Case Report

Brain abscess following meningitis in a neonate: report of three cases

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Abstract

Background: Brain abscess is an infrequent complication of meningitis, including cases caused by Gram-negative enteric bacteria and Klebsiella in neonates. Brain abscess in neonates associated with high morbidity and mortality. Recently, incidence of the disease is increasing because of increased predisposing factors.

Patients: Three cases of brain abscess in neonates are reported, 2 of them were caused by Citrobacter meningitis while another case was caused by Klebsiella abscess following meningitis. All of the abscesses were enormous, and multiple abscesses were observed in 1 case. The abscesses were treated by aspiration and antibiotics. Shunt for hydrocephalus was necessary in all patients. No sources of infection were identified in three cases. The onset of infection was not clear in our cases. Finally, 1 patient could improvement while the other two patients were died. One extremely rare case of Klebsiella brain abscesses was reported.

Conclusion: All neonates with Citrobacter and Klebsiella meningitis should have neuroimaging studies performed due to the substantial risk of associated brain abscesses, even when suspicious signs are absent. Prompt diagnosis and treatment are essential to reduce the neurological morbidity and the risk of death.

Keywords: Brain abscess, Klebsiella, Citrobacter, Neonate, Pediatric neurosurgery.

Introduction

The first report of brain abscesses in neonates was published 100 years ago (1). Brain abscesses are uncommon in neonates, and poses a problem in pediatric neurosurgery because the associated morbidity and mortality have remained significant throughout the antibiotic and computed tomography (CT) era (2- 3).

The incidence of neonatal meningitis varies from 0.3 to 0.5 cases per 1000 live births (4-5). Most cases of neonatal meningitis are associated with neonatal sepsis (6). However, the vast majority of cases of meningitis caused by Gram-negative bacteria and do not result in brain abscess (7).

Klebsiella is a common cause of neonatal septicemia, but it is a very uncommon microbial agent to cause brain abscess. (8).

Infants and neonates with brain abscesses belong to a special group because the prevalence of the predisposing factors differs from that observed in adults and in the general pediatric population (9). The abscesses are often large and multiple (3, 10) and usually occur as complications of bacterial meningitis or bacteremia (2, 9).

Neonatal brain abscesses are often recognized late due to the insidious onset of symptoms. 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 lesioncan grow without raising the intracranial pressure (11).

The classic manifestation of the disease is a triad of seizures, signs of infection, intracranial hypertension and increased head circumference with bulging fontanels (2). The source of infection is unknown in the majority of cases (12-13). The treatment of brain abscesses involves both medical and surgical modalities (14).

In this report, we present the clinical features, treatment, and outcome of three neonates with brain abscesses complicating in adequately treated Citrobacter and Klebsiella meningitis.

Patients

In a period of 7 years, three patients with brain abscess admitted to our hospital (table 1). Brain abscesses were located in temporoparietal, multiple and right frontal (figure 1, 2 and 3) respectively. During the same period of time that these abscesses were encountered, 85 neonate in the same age group were admitted to the hospital for sick children with a purulent meningitis not associated with brain abscess.

Perinatal history & Clinical presentation:

No abnormality of pregnancy was recorded. The gestational period was normal in patients (cases No. 2 and 3), however preterm in case No.1 (33 weeks), delivered by caesarean section. No infant (cases No. 2

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and 3) needed resuscitation or mechanical ventilation at birth. The baby (case No.1) was transferred to the neonatal ICU and was managed conservatively. The examination of the baby was described as normal at birth in every case. No maternal infection was observed in three cases.

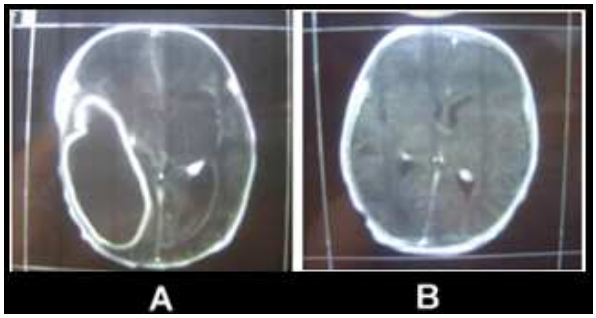

Fig.1 A. T1-W MRI showed a large space-occupying lesion (abscess) in Temporoparietal area of brain; B. shows, 3 months following completion of treatment.

