Neonatal Citrobacter koseri meningitis and brain abscess

U Kariholu, J Rawal, S Namnyak

Citation

U Kariholu, J Rawal, S Namnyak. *Neonatal Citrobacter koseri meningitis and brain abscess*. The Internet Journal of Pediatrics and Neonatology. 2008 Volume 10 Number 1.

Abstract

Citrobacter koseri meningitis is a very rare cause of neonatal meningitis. It is characterized by serious complications like cerebral abscesses and high mortality. This is the first neonatal case of cerebral abscesses in UK following C. koseri meningitis, who survived with no serious neurological deficit. Serial neuroimaging is the key to diagnose cerebral complications early. Neonatal meningitis is a well known serious clinical condition associated with significant morbidity and mortality12 which can be complicated by brain abscess formation and ventriculitis.3456 Although there has been a decrease in the overall mortality in the last decade attributable to improved supportive care and the use of more efficacious antibiotics such as third generation cephalosprorins,7 the incidence and morbidity attributed to this condition has remained largely unchanged.12 Up to forty-five percent of neonatal meningitis is caused by Gram negative bacilli, 123 and is associated with high morbidity7 and mortality of about eighty percent.4 Neonatal meningitis caused by Citrobacter koseri is extremely rare and is often complicated by brain abscess and ventriculitis, with only a few cases reported from the USA,345 India,8 Brazil,9 Israel,10 and Canada.11 In the UK, there have been ten reported cases of Citrobacter meningitis, 12131415 nine of which were C. koseri and one C. freundii.

CASE REPORT

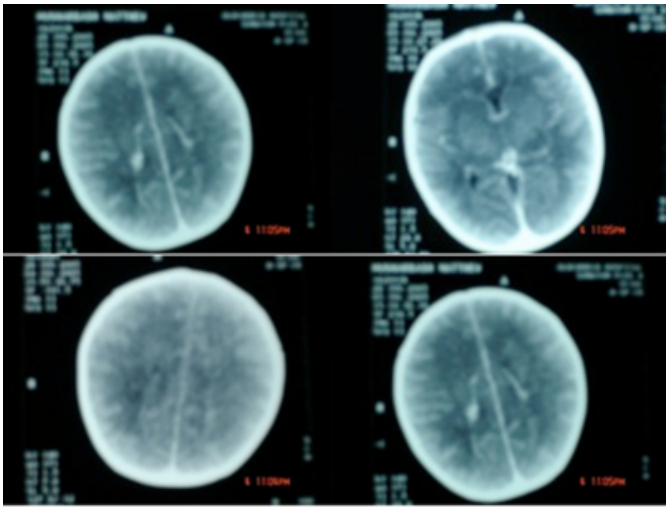
A 39 weeks male neonate, of Caucasian and Arabic parentage, was delivered vaginally by ventouse, following an early rupture of membranes lasting more than 24 hours before delivery. His mother was given 2 doses of intravenous penicillin till four hours before the delivery. His immediate aftercare was uneventful and was discharged home next day, exclusively breastfed.

After five days following discharge he was admitted to the Children's Ward with a two-day history of poor feeding and brief repetitive focal and generalized clonic fits which were managed with intravenous lorazepam and subsequently phenobarbitone.

His initial general physical and systemic examination including vitals was unremarkable. His WCC was within normal limits as well. However his sodium was 158 with urea of 12.5. The chest X-ray and CT scan of head with contrast were normal (Fig 1). Neonatal septicaemia and meningitis was diagnosed and one set of blood cultures was taken. A lumbar puncture yielded a turbid cerebrospinal fluid sample containing 3300 leucocytes per ml with 95% neutrophils, organisms were not seen on direct microscopy and the cultures remained sterile after five days of incubation and enrichment. He was started on empirical intravenous cefotaxime and penicillin G. In view of hypernatraemia, he was slowly rehydrated over 48 hours, when his sodium was back to normal range.

