Surgically Treated Community-Acquired Brain Abscess: Bacteriological Analysis Based on Predisposing Infections

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SUMMARY: Community-acquired brain abscesses are still encountered in clinical practice and cause considerable complications, despite improvements in hygiene in modernized societies. This study aimed to identify potential risk factors pertaining to predisposing infections and microorganisms to facilitate the effective treatment of brain abscesses. Of 121 surgically treated patients with brain abscesses, the most frequent predisposing condition was odontogenic infections (49/121 patients, 40.5%) followed by sinusitis (14/121, 11.6%). Of 121 patients, 51 (42.1%) had no identifiable predisposing infection. Viridans group streptococci (VGS) were the most frequently identified (47%) bacteria in all patients, and anaerobes were more frequently isolated in patients with odontogenic infections (36.7%, *p* = 0.001) than aerobes. Among the patients with no identifiable predisposing infection, the most commonly isolated pathogen was VGS (38.3%); anaerobes occurred significantly less frequently (*p* = 0.045), and old pulmonary tuberculosis was significantly more common (*p* = 0.001) than in the group with identified predisposing infections. There was only one case of staphylococcal infection in 121 patients. The present study indicates that VGS should be the first target for antibiotic treatment when predisposing infections are not identifiable in patients with brain abscesses. Additionally, the association of old tuberculosis with community-acquired brain abscesses is common in these patients.

INTRODUCTION

Despite improvements in hygiene in developed countries, bacterial brain abscesses still occur in a community-acquired form and remain a serious condition that may result in neurological deficits unless treated appropriately (1). To achieve a favorable treatment outcome without delaying appropriate treatment, it is essential to identify the most probable causative organisms and the primary source of infection to determine an effective antibiotic regimen before the results of abscess cultures are available (2). Although various routes of infection in patients with brain abscesses have been identified in previous studies (3), altered patterns of predisposing infections, which may stem from earlier antibiotic treatment of infections in other organs or hygiene improvements, should be considered in the pathogenesis of brain abscesses and thus for postoperative medical treatment. When the predisposing infection is not identified during the first evaluation of the patient, unnecessary overuse of antibiotics may result in antibiotic resistance and further masking of the predisposing infection.

The purpose of this study was to reveal the association between predisposing infections and causative organisms and the commonly isolated pathogen from patients without definite predisposing infection by analyzing patients with community-acquired brain abscesses.

MATERIALS AND METHODS

Characteristics of patients and abscesses: A search of the institutional database was conducted to identify patients with surgically treated brain abscesses from January 2002 to March 2016. This study was approved by our hospital’s institutional review board (IRB 2016-0936). All brain abscesses were defined as a lesion identifiable by either computed tomography (CT) or magnetic resonance imaging (MRI), accompanied by a high signal intensity visible in diffusion-weighted imaging (Fig. 1). Locations of abscesses were classified in accordance with their anatomical location in the brain. The abscesses located in the basal ganglia, thalamus, or brain stem were classified as ‘deep-seated.’

Fig. 1. Preoperative axial post-contrast T1-weighted magnetic resonance imaging (MRI) (A) and diffusion-weighted axial MR images showing a mass lesion of the right occipital region with diffusion restriction (B).
The following information was obtained from the database: patients’ characteristics; symptoms; neurological findings and level of consciousness at admission graded using the Glasgow Coma Scale (GCS); laboratory findings, including white blood cell (WBC) count, C-reactive protein (CRP) level, erythrocyte sedimentation rate (ESR), and culture of abscess aspirates using standard culture methods; locations and volumes of the abscesses on radiological findings; predisposing infections at the time of abscess diagnosis; treatments involving surgery; and administered antibiotics.

Among the patients who were diagnosed with brain abscesses, trauma-related or hospital-acquired cases, abscesses that were preceded by neurosurgical procedures or head trauma, and intracranial tuberculosis were excluded.

