

Original Article

A case series of brain abscesses: an eleven-year retrospective single center study

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Abstract

Introduction: We lack data on the epidemiology and management of brain abscesses in the Middle East. The aim of this study is to report a case series of brain abscesses admitted at a tertiary care center in Lebanon, between January 2008 and December 2018.

Methodology: This retrospective study aimed at determining the demographic data, treatment, and correlations between different studied variables with prognosis of patients that received treatment.

Results: Forty-one patients (30 males) were included with a median age of 37 years (2-85). The analysis showed that the classic triad of fever, headache and neurologic deficit was only present in 12% of patients on admission. The source of infection was contiguous in 36.5%, post surgical in 32%, and distant in 17% of cases. Stereotactic biopsy was performed in 41.5% of patients, and craniotomy in 19.5%. A microorganism was isolated in 63% of patients (26 cases). The most used antibiotics were carbapenems (46%) and glycopeptides (66%). Eighty percent of patient (33) had a good outcome. A worse prognosis was significantly correlated with immunosuppression and multiple cerebral abscesses.

Conclusions: Brain abscess remains a relatively rare condition.

Key words: Brain abscess; stereotactic biopsy; human immunodeficiency virus; antibiotics; patient prognosis.

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Introduction

Intracranial abscesses can be divided into several categories depending on their anatomic location: intraparenchymal brain abscesses, subdural and extradural empyema. Intraparenchymal abscess is a focal collection of pus caused by bacteria, mycobacteria, fungi, protozoa, or helminths in the parenchyma of the brain [1]. This infection is highly debilitating and associated with high mortality [2]. It can arise from a contiguous (otogenic infection, dental infection, sinusitis or mastoiditis) or from a distant spread of a source of infection (congenital cyanotic cardiomyopathy, endocarditis, pulmonary infection, etc.) [3]. These infections can also complicate a head injury, neurosurgery, or meningitis [3]. Intracranial infections remain without any obvious source in approximately 25% to 35% of cases [4,5]. Direct spread accounts for around 50 percent of cases [1]. Distant bacteremia is characterized by multiple cerebral lesions [6].

The treatment and outcome of intraparenchymal abscesses has improved in the recent years, and this can be attributed to the modern neurosurgical techniques, including stereotactic brain biopsy, better culture techniques, antibiotics, and modern non-invasive neuro-radiological imaging. Eradication of the main foci of infection is critical for favorable outcome [2,7,8].

The annual incidence of this disease has rarely been reported in the literature: 0.9 per 100,000 persons-years in Denmark and Minnesota [9,10]. This incidence is higher in the immunocompromised population [11].

Despite its severity, brain intraparenchymal infection has not been extensively studied in Middle Eastern population. The aim of this study is to report the cases of brain abscess recorded in a tertiary care center in Beirut, Lebanon, between January 2008 and December 2018. These cases were reviewed to document the epidemiology, possible causes, treatments, and prognostic factors associated with

outcome. The long-term outcome was not assessed in this study.

Methodology

This study was performed in a tertiary care university hospital. We retrospectively assessed electronic medical records for the past eleven years (between January 2008 and December 2018) searching for “brain abscess”, “brain abscesses”, “cerebral abscess” and “cerebral abscesses” keywords using the International Classification of Diseases (ICD) 10 discharge codes. Only patients that received treatment were selected.

We identified a total of forty-one cases. The following variables were retrospectively assessed by medical record review using a standardized data collection form: sex, age, human immunodeficiency virus (HIV) status, predisposing medical factors, radiologic images with location of the abscess, symptoms, microbiologic cultures, treatment, and outcome.

Brain abscess was defined as a localized lesion, visible on a computerized tomography (CT) or magnetic resonance image (MRI) scan, located in the cerebrum, cerebellum, or midbrain, which met at least one of the following criteria:

A positive culture of intracerebral material or brain abscess at histology or neuroradiological findings suggesting brain abscess plus radiological and clinical response to antimicrobial therapy.

