# Serratia marcescens: an emerging microorganism in the neonatal intensive care unit

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As smaller babies survive in neonatal intensive care units, late-onset septicemia with unusual pathogens appears. Between 1 January and 31 December 1998, in Hacettepe University İhsan Doğramacı Children's Hospital Neonatal Intensive Care Unit, seven infants had S. marcescens isolates. Four babies had septicemia with the microorganism. The case fatality rate was 50 percent in infants with S. marcescens septicemia. The combination of ceftazidime or imipenem with amikacin appears appropriate for the treatment of newborns with Serratia infection.

*Key words: Serratia marcescens, infection, neonatal intensive care unit.*

In the 1990's Group B streptococcus and E. coli were the most frequent bacterial pathogens causing early neonatal sepsis. On the other hand, coagulase negative staphylococci, Klebsiella pneumonia, Pseudomonas aeroginosa, other Gram-negative bacteria and Candida species are the most frequently encountered microorganisms in late-onset sepsis of the newborn[1-3].

Serratia marcescens is a motile, non-sporulating, Gram-negative bacillus classified in the family Enterobacteriacea. It has been recognized as a cause of hospital-acquired infection for the last two decades[4]. These infections were mainly reported in association with altered host defenses. The immaturity of neonatal host defenses is a major risk factor predisposing to bacteremia and sepsis in the newborn. The lack of type-specific antibodies, decreased levels of immunoglobulin G, A and M levels, reduced neutrophil chemotaxis and defective oxidative burst in granulocytes are important factors that contribute to the neonate's (and especially of the preterm infant's) susceptibility to bacterial infection[1-3]. There are reports of Serratia species causing neonatal infection[4-12]. The first time Serratia was isolated in our Neonatal Intensive Care Unit (NICU) was January 1998. Since that time Serratia has been isolated from seven patients and all were S. marcescens. In this report we present our patients with Serratia isolation.

## Material and Methods

In our NICU, every newborn with suspected sepsis undergoes a sepsis work-up which includes complete blood count with differential, urine analysis, C-reactive protein level, chest X-ray, and cultures o fblood, urine and cerebrospinal fluid. All infants requiring mechanical ventilation have routine endotracheal aspirate cultures when the tube is removed or changed and when there is a lower respiratory tract infection proven by chest X-ray. Routine cultures of humidifiers, incubators, ventilators, and disinfectant solutions are performed twice monthly, and cultures of intravenous fluids are performed once monthly.

Bacterial identification was performed by Sceptor System (Becton Dickinson). Antibiotic susceptibilities were determined using Microbroth dilution method, according to NCCLS gudelines (M7-A4).

## Results

Between 1 January-31 December 1998 S. marcescens was isolated from ten cultures of seven infants. The clinical characteristics of these infants are summarized in Table I. Four isolates were from blood, four from tracheal aspirates, one from cerebrospinal fluid and one from bone marrow aspiration culture. All isolates were sensitive to amikacin, imipenem and ciprofloxacin (Table II).

Table I. Clinical Characteristics of the Patients

| Case no. | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|---|
| Gestational age (week) | 37 | 33 | 27 | 33 | 31 | 27 | 32 |
| Birth weight (g) APGAR score | 2300 | 1780 | 600 | 1900 | 1330 | 750 | 2400 |
| (5 min) | 5 | 9 | 2 | 9 | 8 | 6 | 2 |
| Umbilical artery catheterization | - | - | + | - | - | + | + |
| Endotracheal intubation | + | - | + | - | - | + | + |
| Ventilator treatment (days) | 22 | 0 | 3 | 2 | 0 | 20 | 2 |
| Age at diagnosis of infection (days) | 7 | 6 | 23 | 5 | 9 | 45 | 4 |
| First sign of infection | Atelectasis of right lung upper lobe | Hypoactivity Abdominall distention | Bradycardia Abdominal distention | Apnea Hypoactivity | Tachypnea | Apnea Hypoactivity | Diffuse lung infiltrates |
| Blood culture | - | + | + | + | - | + | - |
| CSF culture | - | - | - | - | - | + | ND |
| Bone marrow aspirate culture | ND | ND | - | ND | ND | + | ND |
| Endotracheal aspirate culture | + | - | - | + | + | - | + |
| Total leukocyte count (/mm$^3$) | 18800 | 14600 | 10100 | 19300 | 11500 | 2800 | 11800 |
| Immature: Mature ratio | 0.17 | 0.2 | 0.15 | 0.5 | 0.15 | 0.1 | 0.3 |
| Thrombocytopenia | - | + | + | + | - | - | - |
| CRP level (mg/dl) | ND+ | 0.4 | ND+ | 4.2 | 0.12 | 9.52 | 0.4 |
| Hyperbilirubinemia | - | + | - | + | - | - | + |
| Antibiotic treatment | Imipenem+Amikacin | Cefotaxime+Amikacin | Ceftriaxone+Vancomycin | Ceftazidime+Amikacin | Ceftazidime+Amikacin | Imipinem+Amikacin | Ceftazidime+Amikacin |
| Outcome | Died at 24 days days due to HIE | 13 months old, healthy | Died at 33 days | 9 months old, healthy | 7 months old, healthy | Died at 48 days | 6 months old, healthy |

• Not done due to the unavailability of CRP kit.