Predisposing infections of the patients: All patients were assessed by infectious disease specialists, otolaryngologists, and the dental clinic to identify predisposing infections as a route for the formation of the brain abscess. Predisposing infections were classified as follows: odontogenic, otogenic, sinusitis, meningitis, endocarditis, pulmonary, and other systemic infections. Laboratory tests to identify the focus of infection included blood culture, chest radiography, echocardiography, and craniofacial CT or X-ray. Cerebrospinal fluid (CSF) examinations were performed when the patient was suspected to have ventriculitis caused by abscess extension to the ventricle.

Surgical interventions and abscess cultures: Stereotactic surgery was used in all cases and was classified as burr-hole trephination on the skull followed by abscess aspiration and craniotomy with abscess drainage followed by abscess wall resection. The surgery was performed with the aim of maximum drainage or aspiration of the abscess material. Leksell Stereotactic System® (Elekta, Stockholm, Sweden) was used for the procedure of burr-hole aspiration and Brain Lab® (Munich, Germany) neuronavigation system was used for craniotomy. Abscess materials obtained by abscess aspiration were placed in a sterile culture bottle and sent to the microbiology laboratory for microscopy, culture, and antibiotic-sensitivity tests according to the laboratory’s standard operating procedure. All abscess aspirates were cultured on blood agar, MacConkey agar, and thioglycollate broth medium with 5% CO₂ for detecting aerobic bacteria and phenylethyl alcohol blood agar for anaerobic bacteria, and were incubated at 37°C for 48 h. Empirical antibiotics were preoperatively administered in exceptional cases to patients who underwent delayed surgery.

Patient follow-up: All patients were followed up in our outpatient department with a neurological examination and brain CT or MRI with gadolinium enhancement, between 3 and 6 months after antibiotic treatment.

Statistical analysis: The Statistical Package for Social Sciences (SPSS) version 22.0 (IBM SPSS, Armonk, NY, USA) was used for statistical analysis. Independent t-tests and Mann-Whitney U tests were performed to analyze the equality of means/medians of continuous variables. Chi-square and Fisher’s exact tests were performed to determine independence between categorical variables; p-values ≤ 0.05 were regarded as statistically significant.

Ethical approval: This article does not contain any studies with human participants performed by any of the authors. For this type of study formal consent is not required. No identifying information is included in this article.

RESULTS

Patient characteristics: One-hundred and twenty-one patients with 140 brain abscesses (8 cases of multiple abscesses) were surgically treated between January 2002 and March 2016. Of these, 85 (70.2%) patients were male and 36 (29.8%) were female, with a male-to-female ratio of 2.36:1. The mean age of the group was 50.54 ± 16.15 yr (range: 3–80 yr) with the highest percentage in the 6th decade (33 patients, 27.3%). Seven (5.8%) patients were under 18 yr of age. Of all 121 patients, 61 (50.4%) had underlying diseases, with diabetes mellitus and old tuberculosis being the most common (13.2% and 11.6%, respectively) followed by pulmonary vascular anomaly (5%) and cardiac septal defects (5.8%) (Table 1).

Clinical presentations and laboratory findings: The presenting symptoms, as well as neurological and laboratory findings at first detection of the brain abscess, are summarized in Table 2. The most frequent symptom was a headache (62, 51.2%). Focal neurological deficits, including hemiparesis and speech problems such as dysarthria or dysphasia, were present in 48 (39.7%) patients, and seizures were noted in 30 (24.8%) patients at initial presentation. Fever was present in 25 (20.7%) patients, and the initial GCS score was below 13 in 10 (8.3%) of all 121 patients at the time of diagnosis.

Of 121 patients, 70 (57.9%) patients did not show leukocytosis (WBC < 10,000/µL) and the level of CRP was less than 5 mg/dL in 108 (89.3%) patients at the first laboratory evaluation. Of 119 blood cultures, the same bacteria were isolated in 3 (2.5%) cases, and only 1 out of 103 CSF cultures was positive for the same bacteria that were isolated from the brain abscess.

