Brain abscesses in neonates

A study of 30 cases

DOMINIQUE RENIER, M.D., CÉCILE FLANDIN, M.D., ELIZABETH HIRSCH, M.D., AND JEAN-FRANÇOIS HIRSCH, M.D.

Department of Neurosurgery, Hôpital des Enfants Malades, Paris, France

Since the introduction of ultrasonography and computerized tomography (CT) scanning, brain abscesses are found more frequently in cases of neonatal meningitis and septicemia, particularly when the offending pathogen is *Proteus*. Thirty cases of brain abscess in neonates are reported, 27 of which were caused by *Proteus* species infections. Twenty infants had meningitis and 13 had septicemia. Most of the abscesses were enormous, and multiple abscesses were observed in 17 cases. The frontal region was involved in 22 cases (12 unilaterally and 10 bilaterally). The ventricles were enlarged on the first CT scan in 13 cases.

The abscesses were treated by aspiration and antibiotics in 25 cases, and by antibiotics alone in five. A shunt for hydrocephalus was necessary in 14 infants. Four infants died, three from the initial illness and one from a shunt complication. Subsequent intelligence quotient (IQ) testing was performed in 22 children: eight (36%) have an IQ at or above 80 and eight have an IQ of less than 60. In the 17 children followed for more than 2 years, the proportion with an IQ at or above 80 fell to 24% (four cases). The absence of initial seizures, sterile cerebrospinal fluid, normal ventricles on CT scans, and early aspiration of the abscess seem to be factors portending a better prognosis in terms of epilepsy and mental sequelae.

**Key Words** • brain abscess • bacterial infection • *Proteus mirabilis* • meningitis • septicemia • neonate

**Neonatal** bacterial infections pose a major problem for the neurosurgical community. The incidence has been reported to be between one and 10 cases per 1000 live births, with continued high mortality and morbidity rates. Purulent meningitis during the 1st month of life has been studied by many workers during the last three decades. 

**Clinical Material and Methods**

Thirty newborn infants were treated for brain abscess in the Department of Pediatric Neurosurgery at the Hôpital des Enfants Malades in Paris from December, 1973, to December, 1985. Of these, 28 cases have been observed since 1979 and 23 since 1982.

**Perinatal History**

No abnormality of pregnancy was recorded. The gestational period was normal in 20 cases (38 to 42 weeks), abnormal in five (34 to 37 weeks), and unknown in five. No infant had a birth weight less than 2400 gm. Premature rupture of the membranes, occurring more than 24 hours before delivery, was recorded in two cases. There were six babies delivered by Caesarean section. No internal monitoring device was used and no infant needed resuscitation or mechanical ven-
tilation at birth. The examination of the baby was described as normal at birth in every case.

A maternal infection of the urinary tract was observed in eight cases, with septicemia in one. In six of these eight cases, the same organism was found in the mother's urine and in the infant (Escherichia coli in one, Serratia in one, and Proteus in four).

Clinical Features

Eighteen of the 30 infants were male (a nonsignificant preponderance). The onset of the symptoms occurred during the 1st month of life in all cases (Day 1 to Day 30, median Day 5, mean Day 9), and during the 1st week in 20 cases. The initial manifestation of illness was seizures in 13 infants, signs of infection in 11, respiratory symptoms in two, poor feeding and vomiting in two, and increased head circumference with bulging fontanels in two.

Seizures were the most frequent initial sign, but it must be emphasized that they were even more frequent during the acute course of the illness: 21 infants had seizures, which in nine cases represented status epilepticus. None of the patients with seizures had a normal electroencephalogram (EEG), whereas four of the infants without seizures had a normal EEG. No clear relationship was found between the initial EEG findings and the lesions seen on computerized tomography (CT). None of the single abscesses had focal EEG abnormalities, whereas some of the multiple abscesses had such focal abnormalities.

Bacteriology

Proteus mirabilis was the most commonly found organism, being identified in 27 (90%) of the 30 cases. Escherichia coli accounted for two cases and Serratia marcescens for one. The causative organism was identified in the cerebrospinal fluid (CSF) in 20 (77%) of the 26 patients whose CSF was cultured, in 13 (62%) of the 21 patients whose blood was tested, and in 17 (68%) of the 25 abscesses that were tapped.

Twenty infants had both blood and CSF cultures; both were positive in eight cases. Meningitis without septicemia was observed in six cases, and septicemia without meningitis occurred in four. In two infants, both CSF and blood cultures were negative and the pathogen was found only in the abscess.

Abscess Location

The location and number of abscesses could be precisely studied in 28 patients in whom a CT scan was performed at the time of diagnosis. The abscesses were multiple in 17 (61%) of these cases. The frontal region was involved in 22 cases (79%): unilaterally in 12 cases (in two cases a periventricular abscess extended over the entire hemisphere), and bilaterally in 10 cases (Fig. 1). Most abscesses were enormous. A typical feature was the periventricular location of these abscesses, in direct contact with the ventricle. Some of them communicated with the ventricles, but this was not a constant finding.

