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Profiles of primary brain abscesses and their impact on survival: An international ID-IRI study

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ABSTRACT

Objectives: This study of 331 primary brain abscess (PBA) patients aimed to understand infecting agents, predisposing factors, and outcomes, with a focus on factors affecting mortality.
Methods: Data were collected from 39 centers across 16 countries between January 2010 and December 2022, and clinical, radiological, and microbiological findings, along with their impact on mortality, were analyzed.
Results: The patients had a mean ± SD age of 46.8 ± 16.3 years, with a male predominance of 71.6%. Common symptoms included headache (77.9%), fever (54.4%), and focal neurological deficits (53.5%). Gram-positive cocci were the predominant pathogens, with Viridans group streptococci identified as the most frequently isolated organisms. All patients received antimicrobial therapy and 71.6% underwent interventional therapies. The 42-day and 180-day survival rates were 91.9% and 86.1%, respectively. Significant predictors of 42-day mortality included intravenous drug addiction (HR: 6.02, 95% CI: 1.38-26.26), malignancy (HR: 3.61, 95% CI: 1.23-10.58), confusion (HR: 2.65, 95% CI: 1.19-5.88), and unidentified bacteria (HR: 4.68, 95% CI: 1.76-12.43). Significant predictors of 180-day mortality included malignancy (HR: 2.70, 95% CI: 1.07-6.81), confusion (HR: 2.14, 95% CI: 1.11-4.15), temporal lobe involvement (HR: 2.10, 95% CI: 1.08-4.08), and unidentified bacteria (HR: 3.02, 95% CI: 1.49-6.15).
Conclusion: The risk of death in PBA extends beyond the infection phase, with different factors influencing the 42-day and 180-day mortality rates. Intravenous drug addiction was associated with early mortality, while temporal lobe involvement was associated with late mortality.

Introduction

A brain abscess is a focal intracerebral infection that starts as a localized area of cerebritis and progresses to a collection of pus surrounded by a well-vascularized capsule [1]. Brain abscesses are estimated to occur at a rate of 0.2 to 1.9 per 100,000 person-years [2]. Although rare, brain abscesses remain a significant concern in healthcare due to their potentially poor outcomes. They also hold lasting importance in medical research, given the ongoing challenges in diagnosis and treatment, compounded by the limited availability of reliable evidence and the scarcity of prospective studies.

A primary brain abscess (PBA) is defined as an abscess that develops spontaneously, without prior surgery or trauma, resulting from direct extension or hematogenous spread [3]. PBA can result from the local spread of infection from contagious sites such as sinusitis, otitis, and mastoiditis, or via hematogenous spread from primary bacteremia, infective endocarditis (IE), or other sources of infection [4].

Historically, mortality rates associated with brain abscesses were quite high [5]. However, they have significantly decreased due to advancements in diagnostic tools, such as computed tomography (CT) scans, and improvements in neurosurgical techniques [6,7]. In this international multicenter study, we aimed to explore the infecting agents, predisposing factors, and outcomes of PBA, with a particular focus on the factors affecting mortality.

Methods

Setting

We conducted a retrospective cross-sectional study to analyze PBA. Patients diagnosed with PBA between January 2010 and December 2022 were included in this study. A study protocol outlining the case definition, inclusion criteria, and exclusion criteria was prepared and distributed to the participating centers. The centers then submitted data on patients who met the defined case criteria through a dedicated Microsoft Forms webpage link. Data were collected retrospectively using the Infectious Diseases International Research Initiative (ID-IRI) (https://infectdisiri.com/), an international clinical research platform and global network with members from various regions who voluntarily participate in ID-IRI research projects. Data on PBA cases were collected from 39 centers across 30 cities and 16 countries: Afghanistan, Albania, Bulgaria, the Czech Republic, Egypt, Iran, Italy, Pakistan, Poland, Russia, Saudi Arabia, Slovakia, Slovenia, Syria, Tunisia, and Turkey.

Brain abscess case definition

The diagnosis of PBA was made based on the following two criteria in the presence of clinical signs suggestive of a brain abscess, such as headache, fever, and focal neurological deficits.

1. Evidence of abscess formation on brain magnetic resonance imaging (MRI) or computed tomography (CT).

2. Confirmation of infection through one of the following methods:
   a) Microbiological, molecular diagnostic, or pathological examination of biopsy or drainage samples obtained from the affected area as seen on MRI or CT.
   b) Clinical and imaging improvement following antibiotic treatment.
   c) Identification of the causative pathogen via cerebrospinal fluid culture and/or molecular diagnostic methods or blood culture.

Inclusion criteria

1. Cases that meet the definition of a PBA as described above.
2. Patients with brain abscesses aged $\geq$ 18 years were included in the study.

Exclusion criteria

1. Secondary brain abscesses (resulting from brain injury or brain surgery) and subdural or epidural empyema.
2. Patients with a foreign body, such as a cranioplasty, ventriculoperitoneal shunt implant, or deep brain stimulator.
3. An abscess occurred because of complicated intracranial hemorrhage.
4. HIV (+) patients with intracranial lesions.
5. Patients with intracranial tuberculosis, parasitic infections, and fungal infections.
6. Patients with PBA of undetermined etiology who received empirical antibiotic therapy, as well as treatment for fungi, parasites, or tuberculosis, were also excluded.

