The experiences of non-operative treatment in patients with bacterial brain abscess

S.-Y. Hsiao[1,5], W.-N. Chang[2], W.-C. Lin[3], N.-W. Tsai[2], C.-R. Huang[2], H.-C. Wang[4], C.-M. Su[1], M.-J. Chuang[4] and C.-H. Lu[2]

Departments of 1) *Emergency Medicine,* 2) *Neurology,* 3) *Radiology,* 4) *Neurosurgery, and* 5) *Family Medicine, Chang Gung Memorial Hospital-Kaohsiung Medical Center, Chang Gung University College of Medicine, Kaohsiung, Taiwan*

Abstract

Although treatment of brain abscess requires a combination of antimicrobials and surgical intervention for the infected foci, nonsurgical, empirical treatment is possible and efficient in selected groups of patients. A total of 31 patients were enrolled in this 22-year retrospective study. We describe our therapeutic experiences and attempt to analyze the risk factors that were predictive of therapeutic outcomes. Multiple logistic regression was used to evaluate the relationships between baseline clinical factors and therapeutic outcome during the study period. Of these 31 patients, 25 had community-acquired infections, whereas the other six had nosocomially-acquired infections. Thirteen cases (42%) had a single brain abscess and the other 18 cases (58%) had multiple brain abscesses. Furthermore, the association of bacterial meningitis and brain abscess was found in 81% (25/31) of cases. The overall case fatality rate was 48% (15/31). Significant risk factors for poor outcomes included Glasgow coma scale (GCS) at presentation, presence of septic shock and neck stiffness. In addition, each reduction of one point on the GCS increased the poor outcome rate by 28%. The findings of the study demonstrate that both a higher mortality rate (48%) and worse outcomes were found in this select group of patients. Among the significant prognostic factors, a lower mean GCS at presentation was a major determinant of poor outcome.

Keywords: Bacterial brain abscess, glasgow coma scale, nonsurgical treatment, outcome
Original Submission: 16 January 2010; **Revised Submission:** 11 April 2010; **Accepted:** 30 April 2010
Editor: M. Drancourt
Article published online: 8 May 2010
Clin Microbiol Infect 2011; **17:** 615–620
10.1111/j.1469-0691.2010.03264.x

Corresponding author: C.-H. Lu, Department of Neurology, Chang Gung Memorial Hospital, #123, Ta Pei Road, Niao Sung Hsiang, Kaohsiung Hsien, Taiwan
E-mail: chlu99@ms44.url.com.tw

Introduction

Despite the advent of modern neurosurgical techniques, new antibiotics and new powerful imaging technologies, brain abscess remains a potentially fatal central nervous system infection [1,2]. The treatment of brain abscess requires a combination of antimicrobials, surgical intervention and eradication of primary infected foci [3,4]. Nonsurgical, empirical treatment is possible and efficient in a select group of patients (e.g. brain abscess associated with meningitis, multiple deep-seated abscesses, metastatic abscess, neonates and infants, and abscesses located in the eloquent area of the brain or brain stem where surgical intervention would be inappropriate), especially when the aetiological agent is known with a reasonably high probability as a result of positive cultures from cerebrospinal fluid and /or blood, or drainage from the ear or sinuses [3–16].

To our knowledge, clinical research about non-operative treatment of bacterial brain abscesses are summarized under diverse bacterial brain abscesses or case report studies [3–16], and only one small series of clinical research has focused specifically on the non-operative treatment of bacterial brain abscess [9]. Because of the possible benefits of therapeutic intervention, there is a need for a better delineation of the potential risk factors and clinical features in this specific group of patients.

In the present study, we describe our therapeutic experiences and attempt to analyze the clinical features, neuroimaging findings, clinical scores and measurements to determine the therapeutic outcomes in this special group of patients.

Materials and Methods

We retrospectively reviewed the microbiological records for abscess and blood cultures, medical records and neuroimaging

findings, using pre-existing standardized evaluation forms, for 205 patients with bacterial brain abscesses who were admitted to the Department of Neurology, Kaohsiung Chang Gung Memorial Hospital, between January 1986 and December 2007. Kaohsiung Chang Gung Memorial Hospital, the largest medical center in southern Taiwan, is a 2482-bed acute-care teaching hospital, which provides both primary and tertiary referral care of patients.

