Risk Factors Associated with Poor Outcomes in Patients with Brain Abscesses

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Objective: The purpose of this study was to describe the clinical characteristics, treatment outcomes, and prognostic factors in patients with brain abscesses treated in a single institute during a recent 10-year period.

Methods: Fifty-one patients with brain abscesses who underwent navigation-assisted abscess aspiration with antibiotic treatment were included in this study. Variable parameters were collected from the patients' medical records and radiological data. A comparison was made between patients with favorable [Glasgow Outcome Scale (GOS) ≥4] and unfavorable (GOS <4) outcomes at discharge. Additionally, we investigated the factors influencing the duration of antibiotic administration.

Results: The study included 41 male and 10 female patients with a mean age of 53 years. At admission, 42 patients (82%) showed either clear or mildly disturbed consciousness (GCS ≥13) and 24 patients (47%) had predisposing factors. The offending microorganisms were identified in 25 patients (49%), and Streptococcus species were the most commonly isolated bacteria (27%). The mean duration of antibiotic administration was 42 days. At discharge, 41 patients had a favorable outcome and 10 had an unfavorable outcome including 8 deaths. The decreased level of consciousness (GCS <13) on admission was likely associated with an unfavorable outcome (p=0.052), and initial hyperglycemia (≥140 mg/dL) was an independent risk factor for prolonged antibiotic therapy (p=0.032).

Conclusion: We found that the level of consciousness at admission was associated with treatment outcomes in patients with brain abscesses. Furthermore, initial hyperglycemia was closely related to the long-term use of antibiotic agents.

Key Words: Brain abscess · Glasgow Coma Scale · Glasgow Outcome Scale · Hyperglycemia.
the following characteristics: positive cultures of intracerebral materials, positive blood cultures, or histology of the intracerebral lesion suggesting a brain abscess. Patients with subdural empyema and epidural abscesses, and those who underwent craniotomy for brain abcesses, were excluded. Patient charts were reviewed for the following: age at diagnosis, sex, past history, symptom duration before diagnosis, level of consciousness [assessed by the Glasgow Coma Scale (GCS)], focal neurological status at admission, disease predisposition, various serum parameters [complete blood count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and random blood sugar at admission], microorganisms identified on blood and abscess material cultures, antibiotic regimen, and duration of antibiotic treatment. The radiological parameters including the multiplicity of the lesion, abscess location, and initial and postoperative abscess volumes were also reviewed. Abscess volume was calculated using the formula: $V = \frac{4}{3} \pi abc$, where $a$ is the greatest abscess diameter measured by CT or MRI, $b$ is the diameter $90^\circ$ to $a$, and $c$ is the extent in the coronal direction or approximate number of slices within the abscess multiplied by the slice thickness (Fig. 1).

All patients underwent abscess aspiration under a neuronavigation system (StealthStation, Medtronic, Minneapolis, MN, USA). The operative intervention was performed at the earliest time, if indicated, without preoperative antibiotics so as not to sterilize the cultures. Patients who underwent delayed surgery were administered empirical antibiotics before the operation. During the operation, abscess material was maximally aspirated through a silicone catheter connected to soft collection bags placed in a dependent position and maintained for a minimum of 24 h. A repeat follow-up imaging study was performed routinely in all patients approximately 1–2 weeks postoperatively.

Brain abscess specimens obtained from the surgery were cultured for aerobic and anaerobic bacteria, mycobacteria, and fungi. Antibiotic susceptibility tests were performed on the isolated microorganisms. Immediately after the abscess drainage procedure, the administration of empirical antibiotics was started intravenously until the pathogens were identified. The antibiotic regimen was then targeted against the specific organisms isolated in the culture. The choice of antibiotics for cases with sterile cultures was directed to the most likely organisms based on clinical history and the primary site of infection, if known. The referring physician was later consulted with regard to adjustments or additions to the antibiotics and maintenance of the agents. The outcome was assessed according to the Glasgow Outcome Scale (GOS) at the time of discharge. A favorable outcome (GOS ≥4) was defined as moderate disability (having a disability, but being independent) and good recovery. An unfavorable outcome (GOS <4) was defined as death, persistent vegetative status, or severe disability (conscious, but with disability).

