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George Popescu¹, Marius C. Zaharia¹, Ana-Maria Georghiu¹, Bogdan-Ionuț David¹, Ana-Maria Ioniță¹, Cezar Vijlanescu¹, Radu M. Gorgan^{1,2}

¹ Bagdasar-Arseni Clinical Emergency Hospital, Department of Neurosurgery, Bucharest, ROMANIA

² Carol Davila University of Medicine and Pharmacy, Department of Neurosurgery, Bucharest, ROMANIA

ABSTRACT

Background. Even in the 21st century, infections of the central nervous system and their secondary damage still represents a high mortality condition. Furthermore, brain abscesses (BA) are huge public health issues due to their high mortality and morbidity with high financial implications for the health care system.

Material and methods. In this article, we want to present our clinic`s experience in the management of brain abscesses between 2012 and 2021. A 10 years retrospective study was performed in the 4th Neurosurgery Department of "Bagdasar-Arseni" Clinical Emergency Hospital in Bucharest

Results. In the last 10 years, our clinic admitted 46 patients, 10 women and 36 men. The mean age was 47 years old. The most common symptom was headache (42 cases). In 39 cases, patients had solitary abscesses while seven patients presented multiple abscesses. The therapeutic approach was classic surgery in 37 cases. In four cases abscess drainage was performed and in five cases conservative treatment was used. At discharge, 31 patients were healed and seven patients died.

Discussions. In BA management, antimicrobial therapy is crucial. Thus, identifying the pathogen is crucial for accurate antimicrobial treatment. Unfortunately, in too many cases, the agent remains unknown and empiric treatment is required. Aspiration of the abscesses proved to be safe and with similar results compared to classic surgery.

Conclusions. Brain abscesses remain a high challenge to manage even in the 21st century. Broad-spectrum antibiotic treatment should be applied as soon as possible until the pathogen is identified and specific treatment will be used.

BACKGROUND

Even though trepanation of the skull is one of the first medical procedure performed [10], the first documented surgical intervention of a brain abscess was performed by the S.F Morand in 1952 for a temporoethmoidal abscess [11]. Despite the evolution of techniques

Keywords

brain abscess, stereotactic biopsy, ribosomal DNA amplification

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Corresponding author: G. Popescu

4th Neurosurgical Department, "Bagdasar Arseni" Clinical Emergency Hospital, Bucharest, Romania

george_popescu39@yahoo.com

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First published December 2022 by London Academic Publishing www.lapub.co.uk and technology such as marsupialization proposed by King [12], aspiration tried by Dandy [13] or enucleation of the encapsulated abscess tried by Vincent [14], the first case reported to be successfully treated my medical management was in 1971, by Heineman [15]. However, Vincent [16] proved the efectivness of complete excision of the brain abscess back in 1936.

Even in the 21st century, infections of central nervous system and their secondary damage still represents a high mortality condition [1]. Furthermore, brain abscesses (BA) are a huge public health issue due to its high mortality and morbidity with high financial implication for health care system [2], [3]. Brain abscess represents a puss collections located in the brain parenchyma and a life-threatening emergency. The incidence of BA may widely vary between countries. It is known that developed countries have a lower incidence (about 1-2%) while developing countries may reach an incidence of 8% [4], [5], [6]. The most affected ages are young pediatric population and the elderly with an increased predisposition to male patients.

Brain abscesses are dynamic focal forms of intracranial lesions. Their formation is a long and elaborate process that can be divided in four stages [7], described in Table 1.

Stage	Duration
Early cerebritis	1-4 days
Late cerebritis	4-10 days
Early capsule development	11-14 days
Late capsule development	>14 days

Table 1. Formation of cerebral abscess.

The study of the brain abscess was achieved using CT and MRI scans. The first stage, early cerebritis is characterized by the increase of neutrophil, edema and tissue necrosis. In this stage, the microglias and astrocytes activates. They usually remain activated through whole abscess development [8]. The cytokines TNF-alpha and IL-1 have key roles in the establishment of antibacterial response in the central nervous system [8]. Few studies sugested high level of necrosis factor-alpha, interleukin 1beta and macrophage inflammatory protein-2 are detected from the third week of infection with Staphylococcus aureus [9]. The late cerebritis phase is characterized by a lymphocyte and macrophage infiltrate. Between 11 to 14 days, the development of the capsule begins. In this stage, a highlyvascularized abscess wall is form, limiting the expansion of the infective process, thus preserving the brain function and structure.