The inclusion criteria for non-operative treatment of bacterial brain abscesses were: (i) characteristic computerized tomography (CT) and/or magnetic resonance imaging (MRI) findings; (ii) the aetiological agent was known with a reasonably high probability as a result of positive cultures from cerebrospinal fluid and/or blood, and/or drainage from the ear or sinuses; and (iii) classical clinical manifestations including headache, fever, localized neurological signs and/or consciousness disturbance [1,2]. Patients were excluded if the diagnosis was in doubt and if surgical treatment consisted of either aspiration or excision of the abscess. Thus, only 31 of the 205 patients were enrolled for analysis. The study protocol was approved by the Chang Gung Memorial Hospital Institutional Review Committee on Human Research.

All of the materials from cerebrospinal fluid and/or blood, and/or drainage from the ear or sinuses were cultured for aerobic and anaerobic bacteria, *Mycobacterium* and fungi. Antibiotic susceptibility was determined using the Kirby–Bauer disc diffusion method (Mueller–Hinton II agars; Becton Dickinson Microbiology Systems, Cockeysville, MD, USA). Patients who were initially treated at other hospitals but subsequently transferred to our hospital for further therapy were also included in this study, with initial clinical data collected at those hospitals used for analysis.

Brain abscesses were defined as nosocomial according to the 1988 guidelines of the Centers for Disease Control [17]. Brain abscesses related to head trauma with skull fractures or neurosurgical procedures were classified as a post-neurosurgical form. Otherwise, patients who presented with no distinctive characteristics, and/or who had not undergone invasive procedures, were classified as having a spontaneous form.

The Glasgow coma scale (GCS) score was determined by neurosurgeons or neurologists when the patient arrived at the emergency room. All of the patients received brain CT scans soon after arrival at the emergency room. Follow-up brain CT scans and/or MRI were performed if clinical deterioration was noted, including the acute onset of focal neurological deficits, seizures or status epilepticus, and a progressively disturbed consciousness, as well as post-neurosurgical procedures. Hydrocephalus was judged retrospectively by a dilated temporal horn of the ventricle without obvious brain atrophy and/or an Evan's ratio of more than 0.3 on initial CT scans. The Evan's ratio is the ratio of the ventricular width of the bilateral frontal horn to the maximum biparietal diameter.

We measured the volumes of the brain abscesses on admission CT scans. A radiologist experienced in the interpretation of CT and blinded to the patients' clinical and biochemical data analyzed CT scans to conduct volumetric measurements of brain abscess volumes. All images were processed with the use of VITREA imaging processing software, version 3.9.0.1 (Vital images, Minnetonka, MN, USA, running on an off-line workstation. The volumes were calculated using a semi-automated process. The examiner manually drew regions-of-interest (ROI) in each slice throughout the brain abscess. Automated threshold values, based on Hounsfield unit measurements, were applied to differentiate haematoma from the skull. Contiguous voxels were automatically summed to yield a brain abscess volume. The observer drew the brain abscess twice, at an interval of 1 month. A trained research assistant performed these measurements again. Maps of the ROI used for measurement were stored and then confirmed by a neurosurgeon. Intra-observer and inter-observer reproducibility of these measurements was evaluated by using intraclass correlation coefficients. For brain abscess volume measurements, the intra-observer agreement was $r = 0.99$ and the inter-observer agreement was $r = 0.99$. Furthermore, the 'volumes of brain abscesses' indicates the summation of all the volumes of the brain abscesses if at least two brain abscesses were found.

