Heliyon 9 (2023) e16003

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Research article

Clinical and radiological characteristics of brain abscess due to different organisms in hospitalized patients: A 6-year retrospective study from China

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ARTICLE INFO

Keywords:
Brain abscess
Streptococcus viridans
Confusion
Clinical features
Radiological features

ABSTRACT

Background: Brain abscess (BA) is a rare but life-threatening infection. Early identification of the pathogen is helpful to improve the outcomes. This study aimed to describe the clinical and radiological features of patients with BA caused by different organisms.
Methods: A retrospective, observational study of patients with known etiologic diagnosis of BA in Huashan Hospital Affiliated to Fudan University in China between January 2015 and December 2020 was conducted. Data on patient demographics, clinical and radiological presenting features, microbiological results, surgical treatment, and outcomes were collected.
Results: Sixty-five patients (49 male, 16 female) with primary BAs were included. Frequent clinical presentations included headache (64.6%), fever (49.2%) and confusion (27.3%). *Streptococcus* viridans was associated with thicker wall of abscesses (6.94 ± 8.43 mm for *S.* viridans versus 3.66 ± 1.74 mm for other organisms, $P = 0.031$) and larger oedema (89.40 ± 15.70 mm for *S.* viridans versus 74.72 ± 19.70 mm for other organisms, $P = 0.023$). The independent factor associated with poor outcome identified by multivariate analysis was confusion (Odds ratio 6.215, 95% confidence interval 1.406–27.466; $P = 0.016$).
Conclusions: Patients with BAs caused by *Streptococcus* species had nonspecific clinical signs, but specific radiological features, which might be helpful for early diagnosis.

1. Introduction

With the development of imaging and surgical techniques, the success in the treatment of brain abscess (BA) has increased significantly [1], but it still remains a kind of disease with high disability and its incidence might be underestimated. The reported incidence rate of BA ranged from 0.33 to 0.4 cases per 100,000 population per year in developed countries [2,3], while it was much higher in developing countries [4]. A study in Taiwan revealed that the annual incidence of BA was 1.88/100,000 [5], but accurate figures are not available for large parts of China.

The outcome of patients with BA is improved if the etiologic agent is identified and antimicrobial therapy is targeted. The delay in antibiotic treatment was associated with a 50% increase in mortality risk per day [6], and may lead to unnecessary broad-spectrum

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https://doi.org/10.1016/j.heliyon.2023.e16003
Received 27 September 2022; Received in revised form 22 April 2023; Accepted 28 April 2023
Available online 2 May 2023

antibiotic usage and induce antibiotic resistance. BAs are usually caused by bacteria, although can also be caused by other pathogens including fungi and protozoa, and sometimes polymicrobial infection should be considered [7]. The causative pathogens of bacterial BAs vary according to geographic location, age, underlying medical conditions, and mode of infection [8–10]. A meta-analysis of cohort studies summarised data of 9699 patients from 123 studies and showed that the most common causative microorganisms were *Streptococcus* (34%) and *Staphylococcus* species (18%) [11]. Anaerobes are also described as important contributors to BAs; however, evidence for the presence of anaerobes is limited due to the sensitivity of laboratory diagnosis [12]. Nocardial BA is relatively rare, accounting for approximately 1–2% of all BAs, and its mortality rate is three times higher than that of other types of bacterial BAs [13]. Studies based on pathogen is warranted.

This study aimed to describe the clinical features, microbiology, radiological characterisation, and clinical outcomes of patients with BA due to different organisms in a tertiary hospital in Shanghai, and to investigate important characteristics for early diagnosis.

2. Materials and methods

2.1. Study design and patients

We collected data retrospectively from the electronic patient records of Huashan Hospital Affiliated to Fudan University, a large tertiary hospital in China. Patients discharged between January 2015 to December 2020 were identified using ICD 10 code of BA. Eligible patients fulfilled all of the following criteria: (1) magnetic resonance imaging and/or computed tomography findings of BA; (2) positive microbiological results in intracranial samples or cerebrospinal fluid (CSF) detected by conventional testing or metagenomics next-generation sequencing (mNGS), which were analyzed by two independent senior clinicians to determine whether the results were relevant to BA. Patients with a history of intracranial surgery on admission were excluded.

