



CASE REPORT

Cerebral abscess with cranial hypertension in young infants: a case report and systematic review

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Abstract

Objective: To report a Central Nervous System infection evolving with brain abscess and to address aspects of the treatment of the disease. Results: even with advances in treatment and diagnosis, the pathology has a high mortality. However, the best prognosis is noticed when there is a suspicion through the clinic, neuroradiological images readily available, antimicrobial therapy against commonly encountered agents, and surgical drainage procedures. One study, which combined antibiotic therapy and surgery to drain the abscess, in most of the cases, studied, demonstrated a mortality rate of 12%, and another study, a 42% mortality rate when using antibiotic therapy alone. Another reference suggests the use of antibiotic therapy alone in less severe cases with less neurological impairment. Neurological clinical seguelae can be found in up to 30% of cases. The time of antibiotic therapy still needs to be debated, as well as the surgical indication for drainage. Final Considerations: Pediatric brain abscess is an uncommon disease, still with high morbidity and mortality. Surgical drainage or excision of pediatric abscesses remains the basis of treatment both to relieve the mass effect and to provide a microbiological diagnosis. The literature demonstrates that broad-spectrum antibiotics and access to CT and MRI images decrease the rates of morbidity and mortality. It is concluded that the therapeutic approach involves the administration of broad spectrum intravenous antibiotics and surgical drainage in more complex cases.

Keywords: Cerebral abscess; Intracranial hypertension; Pediatrics.

Introduction

A cerebral abscess (CA) is an infection in the cerebral parenchyma that can arise as a complication of a variety of pathological conditions such as surgery, trauma, and as a result of other primary infections [1]. Most of the time, the clinical symptoms of brain abscess are related to intracranial hypertension (ICH), which is generally associated with secondary brain conditions in children, resulting in high morbidity and mortality, varying between 13% to 20% [2]. Brain abscesses are serious conditions, uncommon in the pediatric population, but of great clinical importance due to significant long-term mortality, demonstrating a prevalence of 0.4% to 0.9% for every 1000 people on a global scale [3].

The pathogenesis of cerebral abscess is explained through two main pathways: contiguity or hematogenic. Infections such as otitis media, mastoiditis, sinusitis, dental infections, trauma, and surgery correspond to the primary sites of contiguous infection. The conditions disseminated by the hematogenous route are more associated with pulmonary, intra-abdominal, pelvic, skin infections,

and congenital cyanotic heart disease, being, therefore, little described as secondary to neonatal infections [4,5].

The microorganisms found are usually grampositive bacteria, such as *Streptococcus viridian's*, *Staphylococcus aureus*, and also gram negative bacteria, related to ear infections and head injuries, such as *Klebsiella pneumonia*, *E. coli, Proteus, and Pseudomonas spp* [6]. In newborns, the main agents are those related to early neonatal sepsis, being *Streptococcus agalactiae* and *E. coli*, and late neonatal sepsis, represented by *Staphylococcus aureus*. Symptoms are related to increased intracranial pressure with episodes of vomiting, nausea, headaches, chronic repercussions in the central nervous system (50 to 80%), followed by poor mental development, epilepsy, and behavior-related disorders [7,8]. In newborns, the clinical manifestations may be nonspecific as occurs in neonatal septic infections, corresponding to diet intolerance, vomiting, cyanosis, apneas or respiratory changes (respiratory distress), hypoactivity, seizures, among other symptoms.

In the clinical suspicion of brain abscess, computed tomography (CT) is requested. The worsening or sudden death of the patient may indicate a rupture of the abscess, a critical complication that leads to high mortality due to the sudden increase in intracranial pressure and intense toxemia caused by the release of purulent content within the ventricles or parenchyma. The treatment indicated is broad-spectrum antibiotics, with good penetration into the central nervous system and reaching aerobic and anaerobic, the duration varies from 6 to 8 weeks, with follow-up by serial CT. Neurosurgery is indicated if there is no improvement, allowing drainage with relief from intracranial hypertension and obtaining material for study [8].

