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CASE REPORT

Bacterial meningoencephalitis and its complications: report of 2 cases in pediatric patients

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Meningitis, bacterial, Empyema, subdural, Pediatrics, Seizures, Meningoencephalitis.

Abstract

Bacterial meningitis is a potentially serious infection with a 100% fatality rate if untreated. The main etiological agents between 2 months and 2 years are Streptococcus pneumoniae and Neisseria meningitidis. This case report presents two previously healthy infants under one year old, with bacterial meningoencephalitis treated at a tertiary pediatric hospital in Paraná, which complicated with subdural empyema and seizures. The research was submitted to the Human Research Ethics Committee and approved under approval number 79898824.3.0000.0097. Analysis of the cerebrospinal fluid isolated pneumococcus in the first patient and meningococcus and herpes virus in the second one. Both received broad-spectrum antibiotic therapy for a long period and underwent surgical drainage with subsequent external ventricular bypass. Subdural effusion is present in 20% to 39% of children with bacterial meningitis, representing one of the main short-term complications of this infection. It frequently appears associated with seizures, present in the two patients reported. Nowadays, the best way to prevent short and long-term complications is through vaccination.

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INTRODUCTION

Bacterial meningitis is a potentially serious infection with a 100% fatality rate if left untreated[1]. Between 2 months and 2 years of age, *Streptococcus pneumoniae* and *Neisseria meningitidis* are the main causative agents[1-3]. This disease affects 7 in every 100,000 children in this age group in the United States and its incidence has been drastically reduced since the introduction of the Haemophilus influenzae vaccine. influenzae and pneumococcal conjugate vaccines - 60% reduction in cases with the latter[3,4].

The clinical presentation is variable and nonspecific; no single sign is pathognomonic. Symptoms and signs depend on the duration of the disease, the host's response to the infection, and the child's age[5-7]. When there is meningeal and brain parenchymal involvement, the disease is defined as meningoencephalitis. Complications described include brain abscess, cerebral vascular thrombosis, and hydrocephalus, which significantly worsen the patient's survival and neurological prognosis. These complications can prolong hospital stays, increase the spectrum of antimicrobial therapy, and even indicate surgical procedures, such as abscess drainage and ventriculoperitoneal shunt[8-10].

The objective of this work is to report two cases of bacterial meningoencephalitis in infants who developed complications of the disease with the aim of disseminating knowledge about the diagnostic and therapeutic approach, contributing to the resolution of similar cases that are frequent in the pediatric population.

METHODOLOGY

This is a descriptive observational case report. The clinical course of the patients was described based on data from their medical records. The articles used as bibliographic references were selected from PubMed and the medical literature collection of the advisors of this case report, and were filtered using the following keywords: bacterial meningitis in pediatrics, complications of bacterial meningitis, subdural empyema, and meningoencephalitis. The research was submitted to the Human Research Ethics Committee and approved under approval number 79898824.3.0000.0097.

CASE REPORT

A healthy 6-month-old female infant developed a fever and a change in urine color 5 days ago. Her mother sought care at a Basic Health Unit, where she was diagnosed with a urinary tract infection and prescribed cephalexin 50 mg/kg/day. On the third day of treatment, she still had a fever and began vomiting and prostration. The caregiver took the patient to a tertiary pediatric hospital, where laboratory tests and a cerebrospinal fluid puncture were performed (Table 1). She was diagnosed with bacterial meningitis, and pneumococcus was later identified in the cerebrospinal fluid by PCR.

The patient was admitted to the infectious diseases ward receiving ceftriaxone 100 mg/kg/day and vancomycin 60 mg/kg/day. Because the vancomycin level was outside the therapeutic target, it was decided to maintain vancomycin

Table 1. Exams laboratory initials of the patients reported.

	Pacient 1	**Pacient 2**
Hemoglobin	8.3 g/dL	9.3 g/dL
Hematocrit	24%	27.5%
Platelets	469000 µL	44000 µL
Leukogram	8070/uL leukocytes 67% neutrophils 7% rods 30% lymphocytes	4760/uL leukocytes 55% neutrophils 18% rods 27% lymphocytes
Protein W reactive	283.3 mg/L	391 mg/L
Cerebrospinal fluid	1840 /mm³ leukocytes 74 % neutrophils 8% lymphocytes 18% monocytes 155/mm³ red blood 184mg/dL proteins 119mEq/L chloride 24mg/dL glucose 5,2 mmol/L lactic acid Bacterioscopic and culture negative PCR positive for pneumococcus	3200 /mm³ leukocytes 77 neutrophils 14 lymphocytes 9 monocytes 1.56/mm³ red blood cells 95mg/dL proteins 128mEq/L chloride <20mg/dL glucose 7.3 mmol/L lactic acid Culture positive for Neisseria Meningitidis subtype B and viral panel positive for Human Herpesvirus type 7

continuously at a dose of 50 mg/kg/day. On the second day of follow-up, the child presented episodes of behavioral arrest, followed by ocular eversion and upper limb spasms lasting less than 5 seconds and resolving spontaneously. An electroencephalogram (EEG) was performed, with a normal result, and a cranial tomography (CT) scan revealed an image suggestive of subdural empyema, which was confirmed with cranial MRI. After evaluation by the neurology team, provoked seizures were considered, and phenobarbital 5 mg/kg/day was initiated. Due to persistent episodes, the minor received phenytoin 15 mg/kg/day intravenously for 2 days, followed by weaning, and began taking levetiracetam 30 mg/kg/day (figure 1). The neurosurgery team opted to drain the empyema with placement of an external ventricular shunt, which was removed after 10 days of evolution.

