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Case Report

Paediatrics Section

Neonatal Brain Abscess due to Extended-Spectrum Beta-Lactamase Producing *Klebsiella pneumoniae*

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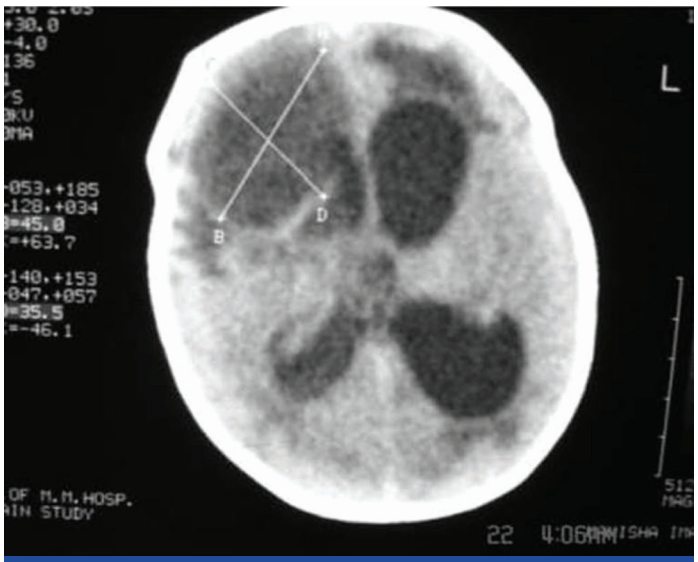
ABSTRACT

Klebsiella pneumoniae (*K. pneumoniae*) causing brain abscess in newborn infants is rare. Presented herein, is a 27-day-old male neonate who developed two frontal lobe abscesses in association with *K. pneumoniae* sepsis and meningitis. Antibiotic susceptibility testing utilizing the double-disk synergy method (Cefotaxime and Amoxycillin-Clavulanate) confirmed the extended spectrum beta-lactamase (ESBL) production by the isolate. He was treated simultaneously with antibiotics (Meropenem and Amikacin) and abscess aspiration through the anterior fontanelle, with less than satisfactory outcome. ESBL producing *K. pneumoniae* brain abscess in neonates is extremely rare in the English literature. Emperical carbapenems and aminoglycoside coverage in neonates with *K. pneumoniae* sepsis and brain abscess, especially in areas with high rate of ESBL producing bacteria may be warranted.

Keywords: Brain abscess, ESBL, *Klebsiella* sepsis

CASE REPORT

A 27-day-old male, term neonate was initially seen for high-grade fever, progressive lethargy and refusal to breastfeed for the last 24 hours. There were three episodes of left sided focal seizures in the preceding six hours, each lasting for about three minutes with spontaneous resolution. He was delivered at term spontaneously to a 24 year old non-consanguineous primipara by the vaginal route. The mother's antenatal period was uneventful and without exposure to ill contacts, radiation or teratogenic drugs. She had a non-reactive ELISA to HIV-I and II. There was no history of prolonged rupture of membrane and difficult or traumatic delivery. She had not received antibiotics either during her antenatal period or during labour. The mother denied any sick contacts in the family. The baby had satisfactory one and five minute Apgar scores of 8 and 9 respectively. The birth weight, length and head circumference were 2550 grams, 46 cm and 34.8 cm respectively. The neonate was discharged on the second day of life from the hospital on exclusive breastfeeding. On admission, he weighed 2660 grams and measured 46.5 cm in length. The head circumference was 37 cm. There was no history of head injury, ear discharge or pyogenic infection in the baby. The physical examination revealed a lethargic and febrile neonate (temperature of 39.1^{0}C). His heart rate was 170/minute; respiratory rate 47/minute and capillary refill time was two seconds. No focus of infection in the skin and ears was identified. The liver and the spleen were palpable 2.5 cm and 1.5 cm below the right and the left costal margins respectively. The anterior fontanelle was tensely bulging and non-pulsatile, measuring 2.8 cm x 3.1 cm. Mild sutural diastasis and prominent scalp veins were noted. He had markedly exaggerated deep tendon jerks of his left upper and lower extremities. Those on his right upper and lower extremities were brisk. Two additional left-sided seizures were noted at the Emergency department which responded to intravenous midazolam injection. He was subsequently put on intravenous phenobarbitone which prevented further seizures. The electroencephalogram was consistent with right frontal lobe seizure activity. The complete blood count revealed the following: hemoglobin (Hb): 11.8 gm/dL, total leukocyte count: 29,700/mm^3 (neutrophils (N): 42%, bands (B): 22%, lymphocytes (L): 34%), platelets: 197,000/mm^3. The erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were elevated at 82 mm (first hour) and 54 mg/L respectively. Routine urine analysis was normal and the culture was sterile. Meropenem (20 mg/kg/dose every eight hours) was added empirically, pending blood cultures. Two sets of aerobic blood cultures yielded growth of *Klebsiella*, identified as *Klebsiella pneumoniae* by conventional laboratory tests. Antibiotic susceptibility testing by Kirby-Bauer disk diffusion method revealed the following values for the antimicrobials tested: Cefotaxime: 14 mm; Ceftriaxone: 12 mm; Ceftazidime: 12 mm; Aztreonam: 16 mm. These values indicated positive screen as per the recommendations of the National Committee for Clinical Laboratory Standard [1] for ESBL production by the isolate. The ESBL production status was confirmed by the double-disk synergy test method using lawn culture of the isolate on Muller-Hinton agar (Hi-media, Mumbai) and exposing them to discs of Cefotaxime (30 µg) and Amoxycillin-Clavulanate (20 µg amoxicillin/10 µg clavulanic acid) arranged in pairs [2]. Amikacin (15 mg/kg 12 hourly) was then added. The lumbar puncture yielded frankly turbid cerebro-spinal fluid (CSF) with an elevated opening pressure. It showed 442 cells with 364 polymorphs. The glucose and the protein contents were 20 mg/dL and 48 mg/dL respectively. The CSF smears showed Gram-negative bacilli and the subsequent cultures were positive



