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Multiple Brain Abscesses Complicating Enterobacter Cloacae Sepsis in a Preterm Neonate with Atypical MRI Appearance: A Case Report

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Abstract

Multiple brain abscesses in neonates are extremely rare and occur as an unusual complication of bacterial meningitis or sepsis. There are many bacterial pathogens reported to cause brain abscesses in newborns; however, brain abscess caused by Enterobacter cloacae has rarely been described previously in neonates and only a few reports exist in English literature. After 4 weeks in the neonatal intensive care unit, a preterm neonate developed multiple brain abscesses as a complication of E. cloacae sepsis which were revealed on TFU and confirmed on MRI. Consequently, a limited craniotomy was performed for the biggest abscess for evacuation of pus and followed by aspiration of other abscesses.

Key Words: Brain abscess, Case study, cystic lesions, Enterobacter cloacae, Magnetic Resonance Imaging (MRI), Nosocomial pathogen, Preterm neonate, Sepsis.

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1- INTRODUCTION

Multiple brain abscesses are prodigious in neonates, and usually occur as complications of bacterial meningitis or bacteremia (1). They are most often caused by Gram-negative bacteria. Enterobacter species are common organisms colonizing the intestinal tract of infants in neonatal units, particularly in low birth weight and preterm infants (2). The accustomed clinical signs of neonatal brain abscesses are nonspecific and subtle, signaling towards a rapidly deteriorating infant; consequently, abscesses are frequently recognized late, and are often large and multiple (3). With a poorly developed immune system, this condition is further aggravated in premature infants.

Prompt radiologic recognition is the first step to appropriate and timely treatment of these potentially catastrophic central nervous system infections (4, 5). Here we describe the case presentation, radiologic findings, and management of an uncommon occurrence of multiple brain abscess secondary to E. cloacae sepsis in a premature infant.

2- CASE PRESENTATION

A preterm male infant was born at 31 weeks of gestational age via C-section due to breech presentation to a 27-year-old mother (gravid 2, para 2). The mother presented to our hospital with spontaneous rupture of the membranes, 1 day prior to delivery, and a single course of corticosteroids was administered. Apart from preterm labor, the mother had no symptoms or signs of infection.

At birth, the newborn's Apgar scores were 7and 9 at 1 and 5 minutes, respectively. Following delivery, the infant was transferred to the neonatal intensive care unit on O_2 via nasal cannula. The initial neonatal intensive care unit course was complicated by respiratory distress syndrome, jaundice and hypocalcemia. He received ampicillin and gentamicin for 48 hours for suspected sepsis which was stopped after negative culture.

On the 4th day, a significant deterioration in the neonate's condition was observed as he started to develop frequent episodes of apnea, temperature instability and tachycardia. Full sepsis evaluation was performed and treatment with ampicillin and Amikacin was initiated. The sepsis screen showed leukocytosis, elevated C-reactive protein (63 mg/l) and thrombocytopenia. Blood culture was positive for Enterobacter cloacae but CSF was negative for this bacterium. According to the blood culture result, treatment was modified to meropenem which was used for 14 days, and Amikacin which was continued for 5 days.

Two weeks later, the newborn experienced numerous episodes of apnea and desaturation that required connection to O2 via nasal cannula. A full sepsis workup was performed and treatment with Amikacin and Tazocin was started. Upon the negative result of the culture and sepsis workup the treatment was stopped after 2 days.

On the 34th day of life, before discharge, a bulging anterior fontanelle was noted by the neonatologist as the only abnormal finding. On the same day, TFU showed multiple bilateral cystic lesions, the largest in the right frontal region and in the left parietotemporal region, without midline shift (**Fig. 1**).

These lesions were confirmed on MRI that was performed on the 38th day of life and revealed bilateral fronto- and parieto-temporal large cystic lesions (4 in the right cerebral hemisphere and 3 in the left one) showing enhancing walls and intra-cystic nodules with diffusion restriction. The largest lesion in the right frontal lobe had 7.8 x 4.4 x 3.3 cm in size (**Fig. 2 A-F**).

