



Cefiderocol in a Preterm Neonate with Multidrug Resistant *Stenotrophomonas maltophilia* Ventilator Associated Pneumonia

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Background and Objective

Ventilator associated pneumonia (VAP) is a serious complication in neonates on mechanical ventilation. The emergence of multidrug-resistant Gram-negative (MDR-GN) infections in this vulnerable population has significant impacts on neonatal morbidity, survival, hospital costs and duration of neonatal intensive care unit (NICU) stay. Cefiderocol, a novel siderophore cephalosporin, with a unique mechanism of action, exhibits potent efficacy against Gram negative bacteria.^(1,2)

We describe the first off-label use of cefiderocol in a 23-day old extremely preterm neonate with MDR-GN *Stenotrophomonas maltophilia* VAP in our unit.⁽³⁾

Pharmacist Intervention

Pharmacist assisted with:

- The drug and therapeutics committee (DTC) approval for off label use.
- Procurement of cefiderocol via the Special Access Scheme (SAS).
- Reviewing drug information and literature. Provide advice on drug preparation, administration and storage.⁽⁴⁻⁸⁾

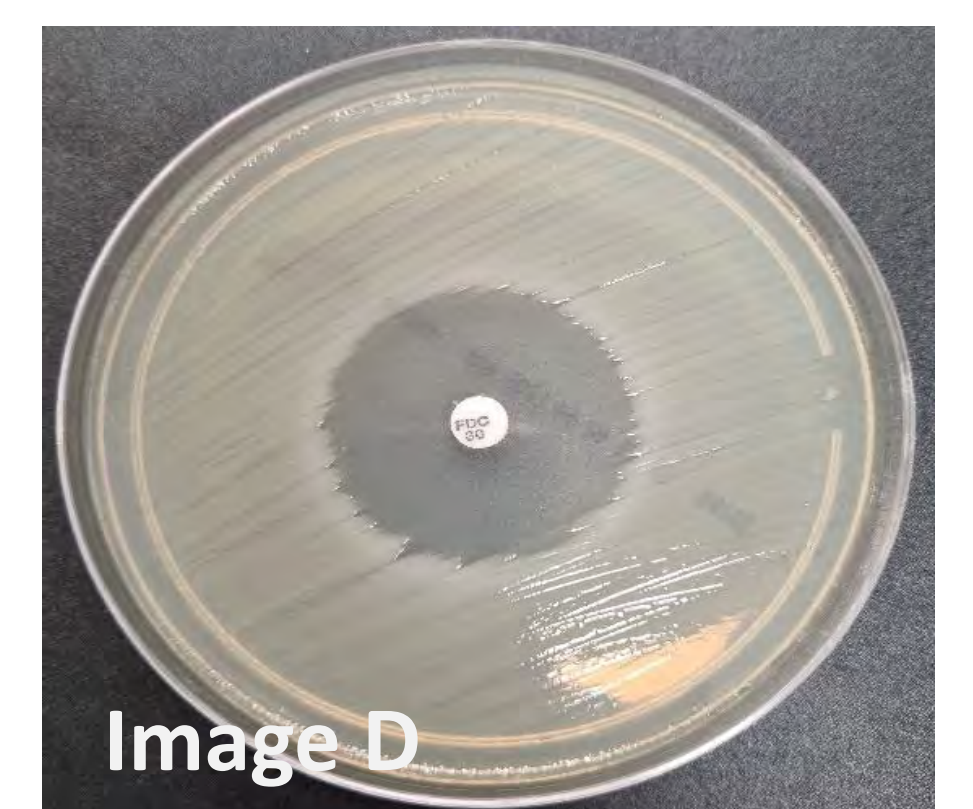
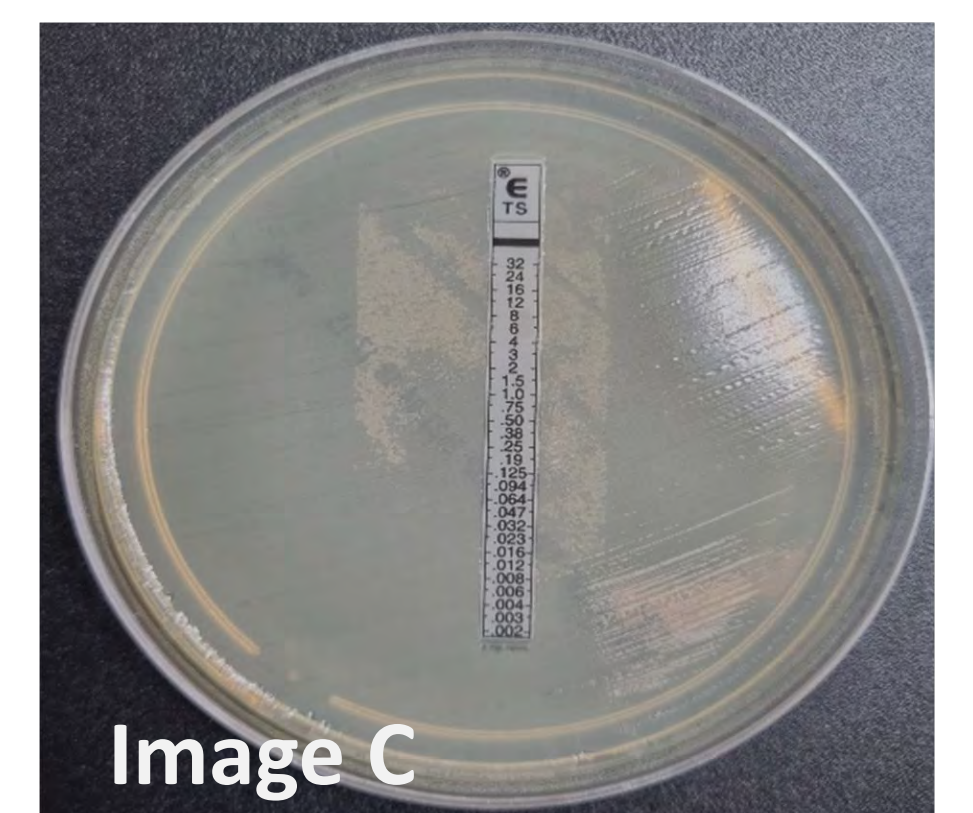
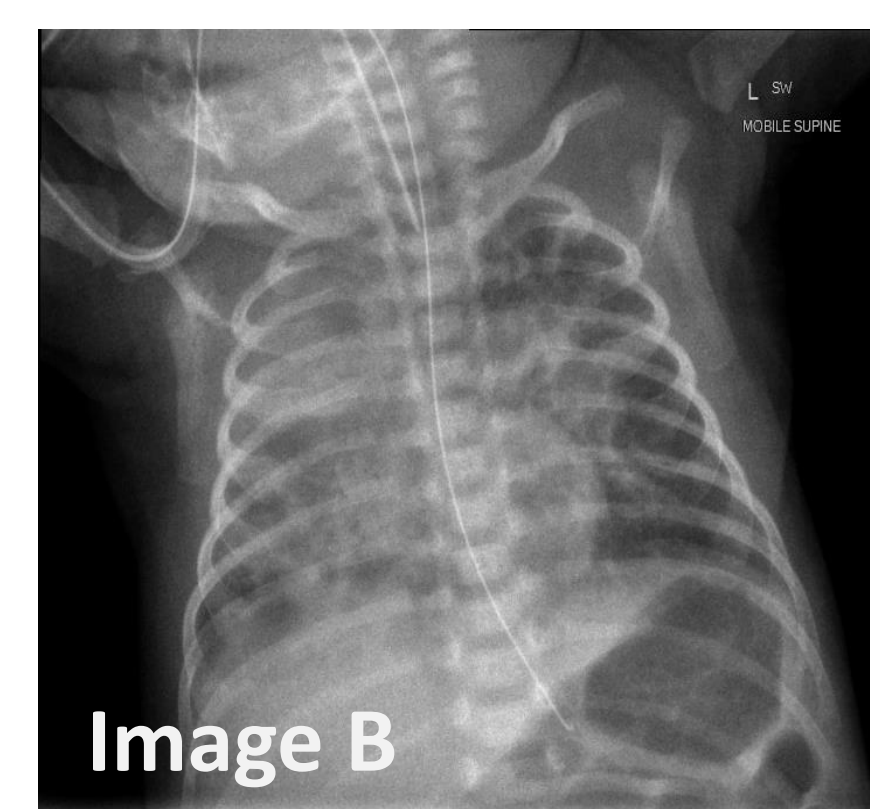
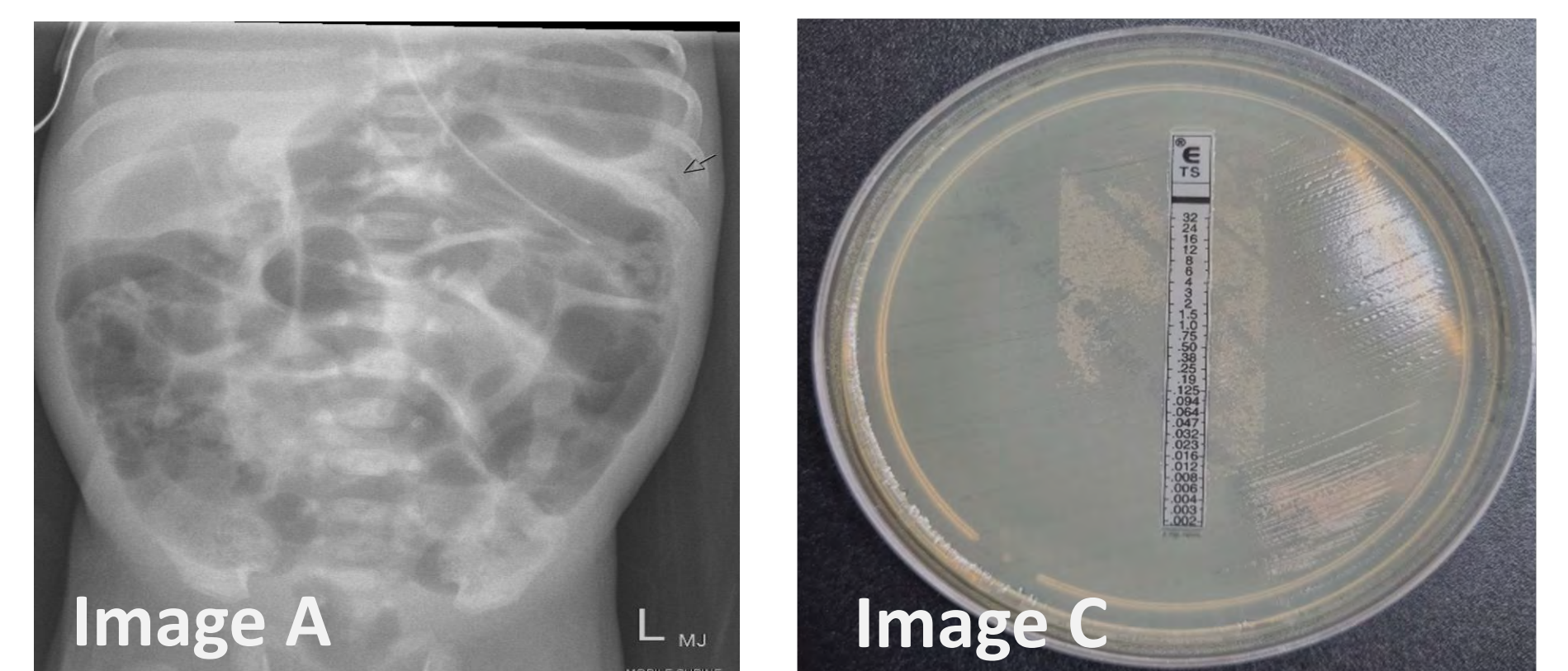
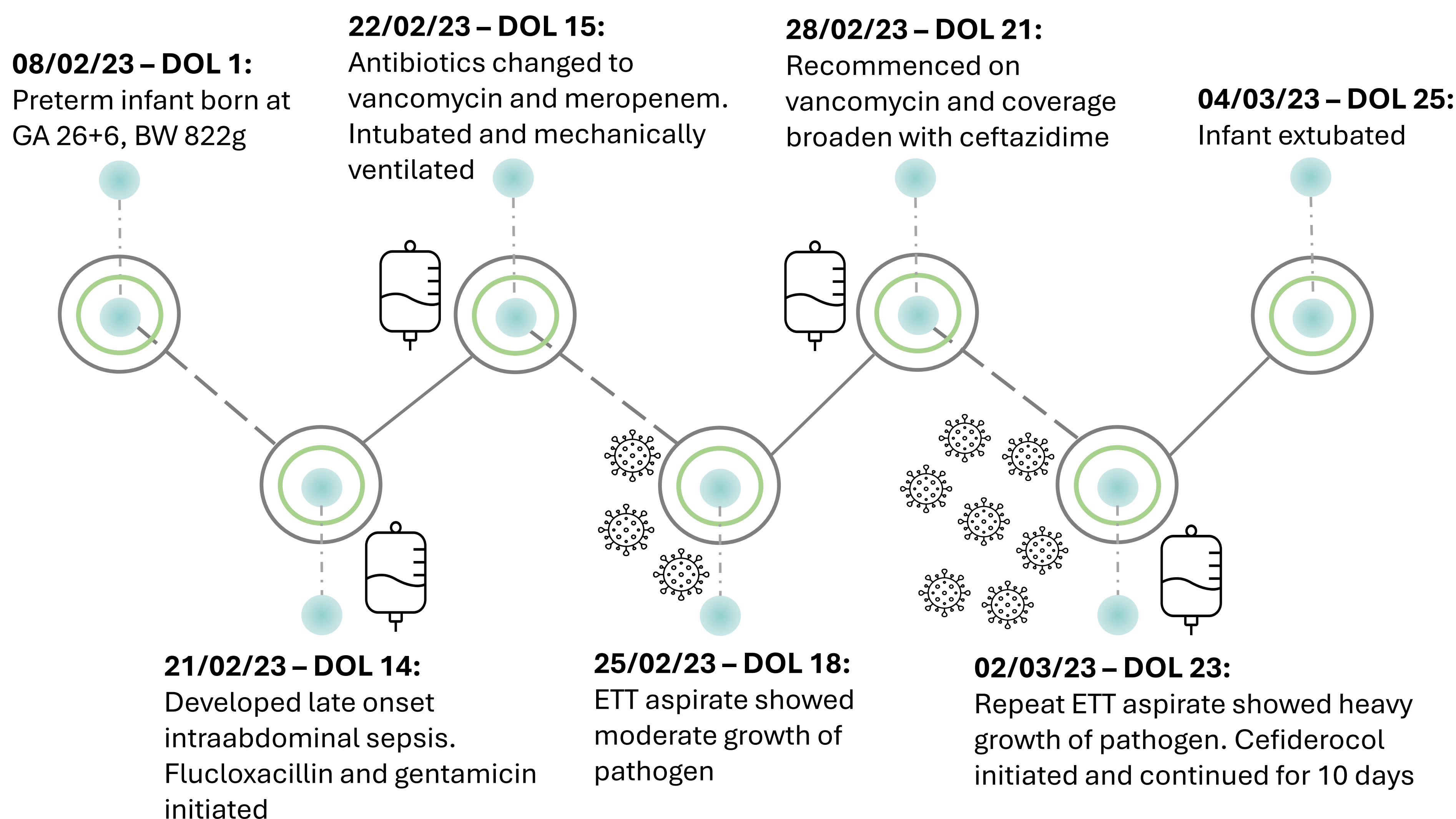
Literature Review