Anonymized details of patient demographics, clinical and radiological presenting features, microbiological results, routine blood examination, Charlson's weighted index of comorbidity [14], treatment, and outcomes were collected from the electronic hospital data. Immunosuppressed status was defined as receipt of corticosteroid (at least 10 mg of prednisone or an equivalent dosage daily) for more than 2 weeks or of antineoplastic chemotherapy or antirejection medication 4 weeks before the onset of BA.

2.2. Magnetic resonance imaging (MRI)

Preoperative MRI scans with enhancement using Verio 3T (Siemens) or Signa Excite 3T (GE) were obtained from 44 patients. For conventional MRI, BAs were identified using hypointense signal in T1-weighted image (T1WI) and hyperintense signal in T2-weighted image (T2WI), with ring-shaped enhancement and extensive surrounding oedema [4]. Meanwhile, conventional MRI with diffusion weighted imaging (DWI) was performed in 30 patients, and hyperintensity was observed in all the pyogenic abscess cavities. The lesion number, size, location, range of oedema and thickness of the abscess wall in cross-section were measured for further analysis. Deep abscesses were defined as those located in the basal ganglia and thalamus of brain, while superficial abscesses were those occurring in other areas such as frontal lobe, parietal lobe, temporal lobe, occipital lobe and cerebellum [15].

2.3. Patient evaluation

The primary outcome measure was Glasgow Outcome Scale (GOS) scores 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 [16]. All clinical samples were identified using standard method, and susceptibility testing was performed using the disc diffusion method recommended by the Clinical and Laboratory Standards Institute guidelines at the clinical microbiology laboratory of Huashan Hospital.

2.4. Statistical analysis

Statistical analyses were performed using IBM SPSS 22.0 package program. Continuous variables were expressed as mean ± SD and compared using the Mann-Whitney *U* test or Student's *t*-test. Categorical variables were expressed as the percentage of the total number of patients analyzed and compared using Fisher's exact test or the $\chi 2$ test, as appropriate. The predictors of poor outcome with $P < 0.2$ determined by univariate analysis were entered into a multivariate logistic regression model to identify the independent predictors of poor outcome. All *P* values were two-sided, with a *P* value < 0.05 considered statistically significant.

2.5. Ethics

This study was approved by the Ethics Committee of Huashan Hospital Affiliated to Fudan University, Shanghai, China. The approval number was KY2020-031 and a waiver of patient consent was granted.

3. Results

3.1. Clinical characteristics

Sixty-five nonduplicate patients (49 male, 16 female) were included in this study. Demographic features were presented in Table 1. The median age was 50.69 ± 16.72 years old. Fourteen patients (21.5%) had comorbid chronic illnesses (hypertension, chronic lung disease, diabetes mellitus, liver disease, or cancer). Six patients (9.2%) were with immunosuppressed status, and 3 of them were with *Nocardia* infection. Furthermore, the most frequent clinical presentations at admission included headache (64.6%), fever (49.2%), and confusion (27.3%). The underlying source of the BA was identified in 10 patients, with 4 having dental infection, 2 with a contiguous ear infection, and 1 with both. Three patients had an upper respiratory infection. Two patients had other concomitant locations of abscesses, including liver, spleen and lumbar spine. Thirty patients (46.2%) underwent burr hole aspiration, and 23 (35.4%) received craniotomy cavity incision for treatment. Mean length of hospital stay was 19.02 ± 12.15 days, and average hospitalization expense was 77.21 ± 43.75 thousand Yuan.