Figure 1

Figure 1: CAT Scans of Head with contrast in first 48 hours of Admission



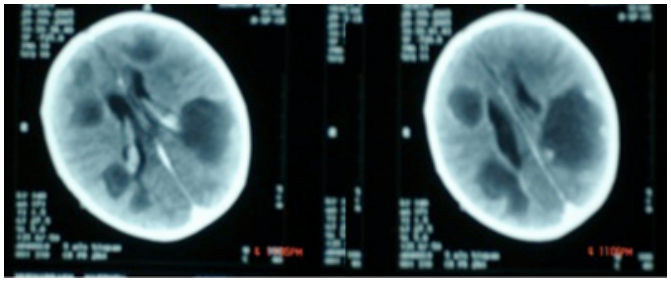
On day 2, the blood cultures yielded gram negative bacilli identified and confirmed by a reference laboratory as C. koseri sensitive to cefotaxime and gentamicin but resistant to penicillin. Hence, penicillin was replaced with gentamicin and therapy continued for a total of seven days. There was a significant improvement in the clinical status and after

spending 6 days on the ward, he was discharged home with cefotaxime to be continued for a further two weeks.

However, three days after discharge, the patient was re-admitted with fever, irritability, inconsolable cry, vomiting and fits. Clinical systemic examination and laboratory results were within normal limits. A repeat CAT scan of head with contrast showed five brain abscesses (Fig 2). The patient was transferred to a Specialist Paediatric Neurosurgical Unit for aspiration of the abscesses. The brain abscesses yielded profuse growth of C. koseri, similar in colonial morphology and antibiotic sensitivity patterns to the blood culture isolate. The therapy was changed to i.v. meropenem and vancomycin. However, the patient continued to have fits for most of the following day, and amikacin was added to the therapy regimen on the following day. There was gradual improvement and the patient was transferred back to us 9 days after aspiration, with the recommendation to continue meropenem and amikacin for a total of six and two weeks respectively.

Figure 2

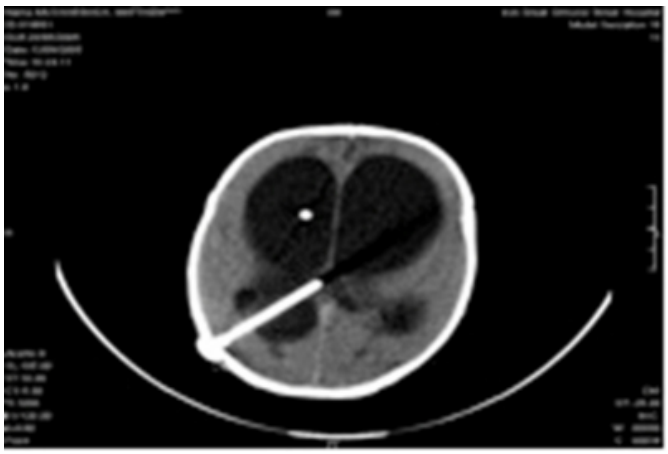
Figure 2 : CAT Scans of Head with contrast on Day 9 after Admission showing cerebral abscesses.



Three weeks after the transfer he was found to be irritable and the head circumference had increased from 34 cm (9^{th} centile) to 37.7 cm (25^{th} – 50^{th} centile) in 21 days and bilateral hydrocephalus was confirmed by CAT scan (Fig3). The patient was transferred back to the neurosurgical unit where endoscopic washout and ventriculostomy of the third ventricle was performed on day 24, followed by the insertion of a ventriculo-peritoneal shunt on day 27. The VP shunt got infected and blocked after two weeks of insertion, that necessitated its removal, intermittent external drainage of ventricles, intravenous vancomycin for two weeks, followed by VP shunt revision on day 42.

Figure 3

Figure 3 : CAT Scan of head post VP shunt insertion for hydrocephalus



The patient was discharged home on day 50. The patient was followed up at four weeks and then two monthly thereafter. At 3 months follow up, the patient was found to be making significant clinical improvement, with only mild developmental delay, but with normal vision and hearing. No relapse of seizures was noted at 6 months follow up.

DISCUSSION

Citrobacter is a genus of gram-negative bacilli, which belongs to family Enterobacteriaceae. C. koseri, is a rare cause of septicemia and meningitis, seldom reported beyond neonatal period.[5,6,8,9,10,11] The infections outside the central nervous system are uncommon although focal infections of bone, joints, lungs, mediastinum, urinary tract, gastrointestinal tract and the umbilicus have been reported.[1,11,16,17]

The source of infection is unknown in the majority of cases, but in some cases it is vertical from mother to the baby [2,18,19] and in others it has been shown to occur as a horizontal nosocomial transmission by unit staff during Citrobacter outbreaks.[20,21,22] In our case the source of infection could not be determined.

