

Clinical Characteristics and Outcome of Primary Brain Abscess: a Retrospective Analysis

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Research Article

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Abstract

Background: Patients with primary brain abscess often present with atypical symptoms, and the outcome is varied. We investigated the demographic, laboratory, and neuroimaging features of patients with brain abscess at our hospital and identified factors associated with their outcome.

Methods: We retrospectively collected the data of patients diagnosed with primary brain abscess at our hospital between January 2011 and December 2020. Their clinical characteristics, predisposing factors, laboratory and neuroimaging findings, treatment, and outcome were analyzed.

Results: Of the 57 patients diagnosed with primary abscess, 51 (89.47%) were older than 40 years and 42 (73.68%) were male. Only eight patients (14.04%) showed the classical triad of headache, fever, and focal neurological deficit. Fourteen patients (24.56%) had comorbidities, of which diabetes mellitus was the most common. Positive pus cultures were obtained in 46.15% of the patients, and gram-negative enteric bacteria were found in 33.33% of them, with *Klebsiella pneumoniae* being the most frequently observed. Surgical treatment, most commonly in the form of stereotactic drainage, was received by 54.39% of the patients. Good outcomes were achieved in 75.44% of the patients. Multivariate logistic regression analysis showed that patients with headache were more likely to have a poor outcome (odds ratio 6.010, 95% confidence interval 1.114–32.407, $p = 0.037$).

Conclusions: Male patients and those older than 40 years were more susceptible to brain abscess than female patients and those younger than 40 years, respectively. Only a few patients showed the classical triad of clinical symptoms. Diabetes mellitus was the most common comorbidity. Positive pus culture results were uncommon, with gram-negative enteric bacteria, especially *Klebsiella pneumoniae*, being the main organisms found. Most patients had a good outcome, and the presence of headache may influence the outcome.

Background

Brain abscess is a focal intraparenchymal infection characterized by an encapsulated collection of pus, immune cells, and other materials following bacterial or fungal infection. It has a prevalence of approximately 0.3–1.3 per ten thousand people per year[1], with a high incidence in developing countries (8%)[2]. It is potentially life-threatening and is often associated with poor outcomes or persistent neurological sequelae. Secondary brain abscess results from open brain injury or brain surgery, whereas primary brain abscess occurs due to hematogenous or contiguous spread of infection (e.g., in patients with pneumonia, bacterial endocarditis, sinusitis, or dental infection) and is not caused by any surgical procedure [3–5]. Most patients with primary brain abscess present with atypical symptoms, which makes diagnosis challenging. Here, we retrospectively collected and analyzed the information of patients diagnosed with primary brain abscess at our hospital in the last ten years to determine the predisposing risk factors, clinical characteristics, and predictors of outcome.

Methods

Inclusion and exclusion criteria

We retrospectively retrieved the electronic medical records of patients diagnosed with primary brain abscess at our hospital between January 2011 and December 2020. Patients who met at least one of the following criteria were included: 1) evidence of infection in brain specimens obtained through surgical aspiration or lesion excision; 2) brain magnetic resonance imaging and/or computed tomography findings of brain abscess and reversal of brain lesion with antibiotic therapy. Patients with secondary brain abscess and those with intracranial empyema, including subdural and epidural abscess, were excluded. This study was approved by the ethics committee of the Second Affiliated Hospital of Fujian Medical University (NO: 2020 – 372).

Clinical and neuroimaging data

Data regarding the patients' demographic characteristics; predisposing factors; clinical characteristics; symptom duration; neurological status at admission; blood and cerebrospinal fluid (CSF) examination results; blood, CSF, and pus culture results; antibiotic treatment; type of surgery; number of abscesses; and location of the brain abscess on magnetic resonance imaging or computed tomography were extracted from electronic medical records. The brain abscess volume (in mm^3) was calculated using the formula $0.5 \times X \times Y \times Z[6]$, where X, Y, and Z were the largest diameters of the abscess in the X-, Y-, and Z-axes, respectively. If there were multiple brain abscesses, the largest abscess was measured.

Outcome assessment

The outcome was evaluated based on the Glasgow Outcome Scale score at discharge (1, death; 2, persistent vegetative state; 3, severe disability; 4, moderate disability; 5, good recovery). A score of 1–3 was regarded as a poor outcome, and a score of 4–5 was regarded as a good outcome.

