

Intra Ventricular Colistin in Neonatal Brain Abscess Management: A Case of Multiple Brain Abscesses

Farhad Abolhasan Choobdar¹, Zahra Soltani^{2,*}, Alireza Nateghian³, Vahid Heidari⁴

¹Department of Neonatal Intensive Care, Ali Asghar Children's Hospital, Iran University of Medical Sciences, Tehran, Iran

²Department of Paediatrics, Fatemeh Zahra Hospital, Iran University of Medical Sciences, Robat Karim, Iran

³Department of Paediatric Infectious Disease, Ali Asghar Children Hospital, Iran University of Medical Sciences, Tehran, Iran

⁴Department of Neurosurgery, Firoozgar Hospital, Iran University of Medical Sciences, Tehran, Iran

Email address:

Choobdar.f@iums.ac.ir (F. A. Choobdar), Drsoltani_zahra@yahoo.com (Z. Soltani), Nateghian.ar@iums.ac.ir (A. Nateghian), V_heidari_md@yahoo.com (V. Heidari)

*Corresponding author

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Abstract: Neonatal Brain abscess is a rare severe neonatal infection requiring careful medical and neurosurgical intervention strategies to reduce morbidity and mortality rates. Gram-negative bacterial agents are the most common pathogens involved in brain abscesses of neonates. The use of wide spectrum antibiotics in combination with neurosurgical drainage of abscesses larger than 2.5 cm is the mainstay of treatment. Colistin is a polymyxin antibiotic used to treat bacterial infections caused by susceptible gram-negative bacteria but with a limited penetration in blood brain barrier. However, there is limited data on using intraventricular Colistin in neonatal intracranial infections. A 12-day-old male neonate with multiple brain abscesses in frontal and parietal lobes is presented. The abscesses were successfully managed with a combination of intravenous antimicrobial agents, intraventricular Colistin and concurrent administration of Interferon- γ . Subsequently, he developed ventriculomegaly which was successfully managed by endoscopic third ventriculostomy. He had an acceptable neurologic outcome. Due to reduced penetration of colistin in blood brain barrier, use of intraventricular Colistin in combination with its intravenous form can be beneficial in management of neonatal brain abscesses. Concurrent administration of Interferon- γ may improve the treatment process and outcome given that reduced secretion of this agent by neonatal T lymphocytes may contribute to a partial immunodeficiency state at this period of life.

Keywords: Brain Abscess, Cerebral Ventriculomegaly, Colistin, Interferon Gamma

1. Introduction

Brain abscess is very rare in neonatal period. It evolves from a localized area of infectious cerebritis resulting from seeding of potent pathogens in cerebral parenchyma [1]. Due to high morbidity and mortality rates, brain abscess still poses a problem in neonatology and pediatric neurosurgery [2].

Most common pathogens involved in brain abscesses are gram negative organisms such as *Proteus*, *Citrobacter*, *Pseudomonas* and *Serratia* species. Increased susceptibility to this group of pathogens in neonates is due to lack of

sufficient immunoglobulin M and complements in this period of life and the propensity of such pathogens in causing necrotizing vasculitis [3, 4].

Brain ultrasound and CT scan are appropriate tools for the diagnosis of neonatal brain abscess and also for follow up after beginning the treatment [5, 6]. MR imaging has a high sensitivity and specificity in detecting brain abscesses but is less utilized due to enough diagnostic information derived from ultrasound and CT Scan studies [2].

Most brain abscesses are managed both medical and surgical. The use of wide spectrum antibiotics in combination with neurosurgical drainage of abscesses larger than 2.5 cm

is the mainstay of treatment [7]. Multi Drug Resistance - Gram Negative bacterial neonatal intracranial infections are a great concern of increased prevalence in some middle and low-income countries which leads to greater morbidity and mortality rates. Colistin is a polymyxin antibiotic used to treat bacterial infections caused by susceptible gram-negative bacteria but has a limited penetration into blood brain barrier and there is limited data on intraventricular administration of Colistin in neonatal intracranial infections, thus, more clinical research is needed to obtain more accurate results [8]. We present a case of neonatal multiple brain abscesses and given a few case report satisfactory results on intracranial Colistin administration in cases similar to ours, we prescribed intracranial Colistin therapy along with intravenous antibiotics in the hope of achieving better therapeutic results.

