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CASE REPORT

Nosocomial Neonatal Meningitis with *Acinetobacter Baumannii* on Myelomeningocele: A Real Therapeutic Challenge

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Abstract: Imipenem-resistant *Acinetobacter baumannii* meningitis is a hospital-acquired infection, the treatment of which constitutes a real therapeutic challenge. In this article, together with a review of the literature, we report two cases of imipenem-resistant *Acinetobacter baumannii* neonatal meningitis following ruptured myelomeningocele, treated with intravenous colistin with favorable results. In recent years, *Acinetobacter baumannii* has become a more and more commonly described pathogen in hospital-acquired infections. However, the cases of meningitis are mainly postoperative and are still not quite frequently described in the literature. Colistin appears to be preferably administered intravenously at a dose of 100.000 IU/kg/day.

Keywords: *Acinetobacter baumannii*, Colistin, Intrathecally, Intravenously, Meningitis, Myelomeningocele.

1. INTRODUCTION

Acinetobacter baumannii is one of the main pathogens in hospital-acquired infections [1] including pneumonia, bacteremia and, less frequently, meningitis [2]. *Acinetobacter baumannii* meningitis resistant to imipenem is a hospital-acquired infection, the treatment of which constitutes a real therapeutic challenge, given the absence of effective antibiotics and the lack of consensus regarding this clinical situation [3]. Colistin, administered intrathecally or intravenously, seems to be effective.

We report two cases of neonatal meningitis due to *Acinetobacter baumannii* resistant to imipenem, treated with intravenous colistin with a favorable outcome.

2. CASE REPORTS

Two newborns, full-term, delivered by caesarean section presented a ruptured myelomeningocele. Initially, the management was done on an outpatient basis. They were admitted to the neonatal intensive care unit, respectively, on the 16th and 4th day of life, the first for convulsion with fever and the second for sepsis.

The first newborn upon admission was conscious, febrile, with generalized clonic seizures, chewing and pedaling, with no signs of respiratory or circulatory distress. The clinical examination showed an axial hypotonia with a bulging anterior fontanel, the cranial perimeter was normal, primitive reflexes and the sucking reflex were weak, in addition to an omphalitis, a polymalformative syndrome comprising ruptured myelomeningocele which was infected, congenital bilateral hip dislocation, arthrogyposis, and bilateral varus clubfoot deformity.

Examination of the cerebrospinal fluid (CSF), by trans-fontanellar puncture, found a slightly cloudy fluid with 780 cells/mm³ predominantly neutrophilic (60%), CSF glucose was 0.04g/l, with a ratio of CSF glucose /glycemia collapsed of 0.054g/l and albumin was 1.26g/l. The Gram stain revealed gram-negative bacilli and the bacterial culture

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a multi-resistant *Acinetobacter baumannii*. Antibiogram was objected a resistance to all antibiotics; especially those used in the newborn (Imipenem, ceftazidime...); this bacteria was sensitive only to colistin. Other findings include an inflammatory syndrome: hyperleukocytosis at $16\ 240\ \text{cells}/\text{mm}^3$ predominantly neutrophilic with a C-reactive protein at $262.8\text{mg}/\text{l}$.

The second newborn was conscious, febrile with signs of sepsis and convulsions including chewing, boxing and revulsion of the eyes with signs of respiratory and circulatory distress. The clinical examination found axial hypotonia with normally tense anterior fontanel; the cranial perimeter was normal, primitive reflexes and sucking reflex were present, in addition to a polymalformative syndrome comprising fissured myelomeningocele, equine varus clubfoot and genu recurvatum deformities bilaterally. Examination of the cerebrospinal fluid, by transfontanellar puncture, found a multi-resistant *Acinetobacter baumannii* sensitive to colistin. Lab test showed an inflammatory syndrome with a C-reactive protein at $301\text{mg}/\text{l}$.

For both newborns, trans-fontanellar ultrasound showed signs of ventriculitis, with tri-ventricular hydrocephalus corroborated by cerebral computed tomography, as well as signs of Arnold Chiari malformation in the first newborn.

After the results of the antibiogram we didn't have any choice in these cases for antibiotics, only colistin was effective, newborns were placed on intravenous colistin at a dose of $100.000\ \text{IU}/\text{kg}/\text{day}$ in 3 doses for 7 weeks and Ciprofloxacin $20\text{mg}/\text{kg}/\text{day}$ in 2 doses for 3 weeks.