The combination of third-generation cephalosporins and metronidazole for 8–12 weeks is the mainstay of initial empiric antimicrobial treatment for bacterial brain abscesses. The choice of final antibiotics was guided by the final culture results from the cerebrospinal fluid and/or blood, and/or drainage from the ear or sinuses. Our standard protocol was to perform follow-up CT scans and/or MRI every 2 weeks during hospitalization. Evaluation of therapeutic outcome after discharge used the Glasgow outcome score (GOS) as: good recovery, moderate disability, severe disability, persistent vegetative state and death [18]. For statistical analysis, a good recovery was defined as a good outcome, whereas moderate disability, severe disability, persistent vegetative state and death were defined as poor outcomes [19]. Two separate statistical analyses were performed. First, the demographic data between the good and poor outcome groups were compared. Categorical variables were compared using a chi-square test or Fisher's exact test. Continuous variables within the two groups were compared using the independent *t*-test for parametric data and the Mann–Whitney *U*-test for nonparametric data. Second, significant variables ($p < 0.05$)

found to be associated with a poor outcome were entered into a forward stepwise logistic regression analysis model, which allowed for simultaneous control of multiple factors. Variables with a zero cell count in a two-by-two table were eliminated from logistic analysis, whereas only variables with a strong association with fatality rate ($p < 0.05$) were included in the final model. All statistical tests were two-tailed. All statistical analyses were conducted using the SAS software, version 13.0 (SAS Statistical Institute, Cary, NC, USA).

Results

The 31 patients included 21 males (mean age 56 years; range 31–84 years) and ten females (mean age 55 years; range 1–74 years). Of these 31 patients, 25 had community-acquired infections, whereas the other six were diagnosed with nosocomially-acquired infections. The associated underlying conditions of the 31 patients are listed in Table 1. Twenty-two cases had more than one underlying disease, whereas the other nine cases did not. Diabetes mellitus, alcoholism and valvular heart diseases were the three most common underlying conditions.

The portal of entry for infection in these 31 cases included haematogenous spread from remote foci (e.g. hepatobiliary tract, cardiopulmonary origin) in 21 cases, contiguous infection from parameningeal foci (e.g. odontogenic origin, otogenic origin or paranasal sinusitis) in four cases, both post-neurosurgical states and haematogenous spread in two cases, and was unknown in four cases. Causative pathogens were found in 23 of the 31 cases. The pathogens were isolated from CSF cultures alone in ten cases, blood cultures alone in five cases, both blood and CSF cultures in four cases, and drainage from the ear or sinuses in four cases. The other eight cases who revealed negative cultures from both CSF and blood, had concomitant bacterial meningitis and the diagnosis was confirmed by serial neuroimaging studies under antimicrobial therapy. Sixty-one percent (61%; 19/31) were infected by a single pathogen, with Gram-negative bacilli being the most prevalent, followed by *Staphylococcus* species and *Streptococcal* species. Mixed infections accounted for 13% (4/31), in which *Acinetobacter baumannii, Escherichia coli, Enterobacter aerogenes* and coagulase-negative *Staphylococcus,* were the implicated pathogens. Twenty-six percent (26%; 8/31) of the patients had a negative culture (Table 2).

Six patients had *Klebsiella* (*K.*) *pneumoniae* brain abscesses, all of whom were diabetic and had concomitant bacterial meningitis. Of these six patients, two had liver abscesses, one had endophthalmitis, one had both endophthalmitis and deltoid pyomyositis, one had purulent pericarditis, and one had septic arthritis. One patient progressed to diabetic ketoacidosis. Fever, disturbed consciousness, septic shock and headache were the four most common clinical features in these 31 cases, accounting for 77% (24/31), 61% (19/31), 55% (17/31) and 52% (16/31), respectively. Other clinical features, median GCS on presentation, median length of hospitalization (days) and median GOS at discharge are listed in Table 3.

The neuroimaging findings of the 31 cases are listed in Table 4. The locations of the abscesses in all 31 cases were supratentorial. In total, 13 cases (42%) had a single brain abscess and the other 18 cases (58%) had multiple brain abscesses. In single brain abscesses, the most common sites for brain abscess were the frontal lobe, temporal lobe and basal ganglion. The left hemisphere was involved more than

TABLE 1. Underlying conditions of the study patients

Underlying conditions	*n* = 31[a]
Diabetes mellitus	12
Alcoholism	7
Valvular heart disease	6
Congenital heart disease	5
End-stage renal disease	4
Liver cirrhosis	3
Chronic ototis media	3
Post-neurosurgical state	2
Atrial fibrillation	2
Coronary artery diseases	2
Drug abuse	2

[a]Twenty-two cases had more than one underlying disease.