Therefore, this study reported a clinical case that occurred in an infant who had a Central Nervous System infection evolving with brain abscess, and due to its severity, morbidity, and unusual evolution in the pediatric population, we aim to address the time of infection and aspects of the treatment of disease.

Methods

Study Design - Case Report

The present study was elaborated according to the rules case report (https://www.careof CARE statement.org/) [9]. The present study is a case report whose bibliographic research used the descriptors: cerebral abscess and intracranial hypertension. The research was carried out through the study of digital articles and virtual books attached to the Google academic, in database platforms such as Scientific Electronic Library Online (SCIELO), PubMed, and in scientific repositories, according to PRISMA (Systematic Review). Used as the main data sources, the most relevant works were selected for the theme for the synthesis and presentation of the information, excluding references that diverged from the purposes covered here.

Patient Information and Clinical Findings, Timeline, Diagnostic, Assessment, Therapeutic, Intervention/

Follow-up and Informed Consent

E.M.C, 1 month and 25 days, female, born and living in the city of Marilia, state of Sao Paulo. She was referred to the pediatric service of Santa Casa de Misericordia de Marilia, with a history of fever, crying, irritability for 1 day, with no respiratory and intestinal symptoms, associated with a bulging fontanelle, nystagmus, and looking in the setting sun. There was no previous trauma. She was admitted to the Emergency Room on 10/18/2019 and performed a cerebrospinal fluid (CSF) puncture, and after the procedure, the patient had a skin motive (livedo reticularis) and groaning, and was referred to the ICU.

A cranial tomography was performed, showing an extra right axial frontal cystic lesion with a midline deviation, greater than 30 mL of content and with apparent skull base origin, followed by a percutaneous puncture via the right coronal suture with an outlet of greenish purulent secretion with a foul odor. Antibiotic therapy was initiated with Ceftriaxone 100mg/kg/day (12/12 hrs), Metronidazole 10mg/kg/day (8/8 hrs) and Oxacillin 50mg/kg/day (6/6 hrs). The next day, the infant remained feverish where bacterial culture was carried out and multi-sensitive E. coli (sensitive to ceftriaxone) was identified in the CSF and brain abscess. On 10/20 the fever ceased and the antibiotics Metronidazole and Oxacillin were suspended, with only Ceftriaxone remaining.

She evolved with a seizure crisis, controlled after an attack dose of Phenobarbital, and another feverish peak occurred again. On 10/22, despite being asymptomatic, she performed а videoelectroencephalogram (video-EEG) that found the presence of mild disorganization and discharges in the left frontal lobe. On the fifth day of hospitalization, there was an improvement in the infectious score (Rodwell's hematological score), but with sodium hydro electrolytic disorder (hyponatremia).

On 10/24, drowsy, fasting, presented a new seizure episode, being medicated and repeated cranial tomography that maintained an earlier pattern. The second puncture was performed via a coronal suture, with drainage of 100 mL of pus, the culture result of which remained with the growth of *E. coli* multi-S. On 10/25, the patient presented a good evolution with a resolution of hyponatremia. Keeping without new seizures, and the serum level of intravenous phenytoin anticonvulsant at 8.6 ug/mL, it was programmed to replace it with oral Oxycarbamazepine. She was discharged from the pediatric ICU and was transferred to an infirmary bed.

On 11/08 the patient was readmitted to the ICU due to a new seizure after the removal of the intravenous

anticonvulsant, she presented episodes of nystagmus and convulsive movements of the upper limbs. A new CT (09/11) was performed, showing a reduction in abscess, but with progression to communicating hydrocephalus and areas of gliosis, with no surgical indication at this time. The IV anticonvulsants were maintained and without new seizures. On 11/11, it evolved with a bulging fontanelle, a new CT scan was performed that showed the same pattern as before and maintained without surgical indication. An echocardiogram was also performed due to the presence of a heart murmur, which revealed the presence of a patent foramen ovale and the absence of vegetation in heart valves. The evolutionary control of the video-EEG (11/11) showed the presence of disorganization in brain waves, however reactive, with nonspecific delta outbreaks (which may correspond to discognitive crises or intracranial hypertension).

