Neonatal Citrobacter koseri meningitis and brain abscess
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Citation

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 mortality which can be complicated by brain abscess formation and ventriculitis. 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 cephalosporins, the incidence and morbidity attributed to this condition has remained largely unchanged. Up to forty-five percent of neonatal meningitis is caused by Gram negative bacilli, and is associated with high morbidity and mortality of about eighty percent. 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, India, Brazil, Israel, and Canada. In the UK, there have been ten reported cases of Citrobacter meningitis, 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 hyponatraemia, 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 readmitted 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 (9th centile) to 37.7 cm (25th – 50th 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 vancomycen 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. 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. The source of infection is unknown in the majority of cases, but in some cases it is vertical from mother to the baby and in others it has been shown to occur as a horizontal nosocomial transmission by unit staff during Citrobacter outbreaks. 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 hydrocephalus consistent with previous observations where brain abscesses occurred in 80% of cases. This is in striking contrast to other gram negative bacterial neonatal meningitis where brain abscesses occurred in as low as 10% of cases. The propensity of the organism to affect neonates and particularly to cause CNS disease, while sparing older age children remains largely unexplained. 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.

Other complications include diffuse necrotizing meningoencephalitis, ventriculitis, hydrocephalus and pneumocephalus / pneumotosis oculi, with severe neurological impairment including seizures reported in 75% of cases and severe delayed development in 50% of cases.

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. 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, 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. 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 with aminoglycoside to be stopped after two weeks. Carbapenems are suggested as alternative antibiotics in resistant cases. 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, but not recommended as these have been shown to cause higher mortality, 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

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