Contiguous focus of infection was defined as secondary to otogenic infection, dental infection, sinusitis, or mastoiditis. A poor outcome was defined as death or invalidating neurological sequela despite

appropriate treatment. The overall mortality was defined as death happening during hospitalization. Immunosuppression was defined by the presence of any of the following: poorly controlled diabetes, any vasculitis or other autoimmune disease that was treated with immunosuppressive agents, positive HIV status with CD4 count of less than 200 mm³.

Statistical Analysis

Data were entered in IBM Statistical Package for Social Sciences for Windows (SPSS version 25) and all the data were analyzed. Ordinal scale data were analyzed as mean with standard deviation or median. The χ^2 test was used for comparison of groups with qualitative variables on nominal scale. A *p* value of 0.05 or less was considered significant and confidence interval of 95% was selected for the analysis.

Ethics approval and consent to participate

The study was approved by the institutional review board at Saint Joseph University, Beirut (approval number TFEM/2018/57).

Results

Between January 2008 and December 2018, 41 cases of brain abscesses were diagnosed and treated. There was 30 (73.2%) males and 11 (26.8%) females (ratio 3:1) with a median age of 37 years (range from 2 to 85 years). Age and sex distribution are shown in Figure 1.

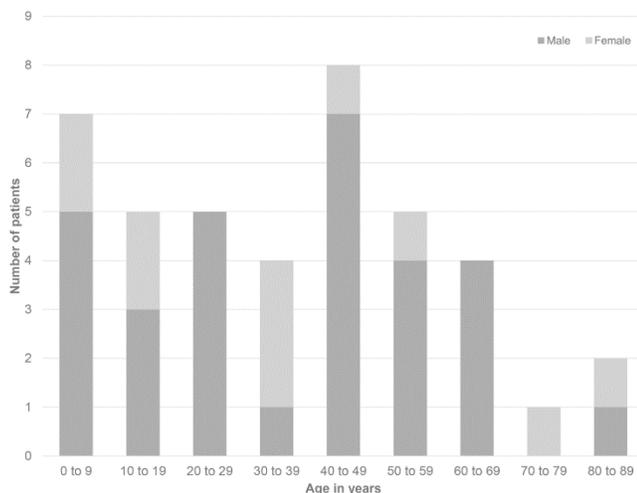
Clinical findings

Neurologic deficit was the most common symptom on admission occurring in 24 (58.5%) patients. Twenty-three (56%) patients had fever and 22 (53.6%) presented with confusion and drowsiness. The classic triad of fever, headache and neurologic deficit was only present in five cases (12%). Patients receiving corticosteroids or other immunosuppressive treatments did not present with initial fever.

Laboratory findings

Two biological serum markers were assessed on admission: white blood cells count and C-reactive protein (CRP) level. The CRP was within the normal range (< 3.5 mg/dL) in 17 patients (41.4%) with a mean of 68 mg/dL. Only 15 patients (36.5%) presented with hyperleukocytosis (defined as white blood cells count of more than 11,000×10⁹ cells per liter).

Figure 1. Age and sex distribution of patients with brain abscesses.



Neuroradiological imaging and source of abscess

Intracerebral abscesses were detected on CT scans in 22 patients (53%), and on MRIs in 16 patients (39%). MRI was used in addition to CT in four patients (9.7%) because of image ambiguity. Twenty-eight patients (68.3%) had a single brain abscess and 13 patients (31.7%) had multiple abscesses detected. The most common site of infection was the frontal lobe (23 patients).

Source of infection was identified in 22 patients (53.6%), out of which 15 had a contiguous and seven had a distant foci of infection. The most prevalent anatomical source for contiguous foci of infection was the ear, nose, and throat (ENT) sphere (12 patients). Six patients had a distant infection (4 pneumonias, 2 endocarditis).

Comorbidities and associated factors

Immunosuppression (18 patients, 44%) and history of neurosurgery (13 patients, 32%) were the most frequent associated factors. Steroid usage and diabetes were amongst the main causes of immunosuppression (12 and 11 patients respectively). Eight patients had HIV infection with a CD4 count < 200 mm³. All HIV patients had the acquired immunodeficiency syndrome (AIDS). Unfortunately, HIV viral load in serum test was not found in the medical records of these patients. Of the neurosurgeries, we identified four cases post cranioplasty or reconstruction for facial deformity, five cases post intracranial hematoma drainage following a trauma, two cases post intracranial mass resection, one case post resection of a cranial dermal sinus and one case post radiological embolization. Characteristics of the studied population are shown in Table 1.

