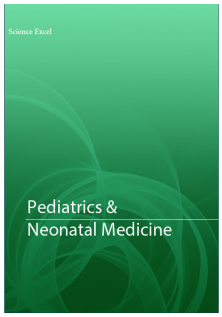
Pediatrics and Neonatal Medicine

Original Article



Bacterial and prognostic profile of nosocomial meningitis in newborns

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- Received Date: 05 Apr 2022
- Accepted Date: 12 Apr 2022
- Publication Date: 15 Apr 2022

Keywords

Brain abscess, Central nervous system, Meningitis in newborns, Myelomeningocele ,Nosocomial infection ,Seizures, Ventriculitis

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Abstract

Introduction: Nosocomial neonatal meningitis is particularly dreadful because it occurs in patients of immature immunity and a developing brain. It is always a challenge for the clinician due to its clinical polymorphism making the diagnosis often difficult

Aim: To study the epidemiological, clinical, bacteriological, therapeutic and evolutionary aspects of neonatal nosocomial bacterial meningitis.

Results: Through our series, we reported fourteen cases of nosocomial meningitis, ie 43% of meningitis recorded over the study period. A male predominance was observed in 57.1%. The newborns were preterm in 28% of cases and had low birth weight in 42% of cases. The germ isolated was Klebsiella pneumoniae in 28.4% of cases. The blood culture was positive in 64% of cases. The same germ was isolated in both blood and the cerebrospinal fluid in 42% of cases. The complications found were: ventriculitis (28.5%), triventricular and tetraventricular hydrocephalus (14.2%) and multiple cerebral abscesses (14.2%). The mortality rate recorded in our series was 28.5%.

Conclusion: Nosocomial meningitis is a serious or even fatal condition requiring early diagnosis and adequate antimacrobial therapy. Prevention remains the best strategy for the battle against this infection.

Introduction

Nosocomial neonatal meningitis is particularly dreadful because it occurs in patients of immature immunity and a developing brain. It is always a challenge for the clinician due to its clinical polymorphism making the diagnosis often difficult. Despite the progress made in its management, neonatal bacterial meningitis (BM) remains alarming due to its high mortality ranging from 8.5 to 15% and the long term neurological complications observed in 20 to 58% of survivors [1].

Patients and methods

Our series is a descriptive retrospective analysis of neonatal nosocomial BM cases confirmed by the isolation of germs in the cerebrospinal fluid (CSF) observed in the neonatal intensive care unit in Marrakesh between January 2016 and December 2020, included all newborns less than 30 days old with meningitis declared after 48 hours of hospitalization. All newborns who have a contraindication to lumbar puncture (LP) or transfontanellar ventricular puncture were excluded from the study, and those treated on clinical, biological and/or radiological signs without bacteriological evidence.

Results

During the study period, 32 cases of meningitis were confirmed, 14 of which were nosocomial meningitis (43%).

Our patients had gestational age that ranged from 35 to 41 weeks of amenorrhea. Preterm babies represented 28% of cases. The ages of hospitalized infants ranged from one to 27 days, with 57% of newborns being less than one week old. The pregnancy was not followed in 36% of the cases. Delivery was by C-section in 21% of mothers. Perinatal distress was noted in four children (28.5%). A male predominance was noted in 57.1% (8 cases).

The initial reason for admission to the neonatal intensive care unit was: neonatal respiratory distress (64%), urinary tract infection (14%), hemorrhagic syndrome (7%), poly-malformation syndrome, neonatal jaundice (7%). The time between hospitalization and the appearance of signs of meningitis varied between 3 and 22 days with an average time of 8 days. The risk factors noted were the presence of a ruptured myelomeningocele in 4 patients (28%) and an umbilical venous catheter in 3 patients (21%).

Fever was the most frequent symptom together with neurological signs (Table 1).

Citation: Elhanafi FZ, Bennaoui F, Mahir N, Slitine NE, Maoulainine FMR. Bacterial and prognostic profile of nosocomial meningitis in newborns. Pediatr Neonatol Med. 2022;2(1):1-4.

Table 1. *Clinical signs revealing meningitis*

Clinical signs	Number of cases	Percentage %
Fever	8	57,1
Hypothermia	1	7,1
Seizure	6	42,8
Groaning	2	14,2
Breast refusal	7	50
Bulging fontanelle	1	7,1
Asymptomatic	3	21,4

Table 2. *Isolated germs in CSF*

Germs	Number	Percentage
klebsiella pneumoniae	4	28,5%
Serratia marcescens	2	14,2%
Acinetobacter baumannii	2	14,2%
Coagulase-negative staphylococci	2	14,2%
Enterococcus spp	1	7 ,1%
Pseudomonas aeruginosa	1	7 ,1%
Enterobacter cloacae	1	7,1%
Group B streptococcus	1	7 ,1%

Table 3. *Germs isolated in blood culture*

Germs	Number	Percentage
Coagulase-negative staphylococci	2	22,2%
Serratia marcescens	2	22,2%
klebsiella pneumoniae	3	33, 3%
Enterococcus faeciu	1	11,1%
Acinetobacter baumannii	1	11,1%

The association of several clinical signs was found in 11 cases (78.5%). Three newborns were asymptomatic. Harmonious and severe intrauterine growth restriction was noted in 6 newborns (42%). The weight of our patients varied between 1050g and 3700g with an average of 2570g.