The levels of anticonvulsants were therapeutic and a Transfontanellar Ultrasound was performed, which maintained the same pattern as the last cranial CT scan (with no signs of intracranial hypertension). On 11/23, presenting hypoactivity and worsening of the general condition. A new skull CT scan was performed, which showed a decrease in abscess, but important hydrocephalus with signs of CSF transudation into the parenchyma. Vancomycin started 15 mg/ kg/dose, EV, 6/6 hours and Cefepime 50 mg/kg/dose, EV, 8/8 hours. On 11/24 there was an improvement in hypoactivity. After 2 days, on 11/26, she was sucking her breast, followed by IV anticonvulsants. On 11/27, the result of the LCR culture was negative. On 11/29, a new CT scan was performed, which showed an increase in hydrocephalus, an abscess similar to the previous one with 3 cm in the right frontal lobe, erasure of furrows, and CSF transudation.

On 11/30/2019, the patient received the vaccines for 2 months, except rotavirus. It was suggested by the Hospital Infection Control Commission to maintain the antibiotic for 56 days of treatment, which would complete 8 weeks of treatment and later programmed DVP (peritoneal ventricle shunt). She presented weight gain and good acceptance of breast milk. One day after the aforementioned date, the serum level of anticonvulsants (phenytoin and phenobarbital) was collected, and after that, the drugs were switched to oral.

On 12/03/2019, a 30 mL CSF puncture was performed, as there was an increase in head circumference, followed by bacterial culture. On 12/05/2019 the result of the culture obtained was negative, and Vancomycin was suspended and de-escalated Cefepime for Ceftriaxone, remaining stable. On December 6, 2019, transferred to home-care to finish treatment. She continued to follow up with motor physiotherapy, occupational therapy, and nutrition. On December 21, 2019, she was readmitted to perform the left peritoneal ventricle shunt due to hydrocephalus, which occurred without abnormalities.

Informed Consent

Those responsible for the patient signed the consent form.

Discussion

A cerebral abscess occurs when there is an infection that affects the cerebral parenchyma, which is usually focal [10]. The main predisposing conditions in children are the adjacent focus of infection, trauma, hematogenous dissemination, neurosurgical procedures, cyanotic heart disease, and immunosuppression [11].

The pathology is rare in adult patients and with an even lower incidence in the pediatric age group. With the development of medicine, it has become rare with an incidence of 0.3-1.8 per 100,000 inhabitants per year. In general, about 25% occur in children and more often between 4 and 10 years of age [3,5,7]. Even with advances in treatment and diagnosis, the pathology has effective mortality [10]. However, the best prognosis is noticed when there is a suspicion through the clinic, neuroradiological images readily available, antimicrobial therapy against commonly found agents, and surgical drainage procedures [12].

Infectious pathogens vary depending on the infection etiology, location, age, and underlying medical [13]. condition Pediatric cultures positive for Streptococcus spp., Staphylococcus spp. and gramnegative enteric bacteria (Proteus spp., Klebsiella pneumonia, Escherichia coli, and Enterobacteriae) [14]. Also, Streptococcus spp. it is commonly associated with sinusitis, otitis media, and endocarditis (the latter with Grupo S. viridans); a series of recent cases suggest a possible increase in the incidence of CA due to group A streptococcus [15]. Staphylococcus spp. (mainly aureus and epidermidis) infections are related to traumatic brain injury, surgery, or skin infections. Neonatal CA may arise from Citrobacter or Proteus meningitis, less frequently from *Escherichia coli* and *Serratia marcescens* [16,17]. The data presented are in agreement with the usual bacteriological flora observed in otorhinolaryngology and infantile meningitis, with Gram-positive cocci in children in the context of otorhinolaryngological disease and Gramnegative bacillus in babies in the context of meningitis [18].

There are reports in some countries that pneumococcal vaccination may contribute in the coming years to a variation in the incidence and etiology of CA [19,20]. Fungi, parasites, and mycobacteria are uncommon pathogens [14]. CA are multiple in most cases

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when the microorganisms are opportunistic. HIV-positive children with low CD4 counts are susceptible to the most common pathogens, namely Toxoplasma, Nocardia, and *Mycobacterium spp* [21]. Fungal abscesses (mainly Aspergillus or Candida) are generally associated with recipients of solid organ transplants or children being treated for leukemia [22].

