

Predictors of Mortality in Brain Abscess

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Abstract

Objective: Brain abscess carries significant morbidity and mortality. Our objective was to elucidate the clinical presentation of brain abscess and to assess predictors of mortality in these patients.

Methods: All patients with a brain abscess presenting to the Aga Khan University Hospital, a tertiary care referral center in Karachi, Pakistan, were studied retrospectively. Statistical analysis involved univariate analysis and a logistic regression model.

Results: Among the 66 patients analyzed, a distant metastatic focus of infection, was the most commonly identified predisposing factor (29%). Otogenic infection was the commonest contiguous source and sinusitis was noticeably absent. Multiple abscesses were frequent (35%). Streptococci were the most common isolates (39%). Lumbar puncture was performed in 44% and steroids administered in 33%. Treatment was surgical in 58%. Most comatose patients were treated conservatively. Overall mortality was 29%. Univariate analysis identified comatose presentation and identification of a distant focus of infection as predictors of mortality. The logistic regression model, however, identified a distant focus of infection as the only independent predictor.

Conclusion: Age greater than 30 years, corticosteroid use, multiple abscesses, performance of lumbar puncture and conservative management had no effect on outcome (JPMA 52:111; 2002).

Introduction

Brain abscess is a focal suppurative process in the brain parenchyma. It usually develops in three clinical settings: (I) the presence of a contiguous focus of infection; (ii) the presence of a distant focus of infection with hematogenous spread and (iii) following cranial trauma or surgery^{1,2}. Some cases are of cryptogenic origin. Diagnosis of brain abscess is based on clinical presentation and characteristic radiological findings.

Although some patients with brain abscess respond to prolonged medical therapy alone, most require surgery for optimal management¹.

Mortality amongst brain abscess cases is declining due to rational use of antibiotics and advances in non-invasive imaging procedures that allow earlier diagnosis and more precise localization³⁻⁵. However, mortality still remains considerably high especially in developing countries^{3,6-8}.

To date, only a few studies are available on the incidence, etiology, clinical course, management and prognosis of brain abscess in Pakistan⁹. This retrospective study describes the demography and etiology, clinical presentation, diagnosis, microbiology,

laboratory findings, treatment and prognosis of patients with brain abscess seen at the Aga Khan University Hospital, Karachi.

Material and Methods

The Aga Khan University Hospital is a 425 bed tertiary care hospital in Karachi and serves as a referral hospital. Selection of patients with brain abscess was carried out using the ICD-9-CM system of classification.

The codes selected were 006.5, 013.30, and 324.0, which represent amebic brain abscess, tuberculous (TB) brain abscess (excludes tuberculoma) and intracranial abscess respectively. Between January 1987 and June 1998 there were 87 patients with intracranial suppuration, 66 of whom had brain abscess while 21 had sub-dural or epidural empyema. Diagnosis of brain abscess was based on clinical presentation and characteristic brain CT or MRI findings. Patients presenting exclusively as meningitis, sub-dural or epidural empyemas were excluded. Mental status was assessed using the Glasgow Coma Score (GCS) and coma defined as a score of less than eight.

Distant metastasis was presumed when an active or resolved focus of infection with potential for hematogenous spread was identified. Congenital heart disease (CHD) was evaluated separately as a predisposing factor.

Data regarding the patients was collected by reviewing the clinical assessment and progress reports, radiology, hematology, pathology, microbiology and other laboratory data. Where patients presented with brain abscess on multiple occasions, only the first presentation was reviewed.

Univariate analysis was performed by means of chi square and Fisher's exact two-tailed tests whenever appropriate. Logistic regression analysis was carried out using the statistical software SPSS (Release 8.0.0, standard version, copyright© SPSS Inc., 1989-97). The log-likelihood ratio test was used to assess the goodness of fit of the model. Results are given as odds ratios with 95% confidence intervals. The odds are expressed as the ratio of mortality to that of survival for a given value of an independent variable.

Results

Amongst the 66 brain abscess patients most (48) were men, giving men:women ratio of about 3:1. This male preponderance was less evident amongst the younger ages (Figure).

