

## CLINICAL INFECTIOUS DISEASE ARTICLES

**Bacterial Brain Abscesses: Factors Influencing Mortality and Sequelae**

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Thirty-nine cases of brain abscess diagnosed since the advent of the computed tomographic (CT) scan were analyzed for factors influencing the outcome. The mortality rate was 13%, and severe sequelae were present in 22% of the survivors. The mean delay between occurrence of the first symptoms and hospitalization was significantly shorter for the 12 patients with poor outcome (death or severe sequelae) than for the 25 who recovered (fully or with moderate sequelae). Moreover, severely impaired mental status and neurological impairment at admission were associated with a poor outcome in terms of both mortality and sequelae. In all cases with fatal outcome or severe sequelae, the diagnosis was made and treatment was initiated within 24 hours of admission. There was no apparent correlation between the outcome and the presence or type of predisposing factors, the radiological, biological, or microbiological findings, or the treatment modalities. Thus, with the advent of the CT scan and the possibility of early diagnosis and treatment, the prognosis of brain abscess appears to be mainly determined by the rapidity of progression of the disease before hospitalization and the patient's mental status on admission.

Since the advent of antimicrobial agents, the mortality rate associated with brain abscess has remained between 20% and 50%, and sequelae have been reported for 30% to 70% of survivors [1-8]. Recently, substantial improvement in the prognosis of brain abscess with a mortality rate between 5% and 20%, has been reported [9-11]. This has been attributed to the advent of more-reliable methods of identification of microorganisms, more-effective antibiotic regimens, new surgical techniques, and, most important, the availability of the computed tomographic (CT) scan [12]. Magnetic resonance imaging (MRI) was recently shown to be more sensitive in the early detection of cerebritis in animal models, but evidence of its superiority over the CT scan in terms of clinical benefit for patients with cerebral abscess has not yet been established [13-15]. The purpose of the present study was to review the cases diagnosed at our institution since the introduction of the CT scan and before the introduction of MRI in order to delineate the clinical, biological, and therapeutic characteristics that are of importance for the diagnosis and outcome of brain abscess.

**Materials and Methods****Patients**

Thirty-nine cases of brain abscesses were diagnosed at the Centre Hospitalier Universitaire Vaudois (Lausanne, Swit-

zerland) from January 1977 to December 1987. All patients had been hospitalized in either the Department of Internal Medicine or the Department of Neurosurgery. The diagnoses were retrospectively traced by the hospitals computerized system. Brain abscess was defined as a localized lesion visible on CT scan that was located in the cerebrum, cerebellum, or midbrain and associated with at least one of the three following criteria: positive blood culture, positive culture of intracerebral material, or histology suggesting an acute brain abscess. Materials obtained from brain abscesses were cultured for aerobic and anaerobic bacteria, fungi, and mycobacteria with use of standard methods. Patients who tested positive for the human immunodeficiency virus and those with suspected *Toxoplasma gondii* encephalitis, *Listeria monocytogenes* meningoencephalitis, or brain abscess due to fungi (in one case, *Cryptococcus*) were excluded.

**Statistical Analysis**

Comparison of groups with continuous variable distribution (age, duration of symptoms) was conducted with use of an unpaired Student's *t*-test. Comparison of groups with discrete variable distribution (predisposing factors, neurological signs, meningismus, microbiological cultures) was performed by means of the  $\chi^2$  test with Yates' correction. A *P* value of  $\leq .05$  was considered significant. Data are given as mean  $\pm$  SD unless stated otherwise.

**Results****Demographic Data**

There were 26 males and 13 females (male/female ratio: 2/1; age: mean, 44 years; and range, 5-80 years) in the study

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**Table 1.** Clinical characteristics of 39 patients with brain abscess, analyzed according to age group.

