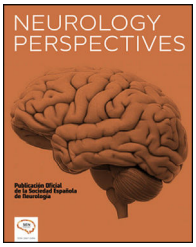
Neurology Perspectives 2 (2022) 160–167

NEUROLOGY PERSPECTIVES

www.journals.elsevier.com/neurology-perspectives



REVIEW

Brain abscess: A narrative review

M.A. Ruiz-Barrera[a,b,d,*], A.F. Santamaría-Rodríguez[a], O.F. Zorro[c]

[a] *Médico Fundación Universitaria Juan N. Corpas, Bogotá, Colombia*
[b] *Estudiante de Maestría en Epidemiología Universidad del Rosario, Bogotá, Colombia*
[c] *Neurocirujano Hospital San Ignacio y Hospital de San José, Bogotá, Colombia*
[d] *Coordinador del grupo de investigación en neurocirugía, Neurociencia, Bogotá, Colombia*

Received 12 September 2021; accepted 23 January 2022
Available online 30 April 2022

KEYWORDS
Brain abscess;
Brain MRI;
Ring-enhancement pattern;
Meningitis;
Cerebritis;
Spectroscopy

Abstract
Background: Brain abscess is a severe focal infection of the central nervous system (CNS) with an annual incidence of up to 8% in developing countries. This article aims to present a comprehensive review of the literature on the pathophysiology, clinical presentation, diagnosis, and treatment of brain abscess.
Methods: We conducted a narrative review of the literature employing the PubMed, Embase, and Google Scholar databases. The terms "brain abscess," "physiopathology," "clinical presentation," and "treatment" were combined using the Boolean operator AND (eg, "brain abscess" AND "physiopathology" or "brain abscess" AND "clinical presentation"). We analysed the titles and abstracts of all articles in English and Spanish, applying no restrictions regarding their publication date, selecting 69 articles for full-text review.
Conclusions: Brain abscess is a frequent infectious disease of the CNS whose prevalence is higher in developing countries. The main pathophysiological mechanisms are related to bacterial spread from adjacent or distal foci. Laboratory findings can be nonspecific. Therefore, neuroimaging and microbiology tests play a fundamental role in establishing the most appropriate treatment for each patient.

PALABRAS CLAVE
Absceso cerebral;
Resonancia Magnética Cerebral;
Patrón de realce en Anillo;

Absceso cerebral: revisión narrativa de la literatura

Resumen
Introducción: El absceso cerebral es una infección focal grave del sistema nervioso central (SNC) con una incidencia anual de hasta el 8% en países en desarrollo. El objetivo de este artículo es

* Corresponding author.
E-mail addresses: miguelangelruizbarrera@gmail.com, investigacion@neurocienciacolombia.com (M.A. Ruiz-Barrera).

https://doi.org/10.1016/j.neurop.2022.01.010

Meningitis;
Cerebritis;
Espectroscopia por resonancia magnética

presentar una revisión exhaustiva de la literatura científica sobre la fisiopatología, cuadro clínico, diagnóstico y tratamiento del absceso cerebral.
Métodos: Se llevo a cabo una revisión narrativa de la literatura en las bases de datos Pubmed, Embase y Google Scholar, empleando los términos 'Brain abscess', 'Physiopathology', 'Clinical presentation' y 'Treatment', combinándolos mediante el operador booleano 'AND' teniendo como término principal 'Brain abscess' (ej: 'Brain abscess' AND 'physiopathology' o 'Brain abscess' AND 'Clinical presentation'). Posteriormente, se analizaron por título y abstract todos los artículos en inglés y español sin restricción respecto a su fecha de publicación, seleccionando 69 de ellos para su revisión a texto completo.
Conclusiones: El absceso cerebral es una patología infecciosa frecuente del SNC cuya prevalencia es mayor en países en vías de desarrollo. Los principales mecanismos fisiopatológicos están relacionados con la diseminación bacteriana por contigüidad o desde focos infecciosos distales. El diagnóstico por laboratorio puede ser inespecífico, por lo cual, las neuroimágenes y las pruebas microbiológicas juegan un papel fundamental permitiendo individualizar el tratamiento de cada paciente.

Introduction

A brain abscess is a focal infection of the central nervous system (CNS) frequently characterised by areas of localised cerebritis and central necrosis surrounded by a well vascularised capsule.[1–5] Brain abscesses account for approximately 8% of all intracranial space-occupying lesions; they are most frequent in men aged 30 to 50 years, and are associated with a mortality rate of up to 53%.[2,6–8]

Before the 1980s and the outbreak of the human immunodeficiency virus (HIV) epidemic, the incidence of brain abscesses in the United States ranged from 0.3 to 1.3 cases per 100,000 person-years.[2,5,8] Currently, the annual incidence of brain abscesses is 1%–2% in developed countries and 8% in developing countries.[5,9,10] According to the United States Centers for Disease Control and Prevention, brain abscesses in that country account for 14% of all post-craniotomy infections.

