THE OUTCOME OF THE PATIENTS WITH CEREBRAL ABSCESSES AFTER INTRODUCTION OF A STANDARDIZED ANTIBIOTIC PROPHYLAXIS

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ABSTRACT

Objective: To analyze the etiopathogenesis, microbial features, therapeutic approach and the outcome of the patients with cerebral abscesses before and after standardised antibiotic prophylaxis. Material and methods: We studied 29 patients with cerebral abscesses that were admitted in the neurosurgery department of The Clinical Emergency County Hospital from Timisoara between 01.01.2000 and 31.12.2005. We decided to study this specific period as it was the most representative for the passing from nonstandardized to standardized treatment. The first cohort of 14 patients, in the period 2000 – 2002 was treated with antibiotics from penicillin’s class or cephalosporins of third generation associated with surgical interventions. The second cohort, in the period 2003 – 2005, was treated with a triple association of antibiotics (metronidazole + ceftriaxone/ceftazidime + oxacillin/vancomycin) for 14 days, together with surgical intervention. CSF samples were taken from all the patients, and for 30% of them there were also taken blood cultures. Results: In 58.62% of the cultures were negative; S. aureus was the most frequently isolated germ from the positive cultures, followed by Pseudomonas and Proteus. Mortality rate for the first cohort was 64.28% while for the second was 13.3%. Conclusions: It’s better to use a standardized treatment for cerebral abscesses, but it’s quite difficult to establish the optimal algorithm by means of prospective studies because of the low number of patients with this kind of pathology. This is why the treatment recommendations are made based on isolated pathogens, the antimicrobial spectrum of the antibiotics, their ability to penetrate the fluid of the abscess and individual reports concerning the efficacy of different therapeutic algorithms.

Key Words: cerebral abscess, brain abscess, antibiotic therapy, surgical treatment, stereotactic aspiration, neurosurgery

INTRODUCTION

Cerebral abscesses are an uncommon entity and even in the largest hospitals there are no more than 4 up to 6 cases per year. Classically, these abscesses arise locally from otorhinolaryngeal infections (one-third of cases), hematogenously from distant infections, or by direct implantation by neurosurgery or penetrating trauma (about 10 percent of cases), though opportunistic infections have become an important consideration upon initial presentation as well. The route is unknown in about 20% of cases.¹⁴
The pathogenic organisms most commonly implicated are of the Streptococcus family; Klebsiella, Staphylococcus aureus, and anaerobes are also frequent. In immunocompromised patients, it is important to include Toxoplasma, Listeria, and Nocardia as possible etiologic agents, as well as fungal pathogens. For the newborns brain abscesses are exclusively due to Proteus and Citrobacter.1,5-7

Abscesses that develop as a result of direct spread of infection from the frontal, ethmoidal, or sphenoidal sinuses and those that occur due to dental infections are usually located in the frontal lobes, while those spreaded from the middle ear are located in the temporal lobes.1 Hematogenous abscesses show a predilection for the territory of the middle cerebral artery.

The cornerstone of early emergency department treatment of brain abscess is administration of antibiotics together with agents that lower the intracranial pressure, all these before the abscess is becoming encapsulated and well localized. Once the abscess is completely formed, total excision and drainage associated with long term antibiotic therapy is the treatment of choice.8 Some neurosurgeons recommend total excision of the abscess, while others prefer repeated aspiration.9,10

The first step before starting the treatment is establishing the exact diagnosis, the dimensions and the number of abscesses, using CT and MRI.1

The medical treatment is recommended if: there is more than one abscess; the abscess is smaller than 2 cm; the abscess is localized deep in the cerebral tissue; minimal associated mass effect; comorbidities that contraindicate the surgical treatment (hemorrhagic diathesis).1,11

Before administering the antibiotic cultures from blood, urine, sputum, or fluid drained from sinuses should be performed. CSF sample can be taken if there is proof of no mass effect (on CT) and if there are signs of meningitis. If possible, it’s better to postpone the antibiotic treatment till after aspiration of the abscess, so we can get reliable culture results.

