Brain abscess in childhood: a 28-year experience

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Brain abscess is an uncommon intracranial suppurative infectious disease, especially in children. The clinical presentation, treatment and outcome of 75 children with brain abscesses admitted to the Department of Pediatric Infectious Diseases at Hacettepe University Faculty of Medicine were retrospectively analyzed. Seventy-five cases of brain abscess within a 28-year period were included in this study. Fever and headache were the most common presenting symptoms. Cyanotic congenital heart disease was the most common predisposing factor. The most common pathogen was Streptococcus spp. Although congenital heart disease remained the most common predisposing factor for development of intracerebral abscess, the rate of immunocompromised diseases as a predisposing factor of brain abscess has increased in recent years, and better management of otogenic infections also influences the prevalence of the disease.

Key words: brain abscess, childhood, predisposing factors.

Brain abscess is an uncommon infectious disease during childhood. Overall, about 25% of brain abscesses occur in children, mostly in the age group of 4-7 years. Brain abscesses in children were traditionally associated with congenital heart defects and with infections of the face, head or brain. The clinical presentation of a brain abscess may be subtle and is influenced by many factors, such as age and the location of the abscess. The classic triad of headache, fever and focal neurological signs was demonstrated in only 9-28% of the pediatric cases[1,2]. Commonly isolated causative organisms are diverse, including aerobic and anaerobic streptococci and staphylococci, but specific pathogens, such as the Citrobacter group, Nocardia, fungi, and *Mycobacterium tuberculosis* are more common in specific groups[1-3].

Before the 1970s, the overall mortality rate from brain abscesses was as high as 30-60%, but it has declined markedly in more recent reports. However, these features may have changed because of aggressive antibiotic treatment for otorhinologic infections and increasing neurosurgical procedures[1,2,4]. The management of brain abscess is both surgical and medical, or medical alone in selected cases. Surgical drainage with antimicrobial therapy is the treatment of choice in most brain abscesses[1,2].

The objective of this study was to characterize the nature of brain abscesses and to identify the risk factors, clinical manifestations and outcome in children.

Material and Methods

This study reviews retrospectively all pediatric cases with brain abscesses treated in the Division of Pediatric Infectious Diseases at Hacettepe University İhsan Doğramacı Children's Hospital in the past 28 years (1982-2010). Medical records of all children (0-18 years) with a discharge diagnosis of 'brain abscess' were analyzed for demographics, presenting signs and symptoms, predisposing factors, imaging, microbiological results, treatment, and short-term outcome. Brain abscess was defined as a macroscopic lesion located in the cerebrum, cerebellum or midbrain, with characteristic features on contrast computed tomography (CT) or magnetic resonance imaging (MRI).

The diagnosis of brain abscess was confirmed when CT and/or MRI showed a localized parenchymal lesion with perilesional brain edema and post-contrast ring enhancement[3]. The imaging findings were corroborated by pus aspiration, culture of the aspirate or pathological findings for a group of patients. For patients who did not undergo surgical intervention, the diagnosis was reinforced by typical clinical symptoms and treatment response. Subdural empyema and epidural abscess were excluded. Abscess content was aspirated during surgery, such as drainage or open craniotomy, in appropriate patients. In addition, the aspirate was transported immediately to the microbiology laboratory for processing in aerobic and anaerobic culture conditions. The patient details reviewed included general patient characteristics, symptoms present upon initial presentation, underlying medical conditions, predisposing factors, location of abscesses, microorganisms isolated, treatment regimen, prognosis, and treatment outcome.

Statistical data were analyzed by chi-square test. A *p* value less than 0.05 was considered statistically significant.

Results

Between 1982 and 2010, 75 children with a diagnosis of brain abscess were identified. The median age of patients with brain abscess was 6.7 years (range: 2 months - 18 years), and the male to female ratio was 1.5 (45 boys, 30 girls). The major presenting symptoms and signs are summarized in Table I. A review of their symptomatology showed that fever and headache were the most common symptoms on initial presentation, noted in 36 children (48%). Nausea and/or vomiting were the second most common presenting symptoms, noted in 27 of the 75 cases (36%). Twenty children (26.6%) had altered consciousness. Among the 35 children with one or more associated focal neurologic deficits, 24 cases had hemiparesis, 15 cranial nerve paralysis, 4 dysphagia, 5 ataxia, 3 diplopia, 3 nystagmus, 2 hydrocephaly, 1 optic atrophy, and 2 spasticity. The classical triad of headache, fever and focal neurological deficit was found in a few groups of cases.