Treatment

The abscesses were treated by aspiration and antibiotics in 25 cases, and by antibiotics alone in five. The age of the patient at first tapping varied from 9 to 66 days (mean 26 days). In 15 (60%) aspiration was performed before the 30th day, and in 10 (40%) after 1 month. Between one and six abscess punctures were necessary for aspiration (mean two, and only one in 14 cases (56%)). In most cases, tapping could be done through the anterior fontanel, guided by real-time ultrasonography.

The antibiotics used changed with the date of treatment. The combination most often given was cefotaxime and gentamicin, but the results appeared better with ceftriaxone and amikacin, which was the combination used in the most recent cases.

Hydrocephalus

Of the 30 patients, 14 infants (47%) had hydrocephalus. Hydrocephalus occurred in 14 (70%) of the patients with meningitis and in none without meningitis. Ventricular dilatation was found on the first CT scan in 13 of the 14 cases of hydrocephalus. All infants with hydrocephalus had shunts placed when the CSF and the abscess were sterilized. When necessary, temporary external ventricular drainage was used until the CSF became sterile. In two cases, the ventricles became noncommunicating cavities, which needed several shunts (two shunts in one case and three shunts in another).

Hydrocephalus occurred less frequently in the 15 infants in whom the abscess was tapped during the 1st month of life (three hydrocephalic cases, 20%) than in the 10 cases where the first aspiration was done later (seven hydrocephalic cases, 70%). This difference is significant (p < 0.04). Four of the five infants who were treated with antibiotics alone developed hydrocephalus.
Neonatal brain abscess

Outcome

All the survivors were reviewed with a follow-up period of 6 months to 12 years (mean 46 months). Neurological examination, psychological and psychometric testing, EEG, and CT were performed. Normal mental level was defined as an intelligence quotient (IQ) or a developmental quotient (DQ), depending on the age of the child at the last assessment, at or above 80.

A series of 36 abscesses in older children treated in the same institution during the same period was studied in order to compare the prognosis of abscesses occurring in newborn infants to those in older children.

Results

Survival

Four infants died, three from their initial illness and one from a shunt complication at 17 months of age. The 10-year actuarial survival rate is 86%.

No deaths occurred in children whose abscess was tapped before the 30th day of life (survival rate 100% vs. 70% in children who were treated later, p < 0.03). This was the only significant factor influencing survival in this series. However, a slightly better survival (although not statistically significant) was found in patients without meningitis or hydrocephalus.

Residual Lesions on CT

In 10 cases, the follow-up CT scans either were normal or had minimal changes. In the remaining 16 cases (62%), dramatic lesions were observed: porencephaly, cerebral atrophy (especially in the frontal region on one or both sides), or large multiloculated cavities. These large residual lesions were less frequent after early tapping of the abscess (before the 30th day) than in those tapped later (43% vs. 71%). However, this difference is not statistically significant. It must be noted that all infants who were treated by antibiotics alone without aspiration have severe residual lesions, compared with only 52% of cases treated by aspiration (chi-square, Fisher's exact test: p = 0.13).

Mental Outcome

Subsequent mental evaluation was conducted in 22 children. Eight (36%) of them have an IQ or DQ of 80 or above and eight have an IQ or DQ of less than 60. In the group of children with a longer follow-up period, the results are worse: four (24%) of the 17 patients with a follow-up period of more than 2 years have a normal mental level, compared with four of the five patients with a shorter follow-up period (chi-square, Fisher's exact test: p = 0.07). The evolution of the mental level can be studied in 16 children who had several psychometric tests during the follow-up period. In most cases, the mental level deteriorates with age (Fig. 2). Therefore, a good early result has no prognostic value, and a long period of follow-up monitoring is needed for determination of the final outcome.

Hydrocephalus and mental retardation are significantly correlated: only one of 10 hydrocephalic children had a normal IQ compared with seven (58%) of 12 children without hydrocephalus (chi-square, Yates' cor-
Epilepsy

The frequency of epileptic sequelae in this series has been studied in another report. The presence of epilepsy could be assessed in 27 children who survived their acute illness. The mean age of onset was 4 years (9 months to 9 years) for generalized or focal seizures, and 2 months for infantile spasms. Sixteen (59%) of these 27 surviving children have seizures. This proportion will probably increase since none of the children without epilepsy has at this time been followed for more than 4 years. Moreover, five of the 11 children without seizures have spikes on their EEG. It is noteworthy that epileptic sequelae are observed almost solely in children who had seizures during the acute illness: among seven survivors who had no neonatal seizures, only one has epilepsy, compared with 15 of the 20 who had seizures during the acute illness (chi-square, Fisher’s exact test: p = 0.02).