Variable	Patient age group			
	0-20 y (n = 7)	20-60 y (n = 19)	>60 y (n = 13)	All ages (n = 39)
Male	4	14	8	26
Female	3	5	5	13
Duration (d) of symptoms before admission (mean ± SD)	36.0 ± 27.3	5.2 ± 8.2	18.5 ± 14.9	15.1 ± 18.7
<i>P</i> value	<i>P</i> < .05		<i>P</i> < .05	
Deaths (%)	0 (...)	3 (16)	2 (15)	5 (13)
Predisposing factors ( <i>P</i> value)	<i>P</i> < .05		<i>P</i> < .05	
Absent (%)	1 (14)	6 (32)	8 (62)	15 (38)
Present (%)	6 (86)	13 (68)	5 (38)	24 (62)
ENT infection	1	8	0	9
Cardiopathy*	3	2	0	5
Lung abscess	0	1	1	2
Other†	2	2	4	8

NOTE. Data are given as numbers of patients except for duration of symptoms before admission (no. of days) and *P* values. Percentages are based on data in each column. ENT = ear, nose, and throat.

\* Cyanotic cardiopathy; three of these patients also had ENT infection.

† Head injury (2), steroid therapy (2), skin infection with bacteremia (2), or endocarditis (2).

group. Most of the brain abscesses diagnosed were in adults aged >30 years (31 of 39; 79%), but six (15%) were observed in children <15 years old (table 1).

Overall, there were 3.6 cases diagnosed per year, i.e., ~1 case per 12,000 hospitalizations (39 of 460,000). Twenty-two patients (56%) were transferred from other hospitals, while 17 were admitted directly to our hospital.

**Presenting Symptoms and Physical Findings**

The duration of symptoms before hospitalization ranged from several hours to 44 days, with a mean of 15.1 days. It was significantly less for the patients between 20 and 60 years of age than for those in other age groups (table 1).

On admission, 56% of the patients (22 of 39) had a headache, the most common symptom. Fever was present in only 41% of the cases (16 of 39) and was not correlated with the presence of predisposing factors or the location of abscess. General seizures (11 patients) or focal seizures (3 patients) prompted hospitalization of 14 patients. On physical examination, all patients presented with neurological signs suggestive of brain lesions: 19 (49%) had focal neurological signs (hemiparesis or focal seizure), 13 (33%) had diffused neurological dysfunction (coma, general seizures, or behavioral disturbances), and 7 (18%) had a hemisindrome and a general seizure. Abscesses in an occipital or temporal location were more frequently accompanied by diffuse signs than were frontal, parietal, or multiple abscesses (table 2).

Meningismus was observed in nine patients (23%) and was associated with fever in six (67%) of them. Five patients also had focal neurological signs, three had neuropsychological disturbances, and one was comatose. Abscesses in an occipital or temporal location were more frequently associated

with meningismus (50%) than frontal or parietal (11%) or multiple abscesses (27%) (table 2). Funduscopic examination was performed on 18 patients: 6 of them (33%) had a papilledema (3 bilateral and 3 unilateral) that was not related to the location of the abscess and did not appear to have prognostic value.

On admission, 19 patients (48%) had a normal mental status (mental status A), 17 (44%) presented with confusion (mental status B), 1 (3%) was stuporous (mental status C), and 2 (5%) were comatose (mental status D).

**Predisposing Factors and Location of the Abscesses**

Twenty-four patients (62%) presented 27 predisposing factors. Fifteen (63%) had an infectious focus (9 otic or sinus

**Table 2.** Location of brain abscess compared with CNS signs at admission and the presence of meningismus in 39 patients.

Variable	No. (%) of patients with indicated abscess(es)			
	F/P (n = 18)	O/T (n = 6)	Multiple (n = 15)	Total (n = 39)
CNS signs*				
Focal	8 (44)	2 (33)	9 (60)	19 (49)
Diffuse	6 (33)	3 (50)	4 (27)	13 (33)
Complex	4 (22)	1 (17)	2 (13)	7 (18)
Meningismus ( <i>P</i> value)	<i>P</i> < .05		<i>P</i> < .05	
Present	2 (11)	3 (50)	4 (27)	9 (23)
Absent	16 (89)	3 (50)	11 (73)	30 (77)

NOTE. F = frontal; P = parietal; O = occipital; T = temporal locations of all single abscess(es). Percentages are based on data in each column.

