Multiple large brain abscesses in a newborn that may have resulted from intrauterine infection

İstemi Han Çelik, Gamze Demirel, Ömer Erdeve, Nurdan Uraş, Uğur Dilmen
Neonatal Intensive Care Unit, Division of Neonatology, Zekai Tahir Barak Maternity Training Hospital


Brain abscess is a focal, intracerebral infection that begins as a localized area of cerebritis and develops into a collection of pus surrounded by a well-vascularized capsule. Here, we report a case with multiple, large brain abscesses diagnosed coincidentally on postnatal day 11. This case is noteworthy because the organized abscesses were present as early as day 11 with no significant neurological signs or symptoms.

Brain abscess in newborns is a very rare disease that may not exhibit the expected neurological signs and symptoms. Depending on the radiological organization, an abscess in a neonate in the first weeks may be the result of an intrauterine infection.

Key words: brain abscess, intrauterine infection, newborn.

Brain abscess is a rare complication of neonatal meningitis that occurs in 1–4% of all cases. It is a focal, intracerebral infection that begins as a localized area of cerebritis and develops into a collection of pus surrounded by a well-vascularized capsule. Early capsulation is seen in 10–13 days. Surgical drainage may be used to treat a brain abscess, but it has become less common. Early diagnosis using radiological modalities such as ultrasonography (USG), computed tomography (CT), magnetic resonance imaging (MRI), and microbiological techniques together with more effective antibiotics have improved treatment. However, the mortality and morbidity rates for neonatal brain abscess remain high, especially following ventricular perforation. An immature immune system, inability to isolate the infection and susceptibility to infection may contribute to the high mortality and morbidity rates in neonates.

The clinical signs of a brain abscess are generally non-specific, and the diagnosis is often coincidental. A microbiological agent cannot be identified in all cases; a negative culture is reported in up to 30% of the cases. Early diagnosis and treatment of brain abscess are essential because of the related high mortality and morbidity.

Here, we report a case with multiple, large brain abscesses diagnosed coincidentally on postnatal day 11. This case is noteworthy because the organized abscesses were present as early as day 11 with no significant neurological signs or symptoms.

Case Report
The subject was a female born at 37 weeks gestation. Her birth weight and head circumference were 2240 g (10-25 percentile) and 32 cm (25-50 percentile), respectively. She was delivered by cesarean section because Doppler USG detected no end-diastolic flow. Her mother had no fever, antibiotic use or infectious disease in the course of pregnancy, and she was admitted to the hospital one day before birth and followed for three days after birth without any complication, including no septic birth. Our patient was firstly followed with her mother in the obstetrics unit. Physical examination was performed after birth and the only pathologic finding was a II/VI degree heart murmur. The neurological examination
was normal. Echocardiography performed on postnatal day 2 revealed patent ductus arteriosus (PDA) and patent foramen ovale (PFO). No invasive procedure was performed on the patient during the follow-up in the obstetrics unit. On the third day, the patient’s temperature was 38°C, and she had abdominal distension and sensibility to pain. She was admitted to the neonatal intensive care unit with suspected early-onset neonatal sepsis. The sepsis screen showed increased interleukin-6 (IL-6; 507 pg/ml, N: 0-20 pg/ml) and C-reactive protein (CRP; 48.97 mg/dl, N: 0-5 mg/dl) levels, and an abdominal X-ray revealed bowel edema. Sepsis and necrotizing enterocolitis were suspected, and penicillin G and netilmicin therapy was started because of antimicrobial coverage of these antibiotics in early-onset sepsis. Feeding was stopped until day 8. The blood and urine cultures were negative. On day 8, IL-6 was 10 pg/ml and CRP did not decrease (45 mg/dl), and the antibiotherapy was changed to piperacillin-tazobactam and amikacin according to the microbial flora of our hospital. The control echocardiogram performed on day 11 revealed PDA with left-to-right shunting, and ibuprofen therapy was initiated. A cranial USG screening given prior to the ibuprofen treatment revealed multiple bilateral hyperechoic lesions, with the largest measuring 38 x 40 mm (Fig. 1). The cranial CT confirmed bilateral frontal and parietal edema and multiple nodular, hypodense organized lesions that were brain abscesses. The patient had no neurological abnormalities. Newborn reflexes such as Moro, sucking and catching were normal and symmetric, and there was no motor deficit. Following neurosurgical consultation, surgical treatment was ruled out. The antibiotherapy was changed to meropenem, vancomycin and metronidazole to cover methicillin-resistant Staphylococcus aureus and beta lactamase-positive Klebsiella pneumoniae, because we did not obtain acute phase response with the previous antibiotics. Abdominal and renal USG showed no abscesses in other areas of the body. The serological markers were negative for toxoplasma, cytomegalovirus, rubella, and herpes viruses. No microorganism could be identified as the source of the brain abscess despite repeated blood cultures. Immunological tests for chronic granulomatous disease, severe combined immunodeficiency, leukocyte adhesion deficiency, and humoral immune deficiency, including tests of the lymphocyte subsets, nitroblue tetrazolium, dihydrorhodamine, and blastic transformation, were all within the normal range (Table I). The only defined risk factor for brain abscess except low birth weight and prematurity was PDA, but it was a low risk factor because the shunt was left-to-right.

