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Original Article

Clinical profile of patients with surgical brain abscesses and etiology in a reference hospital

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Abstract

Introduction: The annual incidence of brain abscesses is 1–2% in developed countries and up to 8% in developing countries. Our aim was to describe the profile and etiological agents of patients with surgical brain infections according to their nosological diagnosis on admission, and to analyze whether the initial diagnosis influenced the neurological deficit at discharge.

Methodology: This was an observational study with convenience sampling. All surgical cases operated between January 2017 and February 2022 with a final diagnosis of an infectious process were included. Three groups were analyzed according to admission diagnosis: a) infection, b) neoplasia, and c) miscellaneous. The time before admission, final histological diagnosis, etiological agent, length of hospital stay, and secondary neurological deficits were investigated. Descriptive and comparative statistics were used.

Results: 24 cases, including 18 (75%) men and 6 (25%) women, of ages 19 to 61 years (average 43.7 years) were studied. Nosological diagnoses on admission were infection in 9 (37.5%) patients, cerebral neoplasia in 9 (37.5%) patients, and miscellaneous diagnoses in 6 (25%) patients. Among the miscellaneous, neoplastic, and infectious groups, 33.3%, 33.3%, and 22.2% of patients were discharged with some neurological deficits with overall neurological morbidity and mortality of 29.6% and 8%, respectively. The etiological agents were *Mycobacterium tuberculosis* (16.6%), *Streptococcus* sp. (13%), *Morganella morganii* (8.7%), *Nocardia* sp. (4.3%), *Cryptococcus* sp. (4.3%), and *Klebsiella* sp. (4.3%).

Conclusions: Nosological diagnosis on admission did not influence the percentage of patients with neurological deficits in our study. *Mycobacterium* was the most frequent etiological agent.

Key words: brain abscess; infection; *Mycobacterium tuberculosis*; *Streptococcus;* morbidity; mortality.

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Introduction

Brain abscesses have an annual incidence of 1–2% in developed countries and up to 8% in developing countries [1]. When clinical and imaging pictures suggest this diagnosis, treatment can be promptly instituted. However, in Latin American countries, and especially in Mexico, the population usually does not seek medical intervention until the disease leads to inability to carry out daily activities. In those circumstances, differential diagnosis may include neoplasia and other non-infectious entities [2]. This situation is especially complicated in patients with human immunodeficiency virus (HIV) infection, where toxoplasmosis and central nervous system (CNS) lymphoma are common pathologies [3]. The aim of this study was to describe the profile of patients with surgical brain infections according to their nosological diagnosis on admission, and to analyze whether these initial diagnoses influenced the neurological deficit at discharge. An analysis of the etiological agents was also carried out.

Methodology

This was an observational study with retrospective convenience sampling.

