



## RESEARCH ARTICLE

### *SERRATIA MARCESCENS* BACTERAEMIA IN PRETERM NEONATE - A CASE REPORT

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#### Abstract

**Background:** *Serratia marcescens* has emerged as opportunist in increasing number of hospital-associated infections in neonatal intensive care unit (NICUs), particularly as bloodstream infections. It is known to cause outbreaks in the NICUs, with high mortality rate in the vulnerable preterm population.

**Case presentation:** We present a case of one and half month-old preterm neonate who had complaints of intolerance to feeding and failure to thrive. Clinical investigation revealed anaemia and increased inflammatory markers. Blood culture showed growth of *S marcescens*. In antimicrobial susceptibility testing, the isolate showed susceptibility to all  $\beta$ -lactams, aminoglycosides and sulfamethoxazole-trimethoprim, but treatment failure occurred with empirical amikacin and piperacillin-tazobactam. Institution of meropenem showed good response.

**Discussion:** In premature babies with very low birth weight along with prolonged NICU stay predisposed them to *S marcescens* infection. The capacity of *S marcescens* to resist antibiotic therapy in vivo in spite of the in vitro sensitivity was exemplified in our case.

**Conclusion:** This case study portrays the important feature of *S marcescens* to develop 'in-vivo' resistance despite being sensitive by 'in vitro' testing which led to therapeutic failure. Carbapenem could be a choice in such treatment failure cases due *S marcescens*.

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#### Introduction:-

Among the rare pathogens in Enterobacterales, *Serratia* spp. was unrecognized as a human pathogen until the 1960s. [1] Even though this species was considered to be an innocuous, non-pathogenic organism, over the last few decades, *Serratia marcescens* have become a significant opportunist causing nosocomial infections. [2]

Recent surveillance studies show that *S marcescens* accounts for only 1-2% of the nosocomial infections which are mostly confined to respiratory tract, urinary tract, surgical wounds and soft tissues. [3] It is less common cause of bacteraemia and rarely associated with endocarditis or central nervous system and ocular infections. [4]

Neonatal age group, use of invasive medical devices, mechanical ventilation and prolonged hospital stay are considered risk factors for *S marcescens* acquisition. [5] It is a well-known cause of nosocomial infectious outbreaks in the neonatal intensive care unit, with a high mortality rate in the vulnerable preterm neonates. [6]

We present a case of bacteraemia due to *S marcescens* with vague signs and symptoms.

### Case history:

#### Presenting concerns and Medical history

One and half month-old newborn female was referred from near by district hospital to the department of Paediatrics in a tertiary care hospital, with a chief complaint of vomiting for last 15 days which was nonprojectile, nonbilious and containing milk. Patient also had complaint of intolerance to feeding and failure to thrive. Feeding by Ryle's tube was given which was not tolerated, hence intravenous fluid was started.

Past history revealed that there was respiratory distress at birth and very low birth weight for which she was managed in NICU of local hospital. Thereafter, she was again admitted there for intolerance to feeding and failure to thrive where she was not responded to treatment and thus referred to the tertiary care hospital.

#### Clinical findings

General condition of patient was poor. She was afebrile with pallor, had wrinkled skin, microcephaly with depressed anterior fontanelle, sparse hair and monkey facies and visible ribs. Neonatal reflexes and tone were average with increased cry. Pulse was 150/min, respiratory rate was 40/min, SPO<sub>2</sub> was 100%. The patient weighed 1.23 kilograms which was categorised under very low weight.

#### Diagnostic focus and assessment

The laboratory tests revealed increased inflammatory markers with C-reactive protein (CRP) 15 mg/L, Serum CK-MB 46 U/L, Serum D-Dimer > 6 µg/ml, Serum LDH- 780 U/L and Serum Ferritin- 356 µg/L. Haematology analysis report showed severe anaemia with haemoglobin 6.6 g/dL, MCH-29 pg and MCV-90.5 fl. White blood cell count was 11,800/L. Peripheral smear report revealed microcytic hypochromic anaemia. RBC were predominantly microcytic, with moderate hypochromia and mild anisopoikilocytosis, Differential leucocyte count showed Neutrophils-55%, Lymphocytes-40%, Eosinophils-2% and Monocytes-3%. Total leucocyte count was 8,000 cells/mm<sup>3</sup>, Platelet count was reduced. Random blood sugar was 71 mg/dL. Renal and Liver function test were within normal range. Neuro-sonography of skull and ultra-sonography of abdomen revealed no relevant pathology.