Seizure was also a common initial presentation, noted in 22 children (29.3%), although none

Table I. Clinical Signs and Symptoms*

	(n: 75)	(%)
Signs and symptoms		
Fever	36	(48)
Headache	36	(48)
Nausea-vomiting	27	(36)
Seizures	22	(29.3)
Altered consciousness	20	(26.6)
Nuchal rigidity	15	(20)
Brudzinski sign	14	(18.6)
Kernig sign	13	(17.3)
Focal neurological involvement		
Hemiparesis	24	(32)
Cranial nerve palsy**	15	(20)
Dysphagia	4	(5.3)
Pathological reflexes	13	(17.3)
Ataxia	5	(6.6)
Diplopia	3	(4)
Nystagmus	3	(4)
Hydrocephaly	2	(2.6)
Optic atrophy	1	(1.3)
Spasticity	2	(2.6)

* More than one symptom can be found in one patient at the same time
**Including facial palsy, ocular palsy, 6th, 9th, and 10th cranial nerve palsies

of the 75 children revealed any history of prior epilepsy.

Predisposing factors were identified in 55 of 75 cases (73.3%). Twenty-five abscesses were secondary to infections involving the brain and adjacent anatomic sites including sinusitis in 4 cases (5.3%), otitis media in 12 cases (16%), orbital cellulitis in 1 case (1.3%), and meningitis in 6 cases (8%). Twenty-five (33.3%) abscesses developed in children with cyanotic congenital heart disease (CCHD), 2 (2.6%) with pulmonary disease, 2 (2.6%) with hematologic disease, and 1 (1.3%) with immunological disease, and 2 cases (2.6%) occurred after head trauma. In addition, no predisposing factor was found in 20 cases (26.6%) in that period. CCHDs were the most common underlying disease group identified in all the cases (25/75; 33.3%). One abscess was secondary to thrombotic thrombocytopenic purpura (TTP)/hemolytic uremic syndrome (HUS), and another was secondary to deficiency of dedicator of cytokinesis 8 (DOCK8). There were no cases related to dental disease (Table II).

Fifty children (66.6%) suffered a single-lesion brain abscess. The remaining 25 children (33.3%) revealed multiple lesions. Nineteen cases were presented in the frontal lobe, 17 in the parietal lobe, 11 in the frontoparietal lobe, and 11 in the temporal lobe, and 10 abscesses were located in the cerebellum. Parietal and/or frontal lobes were most commonly involved (Table III).

Intravenous antibiotics were given to all patients. The kind of antimicrobic drugs were changed according to the time period. Ampicillin-sulbactam, penicillin G and third-generation cephalosporins with or without metronidazole and/or chloramphenicol were given to most cases with brain abscess. The combination of ampicillin-sulbactam, metronidazole and amikacin was the most commonly used treatment in the previous era. In recent years, the most popular and commonly used treatment was the combination of vancomycin, cefotaxime (or another third-generation cephalosporin) and ornidazole (Table IV). In light of the imaging findings and abscess culture results, antifungal treatment (amphotericin B, voriconazole, caspofungin) was used in only 2 cases. According to the results of Gram smear and abscess aspirate cultures, the treatment was reevaluated. Linezolid, meropenem, ampicillin-sulbactam, ceftriaxone, metronidazole, amikacin, and clindamycin were the other therapeutic choices for these cases. Eighteen cases (24%) received antibiotic therapy only; the other 57 patients (76%) received surgical management in addition to antibiotics. Ten patients (17.5%) and 8 patients (44.4%) were treated with medical therapy alone in 1982-1997 and in 1998-2010, respectively. The reasons for not undergoing operation included the relatively small size of the abscesses, multiple and deeply localized abscesses, and improved patient condition following antimicrobial treatment.