Sampling

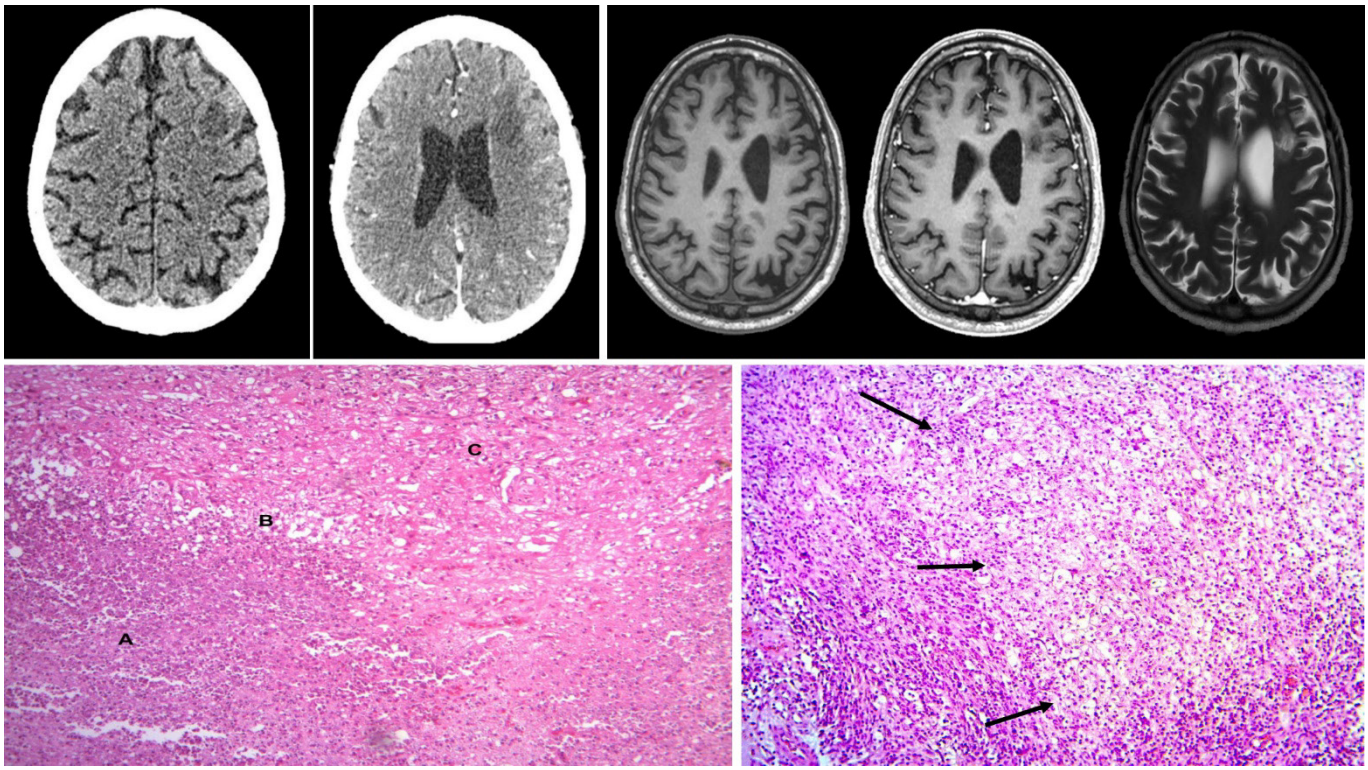
All brain surgeries performed between January 2017 and February 2022 with a final diagnosis of infectious process were included.

Table 1. Cases diagnosed as an infectious process on admission.

ID	Age (years) / Gender	Diagnosis at admission	Location	First symptom	Time between initial symptom-admission (days)	Hospital stay (days)	Added symptoms during stay	Etiological agent	Leucocytes (1000/mL)	Serum Hb (g/dL) at admission	Hto. (%) at admission	Neurological deficit	Status at discharge
B18-200	19/M	Multiple brain abscesses	Bilateral frontal lobes	Headache	23	41	Stupor	*Klebsiella*	4.61	12.9	35.7	Dysarthria and hemiparesis with left predominance	Alive
B19-476	43/M	Multiple brain abscess and subdural empyema	Left temporal lobe	Headache	9	12	None	*Morganella morganii*	14.62	16.4	49.4	None	Alive
B19-492	47/F	Brain abscess	Left frontal lobe	Generalized seizures	10	23	None	*Mycobacterium tuberculosis*	12.82	16	45	None	Alive
B19-522	54/M	2 brain abscesses HIV+	Right parieto-occipital lobes and right frontal lobe	Dizziness	82	15	None	No cultures	4.76	12.7	38.6	None	Alive
B20-322	51/M	Brain abscesses Bacterial endocarditis	Right Frontal and parieto-occipital lobes	Fever and systemic symptoms	33	1	Unknown	No cultures	7.73	8.6	26.8	Patient was sent only for surgery; he returned to cardiology hospital	Alive
B20-382	33/M	Brain abscess	Right frontal and parietal lobes	Headache and left hemiparesis	91	10	None	*Nocardia* sp.	15.71	11.6	34.5	None	Alive
B21-348	60/F	Brain abscess	Left frontal lobe	Headache	103	8	Stupor and left hemiparesis	Gram stain: Gram+ coccus, in chains. No cultures	7.15	11.7	37.9	Left hemiparesis; patient was transferred to other hospital	Alive
B22-89	39/M	Meningitis and brain abscesses	Right frontal lobe and left cerebellar peduncle	Depression and suicidal ideation	8	7	Focal seizures with secondary generalization	*Mycobacterium tuberculosis*	6.86	13.8	40	None	Alive
B22-112	44/M	Brain abscess	Right thalamus	Transient hemiparesis of the left lower limb	70	21	Focal seizures with clonic movements and tonic posture	*Staphylococcus aureus*	10.03	15.3	46.9	None	Alive

F: female; M: male; Hb: hemoglobin; Hto: hematocrit; HIV: human immunodeficiency virus.