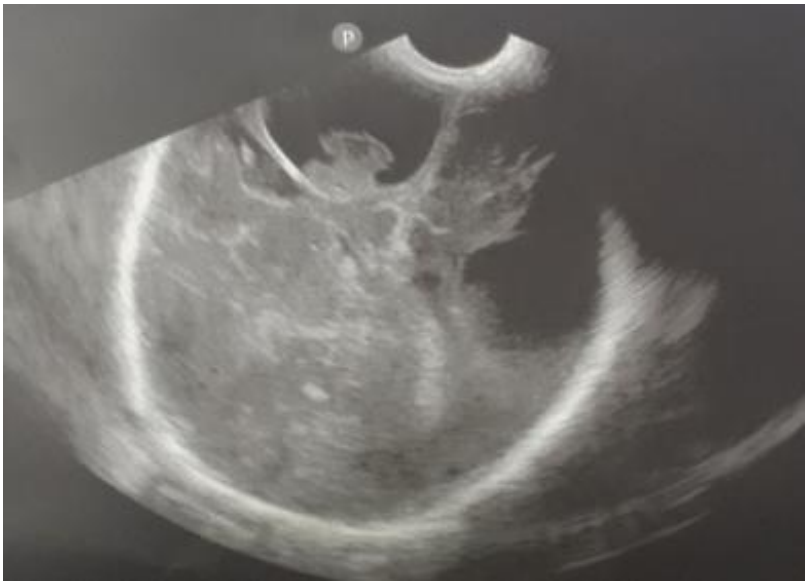

Fig. 1: Cranial ultrasound demonstrated a few well defined anechoic cystic lesions in both cerebral hemispheres with isoechoic nodules inside.