Statistical analysis was performed using the Statistical Package for the Social Sciences software (SPSS 11.5, IBM Corporation, Armonk, NY, USA). Results are presented as the mean± standard deviation of the mean. Univariate analyses (chi-square test, Fisher’s exact test, Student’s t-test) were performed to compare the variables between patients with a favorable outcome or with early response to antibiotics, and those with poor outcomes or with a delayed response to antibiotics. Variables found to have $p<0.1$ in the univariate analyses were entered into a multivariate logistic regression model to identify independent predictors of neurological outcome and the duration of antibiotic use. The correlation between continuous variables was assessed using Pearson’s correlation coefficient. Data were considered statistically significant when their $p$-value was below 0.05.

### RESULTS

#### Patient demographics

The patient demographics are listed in Table 1. There were 41 male and 10 female patients with a mean age of 53 years (range: 14–81 years). Headache, which occurred in 25 patients, was the most common symptom, while 3 patients complained of nausea and vomiting. Motor weakness occurred in 20 patients, and fever was checked in 10 patients on admission. Other symptoms and signs included speech disturbance (8 patients), visual disturbance (4 patients), impaired cognition (3 patients), seizures (2 patients), malaise (2 patients), and sensory changes (2 patients). Clear or mildly disturbed consciousness (GCS ≥13) was evident in 42 patients (82%) and moderately or severely dis-
≥10000/μL] at admission was identified in 24 (47%) patients. The mean WBC count was 11402±632/μL. Mean serum ESR and CRP levels at admission were 34.25±4.08 mm/h and 39.12±8.13 mg/L, respectively. An elevated CRP level (≥10 mg/L) was detected in 31 (61%) patients. The mean plasma glucose level at admission was 147.60±58.37 mg/dL. Twenty-two (43%) of the 51 patients were in a state of hyperglycemia (blood glucose ≥140 mg/dL) on admission.

On brain images, a single lesion was observed in 44 (86%) of the 51 patients and multiple lesions were observed in 7 patients (14%). The abscesses were most commonly found in the frontal lobe (30 patients, 59%), followed by the parietal lobe (12 patients, 24%), temporal lobe (8 patients, 16%), occipital lobe (5 patients, 10%), thalamus (2 patients, 4%), and pons (1 patient, 2%). The mean preoperative abscess volume was 19.11±2.00 cm$^3$ and the residual volume of the abscesses after surgery was 7.03±0.97 cm$^3$ (Table 2).

**Table 1. Summary of demographic features of 51 patients with brain abscesses**

| Parameters | No. of patients (%) |
|------------|---------------------|
| Mean age (years, range) | 53 (14–81) |
| Gender (male vs. female) | 41 (80)/10 (20) |
| Presenting symptoms and signs | |
| Headache | 25 (49) |
| Motor weakness | 20 (39) |
| Fever | 10 (20) |
| Speech disturbance | 8 (16) |
| Visual disturbance | 4 (8) |
| Nausea/vomiting | 3 (6) |
| Cognition impairment | 3 (6) |
| Seizure | 2 (4) |
| Malaise | 2 (4) |
| Sensory change | 2 (4) |
| Incontinence | 1 (2) |
| Mean duration of symptoms (days, range) | 8 (0–45) |
| GCS at admission | |
| ≥13 | 42 (82) |
| <13 | 9 (18) |
| Predisposing factor | 24 (47) |
| Pulmonary infection | 7 (14) |
| Sinusitis | 4 (8) |
| Dental infection | 3 (6) |
| Otic infection | 2 (4) |
| Prior trauma or neurosurgery | 2 (4) |
| Endocarditis | 2 (4) |
| Congenital heart disease | 2 (4) |
| Skin infection | 1 (2) |
| Psoas abscess | 1 (2) |
| Known diabetes mellitus | 10 (20) |
| Immuno compromised (chemotherapy for cancer, chronic renal failure, Addison's disease) | 4 (17) |