Statistical analysis

Statistical analyses were performed using SPSS 22.0. Continuous data were expressed as means \pm standard deviations or medians and analyzed using the independent t-test or Mann–Whitney U test. Categorical data were analyzed using the chi-square test. To identify factors affecting the outcome, we performed multivariate logistic regression analysis of variables with $p < 0.2$ in the univariate analysis. The level of significance was set at $p < 0.05$.

Results

Clinical characteristics

Fifty-seven patients were diagnosed with primary brain abscess during the study period. The mean age was 52.26 ± 14.09 years. Six patients (10.53%) were < 40 years old, 32 (56.14%) were 40–60 years old, and 19 (33.33%) were > 60 years old. Forty-two patients (73.68%) were male and 15 patients (26.32%)

were female. The mean duration of hospitalization was 28.61 ± 15.18 days, and the median symptom duration at admission was six days. The patients' symptoms at admission included headache (52.63%), fever (45.61%), hemiplegia (45.61%), confusion (31.68%), nausea and vomiting (22.81%), epilepsy (14.04%), aphasia (12.28%), and neck stiffness (5.26%).

Predisposing factors and comorbidities

The patients' predisposing factors included adjacent site infection such as paranasal sinusitis (seven patients, 12.28%), chronic otitis media or mastoiditis (five patients, 8.77%), and dental infection (one patient, 1.75%); hematogenous infection such as pneumonia (nine patients, 15.79%) and bacterial endocarditis (one patient, 1.75%); and cyanotic heart disease (one patient, 1.75%). The patients' comorbidities included immunocompromising diseases such as diabetes mellitus (nine patients, 15.78%), tumor (three patients, 5.26%), liver cirrhosis (one patient, 1.75%), and granulocytopenia (one patient, 1.75%).

Results of blood, cerebrospinal fluid, and pus culture

Thirty patients (53%) had elevated white blood cell counts ($> 1,000 \times 10^6/L$) on peripheral blood testing. Blood culture was performed in 25 patients (43.86%), and positive results were obtained in four (16.0%) of them; bacteria of the streptococcus species were isolated in three patients (75%; Table 1). Lumbar puncture was performed in 18 patients (31.58%), and an increased cell count ($> 5 \times 10^6/L$) was observed in the CSF of 17 patients (94.44%), with two patients showing cell counts of $> 1,000 \times 10^6/L$. Moreover, 17 patients (94.44%) showed CSF protein elevation (> 0.45 g/L). CSF culture was performed in 16 patients (28.07%), and positive results were obtained in four of them (25%), with *Streptococcus* being the most commonly isolated organism (two patients, 50%; Table 1). Culture of the pus sample obtained during surgery was performed in 26 patients (45.61%), and positive results were obtained in 12 of them (46.15%; Table 1). In the identified organism, Gram-negative enteric bacteria, including *Proteus mirabilis* and *Klebsiella pneumoniae*, were observed in four patients (33.33%), and staphylococcal and fungal infection were observed in two patients each.

Table 1
Organisms isolated from primary brain abscess culture specimens

Case number	Sex	Age	Culture specimen	Organism
1	M	56	Pus	<i>Sphingomonas paucimobilis</i>
2	M	43	Pus	<i>Staphylococcus aureus</i>
3	M	41	Pus	<i>Proteus mirabilis</i>
4	M	43	Pus	<i>Rhizopus oryzae</i>
5	M	65	Pus	<i>Klebsiella pneumoniae</i>
6	M	45	Blood	<i>Streptococcus anginosus</i>
7	M	57	Pus	<i>Streptococcus anginosus</i>
8	M	38	Pus	<i>Prevotella</i>
9	M	59	CSF	<i>Neisseria cinerea</i>
10	M	20	Blood + CSF	<i>Streptococcus pneumoniae</i>
11	F	60	CSF	<i>Klebsiella pneumoniae</i>
12	M	54	Blood + pus	<i>Enterococcus faecalis</i>
13	M	60	Pus	<i>Staphylococcus aureus</i>
14	M	60	Pus	<i>Klebsiella pneumoniae</i>
15	M	52	Pus	<i>Klebsiella pneumoniae</i>
16	M	33	CSF	<i>Streptococcus intermedius</i>
17	F	48	Blood	<i>Viridans streptococci</i>
18	M	38	Pus	<i>Saccharomyces albicans</i>
CSF, cerebrospinal fluid				

