

Community-acquired brain abscess in Taiwan: etiology and probable source of infection

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Brain abscess is a life-threatening infection caused by spread from infected parameningeal or remote foci. Historically, streptococci have been the predominant organisms reported while brain abscess metastatic from liver abscess caused by *Klebsiella pneumoniae* has been a more recent emerging problem. This study retrospectively analyzed the characteristics of community-acquired brain abscess admitted during an 11-year period. There were 17 men and 7 women with age from 20 to 82 years (median, 41 years). The most common source of infection was liver abscess, followed by otitic infection and sinusitis. The classic triad of fever, headache and focal neurologic deficit was noted in only 25% of cases. Spread of the abscess to multiple lobes was common (n = 6). The most commonly identified organisms were *Streptococcus* spp. (n = 7) and *K. pneumoniae* (n = 5). All 5 cases of *K. pneumoniae* brain abscess also had concomitant pyogenic liver abscess and 4 of them had diabetes mellitus. In this study, brain abscess was common in young patients and in patients with diabetes mellitus. In Taiwan, *Streptococcus* spp. and *K. pneumoniae* are leading etiologies for community-acquired brain abscess. Liver abscess is the most likely source of *K. pneumoniae* brain abscess.

Key words: Brain abscess, *Klebsiella pneumoniae*, liver abscess, *Streptococcus*

Brain abscess is a life-threatening infection caused by spread from infected parameningeal or remote foci [1]. Historically, streptococci were the most frequently isolated organisms, present in 20 to 100% of non-traumatic abscesses [2]. However, the widespread use of antibiotics for upper respiratory tract infections, modern imaging techniques, and the increasing frequency of neurosurgical procedures have possibly changed the epidemiology and clinical spectrum of brain abscesses in recent years [3]. In a previous study of brain abscess by de Louvois et al [4] in 1977 and Yang [5] in 1981, the 3 most frequently identified organisms were streptococci, *Staphylococcus aureus* and *Proteus* spp. In contrast, in more recent studies by Lu et al [6] in 2000 and Cheng et al [7] in 2003, *Klebsiella pneumoniae* was a frequent causative organism of liver abscess metastatic to brain in Taiwan. This retrospective study investigated the etiology and source of infection in patients with community-acquired brain abscess admitted during an 11-year period.

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Materials and Methods

A computerized search was used to identify cases of brain abscess in patients discharged between January 1992 and December 2002. Cases meeting the following criteria were excluded: younger than 18 years old; subdural and epidural empyema; and hospital-acquired infection. Community-acquired infection was defined as clinical evidence of infection developed before admission or within 48 hours after admission. An infection that occurred in a patient who received craniotomy or cerebrospinal fluid (CSF) shunting after discharge was considered as nosocomial. Brain abscess was defined as one or more localized lesions with a characteristic computed tomography (CT) appearance [8,9]. Brain abscess was confirmed by operative and pathologic findings in 20 patients, and by compatible clinical features and CT findings in 4 patients. The pathology of brain abscess was localized inflammation associated with tissue necrosis, which included any stage of maturation (early or late cerebritis, or early or late capsule formation). Fever was defined as body temperature $\geq 37.5^{\circ}\text{C}$; leukocytosis as white blood cell count $\geq 10,000/\text{mm}^3$; thrombocytopenia as platelet count $< 100,000/\text{mm}^3$; and acute renal failure as a rise

in the serum creatinine concentration of 0.5 mg/dL and a rise in the blood urea nitrogen level of 10 mg/dL per day over several days. All materials from brain abscesses were cultured for fungi and aerobic and anaerobic bacteria. Aerobic culture media included blood, chocolate, and thioglycolate broth. Anaerobic cultures were processed in anaerobic chambers using blood agar and thioglycolate isolation. Fungus culture media included chrom agar and sabouraud dextrose agar. Organisms were identified by the Vitek II system and traditional biochemical methods. The following data were collected and analyzed: demographic characteristics, underlying diseases, clinical presentation, probable source of infection, laboratory data, microbiological data and outcome.