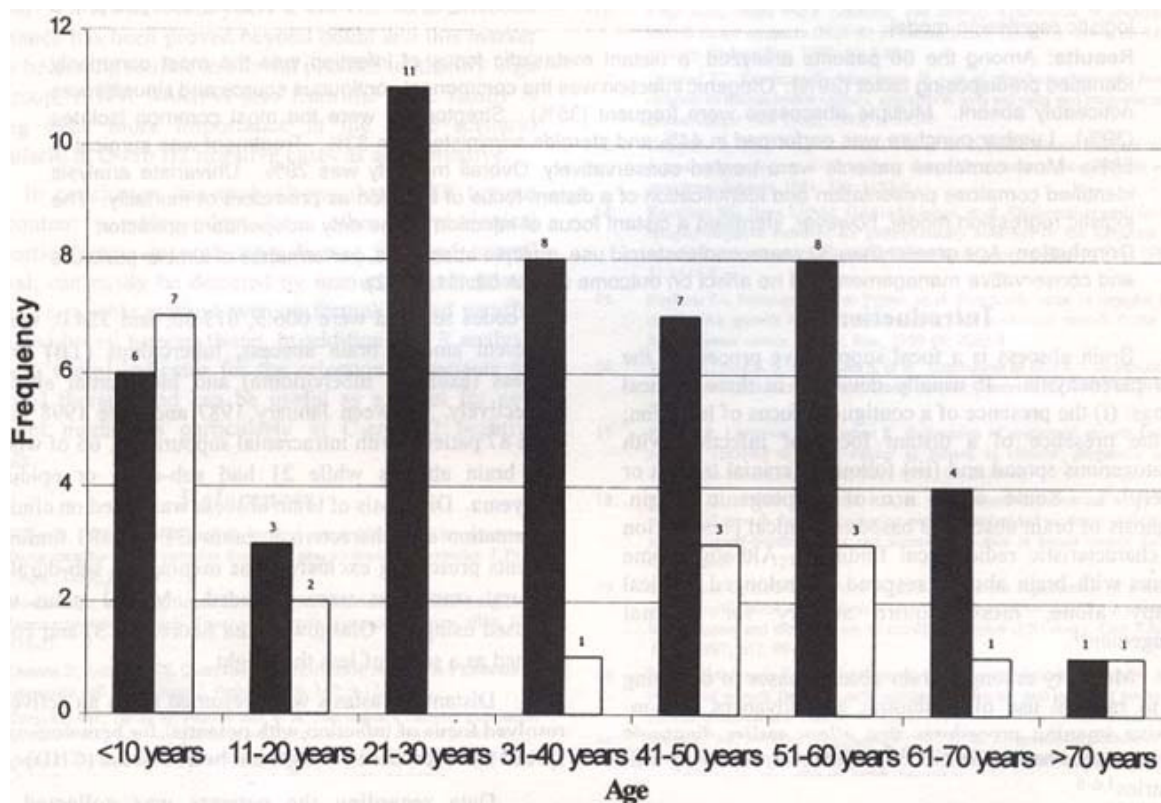


Figure. Age and gender distribution of the 66 patients with brain abscess seen at the Aga Khan University. The black bars represent men while the white bars represent women.

The mean age of the patients was 35 years (range 1 to 79 years).

The distribution of the patients by predisposing factors is summarized in Table 1.

Table 1. Primary sources of infection/predisposing factors in the 66 patients with brain Abscess.

| Primary Source | All Cases (n=66) | | Frequency | | | |
|-----------------------------------|------------------|-------|-----------------------|------|-------------------------|--------|
| | No. | % | Single Abscess (n=43) | | Multiple Abscess (n=23) | |
| | | | No. | % | No. | % |
| Contiguous | 12 | 18.2* | 8 | 18.6 | 4 | 17.4%* |
| Otogenic | 10 | 15.2 | 8 | 18.6 | 2 | 8.7 |
| Acute Otitis Media | 4 | 6.1 | 2 | 4.7 | 2 | 8.7 |
| Chronic Otitis Media | 6 | 9.1 | 6 | 14.0 | 0 | 0.0 |
| Meningitis | 2 | 3.0 | 0 | 0.0 | 2 | 8.7 |
| Trauma | 11 | 16.7 | 11 | 25.6 | 0 | 0.0 |
| Head Injury | 4 | 6.1 | 4 | 9.3 | 0 | 0.0 |
| Post-craniotomy/Surgery | 6 | 9.1 | 6 | 14.0 | 0 | 0.0 |
| Both | 1 | 1.5 | 1 | 2.3 | 0 | 0.0 |
| Distant Metastasis | 19 | 28.8* | 6 | 14.0 | 13 | 56.5* |
| Respiratory Disease | 9 | 13.6† | 3 | 7.0 | 6 | 26.1† |
| Others ‡ | 11 | 16.7† | 3 | 7.0 | 8 | 34.8† |
| Cyanotic Congenital Heart Disease | 7 | 10.6 | 3 | 7.0 | 4 | 17.4 |
| Unknown | 19 | 28.8 | 15 | 34.9 | 4 | 17.4 |

