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First Moroccan Case of Infective Endocarditis Due to NDM-Type Carbapenemase-Producing Serratia marcescens in a Preterm Infant: A Case Report

--Manuscript Draft--

First Moroccan Case of Infective Endocarditis Due to NDM-Type Carbapenemase-Producing *Serratia marcescens* in a Preterm Infant: A Case Report

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Abstract

Serratia marcescens (S. marcescens) is a Gram-negative rod-shaped bacterium belonging to the *Enterobacteriaceae* family, commonly found in various environments. This opportunistic pathogen can cause urinary tract infections, respiratory infections, and septicemia, but endocarditis is particularly rare and concerning due to its rapid and devastating progression. We report the second case in the world of infective endocarditis (IE) caused by *S. marcescens* in a preterm infant born at 34 weeks of gestation. The patient was a preterm male infant born at 34 weeks of gestation, from a triplet pregnancy, admitted to the neonatal intensive care unit on day 2 of life for respiratory distress. The mother, aged 39, had undiagnosed gestational diabetes. Premature rupture of membranes had occurred 10 days before delivery, necessitating prophylactic treatment with amoxicillin. On day 4 of life, the newborn developed a fever with elevated CRP levels and leukocytosis, leading to antibiotic therapy with colistin, imipenem, and amikacin. Blood cultures revealed the presence of carbapenemase-producing *S. marcescens* sensitive to fluoroquinolones. A cardiac ultrasound showed vegetations on the mitral valve, confirming the diagnosis of IE. Despite intensive treatment, the newborn died on day 16 of life due to septic shock. This rare case of endocarditis caused by *S. marcescens* highlights the severity of this infection in preterm infants. Treatment relies on appropriate antibiotic therapy. Prevention requires strict hygiene measures. Further research is needed to establish optimal therapeutic recommendations.

Data Summary

No data were reused or generated in this study

Introduction

Serratia marcescens (S. marcescens) is a Gram-negative rod-shaped bacterium belonging to the *Enterobacteriaceae* family, commonly found in various environments, including water, soil, and plants. It is an opportunistic pathogen responsible for healthcare-associated infections. *S. marcescens* can cause urinary tract infections, respiratory infections, and septicemia. The occurrence of endocarditis is particularly rare but concerning due to its rapidly devastating progression. The natural resistance of this bacterium to many antibiotics, along with its ability to form biofilms, significantly complicates the treatment of this infection.

Infective endocarditis (IE) is an inflammation of the endothelial tissue lining the heart chambers, usually of bacterial origin. This condition represents a medical emergency due to its potential to cause severe complications. The most commonly involved pathogens in endocarditis are staphylococci, streptococci, and enterococci (1).

We report the first case in Morocco of endocarditis caused by *S. marcescens* in a preterm infant born at 34 weeks of gestation, highlighting the diagnostic and therapeutic challenges associated with this infection. To the best of our knowledge, this is the second case of IE reported in the literature due to *S. marcescens* in a premature infant.

Case Report

The patient was a male preterm infant born at 34 weeks of gestation from a triplet pregnancy, admitted on day 2 of life to the neonatal intensive care unit for respiratory distress. The 39-year-old mother had a history of cholecystectomy in 2022 and had experienced three pregnancies with five births (G3P5), as well as undiagnosed gestational diabetes discovered upon admission. Premature rupture of membranes (PROM) had occurred 10 days before delivery, justifying prophylactic treatment with amoxicillin (1g/8h for 7 days) after clinical and biological exclusion of bacterial colonization or infection. Delivery was performed by cesarean section under spinal anesthesia. The amniotic fluid was clear.

At birth, the newborn measured 46 cm, weighed 1.925 kg, and had a head circumference of 31 cm. The Apgar score was 10/10 at 1 minute after birth, and his temperature was 37°C. On day 2 of life, the preterm infant developed respiratory distress with metabolic acidosis, leading to his transfer to the neonatal intensive care unit, where he received continuous positive airway pressure ventilation, which was weaned on day 4 of life, as well as hydration via peripheral intravenous access.

On day 4 of life, the preterm infant presented with fever associated with elevated CRP levels (from 3 to 242 mg/l), leukocytosis (11 G/l) with neutrophilia (7.8 G/l), and normochromic normocytic anemia (Hb at 8.8 g/dl), justifying empirical antibiotic therapy with colistin, imipenem, and amikacin.