Variables in the study and outcome

Patient data on demographics, comorbidities (chronic obstructive pulmonary disease, intravenous (IV) drug addiction, diabetes mellitus, hypertension, malignancy, liver cirrhosis, solid organ transplantation, autoimmune diseases, chronic renal failure, cyanotic heart disease), a potential source of infection (paranasal sinusitis, chronic otitis media or mastoiditis, dental infection, eye infection, IE, hematogenous infection with another focus, unknown source), clinical features (complaints, symptoms, and physical examination findings), imaging findings (location and size of abscesses, single or multiple abscesses, unilateral or bilateral abscesses), conventional microbiological findings (identifying the responsible bacteria using clinical specimens such as abscess, cerebrospinal fluid, and blood culture), molecular diagnostic test results (identifying the responsible bacteria using clinical specimens such as abscess, cerebrospinal fluid), laboratory test results, therapy methods (antimicrobial therapy, surgery or drainage, steroid use), revised antibiotic therapy were recorded. Patients with hematological malignancies, solid organ tumors, and autoimmune diseases who received immunosuppressive therapy or who underwent solid organ transplantation were classified as immunocompromised. Chronic renal failure was defined as a glomerular filtration rate of $<$60 mL/min. The Glasgow Coma Scale (GCS) [8] was used to assess the severity of the patient's clinical findings at the first visit.

Coagulase-negative staphylococci were regarded as causative agents only when isolated from brain abscess specimens.

Molecular diagnostic methods including polymerase chain reaction (PCR)-based techniques, such as multiplex PCR and 16S rDNA PCR were used to detect and identify specific bacterial DNA or RNA.

The clinical outcomes of patients with PBA were assessed based on mortality at 42 days and 180 days after the diagnosis of a brain abscess. We aimed to evaluate mortality attributed to the early infectious phase, stemming from acute infection, and mortality related to the postinfectious phases, characterized by sequelae or seizures. Following this, we conducted separate analyses to identify the factors influencing mortality at both the 42-day and 180-day marks.

Statistical analyses

Categorical variables are presented as numbers and percentages (%). Non-normally distributed variables are expressed as medians with interquartile ranges (IQR). The time at which a brain abscess was diagnosed was selected as the starting point for follow-up. The follow-up was correctly censored on 42nd day and 180th day. Using both observed survival times, we conducted univariate Cox regression analysis for 42- and 180-day mortality. Statistically significant variables in univariate analysis were included in multivariate Cox regression analysis. We present risk measures with hazard ratios (HRs) and 95% confidence intervals (95% CI). Laboratory variables were excluded from the multivariate analysis because of missing data. Additionally, confusion was included in the Cox model instead of the GCS score. Kaplan–Meier survival curves were generated using the significant variables identified in the univariate analysis. We tested the differences between the survival curves using the log-rank test. Restricted mean survival times were estimated with standard errors (SE). Double-sided *P*-values less than 0.05 were considered significant. Statistical analysis and visualization were performed using R version 4.3.1 (A Language and Environment for Statistical Computing. R Foundation for Statistical Computing, Vienna, Austria. https://www.R-project.org/).

Results

Clinical characteristics, comorbidities, and predisposing factors of the patients

This multicenter study included 331 patients diagnosed with PBA. The mean age was 46.8 $\pm$ 16.3 years. Among the participants, 71.6% (n = 237) were male. Patient characteristics are shown in Table 1. Headache was the most common symptom (77.9%), followed by fever (54.4%). Focal neurological deficits were detected in 53.5% of the patients. The classical triad of brain abscesses, consisting of headaches, fever, and focal neurological deficits, was observed in 74 patients (22.4%). Additionally, the majority of patients, 316 (95.5%) presented with at least one of the following symptoms: Headache, fever, or focal neurological deficits.

More than half (52.3%) of the patients had at least one comorbidity. The rates and number of comorbidities and predisposing factors were as follows: diabetes mellitus 15.1% (n = 50), hypertension 8.8% (n = 29), chronic obstructive pulmonary diseases 5.7% (n = 19), malignancy 5.4% (n = 18), autoimmune diseases 2.4% (n = 8), IV drug use 2.1% (n = 7), chronic renal failure 2.1% (n = 7), cyanotic heart disease 8.1% (n = 6), cirrhosis 1.8% (n = 6), solid organ transplantation 5.1% (n = 5). Additionally, 9.4% (n = 31) of the patients were immunosuppressed, including those with malignancies, autoimmune diseases, and solid organ transplantation. Seven patients had a history of IV drug addiction and only one had IE. The source of the brain abscesses was unknown in approximately half (n = 163, 49.2%) of the patients. Among patients with a known source of infection (n = 168), direct spread from contagious tissue was found in 54.8% (n = 92) of patients [chronic otitis media and/or mastoiditis (n = 51, 30%), paranasal sinusitis ([n = 42, 25%], and eye infection [n = 3, 1.8%]). Hematogenous dissemination was found in 45.2% (n = 78) of the patients (dental infection [n = 36, 21.4%], hematogenous infection with another focus, such as pneu-