\* See definitions in text.

infections, 2 skin infections with bacteremia, 2 cases of endocarditis, and 2 pulmonary infections), 5 (21%) had a congenital cyanotic cardiopathy (3 of them associated with an ear, nose, and throat infection), 2 (8%) were receiving corticosteroids, and 2 (8%) had had a prior head injury. Predisposing factors were present in 73% (19 of 26) of the patients <60 years old but in only 38% (5 of 13) of those aged >60 years. Otogenic or sinus infections were all observed in patients <50 years old. Five of the 7 patients >20 years old had either a cyanotic cardiopathy (3 patients) or a prior head trauma (2 patients) (table 1). No patients had undergone a dental or surgical procedure during the 3 months before the diagnosis of brain abscess. Neither the occurrence nor the type of predisposing factors seemed to influence the clinical presentation or the duration between the appearance of the first symptoms and hospitalization. For 38% (15 of 39) of the patients, no predisposing condition was documented. These patients did not differ in terms of the clinical manifestation, location of abscess, or type of isolated organisms.

In cases of a single abscess (24 of 39; 62%), it was mostly located in the frontal lobe (12 patients) or parietal lobe (6 patients) rather than in the occipital (4 patients) or temporal (2 patients). The sites were independent from the presumed origin of infection, except for abscesses caused by an ear or sinus infection (7 of 12 patients [58%] with such abscesses presented with a frontal brain abscess). In the 15 patients (38%) with multiple abscesses, the parietal lobe was involved in all but 3 cases, the occipital lobe in 6 cases, the frontal lobe in 7 cases, and the temporal lobe in 5 cases.

### Laboratory Findings

Peripheral white blood cell (WBC) counts were >10,000/mm<sup>3</sup> in 49% of the cases. Anemia was noted in three cases and thrombopenia (<10,000 blood platelets/mm<sup>3</sup>) in one case. These findings did not influence the clinical presentation or the outcome.

A lumbar puncture (LP) was performed on 17 patients (44%), always before the CT scan. No complication occurred, although 3 patients had papilledema. The decision to perform an LP was mainly related to a clinical suspicion of bacterial meningitis: six patients (35%) had true meningismus with fever and two (12%) were highly confused or in a coma with fever. For two patients (12%) with perforated sinusitis, the LP was performed to rule out meningitis. Seven patients (41%) with hemisindrome (five of whom had fever) also underwent an LP, although retrospective analysis did not disclose a definite indication for the procedure. Analysis of CSF (table 3) revealed bacterial meningitis (criteria: a WBC count of >500/mm<sup>3</sup> and a CSF/blood glucose ratio of <0.3) in only three patients (18%), who had 37,000, 2,470, and 597 WBCs/mm<sup>3</sup> and CSF/blood glucose ratios of 0.02, 0.06, and 0.1, respectively. These 3 patients were febrile and 2 of them had meningismus: 1 died, 1 fully recovered, and 1 had moderate sequelae at follow-up. It was not possible to

**Table 3.** CSF findings for 17 patients with brain abscess.

Determination	No. of patients with given value/no. of patients tested (%)
Opening pressure (mm H <sub>2</sub> O)	
<200	16/17 (94)
≥200	1/17 (6)
Leukocyte count (cells/mm <sup>3</sup> )	
<5	3/17 (18)
5–100	7/17 (41)
100–500	4/17 (24)
>500	3/17 (17)
Protein level (mg/mL)	
<300	5/16 (31)
300–1,000	7/16 (44)
>1,000	4/16 (25)
CSF glucose level (mmol/L)	
<1	3/15 (20)
1–4	4/15 (27)
>4	8/15 (53)
CSF/blood glucose ratio	
<0.3	3/14 (21)
0.3–0.5	4/14 (29)
>0.5	7/14 (50)

determine if ventriculitis or abscess rupture had occurred. Twelve of the 17 patients (71%) had aspecific and mildly altered CSF perturbations compatible with a CNS process, and two patients (12%) with a frontal abscess had entirely normal CSF findings. Eight patients had received antibiotics 2–8 days before the LP; their CSF findings were not different from those observed for the nine patients who had not been treated before the LP. All CSF cultures remained sterile and were not valuable to microbiological diagnosis.

