CASE SERIES

OUTBREAK OF MULTIDRUG-RESISTANT *KLEBSIELLA PNEUMONIAE* SEPSIS IN NEONATAL INTENSIVE CARE UNIT

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ABSTRACT

Klebsiella pneumoniae has played an important role as a cause of infection in the neonatal high risk units around the globe. The widespread use of broad-spectrum antibacterial agents has led to an increase in the emergence of resistance to broad-spectrum cephalosporins and carbapenems. We report an outbreak caused by a strain of *Klebsiella pneumoniae* that was susceptible only to ciprofloxacin and tigecycline and that affected neonates hospitalized in neonatal intensive care unit of Combined Military Hospital Rawalpindi during October 2010. Outbreak investigation was carried to find out the possible source of infection which turned out to be suction tubing of resuscitation table, emergency tray and scissors. The outbreak was resolved by temporarily closing down the nursery and using remedial measures such as disinfection, reinforcing the use of antiseptic techniques and timely treatment of neonates with ciprofloxacin.

KEY WORDS: *Klebsiella pneumoniae,* Extended spectrum beta-lactamase, Ciprofloxacin, Tigecycline.

INTRODUCTION

The genus *Klebsiella* consists of capsulated, gram negative rods, 1-2 μm long non-motile organisms. They are facultative anaerobes and favor moist environments.[1] Carbapenems are first line drugs for the treatment of severe infections caused by *Enterobacteriaceae* expressing extended spectrum beta-lactamases (ESBLs).[2] The emergence of strains of *Enterobacteriaceae* that are resistant to carbapenems in the past years is of great concern. The injudicious use of broad spectrum antibiotics and improper antisepsis has resulted in emergence of multidrug-resistant strains of *K. pneumoniae* causing outbreaks in various settings especially neonatal high risk units.[3]

We present a case series of three neonates from Neonatal ICU (NICU) of a tertiary care hospital, who developed sepsis within five days after they were shifted from the operation theatre. The strain of *Klebsiella pneumoniae* isolated from the blood of all these babies was sensitive only to ciprofloxacin and tigecycline. One neonate, who also had congenital cardiac defects, expired. Two neonates with positive blood cultures and two others who were septicemic but culture negative were managed successfully with injection ciprofloxacin.

CASE SERIES

Our 1st patient was a newborn baby girl resident of Rawalpindi who was hospitalized in NICU of Combined Military Hospital (CMH), Rawalpindi on 9th October 2010. Baby was delivered at 33rd week of gestation by caesarian section. Baby had low birth weight and was tachypneic. APGAR score was 6/10. On systemic examination bilateral crepitations and sluggish reflexes were noted. Provisional diagnosis of respiratory distress syndrome was made and baby was admitted in NICU for further care. Blood complete picture revealed no abnormality. C-reactive protein was 6.5 mg/dL. After Initial resuscitation, Injections cefotaxime and amikacin were advised. On 13th October, condition of baby deteriorated. Further laboratory investigations were requested. Blood was sent for culture and sensitivity. On 17th October blood culture yielded growth of *Klebsiella pneumoniae* which was sensitive to ciprofloxacin and tigecycline only. Patient was started with injection ciprofloxacin while other antibiotics were discontinued. On 20th October, clinical condition of baby started improving when therapy switched over. Baby recovered and was discharged on 30th October 2010.

The 2nd patient was newborn baby girl resident of Rawalpindi who was hospitalized in NICU of CMH on 9th October 2010. Baby was delivered at 30th week of gestation by caesarian section. Baby had low birth weight and was tachypneic. APGAR score was 5/10. On systemic examination bilateral crepitations and sluggish reflexes were noted. Provisional diagnosis of septicemia was made and baby was admitted in NICU for further

care. Blood complete picture revealed no abnormality. C reactive protein was 7 mg/dL. After initial resuscitative measures, patient was started with Injections meropenem, vancomycin and flagyl. Three days after admission condition of baby deteriorated further. Injection ceftazidime was added to treatment. After 3 more days blood picture showed deranged blood counts and mottling all over body, due to which fresh frozen plasma (FFP) infusion, Injection pentaglobulin and platelet concentrates were advised. On 18th October, condition of baby further deteriorated. Blood was sent for culture and sensitivity which later yielded growth of *Klebsiella pneumoniae* which was sensitive to ciprofloxacin and tigecycline only but unfortunately the baby expired one day before the availability of culture & sensitivity report to pediatrician. Baby had also features of Down's syndrome.