TABLE 2. Causative pathogens of the brain abscesses (January 1986 to December 2007)

Organisms	1986 through 1996 *n* = 6 (4)	1997 through 2007 *n* = 25 (11)	*n* = 31 (15)
Gram-negative bacilli (*n* = 11)			
Klebsiella pneumonia	2	4(2)	6 (2)
Other Gram-negative *bacilli*	2 (2)[a]	3 (1)[b]	5 (3)
Staphylococcus species (*n* = 4)			
Staphylococcus aureus	1(1)	2[c]	3 (1)
Staphylococcus epidermidis	0	1(1)	1 (1)
Streptococcus species (*n* = 3)			
Viridans Streptococci	0	3 (1)	3 (1)
Anaerobic Gram-negative *bacillus*	1 (1)[d]	0	1 (1)
Mixed infections (*n* = 5)	0	4[e](3)	4 (3)
Negative culture (*n* = 2)	0	8 (3)[f]	8 (3)

The number of deaths is given in parenthesis.
[a]The causative pathogens were *Escherichia coli* (1) and *Vibrio cholera* (1).
[b]The causative pathogens were *Acinetobacter baumannii* (1) and *Escherichia coli* (1).
[c]The causative pathogens included one oxacillin resistant *S. aureus*.
[d]*Bacteriodes vulgatus*.
[e]*Acinetobacter baumannii*, *Enterococcus* spp.; *Escherichia coli*, *Enterobacter aerogenes*; *Staphylococcus haemolyticus*, *S. epidermidis*, *Enterococcus faecalis*; *Chryseobacterium meningosepticum*, *S. epidermidis*.
[f]The eight cases had concomitant bacterial meningitis and revealed negative cultures from cerebrospinal fluid and/or blood, and/or drainage from the ear or sinuses, and confirmation of the diagnosis was made by serial neuroimaging studies under antimicrobial therapy.

TABLE 3. Demographic features of the study patients

	n = 31
Mean age (years)	55.5 ± 17.5
Sex (male/female)	21/10
Median (IQR) GCS on presentation	9 (7, 15)
Clinical features	
Fever	24
Disturbed consciousness	19
Septic shock	17
Headache	16
Neck stiffness	13
Seizure	11
Motor deficits[a]	10
Nausea/vomiting	10
Hydrocephalus	6
Facial palsy	2
Visual disturbance	1
Median (IQR) length of hospitalization (days)	47 (19, 68)
Median (IQR) GOS at discharge	2 (1, 5)

IQR, interquartile range; GCS, Glasgow coma scale; GOS, Glasgow outcome score.

TABLE 4. Neuroimaging findings

	n = 31
Location of abscess	
Single (*n* = 13)	
Frontal lobe	3
Temporal lobe	3
Basal ganglion	3
Temporo-parietal area	2
Occipital lobe	1
Parieto-occipital area	1
Multiple sites (*n* = 18)	18
Hydrocephalus	6
Rupture into ventricles	9
Median (IRQ) volumes of brain abscess (mm^3)[a]	3 (1.3–22.2)

IQR, interquartile range.
[a]Neuroimaging findings at presentation.

the right, with nine on the left, four on the right and 18 bilaterally on both hemispheres. Other neuroimaging findings including median volume (interquartile range) of the brain abscesses on admission, brain abscess rupture into ventricles and hydrocephalus are listed in Table 4.

All 31 patients received antimicrobial therapy alone, 18 of whom had multiple pyogenic brain abscesses, and 13 were associated with underlying systemic conditions or had concomitant bacterial meningitis. The overall case fatality rates were 46% (6/13) in patients with a single brain abscess and 50% (9/18) in patients with multiple brain abscesses. In total, 16 of the 31 patients survived and the other 15 died. Therapeutic outcomes after discharge were determined by GOS as nine (29%, 9/31) having a normal life, four (13%, 4/31) having moderate disabilities, one (3.2%, 1/31) having severe disabilities, two (6.5%, 2/31) persistent vegetative states, and 15 (48.3%, 15/31) deceased. The median number of hospitalization days, acquisition of infection, types of infection, GCS score at presentation and discharge GOS score are listed in Table 5.