Given the clinical presentation, 3 ml of blood was collected by direct venipuncture and inoculated into a pediatric blood culture bottle (BD BACTEC™ Peds Plus/F, Becton Dickinson) then sent to our laboratory for bacteriological analysis. The blood culture bottle was incubated at 37°C with continuous agitation in a BD BACTEC™ FX system. Bacterial metabolism within the bottle was detected by the automated system after 7 hours and 13 minutes. Direct examination with Gram staining from the positive bottle revealed numerous Gram-negative bacilli. Further subcultures were performed on blood agar, blood agar with inhibitors (nalidixic acid-colistin), Polyvitex chocolate agar, chromogenic agar (CHROMagar), as well as 1/50th diluted broth flooded on Muller-Hinton agar for antibiotic susceptibility testing using the disk diffusion method according to the 2024 recommendations of the Antibiogram Committee of the French Society of Microbiology (CA-SFM). All subcultures were incubated at 37°C in a CO2-enriched atmosphere of 10%.

After 24 hours of incubation, except for the agar with inhibitors, which remained sterile, all subcultures showed a monomorphic appearance with numerous white, moist, and shiny colonies. Analysis by MALDI-TOF mass spectrometry (VITEK MS system, bioMérieux, Marcy l'Etoile, France) identified the species as *S. marcescens*.

Antibiotic susceptibility testing was confirmed by the microdilution method in liquid medium and interpreted according to the 2024 recommendations of the European Committee on Antimicrobial Susceptibility Testing (EUCAST). Indeed, this strain exhibited multidrug resistance. The susceptibility profile with minimum inhibitory concentrations (MIC) is shown in Table 1.

Table 1: Susceptibility Profile of the *S. marcescens* Strain

Antibiotic	MIC (mg/L)	Categorization
Ticarcillin/Clavulanic Acid	64/2	Resistant
Piperacillin/Tazobactam	32/4	Resistant
Cefotaxime	32	Resistant
Ceftazidime	16	Resistant
Cefepime	8	Resistant
Imipenem	8	Resistant
Meropenem	8	Resistant
Ertapenem	4	Resistant

Amikacin	32	Resistant
Gentamicin	8	Resistant
Tobramycin	8	Resistant
Colistin	4	Resistant
Aztreonam	1	Sensitive
Levofloxacin	0.5	Sensitive
Ciprofloxacin	0.25	Sensitive
Tigecycline	0.25	Sensitive
Sulfamethoxazole-Trimethoprim	0.5/9.5	Sensitive
Fosfomycin	32	Sensitive

From the isolated colonies, molecular biology analysis mediated by real-time nested RT-PCR of resistance genes coding for various carbapenemases (CARBA-R©, Cepheid, Sunnyvale, CA) returned positive with detection of the *bla* New Delhi metallo-β-lactamase (bla_{NDM}) gene.

A urine sample collected by a collection bag, as well as cerebrospinal fluid obtained by lumbar puncture, were sent to our laboratory for cytobacteriological analysis. Both samples were sterile with white blood cell counts below their respective thresholds.

On days 5 and 6, blood cultures processed under the same conditions also revealed the same strain of *S. marcescens*. Ciprofloxacin treatment was initiated and the initial antibiotic therapy discontinued.

Despite antibiotic treatment, the preterm infant's respiratory distress worsened on day 8 of life, with the onset of hemodynamic instability requiring intubation and intensification of antibiotic treatment. A transthoracic echocardiogram showed vegetations on the mitral valve (figure 1). Cardiac auscultation revealed a systolic murmur. According to modified Duke criteria (Li et al., 2011), the diagnosis of definite endocarditis was made based on persistent positive blood cultures for the same organism, echocardiographic findings, and the appearance of a new heart murmur.

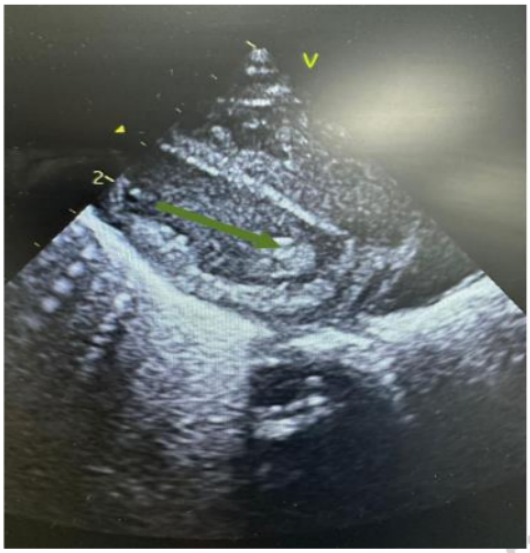

Figure 1 : Echocardiographic image demonstrating a mitral valve vegetation (green arrow) in the setting of infective endocarditis. The irregular, mobile mass is attached to the mitral valve leaflets, causing obstruction and regurgitation. This finding is characteristic of bacterial infection involving the heart valves.

