SEVERE PEDIATRIC SEPSIS CAUSED BY NEISSERIA MENINGITIDIS: A CASE REPORT

JALBĂ (SÎRBU), G.-A.,[1] COREȚCHI, D.,[1*] MORARU, P.-I.,[1,2] PEPTINE, L.,[1,2] RĂILEANU, C.-R., NECHITA, A.[1,2]

https://doi.org/10.35219/efms.2024.3.09

[1]Department of Pediatrics, Clinical Emergency Hospital for Children "Sf. Ioan", Galati
[2]Faculty of Medicine and Pharmacy, "Dunărea de Jos" University of Galati
*diana.coretchi.mg4.8@gmail.com

Abstract

The aim is to report on the aggressive nature of Neisseria meningitidis infection among children and its complications.

Case report: We present the case of a 2-month-old infant who was admitted for fever, diarrhea, moaning, and appetite loss to the Emergency Clinical Hospital for Children "Sf. Ioan" Galați. The infant was admitted to the intensive care unit and underwent clinical evaluation along with extended laboratory investigations. Neurological manifestations began on the first day of hospitalization, starting with tonic seizures. Later, anisocoria and ptosis of the left eye developed over the following days. On the 4th day of hospitalization, positive blood culture for Neisseria meningitidis was obtained and the second blood culture turned out negative. Antibiotic treatment was initiated, and multidisciplinary consultations were conducted to address the ensuing complications.

Discussion: The case highlights the severity of Neisseria meningitidis infection in infants and the rapid progression to neurological symptoms, often accompanied by serious complications. Early management through appropriate antibiotic therapy, aided by a multidisciplinary approach, is essential to limit mortality and sequelae.

Conclusion: Neisseria meningitidis is the cause of serious infections with a high mortality rate and neurological sequelae. The complexity of such cases requires multidisciplinary intervention.

Keywords: child, sepsis, Neisseria meningitidis, complications.

INTRODUCTION

Neisseria meningitidis is an aerobic, Gram-negative diplococcus bacterium commonly known as meningococcus. The most prevalent serogroups are A, B, C, W, X, and Y, distinguished by the type of polysaccharide capsule and are responsible for infections in the general population (2). The majority of cases occur in the pediatric

population, particularly in children under 5 years of age (11). It most commonly occurs with the serogroup B, according to the European Centre for Disease Prevention and Control (3). A variety of laboratory analyses, including blood cultures, can be used to identify the bacterium.

Infections caused by this bacterium are highly aggressive and require urgent therapeutic intervention, with a mortality rate of 4% to 20% within the first two days post-infection (14, 15). The most common conditions include meningococcal meningitis and meningococcal sepsis (12, 13). Post-infection, approximately 10–20% of cases result in sequelae such as behavioral changes, hearing loss, oculomotor impairment, or limb amputations (9).

The septic shock caused by *Neisseria meningitidis* results in aggressive inflammatory responses and coagulation issues that, if not localized, will lead to death quickly. In contrast, meningococcal meningitis accounts for approximately 80% of reported cases (4).

The rate of meningococcal infections has decreased in developed countries due to prophylaxis with conjugate vaccines covering serogroups A, C, W, and Y, as well as monovalent vaccines for serogroup B (7).

Case presentation

A 2-month-old male infant, firstborn via C-section at 38 weeks, with a history of difficult postpartum respiratory adaptation requiring oxygen support at birth, was admitted to the Intensive Care Unit of the Emergency Hospital for Children 'Sf. Ioan' in Galati after being transferred from a secondary hospital. The onset of symptoms, which began a day prior to hospitalization, included fever (T=38.7°C), four episodes of diarrhea, moaning, and loss of appetite.

Family medical history: Mother with pregnancy-induced hypertension.

First clinical examination:

Weight: 6000 g. The infant presented in a severe clinical condition, afebrile at the time of consultation, with extremely pale and mottled skin, a capillary refill time of 4 seconds, moaning, and a depressed fontanel. The heart was rhythmic and well-perfused, with a cardiac rate of 110 bpm and blood pressure of 102/54 mmHg. The

respiratory rate was 35/min, and blood oxygen saturation ranged between 97-100%. The abdomen was bloated, diuresis was observed in the diaper, and the pupils were symmetrically reactive.

The first biological samples reveal the following findings: pancytopenia (leukocytopenia, erythrocytopenia, thrombocytopenia), low hemoglobin levels, an altered coagulogram with elevated INR, PT, APTT, and D-dimer values. Additionally, there are raised levels of C-reactive protein (12.83 mg/dL) and procalcitonin (14.7 ng/mL). Glucose, albumin, calcium, sodium, and iron levels are low. Metabolic acidosis and elevated indirect bilirubin levels are also noted. A blood culture has been collected.

Based on the clinical examination and supported by biological findings, the clinical suspicion is sepsis and disseminated intravascular coagulation (DIC).