The role of glucocorticoids is controversial. Even though steroids may produce temporary improvement of increased intracranial pressure, they can also slower the encapsulation process, promote necrosis, diminish the antibiotic’s penetration into the abscess, enhance the risk of ventricular rupture and alter the CT aspect. Intravenous dexamethasone therapy (10 mg every 6 h) is usually reserved for patients with substantial periabscess edema and associated mass effect and increased ICP.9,11

Abscesses smaller than 2.5 cm and those in the early stages (less than one week) respond well to antibiotic therapy. Typically the treatment consists of 6-8 weeks of intravenous treatment followed by 4-8 weeks of oral treatment. The duration of therapy may be shortened to 3-4 weeks for those abscesses that were drained. The susceptibility of the likely pathogen and the penetration of the agent into the lesion should be considered when choosing an antibiotic.12,13 (Table 1) Usually, high-doses antibiotics are needed. Initial empirical antibiotic choice should take advantage of such information.

- Streptococcus – high doses of penicillin G or third generation cephalosporins (cefotaxime, ceftriaxone); metronidazole should be associated when suspecting the presence of anaerobes resistant to penicillins.
- S. aureus – nafcillin or vancomycin for MRSA;
- Pseudomonas aeruginosa – ceftazidime or cefepime;
- HIV patients need treatment for toxoplasmosis.

Imipenem or meropenem can be used as broad spectrum antibiotics when others are contraindicated, but imipenem was associated with convulsions in patients with brain abscesses.12,14

<table>
<thead>
<tr>
<th>Primary or contiguous source</th>
<th>Streptococi (60-70%)</th>
<th>Cephalosporins 3rd gen (cefotaxime 2g/4h iv or ceftriaxone 2g/12h iv ) plus metronidazole 7.5 mg/kg/6h or 15 mg/kg/12h iv</th>
<th>Penicillin G 20-24mLUqd iv plus metronidazole 7.5 mg/kg/6h or 15 mg/kg/12h iv</th>
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<tbody>
<tr>
<td>S. aureus (10-15%)</td>
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<td>Enterobacteriaceae (25-33%)</td>
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<td>Enterobacteriaceae (25-33%)</td>
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<td>HIV-1 infected</td>
<td>Toxoplasma gondii</td>
<td>Pyrimethamine 200 mg po + Sulfadiazine 1-5 mg po /6h + Folic Acid 10-20 mg /qd po</td>
<td>Vancomycin 1g/12h iv plus cephalosporins 3rd gen</td>
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Table 1. Treatment algorithms according to Sanford guide.14
BSAC (The Infection in Neurosurgery Working Party of the British Society for Antimicrobial Chemotherapy) in the 2000 guide, made the following recommendations for the antibiotic therapy of brain abscesses:15
- Cephalosporin + metronidazole – as empirical treatment if the presumed source is sinogenic or odontogenic;
- Cephalosporin as alternative in cryptogenic metastatic abscesses;
- Ampicillin + metronidazole + ceftazidime/gentamicine for otogenic source of infection;
- Flucloxacillin for abscesses secondary to penetrating trauma or other neurosurgical procedures.

Surgical treatment
The patients that do not meet the criteria for medical treatment need surgical intervention. Currently there are two techniques: stereotactic aspiration and drainage of the abscess under CT or MRI guidance and complete excision via craniotomy or craniectomy.

For best results, it is advisable to drain the abscess before antibiotics are initiated. Single isolated abscess larger than 1.5 cm or multiple abscesses larger than 3 cm should be aspirated. Delaying drainage and decompression is associated with significant morbidity and mortality.

Craniotomy is generally performed for: multi-loculated abscesses; abscess of the posterior fossae; abscesses with no obvious sources; abscesses secondary to trauma; abscesses in which stereotactic aspiration is unsuccessful; altered mental status, intracranial hypertension, without improving in 7 days; abscess that is progressively enlarging.

In addition to surgical drainage and antibiotic therapy, patients should receive prophylactic anticonvulsant therapy because of the high risk (~35%) of focal or generalized seizures.