In almost half of the cases (40%), the origin of BA remains unidentified. In the developed countries, brain abscesses are usually a surgical intervention complication [17]. Before the discovery of antibiotics, the most common isolated pathogen was Staphylococcus aureus [18]. Sometimes, fungal infections and intracranial tuberculosis may present as an abscess [19], [20], [21]. Very often, the pathogenic source is polymicrobial. Even though there is a wide range of pathogens are Staphylococcus aureus and streptococcus viridans in about 40% of the cases.

There were described three types of sources for pathogens to reach the cerebral parenchyma. The first way is due to spread of infection from pericranial contagious focus, in almost half of the cases (25-50%) such as middle ear, dental infections or sinusitis. Dental infections and frontal or ethmoidal sinusitis tend to spread in the frontal lobe, while mastoiditis and chronic otitis media tend to spread through temporal lobe or cerebellum [21].

Hematogenous spread is the second mechanism of pathogenic spread from a distal focus of infections. The most common source is the bacterial endocarditis, but other foci such as lung abscess, skin infections or intraabdominal infections were reported [22]. Hematogenus spread was encountered in 15% to 30% of the cases [23].

The third mechanism is the direct inoculation through head trauma, implantable devices or neurosurgical interventions. This mechanism is the most frequent in the developed countries, having an increased number of road accidents that can lead to head trauma and therefore to brain abscesses [24].

Clinical features of the patients is non-specific and may vary depending on the location of the abscess. The most frequent presentation symptoms are headache and vomiting, due to high intracranial pressure. In more than half of the cases, seizures were reported in literature. The patients may accuse focal neurological deficit and altered states of consciousness. The most common symptoms are displayed in Table 2.

Brain abscess – a still high mortality me	edical condition 401

Symptoms	Frequency (%)	
Fever	54.5-60	
Hemiparesis	20.2	
Headache	72-92.8	
Cranial nerve	39.8	
Meingism	52.2	
Altered level of consciousness	10-100	
Seizure	21-25.3	
Nausea	31-40	
Papilloedema	4,1-50	
GCS at admission		
3-8	10.3	
9-12	28.0	
13-15	61.7	

Table 2. Most common symptoms [27].

Both MRI and CT can be used to emphasize BA, similar features being available for both investigation. However, magnetic resonance imiging has a better ability to differential diagnose the cerebral abscess from other ring-enhancing lesions. A typical CT scan of a brain abscess describe a ring of isodense or hyperdense tissue with uniform thickness and central low attenuation and surrounded by vasogenic edema. Ventriculitis may be present as well and confirmed by the enhancement of the ependyma [27],

However, MRI offers better resolution images compared to CT scan. The specific image of peripheral enhance of contrast substance is emphasized. Differential diagnosis can be performed using diffusion-weighted sequences or spectroscopy, showing central diffusion restriction, a typical aspect of brain abscess [27], [28].

There is no well-defined treatment guidelines for brain abscesses and each case should benefit of tailored treatment strategy. Regardless of chosen therapeutically approach, a rapid broad spectrum antibiotic treatment should be initiated. The most important characteristic of the chosen antibiotic is the penetration of CSF barrier in adequate concentration [29].

Despite de symptomatic treatment, anticonvulsant medication should be initiated as soon as possible for patients with BA [30]. The anticonvulsant treatment must be sustained for at least two years of no seizures for patient and no epileptic activity emphasized on EEG.

Surgical approach of brain abscesses must be taken into consideration when patients present lesions bigger than three cm. A bigger than 5 mm midline shift or brain herniation should be emergency signs for surgical treatment. Moreover, surgical excision of the BA should me the elective treatment when the lesion is located close to the ventricular system. In the last decade, stereotactic CT-guided aspiration became widely used for BA drainage. It is a less invasive maneuver that permits the microbiological analysis of the abscess content, a key factor for a proper antimicrobial therapy. Furthermore, stereotactic CT-guided aspiration is considered as effective as classic surgical intervention [31].