### CT Scan Findings

For all patients, a CT scan was performed: 30 (77%) during the first 3 days of hospitalization, 8 (21%) between days 4 and 10, and 1 (2%) on day 30. All the scans were analyzed for evidence of sinusitis and mastoiditis. Plain films revealed one or several hypodense lesions in 34 cases (87%), hyperdense lesions in 3 cases (8%), and findings consistent with the presence of gas in 2 cases (5%). Surrounding edema was present in 29 patients (74%): 24 had focal neurological signs or meningismus. One patient had diffused cerebral edema. Contrast material was injected in 25 cases (64%): nodular enhancement in 7 patients and ring-enhancing lesions in 18 patients were noted. There was no correlation between the radiological characteristics of the lesions and the time elapsed between the appearance of the first symptoms and the performance of the CT scan.

### Microbiological Findings

A microbiological diagnosis was established in 32 cases (82%), by means of culture of brain abscess material in 28 cases, of blood in 3 cases, and of both in 1 case.

**Table 4.** Microorganisms isolated in cultures of intracerebral material (35 patients), in blood cultures only (3 patients), or in both (1 patient) for 39 patients with brain abscess, in relation to administration of antibiotic therapy (ABT) before surgery.

Variable	ABT before surgery (n = 10)	No ABT before surgery (n = 29)	Total (n = 39)
Culture results (no. [%] of patients)			
Negative	2 (20)	5 (27)	7 (18)
Positive	8 (80)	24 (83)	32 (82)
Blood only*	0/4	3/13	3/17
Intracerebral material	8	20	28
Both	0	1	1
P value	<i>P</i> < .05		
Single species isolated	6 (75)	11 (47)	17 (53)
Multiple species isolated	2 (25)	13 (53)	15 (46)
Isolates (no. [%] of organisms)			
Total	14 (100)	45 (100)	59 (100)
Per patient	1.4	1.6	1.5
Aerobic organisms			
Viridans streptococcus	8 (57)	22 (48)	30 (51)
<i>Streptococcus milleri</i>	2 (25)	7 (32)	9 (30)
<i>Streptococcus milleri</i>	2 (25)	6 (26)	8 (27)
<i>Haemophilus</i> species	1 (12.5)	3 (13)	4 (13)
<i>Staphylococcus aureus</i>	1 (12.5)	2 (9)	3 (10)
<i>Staphylococcus epidermidis</i>	0 (...)	1 (5)	1 (3)
<i>Streptococcus pneumoniae</i>	1 (12.5)	0 (...)	1 (3)
<i>Streptococcus bovis</i>	0 (...)	1 (5)	1 (3)
<i>Actinobacillus actinomycetemcomitans</i>	0 (...)	1 (5)	1 (3)
<i>Eikenella corrodens</i>	1 (12.5)	0 (...)	1 (3)
<i>Pasteurella multocida</i>	0 (...)	1 (5)	1 (3)
Anaerobic organisms			
<i>Fusobacterium</i> species	6 (43)	23 (52)	29 (49)
<i>Fusobacterium</i> species	3 (50)	11 (48)	14 (48)
<i>Bacteroides</i> species	3 (50)	4 (17)	7 (24)
<i>Propionibacterium acnes</i>	0 (...)	5 (22)	5 (17)
<i>Peptostreptococcus</i>	0 (...)	2 (8)	2 (7)
<i>Peptococcus</i>	0 (...)	1 (5)	1 (3)

\* Blood cultures were performed for 17 patients; the three patients whose cultures were positive had no surgery.