Anticonvulsant therapy is continued for at least 3 months after resolution of the abscess, and decisions regarding withdrawal are then based on the EEG. If the EEG is abnormal, anticonvulsant therapy should be continued. If the EEG is normal, anticonvulsant therapy can be slowly withdrawn, with close follow-up and repeat EEG after the medication has been discontinued.1

Mortality rate of brain abscesses decreased in the last years due to standardization of therapy and improvement of the surgical techniques. The comatose patients still have a poor response to therapy. However the mortality rate decreased also in their case from 50% in the past to 15% in the present. Approximately 20% of the survivors remain with sequelae, among which convulsions are the most frequent.1

OBJECTIVES
The aim of our study was to analyze the ethiopathogeny, microbial features, therapeutic approach and the outcome of the patients with cerebral abscesses. On the other hand we wanted to find out if standardised antibioprophylaxis made any difference for these patients.

MATERIAL AND METHODS
We studied 29 patients with cerebral abscesses that were admitted in the neurosurgery department of The Clinical Emergency County Hospital from Timisoara between 01.01.2000 and 31.12.2005. We recorded the next parameters: age, gender, localization of the abscess, probable source, bacteriologic results, radiologic results, type of surgical procedure, type of antibiotic, efficacy of treatment and outcome.

In the studied period we distinguish two cohorts. The first cohort of 14 patients, in the period 2000 – 2002 was treated in a nonstandardized manor. The second cohort, in the period 2003 – 2005 was treated with a triple association of antibiotics (metronidazole, ceftriaxone/ceftazidime, oxacillin/vancomycin) for 14 days, together with surgical intervention.

The algorithm of treatment was adapted from the Sanford guide 2003 and the latest recommendations found in the literature and was next included in the antibiotic prophylaxis protocols of our hospital.13,14

RESULTS
In the first cohort of patients, only 64.28% of patients had a surgical intervention while in the second cohort, all the patients had both surgical intervention and antibiotic treatment. (Fig. 1) 58.62% of the cultures were negative. S. aureus was the most frequently isolated germ from the positive cultures, followed by Pseudomonas and Proteus. (Fig. 2)

Mortality rate for the first cohort was 64.28% while for the second was 15.38%. (Fig. 3) The percentages were compared by Fisher exact test. The association between the two groups was considered to be very statistically significant (p = 0.0065).

DISCUSSION
A PubMed search of the literature using the keywords “brain abscess” was undertaken, and the relevant papers and citations were reviewed.16-18 We shall shortly resume the most relevant findings for our study.
CT and MRI have considerably changed the outcome of brain abscesses. First, these investigations make a clear differentiation between brain abscesses and other cerebral pathology. Also, they identify the exact localization of the abscess, so the surgical procedure will be easier. Serial MRI or CT scans should be obtained on a monthly or twice-monthly basis to document resolution of the abscess. In his study, Roche M et al used CT as the first choice for diagnosing brain abscesses, even though it was proven to be less sensitive than MRI. De Louvois et al, in their review of the bacteriology of abscesses of the CNS, report Streptococcus spp. to be the most common (74%) infecting organism isolated. Fifty-four percent of the streptococci were Streptococcus milleri. Bacteroides spp. was the next most common infecting organisms, found in 24%. S. aureus was found in 20%. Proteus spp. was isolated in 15% of patients, from abscesses located primarily in the temporal lobe. Other reviews note the isolation of Proteus spp. and Klebsiella spp.

The most important microbiological investigation in the management of brain abscess is culture of the abscess fluid or pus. Several researchers report that CSF culture does not contribute significantly to diagnosis. Blood culture was helpful in a small percentage of patients, especially in those patients in whom an operation was not performed.

Association of cefotaxime and metronidazole was the most frequently used algorithm for antibiotic therapy in randomized controlled trials. Penicillin G was added to this algorithm in some cases, or vancomycin when S. aureus infection was suspected. The results of our study were mainly consistent with the ones found in randomized controlled trials. However, it is difficult to establish the optimal algorithm by means of prospective studies because of the low number of patients with this kind of pathology. This is why the treatment recommendations are made based on isolated pathogens, the antimicrobial spectrum of the antibiotics, their ability to penetrate the fluid of the abscess and individual reports concerning the efficacy of different therapeutic algorithms.

CONCLUSIONS

There have been a number of more recent changes in the management of patients with brain abscesses, most notably the introduction of computerised tomography (CT) and refinements in neurosurgical technique that have further improved the prognosis of patients. The use of newer antimicrobial agents has also contributed to the better prognosis of these patients. Still, brain abscess is a serious, life-threatening condition and future research is needed for continuing standardization of its treatment.

REFERENCES