The illness in our case took a fulminant course and developed complications, including brain abscesses and hydrocephalous consistent with previous observations where brain abscesses occurred in 80% of cases.[20,23] This is in striking contrast to other gram negative bacterial neonatal meningitis where brain abscesses occurred in as low as 10% of cases.[23] The propensity of the organism to affect neonates and particularly to cause CNS disease, while sparing older age children remains largely unexplained.[12] The presence of

a specific 32-kD outer-membrane protein has been identified as a neuro-virulence factor that causes the brain abscesses. This protein may provide the organism with tropism for nervous system and associated meningitis and cerebral abscesses.[242526]

Other complications include diffuse necrotizing meningoencephalitis, ventriculitis, hydrocephalus and pneumocephalus / pneumotosis oculi, [315] with severe neurological impairment including seizures reported in 75% of cases [23] and severe delayed development in 50 % of cases.[3] Our case, however, had almost normal neuro-development with normal hearing, normal vision and no seizures at 12 months of follow up.

In our case the CSF did not grow any bacteria, presumably due to prior administration of antibiotics. The organisms were isolated from the blood culture taken before the antibiotics were given and from the pus aspirated from the abscess probably because the antibiotics did not reach the bacteria within the abscess.

Isolation of an uncommon organism like C. koseri from blood and /or CSF should alert the paediatrician about the possible CNS complications and the need for serial neuroimaging to detect cerebral abscesses which can even develop early or late, some times even after treatment.[27] It is not yet clear whether serial neuroimaging in first week could have been beneficial to pick up brain abscesses early in our case

The optimal treatment for C. koseri meningitis and brain abscess is not yet established. Citrobacter strains have been resistant to ampicillin/ amoxicillin/ penicillin and sensitive to third generation cephalosporins/ aminoglycosides/ moxalactam[3] as was the strain isolated from this case. The initial choice of antibiotics in the present case was appropriate, consistent with sensitivity and the recommendations in the literature.[3] These are a combination of third generation cephalosporins and aminoglycosides for a minimum of four to six weeks in the presence of abscesses, following the sterilization of the CSF,[3] with aminoglycoside to be stopped after two weeks. Carbapenems are suggested as alternative antibiotics in resistant cases.[10] Meropenem was used in this child, at the regional neurosurgical unit, in spite of sensitivity to third generation cephalosporins and aminoglycosides, presumably to attain maximum antibiotic concentrations in the CSF, as is the case with meropenem. For reasons of poor penetration, intrathecal and intraventricular antibiotics have been used [12] but not recommended as these have been shown to cause higher mortality,[182829] the reasons for which are not clear.

CONCLUSIONS

The isolation of C.koseri in blood and /or CSF, as found in our patient, suggests that serious and life threatening cerebral complications such as cerebral abscesses may develop despite optimal antibiotic treatment. Regular clinical follow up, supported by early serial neuroimaging and the drainage of abscesses may open new treatment modalities for the prevention of fatal complications. There is a strong need for further investigations on the role of serial neuroimaging and the use of carbapenem antibiotics in C.koseri neonatal meningitis.