#### Therapeutic focus and assessment

Samples for urine analysis and blood culture were processed in bacteriology laboratory. Until the microbiological report came, patient had been started on empiric therapy with injectable piperacillin-tazobactam and amikacin along with multivitamins and nasogastric feeding. Urine culture showed no growth but blood culture sample showed growth of gram-negative bacilli with typically red pigment. Biochemical reaction revealed it as *S marcescens*.



**Figure 1:-** Growth of *S marcescens* on Nutrient Agar at 30°C showing red colour colonies (due to prodigiosin pigment production)

In antimicrobial susceptibility, it was found to be susceptible to all first line (ampicillin, gentamicin and cefazolin) and second line antimicrobials (amikacin, cefotaxime, cefixime, cefoxitin, cefepime, piperacillin-tazobactam, ertapenem and cotrimoxazole). Fortunately, the isolate was sensitive to both antimicrobials added in empiric treatment, these antimicrobials continued for 5 days. But as the patient was not improving, piperacillin-tazobactam was replaced by meropenem was given for 15 days. Two days after institution of meropenem, repeat blood culture was sent which was negative and also the newborn started responding.

Bacteraemia due to *S. marcescens* might be the diagnosis.

### Discussion:-

The journey from fanatical history of red prodigiosin production to the tenth most common cause of bloodstream infection makes the *S. marcescens* one of the recognized entities of Enterobacterales. [7], [8] Owing to its capability to survive under hostile condition, in recent years, it is emerged as an opportunist in growing number of serious hospital-associated infections in NICUs, particularly as bloodstream infections. [9] Surveillance study in USA and Europe showed that it ranked 5<sup>th</sup> amongst gram-negative infections in ICUs. [10]

The newborn in the study was born preterm with very low birth weight and severe anaemia. The preterm birth points towards immature immune system and poor weight gain and anaemia highlighted its immunocompromised condition. Long term hospitalization of this newborn predisposed her to this opportunist present in the hospital environment. It has been found that *Serratia* species are more typically transmitted horizontally to hospitalized patients from health care workers. [11] Ongoing studies indicate that *S. marcescens* produces pore forming hemolysin and cytotoxin which is linked to the extensive host invasiveness and it also releases inflammatory mediators. [12]

A remarkable feature of *S. marcescens* is its ability to produce constitutive high level AmpC  $\beta$ -lactamase due to which it demonstrates clinically significant cross resistance to most  $\beta$ -lactam agents including cephalosporins, monobactams and  $\beta$ -lactam/ $\beta$ -lactamase inhibitors, which often complicates therapy. [13], [14] Further, such derepressed mutants found initially susceptible may become resistant within 3 to 4 days after initiation of therapy. CLSI warrants testing of repeat isolates in such cases. [14] This might be the cause that the newborn was not responding to empirical therapy with piperacillin-tazobactam and responded to meropenem and amikacin. Since repeat blood culture showed no growth, repeat testing could not be done. Although aminoglycosides, fluoroquinolones and 3<sup>rd</sup>-generation cephalosporins have traditionally been effective, but there is now increasing reports of resistance to these classes. [15], [16] This capacity of *S. marcescens* was exemplified by our case, in that even though isolate was susceptible to cephalosporins, it exhibited resistance during clinical use and treatment failure occurred. This finding also supported by other studies. [9], [17]

Carbapenems resist inactivation by chromosomal AmpC and plasmid-mediated ESBL  $\beta$ -lactamases. [13] This is the reason of prescribing meropenem even though cephalosporins were found to be sensitive in vitro. Fortunately, newborn started improving on starting meropenem.

### Conclusion:-

Gram-negative bacilli, including *Serratia*, should be considered in cases of bacteraemia in preterm neonates, especially in immunocompromised condition with long term NICU admission. Lack of response to narrow-spectrum agents, such as penicillin, first-generation cephalosporins and aminoglycosides should heighten the suspicion for *S. marcescens*. Carbapenems should be considered a good choice in such treatment failure cases.

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