3.2. Laboratory and microbiological findings

Thirty-four patients were found to be with elevated peripheral white blood cell counts. Fifty-nine and 6 patients were with positive culture results and mNGS results, respectively. Of the 59 patients with a positive culture result (52 in intracranial samples, 7 in CSF), the most frequent pathogens were *Streptococcus* species [39, (66.1%)], followed by anaerobes [6, (10.2%)], *Nocardia* [4, (6.8%)], and fungi [4, (6.8%)]. The remaining 6 patients had a positive mNGS result (one with intracranial sample and five with CSF), with 2 *S.* species, 1 *Nocardia* farcinica, 1 *Candida* tropicalis,1 *Klebsiella* pneumoniae, 1 *Fusobacterium* nucleatum detected. Totally 4 patients were with polymicrobial infection. *S.* species isolated mostly belonged to the viridans group (97.4%): 16 *Streptococcus* intermedius, 12 *Streptococcus* constellatus, 5 *Streptococcus* anginosus, 2 *Streptococcus* gordoni, 1 *Streptococcus* sanguis, 1 *Streptococcus* mitis, and 1 undifferentiated. All *S.* viridans were susceptible to cefotaxime and levofloxacin, while the susceptibility rates to erythromycin and clindamycin were 44.7% and 34.2%, respectively.

3.3. Foci features

Of the 44 patients evaluated using MRI scans at a median of 1 (interquartile range 0–4) days after hospital admission, 34 (77.3%) had singular BAs and the most common sites were frontal (n = 18; 40.9%) and temporal (n = 5; 11.4%) lobes (Fig. 1A–F), with no deep abscesses observed. The most frequent isolate being *S.* viridans (Table 2). In the 34 singular BAs, the average abscess diameter before surgery was 45.78 ± 13.17 mm, the mean thickness of the abscess wall was 5.78 ± 6.98 mm, and the mean range of oedema was 84.22 ± 18.36 mm. *S.* viridans was associated with thicker wall of abscesses (6.94 ± 8.43 mm for *S.* viridans versus 3.66 ± 1.74 mm for other organisms, $P = 0.031$) and larger oedema (89.40 ± 15.70 mm for *S.* viridans versus 74.72 ± 19.70 mm for other organisms, $P = 0.023$) (Fig. 1A–B), while the difference in abscess diameter was not significant (47.96 ± 10.48 mm versus 41.79 ± 16.84 mm, $P = 0.266$).

Table 1
Demographic and clinical characteristics of patients with brain abscess (N = 65).

Factors	N (%) or (Mean)
Age (years)	50.69 ± 16.72
Sex	
Male	49 (75.4%)
Female	16 (24.6%)
Charlson's weighted index of comorbidity score	
0	51 (78.5%)
1-2	14 (21.5%)
Immunosuppressed status	6 (9.2%)
Symptom	
Headache	42 (64.6%)
Fever	32 (49.2%)
Confusion	18 (27.3%)
Limb weakness	16 (24.6%)
Walking unstable	10 (15.4%)
Concomitant bacteremia	2 (3.1%)
Other concomitant locations of abscesses	2 (3.1%)
Surgical procedures	
Aspiration	30 (46.2%)
Craniotomy	23 (35.4%)
None	12 (18.5%)
Steroids treatment	24 (36.9%)
Pathogen detected	
Streptococcus species	41 (63.1%)
Anaerobe	6 (9.2%)