A total of 59 microorganisms were isolated (table 4). There were 30 aerobic and 29 anaerobic bacteria. Viridans streptococci (9 cases) and *Streptococcus milleri* (8 cases) were the most frequently isolated aerobes, while *Fusobacterium* species were the most frequently isolated anaerobes (14 cases). A single organism was isolated from 17 patients (53%); it was aerobic in 12 cases and anaerobic in 5 cases (in 4 of these, *Bacteroides* species). Multiple organisms were recovered in 15 cases (47%), with a mean of 2.8 bacterial species per patient. Anaerobes, mainly *Fusobacterium* species, were present in almost all these polymicrobial cases (13 of 15; 87%).

Blood cultures were performed for 17 patients and were positive for four. None of these four had had prior antibiotic therapy; two had multiple abscesses. Three patients did not undergo further neurosurgical procedures and fully recovered with medical therapy alone; one was infected with *Staphylococcus aureus*, one with *Actinobacillus actinomycetemcomitans*, and one with both *S. aureus* and *Streptococcus bovis*. In the two cases in which *S. aureus* was isolated, the abscesses originated from skin infections. In the latter case,

cultures of both blood and abscess material were positive for *Bacteroides fragilis*. In two cases (in which *A. actinomycetemcomitans* and *S. aureus* were isolated), the brain abscess was associated with infectious endocarditis.

Culture of intracerebral material remained sterile for seven of the 36 surgical patients (19%). In two cases, preoperative antibiotic therapy (for 16 and 28 days) had been administered, but the gram stain was positive for gram-positive and gram-negative cocci in both cases. In four cases, the diagnosis was based on histologic examination of excised brain material that revealed meningoenkephalitis with numerous inflammatory cells and necrotic tissue highly suggestive of an acute abscess, but direct examination was negative for bacteria or mycobacteria. None of these four patients had had prior antibiotic therapy. Only two of these patients received antibiotics after diagnosis, but all four recovered. The last patient presented with a subdural empyema and a brain lesion characteristic of an abscess. He recovered after drainage of the empyema and administration of antibiotics (direct examination was negative for the presence of bacteria, and cultures remained sterile).

### Surgical Treatment

Surgery was performed on 36 patients (92%). The median delay between hospital admission and surgical intervention was 2 days (0–30 days). A delay exceeding 1 week was observed in only five cases and was related to intercurrent medical problems. It was decided that the early performance of surgery on all these patients was necessary for diagnostic and microbiological purposes.

In 26 patients (72%), the lesions were partially or totally excised. In 10 cases (28%), lesions were aspirated for the main purpose of obtaining material for culture. The surgical technique used did not depend on the location but on the depth of the lesions: excision was attempted only for superficial lesions and stereotaxic aspiration for deeper ones.

### Medical Treatment

Thirty-seven patients (95%) were treated with antibiotics. The median duration of total treatment (intravenous and oral), which was precisely defined for 28 of the 34 antibiotic-treated patients who lived, was 47 days (range, 24–180 days). All these patients were treated parenterally for at least the first 18 days of treatment.

In 10 cases, antibiotic therapy was started before surgical intervention. The duration of treatment before surgery was 2–8 days for the eight patients whose cultures were positive and 16 and 28 days, respectively, for the two patients whose cultures were negative. For one patient of the positive-culture group, antibiotic therapy had to be modified because of the resistance pattern of the isolated microorganisms (*S. aureus*). In the other 7 cases, initial treatment was either simplified (4 cases) or continued without change (3 cases).

In 29 cases, therapy with broad-spectrum antibiotics was started only after surgery (26 patients) or after blood culture (3 patients). The initial choice of antibiotics was appropriate in regard to the sensitivity of the microorganisms isolated from the 24 patients who had positive cultures. However, the antibiotic regimen was simplified for eight patients according to the sensitivity of the microorganisms.