Table 1
General features and microbiological data of patients with primary brain abscesses.

	n (%)		*n* (%)
Male	237 (71.6)	Midline shift	86 (26.0)
Age, mean ± SD	46.8 ± 16.3	Ruptured abscess	30 (9.06)
Comorbidity°	173 (52.3)	Concomitant meningitis, *n* = 239	70 (28.6)
Headache	258 (77.9)	Causative bacteria**	162 (48.9)
Fever	180 (54.4)	Viridian group streptococci	61 (37.7)
Focal neurologic deficit	177 (53.5)	*S. aureus*	23 (14.2)
Confusion	141 (42.6)	*S. pneumoniae*	14 (8.64)
Nausea/vomiting	125 (37.8)	Enterobacteriaceae	14 (8.64)
Seizure	74 (22.4)	Nocardia	9 (5.56)
GCS, median (25-75%)	15.0 (13.0-15.0)	Coagulase-negative staphylococcus	7 (4.32)
Known source of infection*	168 (50.8)	*Pseudomonas spp.*	6 (3.70)
Direct spread	92 (54.8)	*Enterococcus spp.*	3 (1.85)
Dental infection	36 (21.4)	*L. monocytogenes*	2 (1.23)
Hematogenous infection with another focus	28 (16.7)	Oral anaerobic bacteria°	41 (25.3)
Bacterial endocarditis	14 (8.3)	White blood cell (mL), *n* = 278	12300 (9000-16600)
Frontal lobe	128 (38.7)	Neutrophil (mL), *n* = 253	9390 (6700-13892)
Parietal lobe	118 (35.6)	Platelet (mL), *n* = 276	265000 (200000-342500)
Temporal lobe	101 (30.5)	CRP (mg/L), *n* = 253	30.6 (8.51-78.8)
Occipital lobe	73 (22.1)	Procalcitonin (ng/mL), *n* = 100	0.16 (0.05-1.44)
Basal ganglia	21 (6.34)	Creatinine (mg/dL), *n* = 274	0.80 (0.66-1.00)
Cerebellum	20 (6.04)	Steroid therapy, *n* = 312	94 (28.4)
Brainstem	19 (5.74)	Surgery/drainage	237 (71.6)
The longest diameter (mm), median (25-75%), *n* = 299	28 (19-40)	Only antimicrobial therapy	167 (51.7)
Multiple abscesses	93 (28.1)	Mortality	38 (11.9)

° The rate and number are given in the text.
* The denominator of the primary sources of brain abscesses was 168.
** The denominator of the microorganism microbiologically isolated is 162.

monia [*n* = 28, 16.7%], and IE [*n* = 14, 8.3%]). Fever was observed in 49% (*n* = 80) of PBA cases with unknown sources.

Radiological findings

Multiple abscesses were found in 28.1% (*n* = 93) of patients. Among the patients with multiple brain abscesses, 33.3% (*n* = 31) had hematogenous dissemination, while an unknown source was identified in 45.2% (*n* = 42). The frontal lobe is the most affected area, followed by the parietal lobe. The median (IQR) diameter of the longest abscess was 28 (21) mm.

Microbiological findings

Positive cultures were obtained from 55.5% (152 out of 274) of the patients, while molecular diagnostic tests yielded positive results in 71.9% (46 out of 64). Ultimately, the causative bacteria were identified in 48.9% (*n* = 162) of patients (Table 1). In 18 culture-negative patients, the diagnosis was made using diagnostic molecular techniques. In contrast, cultures were positive in eight patients who were negative for molecular diagnostic methods. Multiple bacteria were identified in 19.7% of the cases. Gram-positive cocci were the predominant bacteria, identified in 65.4% of the cases. Viridans group streptococci was the most frequently isolated agents, accounting for 37.7% of cases. Oral anaerobic bacteria were found in 25.3% of the patients. The percentage and the numbers of oral anaerobic bacteria isolated were as follows: *Fusobacterium spp.* 9.87% (*n* = 16), *Peptostreptococcus spp.* 4.93% (*n* = 8), *Parvimonas micra* 4.93% (*n* = 8), *Actinomyces spp.* 4.32% (*n* = 7), *Bacteroides spp.* 3.70% (*n* = 6), *Prevotella spp.* 3.70% (*n* = 6), *Haemophilus aphrophilus* 2.46% (*n* = 4), *Eikenella corrodens* 1.85% (*n* = 3), *Veilonella spp.* 1.23% (*n* = 2), *Aggregatibacterium aphrophilus* 1.23% (*n* = 2), and *Oligella urethralis* 0.61% (*n* = 1).

Hematogenous dissemination was observed in two of our seven patients with coagulase-negative staphylococci.