Results

Demographic data, underlying disease and probable source of infection

During the 11-year study period, a diagnosis of brain abscess was made in 24 patients, 17 men and 7 women. Their age ranged from 20 to 82 years (median, 41 years). Six patients were above 60 years old. The most frequent underlying medical illness was diabetes mellitus (n = 9, 38%) [Table 1]. Probable sources of infection were identified in 11 of 24 patients (46%). The most common probable source of infection was liver abscess, followed by otitic infection and sinusitis, which were suggested by history, examination of the nose, ears, sinuses and CT findings (Table 2).

Clinical presentation

The period between onset of symptoms and admission was as follows: <1 week (n = 18); ≥1 week and <2 weeks (n = 4); ≥2 weeks and <1 month (n = 1); and ≥1 month

Table 1. Underlying conditions of 24 patients with brain abscess

Underlying condition	No. of patients
Diabetes mellitus ^a	9
Alcoholism ^a	3
Cancer ^a	2
Cirrhosis of liver ^a	1
Pulmonary tuberculosis	1
Old cerebrovascular accident ^a	1
Intravenous drug abuser	1
None	13

^aOne patient had concomitant diabetes mellitus, alcoholism and cirrhosis of liver. Two patients had concomitant diabetes mellitus and alcoholism. One patient had concomitant diabetes mellitus, old cerebrovascular accident and colonic carcinoma.

(n = 1). Fever was presented in 71% of cases, headache in 46% and nausea and vomiting in 17%. Mental change was noted in 42% of cases. Focal neurologic deficit was found in 50% of cases including right hemiparesis (n = 7) and left hemiparesis (n = 5). The classic triad of fever, headache and focal neurologic deficit was only noted in 25% of cases. Seizure was seen in 21% of cases (Table 3).

Location and number of brain abscesses

Eighteen patients had solitary brain abscesses. Six patients had multiple brain abscesses (with number of abscesses from 2-7) [Table 2]. Bilateral disseminated abscesses over the cerebral parenchyma were noted in 2 patients. Ventriculitis with abscess formation was seen in 1 patient. Cerebellar abscess was found in 1 patient. Single lobe involvement was found in 14 patients. Thirteen of the 14 patients had solitary abscess.

Laboratory and microbiological data

Leukocytosis was seen in 63% of cases (range, 4500/mm³ to 28,900/mm³) and neutrophils were predominant in all patients. Thrombocytopenia (platelet count, <100,000/mm³) was noted in 2 patients. Acute renal failure developed in 1 patient. Organisms were identified from the pus aspirate in 15 patients. The most commonly identified organisms were *Streptococcus* spp. and *K. pneumoniae* (Table 2). Blood culture was performed in 17 patients. Eight of the 17 patients showed a positive blood culture result including *K. pneumoniae* in 5 patients, *Proteus vulgaris* in 1, β-hemolytic, non-group A, B, D streptococcus in 1, and methicillin-susceptible *Staphylococcus aureus* (MSSA) in 1. Four of the bacteremic patients had an identical organism found in the pus.

Correlation of etiology, source of infection and underlying diseases

K. pneumoniae infection was found in 5 patients (21%). The source of infection appeared to originate from liver abscess in all 5 of these patients. Four of the 5 patients had diabetes mellitus. Viridans streptococcus infection was found in 4 patients but the source of this infection was not identified despite a thorough study including echocardiography. β-Hemolytic, non-group A, B, D streptococcus infection was found in 2 patients. The infection was suspected to have originated from sinusitis in 1 of these patients. MSSA infection was found in 2 patients, 1 of whom had sinusitis and the other chronic otitis media.

Outcome

All of the patients received medical treatment with antibiotics. The mean duration of treatment was 40 days (range, 4 to 60 days). The mean hospital stay was 44 days (range, 4 to 106 days). Twenty patients also received surgical intervention with either craniotomy or stereotactic aspiration and drainage. The overall in-hospital mortality rate was 17% (4/24). Two patients had underlying malignancy (nasopharyngeal carcinoma and colonic carcinoma, respectively). One 82-year-old patient had

underlying diabetes mellitus and pulmonary tuberculosis. The other had sinusitis as the probable source of infection and β -streptococci were identified both in the abscess and blood. The cause of death in 4 patients was classified as severe sepsis and profound shock.