Diagnostic workup and microbiological findings

Drainage of the collections was performed in 26 patients: 17 patients had a stereotactic biopsy and eight had a craniotomy. Myringotomy was performed in one patient. The rest of patients had a lumbar puncture. Thirteen patients, in whom a lumbar puncture was performed, had the following characteristics on cerebrospinal fluid (CSF) analysis:

- Six had a bacterial pattern (hypoglycorrachia, high CSF protein levels and hypercellularity)
- Four had a normal pattern
- Three had a viral pattern (normoglycorrachia, low CSF protein levels and low mononuclear count)

The isolated infecting organisms are detailed in Table 2.

A microorganism was isolated in 26 patients (63%). Eleven patients had organisms that are usually seen in immunocompromised hosts (*Toxoplasma gondii*, *Cryptococcus* sp., *Pneumocystis jirovecii*, and mucormycosis). *Toxoplasma gondii* and *Pneumocystis jirovecii* were mostly isolated in HIV infected patients.

Table 1. Characteristics of 41 patients with brain abscess.

Characteristics	No. (%) of cases
Presenting complaints:	
Fever	23 (56)
Focal neurological deficit	22 (53.6)
Headache	21 (51.2)
Convulsion	21 (51.2)
Nausea/vomiting	19 (46.3)
Unconscious	17 (41.5)
Decreased level of consciousness	10 (24.3)
Location of the abscess¹:	
Frontal	23 (56)
Temporal	11 (26.8)
Parietal	11 (26.8)
Occipital	9 (21.9)
Thalamus	3 (7.3)
Cerebellum	2 (4.8)
Periventricular	2 (4.8)
Protuberance	1 (2.4)
Diencephalon	1 (2.4)
Associated factors:	
Contiguous or distant focus of infection	22 (53.6)
Immunosuppression	19 (46.3)
Post neurosurgery	13 (31.7)
Medical comorbidities ²	10 (24.4)
Head injury	7 (17)
Probable source of infection:	
Acute otitis media	7
Pneumonia	4
Endocarditis	3
Pansinusitis	2
Meningitis	2
Cerebral shunt	1
Frontal sinusitis	1
Retropharyngeal abscess	1
Ethmoiditis	1
Immunosuppression causes:	
HIV ³	8
Renal transplant	3
Sarcoidosis	2
Lupus erythematosus disease	1
Giant Cell Arteritis	1
Good's syndrome	1
Acute lymphoblastic lymphoma	1
Familial Mediterranean Fever	1

¹ Thirteen patients had multiple brain abscesses; ² The medical comorbidities were: Familial Mediterranean fever, lupus erythematosus disease, inflammatory bowel disease, sarcoidosis, spina bifida with meningocele, Crouzon syndrome with hydrocephalus and Schwachman syndrome; ³ HIV: human immunosuppressive virus.

Staphylococcus aureus was grown in patients who had a recent neurosurgery.

Treatments

All patients received intravenous antibiotics initially. Only two patients received intrathecal antifungal therapy. The most used antibiotics were carbapenems (46%) (Meropenem, Imipenem-Cilastatin or Ertapenem) and glycopeptides (66%). Clindamycin was mainly used in the HIV population. It was combined with pyrimethamine in two patients and atovaquone in one patient who had *Pneumocystis jirovecii* infection. Trimethoprim-sulfamethoxazole was administered to eight patients (one of whom had a nocardial infection and one had a pneumocystis infection). Metronidazole was used in eight patients.

Fluconazole was the most frequently used antifungal agent (6 patients). Intrathecal administration of liposomal amphotericin B was performed in one patient (mucormycosis infection).

One patient received acyclovir as monotherapy after identifying a radiological temporal lesion.