Although a large percentage of brain abscesses are polymicrobial, the most frequently isolated pathogens are *Staphylococcus aureus* and *Streptococcus viridans*.[2,8,9] Anaerobic microorganisms are detected in up to 40% of cases, and enteric gram-negative bacilli in up to 33%; the latter are more frequent in patients with otomastoiditis, septicaemia, immunosuppression, or history of neurosurgery.[4,10–12]

The proportion of brain abscesses of fungal aetiology has increased with the use of immunosuppressants and broad-spectrum antibiotics, amounting to approximately 1% of all brain abscesses.[2,8] Brain abscesses associated with *Nocardia* spp. infection may occur as isolated CNS lesions or as part of a disseminated infection, associated with lung or skin diseases, and represent fewer than 1% of all cases.[13]

Pathophysiology

A strong association has been described between the pathophysiological mechanisms of brain abscesses and the predisposing factors (Table 1).[1] Three main pathophysiological mechanisms have been described: inoculation of pathogenic microorganisms normally found on the skin (eg, in the context of head trauma or neurosurgery), contiguous spread of bacteria (eg, mastoiditis, otitis media, sinusitis), and haematogenous spread from distal foci (eg, bacterial endocarditis, lung abscess, skin and dental infections).[2–4,6,10,14–33]

When the blood–brain barrier is damaged (eg, due to brain trauma or a neurosurgical procedure), the brain becomes extremely vulnerable to bacterial infection. According to studies with different animal models, inoculation of at least 102 colony-forming units of a single microorganism is sufficient for a brain abscess to form. These models also showed that the abscess capsule tends to be thinner and more fragile in the vicinity of the lateral ventricles, which may be linked to reduced blood irrigation in this area as compared to the cerebral cortex, for example.[4,5,19,24]

Brain abscess development has classically been divided into 4 stages: *1)* early cerebritis (perivascular infiltration of neutrophils, plasma cells, and mononuclear cells); *2)* late cerebritis (macrophage and fibroblast infiltration is also observed); *3)* early capsule formation; and *4)* late capsule formation. From a histological viewpoint, 5 main areas have been described: *1)* a necrotic centre, *2)* a peripheral area of inflammatory cells, *3)* a capsule, *4)* an area of neovascularisation, and *5)* astrogliosis and perilesional oedema.[3,4,7,15,16,29,34–36]

Symptoms and diagnosis

The most frequent signs and symptoms of brain abscesses are headache (69%), fever (53%), focal neurological deficits (48%), impaired consciousness (48%), nausea and vomiting (47%), papilloedema (35%), meningeal signs (32%), and seizures (25%). Other findings may be linked to predisposing conditions, pathophysiological mechanisms, and the location, number, and size of the lesions.[2–5,7,8,10,28–30,36]

Table 1 Pathophysiological mechanisms, predisposing conditions, and microorganisms frequently isolated in patients with brain abscesses. The anaerobic microorganisms most frequently isolated are *Bacteroides* spp., *Fusobacterium* spp., *Clostridium* spp., *Streptococcus* spp., and gram-negative bacilli.

Pathophysiological mechanisms		
Neurosurgery	Contiguous spread	Haematogenous spread
Predisposing conditions		Commonly isolated microorganisms
HIV infection		*Toxoplasma gondii*, *Nocardia* spp., *Mycobacterium* spp., *Listeria monocytogenes*, *Cryptococcus neoformans*
Neutropaenia		Aerobic gram-negative bacilli, *Aspergillus* spp., Mucorales, *Candida* spp., *Scedosporium* spp.
Transplantation		*Aspergillus* spp., *Candida* spp., Mucorales, *Escherichia coli*, *Enterobacter* spp., *Klebsiella pneumoniae*, *Proteus* spp., *Salmonella* spp., *Nocardia* spp., *Toxoplasma gondii*, *Mycobacterium tuberculosis*
Otitis media or mastoiditis		*Streptococcus* spp., *Bacteroides* spp., *Prevotella* spp., *E. coli*, *Enterobacter* spp., *K. pneumoniae*, *Proteus* spp., *Salmonella* spp.
Sinusitis		*Streptococcus* spp., *Bacteroides* spp., *E. coli*, *Enterobacter* spp., *K. pneumoniae*, *Proteus* spp., *Staphylococcus aureus*, *Salmonella* spp., *Haemophilus* spp
Penetrating trauma or neurosurgery		*S. aureus*, *Staphylococcus epidermidis*, *Streptococcus* spp., *E. coli*, *Enterobacter* spp., *Klebsiella* spp., *Proteus* spp., *Salmonella* spp., *Clostridium* spp
Lung abscess, empyema, bronchiectasis		*Streptococcus* spp., *Fusobacterium* spp., *Actinomyces* spp., *Bacteroides* spp., *Prevotella* spp., *Nocardia* spp.
Bacterial endocarditis		*S. aureus*, *Streptococcus* spp
Congenital heart disease		*Streptococcus* spp., *Haemophilus* spp
Dental infection		Mixed infections of *Fusobacterium* spp., *Prevotella* spp., *Actinomyces* spp., *Bacteroides* spp., *Streptococcus* spp