References

1. Holt DE, Halket S, de Louvois J et al. Neonatal meningitis in England and Wales; 10 years on. Arch Dis Child Fetal Neonatal Ed 2001;84: F85–9
2. Gupta P, Gupta S, Singh NP et al. Vertical Transmission of Citrobacter freundi. Indian Paediatr 2000;38:110–111
3. Doren TI. The Role of Cirobacter in Clinical Disease of Children: Review. Clin
Infec Dis 1999;28:384-94
4. Meier Ann, Chusid Micheal, Sty John. Neonatal Citrobacter meningitis: neurosonographic observations. J Ultrasound Med 1998;17:399-401
5. Aller-Seve-C, Cushid-Michael-J. Citrobacter kosei pneumonia and meningitis in an infant. The Journal of infection 2002;45(1):65-7
6. Dyer J, Hayani KC, Janda WM,et al. Journal of clinical microbiology Oct 1999; 35;3:2686–8
7. Heath PT, Yosoff N K, Baker CJ. Neonatal meningitis. Arch Dis Child
Fetal Neonatal Ed 2003;88: F173-F177
8. Saraswathi K, De A, Gogate A, Fernandes AR. Citrobacter sepsis in infants. Indian
Paediatrics, 1995;32(3):359 – 62
9. Feferbaum R, Diniz EM, Valente M et al. Brain abscess by Citrobacter diversus: case report. Arquivos de neuro-psiquiatria 2000;58(3A):736–40
10. Straussberg R, Harel L, Amir J. Long term outcome of Citrobacter koseri meningitis treated with imipenem/ meropenem and surgical drainage.Infection 2001;9(5):280–2
11. Tse G, Silver M, Shyte H, Jay V. Neonatal meningitis and multiple brain abscesses due to Citrobacter diversus. Pediatr Pathol Lab Med.1997;17(6):977-8226
12. Gwynn CM, George RH. Neonatal Citrobacter meningitis. Arch Dis Child 1973; 48:455–78
13. Malpas TJ, Munoz JJ, Muscat I. Vertical transmission of Citrobacter freundii. Arch
Dis Child 2004;89:F28030
14. Gross RJ, Rowe B et al. Neonatal meningitis caused by Citrobacter koseri. J Cli
Pathol 1973;26(2):138–139
15. Pooboni SK, Mathur SK, Dux A, Hewertson J, Nichani S. Pneumocephalus in neonatal meningitis: diffuse necrotizing meningo-encephalitis in Citrobacter meningitis presenting with pneumatosis oculi and pneumocephalus. Paediatrics
Critical Care Medicine 2004;5(3):393–5.11
16. Rose S J. Neonatal meningitis due to Citrobacter koseri.

J Perinat Med 1979;7:273-5
17. Jansen RD, Meadow WL, Schwartz IK, Ogata ES. 'Bacteriological bit': Citrobacter diversus osteomylitis in a neonate. Clin pediatr 1981;20:79131
18. Papasian CJ, Kinney J, Coffman S, Hollis RJ, Pfaller MA. Transmission of Citrobacter diversus from mother to infant documented by ribotyping and pulsed – field electrophoresis. Diagn Microbiol Infect Dis 1996;26:63–70
19. Harvey BS, Koeuth T, Versalovic J et al. Vertical Transmission of Citrobacter diversus documented by DNA fingerprinting. Infect Control Hosp Epidemiol 1995;16:564–9
20. Lin F-YC, Devoe WF, Morrison C et al. Outbreak of neonatal Citrobacter diversus meningitis in a suburban hospital. Pediatr Infect Dis J 1987;6:50-5
21. William JG, Mariano J, Spurrier M et al. Nosocomial meningitis due to Citrobacter diversus in neonates: new aspect of the epidemiology. J Infect Dis 1984; 21:46–47
22. Morris JG, Lin F-YC, Morrison CB et al. Molecular epidemiology of neonatal meningitis due to Citrobacter diversus : a study of isolates from hospitals in Maryland. J Infect Dis 1986;154:409–14.
23. Graham D, Band JD. Citrobacter diversus brain abscess and meningitis in neonates. J Am Med Assoc 1981;245:1923-5
24. Kline MW, Kaplan SL et al. Pathogenesis of brain abscess formation in an infant rat model of Citrobacter diversus bacteremia and meningitis. J Infect Dis 1998;157:106 – 12
25. Kline MW, Mason EO, Kaplan SL. Characterisation of Citrobacter diversus strains causing neonatal meningitis. J Infect Dis 1998;157:101–5
26. Li J, Musser JM, Beltran P, KlineMW et al. Genotyping heterogeneity of strains of Citrobacter diversus expressing a 32-kilodalton outer membrane protein associated with neonatal meningitis. J Clin Microbiol 1990;28:1760–5
27. Levy RL, Saunder RL. Citrobacter meningitis and cerebral abscesses in early infancy:cure by moxalactam. Neurology 1981;31:1575-7
28. Baker CJ, Kaplan SL. Neonatal sepsis. In: Current therapy in pediatric infectious disease. 3rd ed. St Louis:1993:278
29. Mc Cracken GH Jr, Mize SG. A controlled study of intrathecal antibiotic therapy in gram negative enteric meningitis of infancy. Jpiatr 1996;89:66-72

Author Information

Ujwal Kariholu, SpR Paediatrics
Queens hospital

Jeewan Rawal
Consultant Paediatrics, Queens hospital

Simon Namnyak
Consultant Microbiology, Queens hospital