Figure 1. Tuberculosis abscess.



Computed tomography scan (CTS) and magnetic resonance imaging (MRI) of the lesion. MRI (upper panel). A round, subcortical lesion, hypointense on T1, no enhancement with contrast material and hyperintense on T2 was observed. Histology (lower panel). Tuberculous brain abscess showed a central abscessed area (A), a fibrous capsule (B), and a collarette (C) of foamy macrophages, also observed in the right inferior picture (arrows). H and E, 100 and 400X.

Methods

The patients were grouped according to their admission diagnosis into three groups: a) infection, b) neoplasia, and c) miscellaneous. Miscellaneous diagnoses included neoplastic vs. infectious, autoimmune disorders, syndromic diagnosis, and vascular pathology. The following variables were recorded for each subgroup: gender; age in years; occupation; initial clinical manifestation; axillary temperature at admission; time of evolution before admission; serum levels of hemoglobin, hematocrit, and leukocytes at admission; location of the lesion; computed tomography scan (CTS) and magnetic resonance imaging (MRI) findings; admission diagnosis; evolution; size of the lesion; macroscopic description; histology; etiological agents; treatment; days of hospital stay; and discharge conditions.

Statistical analysis

Descriptive statistics and z tests were calculated for the percentages of patients with some type of neurological deficit at discharge.

Results

From January 2017 to February 2022, 24 surgeries were performed with a final histological diagnosis of infectious inflammatory processes. The patients included 18 (75%) men and 6 (25%) women. Their age range was 19–61 years, with an average of 43.7 years.

The nosological diagnosis on admission was infectious disease in 9 (37.5%) cases, brain neoplasia in 9 (37.5%) cases, and miscellaneous diagnosis in 6 (25%) cases. The last group included one patient with diagnosis of complicated stroke, one with a diagnosis of infection vs. neoplasia, and another with infection vs. autoimmune disease. Three cases had a diagnosis of secondary headache. Except for one patient, no fever was reported before or during hospital admission. Only 35% of the patients had leukocytosis on admission, and except for the patient with endocarditis who was anemic, the others had acceptable levels of hemoglobin and hematocrit.

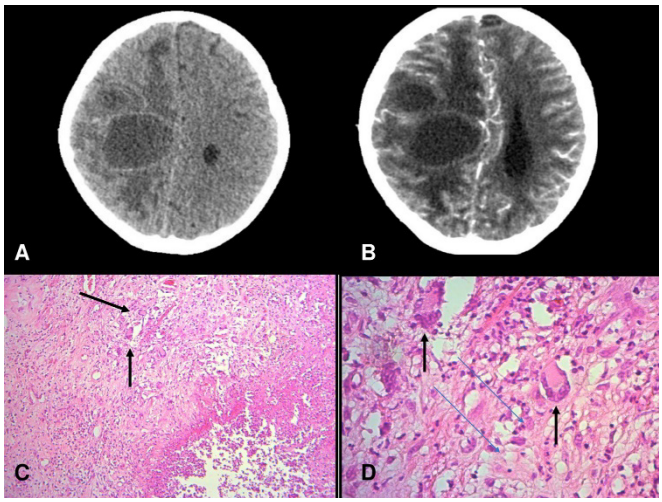
Infectious nosology

Nine patients were admitted with a diagnosis of brain abscess and 1 case was diagnosed as meningitis (Table 1). The main symptom at onset was headache in 4 (44.4 %) patients; 4 patients had seizures, dizziness, depression and suicidal ideation and transient hemiparesis, respectively; only one patient had fever and systemic symptoms. The etiological agents identified were *Klebsiella* sp. (1), *Morganella morganii* (1), *Mycobacterium tuberculosis* (2), *Nocardia* sp. (1), and *Staphylococcus aureus* (1); in 3 cases, no cultures were performed; in the case of meningitis, the etiologic agent was *M. tuberculosis*, and this patient also had parenchymal tuberculosis (TB) abscess, with fibrous wall and a rim of foamy macrophages (Figure 1). The patient with *Nocardia sp.* infection showed a central abscess with a well-defined fibrous capsule and numerous multinucleated giant cells (Figure 2). The average age of the patients in this group was 43.3 years, with a range of 19–60 years. There were 7 (77.8 %) men and 2 (22.2%) women. The average time between the onset of symptoms and hospital admission was 47.7 days, with a range of 8–103 days. The average length of hospital stay was 15.3 days, with a range of 1–41 days.