The comparative results of the clinical features and neuroimaging findings between patients with good and poor outcomes are also listed in Table 5. Statistical analysis of the clinical manifestations and laboratory data between the two patient groups revealed significant findings: GCS at presentation (p 0.001), presence of septic shock (p 0.0001) and neck stiffness (p 0.045). The significant univariate factors and possible confounding factors used in stepwise logistic regression included GCS at presentation and the presence of neck stiffness. The results revealed that, after an analysis of all the above-mentioned variables, only GCS at presentation was independently associated with a with poor outcome, and that each reduction of one point on the GCS increased the poor outcome rate by 28% (p 0.016, OR 0.717, 95% CI 0.547–0.941).

Discussion

In clinical practice, a brain abscess rarely complicates bacterial meningitis and vice versa. In addition, both conditions can develop from contiguous or haematogenous spread from an extradural focus. The association of bacterial brain abscess and meningitis has been found in several situations, including intraventricular rupture of a brain abscess, neonatal central nervous system infections, and brain abscesses caused by *Listeria monocytogenes* [20,21]. To the best of our knowledge, this is the largest series study to show therapeutic experiences among patients who received nonsurgical treatment for bacterial brain abscesses. Most of our patients in this study had associated underlying systemic conditions, concomitant bacterial meningitis or multiple deep-seated abscesses, where surgical intervention would be inappropriate; therefore, the therapeutic outcomes were not satisfactory.

In the present study, we examined the therapeutic outcomes of non-operative treatment of bacterial brain abscesses in selected groups of patients (e.g. brain abscess associated with meningitis, multiple deep-seated abscesses and metastatic abscesses). We conclude that GCS at presentation, presence of septic shock and neck stiffness are risk factors for poor outcomes, and that each reduction of one point on the GCS increases the poor outcome rate by 28%.

Although lumbar punctures should not be performed on patients with a proven brain abscess as a result of increased intracranial pressure, clinicians should be aware of meningitis as a complication of brain abscess. Surgery may be therapeutic and provide tissue samples confirming an infectious process; however, isolating the causative organism from specimens obtained during surgery has been less successful.

TABLE 5. Prognostic factors of the study patients

	Good outcome, *n* = 9	Poor outcome, *n* = 22	Crude OR (95% CI)	p-value	Adjusted OR (95%CI)	p-value
Sex (male/female)	7/2	14/8	0.6 (0.13–2.81)	0.711	–	–
Mean age at onset	48.2 ± 23.4	58.5 ± 13.9		0.139	–	–
Median (IQR) GCS on presentation	15 (12, 15)	8 (6, 15)		0.001	0.717 (0.547–0.941)	0.016
Neuroimaging findings at presentation						
Multiple/single	5/4	13/9	1.16 (0.24–5.53)	1.0	–	–
Involved left hemisphere	5	17	2.72 (0.52–14.17)	0.385	–	–
IVROBA	3	6	0.75 (0.14–4.0)	1.0	–	–
Hydrocephalus	2	4	0.78 (0.12–5.25)	1.0	–	–
Multiloculated	1	3	1.26 (0.11–14.05)	1.0	–	–
Median (IRQ) volumes of brain abscess (mm^3)	2.9 (0.54–4.7)	93.9 (1.6–24.4)		0.238	–	–
Acquisition of infection						
Nosocomially acquired/community acquired	1/8	5/17	2.35 (0.24–23.60)	0.642	–	–
Types of infection						
Post-neurosurgery/spontaneous	0/9	1/21	0.7 (0.55–0.89)	1.0	–	–
Underlying diseases						
Diabetes mellitus	2	10	2.92 (0.49–17.32)	0.418	–	–
Chronic alcoholism	1	6	3.0 (0.31–29.35)	0.639	–	–
Valve heart disease	1	5	2.35 (0.24–23.60)	0.642	–	–
End-stage renal disease	0	4	0.67 (0.51–0.87)	0.295	–	–
Chronic otitis media	0	3	0.68 (0.53–0.88)	0.537	–	–
Liver cirrhosis	1	2	0.8 (0.06–10.11)	1.0	–	–
Neoplasm	0	2	0.69 (0.54–0.88)	1.0	–	–
Drug abuse	1	1	0.38 (0.02–6.85)	0.5	–	–
Clinical features following brain abscess						
Fever/chills	7	16	0.76 (0.12–4.75)	1.0	–	–
Septic shock	0	17	0.36 (0.18–0.72)	0.0001	–[a]	–[a]
Headache	7	9	0.20 (0.03–1.18)	0.113	–	–
Nausea/vomiting	5	5	0.24 (0.05–1.23)	0.105	–	–
Hemiparesis	2	8	2.0 (0.33–12.05)	0.677	–	–
Facial palsy	1	1	0.38 (0.02–6.85)	0.503	–	–
Sensory disturbance	0	1	0.7 (0.55–0.89)	1.0	–	–
Neck stiffness	1	12	9.6 (1.02–90.34)	0.045	8.2 (0.74–90.58)	0.086
Visual disturbance	0	1	0.7 (0.55–0.89)	1.0	–	–
Concomitant with bacterial meningitis	7	18	1.29 (0.19–8.67)	1.0	–	–
Outcome						
Median (IRQ) hospitalization days	53 (41–84)	44 (8–64)		0.391	–	–
Mean GOS at discharge	5.0	1.7 ± 1.2		0.001	–	–