Treatment

All patients received antimicrobial therapy. Most patients (*n* = 237, 71.6%) received interventional therapies such as surgery (*n* = 159, 48%) or endoscopic drainage (*n* = 78, 23.6%), together with antibiotic therapy. Antibiotic therapy was modified in 45.6% of the patients (151 out of 331) for a variety of reasons. Specifically, unresponsiveness to treatment was observed in 25.8% (39 out of 151) of patients, the identification of bacteria in 27.8% (42 out of 151), adverse reactions in 16.5% (25 out of 151), and a switch to oral therapy in 4% (26 out of 151).

Outcomes

During the six-month follow-up period, 26 patients passed away within the first six weeks, while 39 patients died by the end of the six-month period. The 42- and 180-day survival probabilities were 91.9% (*n* = 305) and 86.1% (*n* = 292), respectively (Figure S1).

Table 2 presents the findings from the univariate Cox regression analysis for mortality at 42 days and 180 days following diagnosis. Patients with IV drug addiction had a higher risk of 42-day mortality (HR: 4.96, 95% CI: 1.17-21.0). The presence of at least one comorbidity, malignancy, confusion, low GCS score, and failure to identify bacteria were significant predictors of both 42- and 180-day mortality. Moreover, hematogenous infection (HR: 2.92, 95% CI: 1.34-6.35), parietal lobe involvement (HR: 2.25, 95% CI: 1.20-4.22), temporal lobe involvement (HR: 1.96, 95% CI: 1.05-3.68), multiple abscesses (HR: 2.12, 95% CI: 1.13-3.99), and ruptured abscesses (HR: 3.56, 95% CI: 1.73-7.30) increased the risk of 180-day mortality.

Figure 1 and Table 3 present Kaplan–Meier survival curves and mean ± SE survival times derived from time-to-event analysis. Patients with IV drug addiction had a lower mean ± SE survival time (31.0 ± 6.53 days, $P = 0.03$) compared to the no-drug addiction group (39.9 ± 0.45 days) when considering 42-day mortality. For 180-day mortality, patients with malignancy exhibited a shorter mean ± SE survival time (123 ± 18.30 vs. 164 ± 2.77, $P = 0.002$).

In the multivariate analysis of the 42-day mortality, all variables that were significant in the univariate analysis remained significant (Figure 2). For 180-day mortality, malignancy (HR: 2.70, 95% CI: 1.07-6.81), the presence of confusion at the first visit (HR: 2.14, 95% CI: 1.11-4.15), temporal lobe involvement (HR: 2.10, 95% CI: 1.08-4.08), and failure to identify bacteria (HR: 3.02, 95% CI: 1.49-6.15) were statistically significant.

