Etiology, management and outcome of brain abscess

An 11-year single-center study from China

Chenran Zhang, MD1, Liuhua Hu, MD2, Xuehua Ding, MD, PhD1, Jinxiang Huang, MD1 and Guohan Hu, MD, PHD1

1Department of Neurosurgery, Changzheng Hospital, Second Military Medical University, Shanghai, China.
2Department of Cardiology, Renji Hospital, Shanghai Jiaotong University School of Medicine, Shanghai, People’s Republic of China;
Chenran Zhang and Liuhua Hu contributed equally to this study.

*Corresponding author: Chen-Ran Zhang, Shanghai Institute of Neurosurgery, Department of Neurosurgery, Shanghai Changzheng Hospital, No. 415, Feng-Yang Road, Shanghai, China 200003. Telephone: +86-21-81885692; Fax: +86-21-6358611 E-mail:christopher0708@163.com.

Abstract

Objective: To determine the demographics, management, the variables that affect the outcome in subjects with brain abscesses treated at a single center over an 11-year period.

Methods: The authors retrospectively analyzed data in 60 patients with brain abscesses surgically treated with stereotactically guided aspiration or open craniotomy excision in Shanghai Changzheng Hospital between January 2001 and December 2011. Such variables as age, gender, Glasgow Come Scale (GCS) at admission, clinical presentation, location, number of lesions, predisposing factors, mechanism of infection, etiological agent, and therapy were analyzed independently. Postoperative outcome was appraised using the Glasgow Outcome Scale (GOS) 6 months after surgery; 1–3 points was considered a poor outcome and 4- 5 points a good outcome on this scale.

Results: Eighty-two abscesses were diagnosed and surgically managed in 60 patients. The mean patient age was $47.33 \pm 2.18$ years (range 9-76). The male-to-female ratio in our study was 3.62:1. Most frequent clinical presentations included headache (46; 76.67%), fever (31; 51.67%), and focal neurologic deficits (17 ; 28.33%). The mostly common predisposing factors included
postneurosurgery (10; 16.67%), chronic otitis media (8; 13.33%), congenital heart disease (5; 8.33%), whereas 29 (48.33%) patients had no identifiable predisposing risk factors. The frontal lobe was the most common site of involvement in the patients (19; 31.67%). Stereotactically guided aspiration was the treatment of choice for 36 patients (60%), whereas 18 (30%) of the cases were managed through open craniotomy excision (OCE), and the remaining 6 patients (10%) received radical mastoidectomy combined with OCE therapy. Positive cultures were obtained in only 8 of the cases (13.33%), in which the most common isolate was Streptococcus milleri (6 cases). Outcome was favorable in 78.33% (n=47) of the subjects. The mortality rate in our study was 20% (12 cases). The analysis of variables including sex, age, GCS on admission, symptoms, predisposing risk factors, location of abscess and mode of operation, revealed that only sex (P=0.006; OR=14.003) was associated with poor outcomes.

**Conclusions:** Findings suggest that patients older than 40 years are most susceptible to brain abscess. Gender is the only predictor of favorable prognosis. Mortality due to brain abscess was not directly related to surgery nor surgical technique.

**Keywords** Brain abscess; chronic otitis media; Streptococcus milleri; prognosis

**Background**

Brain abscesses are a common occurrence in the developed world, with an incidence of up to 2% of all space occupying lesions. They are even more common in developing countries, with an incidence of up to 8% [1]. Despite the advent of modern neurosurgical techniques including stereotactic brain biopsy and aspiration, better culture techniques, new antibiotics and modern noninvasive neuroimaging procedures, brain abscess still poses a public health challenge in developing countries.

This report is based on our experience with 82 brain abscesses surgically managed in 60 patients over an 11-year period at one single hospital and analyzes the prognostic factors and strategies of treatment.

**Methods**
Patients and enrollment

Sixty patients with a total of 82 brain abscesses verified by postoperative pathology were surgically treated between January 2001 and December 2011 at the department of Neurosurgery in Shanghai Changzheng Hospital. Demographic data, neurological status at admission, clinical presentation, predisposing factors, anatomical location, number of lesions, surgical techniques, organism culture and the neurological outcome from the electronic hospital data forms of all the patients were retrospectively analyzed (Table 1). Written approval was obtained from the ethics committee of Shanghai Second Military Medical University for this study. A written consent in accordance with the ethical committee standards was given to and signed by participating patients (by post or outpatient follow-up). The consent obtained for patients that died was signed by the same clientele as their duration of hospital stay.