Location of brain abscesses: The most common location of brain abscesses was the frontal lobe (55/121 patients, 45.5%), followed by the parietal lobe (34/121 patients, 28.1%), the temporal lobe (17/121 patients, 14%), the occipital lobe (11/121 patients, 9.1%), and the cerebellum (6/121 patients, 5%). Eight out of 121 patients (6.6%) had underlying abscesses that were preceded by neurosurgical procedures or head trauma, and intracranial tuberculosis were excluded.

Table 1. Patients’ demographic data and underlying diseases at admission

| Underlying disease (%) | 61/121 (50.4) |
|------------------------|--------------|
| DM                     | 16 (13.2)    |
| Old tuberculosis       | 14 (11.6)    |
| Pulmonary vascular anomaly | 6 (5)     |
| Cardiac septal defect  | 7 (5.8)      |
| (VSD or ASD)           |              |
| Liver cirrhosis        | 4 (3.3)      |
| Malignancy             |              |
| (lung cancer 3, hepatocellular carcinoma 1, prostate cancer 1) | 5 (4.1) |
| Immune compromised state or immune disorder | 3 (2.5) |
| (rheumatoid arthritis, post-heart transplantation, previous chemotherapy) | |

DM, diabetes mellitus; VSD, ventricular septal defect; ASD, atrial septal defect.
had deep-seated abscesses. Among the different locations, only the frontal lobe showed a significant association with odontogenic infections ($p = 0.041$).

**Predisposing infections and abscess bacteriology:** Of 121 patients, 74 (61.2%) had identifiable predisposing infections at the first diagnosis of an abscess. The most common predisposing condition was an odontogenic infection (49/121, 40.5%), followed by sinusitis (15/121, 12.4%) (Table 3).

Seventeen different species of bacteria were isolated from the abscess cultures in 83 (68.6%) out of 121 patients. In 78 patients to whom antibiotics were not administered before surgery, abscess cultures were positive in 71 (91%) patients, whereas abscess cultures were positive in 12 (27.9%) patients out of 43 to whom antibiotics were administered preoperatively. The probability of a positive culture result was significantly higher in the group of patients who were not treated with antibiotics before surgery ($p = 0.001$). The most frequently isolated aerobic bacteria were Viridans group streptococci (VGS) (39/121, 32.2%) and *haemophilus* spp. (7/121, 5.8%). Other isolated aerobic bacteria are listed in Table 3.

Anaerobes were isolated from 28 (33.7%) of the 83 patients with positive abscess culture results. Frequently isolated anaerobes included *peptostreptococcus* (10.8%), *fusobacterium* (10.8%), *prevotella* spp. (7.2%), and *parvimonas micra* (6%).

Sixteen patients had polymicrobial infections in which more than 2 different bacterial species were isolated from the abscess, and 67 had monomicrobial infections: 52 aerobic and 15 anaerobic.

Matching patients’ predisposing infections with isolated bacteria, the isolation rate of anaerobes was significantly higher in patients with odontogenic infections than those with other predisposing infections (18 out of 49 patients, 36.7%, $p = 0.003$). Among the anaerobes isolated from the group with odontogenic infections, *peptostreptococcus*...
was the most frequently identified (7/49, 14.3%) (Table 4).

The rate of positive abscess culture was 68.1% in 47 patients who had no identifiable predisposing infection on evaluation, whereas it was 68.9% in 74 patients with identifiable predisposing infection, an insignificant difference ($p = 0.9$). VGS was isolated in 18 out of 47 patients with non-identifiable predisposing infections, making it the most commonly isolated pathogen in this group. The percentage of anaerobic infections was lower in the group with non-identifiable predisposing infections than in the group with an identified predisposing infection, and the difference was statistically significant (12.8% vs. 29.7%, $p = 0.045$). However, there was no significant difference for each isolated bacterium between the 2 groups (Table 4).

Old tuberculosis of the lung was found in 11 out of 47 patients (23.4%) with no identifiable predisposing infections, which was significantly higher than in the group with predisposing infections ($p = 0.001$) (Table 4).

**Surgical interventions, antibiotic treatment, and assessment of abscess resolution:** Of 121 patients, 102 had abscess drainage surgery by burr-hole trephination using the stereotactic method and craniotomy was performed in 19 patients. Among the 19 patients who underwent craniotomy, curettage of the abscess wall was performed in 11 and abscess drainage in 8. No surgical complications were noted in our study group.