MATERIALS AND METHODS

In this article we want to present our clinic`s experience of management of brain abscesses between 2012 and 2021.

A 10 years retrospective study was performed in the 4th Neurosurgery Department of "Bagdasar-Arseni" Clinical Emergency Hospital from Bucharest. It included 46 patients with brain abscesses who benefited of either medical or surgical treatment of brain abscess.

RESULTS

In the last 10 years, in our clinic were admitted 46 patients with brain abscesses, 10 women and 36 men. The mean age was 47 years old, ranging between 16 to 69 years old. A detailed chart of patient`s age is available in Fig.1.



Figure 1. Distribution of patients` age.

The most common symptoms accused by patients at admission were headache (42 cases) and motor deficits (32 patients). Moreover, 24 patients had seizures prior to admission. In 20 cases, aphasia was identified and 14 patients had sings of elevated intracranial pressure such as vomiting. Furthermore, 14 patients had fever over 39 degrees Celsius.



Figure 2. The most frequent symptoms of patients.



Figure 3. Comorbidities of patients.



Figure 4. Main foci of infection

In terms of comorbidities, 23 patients presented infectious diseases prior to occurrence of the brain abscess. Autoimmune diseases were reported in nine cases and seven patients presented diabetes. Moreover, six cases had a history of cancer with radio/chemotherapy. The main sources of the infections disease that led to formation of cerebral abscesses are detailed in the Fig. 4. In the most of cases, osteomastoiditis was the main focus of infection.

Only eight patients affirmed a traumatic history. The rest of them reported no traumatic history or surgeries. In 39 cases, patients had solitary abscess while seven patients presented multiple abscesses. The mean diameter of the abscesses was about 36 mm, ranging between 10 to 63 mm. One third of the lesions were located in the frontal lobe. In 11 cases, the abscess was present in the temporal lobe and in nine patients in the parietal lobe. The distribution of brain abscesses is available in Fig. 5.



Figure 5. Distribution of brain abscesses.

When the abscesses exceed the size of 3 centimeters and cause a mass effect, the same surgical approach as an expansive intracranial process is required, and total resection is the gold standard, especially in the case of encapsulated abscesses.

Therapeutical approach was classic surgery in 37 cases. In four cases abscess drainage was performed and in five cases conservative treatment was used (Fig. 6). Even though only five patients received a conservative treatment, no pathogen grew on the culture in 25 cases. Detailed chart of pathogens identified is available in Fig. 7. In terms of postoperative complications: Two cases had bone flap osteitis. Two patients had extradural hematoma and in four cases abscess recurrence was noted. At discharge, 31 patients were healed and seven patients died. The clinical and neurological state was improved in six cases.



Figure 6. Treatment options of our patients.



Figure 7. The pathogens identified after culture examination.

CASE 1 – SURGICAL APPROACH

First case is a 65-year-old patient, hospitalized for motor aphasia and right hemiparesis, without other medical history. A cerebral MRI scan was performed and revealed high left fronto-parietal space replacement process with imaging appearance suggestive of a brain abscess (Fig. 8).



Figure 8. A fronto-parietal left lesion with suggestive aspect of brain abscess. Important perilesional edema.

Integrating the clinical examination (motor aphasia: right hemiparesis) with the paraclinical investigations (cerebral MRI with contrast substance - frontoparietal left lesion with suggestive aspect of brain abscess and important perilesional edema), the patient presents a neurosurgical indication. The patient underwent surgery and the total ablation of the abscess is performed (Fig. 9). Cultures are taken for the antibiogram and tissue for the histopathological examination. Postoperative brain CT scan confirmed the total removal of the lesion without any signs of hemorrhage. Postoperatively, the patient shows a slow favorable evolution under antibiotic treatment (cefepime 6g with vancomycin 2g), daily intake of anticoagulants, antiedematous treatment, depletives, anti-inflammatory treatment. The smear detects gram negative bacilli. In the antibiogram culture, no germs developed after 5 days of incubation. The skin threads are suppressed seven days postoperatively. The patient is then sent to an infectious disease department for further treatment. At discharge, the patient is in good condition, conscious, cooperative, with partially remitted aphasia and almost completely remitted right hemiparesis.