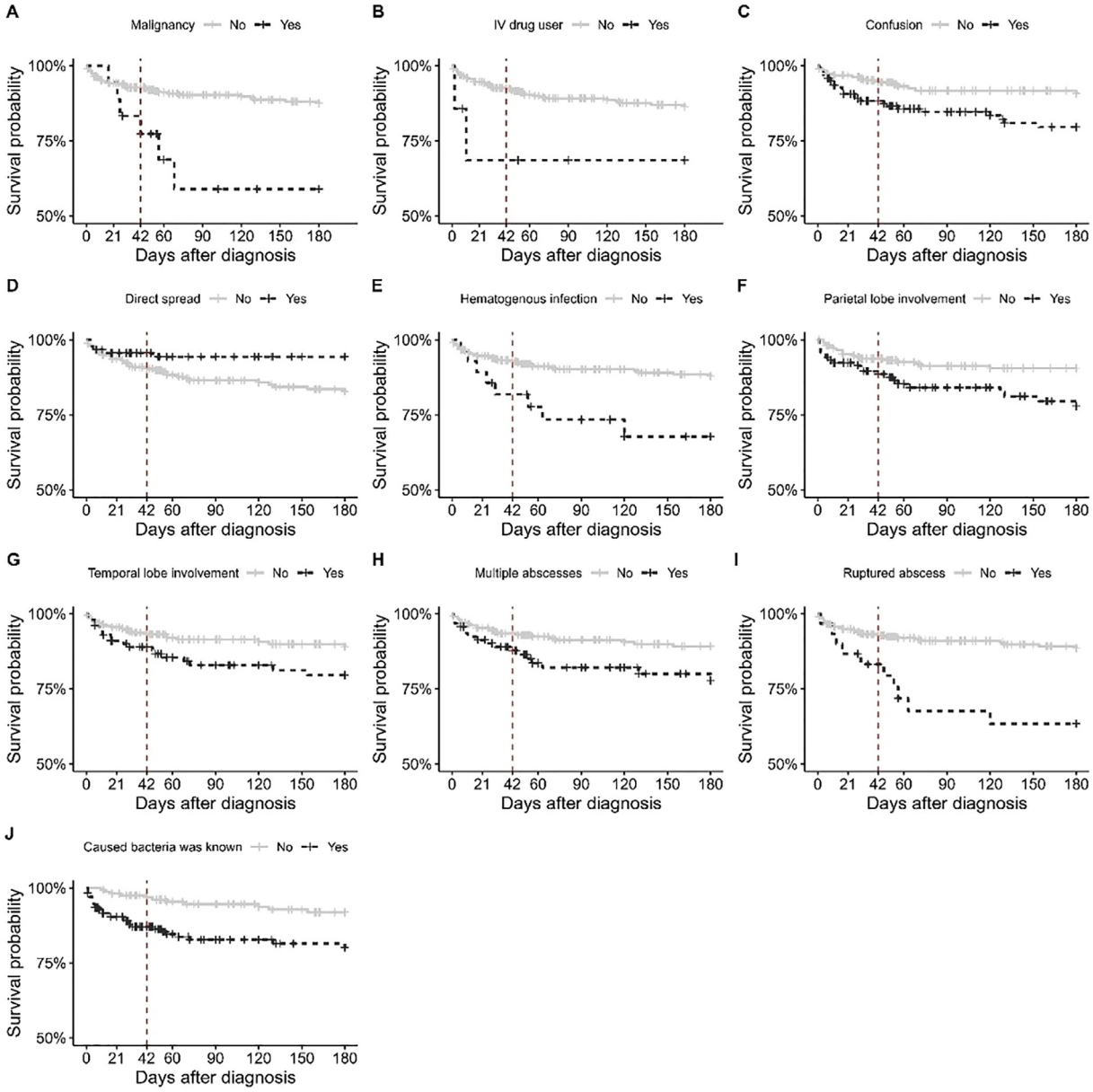

Figure 1. Kaplan–Meier survival curves of clinically significant predictors of 42- or 180-day mortality in the patients with primary brain abscess.

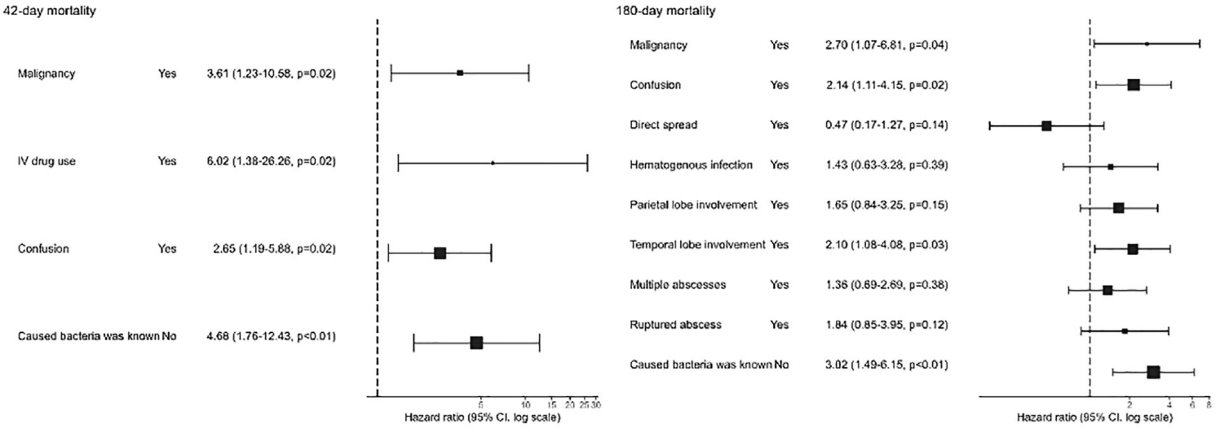

Figure 2. Results of multivariable Cox regression models for 42- and 180-day mortality in the patients with primary brain abscess. Statistically significant variables in the univariate analysis were included in the multivariate Cox regression analysis.

Table 2
Results of the univariable Cox regression analysis for 42- and 180-day mortality in the patients with primary brain abscess.