A communication of brain abscess with the ventricular space has been reported to be a poor prognostic factor due to subsequent hydrocephalus formation which results in higher morbidity rates. Serial imaging studies is essential to diagnose further complications including recurrence of abscess and hydrocephalous formation [9, 10].

2. Case Report

A 12d-old male neonate was presented to Fatemeh-Zahra hospital of Robat Karim city with fever, poor feeding and irritability. He was born full-term with a birth weight of 3.9 kg and a head circumference of 34 cm without birth complications and was discharged home after 24 hours of hospital stay.

At presentation to the hospital, he was ill and irritable. He had an axillary temperature of 39 C. His vital signs were otherwise stable and had acceptable Moro and sucking reflexes. He had no bulge fontanel and the rest of his physical examination was normal. He was performed a full sepsis workup and was started on wide spectrum antibiotics (Cefotaxime and Vancomycin).

His complete blood count showed a WBC count of $12700/\text{mm}^3$ with 27% polymorphs and 66% lymphocytes. C-reactive protein was measured 36 mg/L, and the CSF analysis showed a Xanthochrome appearance with a leukocyte count of $1920/\text{mm}^3$ (80% Polymorphonuclear leukocytes and 30% lymphocytes), $100/\text{mm}^3$ RBCs a glucose concentration less than 1 mg/dl and a protein concentration of 114 mg/dl. Due to presence of meningitis on laboratory results the patient was referred to Ali Asghar Children's Tertiary Care center's neonatal intensive care unit in Tehran city for further evaluation and treatment.

He was started on wide spectrum antibacterial agents in combination with Acyclovir and CSF analysis was repeated after 48 hours which demonstrated a rise in total CSF leukocyte count ($4320/\text{mm}^3$). An emergency brain ultrasound was performed which displayed three echogenic and heterogenic mass like regions two of which located in bilateral frontal lobes and one in parietal lobe periventricular white matter with right frontal lobe lesion communicating with the ventricular space and evidence of ventriculitis was

seen in both lateral ventricles. Subsequently an emergency Brain CT scan was performed which showed four cavitory lesions containing hypodense material in favor of multiple brain abscesses (figure 1).

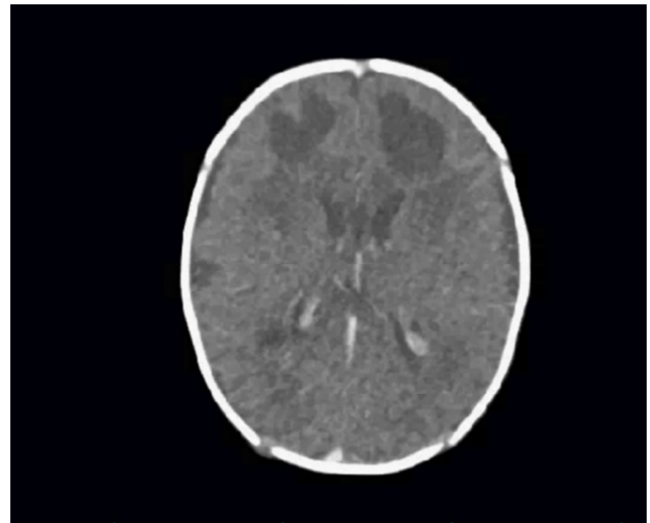


Figure 1. Multiple Brain Abscesses. Four cavitory lesions containing hypodense material without mass effect in white matter of bilateral inferior frontal lobes (measuring 30*30 in Right side and 34*30 mm in left side), Right superior frontal lobe (13.5*13.5 mm) and high parietal lobe (40*22 mm) suggesting multiple brain abscesses.