Neuroimaging findings

All the patients underwent at least one neuroimaging study. Forty-nine patients (85.96%) underwent enhanced brain magnetic resonance imaging, ten (17.54%) underwent enhanced brain computed tomography, and four (0.02%) underwent both. Forty patients (70.17%) had a single abscess and 17 patients (29.83%) had multiple abscesses. The abscess was located in the frontal lobe in 28 patients (49.12%), temporal lobe in 16 patients (28.07%), parietal lobe in 16 patients (28.07%), occipital lobe in 11 patients (19.30%), basal ganglia in 4 patients (7.02%), cerebellum in 9 patients (15.79%), and brainstem in 2 patients (3.51%). The median abscess volume was 9.40 cm³ (95% confidence interval 9.68–17.48),

with small ($< 1 \text{ cm}^3$), medium ($1-10 \text{ cm}^3$), and large ($> 10 \text{ cm}^3$) lesions in 7 (12.28%), 25 (43.86%), and 25 (43.86%) patients, respectively.

Treatment and outcome

Fifty-five patients (96.49%) received antibiotic therapy after admission, and two patients (3.51%) received antibiotic therapy after diagnosis with neuroimaging or surgery. Initial empirical antibiotic therapy included ceftriaxone, metronidazole, piperacillin-tazobactam, vancomycin, or a combination of these drugs, and it was adjusted according to the results of sensitivity testing. The mean duration of antibiotic therapy was 28.16 ± 15.18 days. Thirty-one patients (54.39%) underwent surgery. Among them, 23 (74.19%) underwent stereotactic drainage and 8 (25.81%) underwent craniotomy. At discharge, 14 patients (24.56%) had a poor outcome, including 2 (3.50%) who died, and the remaining 43 (75.44%) had a good outcome. Multivariate analysis was performed to identify factors associated with a poor outcome. The following variables were tested: headache, confusion, age, adjacent site infection, and type of surgery. The presence of headache was independently associated with a poor outcome (odds ratio 6.010, 95% confidence interval 1.114–32.407, $p = 0.037$; Table 2).

Table 2
Risk factors for poor outcome in patients with primary brain abscess

	Good outcome (n = 43)	Poor outcome (n = 14)	Total (n = 57)	Univariate analysis		Logistic regression analysis		
				χ^2	p	OR	p	95% CI
Age, years, n (%)								
< 40	3 (50.00)	3 (50.00)	6	2.305	0.328	0.365		
40–60	25 (78.13)	7 (21.87)	32					
> 60	15 (78.95)	4 (21.05)	19					
Male n (%)	31 (73.81)	11 (26.19)	42	0.017	0.898			
Symptom duration at admission* (days)	5.50	5.50		U = 264.50	0.575			
Duration of hospitalization* (days)	30.00	21.00		U = 231.00	0.194			
Adjacent site infection, n (%)	12 (92.31)	1 (7.69)	13	1.541	0.214	0.051		
Comorbidities, n (%)	10 (71.43)	4 (28.57)	14	0.002	0.965			
Headache, n (%)	26 (86.67)	4 (13.33)	30	4.309	0.038	0.037	6.010	1.114–32.407
Fever, n (%)	18 (69.23)	8 (30.77)	26	0.994	0.319			
Confusion, n (%)	12 (66.67)	6 (33.33)	18	0.510	0.475	0.164		
Hemiplegia, n (%)	18 (69.23)	8 (30.77)	26	0.994	0.319			
Epilepsy	5 (62.50)	3 (37.50)	8	0.841	0.359			
Aphasia	5 (71.43)	2 (28.57)	7	0.000	1.000			
Increased WBC count	22 (73.33)	8 (26.67)	30	0.151	0.697			
Number of abscesses								

	Good outcome (n = 43)	Poor outcome (n = 14)	Total (n = 57)	Univariate analysis		Logistic regression analysis		
				χ^2	p	OR	p	95% CI
Single	31 (77.50)	9 (22.50)	40	0.048	0.827			
Multiple	12 (70.59)	5 (29.41)	17					
Abscess location, n (%)								
Basal ganglia	1 (25)	3 (75)	4	6.82	0.313			
Frontal lobe	22 (78.6)	6 (21.4)	28					
Temporal lobe	12 (75)	4 (25)	16					
Parietal lobe	11 (68.8)	5 (31.2)	16					
Occipital lobe	6 (54.5)	5 (45.5)	11					
Cerebellum	7 (77.8)	2 (22.2)	9					
Brainstem	1 (50)	1 (50)	2					
Abscess volume, n (%)								
< 1 cm ³	6 (85.7)	1 (14.3)	7	1.258	0.620			
1–10 cm ³	20 (80.0)	5 (20.0)	25					
> 10 cm ³	17 (68.0)	8 (32.0)	25					
Surgery, n (%)								
No	17 (65.38)	9 (34.62)	26	3.852	0.132	0.685		
Drainage	18 (78.26)	5 (21.74)	23					
Craniotomy	8 (100.00)	0	8					