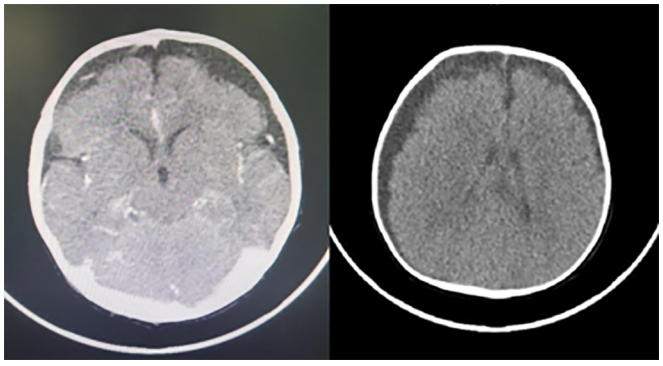


Figure 1. THE left, tomography of skull of patient THE with collection front asymmetric extra-axial collection. On the right, cranial tomography of patient B with bilateral and slightly asymmetric frontotemporal extra-axial collection.

After 10 days of ceftriaxone, antibiotic therapy was transitioned to cefotaxime 200 mg/kg/day due to isolated fever spikes. The patient completed 6 weeks of intravenous antibiotic therapy with continuous vancomycin and cefotaxime . At the end of treatment, a follow-up cranial MRI scan revealed resolution of the collection. The patient was discharged after 42 days of hospitalization, tapering off phenobarbital and receiving levetiracetam , with a follow-up appointment with the neurology and infectious disease teams. The patient was previously healthy, had received two doses of the pneumococcal vaccine, and was late for the second dose of the meningococcal C vaccine available through the National Immunization Program (PNI).

The second patient, a seven-month-old male infant, was equally healthy and, in addition to the PNI vaccinations, had received the meningococcal ACWY vaccine. Two days after hospital admission, the child presented with a difficult--to-control fever, runny nose, dry cough, drowsiness, loss of appetite, and the appearance of erythematous patches on his lower limbs that progressed to his upper limbs. On the morning of the same day of admission, the patient was evaluated at an emergency care unit in his hometown, where a sepsis protocol was established, and he received a dose of ceftriaxone 100 mg/kg.

Initial tests showed a complete blood count with an infectious pattern and hypochromic and microcytic anemia (Table 1), thrombocytopenia, elevated C-reactive protein levels, a partial urine sample negative for infection, and cerebrospinal fluid analysis with a positive culture for Neisseria meningitidis subtype B. For treatment, the patient initially received ceftriaxone 100 mg/kg/day in combination with vancomycin 60 mg/kg/day. On the third day of hospitalization, he presented episodes of generalized tonic- clonic seizures , lasting approximately 3 minutes each, without recurrence after starting phenobarbital and phenytoin . On the same day, an electroencephalogram was performed during sleep and wakefulness without epileptiform discharges. Control exams on the fifth day of hospitalization showed worsening of the infectious pattern of the blood count, negative cerebrospinal fluid culture but with a positive cerebrospinal fluid viral panel for human Herpes virus type 7, and acyclovir 45mg/kg/day was started.

A cranial CT scan on admission revealed an asymmetric extraaxial hypodense collection in the frontal region. Subsequent examinations revealed an increase in this collection, and a cranial MRI confirmed the presence of a subdural empyema. Antibiotic therapy was transitioned to cefotaxime 200 mg/kg/day, and the neurosurgery team performed empyema drainage and an external ventricular shunt. Ten days later, the antibiotic regimen was escalated to cefepime 150 mg/kg/day due to persistent pleocytosis, despite negative cultures in the control CSF . On the thirtieth day of hospitalization, due to clinical and laboratory improvement, the external ventricular shunt was removed, and five days later, the patient was discharged.

DISCUSSION

In Brazil, between 2007 and 2020, approximately 265,000 cases of meningitis were reported and confirmed, 33% of which were of bacterial etiology. Of these, 30% (approximately 26,000 cases) were meningococcal disease and 15% (just over 14,000 cases) were pneumococcal disease[11].

Nuchal rigidity , irritability, confusion or altered mental status, headache, photophobia, nausea, vomiting), often preceded by symptoms of upper respiratory tract infection[5].

The classic triad of fever, neck stiffness, and abnormal mental status occurs in a minority of affected children[5,6]. Symptoms are often nonspecific, and clinical suspicion is essential for diagnosis with CSF puncture.