* Two patients had both contiguous and distant metastatic focus of infection.

† One patient had respiratory disease along with Nocardiosis.

‡ Other sources include septicemia, endocarditis, urinary tract infections, intra-abdominal abscess with septicemia, pneumococcal peritonitis and subcutaneous Nocardiosis. Two patients underwent surgery for esophageal stricture and tricuspid valve replacement.

Of the 47 patients in whom a predisposing factor was identified, 31 (66%) presented with an active primary source of infection. Distant metastasis was the most commonly identified predisposing factor, accounting for the pathogenesis of brain abscess in 19 (29%) patients. In the patients with respiratory disease, two each had pneumonia, bronchiectasis, tuberculosis and nocardiosis and one had pleural effusion. Amongst the patients with CHD, four had tetralogy of Fallot while one each had ventricular septal are summarized in Table 2.

Table 2. Symptoms and Physical Findings amongst the 66 patients with Brain Abscess.

| Symptoms | Frequency | |
|---|-----------|----|
| | No. | % |
| Fever | 40 | 61 |
| Headache | 35 | 53 |
| Nausea/vomiting | 24 | 36 |
| Seizures | 20 | 30 |
| Hemiplegia/paresis | 16 | 24 |
| Stiff neck | 15 | 23 |
| Cranial nerve dysfunction | 15 | 23 |
| Confusion | 9 | 14 |
| Speech disturbance | 9 | 14 |
| Monoplegia/paresis | 4 | 6 |
| Papilledema | 4 | 6 |
| Visual field defects | 2 | 3 |
| Sensory deficits | 2 | 3 |
| No neurological deficits on physical exam | 35 | 53 |

Fever was the most common defect; a shunt between the vena cava and the atrium; and atrial and ventricular septal defects with tricuspid atresia and pulmonary valve stenosis. The mean age of the patients with CHD was ten years. For the other predisposing factors the mean ages ranged from 21 to 44 years. Sinusitis as a predisposing factor was not identified in any patient. Three patients were immunocompromised; one was on immunosuppressant therapy following renal transplant and one each had systemic lupus erythematosus and leukemia. The major presenting symptoms and physical findings presenting complaint (61%), followed by headache (53%). Focal neurological deficits (hemiplegia, monoplegia and/or sensory deficits) were present in 22 (33%) patients. The classic clinical triad of fever, headache and focal neurological deficit was present in only five (8%). At least 13 (20%) patients presented with coma. In 21 (32%) patients, the symptoms had persisted for more than two weeks before presentation. However, most patients (46%) presented with symptom duration of two to 14 days. Examination suggesting cranial nerve (CN) dysfunction was recorded in 15 (23%) patients. Facial weakness was the most common amongst these patients (60%). Other frequently involved nerves were CN III (33%) and CN VI (17%). Amongst 42 patients in whom fundoscopic findings were recorded, only four (10%) had papilledema. All patients were diagnosed based on clinical and radiological findings except the one patient where a tumor was suspected but microscopy showed an abscess. Radiology mostly involved brain CT (95%); MRI was done in six patients, three of whom had a prior CT. Common CT findings included areas of central low attenuation in 30 (46%) patients, ring enhancement in 37 (56%) and surrounding edema in 38 (58%). Hemispheric involvement was similar; the right hemisphere was involved in 26 patients, the left hemisphere in 25. Both hemispheres were involved in 15 patients. Parietal lobe involvement was the most common followed by frontal and temporal lobes. A single abscess was present in 43 (65%) patients while 23 (35%) had multiple abscesses (lesions completely separated by normal parenchyma). Multiloculated lesions not separated by normal brain tissue were considered a single abscess. Distribution of single and multiple abscesses with respect to predisposing factors is summarized in Table 1. Of the 23 patients with multiple abscesses, distant metastatic foci were identified as the primary source of infection in 13 (57%). The lobes most commonly affected by multiple abscesses were the parietal (70%) and frontal lobes (48%). Amongst the 43 patients with a solitary brain abscess, more than one lobe was involved in 20 (47%). Analysis of the distribution of abscess in relation to the clinical setting showed that most patients with a contiguous focus had involvement of the temporal, parietal or cerebellar lobes (81%). Where distant metastases were identified, the parietal, frontal and temporal lobes were mostly involved (80%). Brain abscess samples from the 38 surgically treated patients were sent for microbiology and organisms identified in 25 (66%). Twenty-nine (76%) of these patients had received antibiotics prior to surgery. The organisms identified included 13 microbiologic species; ten bacteria, two fungi, and one protozoon (Table 3).