Discussion

The spectra of clinical presentations of brain abscess range from insidious to fulminant. Some patients have

Table 2. Demographic data, and clinical and microbiological characteristics of patients with brain abscess

Source	Patient no.	Gender/ age (years)	Sites (no.) of suppuration	Culture results			Operation	Outcome
				Intracranial abscess	Blood	CSF		
Liver abscess	1	M/38	F-P	<i>Klebsiella pneumoniae</i>	<i>K. pneumoniae</i>	-	Craniotomy	Survived
	2	M/65	V	<i>K. pneumoniae</i>	<i>K. pneumoniae</i>	-	Craniotomy	Survived
	3	M/55	BCP ^a	-	<i>K. pneumoniae</i>	-	Nil	Survived
	4	F/59	F-L	-	<i>K. pneumoniae</i>	-	Nil	Survived
	5	F/62	BCP ^a	-	<i>K. pneumoniae</i>	-	Nil	Survived
Sinusitis	6	M/21	F-L ^a	β -Hemolytic, non-group A, B, D streptococci	β -Hemolytic, non-group A, B, D streptococci	-	Craniotomy	Died
	7	M/20	F-L	-	MSSA	MSSA	Nil	Survived
Otic infection	8	M/40	T-P-O ^a	<i>Bacteroides fragilis</i>	No growth	-	Craniotomy	Survived
	9	M/20	T-L	<i>Proteus vulgaris</i> , <i>Morganella morganii</i>	<i>P. vulgaris</i>	-	Craniotomy	Survived
Meningitis No identified source of infection	10	M/18	CBL	MSSA	No growth	-	Craniotomy	Survived
	11	F/61	P-L	No growth	No growth	-	Craniotomy	Survived
	12	M/21	T-P	No growth	No growth	-	Craniotomy	Survived
	13	M/41	F-L	Viridans streptococci	-	-	Craniotomy	Survived
	14	F/64	P-L	β -Hemolytic streptococci	No growth	-	Craniotomy	Survived
	15	M/20	F-L	Viridans streptococci	-	-	Craniotomy	Survived
	16	F/66	T-L	<i>Lactobacillus</i> spp.	No growth	-	Craniotomy	Died
	17	M/49	F-T-P	β -Hemolytic, non-group A, B, D streptococci	-	-	Craniotomy	Survived
	18	M/82	P-L	No growth	No growth	-	Craniotomy	Died
	19	M/30	T-L	Peptostreptococci, viridans streptococci, <i>Capnocytophaga</i> spp.	-	-	Craniotomy	Survived
20	F/56	T-P	No growth	No growth	-	Stereotactic craniotomy	Survived	
21	M/29	P-L, P-O	<i>Lactobacillus</i> spp., <i>Haemophilus</i> spp.	-	-	Stereotactic aspiration	Survived	
22	M/57	O-L	No growth	No growth	-	Craniotomy	Survived	
23	F/30	F-L	Unidentified Gram-positive cocci	-	-	Craniotomy	Survived	
24	M/55	F-L	Viridans streptococci	-	-	Craniotomy	Died	

Abbreviations: CSF = Cerebrospinal fluid; F-P = frontoparietal lobes; V = ventriculitis; BCP = bilateral cerebral parenchyma; F-L = frontal lobe; F-T-P = frontotemporoparietal lobes; T-P-O = temporoparietooccipital lobes; T-L = temporal lobe; CBL = cerebellum; P-L = parietal lobe; T-P = temporoparietal lobe; P-O = parietooccipital lobes; O-L = occipital lobe; MSSA = methicillin-susceptible *Staphylococcus aureus*

^aMultiple abscesses.

Table 3. Clinical presentations of 24 patients with community-acquired brain abscess

Presentations	Number of patients (%)
Fever	17 (71)
Headache	11 (46)
Nausea and vomiting	4 (17)
Mental status changes	10 (42)
Focal neurologic deficit	12 (50)
Seizures	5 (21)
Visual acuity loss	2 (8)
Nuchal rigidity	1 (4)
Otalgia	2 (8)

a classic constellation of symptoms and signs, while others have a more subtle presentation [10]. If unrecognized or not treated promptly, brain abscess is associated with a high morbidity and mortality [1].