Diagnosis of brain abscess requires detailed clinical history taking and a thorough physical examination, which help in identifying the predisposing factors and potential pathophysiological mechanisms involved (Table 1). Due to the variable specificity of clinical findings, neuroimaging and laboratory studies are essential tools in the diagnostic process.[30,37]

Lumbar puncture and cerebrospinal fluid (CSF) analysis may be indicated in cases of abscess rupture into the ventricular system or suspected concomitant meningitis; however, there is no consensus on its use due to the high risk of herniation secondary to abrupt changes in intracranial pressure and the high likelihood of obtaining negative culture results.[11,14,23,25,30,33,38] When indicated, lumbar puncture must be performed after neuroimaging studies have ruled out intracranial hypertension.[2] Another alternative is stereotactic aspiration, which enables microbiological study and may also act as an adjuvant therapy.[8,32,39]

In a systematic review and meta-analysis published by Brouwer et al.,[8] the main blood analysis findings were elevated erythrocyte sedimentation rate (72%), leukocytosis (60%), elevated C-reactive protein (CRP) levels (60%), and positive blood culture (28%). The main CSF analysis findings were pleocytosis (71%), elevated protein levels (51%), and positive CSF culture (24%).

Neuroimaging studies enable us to determine the localisation, extension, and characteristics of the lesions.[27] Depending on the radiological pattern, which varies according to the developmental stage of the abscess, several differential diagnoses may be considered, ranging from infectious lesions to tumours.[30]

In up to 85% of cases, contrast-enhanced head CT reveals a lesion with a hypodense nucleus (necrosis) surrounded by a thin contrast-enhancing ring (capsule) and perilesional oedema of variable extension.[2,4,5,10,12,18,26,28,33]

Contrast-enhanced brain MRI is the diagnostic technique of choice due to its high sensitivity and specificity. This technique is able to detect early cerebritis, intraventricular and subarachnoid infectious dissemination, and satellite lesions.[5,10,25,30,40,41] T1-weighted sequences reveal a hypointense lesion surrounded by a isointense or slightly hyperintense halo presenting contrast enhancement (ring-enhancing lesion).[23,30] On T2-weighted FLAIR sequences, perilesional oedema displays signal hyperintensity whereas the capsule appears as a hypointense halo due to the presence of paramagnetic oxygen produced by macrophages.[27,42–44]

These techniques differentiate purulent material from a brain abscess from cell debris generated by tumoural tissue necrosis. On DWI sequences, purulent material is hyperintense, as it restricts the movement of water molecules, whereas the necrotic tissue of a brain tumour is typically hypointense, with a high apparent diffusion coefficient (ADC).[22,44] Another alternative is magnetic resonance spectroscopy (MRS), which detects the presence of amino acids (leucine, valine, acetate, succinate, and alanine) resulting from extracellular proteolysis and bacterial metabolism.[44]

On DWI sequences, bacterial brain abscesses display signal hyperintensity, with low ADC values. Tumoural lesions appear hypointense and present high ADC values. Recognising this pattern decreases diagnostic errors, improving the sensitivity and specificity of MRI.[45]

Table 2 Empirical broad-spectrum antibiotic therapy in patients with brain abscesses.

Indication	Treatment
Standard empirical treatment	Cefotaxime, cefepime, or ceftriaxone, plus metronidazole and vancomycin
Transplant patients, patients receiving immunosuppressants Patients with HIV infection	Cefotaxime, cefepime, or ceftriaxone, plus metronidazole, vancomycin, and trimethoprim-sulfamethoxazole

In MRS images, healthy brain tissue exhibits high concentrations of creatine (3.0 ppm [ppm]), N-acetyl aspartate (2.0 ppm), choline (3.2 ppm), and myo-inositol (3.5 ppm).[43] On MRS images, brain abscesses are characterised by the absence of phosphocreatine, creatine, N-acetyl aspartate, and the trimethyl group of choline-type compounds; images also identify acetate, lactate, and such amino acids as alanine, glycine, valine, leucine, isoleucine, and phenylalanine, as well as fatty acids.[46,47]

Treatment

In most cases, management of brain abscesses combines surgery (drainage, excision, or stereotactic aspiration) and pharmacological treatment (oral, intravenous, or intrathecal antibiotics).[6,11,14,21,23,30,35,48]

Pharmacological treatment

Eligibility criteria for non-surgical treatment are the presence of multiple cerebral abscesses measuring < 1.5 cm diameter, presence of a single lesion measuring < 1.5 cm diameter, lesion location in eloquent areas, and presence of concomitant infection (eg, meningitis, ependymitis).[32,39,48,49]

In order to select the most appropriate drug, we must consider the pharmacokinetic and pharmacodynamic characteristics of each compound, previous treatments, administration routes, the patient's predisposing conditions, the potential pathophysiological mechanism underlying the abscess, and the microorganism involved.[25] Some authors recommend starting empirical antibiotic therapy as soon as samples are collected for microbiological study.[4,5,26,32,39,48,50,51]

Table 3 Antibiotic therapy guided by microbiological study results. Selection of specific antibiotics depends on microbiological study results and antibiotic susceptibility test results. * Microorganisms frequently isolated in mixed infections (combination antibiotic therapy may be needed). ** In patients presenting infection with these microorganisms, treatment should include an aminoglycoside antibiotic (gentamicin 1.7 mg/kg/8 h). ++ In patients presenting infection with these microorganisms, consider adding flucytosine 25 mg/kg/6 h.