**Table 2. Laboratory and radiological findings at admission in study patients**

| Laboratory and imaging findings at admission | No. of patients (%) |
|-----------------------------------------------|---------------------|
| WBC (/μL, mean±SD) | 11402±632 |
| ≥10000/μL | 24 (47) |
| <10000/μL | 27 (53) |
| CRP (mg/L, mean±SD) | 39.12±8.13 |
| ≥10 mg/L | 31 (61) |
| <10 mg/L | 20 (39) |
| ESR (mm/h, mean±SD) | 34.25±4.08 |
| Blood glucose (mg/dL, mean±SD) | 147.6±58.37 |
| >140 mg/dL | 22 (43) |
| Identification of pathogen on blood culture | 2 (4) |
| Single vs. multiple abscess(es) | 44 (86) vs. 7 (14) |
| Abscess location | |
| Frontal | 30 (59) |
| Parietal | 12 (24) |
| Temporal | 8 (16) |
| Occipital | 5 (10) |
| Thalamus | 2 (4) |
| Pons | 1 (2) |
| Initial volume of abscess (cm$^3$, mean±SD) | 19.11±2.00 |
| Postoperative residual volume of abscess (cm$^3$, mean±SD) | 7.03±0.97 |

GCS : Glasgow Coma Scale

Laboratory and radiological findings

Of the 51 patients, leukocytosis [white blood cell (WBC) ≥10000/μL] at admission was identified in 24 (47%) patients. The mean WBC count was 11402±632/μL. Mean serum ESR and CRP levels at admission were 34.25±4.08 mm/h and 39.12±8.13 mg/L, respectively. An elevated CRP level (≥10 mg/L) was detected in 31 (61%) patients. The mean plasma glucose level at admission was 147.60±58.37 mg/dL. Twenty-two (43%) of the 51 patients were in a state of hyperglycemia (blood glucose ≥140 mg/dL) on admission.

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**Microbiological findings**

Abscess pathogens were identified in 25 patients (49%) during a culture study of the abscess material (Table 3). A single organism was isolated from 21 patients and multiple organisms were isolated from 4 patients. Of these isolated microorganisms, 21 (41%) were aerobic and 8 (16%) were anaerobic bacteria. A fungus (Aspergillus) was isolated from 1 patient. The...
most common aerobic bacteria were the *Streptococcus* species (14 cases, 27%), followed by *Gemella morbillorum* (4 cases, 8%), *Staphylococcus aureus* (1 case, 2%), *Proteus mirabilis* (1 case, 2%), and *Klebsiella pneumoniae* (1 case, 2%). The most frequently isolated anaerobic bacteria belonged to the *Prevotella* species (3 cases, 6%), followed by the Peptostreptococcus species (2 cases, 4%), *Fusobacterium nucleatum* (2 cases, 4%), and *Bacteroides intermedius* (1 case, 2%). Blood cultures were performed in 10 patients who presented with fever at admission and were positive in 2 patients (4%). In one patient, *Staphylococcus aureus* was isolated from the blood, as well as from the abscess material. In the other patient, the abscess fluid culture was negative, and the blood culture showed *Streptococcus viridans* growth. Once this pathogen was identified, the patient’s antibiotic therapy was revised accordingly.

**Treatments and outcomes**

The mean duration between admission and surgery was 7.29 days (range : 1–27 days). Of the 51 patients, 6 patients (11.8%) underwent surgery twice because a considerable portion of the abscess remained after the first intervention. Intravenous administration of empirical antibiotics including vancomycin, ceftriaxone, and metronidazole were started after abscess aspiration until the pathogens were confirmed. In the 8 patients who were suspected to be in the cerebritis stage, the antibiotics were started before surgery. Most commonly used antibiotics included a combination of ceftriaxone and metronidazole (22 patients, 43%), sometimes with the addition of either vancomycin or gentamicin. The mean duration of intravenous antibiotic treatment for surviving patients was 42 days (range : 23–66 days). None of the patients received oral antibiotics after they completed a course of parenteral antibiotic therapy. Corticosteroids were selectively administered to patients with severely increased intracranial pressure (9 patients, 18%). During the course of treatment, 8 patients (16%) died, with 3 (6%) deaths being attributed to the abscess itself and 5 (10%) deaths that may have resulted from the underlying pathology. In the latter cases, the cause of death was attributable to the aggravation of a pre-existing disease : 2 patients died of pulmonary infection-related sep-