Table 3. Correlation of microbiology of the abscesses with primary source of infection in the 25 patients with positive culture/smear.

| Primary Source | Microorganism Isolated |
|--------------------|--|
| Contiguous | Proteus (2) *; Staphylococcus aureus (1); Streptococcus species with Proteus (1) |
| Trauma | Staphylococcus aureus (2); Acinetobacter lwoffii (1) |
| Distant Metastasis | Streptococcus intermedius(2); Streptococcus species (1); |
| CHD | Streptococcus pneumoniae (1); Streptococcus species with Pseudomonas aeruginosa and Pseudomonas species (1); Staphylococcus species with Enterobacter species and Nocardia (1) |
| Unknown | Streptococcus species (3) Streptococcus species (2); Staphylococcus species (2); Acinetobacter lwoffii (1); Streptococcus species with Mycobacterium tuberculosis (1); Aspergillus (1); Wangiella dermatitidis (1); Entamoeba histolytica (1) |

* Figures in parenthesis refer to the number of patients in whom these organisms were identified.

Streptococcal species were the most common isolate (39%). Multiple species were identified in four patients.

Lumbar puncture was performed in 29 (44%) patients. This was done before diagnosis in at least 13 (45%) patients. In one patient with pneumococcal peritonitis, blood culture grew Streptococcus pneumoniae, while in another with pneumonia, Streptococcus Chioramphenicol was administered in 15 patients (23%). Surgery involved aspiration in 22 (58%) patients and excision in 16 (42%). Multiple aspirations were required in eight. Mannitol was administered in 25 (38%) patients, corticosteroids in 22 (33%) and anticonvulsants in 13 (20%). Dexamethasone was the most commonly used corticosteroid.

The overall mortality was 29%. Resolution of presenting signs and symptoms was complete in 19 (29%) patients, partial in 28 (43%) and nil in 18 (28%). Abscess relapsed or recurred in ten patients (15%).

Table 4. Factors predicting mortality amongst the 66 patients with brain abscess.

| Prognostic Factors | Mortality | | Univariate Analysis | | Multivariate Analysis | |
|----------------------------|-----------|----|---|--------------|---|--------------|
| | Yes | No | Odds Ratio (95% Confidence Interval) | | Odds Ratio (95% Confidence Interval) | |
| Distant metastasis * | 12 | 7 | 9.8 | (2.9 - 33.5) | 9.9 | (1.6 - 62.4) |
| Coma | 8 | 5 | 6.2 | (1.7 - 23.7) | 2.8 | (0.6 - 13.8) |
| Conservative treatment | 11 | 16 | 2.6 | (0.9 - 7.7) | 1.2 | (0.2 - 5.6) |
| Symptom duration < 2 weeks | 15 | 29 | 2.2 | (0.6 - 7.7) | 4.4 | (0.7 - 27.0) |
| Multiple abscesses | 9 | 14 | 2.1 | (0.7 - 6.4) | 1.2 | (0.2 - 6.8) |
| Age > 30 years | 13 | 24 | 2.1 | (0.7 - 6.4) | 1.1 | (0.2 - 5.5) |
| Steroid therapy | 8 | 14 | 1.7 | (0.6 - 5.2) | 1.4 | (0.3 - 6.3) |
| Lumbar puncture | 10 | 19 | 1.5 | (0.5 - 4.4) | 1.2 | (0.3 - 6.1) |
| Women | 6 | 12 | 1.3 | (0.4 - 4.3) | 0.8 | (0.1 - 5.2) |