Pathogen	Drug
Bacteria	
Actinomyces spp.*	Penicillin G
*Bacteroides fragilis**	Metronidazole
Enterobacteriaceae spp.*	Cefotaxime or ceftriaxone
Fusobacterium spp.*	Metronidazole
Haemophilus spp.*	Cefotaxime or ceftriaxone
*Listeria monocytogenes***	Ampicillin or penicillin G
Mycobacterium tuberculosis	Isoniazid, rifampicin, pyrazinamide, and ethambutol
Nocardia spp	Trimethoprim-sulfamethoxazole or sulfadiazine
*Prevotella melaninogenica**	Metronidazole
*Pseudomonas aeruginosa***	Ceftazidime or cefepime
Staphylococcus aureus	Sensitive: oxacillin or nafcillin; resistant: vancomycin
Streptococcus anginosus and *Streptococcus* spp.*	Penicillin
Fungi	
Aspergillus spp	Voriconazole, amphotericin B
Candida spp.++	Amphotericin B (preparation), fluconazole
Cryptococcus neoformans++	Amphotericin B (preparation)
Mucorales	Amphotericin B (preparation)
Scedosporium apiospermum	Voriconazole
Histoplasma capsulatum	Amphotericin B, itraconazole
Coccidioides spp	Amphotericin B, fluconazole
Zygomycota spp	Amphotericin B, posaconazole
Protozoa	
Trypanosoma gondii	Pyrimethamine + sulfadiazine

Success rates for antibiotic therapy are higher when treatment is started during the stage of early cerebritis, if the lesion measures <1.5 cm diameter, in patients with progression times <2 weeks, and in patients displaying symptom improvement within a week of treatment.[49] Empirical broad-spectrum antibiotic therapy (Table 2) should be maintained for 6–8 weeks, and modified according to microbiological study results to ensure the best possible therapeutic effectiveness (Table 3). Table 4 presents the recommended doses for the different antibiotics described.[4,25–27,51–61]

Patients receiving immunosuppressant or immunomodulatory drugs should receive empirical treatment with third-generation cephalosporins (ceftriaxone or cefotaxime); fourth-generation cephalosporins (cefepime) should be administered if *Pseudomonas* infection is suspected, and combined with metronidazole, vancomycin, or trimethoprim-sulfamethoxazole (the latter in cases of suspected *Nocardia* spp. infection). Voriconazole is suggested for fungal infection, particularly those caused by *Aspergillus*. In cases of *Toxoplasma gondii* infection, voriconazole should be supplemented with pyrimethamine and sulfadiazine.[5,25]

Antibiotic therapy should be administered for 6–8 weeks; treatment for less than 45 days is associated with increased risk of recurrence.[38] Clinical progression allows us to evaluate the efficacy of pharmacological treatment.[25,32] If no significant improvement is observed after a minimum of 2 weeks of treatment, neuroimaging studies should be repeated. Other criteria include normalisation of blood analysis results and acute-phase protein levels.[25] Persistently elevated serum CRP levels after completing the recommended treatment schedule may indicate pharmacological treatment failure.[48,53,62]

Surgery

Neurosurgical management enables microbiological characterisation and reduction of abscess size.[6,11,63–65] Drainage may be performed either with open surgery or with minimally-invasive techniques.[27] Open surgery focuses on draining the purulent material and resecting the capsule to minimise the risk of recurrence. Stereotactic aspiration, on the other hand, is being used increasingly frequently for abscess drainage. However, the decision to choose one technique or the other must be made on an individual basis.[62,66]

Open surgery may be indicated in the following cases: *1)* lesions measuring ≥2.5 cm, *2)* midline shift ≥5 mm, *3)* proximity to the ventricular system, and *4)* brain herniation.[25] Complete surgical resection of the abscess may be indicated in the following cases: *1)* abscesses located in a superficial, non-eloquent area; *2)* suspected fungal, *Mycobacterium tuberculosis*, *Actinomyces* spp., or *Nocardia* spp. infection; *3)* abscesses resulting from a congenital or acquired fistulous path; *4)* multiloculated abscesses; *5)* abscesses caused by parameningeal septic foci; and *6)* failure of previous treatments.[27,62]

With stereotactic surgery and neuronavigation, aspiration can be performed regardless of the phase of the abscess, enabling microbiological and histopathological studies.[23,27,32,33,67] In patients with multiple small abscesses, drainage of the largest lesion should be

Table 4 Dosing of the recommended antibiotics. The doses indicated are for adults with normal liver and kidney function.