IVROBA, intraventricular rupture of brain abscess; GOS, Glasgow outcome scale; GCS, Glasgow coma scale; IQR, interquartile range.
[a]Variables with a zero cell count in a two-by-two table were eliminated from the logistic analysis.

In our series, 81% (25/31) of the cases were associated with bacterial meningitis, brain abscesses with a fulminant course, a high proportion of multiple pyogenic brain abscesses and poor systemic conditions. Ultimately, the decision to perform a lumbar puncture is based on the clinical presentation.

In Taiwan, *Klebsiella* infection is known to commonly cause devastating metastatic septic infection, including pyogenic liver abscess, bacteraemia, pneumonia, endophthalmitis, brain abscess and meningitis [22–25]. Diabetes mellitus and other underlying diseases such as liver cirrhosis and alcoholism appear to be predisposing factors. It has been postulated that hyperglycaemia may enhance capsule formation and thereby increase the virulence of the *Klebsiella* bacilli [23].

For patients with multiple bacterial brain abscesses, and where the largest brain abscess is both >3 cm in diameter and has a significant mass effect noted in the initial CT scan, undergoing both surgical intervention and antimicrobial treatment is recommended [1,3,4,8]. If none of the abscesses has a significant mass effect, antibiotic treatment can be used initially, with regular follow-up by CT scans to evaluate the therapeutic response. Surgical intervention should be performed only if either there is neurological deterioration or if the abscess fails to resolve after antibiotic treatment. The treatment of these patients should be judged on the clinical status, neuroradiographic findings and the therapeutic response, and complete resolution of abscesses for a minimum of 3 months. The duration of antibiotic therapy is dependent on the therapeutic response and neuroradiographic findings, and is usually approximately 8–12 weeks [1,3,4,8].

There are two main limitations to this retrospective study. First, our hospital provides both primary and tertiary referral care for patients, and several patients who were initially treated at other hospitals but subsequently transferred to our hospital for further therapy were also included. Therefore, it is possible that there is reporting bias due to patient selection. Second, the choice of therapeutic strategy for the bacterial brain abscesses was different for each patient according to the preference of his/her doctor, and this may have caused a potential bias in the statistical analysis.

In summary, the present study demonstrates a high mortality rate (48%) and worse outcome in this special group of

patients. Among the significant prognostic factors, a lower mean GCS at presentation was a major determinant of poor outcome. Regardless of the high fatality rate, early diagnosis, the timely use of appropriate antibiotics based on antimicrobial susceptibility testing and correct metabolic derangement are essential for survival.

Transparency Declaration

The authors declare that they have no conflict of interest.