The review only included those patients surgically treated for their BA, confirmed by operation and post-pathology, with stereotactically guided aspiration or open craniotomy excision. A predisposing factor was defined as any event or condition that was directly related to the onset of a BA. Routes of transmission were classified as infection originating through hematogenous spread, contiguous spread, neurosurgical procedures, open head injury, or unknown causes. The neurological status at admission was evaluated using the Glasgow Coma Scale (GCS), whereas outcome was appraised using the Glasgow Outcome Scale (GOS), graded with a five-point score at 6 months after surgery at the outpatient clinic. A score between 0 to 3 points was considered a poor outcome and a score between 4 to 5 points a good outcome. In all cases we conducted standard laboratory tests, including a complete blood count, erythrocyte sedimentation rate, C-reactive protein level, blood cultures and serum chemistry. Case findings were based on the review of microbiology laboratory data for all intracranial samples. All intracranial pus samples were transported to the microbiology laboratory at Changzheng Hospital without delay for microscopy, culture, and sensitivity testing according to the laboratory’s standard
operative procedure.

Patients with the following conditions were excluded from the study: evidence of neurological symptoms unrelated to brain abscess, subject not having undergone drainage procedure or intraoperative pus sampling, patients lost to follow-up during the study period.

**Statistical analysis**

Statistical analysis was performed using SPSS for Windows (SPSS17.0). The groups were compared using the Mann-Whitney U test for continuous variables, and the \( \chi^2 \) test and its continuity correction or Fisher exact test for categorical variables, as appropriate. Univariate analysis, including characteristics of patients and abscesses, were performed to determine the association of clinical results with other factors. Then, logistic-regression analysis was performed to determine the independent association of clinical variables or unfavorable outcomes with other factors. The cutoff in the univariate analysis was \( p<0.20 \). A \( p<0.05 \) was considered statistically significant.

**Medical Regimen**

Initial empirical antimicrobial therapies were selected in accordance with the portal of entry and the anatomical location of the abscess. Our initial empirical antimicrobial therapy includes a combination of vancomycin, ceftriaxone and metronidazole. Between 3 and 5 days later, we either continued with the same treatment or switched to more sensitive antibiotics as soon as the results of sensitivity tests became available. In sum, antibiotic therapy lasted for 4-8 weeks in accordance with the therapeutic response and neuroimaging findings. Infectious disease specialists regularly supervised this treatment.

Low-dose corticosteroid (intravenous Solu-Medrol, given in a dosage of 40mg/12 hours) was used to manage perilesional edema in cases of considerably significant mass effect. However, as this drug can lead to reduced MRI contrast enhancement, delayed capsule formation, increased risk of intraventricular rupture and decreased antibiotic penetration, administration was discontinued as soon as the patient was
stabilized. Seizure prophylaxis or antiepileptic medication was given in all cases and continued for extended periods.

**Surgical therapy**

The surgical options in this study included stereotactically guided aspiration and open craniotomy excision. We recommended surgical treatment for abscesses >2.5 cm, signs of brain herniation secondary to space-occupying lesions or ventricular proximity, abscess growth during medical therapy or uncertain etiology associated with neurological deterioration. On the contrary, these procedures are not recommended in the presence of cerebritis without imaging evidence of necrosis or capsule formation, or when the lesion location is inaccessible.

Stereotactically guided aspiration was the therapy of choice over open craniotomy excision because it is less invasive, thus reducing the likelihood of neurological sequelae. This procedure was carried out in lesions in the vicinity of or at eloquent brain areas, in deep locations (brain stem or basal ganglia region) or ventricular proximity and in patients with multiple abscesses or with a poor general condition. If the size of the abscess on CT or MR images obtained after the first aspiration increased or was not reduced despite antibiotic therapy, aspiration was repeated.