Drug	Dosage
Ampicillin	2 g/4–6 h (IV)
Conventional amphotericin B deoxycholate	0.6–1.0 mg/kg/24 h (doses of up to 1.5 mg/kg/24 h may be considered in patients with aspergillosis or mucormycosis) (IV)
Amphotericin B lipid complex	5 mg/kg/24 h (IV)
Liposomal amphotericin B	5–7.5 mg/kg/24 h (IV)
Cefepime	2 g/8 h (IV)
Cefotaxime	2 g/4–6 h (IV)
Ceftazidime	2 g/8 h (IV)
Ceftriaxone	2 g/12 h (IV)
Ethambutol	15 mg/kg/24 h (oral)
Isoniazid	300 mg/24 h (oral)
Meropenem	2 g/8 h (IV)
Metronidazole	500 mg/6–8 h (IV)
Nafcillin	2 g/4 h (IV)
Oxacillin	2 g/4–6 h (IV)
Penicillin G	2–4 million units/4 h or continuous infusion of 12–24 million units/day (IV)
Pyrazinamide	15–30 mg/kg/24 h (oral)
Pyrimethamine	25–75 mg/24 h (oral)
Rifampicin	600 mg/24 h (oral)
Sulfadiazine	1–1.5 g/6 h (oral)
Trimethoprim-sulfamethoxazole	10–20 mg/kg/day of trimethoprim (administered in 2 or 4 doses) (IV)
Vancomycin	15–20 mg/kg/8–12 h (IV)
Voriconazole	Initial dose of 6 mg/kg/12 h, continuation dose of 4 mg/kg/12 h (IV)

IV: intravenous route.

considered. The remaining lesions may be drained if they are surrounded by marked oedema, if the patient's clinical status worsens, and/or when response to antibiotic therapy is insufficient.[27]

When stereotactic surgery and neuronavigation are not available, intraoperative ultrasound is an alternative technique that may facilitate drainage of the abscess; however, this technique is not recommended in patients with small, deep-seated lesions.[27,68]

Catheter placement in the central region of the abscess for continuous drainage of the purulent material and direct antibiotic administration aims to lower rates of surgical reintervention, although this approach is no longer recommended for routine use.[66] Reintervention may be necessary due to inadequate aspiration, lack of a drainage catheter in large abscesses, history of immunosuppresion, or inadequate antibiotic therapy, among other factors.[2,27,62]

Regarding imaging follow-up, Yamamoto et al.[69] recommend performing a CT study at least once per week, depending on the patient's clinical status.

Conclusions

Brain abscesses are focal infections of the CNS, and account for approximately 8% of all intracranial space-occupying lesions. The most frequently isolated pathogens are *S. aureus* and *Streptococcus viridans*, with anaerobic microorganisms being found in up to 40% of cases. The main pathophysiological mechanisms are: *1)* inoculation of microorganisms normally found on the skin (eg, in the context of head trauma or neurosurgery), *2)* contiguous spread of bacteria (eg, mastoiditis, otitis media, sinusitis), and *3)* haematogenous spread (eg, lung abscess, bacterial endocarditis). The most common signs and symptoms are headache, fever, focal neurological deficits, and impaired consciousness. Laboratory findings are nonspecific, with leukocytosis, elevated CRP levels, pleocytosis, and elevated CSF protein levels being the most frequent findings. In up to 85% of patients, contrast-enhanced head CT may reveal one or several lesions surrounded by a contrast-enhancing ring; these lesions may be better characterised with contrast-enhanced MRI and such other MRI modalities as DWI and MRS. Treatment of brain abscesses is based on 2 main pillars, and should be established on an individual basis. To select the most appropriate pharmacological treatment, we must take into account multiple pharmacokinetic and pharmacodynamic factors, as well as microbiological findings. The indication of neurosurgery, whether open or minimally-invasive, depends on the size, number, and location of the lesions.

Conflicts of interest

None.

Acknowledgements

The authors wish to thank Yanneth Olaya Urrego for her advice regarding microbiology findings.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.neurop.2022.01.010.