The 3rd patient was newborn baby boy resident of Rawalpindi hospitalized in NICU of CMH Rawalpindi on 15th October 2010. Baby was delivered at 32nd week of gestation by caesarian section. Mother was Rh negative and HCV positive. Baby was tachypneic but rest of the general physical examination was unremarkable. APGAR score was 7/10. On systemic examination bilateral crepitations and sluggish reflexes were noted. Provisional diagnosis of prematurity was made and baby was admitted in NICU for further care. All the base line investigations were within normal limits. After initial resuscitation, injections cefotaxime and amikacin were advised. Three days after admission condition of baby deteriorated. Blood was sent for culture and sensitivity. After 3 days, blood culture yielded growth of *Klebsiella pneumoniae* which was sensitive to ciprofloxacin and tigecycline only. Baby was started with injection ciprofloxacin and other antibiotics were discontinued. Next day, clinical condition of baby started improving. Baby recovered completely and was discharged on 2nd November 2010.

Outbreak investigations: The growth of three isolates of *Klebsiella pneumoniae* from blood culture of three different patients in the same unit raised the suspicion of an outbreak. To trace out the possible source of this outbreak a team headed by a microbiologist from Armed Forces Institute of Pathology visited the unit and specimens were collected from different possible sources of infection including healthcare workers, suction tubing of resuscitation table, scissor and emergency tray. All the specimens were cultured on blood and MacConkey agar (Oxoid, UK) and three of these revealed the growth of *Klebsiella pneumoniae* having same biochemical profile and sensitivity pattern as was seen in three patients (Fig 1). NICU was informed immediately. Staff of NICU was in-