Patients with poor response to repeated aspirations and medical treatment underwent complete excision of abscesses through open craniotomy excision (OCE). It was indicated in most BA secondary to open head injury to remove bone chips, foreign bodies and devitalized tissue, in multi-loculated BA that are more likely to have recurrence, in deep-seated abscesses (for example, a cerebellar abscess) and in fungal etiology lesions. Postoperative abscesses where bur hole aspiration would hinder the fusion of the bone flap also underwent complete abscess excision through OCE. Patients with chronic otomastoiditis and cerebellar abscess underwent radical mastoidectomy and OCE.

During surgical procedure, we completely drained the abscess and rinsed the abscess cavity with physiological salinens containing gentamicin until the effluent
was clear. When the abscess broke into ventricular then leading to ventriculitis, we performed external ventricular drainage or lumber puncture combined with intrathecal or intraventricular injection of sensitive antibiotic.

**Imaging**

Preoperative computed tomography (CT) and magnetic resonance imaging (MRI) scans with enhancement were obtained in all patients. On Conventional MRI, pyogenic brain abscesses were hypointense signal in T1WI and hyperintense in T2WI, with ring-shaped enhancement and extensive surrounding edema. Conventional MRI, associated with DWI and MRS were performed when it was difficult to discriminate brain abscesses from cystic or necrotic tumors. MRS in patients with abscess had lactate, amino acids (including valine, alanine, and leucine), and acetate peaks; Spectra for patients with cystic or necrotic tumors showed only lactate peaks. Hyperintensity was seen in all the pyogenic abscess cavities and hypointensity in all the cystic and necrotic tumors on diffusion-weighted images.

**Fig legends**

Fig. 1: Pre- and post-operative MRI images of an abscess of the right basal ganglion region; Fig: 2 Cerebellar multiple abscesses; Fig: 3 Brain abscess complicated with ventriculitis.

**Results**

In our series, there were 47 male (78.33%) and 13 female (21.67%) patients (the male-to-female ratio was 3.62:1), ranging in age from 9 to 76 years (median 47.33 ± 2.18 years) at the time of diagnosis. At the time of admission, 46 (76.67%) patients complained of headaches and 31 (51.67%) had fever, while neurological deficits were present in 17 (28.33%) patients. Fourteen (23.33%) patients had nausea and 17 (28.33%) patients presented with epilepsy. Four (6.67%) patients complained of visual disturbance, which was connected with occipital lesions. Aphasia was observed in two (3.33%) patients. In our study, 52 of the 60 patients (86.67%) had good GCS scores at admission (GCS 14-15/15), which had no effect on the clinical outcome.

Laboratory data had little diagnostic or prognostic value. Twenty-five patients
had elevated peripheral white blood cell counts, all with a predominant leukocytosis. Eleven patients (18.33%) had adjacent localized cranial infection, chronic otitis media (COM), paranasal sinusitis, or tooth abscess as a predisposing factor. Two (3.33%) patients were immunosuppressed on admission. Five (8.33%) patients had congenital heart disease. Sixteen (26.67%) patients had posttraumatic or postoperative abscesses. Twenty-nine (48.33%) patients had no identifiable predisposing cause. The frontal lobe was the most common abscess location in the patients (n=19; 31.67%), followed by temporal (n=13; 21.67%) and occipital (n=10; 16.67%) region. BA were single in 76.67% (n=46) of the subjects and multiple in 23.33% (n=14).

In 60% (n=36) of the cases, the treatment of choice was stereotactically guided aspiration, whereas in 30% (n=18) the abscess was managed through open craniotomy excision, and 6 patients (10%) received radical mastoidectomy combined with OCE therapy. One patient was immunosuppressed after liver transplantation. His left frontal abscess eroded into the skull base and ethmoid sinus. He received Intranasal Ethmoidectomy and further aspiration.

Due to many patients being on antibiotic therapy prior to surgery, positive cultures were obtained in only 8 (13.33%) of the cases, in which the most common isolate was streptococcus milleri (6 cases, 75%).

Of the 60 patients included in this study, outcome was favorable in 78.33% (n=47) of the subjects. The analysis of variables including sex, age, GCS on admission, symptoms, predisposing risk factors, location of abscess and mode of operation, revealed that only male (P=0.006; OR=14.003, 95% CI=2.129~92.081) was associated with good outcomes.

