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Multiple fungal brain abscesses in a neonate: successful treatment with Liposomal Amphotericin B

Cover Page Footnote

Nil

Multiple fungal brain abscesses in a neonate: successful treatment with Liposomal Amphotericin B

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Abstract

Invasive fungal infections are common among infants hospitalized in the Neonatal Intensive Care Unit (NICU). Central Nervous System (CNS) involvement occurs in two third of the disseminated fungal sepsis. Fungal cerebral abscess is one of the severe complications of disseminated fungal sepsis. We report a case of multiple fungal brain abscesses in a term neonate, which was successfully treated with Liposomal Amphotericin B.

Key words: Disseminated candidiasis, brain abscess, sepsis, neonate, Liposomal Amphotericin B.

INTRODUCTION

Neonates who are admitted to the NICU contract invasive fungal infections and these occur in approximately 6-7 per cent of the infants (Hostetter, 2005). There is an inverse correlation of fungal infections with birth weight. If birth weight of an infant is less, greater is the risk of invasive fungal infections (Hostetter, 2005) also states that the frequency of CNS involvement in the setting of disseminated fungal disease is approximately fifty per cent. Abscess formation in the brain is a severe complication of systemic candidiasis.

CASE REPORT

A seven-day-old male neonate was referred to our centre with history of lethargy and seizures. Baby was born to a primigravida mother by Lower Segment Caesarean Section (LSCS), an indication for Pregnancy Induced Hypertension (PIH) at term gestation with history of premature rupture of membrane for nine hours. Baby cried immediately after birth, birth weight was 2.5 kg and the baby was sucking well at breast. However, the baby developed fever on day three with signs/symptoms of lethargy and on day four developed two episodes of tonic seizures. During admission, baby was lethargic, febrile (104°F), Heart Rate (HR) was 156/min, Respiratory Rate (RR) was 66/min, saturation was 90% in room air with sclerema of limbs. CNS

examination revealed hypotonia with elicitable reflexes; pupils were reactive with normal anterior fontanel. Per abdomen-liver was four cm palpable below the right costal margin in the midclavicular line, firm consistency with span of six cm. Other systems were within normal limits. As the baby was diagnosed having septicaemia with meningitis, antibiotics and other supportive treatment were given.

Investigation revealed Total Count (TC)-29,800/mm³, Packed Cell Volume (PCV)-44.2%, Platelet count-25,000/mm³, peripheral smear showing neutrophil predominance (81%), B and cell count-14%, cytoplasmic vacuolation and toxic granules were present. C-reactive protein (CRP) was 12mg/l. Urine routine examination showed presence of yeast cells whereas urine culture was normal. Growth of *Candida* species were seen in blood culture. Neurosonogram revealed presence of cystic lesion with perilesional edema in left putamen and left superior frontal gyrus. Magnetic Resonance Imaging (MRI) scan of brain showed multiple nodular and ring enhancing lesions of varying sizes, involving both the cerebral hemispheres, cerebellar hemispheres, left lentiform nucleus, right sylvian fissure suggestive of multifocal abscesses (Fig. 1). Cerebro Spinal Fluid (CSF) analysis showed presence of lymphocytes. CSF culture was normal.

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Ultrasonography (USG) of kidney was normal, ophthalmological examination was also normal.

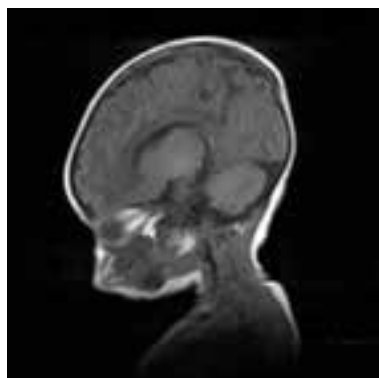


Fig. 1: MRI scan of brain showing multiple abscesses

As the growth of *Candida* species was seen in the blood culture and MRI scan of brain suggestive of multiple abscesses, a diagnosis of fungal cerebral abscess was considered and baby was started on Intravenous (IV) Liposomal Amphotericin B. Liposomal Amphotericin B (3mg/kg/day) was given for six weeks after which the treatment was changed to oral fluconazole for two weeks. Repeat MRI scan of brain showed decrease in size of lesions and perilesional edema (Fig. 2). The baby was attaining milestones normally and neurological examination was normal during follow up.