[Table/Fig-1]: Cranial CECT scan showing a large abscess of 9 cm diameter in the right frontal region, and another 4 cm diameter abscess in the left-frontal region with ventricular communication and marked ventricular dilatation

for ESBL producing *K. pneumoniae*. A trans-fontanelle ultrasound scan showed two well defined space-occupying lesions, one each in the right and the left frontal region with midline shift and marked hydrocephalus. A contrast enhanced cranial computerized tomography (CT) scan [Table/Fig-1] showed a large abscess of 9 cm diameter in the right frontal region, and another 4 cm diameter abscess in the left frontal region. Both the abscesses were communicating with the ipsilateral lateral ventricle which was markedly dilated. The two-dimensional echocardiography was normal. Aspiration of the abscess through the anterior fontanelle yielded 35 ml of purulent material. The smear of the aspirated pus showed Gram-negative bacilli and the cultures once again grew ESBL producing *K. pneumoniae* with a similar sensitivity pattern to that shown in the blood and CSF culture reports. Despite adequate antibiotic coverage and abscess aspiration, the baby developed progressive increase in head circumference with marked ventricular dilatation for which neurosurgical drainage was planned. The mother was informed about the prognosis and she did not give consent to surgical intervention and left the hospital against medical advice.

DISCUSSION

ESBLs are enzymes that hydrolyze oxy-imino beta-lactams such as the third generation cephalosporins (e.g., Ceftazidime, Cefotaxime, and Ceftriaxone) and Monobactams (e.g., Aztreonam) but do not affect Cephamycins (e.g., Cefoxitin and Cefotetan) or Carbapenems (e.g., Meropenem or Imipenem) [1]. They arise by mutations in genes for common plasmid-mediated beta-lactamases that alter the configuration of the enzyme near its active site to increase the affinity and hydrolytic ability of the beta-lactamases for oxy-imino compounds while simultaneously weakening the overall enzyme efficiency. Recent studies on ESBL production in members of *Enterobacteriacae* isolated from clinical specimens showed 9-50 per cent ESBL producers [2]. A study from north India on ESBL production in uro-pathogens showed 26.6 per cent ESBL producers which belonged to *Klebsiella*, *Escherichia coli*, *Enlerobacter*, *Proteus and Citrobacter species* [3]. There are no reports on the prevalence of ESBL producing *Enterobacteriaceae* species causing neonatal infections from India. The passively transferred specific maternal IgG antibody in adequate concentration provides neonatal protection against *Enterobacteriaceae*. Furthermore, specific bactericidal and opsonic antibodies against these enteric Gram-negative bacteria are provided by IgM class of antibody that the neonate actively synthesizes. However, diminished concentrations of immunoglobulins and other immunologic factors along with decreased function of neutrophils and other cells involved in the response to infection occur in both term and preterm infants. Additionally, it has been demonstrated that, in general, newborn infants lack antibody-mediated protection against *Enterobacteriaceae*. Despite these alterations in immune function, systemic infection in newborns is unusual in the absence of obstetric and neonatal risk factors [4]. Brain abscess is rare in the neonatal age-group. *Citrobacter koseri* and *Proteus* species are the most commonly implicated organisms causing neonatal brain abscess in most reports published till date [5]. Although *K. pneumoniae* is a common cause of neonatal sepsis in the newborns of the developing world, it rarely causes brain abscesses in such patients. In all the reported neonates, the brain abscesses were caused by non-ESBL producing *K. pneumoniae* species. In a Polish language report [6] on central nervous system infections caused by ESBL producing *K. pneumoniae* in critically ill neonates by Wojsyk-Banaszak and Szczapa, 27 cases were identified, of which only one neonate had brain abscess which was treated surgically. In most instances of Gram-negative neonatal brain abscesses, maternal genital tract was identified as the source of infection. In one series, 10 of 30 neonates with brain abscesses, maternal urinary tract infection (UTI) was observed in eight cases and it was concluded that in many more the documentation of maternal illness was missing. In the report by Basu et al., [7], the mother had possible UTI during pregnancy which was overlooked. In the neonates described by Pant et al., [8], maternal UTI and prolonged rupture of membranes were the risk factors present. In the present neonate, the presence of most antenatal, intranatal or postnatal risk factors for the development of fulminant *K. pneumonia* infection were excluded and thus, we presume that the infection may have been community-acquired. However, asymptomatic maternal UTI during pregnancy and nosocomial bacterial colonization during the neonate's hospital stay remain noteworthy possibilities.

CONCLUSION

ESBL producing *K. pneumoniae* associated brain abscess in neonates is extremely rare. Emperical Carbapenems and/or Aminoglycoside coverage in neonates with *K. pneumoniae* sepsis and brain abscess, especially in areas with high rate of ESBL producing bacteria may be warranted

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