Three of four patients who had positive blood cultures recovered with antibiotic therapy alone. The positivity of the blood cultures enabled diagnosis in these three cases (two cases of endocarditis and one case of bacteremia originating from the skin). All four patients had multiple abscesses and medical conditions precluding surgical intervention (e.g., coagulation disorders).

All aerobic isolates were sensitive to penicillin, amoxicillin, or ceftriaxone except the three isolates of *S. aureus* (sensitive only to a  $\beta$ -lactamase-resistant penicillin) and *Eikenella corrodens* (sensitive to chloramphenicol). All anaerobic isolates were sensitive to chloramphenicol or metronidazole, and most were also sensitive to penicillin. Thus, the most frequent antibiotic regimen included administration of a  $\beta$ -

lactam agent (penicillin, amoxicillin, or ceftriaxone) with chloramphenicol or metronidazole. Administration of a  $\beta$ -lactamase-resistant penicillin (flucloxacillin) was initiated only in the cases due to *S. aureus* infection.

Corticosteroids were administered to 28 patients (72%). In 16 cases, administration was restricted to the perioperative period (up to 6 days). For 12 patients, corticosteroids were administered for 6–90 days (median, 21 days). There was no detectable difference in the outcome for patients who had and had not received corticosteroids.

### Outcome

Five patients (two males and three females; 13%) died during hospitalization (table 1). Their mean age was 57 years. Predisposing factors were prior head trauma, tetralogy of Fallot, and corticosteroid use (one case each); in two cases, no predisposing factor was detected. In all five cases, a CT scan was performed within 24 hours of admission and surgical intervention was attempted during the first 2 days of hospitalization. For four patients, cultures of brain abscess specimens were positive (for viridans streptococcus and *S. milleri*, either alone or with *Fusobacterium* species), and they were treated with an appropriate antibiotic regimen. The fifth patient's abscess specimen was negative on culture. Four of these five patients were hospitalized a few hours after the first symptoms were noted. Moreover, all had severe neuropsychological conditions or mental impairments on admission: 2 presented with general seizure and mental status B, 1 with a hemisindrome and mental status B, and 2 with mental status D. No other clinical, biological, radiological, or microbiological factors could be correlated with fatal outcome (table 5).

Follow-up neurological examination was performed on 32 of the 34 survivors (94%). The median follow-up period was 12 months (range, 1–84 months). Sequelae were present in 44% (14 of 32) of the cases. In 7 cases, these sequelae were considered severe since they had led to modification of social and professional activities (5 patients had seizures and 2 had hemiparesis). Seven patients had only moderate sequelae not impairing daily life. Seventy-five percent (12 of 16) of the patients between 20 and 60 years old had moderate to severe sequelae, as compared with none of the six patients younger than 20 years old and 20% (2 of 10) of the patients older than 60 years of age.

The mean delay between the appearance of the first symptoms and hospitalization for the 37 patients evaluable at follow-up was 12.3 days. This delay was significantly shorter for the 12 patients who died or had severe sequelae than for the 25 patients for whom the outcome was better (4.3 and 16.1 days, respectively). The presence of sequelae was correlated with the severity of the mental status on admission, since most of the patients who recovered (fully or with moderate sequelae) were of mental status A (17 of 25; 68%) and the

**Table 5.** Outcome for 37 evaluable patients\* with brain abscess as compared with clinical characteristics.

Variable	No. of patients with given outcome <sup>†</sup>		
	Death or severe sequelae (n = 12)	Recovery and moderate sequelae (n = 25)	Total (n = 37)
Male	7	17	24
Female	5	8	13
Age (y)	48.6 ± 15.3	41.4 ± 22.0	43.8 ± 20.0
Duration (d) of symptoms before admission	4.3 ± 5.7	16.1 ± 12.2	12.3 ± 11.9
P value	P < .003		
Fever			
Present	6	9	15
Absent	6	16	22
Mental status <sup>‡</sup>			
A	1	17	18
B	8	8	16
C or D	3	0	3
Intracranial material culture			
Positive	10	22	32
Negative	2	3	5

\* Two patients lost at follow-up.