	42-day mortality		180-day mortality	
	Yes, $n = 26$	HR (95% CI)	Yes, $n = 39$	HR (95% CI)
Gender (Female)	8 (8.5)	1.09 (0.47-2.50)	10 (10.6)	0.83 (0.40-1.71)
Age, mean ± SD	48.6 ± 16.2	1.00 (0.98-1.02)	51.3 ± 18.8	1.01 (0.99-1.03)
Comorbidity	19 (11.0)	2.61 (1.10-6.21)*	30 (17.3)	3.40 (1.61-7.17)*
DM	3 (6.0)	0.75 (0.22-2.48)	5 (10.0)	0.84 (0.33-2.14)
Hypertension	3 (10.3)	1.38 (0.41-4.60)	4 (13.8)	1.19 (0.42-3.35)
COPD	3 (15.8)	2.15 (0.65-7.17)	5 (26.3)	2.31 (0.90-5.90)
Malignancy	4 (22.2)	3.10 (1.07-9.00)*	6 (33.3)	3.59 (1.50-8.60)*
IV drug use	2 (28.6)	4.96 (1.17-21.0)*	2 (28.6)	3.64 (0.87-15.1)
CRF	2 (28.6)	4.00 (0.94-16.9)	2 (28.6)	2.43 (0.58-10.1)
CHD	1 (16.7)	2.32 (0.31-17.1)	2 (33.3)	3.36 (0.81-14.0)
SOT	0 (0.0)	–	1 (20.0)	1.93 (0.26-14.1)
Headache	19 (7.4)	0.76 (0.32-1.81)	29 (11.2)	0.83 (0.40-1.70)
Fever	14 (7.8)	0.98 (0.45-2.12)	20 (11.1)	0.87 (0.46-1.63)
FND	14 (7.9)	1.05 (0.48-2.26)	23 (13.0)	1.29 (0.68-2.44)
Confusion	16 (11.3)	2.26 (1.03-4.99)*	24 (17.0)	2.30 (1.21-4.39)*
Nausea/vomiting	9 (7.20)	0.88 (0.39-1.97)	13 (10.4)	0.80 (0.41-1.56)
Seizure	5 (6.8)	0.81 (0.30-2.14)	9 (12.2)	1.03 (0.49-2.18)
GCS, median (25-75%)	14 (9-15)	0.81 (0.73-0.90)*	14 (9-15)	0.81 (0.74-0.89)*
Source of infection	12 (7.1)	0.80 (0.37-1.74)	16 (9.5)	0.63 (0.33-1.19)
Direct spread	4 (4.4)	0.46 (0.16-1.34)	5 (5.4)	0.36 (0.14-0.92)*
Dental infection	2 (5.6)	0.67 (0.16-2.83)	2 (5.6)	0.42 (0.10-1.72)
Hematogenous infection	5 (17.9)	2.59 (0.98-6.88)	8 (28.6)	2.92 (1.34-6.35)*
Bacterial endocarditis	2 (14.3)	1.89 (0.45-8.00)	2 (14.3)	1.29 (0.31-5.35)
Frontal lobe	11 (8.6)	1.18 (0.54-2.56)	13 (10.2)	0.81 (0.42-1.58)
Parietal lobe	13 (11.0)	1.88 (0.87-4.06)	21 (17.8)	2.25 (1.20-4.22)*
Temporal lobe	11 (10.9)	1.69 (0.78-3.67)	18 (17.8)	1.96 (1.05-3.68)*
Occipital lobe	5 (6.9)	0.80 (0.30-2.11)	11 (15.1)	1.27 (0.63-2.55)
Basal ganglia	0 (0.0)	–	2 (9.5)	0.78 (0.19-3.23)
Cerebellum	1 (5.0)	0.60 (0.08-4.42)	1 (5.0)	0.37 (0.05-2.72)
Brain stem	1 (5.3)	0.63 (0.08-4.62)	1 (5.3)	0.41 (0.06-2.95)
Longest diameter, median (25-75%)	30.0 (25.5-40.0)	1.00 (0.98-1.03)	33.0 (23.1-43.0)	1.01 (0.99-1.03)
Multiple abscesses	11 (11.8)	1.92 (0.88-4.19)	17 (18.3)	2.12 (1.13-3.99)*
Midline shift	7 (8.1)	1.05 (0.44-2.51)	12 (14.0)	1.25 (0.63-2.47)
Ruptured abscess	5 (16.7)	2.42 (0.91-6.42)	10 (33.3)	3.56 (1.73-7.30)*
Concomitant meningitis	8 (11.4)	1.42 (0.60-3.39)	13 (18.6)	1.90 (0.92-3.91)
Bacteria not identified	21 (12.4)	4.42 (1.67-11.7)*	28 (16.6)	2.96 (1.47-5.96)*
White blood cell (mL), $n = 278$	12000 (9950-15100)	1.00 (0.99-1.00)	12170 (9200-15200)	1.00 (0.99-1.00)
Neutrophil (mL), $n = 253$	11108 (7820-13381)	1.00 (0.99-1.00)	11500 (7500-13720)	1.00 (0.99-1.00)
Platelet (mL), $n = 276$	237000 (165500-316250)	1.00 (0.99-1.00)	246500 (164750-331250)	1.00 (0.99-1.00)
CRP (mg/L), $n = 253$	39.5 (19.9-58.4)	1.00 (0.99-1.01)	36.0 (10.8-50.0)	1.00 (0.99-1.00)
Procalcitonin (ng/mL), $n = 100$	7.07 (0.25-19.5)	1.17 (1.09-1.26)*	2.25 (0.11-11.8)	1.17 (1.10-1.26)*
Creatinine (mg/dL), $n = 274$	0.90 (0.74-1.20)	1.03 (1.01-1.05)*	0.80 (0.70-1.05)	1.02 (1.00-1.05)*
Surgery/drainage	17 (7.2)	0.74 (0.33-1.67)	25 (10.5)	0.70 (0.36-1.34)

Categorical variables were presented as row percentages.
* $p < 0.05$
CHD: Cyanotic heart disease, COPD: Chronic obstructive pulmonary disease, CRF: Chronic renal failure, DM: Diabetes mellitus, FND: Focal neurologic deficit, HR (95% CI): Hazard ratio (95% confidence interval), IV: Intravenous, SOT: Solid organ transplantation.