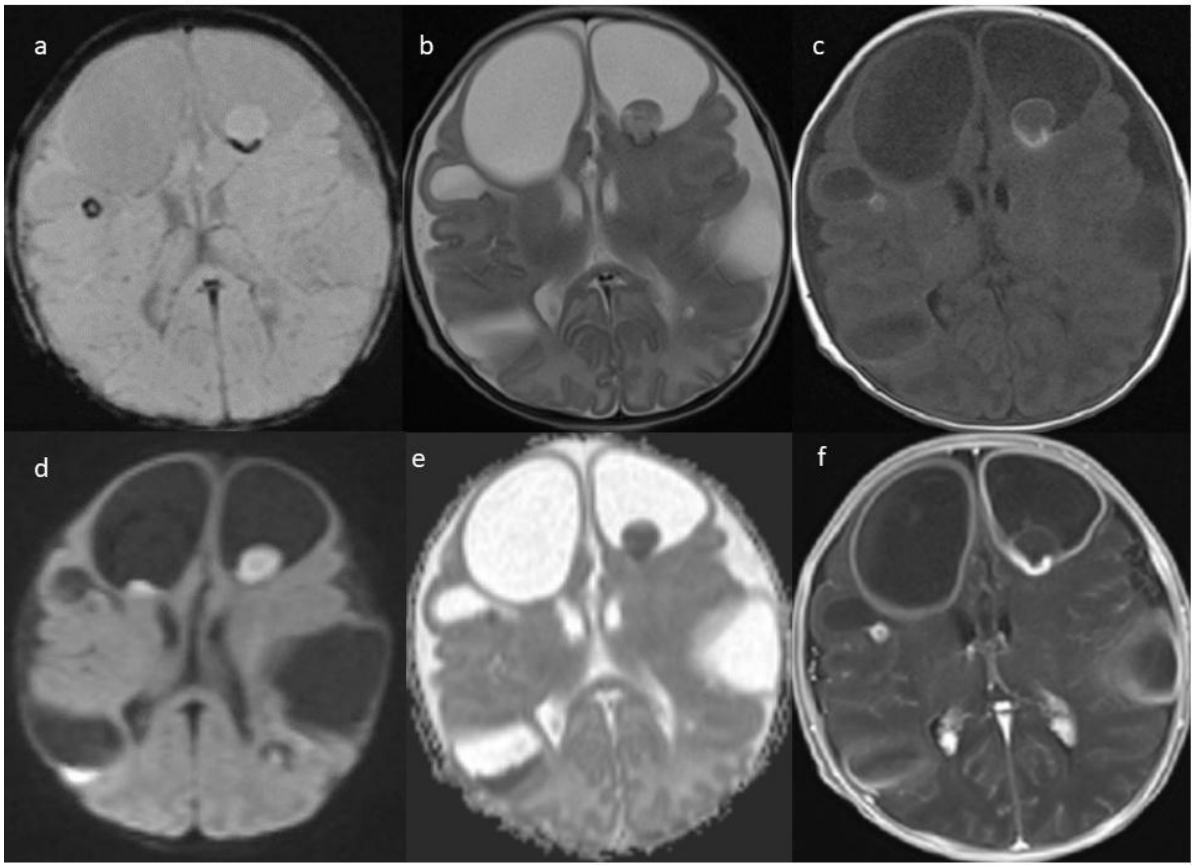

Fig. 2: Preoperative MRI appearance of brain abscesses. a. GRE/T2*WI showing hemorrhagic elements in the abscesses. b. FSE/T2WI, c. SE/T1WI and f. SE/T1WI post-contrast demonstrated the cystic nature of the abscesses filled mainly with fluid, with enhancing walls and containing perimural nodules. d. DWI and e. ADC map showed diffusion restriction limited to the nodules.

However, the infant remained stable until the 39th day of life when he developed significant frequent apneic episodes and desaturation again. Raised C- reactive protein (35 mg/I) was found in the Initial sepsis workup; and treatment with Tazocin and amikacin was started. Blood culture was negative again, and CSF analysis remained normal. However, urine culture was positive for Enterobacter cloacae, which was sensitive to Tazocin, but resistant to amikacin. Thereupon, amikacin was stopped and Tazocin continued, subsequently switched to meropenem after review of literature addressing Enterobacter infections.

Two weeks after the MRI scan, in view of lacking improvement on TFU it was decided to perform craniotomy for the biggest lesion in the left hemisphere and minimal invasive aspiration of other lesions after confirming pus coming out of the biggest one (**Fig. 3**).

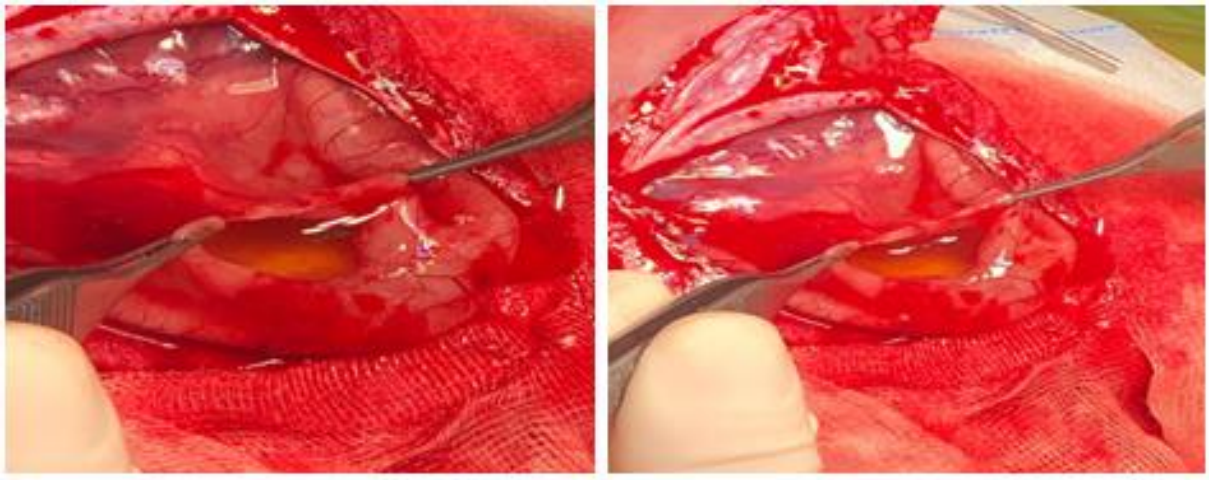

Fig. 3: Intraoperative pictures show pus inside the biggest lesion before craniotomy.

The microbiological examination and culture of the obtained material was sterile. Serial CT scanning and brain MRI were performed to monitor the efficacy of treatment (**Fig. 4 A-F**) and antibiotic therapy (meropenem and vancomycin) was continued for 6 weeks.

At the most recent pediatric neurology follow up at 3 months of age, the infant showed a significant improvement, and he accomplished all neurodevelopmental milestones expected of age.