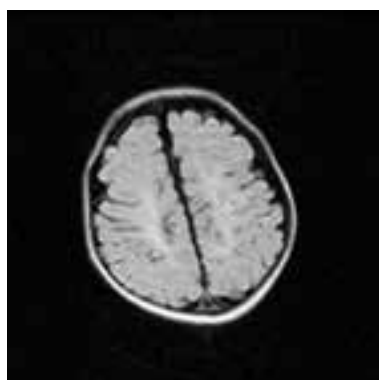


Fig. 2: MRI brain showing resolution of abscess following treatment.

DISCUSSION

Factors which contribute to neonates being susceptible to fungal infections after being hospitalized to NICU include birth weight less than 1500 grams, Apgar score of less than five at five minutes, percutaneous catheters, prolonged use of broad spectrum antibiotics, indwelling central venous catheters,

abdominal surgery, total parental nutrition, parental lipids, endotracheal intubation and duration of stay in NICU for more than seven days. These factors contribute to developing *Candida* infections, leading to late onset sepsis in NICU; the infections being the third most common cause (Hostetter, 2005).

The skin and the gastrointestinal tract are the most common areas of fungal colonization. Colonization with ubiquitous fungal sepsis occurs at least in 25 per cent of very low birth weight neonates. Approximately seven per cent of neonates having birth weight of less than 1500 grams develop invasive *Candida* infections (Hostetter, 2005). Most neonates with more than 2500 grams get blood borne *Candida* infections. This occurs along with congenital anomalies, and congenital or acquired immunodeficiency (Cevit et al., 1999). Newborns in NICU may also be having presence of candiduria. In addition, renal candidiasis may also be present in these newborns in many cases (Hostetter, 2005). One reliable indicator of *Candida* infection is the isolation of *Candida* species from a catheterized specimen or even through suprapubic aspiration. Further, blood culture as well as renal imaging should also be contemplated.

Disseminated candidiasis may affect kidneys as well as brain. Neonates with systemic fungal infections may have severe complication like abscess formation in the brain (Marcinokowski et al., 2001). CNS is involved in two third of cases of systemic candidiasis in premature infants. In patient with candidal endocarditis, 80 per cent also have CNS candidiasis (Singh et al., 2006). Neuropathologic lesions in cerebral candidiasis include meningitis, ependymitis, micro abscesses, macro abscesses produced by noncaseating granulomata, thrombosis, secondary infarction, vasculitis from invasion of vessel wall, mycotic aneurysm, fungal ball, haemorrhage or haemorrhagic necrosis, demyelization and transverse myelitis (Singh et al., 2006). Mortality rates approach 30 per cent for disseminated candidiasis (Hostetter, 2005).

Evaluations in disseminated candidiasis include ophthalmologic examination, echocardiography, USG of abdomen and neurosonogram. Lumbar

puncture is advised to evaluate disseminated candidiasis. CSF analysis was normal in our case. A study done by Fernandez et al., (2006) revealed that in fungal meningitis, CSF analysis was varied whereas pleocytosis was inconsistent and hypoglycorrhachia was common. In 74 per cent of cases, *Candida* species could be isolated.

Conventional antifungal agents used in the treatment of disseminated fungal infection often provide unsatisfactory results and have high incidence of severe adverse effects. A study done by Scarcella et al., (1998) showed high efficacy of liposomal Amphotericin B in the treatment of disseminated fungal sepsis without any side effects. We administered Liposomal Amphotericin B, which is an alternative to conventional Amphotericin B. Cerebral abscesses were reduced in size and perilesional edema was also resolved after four weeks of treatment. Blood counts, liver enzymes, electrolytes and renal parameters were monitored regularly during treatment, which were within normal limits.

Invasive fungal infections are common in neonates in NICU, especially in premature babies. In case of sepsis, not responding to common antibiotics, fungal septicaemia may be considered, evaluated and appropriate antifungal treatment should be initiated at the earliest.

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