The treatment duration was not evaluated in the studied population due to the lack of information in some medical records (some patients were on prophylactic antibiotic treatment before their admission), and some patients were transferred to other facilities.

Patients' outcome and factors correlated with poor outcome

The overall in hospital mortality was 19.5% (8 patients), with three deaths attributed to AIDS

complications, two deaths attributed to advanced neoplasia (Acute lymphoblastic lymphoma and non-Hodgkin lymphoma) and three deaths possibly caused by a lack of source control of the infection (mucormycosis and *Cryptococcus neoformans* abscesses). Eleven patients (26.8%) recovered but sustained neurological sequelae: 7 patients remained epileptic, one experienced amnesia, one had a frontal lobe syndrome and one had hemiplegia.

The length of stay in the hospital ranged from 3 to 233 days with an average of 35 days and a standard deviation of 15 days. Ten patients were switched to an oral antibiotic after definitive culture results, with amoxicillin-clavulanate and / or fluoroquinolone being mostly prescribed.

Several factors have been statistically studied and were found to have a correlated with a poor outcome:

- Immunosuppression was correlated with a poor prognosis ($p = 0.02$): death occurred only in immunosuppressed patients
- Multiple cerebral abscesses were correlated with a poorer prognosis compared to single abscesses ($p = 0.05$): 6 out of 13 patients with multiple abscesses died

There was no significant correlation between diabetes, anatomic location of the abscess, or the clinical presentation and the outcome.

Patients presenting with abscesses following a fracture of the skull or a neurosurgery had a better prognosis.

Table 2. Microorganisms isolated in brain abscesses of patients.

Causative agent	Contiguous focus of infection	Medical comorbidities ¹	HIV ² positive	Post neurosurgery	Cranial trauma	Total no.
<i>Toxoplasma gondii</i>	0	0	7	0	0	7
<i>Streptococcus pneumoniae</i>	2	0	0	0	1	3
<i>Staphylococcus aureus</i>	1	1	0	1	0	3
<i>Staphylococcus epidermidis</i>	1	0	0	0	1	2
<i>Streptococcus milleri</i>	1	1	0	0	0	2
<i>Staphylococcus aureus</i> methicillin resistant	1	0	0	1	0	2
<i>Streptococcus mitis</i>	1	0	0	0	0	1
<i>Nocardia</i> sp.	0	1	0	0	0	1
<i>Peptococcus</i> sp.	0	1	0	0	0	1
<i>Klebsiella pneumoniae</i>	0	1	0	0	0	1
Mucormycosis infection	1	0	0	0	0	1
<i>Cryptococcus</i> sp.	0	1	0	0	0	1
<i>Pneumocystis jirovecii</i>	0	0	1	0	0	1
No causative agent identified	5	3	0	3	4	15

¹ The medical comorbidities include diabetes, renal transplant, sarcoidosis, lupus erythematosus disease and familial Mediterranean fever; ² HIV: Human immunosuppressive virus.

Discussion

To our knowledge, this is the largest case series to report data on patients with brain abscesses done in the Middle East. One case series reported 26 cases in Saudi Arabia and was published in 1980s [12]. Only a few case reports have been recently published from this region [13,14]. Several studies describing series of patients with a brain abscess, whenever focused on a specific population [15] or all cases [16–19], have been reported in the medical literature.

Epidemiology

The sex ratio (male to female) in our study is comparable to the one reported by Zhang *et al.* [20], but differs from the one reported by Carpenter *et al.* (1.27 to 1) [21].

The median age in this study is comparable to the one reported by Carpenter *et al.* [21]. We described the cases of seven children, between the ages of 2 to 9 years old (17% of cases). Patients younger than 18 years old accounted for 29.2% in this study. In contrast, in cases reported by Carpenter *et al.* [21] only 4% of their population were children under 10 years old, and 14% of their patients were under the age of 18. The majority of brain abscesses occur in the first two decades of life because of the frequency of sinus and middle ear infections in these ages [17].

The classic triad of fever, headache and neurologic deficit was found in more cases in our study compared to the one done by Zhang *et al.* [20]. According to Renton *et al.* [22], this combination helps to establish a correct diagnosis but its sensitivity remains low.