Neoplastic nosology

There were 9 cases of presumed neoplastic nosology and the etiological agents identified were TB (1), anaerobic bacteria (1), *Streptococcus intermedius* (1), *Streptococcus anginosus* (1), and *Cryptococcus gattii* (1); in one case, a polymicrobial infection by *Escherichia coli* and *Staphylococcus aureus* was documented; in 3 cases, there was no bacterial growth in the culture media, including the case with a necrotic abscessed neoplasm. Cryptococcoma showed an extensive fibroglial reaction, islands with numerous yeasts, discrete lymphoplasmacytic infiltrates, and few multinucleated giant cells (Figure 3). Average time between symptom onset and hospital admission was 69 days, with a range of 8–203 days.

Figure 2. Nocardia abscess.



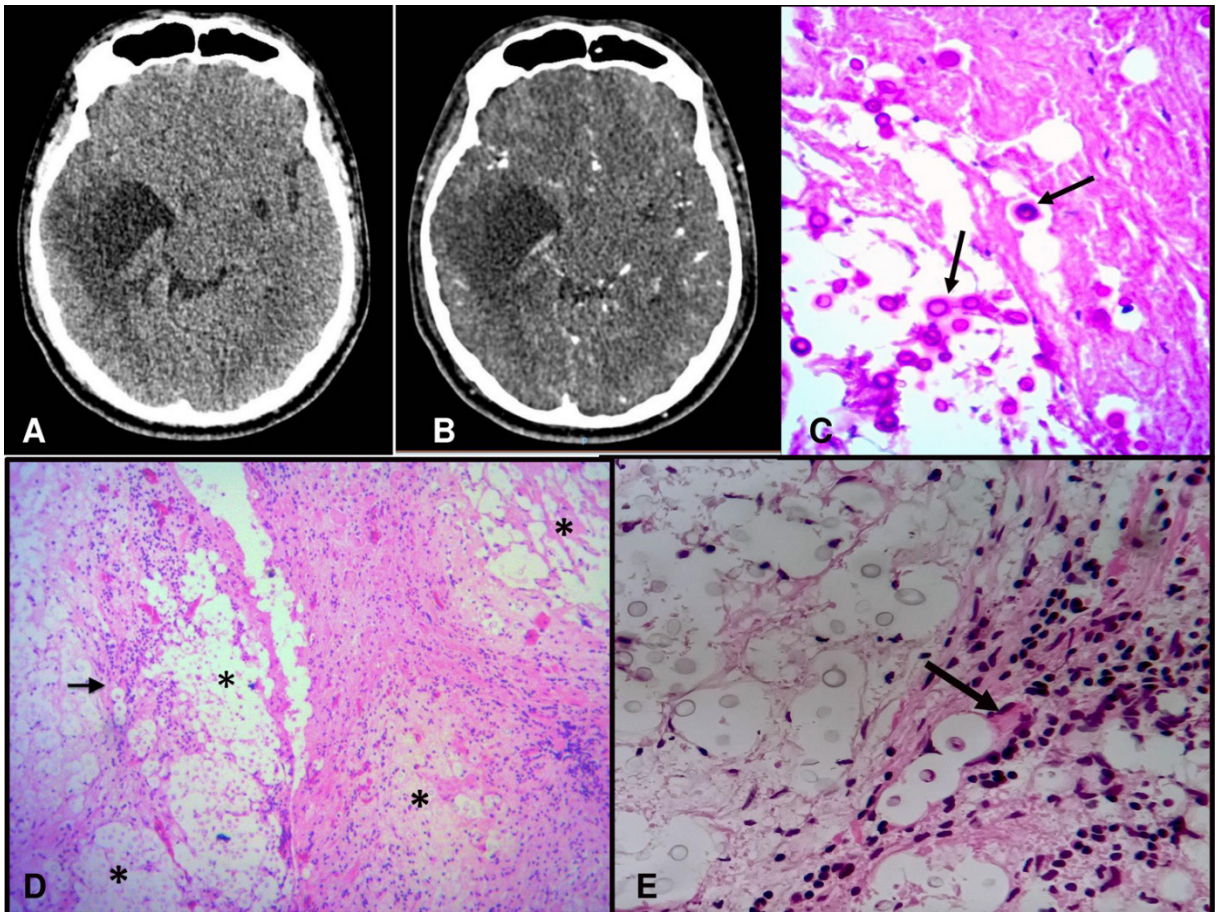
Computed tomography scan (CTS) brain axial sections (A–B). (A) A cortico-subcortical (23.61 × 16.99 mm) and a white-matter (41.97 × 39.42 mm) lesions, were observed. (B) The lesions had discrete ring enhancement with contrast material. Histology (C–D) Abscessed necrotic center, with a fibrous wall with numerous multinucleated giant cells (arrows) Left, 100X, right 400X, H&E.