The etiological diagnosis can be obtained through the culture of the abscess pus, acquired by stereotactic biopsy or complete aspiration, instead of an excised craniotomy [16,19, 23-27]. In some cases, neurosurgery is not indicated and therapy should be performed and continued empirically, with monitoring of clinical and radiological improvement [19,24,28,29]. CAS can result from the extension of infection through blood flow from a distant focus (dental, sinus, otological, endocarditis, lung or skin infections) [30,31]. In newborns, it prevails in cases of meningitis or hematogenous dissemination of distant local infection [17,32].

The patient initially had fever and irritability. Later, she developed nausea, vomiting, and seizures. In the literature, the most common symptoms of brain abscess are fever, disturbance of consciousness, nausea, focal signs, and seizures [33]. In infants with ICH, the findings may be vomiting, intermittent unconjugated eye movements, drowsiness, lethargy, presence of focal neurological signs, and the occurrence of seizure [34]. Seizures develop in 25% of cases and can be the first manifestation of brain abscess [35].

Corroborating the results described in the present study, Sahbudak et al [29] showed in a retrospective descriptive study carried out in Turkey with 18 children, with a mean age of 48 months with cerebral abscess, among them 22% were less than 1 year old, the most common symptoms on admission were fever, nausea, and vomiting, in addition to 22% having a bulging fontanelle.

On physical examination, the patient in the study revealed a bulging fontanelle, nystagmus, and looking in the setting sun, without the occurrence of trauma. In addition, during evolution, there was a reduction in abscess and the presence of communicating hydrocephalus and areas of gliosis. A cerebral abscess can affect the flow of CSF through ventricular flow, a function of the subarachnoid space, or by cerebral venous compliance [36], causing hydrocephalus to appear. Intracranial hypertension secondary to cerebral abscess causes compensation at the expense of decreasing the volume of cerebrospinal fluid and blood since the brain mass is less compressible and can cause decreased tissue perfusion and worsening cellular damage due to ischemia [34].

In 14 days, a brain infection evolves with a collection of pus encapsulated in the brain parenchyma and

subsequent early cerebritis to the late capsular stage [37]. Pathogens can spread to the brain through a contiguous location (middle ear, mastoid, and paranasal, sinus infections) or a discontinuity of the skull (trauma or neurosurgery). The location of the CA is related to the source of the primary infection. It most often affects the frontal lobe (secondary to frontal sinusitis, ethmoid or dental infection), followed by parietal and temporal lobes (acute otitis media, mastoiditis, or sphenoid sinusitis) and less frequently located in the cerebellum and brain stem, of otogenic or hematogenic origin [20.27.38].

Cerebral abscesses begin with areas of cerebritis and progress into discrete collections of encapsulated pus, over stages (initial cerebritis, late cerebritis, initial capsular, and late capsular) [39], which the imaging resources depend on the phase infection [40]. Blood tests are the first to be performed in the emergency room to assess the presence of altered inflammatory markers due to infection (probability of being normal is high) and investigation of hematogenous dissemination. They are primarily the leukocyte count (if altered, leukocytosis is more frequent than leukopenia), C-reactive protein, erythrocyte sedimentation rate, and blood cultures [10].

In the face of neurological involvement, lumbar puncture can be performed for physical-chemical analysis of cerebrospinal fluid (CSF) and subsequent culture for a specific etiology, even if at low risk [16,20,25,29]. It is worth mentioning that the puncture should not be performed routinely and is contraindicated in the case of non-communicating obstructive hydrocephalus and brain dislocation, possible consequences of the mass effect of the CA [41]. In cases where it can be performed, the count of white blood cells, glucose, and protein content can show great variability [20,26]. However, leukocytosis, hyperproteinorrhachia, and normal or reduced glucose are more frequent [3,18,26].