CSF : Cerebrospinal.
Fluid, HIE : Hypoxic-Ischemic Encephalopathy.
ND : Not Done.

Table II. Susceptibility Patterns of Different Isolates of S. Marcescens

| Case | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|---|
| TMP/SMX | R | R | S | – | R | S | R |
| Sulbactam-Ampicillin | R | R | R | R | R | R | R |
| Ceftazidime | S | S | S | S | S | R | S |
| Cefotaxime/Ceftriaxone | S | S | S | R | R | R | R |
| Imipenem | S | S | S | S | S | S | S |
| Ciprofloxacin | S | S | S | S | S | S | S |
| Amikacin | S | S | S | S | S | S | S |
| Netilmicin/Tobramycin | R | R | S | – | R | – | – |

R : Resistant.
S : Sensitive.
TMP/SMX : Trimethoprim-sulfamethoxazole.

## Discussion

Severe illness due to S. marcescens is generally seen in immunocompromised patients such as the elderly and neonates. In newborns the organism can be responsible for sepsis and meningitis, which have a high case fatality rate[10]. Studies in the 1970's suggested that neonatal colonization and infection were rare events, but from 1980 to 1999, reports of S. marcescens epidemics in NICU's have increased[4,9,10]. Before January 1998, Serratia had not been isolated from cultures in our NICU. At the time, neither overcrowding nor patient admission from other hospitals had ocurred in our NICU.

The symptoms of infection were non-specific, such as hypoactivity, abdominal distention and apnea (Table I). The day of onset of symptoms ranged between four to 45 days, which suggests late sepsis with acquisition of the microorganism from the NICU. Endotracheal intubation and mechanical ventilation were required in five of the cases. There was no growth in urine cultures. In one patient (Case 2), hemolysis with jaundice that could not be controlled by photoherapy and required two exchange transfusions was observed. Other reasons for hemolysis were excluded in that patient, thus, it was thought to be due to S. marcescens infection. To our knowledge, this symptom has not been observed before in newborns with Serratia septicemia.

It has been shown that Serratia is a human pathogen capable of causing significant mortality and morbidity, with the small premature infant being most at risk of serious infection[7]. In our series, three of the babies with Serratia infection died. One of them (Case 1) was a debilitated baby with severe neurological sequelae due to hypoxic-ischemic encphalopathy (HIE). This baby had S. marcescens grown only in endotracheal aspirate culture. The other two babies (Cases 3 and 6) were premature and extremely low birth weight babies, prone to nosocomial infections. Since two out of four of the babies with S. marcescens septicemia died, the case fatality rate attributable to S. marcescens septicemia was 50 percent. Zaidi et al.[10] reported a 60 percent mortality rate for newborns weighing 2500 g or less with S. marcescens infection. In the series of van Ogtrop et al.[9], septicemia had a mortality rate of 100 percent in preterm newborns. In our series, the surviving infants with S. marcescens septicemia had a greater birth weight and gestational age than the ones that died. At the moment, Case 2 is 13 months and Case 4 is nine months old. The other two babies with S. marcescens growth only in endotracheal aspirate cultures (Case 5 and Case 7) are seven and six months old, respectively. All the babies with S. marcescens infection are being followed up. No late complication of infection nor any neurological sequelae has been observed in these four babies.

After the emergence of Serratia strains, environmental samples were taken from incubators, humidifiers, suction jars, soaps, intravenous solutions, sinks and stethoscopes. Extensive investigation and cultures failed to identify any environmental reservoir of S. marcescens. Since colonization on hands of the personnel had been reported to be responsible for spread of the microorganism, strict handwashing policies were re-introduced. Since June 1998, only one case with S. marcescens growth has been identified, in August 1998. In our NICU for the last five years, the standard treatment protocol for late-onset neonatal sepsis has been the combination of cefotaxime or ceftriaxone with amikacin. As smaller babies began to survive in our NICU, combination of an antipseudomonal cephalosporin with vancomycin was introduced in April 1998 as an alternative empyric late-onset sepsis treatment protocol for catheter-related sepsis.

Serratia species are known to carry chromosomally inducible beta-lactamase. Exposure to a beta-lactam antibiotic results in induction of expression of the enzyme, which persists as long as the inducer is present. Depressed mutants secreting beta-lactamase may colonize in an NICU and then be transferred to the patients later. Since in our series none of the isolates was susceptible to sulbactam ampicillin, and only 40 percent were

susceptible to cefotaxime or ceftriaxone, we think that our isolates also carry the enzyme. When we consider the high resistance levels with sulbactam ampicilin and cefotaxime or ceftriaxone for S. marcescens, a combination of ceftazidime or imipenem with amikacin seems appropriate for the treatment of newborns with Serratia infection.

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