Table 2. Cases with a nosological diagnosis of neoplasia on admission.

ID	Age (years) / Gender	Diagnosis at admission	Location	First symptom-sign	Time between initial symptom-admission (days)	Hospital stay (days)	Added symptoms during stay	Etiological agent	Leucocytes (1000/mL)	Serum Hb (g/dL) at admission	Hto (%) at admission	Neurological deficit	Status at discharge
B17-98	48/F	Brain metastasis, probably lung origin	Left frontal lobe	Seizures	79	38	Headache	*Mycobacterium tuberculosis*	Not available	12	37	None	Alive
B17-100	29/M	Glioma	Right frontoparietal lesion	Headache	10	18	Generalized seizures	Anaerobic bacteria	Not available	13	38	Sensory transcortical aphasia	Alive
B17-238	51/M	Low-grade glioma	Right frontal lesion	Facial asymmetry	10	13	Headache, left hemiparesis	*Streptococcus intermedius*	Not available	14	38	None	Alive
B17-816	31/F	Pituitary adenoma	Hypophyseal fossa	Progressive loss of vision	203	4	Headache	Negative culture	8.61	11.1	33	Persistence of previous visual deficit	Alive
B20-123	29/M	Glioma	Left parietal lobe	Right facial and corporal hemiparesis	8	13	Tonic-clonic seizures	*Streptococcus anginosus*	14.26	17.3	51	Seizures	Alive
B21-43	61/M	Metastasis vs Glioblastoma	Right frontoparietal lobes and left parietal lobe	Focal seizures: hemifacial and twitching	83	22	Right hemiparesis	Negative cultures	11.52	13.1	41	Sudden death, cardio-pulmonary arrest	Abscessed metastasis. Death.
B21-459	39/M	Glioma	Right temporo-parietal lesion	Headache	120	25	Behavior changes, left hand tremor	*Cryptococcus gattii*	16.76	14.9	43.1	None	Sudden death, pulmonary embolism
B22-27	57/M	Malignant glioma	2 lesions; right temporal lobe	Headache	91	33	None	*Escherichia coli* and *Staphylococcus aureus*	9.69	15.1	44.9	None	Alive
B22-102	57/M	Glioma	Right temporo-parietal and occipital lobes	Headache	17	24	Intensification of headache, vomiting, tachypnea	Negative cultures	13.02	17.7	52	None	Alive

F: female; M: male; Hb: hemoglobin; Hto: hematocrit.

Figure 3. *Cryptococcoma*.



(A–B) Magnetic resonance imaging (MRI). Right frontoparietal, subcortical, heterogeneous lesion with irregular, poorly defined borders, hypointense in T1 (A), and with slight central contrast enhancement (T1, B). (C) Upper right corner, mucicarmine stain showing numerous cryptococci with red capsule (arrow). (D) Cerebral cryptococcoma (*) showed numerous yeasts in a mucinous background, forming islands surrounded by reactive fibroglial tissue. A giant multinucleated cell (arrow) is observed (100X). (E) Lymphoplasmacytic inflammation and a giant multinucleated cell (arrow) ingesting a cryptococcus. H and E, 400X.

The average length of hospital stay was 21.1 days, with a range of 4–38 days (Table 2).