The first type of image performed is CT [5,18,27], as it is available in the emergency room and can clarify the characteristics of the suspected lesion; then, magnetic resonance imaging (MRI) can be performed to confirm the diagnosis and improve the characterization of the abscess. In the study by Felsenstein et al. [5], all patients whose first image was MRI, CA were detected. Thus, MRI is suggested as the gold standard image for diagnosis; also recommends its use in follow-up. The magnetic resonance exam is superior to Computed Tomography for investigating CA since it is more sensitive, the contrast of less toxicity [39], and the ability to provide an early diagnosis to the capsular stage, identifying lesions with risk of complications early [42]. However, the age range of infants and young children is a limiting factor due to the need for long-term sedation for MRI to be performed.



Empirical antibiotic therapy should be initiated based on the likely associated pathogens that depend on the probable precipitating source of infection and the results of Gram stain. The antibiotic regimen can be modified, if necessary, once the results of aspirated pus culture are available [43].

The choice of empirical therapy should be based on predisposing conditions and, consequently, the microorganism that may be involved, should be directed towards bactericidal and non-bacteriostatic agents, using drugs that can cross the blood-brain barrier (lipophilic, with low molecular weight and low connection with plasma protein) and safe enough to be administered in high doses even for a long time [44-46].

Seneviratne Rde (2003) [47] described a study with 41 patients with brain abscess, in which 30% of the cases had congenital heart disease as a predisposing factor, the antibiotic used consisted of cefotaxime and metronidazole and the result of the treatment was satisfactory. In 2004, Jansson described 66 cases of brain abscess initially treated with cefotaxime, sixty-two of these patients were additionally treated with metronidazole, and surgery was also performed on 53 patients, with mortality in this study being 12%. Goodkin et al. (2004) [16] reported that in cases of abscess <2 cm in diameter, multiple abscesses in newborns, antibiotic treatment was used alone, however, the mortality rate was 42%.

Arlotti et al. (2010) [48] provided recommendations on the treatment of brain abscesses, which can be medicated or surgical. According to these recommendations, drug treatment alone can be considered in patients without severe neurological symptoms or impaired admission (Glasgow scale greater than 12), with a small abscess (<2.5 cm) or multiple abscesses, and in case of contraindication to surgery; in addition, antibiotics represent adjunctive therapy after surgery for large brain abscesses or brain abscesses causing a mass effect.

In pediatric patients, the most common combination of intravenous antibiotics is a third-generation cephalosporin associated with metronidazole and, in some cases, vancomycin [49]. Some studies also report the possible use of meropenem alone or in combination with other drugs [6,49]. In addition, Krzysztofiak et al. (2017) [50] showed the effective use of linezolid in pediatric patients, with clinical and radiological evidence of improvement.

Antimicrobial agents must be started intravenously and can then be switched to oral therapy, depending on the clinic, biochemical and radiological improvement [14]. Arlotti et al. (2010) considered a general treatment of 4 to 6 weeks for patients who underwent surgical treatment and enteral therapy for 6-8 weeks for patients treated with only drug therapy or with complicated brain abscesses [48].

The appropriate duration of antimicrobial therapy for brain abscess remains unclear. A 6 to 8-week course antibiotics has traditionally of parenteral been recommended, as long as the etiologic organisms are susceptible and adequate surgical drainage is achieved [51,52]. In selected cases with uncomplicated infection and complete surgical remission of a well-designed abscess, shorter courses of treatment (3 to 4 weeks) are sufficient [52]. However, many studies recommend 2 to 3 months of additional oral antimicrobial therapy to prevent relapse [53]. More complex cases may require a longer duration of treatment and rigorous clinical and radiographic follow-up. Repeated cranial tomography and magnetic resonance imaging will eventually show a decrease in the size of the abscess, disappearance of the surrounding edema, and less enation of the enhancement ring. These improvements are usually seen within 1 to 4 weeks of management, but complete radiographic resolution often extends over several months of follow-up [12].