First-choice antibiotics administered to the patients before the result of their abscess culture was obtained were ceftriaxone and metronidazole. The antibiotics were later changed according to the result of the abscess culture. The mean duration of intravenous antibiotics administration was 46.84 ± 24.18 days.

**Treatment outcomes and long-term follow-up:** The median follow-up time was 21 months (range: 0.5–122 months) from the first diagnosis of the brain abscesses. The 2 mortality cases were caused by septic shock and pulmonary thromboembolism. All patients, except for the 2 mortality cases, recovered completely, with an improvement in their symptoms and improved neurological presentation compared to the time of diagnosis. Ten out of 121 patients were complicated by ventriculitis at the time of first diagnosis. The mean duration of intravenous antibiotics administration for patients with and without ventriculitis was 46.46 ± 25.64 days.

**Table 4. Comparison of clinical characteristics and isolated microbial organisms between groups with and without identifiable predisposing infections at admission**

|                        | Patients without identifiable predisposing infection | Patients with predisposing infection | $p$-value |
|------------------------|------------------------------------------------------|------------------------------------|-----------|
| Age                    | 48.7 ± 17.33                                         | 51.7 ± 15.36                       | 0.32      |
| DM                     | 8 (17)                                               | 8 (11)                             | 0.33      |
| Old tuberculosis       | 11 (23.4)                                            | 3 (4.1)                            | 0.001     |
| Pulmonary vascular anomaly | 5 (10.6)                       | 1 (1.4)                           | 0.032     |
| Cardiac septal defect  | 2 (4.3)                                              | 5 (6.8)                            | 0.71      |
| Liver cirrhosis        | 1 (2.1)                                              | 3 (4.1)                            | 0.5       |
| Malignancy             | 2 (4.3)                                              | 3 (4.1)                            | 0.64      |
| Immune compromised state or immune disorder* | 2 (4.3)                       | 1 (1.4)                            | 0.56      |
| Duration of intravenous antibiotics (days ± SD) | 46.46 ± 25.64                                       | 47.06 ± 23.47                      | 0.9       |
| Abscess culture        | Positive in 32 (68.1)                                | Positive in 51 (68.9)              | 0.9       |
| Anaerobic infection    | 6 (12.8)                                             | 22 (29.7)                          | 0.045     |
| Polymicrobial infection| 4 (8.5)                                              | 12 (16.2)                          | 0.17      |
| **Gram positive aerobes** |                                                     |                                    |           |
| *Actinomyces* spp.     | 1 (2.1)                                              | 2 (2.7)                            | 0.67      |
| *Listeria monocytogenes* | 1 (2.1)                        | 0                                  | 0.39      |
| *Nocardia* spp.        | 3 (6.4)                                              | 1 (1.4)                            | 0.16      |
| *Staphylococcus intermedius* | 0                          | 1 (1.4)                            | 0.61      |
| *Streptococcus agalactiae* | 0                                         | 2 (2.7)                            | 0.37      |
| *Streptococcus pneumoniae* | 0                                          | 3 (4.1)                            | 0.23      |
| **Viridans group streptococcus** | 18 (38.3)                        | 21 (28.4)                          | 0.26      |
| **Gram positive anaerobes** |                                                   |                                    |           |
| *Clostridium* spp.     | 0                                                    | 2 (2.7)                            | 0.37      |
| *Parvimonas microa*    | 2 (4.3)                                              | 3 (4.1)                            | 0.65      |
| *Peptoniphilus asaccharolyticus* | 0                          | 1 (1.4)                            | 0.61      |
| *Peptostreptococcus microa* | 2 (4.3)                       | 7 (9.5)                            | 0.25      |
| *Propionibacterium acnes* | 0                                            | 1 (1.4)                            | 0.65      |
| **Gram negative aerobes** |                                                   |                                    |           |
| *Haemophilus* spp.     | 3 (6.4)                                              | 4 (5.4)                            | 0.56      |
| *Klebsiella pneumoniae* | 1 (2.1)                                             | 5 (6.8)                            | 0.25      |
| *Pseudomonas* aeruginosa | 2 (4.3)                      | 0                                  | 0.15      |
| **Gram negative anaerobes** |                                                   |                                    |           |
| *Fusobacterium nucleatum* | 3 (6.4)                       | 6 (8.1)                            | 0.51      |
| *Prevotella* spp.      | 1 (2.1)                                              | 5 (6.8)                            | 0.25      |