Miscellaneous cases

This group included 6 cases (Table 3). In the case of vascular nosology, the patient had had a cerebral infarction 4 months earlier, and an abscess with 30 cc of purulent material developed adjacent to that area. The culture did not exhibit any growth, but he had received antibiotics prescribed by his family physician, before admission. The case with an infectious vs. autoimmune disease was clinically diagnosed as severe rhombencephalitis with vasculitis and vascular endothelial damage. The final diagnosis was culture-documented TB. Three patients who were admitted with headaches of secondary origin had abscesses. TB and *Streptococcus pneumoniae* were identified in one case; *M. morganii* and *E. coli* grew in culture in the second case; and *Streptococcus* sp. were involved in the last one. One patient with frontal lesions had negative culture results. Average time between symptom onset and hospital admission was 83.1 days, with a range of 2–206 days. The average length of hospital stay was 31 days, with a range of 10–93 days.

Clinical evolution

Of the 24 patients studied, 15 (62.5%) showed adequate evolution and were discharged without neurological deficits; 7 (29.1%) patients had neurological deficits; and finally, 2 (8.3%) sudden deaths, both in the group admitted as neoplasia, were recorded. The patient with abscessed-brain metastasis died of cardiorespiratory arrest and the patient with cryptococcoma died of pulmonary thromboembolism.

In the miscellaneous, neoplastic, and infectious groups, 33.4%, 33.4%, and 22.2% of the patients, respectively, were discharged with some neurological deficit; however, the z-test for percentages had a $p = 0.80$. Therefore, there were no significant differences in neurological sequelae between the groups.

Discussion

All the patients included in this study had brain abscesses. Although fever and leukocytosis were not frequent findings (4.1 and 35% respectively), their presence supports an infectious etiology.

Of the 9 cases in the infectious group, 2 (22.2.%) had TB. Interestingly, these two cases showed lesions with central abscesses surrounded by foamy macrophages and a fibrous wall with adjacent granulomatous tissue. Caseous granulomas are usually expected to be seen in the setting of TB; however, in these cases, central abscesses with a ring of foamy macrophages were observed. The two cases had an acute evolution and while one patient started with seizures, the other presented depression and suicidal ideation. None were immunosuppressed, nor was pulmonary or systemic infection documented. In general, there are reports of isolated cases of TB brain abscesses in patients with HIV [4], or TB brain abscess in immunocompetent patients with infectious systemic involvement [5-6]. In our cases, TB presented as a brain abscess with no apparent systemic involvement in immunocompetent subjects. It is important to note that

Table 3. Cases with miscellaneous diagnoses on admission.

ID	Age (years) / Gender	Diagnosis at admission	Location	First symptom-sign	Time between initial symptom-admission (days)	Hospital stay (days)	Added symptoms during stay	Etiological agent	Leucocytes (1000/mL)	Serum Hb (g/dL) at admission	Hto (%) at admission	Neurological deficit	Status at discharge
B17-337	61/M	Previous brain infarct & lesion with irregular peripheral contrast enhancement in the area of encephalomalacia of previous infarct	Right Parieto-temporal lobes	Headache	2	38	Generalized seizures	No culture of purulent discharge	6.51	13.3	39.9	Aphasia	Alive
B17-574	37/F	Headache of secondary origin	Left frontal lobe	Headache	172	10	None	*Mycobacterium tuberculosis* and *Streptococcus pneumoniae*	6.35	13.2	39.9	None	Alive
B19-369	34/F	Headache of secondary origin	Left frontal lobe	Headache	206	15	Generalized seizures	*Morganella morganii* and *E. coli*	15.25	14.2	42.7	None	Alive
B20-164	48/M	Neoplasia vs. infection	Left frontal lobe	Right hemiparesis	8	18	None	No growth	8.7	14.1	43.6	None	Alive
B21-458	30 M	Immune-mediated vs infectious: rhombencephalitis	Multiple lesions in pons, and cerebellum	Mixed dysarthria	95	93	Fatigue-patient required gastrostomy and tracheostomy	*Mycobacterium tuberculosis*	4.18	15.4	45.2	Pancerebellar syndrome	Alive
B21-134	46/M	Headache	Right parietal lobe	Headache	16	12	Right hemiparesia	*Streptococcus* sp.	7.55	17	50.5	None	Alive

F: female; M: male: Hb: hemoglobin; Hto: hematocrit.

granulomatous reaction surrounded the abscess; therefore, the biopsy should not be taken from the abscessed-central necrotic region, but rather from the area that is reinforced with contrast. Although no cultures were taken in 3 cases, the presence of *Klebsiella* sp., *Nocardia* sp., *S. aureus*, and *M. morganii* was documented in the rest. One (11.1%) patient had immunodeficiency (human immunodeficiency virus, HIV+) and two (22.2%) patients were discharged with neurological deficits. In a series of 57 patients diagnosed with primary abscesses, 24.5% had a poor prognosis, including two deaths [7].