A higher percentage of brain abscesses complicating a head injury or neurosurgery was found in this study compared to the study done by Carpenter *et al.* [21]. This may be due to a decreasing frequency of ENT infections complicated by intracerebral abscesses, as a result of better vaccination rates.

Previous studies have demonstrated that hematogenous dissemination of an infection arising from a distant location, accounts for approximately 6% of cerebral abscesses. [23,24] Our study showed that 17% of the abscesses reported were secondary to a distant foci (endocarditis and pulmonary). This emphasized on the importance of looking for distant infections when no apparent origin for a brain abscess can be found. It may help in controlling the source of infection and preventing further complications.

Several articles [20,21] reported brain abscesses originating from complications of cyanogenic heart disease but no such cases were observed in this study.

The percentage of single brain abscesses in this study was comparable to the reported ones by Zhang *et al.* [20] and Landriel *et al.* [25].

Treatment

Previous studies proved that aggressive antibiotic therapy alone cannot substitute for an abscess drainage [4]. Prolonged antibiotic treatment (4 to 8 weeks) combined with a surgical excision or drainage of the brain abscess remains the treatment of choice [26]. Some recommend a complete surgical excision of the abscess while others favor repeated drainage. Since repeated drainage is less invasive, it became the standard of care [27]. Stereotactic CT guided aspiration can reach difficult regions of the brain. Most of our patients were subjected to a drainage technique (63.4%). This study revealed that performing drainage improved the prognosis of patients. This correlation between drainage of abscesses and better prognosis was demonstrated in the literature [7,21].

Causative microbiological findings

A causative organism was isolated in most of the reported patients. Negative microbiology cultures in some cases were probably secondary to antibiotics received before admission. The most frequently isolated microorganisms were: *Staphylococcus aureus*, *S. milleri*, *S. epidermidis*, *Streptococcus pneumoniae* and *Peptococcus* sp.; these microorganisms are reported frequently in the literature [28]. *Staphylococcus aureus* was mostly isolated from patients with a history of neurosurgery. This bacteria colonizes the skin and surgical incisions may increase its risk of infection [3]. *Toxoplasma gondii* and pneumocystis infections were mostly isolated in HIV infected patients in this study. This underlines the importance of early diagnosis and treatment of HIV infection [29], especially in the Middle Easter population.

Draining a brain abscess will not only help culture the causative organism but will also aid in controlling the source of infection. Treating a specific organism is much simpler than keeping patient on broad spectrum empirical therapy.

Prognosis and mortality

The overall in hospital mortality rate in this study was within the range reported in the literature [28]. Among the HIV positive, two out of eight patients died, and three had some residual sequelae. Among the thirteen postoperative infections, four patients had neurological sequelae and no mortality was

encountered. Six out of ten immunosuppressed patients died, (HIV positive patients not included), and one had sequelae after completing the course of treatment.

Strengths and limitations of the study

The study highlights several important points: This is probably one of the largest case series reporting the epidemiology and microbiology of brain abscesses from a Middle Eastern region, with an HIV subpopulation. Distant sources of infection should be systematically looked for. It also demonstrated that draining the abscess was associated with a better prognosis, and that multiple abscesses or immunosuppression were associated with a worse outcome. Diagnosing and treating HIV infections in earlier stages could prevent these complications.

This is a monocentric retrospective study, and could have selection, recall and information bias. The absence of follow-up to determine long term outcome, and the absence of some details for many patients on the duration of antibiotic treatment, are significant limitations.

Conclusions

Despite a decline in mortality rates in the era of evolving neuroradiological techniques, brain abscess remains a serious condition with high mortality and morbidity. This study reports a case series of brain abscesses from a Middle Eastern center. Immunosuppression and multiple brain abscesses were found to be associated with poor outcome, whereas early drainage significantly improved the prognosis of these patients.

Authors' contributions

RW drafted the original manuscript. NC, MC and EH helped to draft the manuscript. GS participated in the design of the study. JC, HT and HM conceived the study and participated in its design and coordination. All authors read and approved the final manuscript.

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