References

1. Mathisen GE, Johnson JP. Brain abscess. *Clin Infect Dis* 1997; 25: 763–781.
2. Lu CH, Chang WN, Lin YC *et al.* Bacterial brain abscess: microbiological features, epidemiological trends and therapeutic outcomes. *QJM* 2002; 95: 501–509.
3. Lu CH, Chang WN, Lui CC. Strategies for the management of bacterial brain abscess. *J Clin Neurosci* 2006; 13: 979–985.
4. Sharma BS, Gupta SK, Khosla VK. Current concepts in the management of pyogenic brain abscess. *Neurol India* 2000; 48: 105–111.
5. Obana WG, Rosenblum ML. Nonoperative treatment of neurosurgical infections. *Neurosurg Clin N Am* 1992; 3: 359–373.
6. Barsoum AH, Lewis HC, Cannillo KL. Nonoperative treatment of multiple brain abscesses. *Surg Neurol* 1981; 16: 283–287.
7. Daniels SR, Price JK, Towbin RB, McLaurin R. Nonsurgical cure of brain abscess in a neonate. *Childs Nerv Syst* 1985; 1: 346–348.
8. Rosenblum ML, Hoff JT, Norman D, Edwards MS, Berg BO. Nonoperative treatment of brain abscesses in selected high-risk patients. *J Neurosurg* 1980; 52: 217–225.
9. Berg B, Franklin G, Cuneo R, Boldrey E, Strimling B. Nonsurgical cure of brain abscess: early diagnosis and follow-up with computerized tomography. *Ann Neurol* 1978; 3: 474–478.
10. Vaquero J, Cabezudo JM, Leunda G. Nonsurgical resolution of a brain-stem abscess: case report. *J Neurosurg* 1980; 53: 726–727.
11. Bertoldi RV, Sperling MR. Norcardia brain stem abscess: diagnosis and response to medical therapy. *Bull Clin Neurosci* 1984; 49: 99–104.
12. Ruelle A, Zerbi D, Zuccarello M, Andrioli G. Brain stem abscess treated successfully by medical therapy. *Neurosurgery* 1991; 28: 742–746.
13. Lorber B. Listeriosis following Shigellosis. *Rev Infect Dis* 1991; 13: 865–866.
14. Wang H, Kuo M, Huang S. Medical cure of a brainstem abscess and serial brainstem auditory evoked potentials. *Dev Med Child Neurol* 1992; 34: 911–915.
15. Carpenter JL. Brain stem abscess: cure with medical therapy, case report and review. *Clin Infect Dis* 1994; 18: 219–226.
16. Kohno K, Ohue S, Sadamoto K, Takeda S, Sakaki S. Rupture of brain stem abscess into fourth ventricle: MR demonstration. *J Comput Assist Tomogr* 1993; 17: 498–499.
17. Garner JS, Jarvis WR, Emori TG, Horan TC, Hughes JM. CDC definitions for nosocomial infections. *Am J Infect Control* 1988; 16: 128–140.
18. Jennett B, Bond M. Assessment of outcome after severe brain damage. *Lancet* 1975; 1: 480–484.
19. Weisfelt M, van de BD, Spanjaard L, Reitsma JB, de Gans J. A risk score for unfavorable outcome in adults with bacterial meningitis. *Ann Neurol* 2008; 63: 90–97.
20. Lee TH, Chang WN, Su TM *et al.* Clinical features and predictive factors of intraventricular rupture in patients who have bacterial brain abscesses. *J Neurol Neurosurg Psychiatry* 2007; 78: 303–309.
21. Eckburg PB, Montoya JG, Vosti KL. Brain abscess due to *Listeria monocytogenes*: five cases and a review of the literature. *Medicine (Baltimore)* 2001; 80: 223–235.
22. Lee SS, Chen YS, Tsai HC *et al.* Predictors of septic metastatic infection and mortality among patients with *Klebsiella pneumoniae* liver abscess. *Clin Infect Dis* 2008; 47: 642–650.
23. Lu CH, Chang WN, Chang HW. *Klebsiella* meningitis in adults: clinical features, prognostic factors and therapeutic outcomes. *J Clin Neurosci* 2002; 9: 533–538.
24. Liliang PC, Lin YC, Su TM *et al. Klebsiella* brain abscess in adults. *Infection* 2001; 29: 81–86.
25. Tang LM, Chen ST, Hsu WC, Chen CM. *Klebsiella* meningitis in Taiwan: an overview. *Epidemiol Infect* 1997; 119: 135–142n.