Phenobarbital was administered to stop convulsions. Local dressing for myelomeningocele was done twice daily, with the isolation of newborns, given the high risk of contamination.

Bacteriological surveillance was performed by sampling the cerebrospinal fluid from the trans-fontanellar puncture, which had become sterile by the tenth day. Normalization of CSF glucose and albumin levels was achieved after 24 days. We were continued 7 weeks for treatment because they were severe cases of ventriculitis caused by *Acinetobacter baumannii* multi-drug resistant.

No adverse effects were observed; especially, no neurological worsening or renal failure was observed. The short-term evolution was favorable. The patients were then transferred to the neurosurgery department after seven weeks of treatment for surgical treatment of myelomeningocele; then, to the pediatric orthopedic surgery department for treatment of the limb malformations.

3. DISCUSSION

Neonatal bacterial meningitis is responsible for high mortality and long-term neurological sequelae, its incidence is between 0.25 and 0.32 per 1000 live births. In developing countries, the incidence of neonatal bacterial meningitis is underestimated. In newborns with documented sepsis and premature infants, the incidence is significantly higher. Neonates are more exposed to meningitis because of the immaturity of cellular immunity and the absence of specific clinical signs, making the diagnosis of meningitis more difficult in newborns [4].

Acinetobacter baumannii meningitis is rare and treatment, a real therapeutic challenge. Because of the immunoincompetence of cerebrospinal fluid (CSF), the treatment must include bactericidal antibiotics with good tissue diffusion, which must be in high doses parenterally because of the poor diffusion of the majority of available molecules. In our case, the therapeutic challenge was to find a molecule that would be both effective against *Acinetobacter baumannii*, which is a multi-resistant germ, and have a good neuro-meningeal diffusion in order to reach the effective concentrations without being toxic [5].

The rising incidence of multi-drug resistant gram-negative infections and carbapenem-resistant Gram-negative since 2000s in pediatric intensive care units continues to challenge clinicians. The lack of new antibiotics to combat these infections have led to the revival of colistin; an old class of cationic, cyclic polypeptide antibiotics. Colistin may have a role in the treatment of infections caused by multidrug-resistant Gram-negative bacteria in critically ill children, including *Acinetobacter* species, *Pseudomonas aeruginosa*, *Enterobacteriaceae* species. However, the patients have to be followed for side effects throughout colistin treatment, not for only early stage. And the clinicians should be aware of the increase in the rate of nephrotoxicity in patients receiving a concomitant nephrotoxic agent [6]. We continued 7 weeks of treatment because they were severe cases of ventriculitis caused by *Acinetobacter baumannii* multi-drug resistant.

In addition, an antibiotic that is effective in this context such as colistin seems to be preferably administered either intrathecally *via* lumbar injections and/or a ventricular catheter, or intravenously, even if it has a poor diffusion across the hemato-meningeal barrier. Administration of colistin intrathecally has rarely been mentioned in the literature [7].

The cases of imipenem-resistant *Acinetobacter baumannii* meningitis described in the literature were all secondary to a neurosurgical procedure [8]; this was not the case with our patients whose infection was secondary to ruptured myelomeningocele. Myelomeningocele is a defect that is usually repaired surgically in the early days of life in developed countries to minimize the risk of meningitis [9].

Outpatient care of children with myelomeningoceles requires interdisciplinary collaboration. Unfortunately, in our context, from the first days of life, it is the parents who carry out the outpatient management inadequately, for that matter. This is due to the lack of means and the unavailability of health-care centers.

The local use of colistin is a solution for treating imipenem-resistant *Acinetobacter baumannii* meningitis [10]; but the intravenous use showed its effectiveness at a dose of 100.000 IU/kg/day for 7 weeks as was the case of our patients who evolved well without exhibiting any side effects.

CONCLUSION

Nosocomial meningitis is a rare, though severe, entity in the newborn and *Acinetobacter baumannii* is exceptionally implicated. The emergence of multi-resistant strains of *Acinetobacter baumannii* can sometimes be a therapeutic impasse. Colistin remains the ideal treatment choice for *Acinetobacter baumannii* meningitis, whether intravenously administered.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

HUMAN AND ANIMAL RIGHTS

No animals/humans were used for studies that are the basis of this review.

CONSENT FOR PUBLICATION

Not applicable.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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Declared none.

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