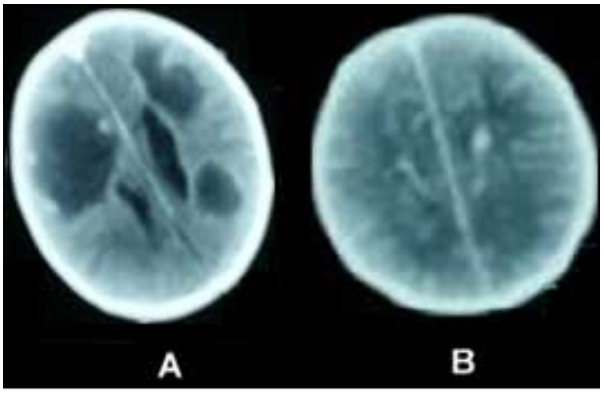

Fig.2 A. Computerized tomography scans in neonate showing multiple brain abscesses; B. Treatment of brain abscess 1 month after admission.

The onset of the symptoms occurred during the 1st month of life in two cases (Day 26 and Day 28), and during the 1st week in 1 case. The initial manifestation illness were 'high-grade fever, vomiting, poor feeding, lethargy', 'fever, seizures, poor feeding,
Vomiting' and "high-grade fever, seizures, poor feeding, neck stiffness, alteration of consciousness" in patients (cases No. 1-3), respectively.
In the neonate (cases No. 2), rapid enlargement of the head took place in the third week of life; this was reported to be about two inches in one week.

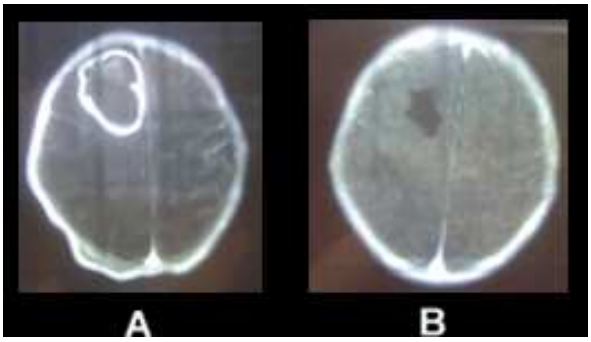

Fig.3 A. T1-W MRI showed a large space-occupying lesion (Abscess) in Right frontal area of brain; B. shows, 2 months following completion of treatment.

Diagnosis &Management &Outcome:

A T1-W magnetic resonance imaging (MRI) (cases No. 1 and 3), computed tomography scan (CTS) with and without intravenous contrast (cases No. 2) and cranial ultrasonography were used to confirm the diagnosis. Imaging study showed brain abscess. The abscesses were enormous in size in all cases and caused significant enlargement of the head in the three patients who reached the neurosurgical service.
Two patients (cases No. 2 and 3) of meningitis were caused by Citrobacter, and klebsialla caused one (case No. 1), followed by brain abscess.
Erythrocyte sedimentation rate (ESR) was elevated in all patients. The causative organism was identified in the cerebrospinal fluid (CSF) in all of patients. Blood culture was positive in 1 patient (case No.3). Cultures obtained from the abscess showed Klebsiella and Citrobacter as the causative agents in (cases No. 1) and (cases No. 2 and 3), respectively.
Once the diagnosis is confirmed, additional studies with the goal of identifying the predisposing factors and the source of infection will be guided by the patient's history and physical examination. The widely open sutures in the newborn allow for progressive enlargement of the head as the abscess enlarges in the affected hemisphere due to the apparent inability of infantile white matter to ward off infection.
First-line intravenous antibiotics were started for treatment of meningitis (cases No. 1) duration of 20 Approximately one week after discharge, the neonate was admitted in neonate ICU on the 26th day of delivery in hospital with brain abscess.
The patients (cases No. 2 and 3) admitted on the5th, 28th day of delivery in the hospital with primary diagnosis of meningitis. They received intravenous antibiotic for 1 and 2 week respectively, and were then identified brain abscess following meningitis.

Table 1. Clinical characteristics of patients with Brain abscess

	Case		
	1	2	3
Age and admitted(Day) /Sex	28/F	5/M	26/F
Signs, Symp	High-grade fever, vomiting, poor feeding, lethargy	Fever, seizures, poor feeding, vomiting	Fever, seizures, poor feeding, vomiting, neck stiffness, alteration of consciousness,
Location	Temporoparietal	Multiple	Right frontal
Predisposing factor	Meningitis	Meningitis	Meningitis
Microbiology(Abscess culture)	Klebsiella	Citrobacter	Citrobacter
Management	Antibiotic therapy + drainage of Abscess +Irrigation+ EVD+ ventriculo-peritoneal Shunt	Antibiotic therapy +drainage of Abscess + EVD + ventriculo-peritoneal Shunt	Antibiotic therapy +drainage of Abscess + Irrigation + ventriculo-peritoneal Shunt
Antibiotic therapy/duration	40day	65day	48day
Followup(month)	4	5	26
Birth weight(g)	1450	3400	3500
***Birth HC(cm)**	32	33	35
CSF Analysis(admitted day)			
WBCs(cells/µL)	720	2400	200
Neutrophils	92%	71%	90%
RBCs(cells/µL)	3	30	10
Protein (mg/dL)	210	360	420
Glucose (mg/dL)	32	< 20	59
blood culture(admitted day)	Negative	Negative	Citrobacter
Apgar score(1, 5, 10 minute after birth)	3/6/7	6/8/9	5/8/9
Outcome	Death	Death	well, hydrocephalus