<sup>†</sup> Except categories of age and duration of symptoms before admission, which show data as mean ± SD.

<sup>‡</sup> See definitions in text.

three patients with the worst mental status (namely, C or D) died (table 5). There was no correlation with microbiological findings, antibiotic regimens, or type of surgical intervention.

## Discussion

Although brain abscess is a rare disease, its prognosis is poor. In most series mortality rates of 30% to 50% were reported, but two recent reports have documented rates of 4% to 20% [9, 10], figures that are similar to the 13% rate observed in the present series. This improvement has been attributed to several factors, among which early diagnosis by means of CT scan was thought to be the most important [2, 10, 16–19]. Hence, in a series that compared periods before and after the advent of the CT scan, the excessive mortality associated with brain abscess observed in the first period could be explained entirely by delay in the diagnosis [10]. The increased sensitivity of MRI observed in the diagnosis of experimental brain abscess appears to be of limited value in humans because there is already a lesion obvious on CT scan when the patient presents [20]. Neurological sequelae which occurred in 46% of our cases, were severe enough to alter social or professional capacities of half of those patients.

Death and severe sequelae were mostly observed in patients who presented with a severe neurological impairment on admission and were associated with a significantly shorter delay from the onset of symptoms to admission. Moreover, all patients who died had undergone a CT scan within the first 24 hours after admission, and none of the factors analyzed (location and number of the abscesses, presence of a predisposing factor, type of microorganisms isolated, and type of surgery performed) influenced the outcome except the patient's initial clinical impairment and a slightly older mean age, although the latter was not a significant factor. These data indicate that, although CT scan is likely to have contributed to the decreased mortality observed in recent series, further improvement in the prognosis of cerebral abscess will now mainly depend on earlier admission and better management of predisposing conditions.

Predisposing factors, present in 62% of our patients, were not equally distributed in the different age groups, in contrast with other studies [3, 18, 21–24], and seem to be more frequent in patients <50 years old. Direct spread from an otic or sinus infectious focus was the most frequent source of brain abscess in young adults in our series, although globally less frequent than in other series [2, 7, 10, 22], and was never noted in patients older than 60 years. The incidence of brain abscess due to congenital heart disease (12% of our cases) can be expected to be lower in the future, thanks to recent advances in cardiovascular surgery [7, 21, 22, 25, 26]. Skin infections (with or without endocarditis) and pulmonary abscesses (often related to bronchiectasis) should be recognized as other potential sources of infection. With early and appropriate management of predisposing conditions, the overall incidence of brain abscess should decrease; however, the proportion of patients without predisposing conditions (38%) or with less-well-defined predisposing conditions (e.g., head injury or steroid therapy) remains a difficult clinical problem, particularly among the elderly.

Short duration of symptoms before hospitalization characterized patients of ages 20–60 years and those with a poorer outcome: it identified a patient subgroup with an important clinical impairment at admission. All patients presented with symptoms pointing to involvement of the CNS, but only 49% had focal neurological manifestations; these patients had multiple abscesses slightly more frequently. Presence of fever does not appear to be a diagnostic clue. Presence of meningismus seems to be more frequently related to an occipital or temporal location of abscess. Our series highlights the diagnostic difficulties in regard to patients with nonspecific clinical presentation and indicates that a high index of suspicion should be maintained even in the absence of the classical manifestations of brain abscess [4, 27–29].