References

1. Bodilsen J, Dalager-Pedersen M, van de Beek D, Brouwer MC, Nielsen H. Risk factors for brain abscess: a nationwide, population-based, nested case-control study. Clin Infect Dis [Internet]. 2020 Aug 14;71(4):1040–6 Available from: https://academic.oup.com/cid/article/71/4/1040/5603189.
2. Bokhari MR, Mesfin FB. Brain Abscess [Internet].StatPearls; 2021. Available from: http://www.ncbi.nlm.nih.gov/pubmed/28722871.
3. Cantiera M, Tattevin P, Sonneville R. Brain abscess in immunocompetent adult patients. Rev. Neurol. 2019;175:469–74.
4. Sonneville R, Ruimy R, Benzonana N, Riffaud L, Carsin A, Tadié J-M, et al. An update on bacterial brain abscess in immunocompetent patients. Clin Microbiol Infect [Internet]. 2017;23(9):614–20 Available from: https://linkinghub.elsevier.com/retrieve/pii/S1198743X17302598.
5. Tunkel AR. G-BJC Absceso cerebral.Enfermedades Infecciosas Principios y Práctica Mandell. Douglas, Bennett. Madrid: Elsevier Inc; 2021. p. 1248–61.
6. Brook I. Microbiology and treatment of brain abscess. J. Clin. Neurosci. 2017;38:8–12.
7. Vargas Rodríguez LJ, Teresa Alvarado M, Suárez Chaparro ÁF. Absceso cerebral: diagnóstico, manejo, complicaciones y pronóstico. Revista Chilena de Neurocirugía. 2019;44(1):60–8.
8. Brouwer MC, Coutinho JM, van de Beek D. Clinical characteristics and outcome of brain abscess [Internet]. Neurology. 2014;82:806–13 Available from: https://n.neurology.org/content/82/9/806.
9. Wu S, Wei Y, Yu X, Peng Y, He P, Xu H, et al. Retrospective analysis of brain abscess in 183 patients. Med. Int. 2019 Nov;98(46):e17670 Available from: https://journals.lww.com/10.1097/MD.0000000000017670.
10. Patel K, Clifford DB. Bacterial Brain Abscess. The Neurohospitalist [Internet]. 2014 Oct 10;4(4):196–204 Available from: http://journals.sagepub.com/doi/10.1177/1941874414540684.
11. Yoshikawa TT. GSJ Brain Abscess Specialty Conference, 121; 1974;207–19.
12. Brandão E, Rosas MJ, Abreu P, Linhares P, Vaz R. Intracerebral abscess: A rare complication of deep brain stimulation. Neurocirugia. 2013;24:33–6.
13. Lin YJ, Yang KY, Ho JT, Lee TC, Wang HC, Su FW. Nocardial brain abscess. J. Clin. Neurosci. 2010;17:250–3.
14. Pisculli ML, Barker FGFC. Postoperative infections of the head and brain.Yoummans and Winn Neurological Surgery. 7th ed. Philadelphia: Elsevier Inc; 2017. p. 319–30.
15. Sáez-Llorens X, Nieto-Guevara J, Brain abscess. Handb. Clin. Neurol. 2013;112:1127–34.
16. Muzumdar D, Jhawar S, Goel A. Brain abscess: an overview. Int. J. Surg. 2011;9:136–44.
17. Erdoğan E, Cansever T. Pyogenic brain abscess. Neurosurg. Focus. 2008;24.
18. Calfee DP, Wispelwey B. Brain Abscess. Semin. Neurol. 2000;20(3):353–60.
19. Mendes M, Moore P, Wheeler CB, Winn HR, Rodeheaver G. Susceptibility of brain and skin to bacterial challenge. J. Neurosurg. 1980;52:772–5.
20. Onderdonk AB, Kasper BJ, Mansheim TJ, Louise SL, Gorbach SLBJG. Experimental animal models for anaerobic infections. Rev. Infect. Dis. 1979;2(2):291–301.
21. Hall WA, Truwit CL. THE surgical management of infections involving the cerebrum. Neurosurgery [Internet]. 2008;62