Figure 9. Postoperative cerebral CT scan that shows the complete removal of the abscess.

CASE 2 - CONSERVATIVE APPROACH

The 35-year-old patient is hospitalized in the 4th Neurosurgery Service of "Bagdasar Arseni" Emergency Hospital for visual field disorders and balance disorders with sudden onset approximately 24 hours ago. The cerebral MRI scan performed by the patient revealed multiple intracranial expansive processes in etiological observation. Based on the investigations carried out, the associated pathology (infective endocarditis with Klebsiella and Streptococcus), the clinical and neurological consultation, the diagnosis of multiple cerebral abscesses is established.



Figure 10. Expansive intracerebral processes, mostly supratentorial, one millimeter infratentorial, with an MRI appearance suggesting an infectious substrate - brain abscesses.

A whole-body CT-scan was performed and showed liver abscess as well.



Figure 11. Liver lesion with a CT appearance suggestive of an infectious inflammatory substrate (abscess).

The condition and its therapeutical options are presented to patient and her relatives (surgical for the right occipital lesion, conservative according to the antibiotic scheme recommended on the "wait and see" principle) and they opt for conservative treatment, in full knowledge of the possible risks/benefits. Under maximum antibiotic treatment 2fl/day, (Meropenem 6g/day, Vancomycin Gentamicin 80mg 2fl/day) associated with treatment (corticosteroid with symptomatic Dexamethasone), the patient's evolution is slowly favorable, with quasi-total remission of symptoms at the time of discharge. Imaging investigations (repeated head CT, repeated cerebral MRI) show the dimensional decrease of infectious processes from the liver and brain.



Figure 12. MRI 4 weeks after conservative treatment. Regression of the lesions.

She was discharged almost four weeks later, afebrile, conscious, cooperative, without neurological deficits and referred to cardiovascular department for the surgical intervention in the field of cardiovascular surgery. She will return for clinical and imaging follow-up according to the schedule.



Figure 13. Comparison of the lesions at admission (right) vs discharge (left).

At two months follow-up check, patient's clinical and neurological state were improved. MRI performed showed an important downsize of the main two foci (right occipital lesion and left parietal lesion) and the complete remission of other lesions (Fig. 14).



Figure 14. 2 months after discharge MRI. Important shrink of the main foci (right occipital lesion and left parietal lesion) and complete remission of the other lesions. No edema was emphasized.

DISCUSSION

In BA therapy, antimicrobial therapy is crucial. Thus, identifying the pathogen is crucial for an accurate antimicrobial treatment. Unfortunately, in too many cases, the agent remains unknown and empiric treatment is required. In our clinic, the pathogen was not identified in 65% of cases (25 cultures were sterile and in five cases patients chose the conservative treatment). Therefore, seven patients lost their lives in the process, despite the maximal therapy. M Al Masalma et al [32] the authors used ribosomal DNA amplification and achieved pathogen identification in 9 of 21 culture-negative BA, identified 44 distinct bacterial species not previously described in BA, and determined polymicrobial infections at a significantly higher rate than by culture. This way more targeted treatments could be used for a better outcome of the patients.

Even though brain abscesses are more frequently identified in low/middle-income countries, they did not completely disappear from developed countries. In developed countries, most cases of BA occurred at immunocompetent patients after surgical interventions such as neurosurgical interventions or after professional tooth cleaning procedures, as LP Pallesen et al described in their article [25]. However, brain abscesses remain one of the most feared neurosurgical intervention complication. In the last decades, the number of BA increased in developed countries due to a higher number of neurosurgical intervention.