In the absence of clinical and radiological improvement within 1 to 2 weeks, a neurosurgical intervention must be performed [45]. Depending on the characteristics, location, and some abscesses, it is possible to perform a stereotaxic or endoscopic aspiration of the abscess, instead of open surgery (craniotomy with excision) [55]. Studies involving mortality rates are more frequent in patients with lower scores on the Glasgow coma scale, rupture of the intraventricular abscess [5,29] congenital immunosuppression, organ transplantation, tumors being treated with maternal chemotherapy, premature newborns, or malformations [5]. A total recovery rate from infection of about 60-70% is reported in the case of early diagnosis and adequate therapy [20]. However, a smaller percentage of 50% of the cases can be explained by the delayed intervention, the presence of a greater number of patients with neurological deficiency on admission, and severe predisposing conditions [41].

Third-generation cephalosporins (ie, cefotaxime, ceftriaxone, ceftazidime) are suitable choices for the therapy of aerobic gram-negative organisms and provide coverage against strep isolates. Ceftazidime adds activity against Pseudomonas aeruginosa [12]. Metronidazole also penetrates the central nervous system (CNS) very well and has good oral absorption capacity. Because of its unique activity against anaerobes, metronidazole should be used as part of antibiotic therapy [56]. Intracavitary administration of antibiotics can be useful only in patients with large abscesses, of low resolution, who remain with positive culture despite the administration of adequate parenteral therapy [57].

The intraventricular rupture of a brain abscess re-

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presents a serious complication associated with a mortality rate of more than 80%. An aggressive approach that includes open craniotomy with debridement of the abscess cavity, followed by the placement of a ventriculostomy catheter for external drainage and potential intraventricular administration [58]. The use of corticosteroids for the treatment of brain abscesses is controversial. These agents are generally indicated for the control of intracranial hypertension and are associated with the risk of herniation or significant symptoms such as cerebral edema [12]. Severe cerebral edema may require administration of intravenous mannitol. Steroids interfere with the inflammatory response, delay the encapsulation, increase the development of necrosis, potentially reduce the concentrations of antibiotics within the purulent collection and alter the CT images [59].

Anticonvulsants are recommended in children who have developed seizures to potentially prevent new episodes. The duration of anticonvulsant therapy must be individualized and guided by electroencephalographic studies (EEG) in the follow-up phase of the disease. Most authors recommend at least 3 months of prophylaxis if they no longer occur [12]. Clinical sequelae can be found in about 30% of patients and are mainly epilepsy, motor, visual and auditory deficits, and hydrocephalus [29]. Surgically inaccessible lesions, early cerebritis, several small abscesses, and significant medical comorbidities are indicated treatments with only non-surgical methods. Despite the consensus for surgical drainage of the abscess, there is no agreement on surgical care for these patients. The duration of antibiotic therapy, the choice between oral and intravenous routes, the intervals, and the duration of these have yet to be debated [60,61].

Final Considerations

Pediatric brain abscess is an uncommon disease, yet with high morbidity and mortality. In the future, it is believed that evaluating changes in the epidemiology of brain infections is crucial for prognosis and treatment, seeking to take into account, on the one hand, the progressive decrease in some predisposing factors, such as HIV immunosuppression, congenital heart diseases, on the other hand, On the other hand, the decrease in vaccination coverage, the increase in resistance to antibiotics, and the of with growing number patients iatrogenic immunodeficiencies. Prospective multicenter studies are needed to achieve more significant evidence, particularly in the treatment of brain abscesses. Surgical drainage or excision of pediatric abscesses remains the basis of treatment both to relieve the mass effect and to provide a microbiological diagnosis. The literature demonstrates that

broad-spectrum antibiotics and access to CT and MRI images decrease the rates of morbidity and mortality. It is concluded in the case in question that the follow-up with a neurologist should be done throughout life, as it presents important neurological sequelae, given the complexity that the pathology presents, the therapeutic approach involves the administration of broad-spectrum intravenous antibiotics and surgical drainage in more complex cases.

Conclusion

Those responsible for the patient in the present study have the perspective that the interaction of a multidisciplinary medical team will favor the resolution of illnesses and the progression to a stable condition of the patient.

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Conflict of interest

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