*Head circumference at time of birth

Abscesses were treated by multiple irrigation and aspiration (I&A) and optimal antibiotics for 40, 60 and 48 day for the patients (cases No. 1, 2 and 3) respectively.

All of patients used antibiotic therapy based on original and published data. The antibiotic used was changed with the date of treatment

Hydrocephalus occurred in all patients. All infants with hydrocephalus had shunts placed when the CSF and the abscess were sterilized. These shunts subsequently blocked and were revised. On occasion, temporary external ventricular drainage was used until the CSF became sterile. Postoperatively, cases were followed for 4, 5 and 26 months respectively. We assessed the outcomes using previous laboratory tests and imaging studies. in none of our cases could a definite portal of entry for the infection be ascertained.

Despite antibiotic therapy two infants died, from a shunt complication (case No.1), and from seizures and cardiopulmonary arrest (case No.2) at 4 and 5 months of age, respectively. The patient (cases No.3) was discharged from the hospital 2 months later, well and hydrocephalus without neurological deficit.

Discussion

We have presented three cases of brain abscess in neonates after menengitis caused by Citrobacter and Klebsiella.

Although Brain abscesses are uncommon complications of bacterial meningitis in neonates**,** but its high mortality and morbidity necessitates finding appropriate diagnostic and management methods (9-15). Brain abscesses occur as complications of bacterial meningitis or bacteremia (9-15). The microbial agents that are commonly involved in the pathogenesis of neonatal brain abscesses are gram-negative bacilli (9-15). Some microorganisms, such as Citrobacter, is characterized by unusual propensity for causing brain abscesses, whereas others, such as Klebsiela, rarely are implicated in the pathogenesis of this infection during the first months of life (8, 9-15).

To our knowledge, only a few cases of Klebsiela brain abscesses in neonates have been reported previously in the English literature (8, 16-20). Basu S et al. (8) reported one case of brain abscess after sepsis caused by Klebsiela pneumonia. Theophilo et al. (16) reported one case of Klebsiella abscess following meningitis in a term neonate who had under goner resuscitative intervention at birth.

Pragya P et al. (19) reported two premature infants who developed multiple brain abscesses following Klebsiella pneumonia infection. Qureshi UA et al. (18) reported one case of Klebsiella brain abscess in a term neonate and Anca IA et al. (20) reported two cases of brain abscesses Klebsiella in neonates, diagnosed by transfontanellar (TF) ultrasound and cranial MRI. In one of the largest series of 30 neonates with brain abscess in a tertiary center, no case was attributed to Klebsiella (15).

Citrobacter is a genus of gram-negative bacilli, which belongs to family Enterobacteriaceae (21). Meningitis caused by Citrobacter diversus has been reported sporadically and in small outbreaks in the United States and Europe, However, the vast majority of cases of meningitis caused by Gram-negative bacteria do not result in brain abscess(7). Citrobacter accounts for up to 4% of neonatal meningitis cases (21).

Renier D et al. (15) reported 30 brain abscesses in neonates. They were treated by aspiration and antibiotics in 25 cases, and by antibiotics alone in five.

Allen M et al. (22) reported 13 neonate brain abscesses following meningitis due to Citrobacter, with mortality approaching 50 percent and neurologic residua in 40 percent.

Overall, approximately 30% of neonates with Citrobacter meningitis die and 50% sustain some damage to the CNS (23).

Despite antibiotic therapy case No.1 died, from a shunt complication. This may be occurred due to shunt failure. It is also possible for the patient (case No.2).

The source of infection is unknown in the majority of cases, but in some cases it is vertical from mother to the baby (12-13). In our cases the source of infection could not be determined.