The only definite means of diagnosis remains the determination of the etiologic agents. LP was not helpful in this respect since all the CSF specimens remained sterile in culture. Moreover, this procedure is risky [18, 23, 30], although

there were fortunately no complications in our series. CSF analysis offers only nonspecific evidence of CNS involvement; it reveals signs of mild to severe inflammation in almost all cases, a finding that has no prognostic value. Even the presence of biological signs suggestive of bacterial meningitis in three patients (none of whom had focal neurological signs) was not related to the type of preexisting condition, the location of the abscess, or the presence of microorganisms in the intracerebral material. The use of LP should initially be restricted only to patients with true meningismus and diffuse CNS signs, as a means of ruling out bacterial meningitis. For patients with focal CNS signs or without meningismus, initiation of antibiotic therapy (after culture of blood and a specimen from any suspected focus of infection) followed by a CT scan will lead to the detection of a focal intracranial process with minimal iatrogenesis.

Surgery is the only procedure allowing optimal microbiological documentation and should not be delayed. Antibiotic pretreatment for <10 days does not reduce the rate of positivity of cultures of intracerebral material. The precise identification of the isolated microorganisms led to simplification of the antibiotic regimen for 12 patients in our series and to modification of the treatment because of the resistance of *S. aureus* in one case. The choice between excision or stereotactic aspiration was mainly dictated by the depth of the lesion. There has been no detectable difference in outcome for the patients who have undergone either one of these two procedures, although some authors have observed an increased rate of sequelae, mainly epilepsy, after complete or partial excision [2, 10, 31, 32]. In very highly selected patients, non-surgical treatment with antibiotics alone can be successful. Several authors recommend medical therapy, particularly in cases in which the abscess is <2 cm in diameter, when the lesion is of high density (suggesting cerebritis [28, 30, 33, 34]) or when multiple abscesses are present [24, 35–37]. This conservative approach appears to be most appropriate when the responsible microorganisms have been identified by blood culture, which may occasionally be positive (4 of 17 in our series). Such cultures should therefore always be performed, in particular when no prior treatment has been given.

The combination of a  $\beta$ -lactam agent with chloramphenicol or metronidazole generally has been recommended as standard treatment for bacterial brain abscesses. In contrast with findings in other studies, the type of microorganisms isolated was not related to the origin of the infection in our study. The recognition of an infectious focus as a potential source is not helpful in choosing an antibiotic regimen, except when a cutaneous source is a possibility, in which case a  $\beta$ -lactamase-resistant  $\beta$ -lactam agent should be used to cover *S. aureus*. Although all anaerobes we discovered were sensitive to  $\beta$ -lactam antibiotics, patients may benefit from the good penetration of chloramphenicol or metronidazole into the CNS [24, 35, 36]. Overall duration of treatment should

be 2 months, with the parenteral route of administration used for at least the first 2 weeks, as usually recommended [34–36]. When cultures are negative but histologic evidence of an acute inflammatory process or the presence of organisms on gram stain is noted, treatment of patients with a standard combination (a  $\beta$ -lactam agent with chloramphenicol or metronidazole) or a  $\beta$ -lactamase-resistant  $\beta$ -lactam agent (in cases of skin infection) is recommended. However, some patients can recover without any medical treatment.

Twenty-eight patients received corticosteroids. No detectable difference in outcome was observed between the patients who had received corticosteroids and those who did not. This finding is in accordance with those in other studies [2, 29, 38]. Therapy with corticosteroids appears to be indicated only in cases of massive symptomatic cerebral edema.

In conclusion, our study confirms that the mortality rate associated with brain abscess might be as low as 13%. Presentations at admission are very heterogenous, and no clinical or biological elements are diagnostic. Initial LP should be performed only in cases in which bacterial meningitis is highly suspected on account of meningismus and diffuse CNS signs. In other cases, a CT scan will determine the location of a focal brain process. Even though a brain abscess can be successfully treated with antibiotics alone in some cases, surgery (mainly stereotactic aspiration) permits a precise microbiological documentation, thus allowing establishment of the best antibiotic regimen.

The only factor that definitely influences mortality and sequelae is the clinical presentation at admission. Efforts should be directed toward better recognition and management of predisposing conditions, actions that seem to be the only means of improving outcome for patients with bacterial brain abscess.

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