3- DISCUSSION

Brain abscesses occur as complications of bacterial meningitis or bacteremia (1). The microbial agents that are commonly involved in the pathogenesis of neonatal brain abscesses are Gram-negative bacilli (1, 6). In recent years, Enterobacter cloacae has emerged as an important nosocomial pathogen in neonatal units (7). Lee et al. isolated E. cloacae as the leading microorganism in neonatal Gram-negative bacilli sepsis (8).These bacteria can cause fulminant late-onset sepsis, a condition associated with relatively high mortality and morbidity (9).

The source of infection in our case is unknown. Both vertical transmission from the mother and horizontal transmission as nosocomial infection have been described (10, 11). Vertical transmission is unlikely, as there is not any known infection risk factor in the maternal obstetrical history. Furthermore, the baby was delivered by C-section, and became symptomatic after 3

days of life. However, nosocomial infections occur later and are more likely to result in brain abscesses.

E. cloacae brain abscess following sepsis in a neonate is extremely rare. In most published cases, neonatal brain abscesses are caused by Citrobacter species, and more frequently associated with meningitis. Citrobacter species are well-known to cause meningitis and cerebral abscesses develop in 77% of cases (10).

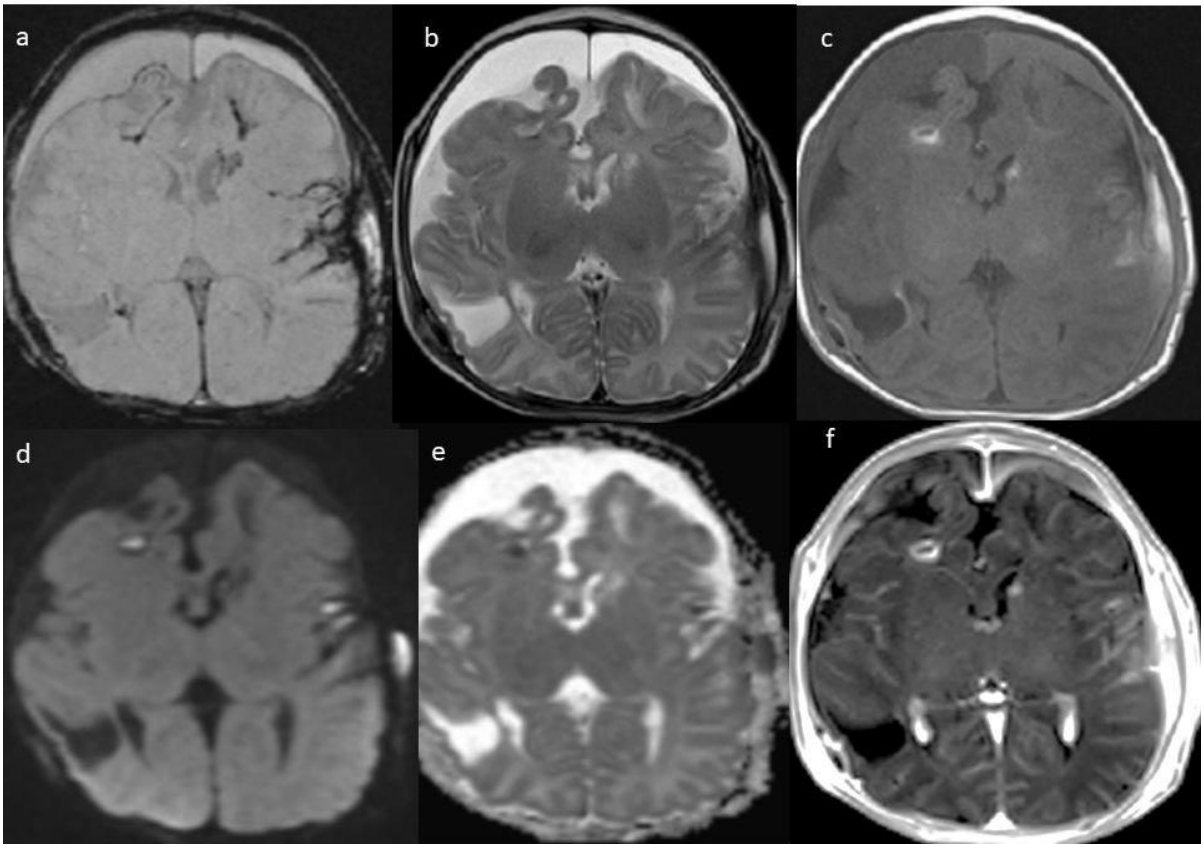

Fig. 4: Post-operative MRI (a. GRE/T2*WI, b. FSE/T2WI, c. SE/T1WI, d. DWI, e. ADC map, f. SE/T1WI post-contrast) in roughly corresponding sections demonstrated improvement after the surgical procedures.

