complicates therapy(1,5,7). Troillet, *et al.*(8) reported imipenem resistance in 11% of the clinical isolates of *Serratia* species. Ito, *et al.*(9) concluded that 19% of *S. marcescens* clinical isolates were resistant to imipenem. Imipenem resistance is achieved by a metallo-beta-lactamase that does not confer resistance to meropenem(10). In another study, *S. marcescens* isolates were not resistant to imipenem, but the resistance rate to meropenem was 89%(9). Thus, susceptibility to the antimicrobials may differ in a manner that is dependent on whether these antibiotics were previously used in the units. Although our clinical *S. marcescens* isolates were susceptible to gentamicin and imipenem on an antibiogram, these isolates exhibited resistance during clinical use and treatment failure occurred. Four of our neonates (cases 1,5,6 and 7) had already received imipenem before the onset of *S. marcescens* sepsis. However, seven neonates with sepsis were successfully treated with meropenem. This pattern may be explained by *in vitro* or *in vivo* susceptibility. The possible development of resistance to imipenem may be related to its long-term exposure in our NICU.

However, meropenem had not been used previously.

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