- Use of cefiderocol has been reported in 2 preterm infants at 27 and 31-week gestation with MDR-GN late onset sepsis (LOS) and necrotising enterocolitis and MDR-GN LOS respectively.^(4,5)
- Katsube et al. reviewed and modified an adult pharmacokinetic model to predict and propose cefiderocol dose regimens for paediatrics (birth to < 18 years old). Based on this study, the dosing regimen of 30mg/kg every 8 hours was chosen.⁽⁶⁾

Clinical Features

- A preterm neonate was born with gestational age 26+6 weeks and birth weight of 822g. She had a stable clinical course until day 14 of life.
- **21/02/23 - Day of life (DOL) 14:** She developed late onset intraabdominal sepsis on suspicion of necrotising enterocolitis (NEC) with abdomen distension, apnoeas and raised inflammatory markers (C-reactive protein (CRP) and procalcitonin (PCT)). Flucloxacillin and gentamicin were initiated as per sepsis protocol. She became increasingly lethargic with respiratory deterioration. An abdominal x-ray (AXR) showed multiple dilated gut loops (**image A**) and suspicious intraluminal gas. Antibiotics were changed to meropenem and vancomycin. The neonate was intubated and mechanically ventilated.
- **25/02/23 - DOL 18:** The endotracheal tube (ETT) aspirate returned a moderate growth of *Stenotrophomonas maltophilia*. A chest x-ray (CXR) showed right upper lobe collapse/consolidation (**image B**). A repeat AXR showed no evidence of NEC. Both her CRP and PCT were slightly improving.
- **28/02/23 - DOL 21:** Her respiratory status continued to deteriorate, consistent with severe VAP. Infectious diseases (ID) team advised that the *Stenotrophomonas maltophilia* was intrinsically resistant to meropenem. Vancomycin was recommenced to provide broad Gram positive cover and meropenem was changed to ceftazidime. Her blood culture remained negative.
- **02/03/23 - DOL 23:** A repeat ETT culture demonstrated heavy growth of *Stenotrophomonas maltophilia*. ID team reported that this isolate was resistant to trimethoprim/sulfamethoxazole (**image C**), ciprofloxacin and ceftazidime but susceptible to cefiderocol (**image D**). Following discussions between the neonatal and infectious diseases teams and the parents, cefiderocol was initiated. The infant had difficult and limited IV access. She was on continuous infusions of total parenteral nutrition, lipids and morphine. With the lack of information on drug compatibility, a shorter infusion time of 1 hour was chosen.
- **04/03/23 - DOL 25:** Her clinical condition improved following 48 hours of cefiderocol and she was extubated. Cefiderocol was continued for a total of 10 days and was well tolerated without any observed adverse effects.

Case Progress and Timeline



Picture of infant reproduced with permission

GA = Gestational age; BW = Birth weight; DOL = Day of life; ETT = Endotracheal tube; Pathogen = *Stenotrophomonas maltophilia*.

Images:

A. Abdominal x-ray showing multiple dilated gut loops.

B. Chest x-ray showing right upper lobe collapse/consolidation.

Susceptibility testing results for *Stenotrophomonas maltophilia*:

C. Gradient diffusion (E-test) with trimethoprim/sulfamethoxazole showing resistance.

D. Disc diffusion with cefiderocol showing susceptibility with a 28 mm zone diameter.

Discussion

Cefiderocol is an emerging antibiotic and demonstrates good promise in the treatment of MDR-GN infections.^(1,2,9,10) It is recognised that more research is urgently needed in neonates and children and the World Health Organization has listed cefiderocol as a priority antibiotic to be further developed for the paediatric population.⁽¹⁰⁾

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