On day 20, the patient’s head circumference was 32.8 cm. Lumbar puncture (LP) was not performed because the patient was receiving an antibiotic regimen and there was a risk of brain shift. A cranial MRI performed on day 22 revealed multiple bilateral abscesses and a 5-mm shift in the central line; the largest abscess was 40 x 35 mm (Fig. 2). Antibiotherapy was continued following a second neurosurgical consultation. Ultrasonographic follow-up was performed weekly, and lesions became cystic and decreased after day 40. On day 44, the neurological examination was normal and no convulsions were observed. Antibiotherapy was continued for six weeks according to the literature, and oral amoxicillin-clavulanate was prescribed upon discharge. The patient’s neurological examination was normal at discharge. On day 56, a follow-up cranial MRI was performed and revealed decreased lesions (the largest measured 35x25 mm), and her head circumference was 36 cm. A cranial MRI at 8 months showed a 40x24 mm cystic, encephalomalacic lesion (Fig. 3). Her mental and motor development was consistent with six months and her head circumference was 42.5 cm. She had no focal deficit.

Fig. 1. A cranial USG shows multiple bilateral abscesses on the 11th day, with the largest measuring 48x28 mm in the right frontal lobe. Multiple brain abscesses were seen in the other cortical area with a 5 mm mean diameter.
Discussion

Intracerebral abscesses occur when microorganisms from a contiguous infection in non-neural tissue invade the brain parenchyma. The infection may reach the brain through hematogenous spread, or it may be the result of a direct mechanical introduction such as a penetrating trauma or a surgical procedure. Hematogenous spread is the primary cause of intracerebral abscess in the neonate. Low birth weight and prematurity are known risk factors for neonatal infections including brain abscess. Secondary to sepsis, abscess formation begins when the microorganism invades the parenchyma. Hematogenous seeding can occur from anywhere in the body, and it stems from infections such as osteomyelitis, endocarditis or cutaneous infection. Dermal sinuses and devices used for fetal scalp blood sampling are risk factors for direct mechanical introduction. Meningitis is a major risk factor for brain abscess. Brain abscess is found in 1–4% of neonatal meningitis cases. Congenital heart disease with right-to-left shunt is a risk factor for brain abscess at all ages. Brain abscesses occur less frequently in neonates than in other age groups. Immune deficiency is a risk factor for brain abscess. Chronic granulomatous disease, severe combined immunodeficiency, leukocyte adhesion deficiency, humoral immune deficiency such as IgA deficiency, and lymphocyte deficiency such as DiGeorge syndrome are detectable immune diseases in neonates. Our patient had clinical sepsis, but the blood culture was not positive. We could not find a source of hematogenous seeding or an anatomical malformation such as dermal sinus. The patient’s immunological screen was normal. The only risk factor other than low birth weight and prematurity that we could identify was a low-risk PDA. The lesions were organized when the diagnosis was made on day 11. Previous studies have reported early encapsulation of the infection within 10–13 days followed by organization of the abscess. The abscess formation may have started in utero. The mother had no risk factors such as sepsis, vaginal lochia or an invasive procedure such as fetal scalp monitoring or amniocentesis; however, it is unlikely that such an advanced lesion could have developed postnatally, and the mother may have had an undetected intrauterine infection.