### Table 3. Microorganisms isolated from the brain abscess samples

| Microorganism       | No. of patients (%) |
|---------------------|---------------------|
| Sterile culture     | 26 (51)             |
| Identification of pathogen from abscess | 25 (49) |
| Aerobic organisms   | 21 (41)             |
| *Streptococcus* spp. | 14 (27)             |
| *Gemella morbillorum* | 4 (8)              |
| *Staphylococcus aureus* | 1 (2)             |
| *Proteus mirabilis* | 1 (2)               |
| *Klebsiella pneumoniae* | 1 (2)         |
| Anaerobic organisms | 8 (16)              |
| *Prevotella* spp.   | 3 (6)               |
| *Peptostreptococcus* spp. | 2 (4)          |
| *Fusobacterium nucleatum* | 2 (4)        |
| *Bacteroides* intermedius | 1 (2)       |
| Fungus (*Aspergillus* | 1 (2)              |

### Table 4. Results of univariate and multivariate analyses for treatment outcomes in patients with brain abscesses

| Factors | Favorable outcome (GOS ≥4, n=41) | Unfavorable outcome (GOS <4, n=10) | \( p \) value | Multivariate analysis*<br>\( p \) value | Odds ratio | 95% CI |
|---------|----------------------------------|-----------------------------------|----------------|----------------------------------------|------------|-------|
| Age (years, mean±SD) | 51±2.8 | 60.8±5.58 | 0.164 | NA | NA | NA |
| Gender (male) | 34 (83%) | 7 (70%) | 0.389 | NA | NA | NA |
| Duration of symptoms (day) | 9.14±1.88 | 5.2±2.81 | 0.338 | NA | NA | NA |
| GCS ≥13 | 37 (90%) | 5 (50%) | 0.003 | 0.052 | 6.039 | 0.982–37.118 |
| Presence of predisposing factors | 18 (44%) | 6 (60%) | 0.485 | NA | NA | NA |
| Known diabetes mellitus | 8 (20%) | 2 (20%) | 1.000 | NA | NA | NA |
| Immunocompromised | 2 (5%) | 2 (20%) | 0.168 | NA | NA | NA |
| WBC (μL, mean±SD) | 11255±679 | 12006±1698 | 0.643 | NA | NA | NA |
| ESR (mm/h, mean±SD) | 31.78±3.64 | 44.4±14.74 | 0.224 | NA | NA | NA |
| CRP (mg/L, mean±SD) | 30.15±6.67 | 75.93±29.54 | 0.024 | 0.440 | 1.006 | 0.992–1.020 |
| Blood glucose (mg/dL, mean±SD) | 18.7±2.26 | 21.47±4.30 | 0.588 | NA | NA | NA |
| Identification of pathogen on abscess culture | 18 (44%) | 7 (70%) | 0.173 | NA | NA | NA |
| Multiple operations | 5 (12%) | 1 (10%) | 1.000 | NA | NA | NA |
| Multiple abscesses | 5 (12%) | 2 (20%) | 0.612 | NA | NA | NA |
| Initial abscess volume (cm³, mean±SD) | 18.7±2.26 | 21.47±4.30 | 0.588 | NA | NA | NA |
| Postoperative residual abscess volume (cm³, mean±SD) | 6.71±1.07 | 8.38±2.73 | 0.525 | NA | NA | NA |