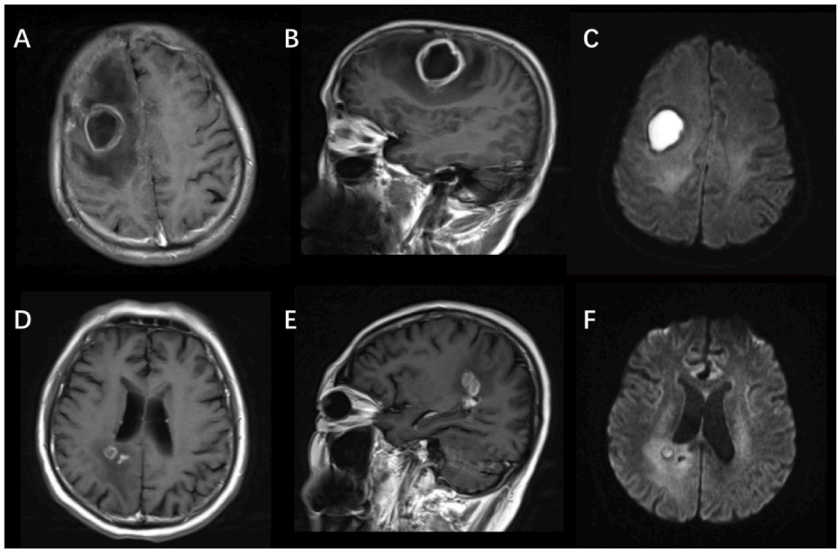

Fig. 1. Example of preoperative magnetic resonance imaging of brain abscess caused by *Streptococcus* species (A–C) and *Nocardia* farcinica (D–F). (A–B) contrast-enhanced T1-weighted image shows a hypointense necrotic center with pus, ring-shaped enhancement of the abscess wall, and a hypointense zone of oedema surrounding the abscess. (C) Diffusion-weighted image shows a hyperintense signal within the abscess. (D–F) contrast-enhanced T1WI and DWI show multiple abscesses due to *N*ocadia farcinica.

Table 2
Microbiological and radiological findings of patients with brain abscess.

Organism	Number of abscess	No. of patients (n = 44)
Streptococci viridans		
	Single	22
	Multiple	3
Nocardia		
	Single	3
	Multiple	2
Fungi		
	Single	3
	Multiple	1
Staphylococcus spp		
	Single	1
	Multiple	2
Anaerobe		
	Single	2
	Multiple	1
Others		
	Single	3
	Multiple	1

3.4. Outcomes

At discharge, poor outcome was observed in 11 patients (16.9%), including 2 (3.1%) who died both with *Nocardia* infection, and the remaining 54 (83.1%) had a good outcome. The statistically significant factors associated with poor outcome by univariate analysis ($P < 0.2$) were age, headache, confusion, and *Nocardia*. The independent factor associated with poor outcome identified by multivariate analysis was confusion (odds ratio [OR] 6.215, 95% confidence interval [CI] 1.406–27.466; $P = 0.016$) (Table 3).

4. Discussion

This study provides a detailed overview of the clinical and radiological presentation, microbiological features, treatment, and outcomes of patients with BA caused by different pathogens. The male predominance in BA noted in this study was consistent with previous studies [5,11]. Most patients in this study had good clinical conditions. Headache and fever were the most common symptoms in BA based on previously published data [17,18], and they were also observed in 64.6% and 49.2% of patients in this study.

The frontal lobe was the most common abscess location in the patients, as described previously [8], suggesting that abscesses might be due to sinusitis [19]. A previous study found that deep abscesses had significantly thicker walls compared to superficial abscess ($P =$

Table 3
Univariate and multivariate analyses of predictor of poor outcome in patients with brain abscess.

Predictors	Good outcome (n = 54)	Poor outcome (n = 11)	Univariate analysis	Multivariate logistic regression analysis		
			P-value	OR	*P*-value	95% CI
Age (years)	49.09 ± 16.76	58.55 ± 14.75	0.086	0.968	0.203	0.921–1.018
Male	40 (74.1%)	9 (81.8%)	0.718			
Headache	37 (68.5%)	5 (45.5%)	0.176	0.560	0.461	0.120–2.615
Fever	26 (48.1%)	6 (54.5%)	0.699			
Confusion	11 (20.4%)	7 (63.6%)	0.007	6.215	0.016	1.406–27.466
Surgery			0.907			
None	10 (18.5%)	2 (18.2%)				
Aspiration	24 (44.4%)	6 (54.5%)				
Craniotomy	20 (37.0%)	3 (27.3%)				
Immunosuppressed status	4 (7.4%)	2 (18.2%)	0.266			
Increased WBC count	27 (50.0%)	7 (63.6%)	0.409			
Streptococcus species	35 (64.8%)	6 (54.5%)	0.517			
Nocardia	3 (5.6%)	2 (18.2%)	0.196	3.496	0.288	0.348–35.152

OR odds ratio; *CI* confidence interval.