Discussion

In this study, we observed a 42-day mortality rate of 7.8%, which increased to 11.8% over a 180-day follow-up period for patients with PBA. Our study emphasizes that the presence of malignancy, confusion, and the identification of bacteria upon admission serve as prognostic indicators of mortality risk in both the early and late periods. In contrast, IV drug addiction, which is linked to severe infection, predicted early mortality, whereas temporal lobe involvement was linked to late mortality. To our knowledge, this is the largest case series of PBA ever reported in the literature.

PBA mortality has been reported to range from 3.5% to 23.4%, depending on the follow-up period of the studies [3,9-11]. Bodilsen et al. reported a 30-day mortality rate of 15% and a one-year mortality rate of 21%, demonstrating that the risk of death due to brain abscesses persisted in the postinfection period [12]. Furthermore, they reported a significantly higher mortality rate in patients with brain abscesses than in the control group, even years later. The exact causes of mortality following the infectious phase remain unclear, although seizures, neurological deficits, and complications may be influential factors. Our results show that temporal lobe involvement, which was not initially associated with mortality, became a significant risk factor for mortality. We could not confirm a clear association between temporal lobe involvement and seizures in the postacute period or a high complication rate. When the temporal lobe is involved, there is a higher likelihood of unfavorable clinical outcomes, such as epilepsy or other complications, resembling the progression observed in herpetic encephalitis, which is recognized for its postinfection complications, including sequelae and seizures [13,14]. The long-term complications of temporal lobe involvement require further clarification.

The majority of our patients were male, which aligns with the existing literature [3,9,10,15]. Headache was the most common symptom, observed in half of patients. In addition, the classic triad of symptoms associated with brain abscesses, headache, fever, and focal neurological deficits was observed in approximately one-fifth of patients presenting with a relatively silent clinical form. The presentation of symptoms is similar to that of brain abscesses that

Table 3
Mean survival times by clinical predictors for 42- and 180-day mortality in the patients with primary brain abscess.

	42-day mortality		180-day mortality	
	Mean survival time (days) ± SE	Log-rank *P*	Mean survival time (days) ± SE	Log-rank *P*
Malignancy		0.03		0.002
No	39.8 ± 0.48		164 ± 2.77	
Yes	38.7 ± 1.77		123 ± 18.30	
IV drug user		0.02		0.06
No	39.9 ± 0.45		162 ± 2.8	
Yes	31.0 ± 6.53		126 ± 32.2	
Confusion:		0.04		0.009
No	40.6 ± 0.49		168 ± 3.16	
Yes	38.5 ± 0.85		154 ± 5.04	
Direct spread		0.1		0.03
Yes	39.4 ± 0.57		171 ± 4.06	
No	40.4 ± 0.76		158 ± 3.58	
Hematogenous infection		0.05		0.005
No	39.9 ± 0.47		164 ± 2.79	
Yes	37.6 ± 1.90		137 ± 13.02	
Parietal lobe involvement		0.1		0.009
No	40.3 ± 0.49		166 ± 3.11	
Yes	38.7 ± 0.95		153 ± 5.54	
Temporal lobe involvement		0.2		0.03
No	40.2 ± 0.50		166 ± 3.06	
Yes	38.7 ± 0.98		153 ± 5.97	
Multiple abscesses		0.09		0.02
No	40.2±0.49		166 ± 2.99	
Yes	38.6±1.06		152 ± 6.48	
Ruptured abscess		0.07		< 0.001
No	40.0 ± 0.46		165 ± 2.72	
Yes	37.4 ± 2.02		130 ± 13.05	
Causative bacteria were identified		0.001		0.001
Yes	41.4 ± 0.33		171 ± 2.74	
No	38.1 ± 0.83		152 ± 4.86	

SE: Standard error.

have been previously documented in the literature [4,16,17], which can sometimes result in a delay in diagnosis, especially PBA.

Previous studies have reported that the rate of unidentified pathogens in PBA ranges from 40% to 84% [3,9,11,15]. Likewise, in our study, half of the cases did not have an identified pathogen. While the majority of pathogens were detected through culture, PCR demonstrated higher positivity rates. Nevertheless, our findings underscore the critical importance of pathogen identification in reducing mortality for patients with brain abscesses. Identifying pathogens—regardless of the method used—illustrates how targeted therapy can significantly improve outcomes in infectious diseases. On the other hand, the integration of molecular diagnostic methods has notably enhanced the identification of causative pathogens of brain abscesses. However, these techniques are not flawless and can produce false-positive results by detecting non-pathogenic bacteria [18,19]. In conclusion, mortality rates, which have been decreasing over time [2], are expected to decrease further with advances in molecular diagnostics.