An emergency neurosurgery consultation was conducted and the neurosurgeon inserted an Extra Ventricular Device (EVD) with a 16-gauge angiocath in the right frontal lobe abscess cavity and aspirated 10 milliliters of pus-like fluid. According to consultation with Pediatric Infectious Disease Specialist, the patient was started on daily intraventricular Colistin through EVD and his Intravenous antibiotics were replaced by Colistin, Rifampin and Ciprofloxacin. He also received interferon gamma (IFN- γ) injections every other day for a period of two weeks.

TORCH study and polymerase chain reaction (PCR) for Herpes Simplex virus, Cytomegalovirus, Enteroviruses and Coronavirus disease 2019 were negative. Repeated blood and CSF cultures were sterile. An immunologic study including a complete Immunoglobulin analysis, flowcytometry and dihydrorhodamine (DHR) test was conducted which showed no evidence of any underlying primary immunodeficiency disorder.

Our patient received 21 days of intraventricular Colistin and 28 days of intravenous antibiotics and was discharged home with complete remission of the abscesses, an acceptable physical condition and a head circumference of 40 cm.

The patient's health condition was followed via serial outpatient visits which he was doing well. By two and half months of age he could hold up his head and smile at people and bring his hands to his mouth. But a week later his head circumference started to rise rapidly and he developed sun set eyes. A Brain CT scan study showed marked bilateral frontal lobe atrophy and porencephalic cysts joining in the frontal horns of lateral ventricles and one porencephalic cyst in the

region near right occipital horn. Thereupon, he was admitted to the hospital and undergone an endoscopic third ventriculostomy neurosurgery procedure to reduce the intra cranial pressure (ICP). The procedure was successful and on serial follow-ups after discharge there were no signs of recurrence of raised ICP and no need to prepare a Ventriculo-Peritoneal Shunt.

3. Conclusion

Neonatal brain abscess is a rare condition with poor neurodevelopmental outcomes. Our patient had developed multiple brain abscesses which were managed successfully via thorough medical and neurosurgical treatments. Multi Drug Resistance – Gram Negative bacterial neonatal infections including intracranial infections is a great concern of increased prevalence in some middle and low-income countries which leads to greater morbidity and mortality rates [8]. Thus, despite negative blood and CSF culture results which might be due to technical issues, our patient was started on Intravenous Colistin in combination with Rifampin and Ciprofloxacin.

Due to limited penetration of Colistin into the blood brain barrier, simultaneous administration of Colistin via an EVD may enhance survival and improve neurodevelopmental outcomes [8, 11]. However, there is limited data on using intraventricular Colistin in neonatal intracranial infections. Alaoui *et al.* successfully treated a 4-day-old neonate with meningitis and ventriculitis by the means of intraventricular Colistin administration and Ziaka *et al.* reported that combination therapy with intravenous and intraventricular Colistin provides a higher concentration of drug in the CSF [12, 13]. On the same day of diagnosing the brain abscesses, and in combination with intravenous antibiotics, our patient was started on a daily dose of 0.2 mg/kg Colistin through EVD which was continued for a duration of 3 weeks.

Studies show INF- γ secretion by T-Lymphocytes results in adequate phagocytosing response in facing some viral, bacterial and fungal infections. Inadequate INF- γ production by neonatal T-Cells may contribute to decreased response of the immune system to specific pathogens thus increases morbidity and mortality in severe neonatal infections. Administration of INF- γ in severe infections of neonates may result in a better infection control [14, 15]. For this reason, our patient was administered a two-week period of INF- γ injections beginning soon after the diagnosis of brain abscesses.

Despite successful management and treatment of the abscesses a less satisfactory neurologic outcome is expected in our patient due to communication of abscesses with the ventricular space and the subsequent massive hydrocephalus and prominent frontal lobe atrophy. Serial follow-ups in terms of precise neurodevelopmental tracking are needed to

provide an appropriate support plan in order to supply beneficial rehabilitation programs.

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