A group of appropriate cases underwent surgical operation. A surgical treatment and aspiration (n: 30, 40%) or resection (n: 27, 36%) was performed in 57 (76%) of the 75 patients (Table IV). Repeated drainage

Table II. Predisposing Factors

	(n)	(%)
Cyanotic congenital heart disease	25	(33.3)
Otogenic	12	(16)
Meningitis	6	(8)
Sinusitis	4	(5.3)
Trauma	2	(2.6)
Immunosuppression*	3	(3.9)
Pulmonary origin	2	(2.6)
Orbital cellulitis	1	(1.3)
Unknown	20	(26.6)

*This group includes 1 child with deficiency of dedicator of cytokinesis 8 (DOCK8), 1 child with acute lymphoblastic leukemia (ALL) and 1 child with thrombotic thrombocytopenic purpura/hemolytic uremic syndrome (TTP/HUS).

Table III. Localization of Abscesses

(n)	(%)	
Supratentorial		
Frontal lobe	19	(25.3)
Temporal lobe	11	(14.6)
Parietal lobe	17	(22.6)
Occipital lobe	4	(5.3)
Frontoparietal lobe	11	(14.6)
Parietooccipital lobe	5	(6.6)
Temporoparietal	3	(4)
Temporoparietooccipital	3	(4)
Infratentorial		
Cerebellum	10	(13.3)
Brain stem	6	(8)

of the abscess was needed in only 3 cases. Intraventricular vancomycin and amikacin were given to only 1 case for 5 days, and endoscopic sinus drainage was performed in 2 cases that had sinusitis. Surgery was not performed in 18 cases (24%) who were treated with antimicrobials alone.

The 57 individuals who received surgical intervention had abscess pus cultures, 25 of which revealed the presence of pathogens (Table V). Polymicrobial pathogens were isolated from 3 patients. *Staphylococcus aureus* and *Streptococcus viridans* were the most common microorganisms, determined in 5 patients each. *Proteus mirabilis* was cultured from 3 patients. *Streptococcus constellatus, Streptococcus pneumoniae, peptostreptococci,* and *Peptococcus niger* were detected in 2 patients each. *Coagulase-negative staphylococci, Streptococcus anginosus,* Klebsiella spp, Ekinella spp, Fusbacterium spp, Bacteroides spp, and Aspergillus spp were isolated from 1 patient each. Microorganism-positive blood culture result was noted in only 1 patient who also had positive pus culture result for the same microorganism, *S. viridans*.

Three (4%) of the 75 abscess episodes resulted in death before hospital discharge.

Discussion

Brain abscesses are uncommon in children. The clinical presentation of brain abscess is related with multiple factors, including lesion location, pathogen and host immune status. Although headache, fever and vomiting each occur in 60-70% of the patients, the presentation of brain abscess in infants and children may be nonspecific[1]. Fever (48%) and headache (48%) were the most common symptoms of brain abscess at initial presentation in our study population. The clinical manifestations in our patients were compatible with the results of a number of other analogous studies[3,5-8]. Focal neurological signs were present in 35 (46%)

Table IV. Treatment Modalities and Outcome

	n	%
Medical treatment	75	100
Sulbactam-ampicillin + amikacin + metronidazole	14	18.6
Penicillin G + chloramphenicol + metronidazole	12	16
Sulbactam-ampicillin + metronidazole	8	14
Vancomycin + cefotaxime + ornidazole	7	9.3
Penicillin G + chloramphenicol	4	5.3
Sulbactam-ampicillin + chloramphenicol	3	4
Vancomycin + cefotaxime + metronidazole	3	4
Other*	24	32
Surgical treatment	57	76
Aspiration	30	40
Resection	27	36
None	18	24
Death**	3	4

*Combination therapies with netilmicin, ticarcillin, fluconazole, meropenem, linezolid, amphotericin B, voriconazole
**Death occurred before hospital discharge.

of the cases. This finding was also similar to those previously reported[1,3].