*Rheumatoid arthritis, post-heart transplantation, previous chemotherapy.*
triculitis was $55.25 \pm 24.85$ and $46.18 \pm 24.13$ days, respectively, which was not significantly different ($p = 0.31$). Patient recovery was not affected by the presence of ventriculitis during the treatment. There was no case of recurrence on follow-up examination.

**DISCUSSION**

Although the incidence of brain abscesses has reportedly been decreasing and treatment outcomes have been improving compared to the past (1,4), the value of bacteriological evaluation in community-acquired cases without identifiable predisposing infections has not yet been assessed.

Reports of fever have varied in previous studies. Whereas several studies reported fever as the most frequent presentation (4–6), some reported that fever was not diagnostically helpful (7–9). In the present study, fever was present in only 20.7% of patients, whereas the 2 most common presentations at the first diagnosis were headaches and focal neurologic deficits. This may be due to the improved accessibility of medical evaluation tools for early diagnoses, such as CT or MRI, for symptoms of headaches or neurological impairment, compared to the past. Furthermore, unlike in previous reports, patients with fever of another focus than the brain abscess itself might not be included in our study, since we excluded brain abscess cases secondary to head trauma or neurosurgical procedures.

Compared to previous studies, cases of pulmonary infection, head and neck infections, or endocarditis occurred relatively less frequently in the present study (6,10,11). Early antibiotic treatment for infections of the lung or head and neck sites, such as otitis media and paranasal sinuses, may result in a lower incidence of such infections as suggested in a previous study by Tonon et al. (11). On the contrary, the frequency of odontogenic infection in the present study of community-acquired brain abscesses was relatively high compared to previous reports. Laulajainen-Hongisto et al. suggested that the modern practice of increasingly preserving teeth compared to the past may lead to a potentially higher risk of odontogenic infection, which may explain the rising number of brain abscesses due to odontogenic infections (12). Exclusion of hospital-acquired, trauma-related, and iatrogenic cases in the present study may also explain the lower incidence of hematogenous spread from other infection sites.

The rate of positive abscess cultures varies in earlier reports, from 41% to 73.4% (1,4,6,11). We identified positive cultures in the abscess aspirate of 91% of patients who did not receive preoperative antibiotics, a number higher than previously reported (11). Therefore, appropriate abscess aspiration before the administration of antibiotics may be essential for an accurate microbiological diagnosis of the infection.

Frequent isolation of anaerobes from abscesses in individuals with odontogenic infections in our assessment is consistent with the results from previous studies (7–9,13). However, unlike in previous studies in which staphylococcus spp. were most commonly identified (4,7,14), there was only one case of staphylococcal infection in our assessment. The lower incidence of staphylococcal infections compared to other studies can be attributed to the exclusion of abscess cases of traumatic origin or postural infections in our assessment of community-acquired brain abscesses. Based on a study by Laulajainen-Hongisto et al., the use of vancomycin for medical treatment in the postsurgical management of brain abscesses has increased since 1980 (12). However, the low rate of staphylococcal infections in community-acquired brain abscesses in our study suggests that the use of vancomycin, which targets methicillin-resistant staphylococcal spp., may be unnecessary.

Nocardial infections are known to account for a minority of brain abscesses (4,15) and have been reported more frequently in immunocompromised patients (16); however, except for one case of an immunocompromised patient with a history of heart transplantation, 3 out of 4 brain abscesses of nocardial infection origin occurred in immunocompetent patients in the present study.