The mortality rate in our study was 20% (12 cases). Ten patients died in the immediate postoperative period from complications and 2 patients who had received operation due to glioblastoma died after discharge. Of the 10 patients who died in hospital, two were immunosuppressed at the time of diagnosis and died from multisystem organ failure. Two mortalities were the result of lethal complications not directly related to the surgical procedure: hematoma in the midbrain and operative area, respectively. In three patients, the abscesses broke into the ventricular system
and the patients died from ventriculitis and infectious shock. The other three deaths were due to postoperative brain herniation from high intracranial hypertension. Seizures were the most common form of post-operation complication and were treated with thorough anti-epileptic therapy. After discharge from the hospital, the patients were monitored at the outpatient clinic for 7~19 months. After 15 months, 12 patients were lost to follow-up and of the remaining patients who could be assessed, neurological scores remained unchanged. In the follow-up period, none of the patients who survived showed clinical or neuroimaging signs of recurrence.

**Discussion**

The male-to-female ratio in our study was 3.6:1; that is, males were found to be more affected than females in the present study, irrespective of the age group. Similar observations have been reported in different parts of the world [2,3,4]. However, Federico Landriel et al [5] reported 59.3% of the patients with intracranial abscesses were female.

In our study, the mean age of the patients was 47.33±2.18 years (range 9-76); 42 subjects (70%) were older than 40 years. Our results were similar to previous report [5] with respect to susceptible age. On the contrary, some authors reported that brain abscess occurs in the younger age group, usually during the first three decades of life [5,6,7,8]. In Manzar N’s study, 34 subjects (64.2%) were older than 15 years and the majority of patients were younger than age 40 years [4]. Similarly, in a study carried out by Sinha et al, 74.89% of the patients were younger than 40 years [3].

In our series, 86.67%(52/60) of the patients had good a GCS score at admission (GCS 14-15/15) , which had no bearing on the clinical outcome. Similarly, in Landriel F’s study, 79.6% of the patients had a good GCS score at admission [5]. In view of this distribution, we can draw no conclusions regarding the effect of neurological deterioration on the outcome; however, there is adequate evidence that this is one of the most important factors determining prognosis [9,10,11]. Previous studies found an alteration in the level of consciousness present in up to two-thirds of patients [12,13]. In Manzar N’s study, 69.8% of the patients were brought to the hospital with an
altered state of consciousness [4]. The level of consciousness at presentation has been shown by other authors to be of great prognostic value [14,15].

In our study, symptoms on presentation did not correlate with the GOS results at 6 months. Headache was the most common symptom documented, occurring in 76.67% of the subjects. Similar results have been reported in several other studies. This was followed by fever and focal neurologic deficits in 51.67% and 28.33% of the patients, respectively. Despite being the most common, the “classic” triad of headache, fever and focal neurological deficits was seen together in only 5% (n=3) of the cases. We consider that this classic presentation described by Renton et al is helpful but actually has low sensitivity [5,10,11,16,17,18,19,20]. Seizures were present in the 28.33% of the cases, comparable to incidence rates presented in other large series [9,15].

The route of transmission was contiguous infection in 18.33% (n=11) of the cases and this determined which region of the brain was affected. For example, otogenic infections were associated with temporal or cerebellar abscesses. However, 41.18% of the frontal lesions had unknown predisposing causes.

In most large series of brain abscesses from developing countries, middle ear infection has been reported to be the most common source of intracranial suppuration and this is reflected in our study (8/60=13.33%). However, there has been a decline in developed countries in cases of CSOM [21]. Five patients had underlying congenital heart disease (8.33%).

Abscesses of unknown causes accounted for 48.33% (n=29) of the subjects in our series, a percent higher than the values reported for other series [4,5,10,11,18]. The frontal lobe was the most common abscess location in the patients (31.67%), followed by the temporal (21.67%) and occipital (16.67%) regions. However, in a study carried out by Cavoğlu H et al, the temporoparietal region was the most commonly affected location [15]. BA were single in 76.67% (n=46) of the subjects and multiple in 23.33% (n=14), which were similar with the findings presented in Landriel F’ series [5].