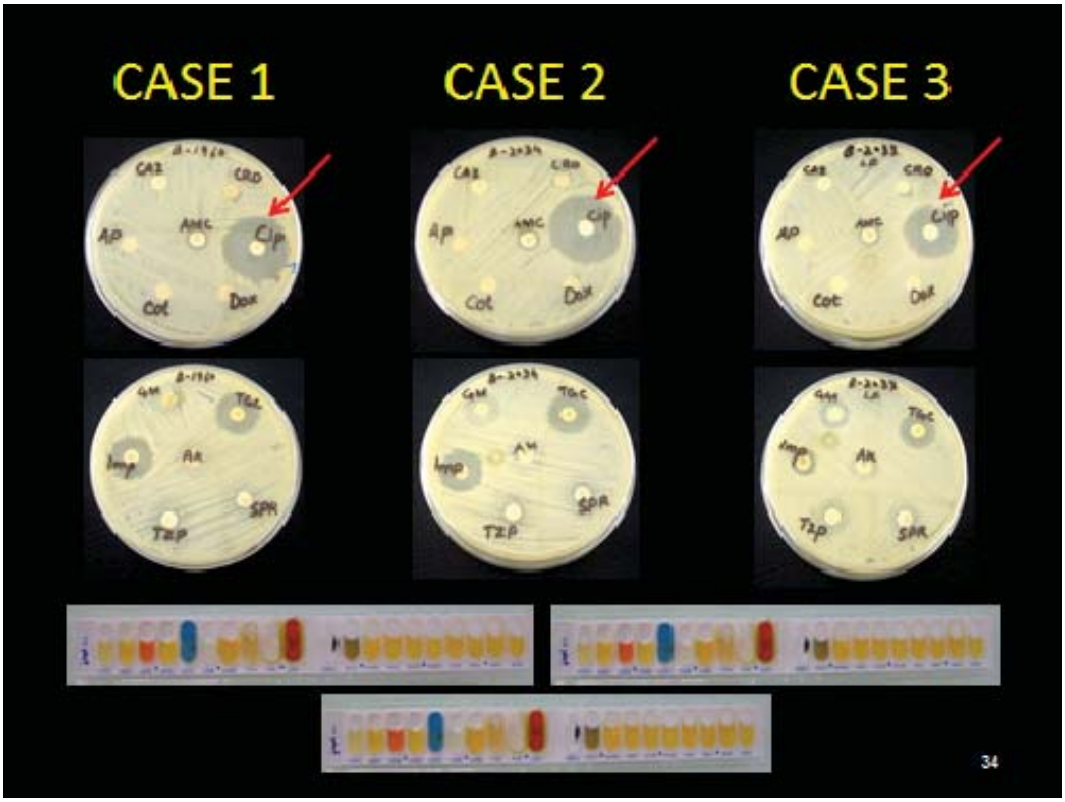

Fig. 1: Three strains of *Klebsiella pneumonia* showing similar antibiogram.

structed to adopt strict antiseptic techniques. Ciprofloxacin was included in the treatment regimen. In addition to the cases mentioned two other babies of the unit with suspected septicemia were also put on injection ciprofloxacin & responded to treatment while their blood cultures were negative. NICU was temporarily closed down. Proper sterilization & disinfection of instruments and NICU were advised. Considering operation rooms as a possible source of infection, as all the cases were delivered by caesarian section, 18 specimens were also collected from OT & its staff but no such growth was seen in cultures of OT specimens.

DISCUSSION

Klebsiella was named after the German bacteriologist of nineteenth century Edwin Klebs (1834-1913). Genus Klebsiella consists of capsulated, Gram negative rods. They are non-motile but express fimbriae. They grow at 12-43°C (optimum 37°C) and are killed by moist heat at 55°C for 30 min.[4] Klebsiella may survive dying for months and cultures remain viable for many weeks at room temp. They are facultative anaerobes and favour moist environment for their growth. *K. pneumoniae* is responsible for causing severe potentially fatal pneumonia and septicemia and is frequently implicated in healthcare-associated outbreaks in ICUs.[5] Nosocomial infections occur more frequently in premature infants, patients in neonatal intensive care units as in our case, and hospitalized individuals who are immunocompromised.[6]

The global dissemination of firstly the ESBL producing *K. pneumoniae* and then the strains that are resistant to carbapenems is a matter of great concern to public health services worldwide.[7] Reported mortality due to ESBL producing strains of *K. pneumoniae* is 25%.[8] In a recent outbreak occurred in India, 14 phenotypically identical *K. pneumoniae* strains were isolated in neonatal ICU which were multi-drug resitant. These strains were isolated from disinfectant solution, suction fluid, water tap and hands of HCWs.[9] All these strains were sensitive to imipenem. Strains that are resistant to carbapenems are also frequently resistant to aminoglycosides, tetracyclines and fluoroquinolones.[10] The strains resistant to carbapenems were first reported in US in 1996. The first outbreak outside the United States was documented in Israel in 2004.[11] The indiscriminate and injudicious use of broad-spectrum antibiotics is responsible for rapid spread of multidrug-resistant bacteria around the globe.[12]

Healthcare-associated outbreaks of multidrug-resistant bacteria represent an emerging threat in all kinds of medical departments but especially in neonates and immunocompromised patients.[13] Because of the clinical and financial burden resulting from these outbreaks, all efforts should be made to minimize the risk of nosocomial spread by good hand hygiene especially use of alcohol based hand sanitizers, sterilization and disinfection of equipment in the wards and ICUs and use of disposable instruments.[14] Environmental decontamination should be regularly carried out and vascular and urinary catheters should be optimally managed. Sources of infection should be identified and removed.[15]

CONCLUSION

Klebsiella pneumoniae septicemia is a life threatening condition especially in neonates. The ability of organism to survive in hospital settings predisposes to nosocomial infections. The majority of outbreaks result from negligence in hospital infection control practices. Strict hospital infection control measures are the only key to control such infections. The existing infection control protocols should regularly and carefully be reviewed and modified. Fortunately in our case the isolate was susceptible to ciprofloxacin but we may not be so fortunate in future. Therefore, a policy for judicious use of high-risk antibiotics must be devised which would not only result in prevention of these outbreaks but also delay the emergence of more resistant and potentially epidemic strains.