Discussion

The average age of the study participants was 52 years, and 56.14% of them were aged between 40 and 60 years. There are inconsistent reports of the age predilection of brain abscess. Some studies show that individuals older than 40 years are more susceptible to brain abscess[4, 7, 8], whereas others show that

brain abscess occurs more often in individuals younger than 40 years[9, 10]. The average age of participants in a meta-analysis conducted in 2014 was 33.6 years[1]. Therefore, the age group that is most affected is difficult to determine, and it may depend on the underlying predisposing factors for brain abscess. Moreover, we found that regardless of age, men were more susceptible to brain abscess than women, with a ratio of 2.8:1. Other authors have reported similar findings[7, 11], although a female predilection was observed in one of these studies[7]. Headache, fever, and hemiplegia were the most common symptoms in our study, occurring in 52.63%, 45.61%, and 45.61% of the patients, respectively; this was consistent with previous reports[1, 8, 12]. Headache, fever, and focal neurological deficit are regarded as the classical symptoms of brain abscess. However, few patients experience all three symptoms simultaneously[1]. In our study, the classical triad of headache, fever, and hemiplegia was only observed in eight patients (14.04%); this was lower than the previously reported rate of 20%[1]. The presentations were insidious and atypical, and the absence of this classical clinical triad decreases the likelihood of brain abscess being suspected on initial examination.

Here, 42.11% of the patients had some predisposing factor, and 22.81% (13 patients) had adjacent site infection, including paranasal sinusitis, chronic otitis media, mastoiditis, and dental infection. A previous study in a developing country found that otitis media was the most common source of intracranial suppuration[7]. However, this was not the case in our study, possibly due to improvements in the treatment of otitis media in recent decades. It is important to recognize predisposing factors because eliminating the underlying infection helps to avoid prolonged infection. Comorbidities, including diabetes mellitus, tumor, liver cirrhosis, and granulocytopenia, were noted in 24.56% of the patients in our study. Other comorbidities, including human immunodeficiency virus infection, autoimmune disease, and immunosuppressive therapy, were reported in a previous study[13]. However, none of our patients had these comorbidities, and diabetes mellitus was the most common comorbidity observed in this study. The relationship between diabetes mellitus and susceptibility to infection has been reported[14]. Impaired glucose control may affect host defense and increase the risk of brain abscess.

Only half of the patients in this study had an elevated peripheral white blood cell count. Indicators of inflammation such as white blood cell count, erythrocyte sedimentation rate, and C-reactive protein level play a limited role in the diagnosis of brain abscess[1]. An increased cell count in the CSF, which indicates leptomeningeal affection, was found in 94.44% of the patients who underwent lumbar puncture in this study, and this finding helped us determine the nature of the brain lesion in those patients. However, not all patients with brain abscess show leptomeningeal involvement, and the role of lumbar puncture in its diagnosis is limited. Moreover, lumbar puncture should be performed with caution. There are reports of clinical deterioration after lumbar puncture due to exacerbation of the brain tissue shift caused by the brain abscess, which may lead to death[1]. The rate of CSF culture positivity in our study was 25%, which is similar to the rate of 24% reported in a previous study[1]. Therefore, it is difficult to determine the causative organism solely based on the result of CSF culture.