In this study, 33.3% of patients had CCHD as their underlying medical condition. In concordance with most published reports, CCHD and otogenic infections were the most common predisposing factors in our series[1,5,9]. A change in the epidemiology was revealed since the 1990s, owing to a decreasing incidence of otogenic infections and a relative increasing number of immunocompromised patients, which was a similar finding in some previous reports[9,10]. This may be explained by the implementation of 7-valent pneumococcal conjugate vaccine into the Turkish national immunization schedule in 2008 and the increased rate of influenza vaccination in recent years. Our patients had more frontal and parietal abscesses. This may also reflect the trend towards better and more aggressive management of otogenic disorders, as similar to some other reports[11]. Of the three children identified as immunosuppressed, only one was positive for fungi. Immunosuppression among study participants has been increasingly reported in recent years[9,10]. Availability of improved diagnostic techniques has likely led to some kind of rare immunological diagnosis. We could identify no underlying reason in 20 patients (26.6%) in our study, similar to the finding of a previous report[3].

Table V. Pathogens Isolated from Patients with Brain Abscess*

	(n)
A. Aerobes	
I. Gram-positive cocci	
i. Streptococcus spp.	
a) S. viridans	5
b) S. pneumoniae	2
c) S. constellatus	2
d) S. anginosus	1
ii. Staphylococcus spp.	
a) S. aureus	5
b) Coagulase-negative staphylococcus	1
II. Gram-negative organisms	
a) Proteus mirabilis	3
b) Klebsiella pneumoniae	1
B. Anaerobes	
I. Gram-positive cocci	
a) Peptostreptococcus	2
b) Peptococcus niger	2
c) Eikenella corrodens	1
II. Gram-negative bacilli	
a) Fusobacterium spp.	1
b) Bacteroides spp.	1
C. Fungi	
a) Aspergillus fumigatus	1

**Polymicrobial pathogens were isolated from three patients.*

Sterile pus cultures were found in 56% of cases. This represents quite a high rate of sterile cultures that has been described in the previous studies, which varied between 10% and 32% [2,3,5,9]. This may be explained by the previous antimicrobial treatment and perhaps difficulty in isolating microorganisms or inadequate sampling technique. Sixteen (28%) of our patients had pathogens including Streptococcus spp and Staphylococcus spp in the cultures. Seven (12.2%) of our patients had anaerobic pathogens including Peptococcus, Peptostreptococcus, Fusobacterium, and Bacteroides spp, in concordance with the literature[4,12-14].

Treatment of brain abscess requires a combination of antimicrobials and surgical intervention. In our institution, we treated 18 patients (24%) with antimicrobial therapy alone. Our ratio represents a relatively high rate of medical therapy alone. Auvichayapat et al.[15] and Goodkin et al.[9] treated 14.7% and 12.5% of their cases, respectively, with medical therapy alone. By comparing our current cases with our earlier cases, 10 patients (17.5%) and 8 patients (44.4%) were treated with medical therapy alone in 1982-1997 and in 1998-2010, respectively. This difference was statistically significant (p: 0.019). This may be explained by the difficulty in surgical drainage for multiple, small and deeply localized brain abscesses and also new effective therapeutic modalities.

Until the 1970s, the mortality rate was as high as 36%, but it subsequently declined after the 1980s. The mortality from brain abscess has decreased with the use of CT or MRI and prompt antibiotic and surgical management, but it remains relatively high (15%)[1,9]. The mortality rate in our series was very low (4%). It was similar to the results of the study reported by Shachor-Meyouhas et al.[2], but in contrast, it was quite low compared to the other results reported previously. Our low mortality rate may reflect the earlier and more accurate diagnosis resulting from the development of new imaging modalities and

appropriate antimicrobial and surgical therapies in our hospital.

By comparing our current data with our earlier cases, 57 patients and 18 patients were treated with the diagnosis of brain abscess in 1982-1997 and in 1998-2010, respectively. The decreasing ratio of patients may be explained by the early diagnosis and the development of surgical procedures for CCHD. Despite the availability of new therapeutic strategies and the development of better neurosurgical techniques, CHD remained the most common predisposing factor. None of the brain abscesses in recent years occurred in the setting of otogenic infections. Compared with the previous era, important historical trends were identified, including a reduction in the number of abscesses that occurred in the setting of otogenic infection. This is probably the direct result of improvement in diagnoses and the increased use of more effective antibiotics for the treatment of sinusitis and otitis. In recent years, immunocompromised states have become an important predisposing factor for the development of brain abscesses. Despite the relative increasing ratio of immunosuppression caused by aggressive therapeutic modalities and longer life span for these conditions, three of the patients who died were reported before the 2000s.

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