The CSF study showed pleocytosis> 100 elements / mm (variable between 400-7860 elements) in 50% of our patients with perineuronal net predominance in 71% of cases. Lack of cellular response was noted in 21.4% of cases. CSF/serum glucose ratio was less than 0.4 in 11 patients (78%). The CSF protein concentration was variable between 1.9 and 8.5g / l. The CSF culture was positive in all cases. Klebseilla pneumoniae was found in 28.5% of cases (Table 2). The blood culture was positive in 9 cases (64%) (Table 3).

A 42% match was found between the germ isolated in the blood and the CSF. The c-reactive protein (CRP) was positive above 30 mg / l in 71% of cases. On the complete blood count, thrombocytopenia was found in 32% of the newborns, while 50% were anemic and leukopenia was noted in 21% of cases. Transfontanellar ultrasound performed systematically in all patients, it showed an aspect of ventriculitis in four newborns, and triventricular hydrocephalus in two patients. Brain CT was performed in six patients and identified; multiple brain abscesses in two cases, tetraventricular hydrocephalus in two patients, triventricular hydrocephalus in one patient and subarachnoid hemorrhage associated with diffuse cerebral edema in one patient.

As we are in a context of nosocomial infection, the antimacrobial therapy initially prescribed according to our microbial ecology of the neonatal intensive care unit was imipenema associated with amikacin and ciprofloxacin then adapted according to the isolated germ and the antibiogram.

Eleven patients received ciprofloxacin (78%), three patients received colistin two of them by intrathecal route, vancomycin was administered in two patients. The duration of treatment was from 14 to 60 days. None of our patients had corticosteroid therapy. Phenobarbital was administered in 35.7% of cases. An external bypass was performed in two patients for active hydrocephalus. The length of hospitalization varied between 17 to 68 days with an average length of 24.2 days.

The mortality rate recorded in our series was 28.5%, half of which have harmonious and severe intrauterine growth restriction. Septic choc was the main cause of death in 50% of cases. The bacteria involved was gram-negative bacilli in all cases: Acinitobacter baumannii (1case), Pseudomonas aeruginosa (1case), Serratia marcescens (1case), Klebsiella pneumoniae (1case). Psychomotor restriction was observed in three patients (30%) and unprovoked seizures and epilepsy in two patients.

Discussion

A nosocomial infection (NI) is an infection that was not present or incubating upon admission. Therefore, it is accepted that an infection occurring more than 48 hours after admission, or directly linked to an act of care (regardless of its date of occurrence), is nosocomial [1]. The hospitalized newborns are sometimes in an unstable clinical state, often present serious conditions which may justify the use of invasive procedures. It is frequent that very early preterm babies have longer hospital stay which increases the risk of NI. Preterm and low birth weight are the perinatal risk factors most frequently linked to neonatal BM [2], this is explained by the high permeability of the blood-brain barrier, especially at the level of the choroid plexuses, the absence of polynuclear cells and immunoglobulins G in the CSF allow faster growth of germs. The rate of nosocomial BM is underestimated: in preterm babies, the risk of 1.4% of nosocomial BM (5% of LP performed) is much higher than that of primary meningitis [3]. These 2 risk factors were found in our study with a respective frequency of 28 and 42%. A male predominance was found with a sex ratio M / F equal to 1.3 [3], the same results was noted in our study.

The signs of meningitis we noticed are those of infection with fever 57.1%, breast refusal 50% and seizures which represented 42% of cases. Fever and breast refusal were the 2 most frequently found in the study of Ben hamouda et al [4]. In the study of Devi et al. (2017) seizure and lethargy were the most common clinical symptoms [5]. In Khalesi et al. (2014), seizure was revealing sign in 55% of neonatal meningitis [6]. However, 37% of neonatal BMs have no neurological signs [7], 21.4% of newborns in our study had no clinical signs of meningitis, and LP was performed after an increase in CRP and / or a positive blood culture.

The severity of nosocomial neonatal BM requires early diagnosis. A LP should be performed in any newborn suspected of septicemic infection after clinical stabilization. Positive culture is essential for diagnostic certainty [8].

Biological assessment of the CSF guides the diagnosis: a CSF protein concentration greater than 1.20 g / L and, above all, a CSF / blood glucose ratio of less than 0.40 are in favor of BM. A hypercytosis, greater than 21 / mm^3 in the CSF has a sensitivity of 79% and a specificity of 81% [3,9,10]. However, an absence of cellular reaction when the LP is done very early is possible in the invasion phase of CSF, therefore; it does not disprove the diagnosis which is confirmed in this case only by culture [10], this was noticed in our study as well where the cellular reaction was absent in 21.4% of patients.