The surgical approach evolved as well in the last decades. Aspiration of the abscesses proved to be safe and with similar results compared to classic surgery. Furthermore, stereotactic guided aspiration of the BA proved to be superior to classic surgery in the hardly accessible areas such as infratentorial space. K. Elango et al [26] presented in their paper the stereotactic CT-guided aspiration of a brainstem abscess of a 38 years old female. The patient clinical and neurological state were improved after surgical intervention and aggressive antibiotic therapy. Furthermore, the authors consider CT-guided aspiration the best approach for deep lesions such as a brainstem abscess due to its minimally invasiveness and minimal morbidity and mortality [33], [34].

CONCLUSION

Brain abscesses remain a high challenge to manage

even in the 21st century. Rapid broad spectrum antibiotic treatment should be applied as soon as possible until the pathogen is identified and specific treatment will be used. Signs of intracranial pressure, midline shift >5 mm or abscesses >3 cm should be strong arguments for an invasive approach of the lesion. Even though less invasive surgical approaches were developed in the last decades (such as stereotactic CT-guided aspiration) the evolution of the patients is hard to predict due to their primary foci and their comorbidities. Conservative treatment is worth trying in cases with multiple lesions, located deep or in eloquent areas, with dimensions smaller than 3 centimeters, in cases where we know the pathogen and the starting point and the patient's neurological condition allows this.

REFERENCES

- Muzumdar D. Central nervous system infections and the neurosurgeon: a perspective. International journal of surgery (London, England). 2011;9(2):113-6.
- 2. Mathisen GE, Johnson JP. Brain abscess. Clinical Infectious Diseases. 1997 Oct 1:763-79.
- Menon S, Bharadwaj R, Chowdhary A, Kaundinya DV, Palande DA. Current epidemiology of intracranial abscesses: a prospective 5 year study. Journal of medical microbiology. 2008 Oct 1;57(10):1259-68.
- 4. Bernardini GL. Diagnosis and management of brain abscess and subdural empyema. Current neurology and neuroscience reports. 2004 Dec;4(6):448-56.
- Moorthy RK, Rajshekhar V. Management of brain abscess: an overview. Neurosurgical focus. 2008 Jun 1;24(6):E3.
- Sharma BS, Gupta SK, Khosla VK. Current concepts in the management of pyogenic brain abscess. Neurology India. 2000 Apr 1;48(2):105.
- 7. Ersin E, Tufan C. Pyogenic brain abscess. Neurosurg Focus 2008;24(E2):1e10.
- Kielian T, Esen N, Liu S, Phulwani NK, Syed MM, Phillips N, Nishina K, Cheung AL, Schwartzman JD, Ruhe JJ. Minocycline modulates neuroinflammation independently of its antimicrobial activity in staphylococcus aureus-induced brain abscess. The American journal of pathology. 2007 Oct 1;171(4):1199-214.
- Salzman C, Tuazon CU. Value of the ring-enhancing sign in differentiating intracerebral hematomas and brain abscesses. Archives of internal medicine. 1987 May 1;147(5):951-2.
- Chauvet D, Sainte-Rose C, Boch AL. The mystery of prehistoric trepanations: Is neurosurgery the world eldest profession?. Neuro-chirurgie. 2010 Oct 1;56(5):420-5.
- 11. Canale DJ. William Macewen and the treatment of brain

abscesses: revisited after one hundred years. Journal of neurosurgery. 1996 Jan 1;84(1):133-42.