The rate of pus culture positivity in our study was 46.15%, which is far lower than the previously reported rate of approximately 70%[1, 13]. This may be because we initiated antibiotic therapy before obtaining

samples for culture, and the standard culture protocol followed at our hospital may result in certain organisms going undetected. The use of next-generation bacterial sequencing may help to identify more pathogens. In our study, gram-negative enteric bacteria were the most common pathogens observed in pus, and ceftriaxone, which is effective against gram-negative bacteria, was often initially administered as empirical antibiotic therapy. In previous studies, the most commonly observed bacteria in patients with brain abscess were those of the streptococcus species. However, various pathogens, including staphylococci, gram-negative enteric bacteria, and fungi, have been isolated from brain abscess specimens[1, 13]. Moreover, a previous study reported the frequent occurrence of the gram-negative enteric bacteria *Klebsiella pneumoniae* in Asian patients[1]; it caused 10% of all brain abscesses in Taiwan. Multiple abscesses due to *Klebsiella pneumoniae* are often found in organs such as the brain, liver, and lungs, especially in patients with diabetes mellitus or liver cirrhosis. In our study, *Klebsiella pneumoniae* was found in the pus of four patients, and one patient with diabetes had comorbid liver abscess.

The most common brain abscess location in our study was the frontal lobe, followed by the temporal and parietal lobes, and most of the patients had single lesions. This result is consistent with a previous report[1, 7]. However, another study found that the temporoparietal region is the most common brain abscess location[15]. The location of a brain abscess partly depends on the route of infection transmission. Paranasal sinusitis is often associated with a frontal lobe abscess and otitis media and mastoiditis are associated with temporal lobe or cerebellar abscesses.

Here, 54.39% of the patients underwent surgery. Most of them underwent stereotactic drainage, while others underwent craniotomy. The rate of surgical treatment was lower than that reported previously, (60–87%)[1, 7, 8]; the reason for this is unclear. Further research is needed to determine the reason for this difference. Although craniotomy was once thought to be associated with lower recurrence and mortality rates than stereotactic drainage[16], with increasing availability of computed tomography, the difference between craniotomy and stereotactic drainage has become uncertain. A previous study found no difference in the effects, outcomes, and complications of these two surgical techniques[7]. Even after surgical treatment, long-term antibiotic therapy (4–8 weeks) was necessary. Moreover, 75.44% of the patients in our study had a good outcome, and only two patients died. The mortality rate, which was approximately 8–53% before 2014, has decreased in the recent decades[17], and it has been reported as 4.3% in 2018[13]. The mortality rate in our study was lower than that in previous studies. We believe that this may reflect improvement in the treatment of brain abscess, although selection bias related to patient recruitment from our hospital, which is a tertiary hospital, should be considered. Previous studies have reported inconsistent findings regarding the factors associated with outcome. Landriel et al.[4] found that age, immunosuppression, and hematogenous spread were associated with a poor outcome. Zhang et al. [7] revealed that gender was associated with an unfavorable outcome. Another study[15] found that consciousness at presentation had prognostic value. Nevertheless, our findings indicate that headache, and not confusion, age, adjacent site infection, or type of surgery, influenced outcome. As a classical symptom of brain abscess, headache indicates possible intracranial hypertension, which may lead to a poor outcome.

This study has several limitations. First, the sample size was small. Second, it was a retrospective, single-center study. Consequently, our findings may not be generalizable to patients in different regions, and some data, including inflammatory marker levels, could not be collected and analyzed. Multicenter studies with larger samples should be conducted in the future.

Conclusions

In conclusion, we retrospectively analyzed the data of 57 patients diagnosed with primary brain abscess over ten years. We found that men were more susceptible to primary brain abscess than women, and the most common comorbidity was diabetes mellitus. Gram-negative enteric bacteria, especially *Klebsiella pneumoniae*, were the most common pathogens. The presence of headache may be associated with a poor outcome.

Abbreviations

CSF: cerebrospinal fluid

Declarations

Ethics approval and consent to participate

This study was approved by the ethics committee of the Second Affiliated Hospital of Fujian Medical University (NO: 2020-372). All methods were performed in accordance with the relevant guidelines and regulations. As per national legislation and institutional guidelines, it was not necessary to obtain written informed consent to participate from the participants of this study. And the ethics committee of the Second Affiliated Hospital of Fujian Medical University approved the waiver for the need of informed consent.

Consent for publication

Not applicable

Availability of data and materials

Data are available from the corresponding author upon reasonable request.

Competing interests

None

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Author Contributions

LW and JH designed the study. LW, JH, and HW conducted the medical record review. LW, JH, HW, and HH performed the data collection. LW, BW, and WW conducted the statistical analysis. LW, HH, and JH wrote the manuscript. JH and HW contributed equally to this article and can be considered as co-first authors. All the authors critically read and approved the final manuscript.

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