Epilepsy and mental deficiency are significantly correlated: two of 14 epileptic children tested have a normal IQ compared with six of eight children without seizures (chi-square, Fisher’s exact test: p = 0.01). Epilepsy is highly correlated with hydrocephalus: 100% of hydrocephalic children have epilepsy compared with a 27% rate in children without hydrocephalus (chi-square, Yates’ correction: p = 0.0005). Epilepsy is also correlated with meningitis: 78% of the children who had meningitis have epilepsy, versus 17% of those children who did not (chi-square, Fisher’s exact test: p = 0.03). The other factors increasing the risk of epilepsy are late tapping or no tapping of the abscess and severe residual lesions on CT scans; however, these subgroups are too small to provide statistically significant differences.

Comparison With Older Children With Brain Abscesses

The authors reviewed a series of 36 brain abscesses in older children treated with the same protocol as in the present series. Nineteen of the abscesses were due to cyanotic heart disease and 17 to miscellaneous causes (mainly ear, nose, and throat infections). These two groups have been distinguished because it has been shown in another report that their prognosis is clearly different. The prognosis is worse in the neonatal series than in the older children as far as residual lesions on CT, epileptic sequelae, and mental outcome are concerned (Table 1).

Discussion

The first reports of brain abscesses in neonates were published 90 years ago. Since that time, these lesions have been regarded as very uncommon. However, during the last decade their incidence has increased: 28 of our 30 cases were observed after 1978. Clearly, the current use of CT and ultrasonography is responsible for this apparent increase in incidence. It is likely that these abscesses were formerly misdiagnosed, a fact that could explain (at least in part) the high mortality and morbidity rates in the published series of neonatal meningitis. In fact, the only abscesses in neonates in previous decades were described in pathological studies. It is noteworthy that, in most series of neonatal meningitis, the most frequent responsible pathogens are E. coli and group B Streptococci,

Brain abscesses in neonates are caused by Gram-negative pathogens in all the published cases and are frequently linked to meningitis. Both features are atypical of brain abscesses in older children. The high frequency of Gram-negative organisms in neonatal meningitis is well known, varying from 47% to 83%. However, it is noteworthy that brain abscesses have not been described in all Gram-negative neonatal meningitis, but almost solely in those cases caused by Proteus and Citrobacter species. In a review of 53 cases of Citrobacter neonatal meningitis reported in the literature by Graham and Band, a brain abscess was identified in 77%. They compared this to 10% of the 159 cases of non-Citrobacter Gram-negative enteric meningitis studied by the Neonatal Meningitis Cooperative Study Group. In the series published by Dulac, et al., a brain abscess was observed in 10 of the 12 cases of Proteus meningitis.

The susceptibility of newborns to Gram-negative infections is well established, and is explained by the
Neonatal brain abscess
deficiency of both placently transferred immunoglobulin M antibodies and complement. Abnormalities of pregnancy and delivery have been described by many authors as predisposing factors to Gram-negative infections of the newborn: prematurity, urinary tract infections and the nursery environment are the source of neonatal meningitis and brain abscesses, then this raises important issues for their prevention.

The route of infection to the brain is debatable. Theoretically, spread of infection can follow two different paths: blood or CSF. Direct extension of infection to the CSF from the middle ear has been described. In our series, six infants had meningitis without septicemia and one had an otitis prior to the time of diagnosis. Four other infants had septicemia involving the midline structures, fornix, and corpus callosum. These lesions are particularly characteristic of Proteus infections. In addition to the lesions due to meningitis are the lesions left by the abscesses, which are in most neonatal cases much more severe than those due to abscesses in older children.

Moreover, the functional results are better after early tapping, and worse when no tapping was done.

Four deaths among these 30 neonates with central nervous system infections (three deaths in the 20 infants with proved meningitis) represents a dramatic improvement as compared with previously published series. In our institution, no death has occurred since May, 1984, among neonates with brain abscess (12 cases in this series and six more cases since 1986). Improvement in antibiotic therapy is obviously an important factor: the use of new cephalosporins in conjunction with aminoglycosides plays a major part. The combination of gentamicin with cefotaxime and more recently amikacin with ceftriaxone has given very good results in terms of survival. Early aspiration of the abscesses is another important factor in this improvement, since no deaths occurred when the abscess was tapped before the 30th day of life.

The morbidity rate still remains high. Of 17 children with long follow-up periods (more than 2 years), only four are normal intellectually and without seizures. Such dismal results have a histopathological basis: this includes the multiplicity of cerebral hemorrhagic infarcts and necrosis described in neonatal meningitis. Involving the midline structures, fornix, and corpus callosum. These lesions are particularly characteristic of Proteus infections. In addition to the lesions due to meningitis are the lesions left by the abscesses, which are in most neonatal cases much more severe than those due to abscesses in older children.

The usefulness of aspiration in the treatment of brain abscess in neonates requires discussion, since in most cases the etiological organism is identified from the CSF or the blood cultures, and since there is no sign of raised intracranial pressure. However, in our series, the residual lesions seen on CT were more frequent and severe in nonaspirated cases, and were smaller when the puncture was performed during the 1st month of the illness.

References

Manuscript received March 3, 1988.
Address reprint requests to: Dominique Renier, M.D., Department of Neurosurgery, Hôpital des Enfants Malades, 149 rue de Sèvres, 75730 Paris Cedex 15, France.

D. Renier, et al.