0.004) [15]. However, no deep abscess was observed in this study, which made it difficult to draw a direct comparison. The radiological features of abscesses caused by *S.* species included singularity, large size, thick wall, and obvious oedema. The presence of *Streptococcus* intermedius has been reported to be associated with abscess size [12]. The results of the present study showed that the thickness of the abscess wall and diameter of oedema in the *S.* species group (N = 22) were larger than that in the non-*S.* species group (N = 12) ($P = 0.031$; $P = 0.023$), and no statistically significant difference was observed in lesion diameter. This suggests that different pathogens have distinct imaging presentation, which may contribute to early intervention. However, studies analysing the relationship between pathogens and imaging presentation are scarce, so further studies should be conducted.

S. species, including *S.* milleri group, *S.* pneumoniae, etc., are the most common bacteria isolated from patients with BAs [20,21]. Third-generation cephalosporin resistance has been reported in less than 8% of *Streptococci* mitis/oralis isolates in the Netherlands [22]. According to data from the China Antimicrobial Surveillance Network (CHINET) (http://www.chinets.com) in 2021, the resistance rates of *Streptococcus* viridans to cefotaxime, levofloxacin and clindamycin were 0%, 13.1% and 52.3%, respectively. The strains in the present study showed higher susceptibility to cefotaxime and levofloxacin.

It was reported that patients who presented with a nocardial BA were older and immunosuppressed [23]. The percentage of immunosuppressed patients was much higher in the nocardial BA group (3/5, 60%) than in the non-nocardial group (3/60, 5.0%) ($P = 0.004$). However, the median age of patients with nocardial BAs was 56.60 ± 25.41 years old, which was not statistically older than that of patients infected with other pathogens ($P = 0.607$). Moreover, the location, size, and appearance of nocardial BAs cannot be used to differentiate these from other causes of BA. *Nocardia* farcinica BA has a high mortality rate, as high as 20% in immunocompetent patients and 55% in immunocompromised patients [24], consistent with the finding of this study. Although it turned out not to be an independent factor related to poor outcome in the multivariate analysis, we still hope to increase awareness of this rare infection, especially in immunocompromised hosts. Early identification of the pathogen and appropriate identification of specific nocardial species are crucial for initiating appropriate antibiotic therapy to improve patient survival.

Metagenomics next-generation sequencing, which has been used in clinical practice for several years, represents an innovative strategy for detecting potential pathogens including bacteria, viruses, fungi, and parasites [25–27]. In this study, 6 patients were found to have positive mNGS results in intracranial sample and CSF, with 2 *S.* species, 1 *Nocardia* farcinica, 1 *Candida* tropicalis,1 *Klebsiella* pneumoniae, 1 *Fusobacterium* nucleatum detected. A previous report showed the sensitivity and specificity of mNGS for diagnosing infectious disease were 50.7% and 85.7%, respectively, and these values outperformed those of culture, especially for *Mycobacterium* tuberculosis (OR, 4; 95% CI, 1.7–10.8; $P < 0.01$), viruses (mNGS only; $P < 0.01$), anaerobes (OR, ∞; 95% CI, 1.71-∞; $P < 0.01$) and fungi (OR, 4.0; 95% CI, 1.6–10.3; $P < 0.01$) [28]. Despite decreased sensitivity for pathogen detection owing to interference of high nucleic acid background in some samples and relatively expensive cost, mNGS can be a complementary and helpful technology for pathogenic confirmation in certain clinical situations. Up till now, multiple articles have showed the value of mNGS in pathogen detection in meningitis, bloodstream infection, pneumoniae and urinary tract infection. However, data of the diagnostic efficacy of mNGS still lacks in the field of BA. Hu et al. reported 4 surgical samples of BA were detected by NGS and *Bacteroides* fragilis, *S.* intermedius, *Prevotella* oralis, and *Fusobacterium* nucleatum or combinations of them were found, while only 2 of them were with positive culture results [29]. The value of mNGS in the etiological diagnosis of BA was also highlighted by a series of case reports [30–33], especially for some uncommon pathogen, namely *Nocardia* and *Mycobacterium* isolates. More studies, especially large scale prospective studies should be conducted to analyze and evaluate diagnostic value of mNGS in BA.