Clinical manifestations: The clinical signs and symptoms of brain abscesses are nonspecific. In the neonate, a brain abscess is a potential cause of irritability, a bulging fontanel, and a rapid increase in head circumference. Focal neurological deficits related to the site of the abscess may be present, depending on the size of the lesion, presence of surrounding edema, virulence of the infectious microorganisms, and signs of infection (15, 24, and 25). The most common presentation is vomiting due to raised intracranial pressure. Seizures and poor feeding have been reported in these cases (15, 24, 25), which was the case in our patients.

Diagnosis& Management& Treatment: Brain abscesses in neonate should be managed by a multidisciplinary team that includes neurosurgeons and infectious disease practitioners (24).

Improved imaging techniques combined with improved culturing techniques and advances in surgical and medical management of brain abscesses have contributed to the reduction in the mortality rate, which has been seen over the last century (26). However, this condition remains that brain abscesses in neonates were formerly misdiagnosed, a fact that could explain, the high mortality and morbidity rates in the published series of neonatal meningitis(4).

Evaluation of the CSF is important in determining the etiology and then in deciding the most appropriate therapy. Typical CSF findings in acute bacterial meningitis include: raised WBC count, reduced CSF glucose and raised CSF protein (27).

Since abscesses may grow very large in neonates before manifesting clinical signs, any patients with Citrobacter and Klebsiella meningitis should have CT scans, MRI(20) or Ultrasound examination(18, 20) of the head performed when meningitis is diagnosed and frequently thereafter until abscess is confirmed or excluded(28).

Ultrasound examination proved to be an excellent tool not only for the initial diagnosis but also for the follow-up brain abscess in neonate (18, 20). On account of its high resolution, MRI scans are extremely useful, but compared to the ease of use and the excellent accuracy of TF ultrasound, MRI might be a second imagistic option (20), as mentioned above, are considered for our patients.

Complications and the need for serial neuroimaging to detect cerebral abscesses which can even develop early or late, sometimes even after treatment (29). Serial imaging studies are conducted to assess the effectiveness of antibiotic therapy (24). It is not yet clear whether serial neuroimaging in first week could have been beneficial to pick up brain abscesses early in our cases.

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 size and stage, as well as the age and initial neurological status of the patient all influence the treatment strategy (14). Surgical and medical approaches each have advantages and disadvantages. Medical therapy saves the patient from the stress and complications of the surgery, especially in neonate, who present with significant surgery related neurological deficits and hemorrhage (14, 26). On the other hand, surgical therapy provides samples for accurate diagnosis, reduces the mass of the abscess, improves the efficacy of the drug used for treatment, and in some conditions allows intrathecal, intraventricular, or intracavitary administration of the antibiotic agent (30).

Typically, abscesses > 2.5 cm require surgical intervention (24). The duration of the antibiotics course is usually 6–8 weeks and longer for immunocompromised patients (24). If possible, antibiotics should be held until after surgery to reduce the possibility of a sterile culture obtained intra operatively (24), as mentioned above, are considered for our patients.

Complications are severe in preterm neonates with brain abscess. Treatment of brain abscess includes prolonged antibiotic therapy and neurosurgical drainage. Multiple aspirations are necessary for cases that do not respond to single aspiration (31). Abscess recurrence has been found to be more common after aspiration than surgical extirpation (24).

Due to the rare occurrence and serious outcome of brain abscess in neonate, it is both impractical and ethically difficult to conduct prospective, randomized clinical trials to determine.

Brain abscess following meningitis in a neonate caused by Klebsiella is extremely rare, with only a few cases reported from the India (8, 17-19), Brazil (16)and Romania(20).

Bacterial brain abscesses in neonate remain a serious central nervous system problem despite advances in neurosurgical, neuroimaging, and microbiological techniques and the availability of new antibiotics. The successful treatment of brain abscesses requires surgery, appropriate antibiotic therapy, and eradication of the primary source; nevertheless many controversial issues on the management of this serious infection remain unresolved.

Neurologic function and imaging findings should be closely monitored while the therapy is commenced, particularly in patients who are treated medically.

When evaluated neonates bacterial brain abscesses, follow with meningitis, the speed with which the operation is made, rather than the type of operation, is the factor that most affects the final condition of these patients.

*In conclusion***,** Prompt diagnosis and treatment are important factors to gain best results. The morbidity rate still remains high. The problem of resulting hydrocephalus remains, however, and account for the death of two of our patients.

All neonates with Citrobacter and Klebsiella meningitis should have neuroimaging studies performed due to the substantial risk of associated brain abscesses.

It is important to observe the patient carefully by TF ultrasound, CT or MR imaging until the abscess has completely resolved.

There is a strong need for further investigations on the role of serial neuroimaging and the use of new antibiotics in Klebsiella brain abscess following neonatal meningitis.

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