In our series, stereotactically guided aspiration was the treatment of choice for 36
patients, whereas 30% of the cases were managed through open craniotomy excision, and 6 patients received radical mastoidectomy combined with OCE therapy. The results of these surgical techniques presented no significant differences in terms of outcome or associated complications. The effectiveness of stereotactically guided aspiration and open craniotomy excision differs across multiple reports. Xiao et al, who reported similar effectiveness between the two procedures but significantly lower mortality (p=0.02) with open craniotomy excision [11]. Mampalam et al reported less BA recurrence in open craniotomy than in stereotactic aspiration [12]. Ratnaike TE et al reviewed the Ovid Medline database 1950-2009 with the year range limited to 1990-2009 to identify all articles relating to brain abscess. They found the high mortality rates from aspiration in the pre-computer tomography era decreased dramatically after computer tomographic scanning became available. In their review, the mean mortality for aspiration post-1990 was 6.6% for publications with more than five patients. With surgical excision by craniotomy, the mean mortality in the same period was 12.7%. They concluded that aspiration may be the first surgical choice in patients with supratentorial parenchymal brain abscesses [22].

In our series, negative cultures totaled (52/60)86.67%. This is much higher than the rates observed by other authors [4,5,9,15,23]. Monomicrobial etiology was found to be a feature of brain abscesses in our study, and the same trend has been noted in various studies throughout the world [4,25,26,27]. Where cultures are negative, empiric therapy must be administered against the suspected causative agent. The following are the possible reasons for the high culture negative rate. Firstly, due to the loose antibiotic management policy in China, the preventative use of antibiotics is very common. Secondly, the intracranial pus samples could not be transported to the microbiology laboratory promptly. Lastly, owing to the defect of experiment method, some special organisms, such as anaerobic bacteria, could not be cultured under common circumstance.

Saito et al diagnosed culture-negative brain abscess with Streptococcus intermedius infection through direct nucleotide sequence analysis of the 16s ribosomal RNA gene [28]. Al Masalma et al performed a 16S rDNA-based
metagenomic analysis of cerebral abscesses from patients diagnosed from 2006 through 2010. By detecting polymicrobial infections in 19 patients, their strategy was significantly more discriminatory and enabled the identification of a greater number of bacterial taxa than did culture and conventional 16S rDNA polymerase chain reaction (PCR) and sequencing, respectively (P < 0.01). They concluded that cloning and sequencing of PCR-amplified 16S rDNA is a highly valuable method to identify bacterial agents of brain abscesses [29].

The outcome of the patients was assessed using the Glasgow Outcome Scale. Of the 60 patients included in this study, outcome was favorable in 78.33% (n=47) of the subjects. The mortality rate in our study was 20% (12 cases). This is similar to the rates observed by other authors, who have reported mortality rates between 8% and 53% [19]. The analysis of variables including sex, age, GCS on admission, symptoms, predisposing risk factors, location of abscess and mode of operation, revealed that only female was associated with poor outcomes. However, Manzar et al reported that the most important factors influencing mortality was the neurologic condition of the patient at the time of admission [4]. Landriel et al revealed that age, immunosuppression and hematogenous spread were all associated with poor outcomes [5]. As far as therapeutic effect is concerned, Park SH et al demonstrated that MRI plus FDG-PET improved the accuracy of assessing therapeutic responses to antibiotics treatment of brain abscess and aided in optimizing therapy [30].

**Conclusions**

In our study, patients older than 40 years are the most susceptible to brain abscess. Male is the only predictor of favorable prognosis. Mortality of brain abscess was not directly related to surgery or surgical technique. However, a large-scale prospective multi-center study is recommended for further evaluating the ethnic and geographic differences and other risk factors for brain abscesses in underdeveloped countries like China.

**Competing interests**

The authors declare that they do not have any financial or non-financial competing interests.
Authors’ contributions
ZCR conceived the concept and design of the study. Data was gathered by HLH and HJX. ZCR and DXH performed the data analysis. ZCR, HLH and HGH wrote the manuscript. All authors read and approved the final manuscript.

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The Institute for Medical Statistics at the Second Military Medical University provided assistance on data analysis with SAS.

References


Table 1. Predictors of Unfavorable Outcomes in intracranial abscesses

<table>
<thead>
<tr>
<th>Variables</th>
<th>Favorable Outcomes (n=47)</th>
<th>Unfavorable Outcomes (n=13)</th>
<th>Total (n=60)</th>
<th>p Value</th>
<th>P, Regression (OR, 95% CI)</th>
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OR, odds ratio; CI, confidence interval;