The germs most frequently isolated in our study were *Klebsiella pneumoniae* (28,5%), Acinitobacter baumannii (14,2%), Serratia marcesens (14,2%), coagulase negative Staphylococcus A (14,2%). In Hassan Boskabadi et al , the most common microorganisms were Klebsiella pneumoniae (49%), Enterobacter aeruginosa (14%), and Acinetobacter baumannii (6%)[11].in one study, *Klebsiella* pneumoniae, Coagulase negative staphylococci, and Enterococcus faecalis were the most common bacterial infectious agents [5,11].

The mainly aerobic blood culture that usually precedes the LP; was positive in 61.4% of cases with a mismatch of germs in 3.5% of cases [10]. A multicentric study in the National Institute of Child Health on 134 low birth weight newborns with confirmed meningitis showed that the pathogens responsible for meningitis were similar to those associated with sepsis, and that one third of these newborns did not have positive blood cultures [8]. In our series, the blood culture was positive in 64% with a germ mismatch in 22% of cases.

Meningitis due to *Klebsiella* pneumonia is a rare disease [12]. They are poorly described and yet their mortality is high. They seem to occur before 1 year, or around the age of 55, and can occur in patients without specific medical history [13]. Serratia marcescens is an enterobacterium that causes a multitude of infections and nosocomial epidemics including meningitis; found mainly in neonates and neurosurgery [14]. Regarding Acinetobacter baumannii is a nosocomial pathogen of increasing importance. The authors of one evaluation of children with nosocomial meningitis reported that Acinetobacter accounted for 11.2% (20/178) of cases [5]. In large series in the USA and Taiwan, Acinetobacter ranked the fifth most common genus to be associated with nosocomial meningitis [15,16]. Nosocomial infections associated with Acinetobacter baumannii lead to high mortality [17].

Today, coagulase-negative staphylococci (CoNS), as typical opportunists, represent one of the major nosocomial pathogens, having a substantial impact on human life and health [18]. CoNS is sometimes a contaminant, it has increasingly been recognized as a cause of clinically significant nosocomial bloodstream infections, particularly in neonates [19,20]. The cases of CoNS meningitis in our series were symptomatic with a pleocytosis in the CSF study and a positive culture.

Enterobacter cloacae is a rare but severe agent particularly affecting preterm babies and hypotrophic newborns. The prevalence of Enterobacter cloacae in neonatal nosocomial infections is variable according to studies from 4 to 10% of systemic infections. These E. cloacae infections are severe and result in sepsis and meningitis [21]. The case noted in our series was a preterm 35 weeks old presented with multiple brain abscesses requiring an intrathecal use of colistin.

Meningitis caused by Pseudomonas aeruginosa are rare, and always defined as nosocomial. Only old epidemiological studies put forward a figure of 10% of Pseudomonas aeruginosa among Gram-negative meningitis [22]. We recorded one case of Pseudomonas aeruginosa meningitis which occurred in a newborn baby with myelomeningocele and whose outcome was unfavorable.

Bacterial meningitis can cause acute complications such as brain parenchymal vasculitis, ventriculitis and systemic complications such as pneumonia and septic shock [23]. In agreement with data in the literature, complications such as ventriculitis, hydrocephaly and abscesses were more frequent in Gram-negative meningitis [24]. Neonatal meningitis is responsible for 25–50% of deafness, blindness, cerebral palsy, seizure, hydrocephalus, or cognitive impairment of surviving infants [25].

The contribution of neuro-radiological investigations, in particular transfontanellar ultrasound and brain CT is essential for highlighting the immediate complications which influence the vital prognosis and increase the risk of neurological longterm complications [4].

Rapid initiation of appropriate broad-spectrum antimicrobial therapy in response to suspected neonatal meningitis is critical to optimize the outcomes. While waiting for the bacteriological results, the choice of antimicrobial therapy is probabilistic and must take into consideration the local bacterial epidemiology, the resistance profile of the germs circulating in the neonatal unit and the circumstances of the disease [2].

The potential indications for fluoroquinolones in newborns are relatively limited, and are represented by Staphylococcal, Enterobacter, and even Gram-negative meningitis [26]. This class of antibiotic can be used as a curative treatment in nosocomial neonatal meningitis caused by bacteria resistant to traditional antibiotics (ceftazidime or imipenem type) combined with an aminoglycoside

However, in coagulase-negative Staphylococcal meningitis, the combination of vancomycin with an aminoglycoside remains the treatment of choice [27]. The recommended duration of a antimicrobial therapy is 21 days. It is extended to 6 or even 12 weeks in the event of a brain abscess or ventriculitis.

Steroid administration has not been shown to be beneficial as an adjunct to antimicrobial therapy in neonatal BM [28].

At the end, newborns with meningitis management, regardless of the involved pathogen, requires a specific follow-up protocol. It is based on the early detection of complications, in particular seizures (clinical + EEG) [3].

Conclusion

Nosocomial meningitis in newborns is an infrequent but serious infection causing long-term complications both psychomotor and neurocognitive. They are characterized by clinical polymorphism and often occur in patients with risk factors. Early diagnosis and management based on broad-spectrum antimicrobial therapy will minimize its complications. Prevention remains the best strategy for the fight against this infection.

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