Despite intensive antibiotic therapy, the newborn did not improve and died on day 16 of life from septic shock with multiple organ failure.

Discussion

S. marcescens is an opportunistic pathogen that can cause significant hospital outbreaks, particularly in neonatal units (2–4). Preterm infants are especially susceptible to infections and colonization due to the immaturity of their immune systems. The risk of infectious complications is further exacerbated by other high-risk pregnancy factors, such as gestational diabetes and multiple pregnancies (5,6). Our case exhibited all the aforementioned risk factors for infection.

Premature rupture of membranes (PROM) is a common complication in multiple pregnancies (7). Prophylactic antibiotic treatment, usually with amoxicillin, is used to prevent progression to chorioamnionitis. However, this treatment can lead to the selection of antibiotic-resistant pathogenic bacteria, which may cause massive maternal-fetal colonization (8). Among the hospital-acquired bacteria naturally resistant to amoxicillin are *Enterobacteriaceae* (e.g., *Klebsiella pneumoniae,* S. *marcescens, Enterobacter cloacae*), and non-fermenting bacilli (e.g., *Pseudomonas aeruginosa, Acinetobacter baumannii*). Additionally, the overuse of broad-spectrum antibiotics like colistin creates selective pressure that favors the emergence of infections caused by *S. marcescens*, which is naturally resistant to this drug.

To the best of our knowledge, this is the second reported case of IE due to *S. marcescens* in a preterm infant and the first reported in Morocco. According to the literature, the rare cases of *S. marcescens* endocarditis typically occur in adults, particularly in intravenous drug users (9). There are three published pediatric cases of IE caused by *Serratia sp.* with only one case involving *S. marcescens* in a preterm infant (10). The other cases involved a 7-year-old burn victim infected with *S. marcescens* and a preterm infant who underwent cardiac surgery complicated by IE due to *S. liquefaciens* (11,12).

According to the literature (13), the presence of a venous catheter, bacteremia caused by *S. marcescens*, and the absence of a primary infectious focus suggest that the bacteremia was likely catheter-related. The appearance of a New valvular regurgitation, the presence of mitral vegetation on echocardiography, and two positive blood cultures for *S. marcescens* taken 12 hours apart confirm a definite endocarditis diagnosis based on Li et al.'s criteria (13). In our case, the occurrence of endocarditis can be explained by the persistence of bacteremia, associated with the immaturity of the newborn's cardiac endothelium, in the absence of identified cardiac lesions or malformations.

S. marcescens possesses an inducible, low-level chromosomal cephalosporinase of the Amp-C type, which provides natural resistance to aminopenicillins, first-generation cephalosporins, and aminopenicillin/inhibitor combinations. Treatment with beta-lactams, particularly clavulanic acid, cefoxitin, and imipenem, can induce overproduction of this enzyme, leading to resistance to penicillins and cephalosporins (14). In our patient, the reduced diameter around the imipenem disk raised two possible hypotheses: Amp-C hyperproduction associated with reduced permeability or carbapenemase production. Molecular analysis confirmed the production of an NDM-type metallo-beta-lactamase. This enzyme is a class B carbapenemase according to the Ambler classification. In *Enterobacteriaceae*, the genes encoding this enzyme are primarily associated with IncX3 plasmids, which can easily be transferred from one bacterium to another (15,16). These plasmids often carry other resistance genes, conferring pan-resistance to antibiotics (17).

Currently, there is no consensus on the treatment of IE caused by *S. marcescens*. Several agents have been tested with variable results, including cefepime, piperacillin/tazobactam, and fluoroquinolones (18). In our case, high-dose fluoroquinolone therapy proved ineffective. In the absence of fosfomycin and newer antimicrobial agents, infection with a multidrug-resistant *S. marcescens* strain represents a therapeutic dead end, significantly complicating patient management.

Conclusion

This rare case of IE caused by *S. marcescens* underscores the danger posed by this opportunistic pathogen to vulnerable individuals and its rapidly disastrous progression. Treatment relies on bactericidal antibiotic therapy. This infection is preventable through the adoption of strict hygiene measures. Further studies are needed to establish therapeutic guidelines.

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