REFERENCES

1. Podschun R and Ullmann U. Klebsiella spp. as nosocomial pathogens: epidemiology, taxonomy, typing methods, and pathogenicity factors. Clin Microbiol Rev 1998; 11: 589-603.
2. Paterson DL. Recommendation for treatment of severe infections caused by *Enterobacteriaceae* producing extended-spectrum beta-lactamases (ESBLs). Clin Microbiol Infect 2000; 6: 460-3.
3. Gur D, Hascelik G, Aydin N, Telli M, Gultekin M, Ogulnç D, *et al*. Antimicrobial resistance in gram-negative hospital isolates: results of the Turkish HITIT-2 Surveillance Study of 2007. J Chemother 2009; 21: 383-9.
4. Abbasi SA, Karamat KA, Hafeez A, Ali S, Luqman M. An outbreak of neonatal sepsis in a nursery. Pak Paed J 1997; 21:149-53.
5. Roy I, Jain A, Kumar M, Agarwal SK. Bacteriology of neonatal septicaemia in a tertiary care hospital of northern India. Indian J Med Microbiol 2002; 20:156-9
6. Zhanel GG, DeCorby M, Laing N, Weshnoweski B, Vashisht R, Tailor F, *et al*. Antimicrobial-resistant pathogens in intensive care units in Canada: results of the Canadian National Intensive Care Unit (CAN-ICU) study, 2005-2006.; Canadian Antimicrobial Resistance

Alliance (CARA). Antimicrob Agents Chemother 2008; 52: 1430-7.

7. Hawkey PM. Prevalence and clonality of extended-spectrum beta-lactamases in Asia. Clin Microbiol Infect 2008; 14: 159-65.

8. Siu LK, Lu PL, Hsuch PR, Lin FM, Chang SC, Luh KT, et al. Bacteremia due to extended spectrum beta lactamase producing *Escherichia coli* and *Klebsiella pneumoniae* in a pediatric oncology ward: Clinical features and identification of different plasmids carrying both SHV-5 and TEM-1 genes. J Clin Microbiol 1999; 37: 4020-7.

9. Feizabadi MM, Etemadi G, Yadegarinia D, Rahmati M, Shabanpoor S, Bokaei S. Antibiotic-resistance patterns and frequency of extended-spectrum beta-lactamase-producing isolates of *Klebsiella pneumoniae* in Tehran. Med Sci Monit 2006; 12: 362-5.

10. Rastogi V, Nirwan PS, Jain S, Kapil A. Nosocomial outbreak of septicaemia in neonatal intensive care unit due to extended spectrum â-lactamase producing *Klebsiella pneumoniae* showing multiple mechanisms of drug resistance. Indian J Med Microbiol. 2010; 28: 380-4.

11. Leavitt A, Navon-Venezia S, Chmelnitsky I, Schwaber MJ, Carmeli Y. Emergence of KPC-2 and KPC-3 in carbapenems resistant Klebsiella pneumoniae strains in an Israeli hospital. Antimicrob Agents Chemother 2007; 51: 3026-9.

12. Babay HAH. Ciprofloxacin resistance among bacterial isolates in a teaching hospital in Riyadh Saudi Arabia 2001-2005. Pak J Med Sci 2007; 23: 39-42.

13. Raineri E, Crema L, Dal ZS, Acquarolo A, Pan A, Carnevale G, et al. Rotation of antimicrobial therapy in the intensive care unit: impact on incidence of ventilator-associated pneumonia caused by antibiotic-resistant Gram-negative bacteria. Eur J Clin Microbiol Infect Dis 2010; 29: 1015-24.

14. Corona A, Raimondi F. Prevention of nosocomial infection in the ICU setting. Minerva Anestesiol 2004; 70: 329-37.

15. Siddiqui S, Hussein K, Manasia R, Samad A, Salahuddin N, Zafar A, Hoda Q. Impact of antibiotic restriction on broad spectrum antibiotic usage in the ICU of a developing country. J Pak Med Assoc 2007; 57: 484-7.

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