Before the era of human immunodeficiency virus infection, brain abscess accounted for about 1 in 10,000 general hospital admissions with 1500 to 2500 cases treated in the United States each year [11]. During the 11-year-period of this study, there were 352, 167 admissions in our hospital. The ratio of admissions due to community-acquired brain abscess was 0.68 in 10,000, which is lower than previous study and may be attributable to exclusion of pediatric and postneurosurgical patients.

Brain abscess is the most common focal suppurative intracranial process [12]. It is usually related to contiguous infection or hematogenous spread from a remote site. A quarter of all brain abscesses arise hematogenously, most commonly from a cardiac or pulmonary source [13]. In a recent study, viridans streptococci and *K. pneumoniae* were the 2 prevalent pathogens associated with hematogenous spread [14]. Metastatic septic abscess of *K. pneumoniae* septicemia in diabetic patients was reported to have a high mortality rate [14]. In contrast, all 6 patients in this study with intracranial abscess secondary to a hematogenous spread from pyogenic liver abscess caused by *K. pneumoniae* survived. We also found that 83% of patients with *K. pneumoniae* intracranial abscess had underlying diabetes mellitus. Contiguous infections (25%) identified in this study included sinusitis, otitic infection and meningitis.

In a previous study, the classic triad of headache, fever, and focal neurologic deficit was present in fewer than half of patients with brain abscess [15]. In this series, only 25% of patients fulfilled the classic triad, indicating that the classic triad is not sensitive for the diagnosis of brain abscess.

In a previous study, routine laboratory tests, including peripheral white blood cell count, were not helpful in diagnosing brain abscess [16]. Abscesses of the central nervous system with negative cultures have been reported in 9 to 63% of patients [4]. Aerobic or microaerobic streptococcal spp. are isolated in up to 70% of brain abscesses [17,18]. In this series, liver abscess was the most common probable source of brain abscess, and was uniformly caused by *K. pneumoniae*. *K. pneumoniae* has been reported to be the leading causative organism of pyogenic liver abscess [5,18], and as the predominant pathogen of community-acquired meningitis [19]. An increasing incidence and high proportion of *K. pneumoniae* community-acquired bacterial meningitis during 1993 to 1998 was reported, but the reason remained unclear [20]. The high prevalence of serotype K1 has been implicated as the reason for the increased incidence of invasive *K. pneumoniae* diseases in this country [21]. Diabetes mellitus was the most common underlying disease, followed by other debilitating diseases such as liver cirrhosis, neoplasm and end-stage renal disease. Metastatic septic abscess is a devastating complication of *K. pneumoniae* septicemia. The incidence of metastatic septic lesions of meningitis caused by *K. pneumoniae* bacteremia and hepatobiliary infection such as pyogenic liver abscess has been reported to be as high as 15.6% [19].

Most of the patients in this series with sinusitis and otitic infection as the source were young men. None of the 5 patients had underlying disease except for one who had diabetes mellitus. The route of spread from sinusitis and ear infection is usually through thrombophlebitis and septic implantation. Parameningeal foci such as sinusitis and otitic and odontogenic infections have accounted for 40 to 70% of cases reported since 1936 [2,22]. The incidence of abscesses due to otitic infections has decreased from approximately 35% to 20% since 1936 and may be attributable to enhanced recognition, early antibiotic therapy, and more aggressive management of ear infections [8]. The incidence of abscesses due to pulmonary infections and sinusitis has remained about 15% since 1936 [8].

Mortality from brain abscess has been significantly reduced since 1940 because of antimicrobial therapy and improved diagnostic imaging techniques. With the use of CT scan as the diagnostic tool, lower mortality, ranging from 0 to 30%, has been reported [23]. Mortality among treated patients was related to older age, male gender, altered sensorium and a pulmonary source [2].

The mortality rate in this study was 17%, which was compatible with previous studies [2,5,9,11].

In conclusion, we found that intracranial abscess often occurs in young patients and in patients with diabetes mellitus. In Taiwan, *Streptococcus* spp. and *K. pneumoniae* are leading etiologies for community-acquired brain abscess. Liver abscess should be considered a probable source in all cases of *K. pneumoniae* brain abscess.

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