(suppl_2) SHC519–31. Available from: https://academic.oup.com/neurosurgery/article/62/suppl_2/SHC519/2581130.
22. Carroll MW, Jeon D, Mountz JM, Lee JD, Jeong YJ, Zia N, et al. Efficacy and safety of metronidazole for pulmonary multidrug-resistant tuberculosis. Antimicrob Agents Chemother [Internet]. 2013 Aug;57(8):3903–9 Available from: https://aac.asm.org/content/57/8/3903.
23. Zhang Chenran, Liuhua Hu, Xiaojun Wu GH. A retrospective study on the aetiology, management, and outcome of brain abscess in an 11-year, single-centre study from China. BMC Infect. Dis. 2014;14(311):1–7.
24. Slazinski T, Brain abscess. Crit. Care Nurs. Clin. North Am. 2013;25:381–8.
25. Brouwer MC, Tunkel AR, McKhann GM, van de Beek D. Brain Abscess. New England J Med [Internet]. 2014;371(5):447–56 Available from: http://www.nejm.org/doi/10.1056/NEJMra1301635.
26. Honda H, Warren DK. Central nervous system infections: meningitis and brain abscess. Infect Dis Clin North America [Internet]. 2009 Sep;23(3):609–23 Available from: https://linkinghub.elsevier.com/retrieve/pii/S0891552009000373.
27. Lu C-H, Chang W-N, Lui C-C. Strategies for the management of bacterial brain abscess. J Clin Neurosci [Internet]. 2006 Dec;13(10):979–85 Available from: https://linkinghub.elsevier.com/retrieve/pii/S0967586806004814.
28. Sahbudak Bal Z, Eraslan C, Bolat E, Avcu G, Kultursay N, Ozkinay F, et al. Brain abscess in children: a rare but serious infection. Clin Pediatr [Internet]. 2018 May 3;57(5):574–9 Available from: http://journals.sagepub.com/doi/10.1177/0009922817733301.
29. Mameli C, Genoni T, Madia C, Doneda C, Penagini F, Zuccotti G. Brain abscess in pediatric age: a review. Childs Nerv. Syst. 2019;35:1117–28.
30. Helweg-Larsen J, Astradsson A, Richhall H, Erdal J, Laursen A, Brennum J. Pyogenic brain abscess, a 15 year survey. BMC Infect. Dis. 2012;12.
31. Sankararaman S, Riel-Romero RMS, Gonzalez-Toledo E. Brain abscess from a peritonsillar abscess in an immunocompetent child: a case report and review of the literature. Pediatric Neurol [Internet]. 2012 Dec;47(6):451–4 Available from: https://linkinghub.elsevier.com/retrieve/pii/S088789941200402X.
32. Radoi M, Ciubotaru V, Tataranu L. Brain abscesses: Clinical experience and outcome of 52 consecutive cases. Chirurgia (Romania). 2013;108:215–25.
33. Wispelwey BSM. Brain Abscess. Sminars Neurol. 1992;12(3):273–8.
34. Fennelly AM, Slenker AK, Murphy LC, Moussouttas M, DeSimone JA. Candida cerebral abscesses: a case report and review of the literature. Med Mycol [Internet]. 2013;51(7):779–84 Available from: https://academic.oup.com/mmy/article-lookup/doi/10.3109/13693786.2013.789566.
35. Carpenter J, Stapleton S, Holliman R. Retrospective analysis of 49 cases of brain abscess and review of the literature. European J Clin Microbiol Infect Dis[Internet]. 2007 Jan 9;26(1):1–11 Available from: http://link.springer.com/10.1007/s10096-006-0236-6.
36. Miranda HA, Castellar Leones SM, Elzain MA, Moscote-Salazar LR. Brain abscess: Current management. J Neurosci Rural Practice [Internet]. 2013 Dec 26;04(S 01):S67–81 Available from: http://www.thieme-connect.de/DOI/DOI?10.4103/0976-3147.116472.
37. Anderson N, Koshy AA, Roos K. Bacterial, fungal and parasitic diseases of the nervous system.Neurology in Clinical Practice. 8th ed. Elsevier Inc; 2022. p. 1214–25.
38. Chow F. Brain and spinal epidural abscess. CONTINUUM: Lifelong Learning in Neurology [Internet]. 2018 Oct;24(5):1327–48 Available from: http://journals.lww.com/00132979-201810000-00007.
39. Lee HS, Kim JH, Kim YH, Lee S. Surgically treated community-acquired brain abscess: Bacteriological analysis based on predisposing infections. Jpn. J. Infect. Dis. 2018;71:191–6.
40. Ausman JI, Gadgil N, Patel AJ, Gopinath SP. Surgical Neurology International Open craniotomy for brain abscess: A forgotten experience? [Internet] Available from: http://www.surgicalneurologyint.com.
41. Baddley JW, Salzman D, Pappas PG. Fungal brain abscess in transplant recipients: Epidemiologic, microbiologic, and clinical features. Clin. Transpl. 2002;16:419–24.
42. Thurnher MM, Sundgren PC. Intracranial infection and inflammation.Diseases of the Brain, Head and Neck, Spine 2020–2023: Diagnostic Imaging [Internet]; 2020. p. 59–76. Available from:: http://link.springer.com/10.1007/978-3-030-38490-6_6.
43. Villanueva-Meyer JE, Mabray MC, Cha S. Current clinical brain tumor imaging. Neurosurgery [Internet]. 2017 Sep 1;81(3):397–415 Available from: https://academic.oup.com/neurosurgery/article/81/3/397/3806788.
44. Zimmerman RD. Physiological imaging in infection, inflammation and demyelination: overview. Clinical MR Neuroimaging: Physiological and Functional Techniques. 2nd ed. London: Cambridge University Press; 2010. p. 405–25.
45. Chang Shih-Chin, Laia Ping-Hong, Chen Wei-Liang. Diffusion-weighted MRI features of brain abscess and cystic or necrotic brain tumors Comparison with conventional MRI. J Clin Imaging. 2002;26:227–36.
46. Irene Martínez-Pérez, Angel Moreno, Juli Alonso. Diagnosis of brain abscess by magnetic resonance spectroscopy. J. Neurosurg. 1997;86:708–13.
47. de Simone M, Brogna B, Sessa G, Oliva G, Guida B, Magliulo M. Valuable contribution of magnetic resonance spectroscopy in differentiation of brain abscess from glioma. Infect Dis [Internet]. 2017 Dec 2;49(11–12):871–3 Available from: https://www.tandfonline.com/doi/full/10.1080/23744235.2017.1331464.
48. Erdoğan E, Cansever T. Pyogenic brain abscess. Neurosurg Focus [Internet]. 2008;24(6):E2 Available from: https://thejns.org/view/journals/neurosurg-focus/24/6/article-pE2.xml.
49. Amornpojnimman T, Korathanakhun P. Predictors of clinical outcomes among patients with brain abscess in Thailand. J Clin Neurosci [Internet]. 2018 Jul;53:135–9 Available from: https://linkinghub.elsevier.com/retrieve/pii/S0967586818302820.
50. Somand DM, Meurer WJ. Central nervous system infections. Rosens's Emergency Medicine. Philadelphia: Elsevier Inc; 2016. p. 1328–40.
51. Mampalam TJ, Rosenblum ML. Trends in the management of bacterial brain abscesses: a review of 102 cases over 17 years. Neurosurgery [Internet]. 1988 Oct;23(4):451–8 Available from: https://academic.oup.com/neurosurgery/article-lookup/doi/10.1227/00006123-198810000-00008.
52. Munshi MA, Rella A, Del Poeta M. Fungal infections of the CNS. In: Gracía-Moncó JC, editor. CNS infections: A clinial Approach. London: Springer; 2014. p. 119–29.
53. Jamjoom AB. Short course antimicrobial therapy in intracranial abscess. Acta Neurochirurgica [Internet]. 1996 Jul;138(7):835–9 Available from: http://link.springer.com/10.1007/BF01411262.
54. Pappas PG, Kauffman CA, Andes D, Benjamin Daniel K, Calandra TF, Edwards John Jr E, et al. Clinical Practice Guidelines for the Management of Candidiasis: 2009 Update by the Infectious Diseases Society of America. Clin Infect Dis [Internet]. 2009;48(5):503–35 Available from: https://academic.oup.com/cid/article-lookup/doi/10.1086/596757.
55. Mathisen GE, Johnson JP. Brain abscess. Clin. Infect. Dis. 1997;25(4):763–79.
56. Sveinsson ÓÁ, Ásgeirsson H, Ólafsson IH. Brain abscess - overview. Læknablaðið [Internet]. 2013 Jan 1;2013(01):25–31 Available from: http://laeknabladid.is/tolublod/2013/01/nr/4735.