Under normal conditions, there are <5-10 leukocytes/mm^3 in the CSF , with a predominance of mononuclear cells, and in neonates, there may be up to 30 leukocytes/mm^3. The CSF analysis of bacterial meningitis includes the presence of pleocytosis (100-10,000 leukocytes/mm^3) with a predominance of polymorphonuclear cells from the first 24 hours of bacterial aggression. The normal value of CSF protein is between 45-50 mg/dL and in bacterial meningitis it is usually

significantly increased (around 135 mg/dL). Glucose, which is related to serum glycemia, is usually low (<40 mg/dL) due to bacterial metabolism. On admission, both patients presented CSF with pleocytosis, increased protein levels , and low glucose levels , as shown in Table 1[12].

In cases of bacterial meningitis, the presence of leukocytosis above 11000-12000/mm³ in the leukogram is expected. The infants mentioned did not present leukocytosis, but had elevated C-reactive protein levels compatible with the infectious condition[12]. Both presented anemia considered to be of transinfectious etiology , which was untreated and resolved spontaneously in subsequent control exams.

The diagnosis is confirmed by isolation of a bacterial pathogen from cerebrospinal fluid culture; isolation of bacteria from blood cultures in a patient with cerebrospinal fluid pleocytosis; or detection of a bacterial pathogen in CSF by molecular methods. Both patients obtained culture results through molecular analysis, performed in a state laboratory in partnership with the tertiary hospital. In simple CSF culture, there was no bacterial growth in either sample, demonstrating the importance of more sensitive methods for accurate pathogen isolation[6-8].

The second patient reported presented a positive viral panel for Herpesvirus type 7, which presents with a clinical picture of fever followed by a sudden rash. This virus, once acquired, can remain latent after primary infection. Herpesvirus type 7's mechanism of invasion of the central nervous system remains poorly studied and may be associated with encephalitis[13]. To confirm primary infection with this virus, the ideal is to evaluate PCR in the cerebrospinal fluid and compare it with the IgG antibody titer in the serum. In a study by Schwartz[14], the genetic material of herpesvirus type 7 was confirmed in 57 of the 2,972 children tested with neurological disease. Only 3 adolescents had primary infection (low-avidity IgG), and 18 children had possible disease due to the virus after inconclusive serological tests and no alternative cause other than clinical. The others presented IgG with high avidity (probable previous infection) and/or an alternative cause for the condition, with neurological disease caused by herpes type 7 being ruled out[14]. In the case presented, the viral panel of the cerebrospinal fluid was not confirmed by serology and the bacterial etiology was considered as the main etiology given the compatible clinical and laboratory findings and clinical improvement with the antibiotic therapy employed.

Antibiotic treatment should initially be empirical with vancomycin and ceftriaxone, and after culture results, the causative agent should be targeted. The duration of therapy averages 7 to 14 days[9,10]. Our patients initially received this therapeutic regimen but required additional regimens and longer treatment times due to the complications they presented.

The patients described were 6 and 7 months old at the time of diagnosis. According to a cohort study by Vasilopoulou et al., age less than 12 months at the time of diagnosis was considered a risk factor for both short- and long-term neurological complications[15].

Short-term complications include the two main complications reported in the patients: subdural effusion and seizures. Subdural effusions occur in 20% to 39% of children with bacterial meningitis. Most of these subdural effusions are asymptomatic and resolve spontaneously. Effusions are diagnosed by imaging tests in patients with neurological deterioration, with MRI being the most common . Magnetic resonance imaging (MRI) is the gold standard. Through it, the purulent collection appears hyperintense on T1 and isointense on T2, and gadolinium enhancement delimits the periphery of the lesion. Indications for drainage include the presence of infected subdural empyema, focal neurological signs or symptoms, or increased intracranial pressure. Seizures may be associated with the presence of empyema and develop early and are easily controlled, rarely leading to permanent neurological complications[15,16].

Long-term complications include hearing loss, cognitive impairment, hydrocephalus, learning disabilities, and epilepsy[16]. After hospital discharge, the patients reported undergoing outpatient consultations with pediatric neurology and infectious disease specialists, with no complaints of hearing loss and no new episodes of seizures. The team's care plan requires long-term follow-up for possible intervention if complications arise.

The most effective prevention of complications from bacterial meningitis is prevention through vaccination[16]. Vaccines against the three main organisms causing bacterial meningitis are currently available in the National Immunization Program (PNI): Haemophilus influenzae serotype B (Hib), Streptococcus pneumoniae , and Neisseria meningitidis (capsular groups A, C, W, and Y). In the first reported case, the infant was late in receiving meningococcal C vaccination and had not yet received the pneumococcal booster vaccine administered at 12 months of age by the National Immunization Program (PNI). The second patient, who did not have a late vaccination, received a dose of the meningococcal ACWY vaccine and ended up contracting serotype B, which is only available in private vaccines.

CONCLUSION

This publication reported two infants with short-term complications of bacterial meningoencephalitis, highlighting the importance of clinical suspicion for diagnosis and appropriate treatment. Bacterial meningitis in infants is a serious, life-threatening disease that can cause complications and is preventable with vaccination.

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