In a case series of neonatal sepsis due to E. cloacae in very low birth weight infants, 55% of infants had apnea, 58% had desaturation and tachycardia as a presenting sign of sepsis, while the most common laboratory finding was thrombocytopenia, and raised C-reactive protein (9). The clinical signs and symptoms of brain abscesses are nonspecific. Infants who have brain abscess initially may exhibit no apparent neurologic symptoms other than increased irritability, and bulging fontanel (1). Neurologic deficits are less obvious in extremely preterm infants (12). The clinical presentation of a brain abscess depends mainly on the presence of raised intracranial pressure. In neonates the fontanels and the cranial sutures are still open and an intracranial mass lesion can grow without raising the intracranial pressure (13).

The virulence associated properties of this microorganism have not been fully explained. The brain most likely was infected by the hematogenous route during

the preceding episode of Enterobacter bacteremia at 4 days of life. The abscesses caused by hematogenous dissemination are more commonly multiple, multiloculated, and are frequently found in the distribution of the middle cerebral artery (14). Clinical observations and experimental data have shown that the frontoparietal region is the most favorable site of abscess formation after hematogenous dissemination (15). It is worth noting that the right to left shunt that normally may be present in the first days of life, might have facilitated the hematogenous dissemination of bacteria to the brain by bypassing the defense mechanisms of lung macrophages (16).

After the bulging anterior fontanelle was noted on the 34th day of life, TFU indicated the presence of brain abscesses. The typical MRI appearance confirmed the diagnosis. MRI provides very characteristic images of bacterial brain abscesses: a capsule that is hyperintense on T1-weighted images and hypointense on T2-weighted images and enhances after administration of contrast material. Importantly, a hyperintense signal of the contents of the abscess can be seen on diffusion-weighted imaging (DWI) with corresponding low values of the apparent diffusion coefficient (ADC) on ADC maps. This is due to restriction of water diffusion within the abscess, which was also observed in our patient (17). In the presented case we faced the unusual appearance of brain abscesses which were mostly cystic (with signal intensity (SI) of thick fluid, without diffusion restriction) and contained perimural nodules with SI typical of abscesses, reported above. We have not found similar descriptions in the literature; such an appearance was neither discussed in papers devoted to brain abscesses (18) nor to cystic tumors with mural nodules (19).

In our case, E. cloacae was isolated in the initial blood culture (day 4), and later was isolated in the urine culture (day 39) whereas CSF and aspiration material culture were sterile; so, antibiotics were given according to these results. Indeed, aspiration material culture can be sterile due to previous antibiotic therapy, as in our case in which the newborn had been exposed to 14 days of meropenem before operation.

The treatment of brain abscesses involves both medical and surgical modalities. The nature of the abscess, its anatomic location, the number of abscesses and their sizes and stages, will all influence the treatment strategy (20). Walled off abscesses larger than 3 cm diameter and smaller deep-seated white matter abscesses are unlikely to respond to medical treatment alone. Standard therapy for such lesions should be surgical evacuation followed by appropriate antibiotic administration (21).

In general, there are no precise guidelines for treatment of brain abscesses. Each case must be individualized and treated on its own merits. In our case, the brain abscesses were too large to be treated only with antibiotics. Therefore, burr holes placement and simple abscess drainage was the surgical therapy of choice. The ability of carbapenems to penetrate CSF and macrophage makes those drugs a logical option to treat Enterobacter infection. Meropenem appears to have a better safety profile and thus would be the preferred choice in neonates (22). Long-term neurodevelopment follow up and neuroimaging studies are indicated.

4- CONCLUSION

We have reported a case of premature infants with the rarely occurring multiple Entrobacter cloacae brain abscesses, arising as a complication of sepsis. Brain abscess in neonates usually presents with nonspecific symptoms and signs. Early radiologic recognition, preferably by contrast-enhanced MRI, prompt treatment, and optimal follow-up is important to

reduce the neurological morbidity and the risk of death.

5- FUNDING

None.

6- CONFLICTS OF INTEREST

None.

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