NDM-1 *Klebsiella pneumoniae* sepsis in premature neonate – successful treatment and NICU outbreak study

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Background

Enterobacteriaceae (EB) are responsible for 15-40% of late onset sepsis (LOS) in premature neonates. *Klebsiella* sepsis is associated with an especially high risk of mortality. Carbapenem-producing Enterobacteriaceae (CPE) nosocomial outbreaks in NICUs are having been more frequently reported worldwide. CPE New Delhi metallo- β -lactamase (NDM-1) producers remain susceptible to only two bactericidal antibiotics (colistin and fosfomycin) and a single bacteriostatic antibiotic (tigecycline). The optimal therapy is unknown because of the paucity of reports and lack of studies. Since 2008, several nosocomial NDM-1 producing *K. pneumoniae* NICU outbreaks were reported. We report the first NDM-1 *K. pneumoniae* outbreak in an Israeli NICU and describe the successful treatment of a neonate who developed NDM-1 *K. pneumoniae* late onset sepsis and pneumonia.

Case Report

6-day old premature male (Patient B), was born at 28-weeks of gestation, with a birth weight of 970 grams, the first of discordant twins. At the age of 6 days he developed sepsis. The EB isolate was identified as *K. pneumoniae*. CSF and urine cultures were negative. The bacteria continued to grow on days 8, 9 and 10, with the first negative culture obtained on day 10 (Figure 1). The final microbiological identification of NDM-1 *K. pneumoniae* was completed, and the antibiotic treatment was switched from Meropenem + Amikacin to combination of **Coliracin** (25000unit/kg/dose three times daily), **Tigecycline** (1mg/kg/dose twice daily) and **Fosfomycin** (50mg/kg/dose twice daily). On chest X-Ray the diffuse infiltrate of the right lung appeared (Figure 2 – X-ray). At day 12 Broncho-alveolar lavage (BAL). The NDM-1 *K. pneumoniae* was isolated in the culture of BAL aspirate fluid. After BAL clinical improvement was observed, and the following blood cultures were negative. The infant was discharged from the hospital on Spironolactone and Hydrochlorothiazide due to BPD at the chronological age of 117 days. At the follow-up visit, he was noted to have only mild developmental delay.

Outbreak Investigation

Exposed neonates were rectally screened for disclosure of cross-transmission. Four out of twenty four other neonates were found positive; Total of 21% (5/24) of the NICU patients were NDM-CPE carriers.

The source of this outbreak was linked to a neonate who was born in a hospital outside Israel after surrogate pregnancy. This premature baby had been hospitalized in a NICU in the country of his surrogate mother (Caucasus region) after delivery, and was transferred to Israel with his biological parents at the age of 3 days. The source neonate was screened on admission for CPE according to standard policy by rectal swab culture and found negative, before the outbreak screening swab was found.

NDM-1 *K. pneumoniae* was then detected in the original sample of patient A by PCR and by enrichment culture. During 109 days, till the last NDM-CPE carrier was discharged, cross transmission was not detected. No new cases of CPE were recovered until March-2018. The carriers were found positive **100-312 days** post disclosure.

Conclusions

- NDM-1 *K. pneumoniae* neonatal sepsis can be successfully treated with **Coliracin, Tigecycline and Fosfomycin** combination.
- In **high risk patients** for CPE, **PCR and/or enrichment culture** of the rectal swab are crucial for **identification of CPE.**

Figure 1 Timeline

Fig.2- Chest X-Ray