*Variables with \( p \leq0.1 \) in the univariate analysis were entered into a multivariate analysis. CI : confidence interval, CRP : C-reactive protein, ESR : erythrocyte sedimentation rate, GCS : Glasgow Coma Scale, GOS : Glasgow Outcome Scale, NA : not available, SD : standard deviation, WBC : white blood cell
The results of comparison analyses between the patients with favorable and unfavorable outcomes are shown in Table 4. In the univariate analyses, admission variables associated with patient outcome included an initial GCS score <13 (p = 0.003), a high level of serum CRP (≥10 mg/L, p = 0.024), and hyperglycemia (≥140 mg/dL, p = 0.016). Among these, only a GCS score <13 [p = 0.052, 95% confidence interval (CI) 0.982–37.118] was likely to be an independent risk factor for poor patient outcome in the multivariate logistic regression analysis.

To assess the clinical and radiological factors that were associated with the response to antibiotics, the patients were divided into two groups: 1) early responder group (duration of antibiotics <6 weeks) comprising 25 patients, and 2) delayed responder group (death or using antibiotics for ≥6 weeks) comprising 26 patients. The mean WBC count and plasma blood sugar level in the delayed responder group were significantly higher than in the early responder group (12639/μL vs. 10116/μL, p = 0.045; 171.57 mg/dL vs. 122.84 mg/dL, p = 0.003, respectively) (Table 5). In the multivariate analyses, the independent risk factor for prolonged antibiotic use was hyperglycemia (p = 0.032, 95% CI 1.002–1.040). There was a positive correlation between the initial blood sugar level and the duration of antibiotic use (r = 0.471 and p = 0.001) (Fig. 2).

### DISCUSSION

Brain abscesses are considered serious and life threatening in-
Infections. The mortality rate associated with brain abscesses was reported to be as high as 40% in the 1980s. Advances in radiographic scanning, the development of novel surgical techniques, and the availability of newer antibiotics have all helped decrease the mortality rate in patients with brain abscesses. Recently, Tseng and Tseng have published the clinical outcomes of their patients with brain abscesses, of which 16.9% died during hospitalization. The deaths were caused by underlying systemic infection or the terminal stage of cancer and not by the abscess itself. Similarly, in our series, the overall mortality rate was 16% (8 patients) and the majority of these deaths were related to systemic infections, heart attacks, or aggravation of their pre-existing diseases. Only 3 patients died because of the brain abscess itself. This finding suggests that, although the current therapeutic strategy for controlling these abscesses is highly effective, the decisive factor for patients’ survival still depends on their ability to recover from their medical comorbidities.

Headache has been reported as the most common presenting symptom of brain abscesses. Several case series have reported headache, fever, and altered mental status as the most frequent presenting symptoms, while less commonly observed symptoms include nausea, vomiting, and focal neurological symptoms and signs. However, Kao et al. reported that fever was not helpful diagnostically. In a study with pneumococcal brain abscesses, fever was found in only 29% of patients, while 86% had focal deficits and 81% had headaches. In the present series, headache was the most frequent single symptom (49%). Forty percent of patients had motor weakness, either hemiparesis or monoparesis, 18% had moderately or severely disturbed consciousness, and 16% had speech disturbances. Fever was present in 20% of the patients. Overall, it seems that headache and focal neurological deficits including motor deficits and dysarthria are the most frequent presenting symptoms, with fever being common, but not invariable, since the systemic inflammatory response to an abscess may be minimal. Chun et al. demonstrated that old age, male gender, altered sensorium on admission, and abscesses with a pulmonary source were associated with poor outcomes in patients with brain abscesses. Other studies found that the mortality among treated patients correlated significantly with the initial neurological grade. Seydoux and Francioli also revealed that death and severe sequelae were related to the severity of neurological impairment on admission and to a shorter duration from symptom onset to admission. In the present study, patients with a low GCS score on admission had a greater likelihood of an unfavorable outcome than those with minimal mental disturbances when all potential confounds had been adjusted for in the multivariate analysis.