Great variability was observed in the etiological agents in the "neoplasia" group: TB, fungi, *S. aureus*, *S. intermedius*, *S. anginosus*, *E. coli,* and anaerobic bacteria; however, in three cases, the cultures were negative. The initial symptoms were headaches (44.4%) and seizures (22.2%). In two patients, seizures also occurred during the course of the disease. *Streptococcus* was the etiological agent in two cases. *S. anginosus* is part of the microbiome of the oral cavity and gastrointestinal tract but is also a frequent cause of brain abscesses [8].

The case associated with *Cryptococcus gattii* had 120 days of evolution and was diagnosed as high-grade glioma. However, during the surgical approach, a gelatinous, poorly vascularized lesion was observed, and a frozen section study showed the presence of *Cryptococci*. Although rare, cryptococcomas can mimic brain neoplasms with a chronic course [9,10].

Multiple lesions were frequently observed in the miscellaneous-group. In addition, the percentage of affected women in the miscellaneous group was higher than in the neoplastic (22.2%) and infectious (22.2%) groups. TB was the etiological agent in two cases. *S. pneumoniae*, *E. coli*, and *M. morganii* were also identified in other patients. One case of TB presented clinically as rhombencephalitis, although MRI revealed multiple lesions in the cerebellum, pons, and supratentorial white matter. Cerebellar biopsy showed an infiltrate of foamy macrophages, with PAS+ granular material, forming perivascular collarettes (reminiscent of what was described in Whipple's disease caused by *Tropheryma whippelii*). This PAS+ material can also be observed in histoplasmosis and *Mycobacterium avium* infection [11]. Parenchymal macrophages without PAS+ material, CD3+ lymphocytes, and a few CD20+ lymphocytes were also observed.

The time of evolution before hospital admission varied according to the admission diagnosis. In this series, patients admitted with a diagnosis of neoplasia had a longer evolution before admission than the other two groups. Neurological deficits at discharge were observed in 29% of patients. No significant differences in neurological deficits were observed between groups.

Two deaths occurred in the group with initial diagnosis of neoplasia; one of them might have been prevented by heparin prophylaxis [12].

The overall mortality rate was 8.3%, and deaths were not directly due to infection. In a series of 71 patients reported by Gutierrez *et al*., the mortality rate associated with brain abscesses was 21% [13]. In a series of 1,384 brain abscesses in Denmark with a mean follow-up of 6 years, it was shown that the mortality rate at 1 year was 21% compared to 1% in the control group. Furthermore, in patients who survived for more than one month, new-onset epilepsy developed in 32% of the patients compared to 2% in the control population [14].

Limitations

This study employed a convenience sample characterized by a relatively limited number of cases. Nonetheless, it offered a fundamental insight into the behavior of these infectious processes that remain unresponsive to conventional medical interventions.

Conclusions

Surgical brain abscesses were more frequent in men (75%) than in women and patients may have chronic symptoms during 200 days or more before seeking medical care. Initial diagnosis of an infectious process was made in only 37.5% of the patients. The most frequent causative agents were *Mycobacterium tuberculosis* (20.8%), *Streptococcus* (12.5%), and *Morganella morganii* (8.3%). Nosological diagnosis at admission did not affect the percentage of neurological deficits at discharge. TB continued to be a great simulator, with manifestations such as brain abscesses and acute rhombencephalitis. Thus, differentiating between brain infections, neoplasia, and vascular events is not always easy and requires complete clinical evaluation and multidisciplinary teamwork.

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Ethical approval

The study protocol was approved by the Ethics and Research Committee of the institution (protocol 125-22), and the research was conducted ethically in accordance with the

World Medical Association Declaration of Helsinki. In retrospective studies like this one, where the identity of the patients is not exposed, Ethics and Research Committees do not require a consent letter.

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Conflict of interests: No conflict of interests is declared.