* Distant metastasis is the sole significant predictor of mortality

Table 4 summarizes the univariate and multivariate analysis of the various prognostic factors studied. Univariate analysis showed that coma on admission and the identification of a distant metastatic focus were significant predictors of mortality.

Logistic regression identified a distant metastatic focus to be the sole independent predictor of mortality. Symptom duration of less than two weeks was the only other variable with an odds ratio that increased from univariate (2.2) to multivariate analysis (4.4); however, it did not achieve statistical significance.

Discussion

This series represents a large collection of brain abscess patients from the Indian subcontinent. Most of our data is comparable to previous series. The mean age and age distribution of our patients and the overall male preponderance is similar^{3,4,6-8,10-12}. Children (less than 14 years) comprised 21% of our patients and the boys: girls ratio was 1:1.3; both these observations are in contrast to other series where fewer children with brain abscess are reported and the gender distribution shows a male preponderance.^{5,6,13-15}

A striking feature in our review is the high number of abscesses (29%) secondary to metastasis from a distant focus of infection^{4,5,7,10,14}. Metastases from a distant focus of infection usually embolize to the distribution of the middle cerebral artery, affecting the parietal, frontal and temporal lobes. This probably accounts for both the high frequency of parietal lobe involvement (62%) and the number of patients (35%) with multiple abscesses. None of our patients presented with, or had a history of sinusitis, an important predisposing factor^{4,7,15}.

Presenting symptoms and findings were similar to other series. There was no difference in presentation of patients with single or multiple abscesses, as noted before⁸. An unusual feature was that almost one-third of our patients presented with symptom duration of greater than two weeks^{15,16}. This may reflect a delay in diagnosis and referral to the hospital. Fewer patients had papilledema as compared to other reports^{3,7,8,11,15}.

Correlation between microbiologic species isolated and the primary source is shown in Table 3. These findings are consistent with previous series^{4,7}. Our series yielded a considerably lower number of anaerobes (13%)^{4,10,15}. This may in part be due to inappropriate sampling or culture techniques. Streptococci were the most common isolates (39%) as in other series^{4,6,10,14}. Multiple species were isolated in 11% and culture was sterile in 38% of the samples; likely a reflection of the poor recovery of anaerobes and prior antibiotic use in our patients.

Interestingly, lumbar puncture was performed frequently, as in other series^{3,4,7,11,15}. This procedure is relatively contraindicated given the risk of herniation or rupture of the abscess into the ventricles. Furthermore, CSF findings are of little diagnostic value⁴. Even though many patients were managed conservatively^{3,4,7,8,15}, this did not influence the eventual outcome. Management was surgical in 69% patients with non-comatose presentation, and predominantly conservative in those who presented comatose. This finding is contrary to that indicated by others³. The reasons cited for conservative management in these patients included multiple medical problems, deep location of the abscesses and lack of stereotactic facility and refusal to undergo surgery. Management was surgical in 48% patients with multiple abscesses; usually conservative management is recommended for such patients^{2,3}. The use of corticosteroids in the management of brain abscess is controversial. Of interest is the use of steroids in 33% patients in our series. Neither steroid use, nor the performance of lumbar puncture was an independent

predictor of mortality. Overall mortality is comparable to other series^{4,6-8,15}.

The strength of our study lies in the use of a logistic regression model to identify independent predictors of mortality in patients with brain abscess. The presence of multiple abscesses, performance of lumbar puncture, use of corticosteroids and conservative management were not important determinants of the outcome. Comatose presentation showed a trend towards significance; the lack of statistical significance may reflect the limited power of our study. Presence of distant metastasis remains the only factor that independently predicted mortality in our series of patients with brain abscess.

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