Cerebral abscesses can occur in a variety of clinical settings. Direct spreading from an ear infection, sinusitis, or dental infection is the major cause for developing an abscess. This contiguous spreading of infection from adjacent sites has been reported in nearly half of all brain abscess cases in the past. However, in our series, only 13 (26%) of the patients had a contiguous focus of infection as their predisposing cause (4 sinus, 3 dental, and 2 ear infections). Similar to our findings, Carpenter et al. also found that 24% of patients with brain abscesses had primary infections in their head and neck. Aggressive and widespread therapy for the primary infections in the adjacent area is likely to lead to a corresponding decrease in the incidence of brain abscesses associated with these conditions. In addition to a documented focus of infection, patients with certain medical conditions have an increased risk of infection. Many of these conditions, including diabetes and cancer, reduce the immune response in the patient. In this series, 14 (28%) patients had a medical condition that might have increased their susceptibility to infection: diabetes mellitus in 10 patients and an immunocompromised state in 4. This is in accord with other series, in which diabetes has been shown to be an important predisposing factor. Kao et al. reported that patients with underlying diabetes and liver disease had a higher mortality. However, in the present study, we failed to find any apparent correlation between outcomes and the presence or type of predisposing factors.

Identifying the offending pathogens is crucial for managing abscesses more efficiently. However, a lumbar puncture to obtain cerebrospinal fluid may be contraindicated in a patient with a brain abscess because raised intracranial pressure may lead to brainstem herniation and death. Blood cultures are often helpful in some patients, especially those who did not undergo an operation, and in patients whose abscess fluid cultures were negative. In addition, if the abscess is thought to be the result of hematogenous spreading, a blood culture is indicated.

The introduction, in the 1980s, and subsequent widespread acceptance of CT-guided stereotactic aspiration for brain abscesses, a minimally invasive procedure with low morbidity and mortality, has allowed rapid and effective surgical drainage of many brain abscess cases. In turn, this has enabled the culturing of pus and the identification of the organism(s) responsible, with high rates of resolution and a good outcome. Some studies have advocated nonsurgical treatments for patients who are poor candidates for surgery or for those with surgically inaccessible lesions. The major drawback to this approach is the potential toxicity involved in the prolonged administration of empirical antimicrobial therapy. Even in regions with limited accessibility such as the brain stem or eloquent areas among patients with a high risk for surgery or with multiple brain abscesses, stereotactic aspiration combined with antibiotic treatment can be safely applied in most cases. In our center, we attempt to treat most of the lesions suspected to be brain abscesses on imaging and clinical manifestations by aspiration and drainage guided by navigation, except during the stage of cerebritis. This approach not only achieves a reduction of the mass effect, but also severs abscess materials for identifying the infecting pathogens, and thus for facilitating antibiotic selection. Although the excision of abscesses may shorten the clinical course, no further improvement in the outcome has been observed.
These findings suggest that hyperglycemia is likely the result of a central nervous system insult leading to disturbed blood-glucose regulation mechanisms, rather than the result of systemic insults; thus, hyperglycemia may be a useful predictor of treatment outcome and the responsiveness of postoperative medical treatment in patients with brain abscesses.

This study had several limitations inherent to its retrospective design. As with any observational study, there remains a possibility that unmeasured confounds influenced our findings. In addition, our study did not include patients who underwent a craniotomy with their abscess excision, which might have an independent effect on the outcome. We assessed a single random blood glucose level on admission to define hyperglycemia without measuring glycosylated hemoglobin (HbA1c). Although we attempted to define the medical condition of the patients clearly, including pre-existing diabetes, by performing a critical review of the patients’ medical histories, it is likely that we also included patients with undiagnosed diabetes, which might have introduced an important bias in our analysis.

**CONCLUSION**

In this retrospective study of 51 patients with brain abscesses, we found that the GCS score on admission was associated with the patients’ outcomes. The overall mortality rate was 16%; however, the majority of the deaths were caused by patients’ pre-existing critical medical conditions and not by the abscesses themselves. In survivors, the response to a combination therapy of abscess drainage followed by parenteral antibiotic administration was excellent. An elevated blood glucose level on admission was associated with a prolonged use of antibiotics.

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