57. Canpolat M, Ceylan O, Per H, Koc G, Tumturk A, Kumandas S, et al. Brain abscesses in children. J Child Neurol [Internet]. 2015 Mar 15;30(4):458–67 Available from: http://journals.sagepub.com/doi/10.1177/0883073814549247.
58. Brouwer MC, van de Beek D. Epidemiology, diagnosis, and treatment of brain abscesses. Curr Opin Infect Dis [Internet]. 2017 Feb;30(1):129–34 Available from: http://journals.lww.com/00001432-201702000-00018.
59. Osenbach RK, Loftus CM. Diagnosis and management of brain abscess. Neurosurgery Clin North America [Internet]. 1992 Apr;3(2):403–20 Available from: https://linkinghub.elsevier.com/retrieve/pii/S1042368018306715.
60. Bodilsen J, Brouwer MC, Nielsen H, van de Beek D. Anti-infective treatment of brain abscess. Expert Rev Anti-infective Therapy [Internet]. 2018 Jul 3;16(7):565–78 Available from: https://www.tandfonline.com/doi/full/10.1080/14787210.2018.1489722.
61. Miniar T, Amel BA, Khalil S, Khaled Ben Helal BH, Med Naji Gueddiche G, Tilouche TS, et al. Pyogenic brain abscess in children: a Tunisian multi-center experience. African Health Sci [Internet]. 2018 Aug 14;18(3):560 Available from: https://www.ajol.info/index.php/ahs/article/view/176125.
62. Neidert MC, Karlin K, Actor B, Regli L, Bozinov O, Burkhardt JK. Preoperative C-reactive protein predicts the need for repeated intracerebral brain abscess drainage. Clin. Neurol. Neurosurg. 2015;131:26–30.
63. Gruszkiewicz J, Doron Y, Peyser E, Borovich B, Schächter J, Front D. Brain abscess and its surgical management. Surg. Neurol. 1982;18(1):7–17.
64. Wang X, Sun Y, Zhang Q. [Drainage of otogenic brain abscess under imaging guidance] Zhonghua er bi yan hou tou jing wai ke za zhi. Chinese J Otorhinolaryngol Head Neck Surgery [Internet]. 2015 Oct;50(10):848–50 Available from: http://www.ncbi.nlm.nih.gov/pubmed/26696480.
65. Yu X, Liu R, Wang Y, Zhao H, Chen J, Zhang J, et al. CONSORT: May stereotactic intracavity administration of antibiotics shorten the course of systemic antibiotic therapy for brain abscesses? Med. Int. 2017 May;96(21), e6359 Available from: https://journals.lww.com/00005792-201705260-00001.
66. Ratnaike TE, Das S, Gregson BA, Mendelow AD. A review of brain abscess surgical treatment–78 years: aspiration versus excision. World Neurosurg. 2011;76(5):431–6.
67. Höhne J, Brawanski A, Schebesch KM. Fluorescence-guided surgery of brain abscesses. Clin. Neurol. Neurosurg. 2017;155:36–9.
68. Park H, Lee Y, Oh S, Lee HJ. Successful treatment with ultrasound-guided aspiration of intractable methicillin-resistant staphylococcus aureus brain abscess in an extremely low birth weight infant. Pediatric Neurosurgery [Internet]. 2015;50(4):210–5 Available from: https://www.karger.com/Article/FullText/381749.
69. Yamamoto M, Fukushima T, Hirakawa K, Kimura H, Tomonaga M. Treatment of bacterial brain abscess by repeated aspiration. follow up by serial computed tomography. Neurologia Medico-Chirurgica [Internet]. 2000;40(2):98–105 Available from: http://www.jstage.jst.go.jp/article/nmc/40/2/40_2_98/_article.