Viridans streptococci, which are part of the normal oral and gastrointestinal flora and commonly cause dental infections, IE, brain abscesses, and neutropenic sepsis [20], were found to be the most common pathogens in PBA cases in our study, which is consistent with the results of previous studies [9,11,15]. These bacteria are thought to easily infect the brain via a hematogenic route. Their tendency to form abscesses is likely due to specific virulence factors, such as enzymes that digest the host tissue and factors that help them bind to fibronectin and laminin in the extracellular matrix [21]. The incidence of brain abscesses in patients with IE has been reported to be higher in IV drug addicts than in non-addicts [22]. However, data on the prevalence of IE due to IV drug addiction in patients with brain abscesses are lacking. In our study of PBA cases, 86% of IV drug addictions were not associated with IE. We attribute these lower-than-expected rates to the fact that IE in IV drug addiction is more commonly associated with right heart involvement. By contrast, brain abscesses were more common in patients with left-sided cardiac involvement. In addition to the conflicting findings on brain abscesses and IE among IV drug addictions, we also found that IV drug addiction was associated with a higher early stage mortality rate and shorter survival time in patients with PBA. This suggests that drug abuse affects the immune system, increases the risk of infection development [23], and might increase mortality, even without endocarditis. Another factor affecting the outcome was malignancy; the presence of concurrent malignancy in patients with PBA significantly increased mortality.

A low GCS score at the first visit was associated with poor PBA outcomes [10]. However, confusion, an easy-to-detect finding on admission, was not reported to indicate mortality in PBA in the literature, yet [3,9,15] and we found that it was a strong predictor of mortality in this study. In addition, the presence of confusion may indicate postinfection complications such as seizures and neurological deficits.

The large sample size in our study increased the reliability of our findings and provided a more accurate reflection of the relationship between confusion and mortality. This study has some limitations owing to its retrospective design. First, as with any observational study, unmeasured confounders may have influenced our results. Second, we did not have data on sequelae and seizures that developed after the infection period to assess their potential effect on mortality over time. Third, differences in diagnostic methods and treatment regimens across centers could have led to variability in clinical outcomes. Comprehensive information regarding the PCR methods and kits utilized was not provided. As a result, we were unable to evaluate the heterogeneity of these methods as a limitation. Finally, the lack of an attributable cause of death, particularly in patients with malignancy, is another limitation of this study.

Conclusion

Our study highlights that the factors influencing the 42-day and 180-day mortality in PBA may differ. According to our data, the factors associated with the acute infectious process led to higher short-term mortality rates, with additional contributions to long-term mortality stemming from destructive processes, such as temporal lobe involvement.

CRediT authorship contribution statement

Meyha Sahin: Data curation, Conceptualization, Investigation, Methodology, Resources, Validation, Visualization, Writing – original draft, Writing – review & editing. **Ali Mert:** Supervision, Validation, Visualization, Writing – review & editing. **Ahmet Naci Emecen:** Formal analysis. **Natalija Planinc Strunjas:** Data curation. **Lenka Fasanekova:** Data curation. **Ayse Batirel:** Data curation. **Ilad Alavi Darazam:** Data curation. **Shabboo Ansari:** Data curation. **Ghazaleh Golchoub Firouzjaei:** Data curation. **Roman Stebel:** Data curation. **Elif Tukenmez Tigen:** Data curation. **Buket Erturk Sengel:** Data curation. **Olga Dzupova:** Data curation. **Maya Belitova:** Data curation. **Maha Abid:** Data curation. **Nazife Duygu Demirbaş:** Data curation. **Serpil Erol:** Data curation. **Halil Kul:** Data curation. **Abdullah Umut Pekok:** Data curation. **Tülay Ünver Ulusoy:** Data curation. **Handan Alay:** Data curation. **Zahra Mohtasham Amiri:** Data curation. **Antonio Cascio:** Data curation. **Mehmet Kürşat Karadağ:** Data curation. **Entela Kolovani:** Data curation. **Nikolay Mladenov:** Data curation. **Ergys Ramosaco:** Data curation. **Oğuz Reşat Sipahi:** Data curation. **Gamze Şanlıdağ:** Data curation. **Amani El-Kholy:** Data curation. **Gulay Okay:** Data curation. **Natalia Pshenichnaya:** Data curation. **Mustafa Serhat Şahinoğlu:** Data curation. **Sevil Alkan:** Data curation. **Mehmet Özdemir:** Data curation. **Bilal Ahmad Rahimi:** Data curation. **Gulden Eser Karlidag:** Data curation. **Şafak Özer Balin:** Data curation. **Anna Liskova:** Data curation. **Anas Jouhar:** Data curation. **Fahad Almajid:** Data curation. **Xhumari Artur:** Data curation. **Mehmet Çelik:** Data curation. **Asfandiyar Khan:** Data curation. **Massimiliano Lanzafame:** Data curation. **Andrea Marıno:** Data curation. **Arzu Şenol:** Data curation. **Serkan Oncu:** Data curation. **Mustafa Uğuz:** Data curation. **Joanna Zajkowska:** Data curation. **Hakan Erdem:** Supervision, Validation, Visualization, Writing – review & editing.

Declarations of competing interest

The authors have no competing interests to declare.

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Ethical approval statement

The study protocol was approved by the Istanbul Medipol University Ethics Committee (ethical approval numbers and dates: E-10840098-772.02-6170 and 14.10.2022).

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ijid.2024.107228.

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