This study found that independent risk factors for poor outcome in patients with BA was confusion, in agreement with the result presented on a previous study from Thailand [34]. Previous studies have reported some other prognostic factors for BA. Cho et al. reported that higher Sequential Organ Failure Assessment, pre-existing hemiplegia, and higher Charlson comorbidity index were associated with unfavorable clinical outcomes [10]. Widdrington et al. reported that a reduced Glasgow coma scale (GCS) (OR, 16.6; 95% CI, 5.63–48.93; $P < 0.001$), focal neurological deficit (OR, 5.50; 95% CI, 1.67–18.08; $P = 0.003$), and seizures (OR, 3.68; 95% CI, 1.26–10.78; $P = 0.014$) at presentation were independently associated with an unfavorable clinical outcome (death or disability) [17].

A study including 109 patients with BA in France during a period of 13 years found that initial GCS ≤14 and comorbidities (Charlson scale ≥2) were associated with poor neurological outcome while oral antibiotic switch was associated with better neurological outcome, and total duration of antibiotic treatment was significantly linked to the length of hospital stay ($P = 0.017$) [35]. A study from China found that female gender was related to poor outcome [4]. The choice of surgical method is also a debated subject. A retrospective analysis of BA in 183 patients showed that patient who underwent aspiration were more likely to experience reoperation, while open craniotomy excision was related to complications [36], while another study found no significant difference in outcome according to GOS at discharge between the 2 procedures [20]. This study also showed that surgical treatment did not affect outcome of patients at discharge, but more studies including data of long-term follow-up should be carried out to ascertain the conclusion.

This study had several limitations. First, due to the rarity of this disease, this was a retrospective observational study that was not specifically designed to compare the difference among BA caused by different organisms. Lack of MRI data in some patients and the small number of BA with other microorganisms compared to the number of those with *S.* species limit the validity of the conclusions. We believe that our data is valuable as we included a relatively large cohort of 65 patients and only patients with positive results in intracranial abscess culture or CSF were included. In addition, the choice and duration of individual antibiotic was not reported because changes of antibiotics were common during treatment. The efficacy of individual antibiotic choice was hard to evaluate since the number of each pathogen subgroup was relatively small. Finally, relevant data of mNGS, such as sequencing depth, was not available due to the retrospective design of this study. Further prospective studies with a larger sample size should be conducted to increase our understanding of this disease.

5. Conclusion

BA is a rare but dangerous disease. This study demonstrated the clinical and radiological characteristics of BA caused by different organisms, and showed that confusion was the independent factor related to poor outcome and *S.* viridans was associated with thicker wall of abscesses and larger oedema, suggesting that future therapy of BA should consist of early diagnoses with microbiological analyses.

Author contribution statement

Jiachun Su: Performed the experiments; Analyzed and interpreted the data; Wrote the paper.
Bin Hu: Analyzed and interpreted the data; Wrote the paper.
Yixin Zhang: Performed the experiments.
Ying Li: Conceived and designed the experiments.

Data availability statement

Data included in article/supp. material/referenced in article.

Funding

This research was supported by the National Nature Science Foundation of China (grant number 81603163 and 81903673), Funding of Huashan Hospital (grant number 2020QD097). We declare that the funding source did not play any role in study design, data collection, statistical analysis and data interpretation.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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