A broad spectrum of possible etiological agents can be assessed by pus, blood and cerebrospinal fluid cultures. Up to 40% of blood cultures are sterile; this may be the result of the bacteriological procedure. Our patient’s culture was negative in repeated blood tests. A positive culture is important for making an accurate diagnosis. In most cases, similar to ours, an antibiotic regimen reduces the positive blood culture rate. Streptococcus intermedius, group B streptococcus and Peptostreptococcus are the primary causative agents. Staphylococcus species such as Staphylococcus aureus and S. epidermidis are secondary causative agents. Citrobacter, Klebsiella, Enterobacter, Serratia,
and Edwardsiella species are gram-negative etiological agents. *Proteus mirabilis* was reported to be the most common etiological agent in one series. Possible etiological agents also include fungi; among them, *Aspergillus* and *Candida* species are the leading causes of brain abscesses. In addition, *Mycoplasma* and *Ureaplasma* can cause brain abscesses. Laboratory tests have limited value for the diagnosis of brain abscess. Peripheral white blood cell count and acute phase reactants such as IL-6 and CRP may be normal or elevated. Our patient’s IL-6 and CRP values were high, and after antibiotherapy, follow-up values were in the normal range. LP should be reserved for patients who have suspected meningitis and no signs of increased intracranial pressure or focal neurological deficits because of the potential risks such as herniation. We did not perform LP on our patient due to the risk of a brain shift because of multiple and large brain abscess, and because she had been receiving antibiotherapy for eight days before the brain abscess diagnosis. LP would have provided little diagnostic assistance in the present series.

Clinical manifestations of a brain abscess vary according to the stage of the disease, the relative virulence of the infecting organism, the host immune status, localization of the abscess, the number of lesions, and the presence or absence of associated meningitis or ventriculitis. Fever is usually a non-specific symptom and may be found in 50–80% of the cases. Increased intracranial pressure and mass effect cause neurological symptoms. Hypoactivity, hypotonia, eating difficulties, vomiting, irritability, alterations in the level of consciousness, and focal neurological deficits are symptoms of a brain abscess. An examination may detect a bulging fontanel, increased head circumference and widening of the sutures. Focal or generalized convulsions may occur. Our patient’s initial symptoms of fever and abdominal distension and sensitivity improved in five days. She had no neurological symptoms during the illness and showed no neurological deficit or symptoms, despite having multiple large lesions. Although she showed no neurological deficits during the acute phase of her illness, she may experience neurological sequelae later in life, such as cerebral palsy, learning difficulties, hearing and visual problems, and mental and motor retardation.

Ultrasonography (USG) is a safe and accurate method for detecting complications of central nervous system infection; however, small abscesses and subdural collections cannot be seen by USG. CT can detect all stages of abscess formation, and the widespread use of CT has dramatically modified the management of brain abscesses. CT is used for early diagnosis, treatment and follow-up. The edema that characterizes brain abscesses can be detected by MRI. MRI produces better resolution of soft tissue than does a CT scan, but MRI does not add significant information.

Fig. 2. A cranial MRI shows multiple bilateral abscesses on the 22nd day, with the largest measuring 40 x 35 mm on the right frontoparietal lobe. There was a 5 mm right-to-left shift at the midline.
for the management of the abscess. We performed CT for immediate radiologic evaluation after USG diagnosis instead of MRI because MRI poses technical difficulties such as need of sedation, anesthesia and long period of immobility, which is impossible in an infant without anesthesia. Diagnosis using USG, CT and MRI has contributed to the decrease in mortality and morbidity rates seen in recent years. Our patient was diagnosed using USG, and immediate confirmation was made by CT; USG and MRI were used for follow-up, surgical decision and postoperative follow-up, respectively. These imaging technologies can be used to easily diagnose and follow a brain abscess that has characteristic lesions.

Successful treatment of a brain abscess requires a multidisciplinary approach that includes a neonatologist, neurosurgeon and infectious diseases specialist. Empirical therapy must be started immediately and managed with blood culture results, host response and neuroimaging. No consensus exists on the duration of antibiotic therapy; however, 6–8 weeks of intravenous therapy is the recommended time period. The roles of surgical treatment are to provide a specimen of purulent material for bacteriologic analysis and culture, to remove the material to lower intracranial pressure, to decrease the mass effect of the abscess, and to decompress and irrigate the ventricular system. Surgical intervention can be in the form of either aspiration or craniotomy. The mortality rate for brain abscess is between 9% and 32%. Preoperative neurological examination is important for the prognosis. Recurrence is probable.

In conclusion, brain abscess in newborns is a very rare disease that may not exhibit the expected neurological signs and symptoms. Depending on the radiological organization, an abscess in a neonate in the first weeks may be the result of an intrauterine infection.

REFERENCES