In the results of the present study, among 47 patients without identifiable predisposing infections, there were 2 with cardiac septal defects and 5 with pulmonary vascular anomalies first detected during the diagnosis of the brain abscesses. Therefore, we advocate that routine cardiac and pulmonary evaluations, such as echocardiography and chest CT, should be performed to detect cardiac or pulmonary pathologies as potential sources of brain abscesses. Moreover, some authors have suggested the possibility of congenital heart diseases, such as patent foramen ovale or pulmonary arteriovenous fistula, in certain patients with cryptogenic brain abscesses (17). We found, however, no significant association between congenital heart disease or pulmonary vascular anomaly and brain abscesses without identifiable predisposing infection due to the limited number of such cases in our assessment.

The percentage of patients without identifiable predisposing infections was higher in our assessment (42.1%) than in other studies (6,9,10). In a study by Xiao et al., an improved outcome was noted for patients without known predisposing factors (9). However, in our study, there was no difference in the treatment outcome and the duration of intravenous antibiotics administration related to the presence of predisposing infections or the result of the abscess culture. Anaerobic infections occurred significantly less frequently and VGS was the most commonly isolated bacteria in the group with no predisposing infections (Table 4). Pulmonary vascular anomalies and old tuberculosis were the 2 conditions most frequently present in the group with no identifiable predisposing infections in the present study. Considering that the general incidence of tuberculosis is 145.6 per 100,000 people in Korea (18), the incidence of 11.6% of old tuberculosis in 121 patients in our assessment is considerably higher. Although the role of old tuberculosis in the pathogenesis of brain abscesses has not been reported, we assumed that the inflammatory pathology of pulmonary tuberculosis could form an arteriovenous shunt in the microvasculature of the lung. The cause of pulmonary arteriovenous malformations is known to usually be of congenital origin; however, some authors reported cases of pulmonary arteriovenous malformation in association with pulmonary tuberculosis and suggested the recruitment of local pulmonary and systemic arteries to the inflammatory mass as the pathogenic mechanism for these cases (19,20).

Abscess aspiration by stereotactic surgery, using either neuronavigation or a stereotactic frame, was sufficient to obtain adequate amounts of abscess aspirate for microbial
diagnosis and to relieve the mass effect of the abscess. As reported in previous studies, stereotactic aspiration was safely performed in all patients included in the present study, including individuals with abscesses in the basal ganglia or thalamus, with no surgical complications, enabling the identification of causative organisms for effective postoperative antibiotic therapy from abscess cultures (7,21,22).

There was no case of recurrence during the follow-up period in our assessment, which was attributed to the treatment of the source of infection in the patients with identifiable predisposing infection and the choice of appropriate antibiotics according to the result of the culture from abscess aspirates.

There were several limitations to this study. First, the limited number of patients limited the power to identify the association between identified predisposing infections and isolated pathogens. Though a significant association of old pulmonary tuberculosis with the brain abscesses without identifiable predisposing infection was identified in the present study, subgroup risk analysis in both prospective and retrospective manners should be performed to confirm it as a risk factor for brain abscesses. Second, due to the retrospective analysis of the patients, an accurate evaluation of the treatment outcome was limited for individual initial presentations. Therefore, future research should focus on recruiting more patients and should implement long-term follow-up and a more thorough review of patients in a prospective manner. However, to our knowledge, our study is the first to analyze the bacteriology in patients with brain abscesses with no predisposing infections. Our results will help clinicians to determine appropriate antibiotic therapy for the prompt treatment of brain abscesses when the predisposing infection is not identifiable on the first evaluation.

In conclusion, abscess aspiration using stereotactic surgery can be safely performed in patients with brain abscesses to facilitate an early diagnosis and appropriate antibiotic treatment. Even if predisposing infections are not identifiable during the systematic evaluation of patients with brain abscesses, VGS should be the first target for antibiotic treatment. The high incidence of old pulmonary tuberculosis may indicate a role as a potential route for antibiotic treatment. The high incidence of old pulmonary tuberculosis secondary to Mycobacterium tuberculosis empyema, Ann Thorac Surg. 2002;74:1229-31.

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Conflict of interest None to declare.

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