- 12. King JEJ. The treatment of the brain abscess by unroofing and temporary herniation of abscess cavity with avoidance of usual drainage methods, with notes on the management of hernia cerebri general. Surg Gynecol Obstet 1924;39:554e68.
- 13. Dandy WE. Treatment of chronic abscess of the brain by tapping: preliminary note. Journal of the American Medical Association. 1926 Oct 30;87(18):1477-8.
- 14. Sargent P. Remarks on drainage of brain abscess. British Medical Journal. 1928 Dec 12;2(3543):971.
- Heineman HS, Braude AI, Osterholm JL. Intracranial suppurative disease: early presumptive diagnosis and successful treatment without surgery. JaMa. 1971 Dec 6;218(10):1542-7.
- Vincent C. Sur une méthode de traitement des abcès subaigus des hémisphères cérébraux: large décompression, puis ablation en masse sans drainage. Gaz Méd de Fr. 1936 Feb 1;43:93-6.
- Moorthy RK, Rajshekhar V. Management of brain abscess: an overview. Neurosurgical focus. 2008 Jun 1;24(6):E3.
- Yang SY. Brain abscess: a review of 400 cases. Journal of neurosurgery. 1981 Nov 1;55(5):794-9.
- Hanamsagar R, Hanke ML, Kielian T. Toll-like receptor (TLR) and inflammasome actions in the central nervous system. Trends in immunology. 2012 Jul 1;33(7):333-42.
- 20. Konat GW, Kielian T, Marriott I. The role of Toll-like receptors in CNS response to microbial challenge. Journal of neurochemistry. 2006 Oct;99(1):1-2.
- 21. Mathisen GE, Johnson JP. Brain abscess. Clinical Infectious Diseases. 1997 Oct 1:763-79.
- Kawamata T, Takeshita M. Patent Foramen Ovale as a Possible Risk Factor for Cryptogenic Brain Abscess: Report of Two Cases. Neurosurgery. 2002 Mar 1;50(3):674-5.
- 23. Horiuchi Y, Kato Y, Dembo T, Takeda H, Fukuoka T, Tanahashi N. Patent foramen ovale as a risk factor for cryptogenic brain abscess: case report and review of the literature. Internal Medicine. 2012;51(9):1111-4.
- Pallesen LP, Schaefer J, Reuner U, Leonhardt H, Engellandt K, Schneider H, Reichmann H, Puetz V. Multiple brain abscesses in an immunocompetent

patient after undergoing professional tooth cleaning. The Journal of the American Dental Association. 2014 Jun 1;145(6):564-8.

- 25. Mace SE. Central nervous system infections as a cause of an altered mental status? What is the pathogen growing in your central nervous system?. Emergency Medicine Clinics. 2010 Aug 1;28(3):535-70.
- 26. Calfee DP. Wispelwey (2000). InBrain abscess. Seminars in neurology (Vol. 20, pp. 353-60).
- Campioli CC, Almeida NE, O'Horo JC, Garrigos ZE, Wilson WR, Cano E, DeSimone DC, Baddour LM, Van Gompel JJ, Sohail MR. Bacterial brain abscess: an outline for diagnosis and management. The American Journal of Medicine. 2021 Oct 1;134(10):1210-7.
- Lai PH, Ho JT, Chen WL, Hsu SS, Wang JS, Pan HB, Yang CF. Brain abscess and necrotic brain tumor: discrimination with proton MR spectroscopy and diffusion-weighted imaging. American Journal of Neuroradiology. 2002 Sep 1;23(8):1369-77.
- 29. de LOUVOIS J. Bacteriological examination of pus from abscesses of the central nervous system. Journal of clinical pathology. 1980 Jan 1;33(1):66-71.
- Legg NJ, Gupta PC, Scott DF. Epilepsy following cerebral abscess a clinical and eeg study of 70 patients. Brain. 1973 Jun 1;96(2):259-68.
- Hirata S, Kobayashi M, Ujihara M, Takabatake K, Wakiya K, Fujimaki T. Aspiration Surgery with Appropriate Antibiotic Treatment Yields Favorable Outcomes for Bacterial Brain Abscess. World Neurosurgery. 2022 Sep 1;165:e317-24.
- Al Masalma M, Lonjon M, Richet H, Dufour H, Roche PH, Drancourt M, Raoult D, Fournier PE. Metagenomic analysis of brain abscesses identifies specific bacterial associations. Clinical Infectious Diseases. 2012 Jan 15;54(2):202-10.
- 33. Patel K, Clifford DB. Bacterial brain abscess. The Neurohospitalist. 2014 Oct;4(4):196-204.
- Chen MH, Kao HW, Cheng CA. Complete resolution of a solitary pontine abscess in a patient with dental caries. The American journal of emergency medicine. 2013 May 1;31(5):892-e3.