On the first day in the hospital, broad-spectrum antibiotic treatment with intravenous Ceftriaxone was initiated. However, due to clotting disorders and elevated inflammatory markers, the treatment was escalated to i.v. Meropenem and Linezolid.

It was also supplemented with human immunoglobulin intravenous, antifungal treatment intravenous., isoRh and isogroup resuspended erythrocyte concentrates, isoRh and isogroup fresh frozen plasma, diuretics, and infusions for hydro-electrolytic and acid-base rebalancing.

On the first day of hospitalization, the patient associates tonic clonic seizure with nystagmus with a capped gaze and eyeball deviation, managed with intravenous Levetiracetam.

On the second day of hospitalization, clinical examination revealed: an extremely severe general condition, subfebrile state, and extreme agitation with continuous moaning. The skin appeared very pale and mottled, with a capillary refill time of 4 seconds. A grade II/VI systolic murmur was detected, with a cardiac frequency of 130 bpm and blood pressure of 98/75/79 mmHg. Blood oxygen saturation was 93%, with evident chest-abdominal swings. Diuresis was 2.9 mL/kg/h. The anterior fontanel was tense, and the pupils were slow to react.

First transfontanellar ultrasound: non dilated ventricular system with mild asymmetry.

The neurological examination reveals the following findings: extremely severe clinical condition, tense anterior fontanel, absent reflexes, and frowning. Clinical suspicions include sepsis, encephalitis, and febrile seizures. Continue treatment with intravenous Levetiracetam and add oral Phenobarbital, intravenous glucocorticoids, and intravenous mucolytics.

On the 4th day of hospitalization, the patient remains in an extremely severe condition, presenting with hypertonia, edema of the lower limbs and scrotum, and anisocoria (left pupil larger than the right). A second transfontanelar ultrasound is performed, revealing: asymmetry of the bilateral fronto-parietal subarachnoid space, a left fronto-parietal hypoechoic-transonic collection, with a maximum thickness of 16 mm. It maintains ventricular asymmetry, with a slightly inhomogeneous aspect of the right frontal horn. A cranial CT scan was performed to provide greater diagnostic precision. The imaging revealed dilated pericerebral fluid spaces and asymmetry at the frontal level. Additionally, a subdural hypodense collection with a maximum thickness of 18 mm was identified, along with parafluid densities in the pericerebral fluid spaces.

On the 5th day of hospitalization, the blood culture results indicate a positive finding for Neisseria meningitidis. The pathogen is found to be susceptible to Cefuroxime, Ceftriaxone, Meropenem, Rifampicin, Trimethoprim-Sulfamethoxazole, and Chloramphenicol. Based on these findings, it is decided to reintroduce treatment with Ceftriaxone. Clinically, the patient mentains extremely severe conditions associated with palpebral edema.

The neurosurgical examination reveals a somnolent patient who is poorly responsive, does not open his eyes, and exhibits spontaneous symmetric limb movements of low amplitude. The recommendation is to perform a brain MRI with contrast for further evaluation.

6^{th} day in hospital: The brain MRI reveals left extranevraxial fluid accumulation with an appearance suggestive of a hydroma. No evidence of empyema or hemorrhage is observed. Upon re-examination by the neurologist, the patient is noted to have no seizures but continues to exhibit palpebral edema of the left eye and eyeball deviation.

Based on these findings, it is decided to reduce the doses of Phenobarbital and

Acetazolamide and to switch the mode of administration of Levetiracetam from intravenous to oral.

8th day in hospital: transfontanellar ultrasound with stationary appearance comparative to previous examination.

14th day in hospital: MRI re-evaluation stationary appearance comparative with previous examination.

The patient demonstrates a progressive and favorable clinical course, with no further seizures. Given the improvement in laboratory findings under antibiotic treatment, the patient is discharged on the 22nd day. The discharge plan includes continued oral antiepileptic treatment with Phenobarbital and Levetiracetam, as well as scheduled neurological and ophthalmological re-evaluations during the recovery period.

Table 1. Succesive characteristics of biological data

Biological analysis	1st day	2nd day	6th day	15th day	20th day
Hemoleucogram	Leukopenia, erhitrocytopenia, thrombocytopenia, Low Hemoglobin	thrombocytopenia	Leukocytosis, erhitrocytopenia, Low Hemoglobin	Leukocytosis, thrombocytosis	Thrombocytosis,
Coagulation	D-dimers, INR, APTT, PT ↑	D-dimers,PT, INR↑	D-dimers, INR↑	D-dimers ↑ APTT ↓	N
C-reactive Protein	12,83mg/dl	23,67 mg/dl	4,41 mg/dl	24,57mg/dl	<0,5mg/dl
Procalcitonin	14,7ng/ml	16,2ng/ml	0,508 ng/ml	7,81ng/ml	N
Transaminase	N	N	N	N	N
ESR	N		↑	↑	
LDH	N	↑	N	↓	N
CK	N	N	N	N	N
Glucose	66,6 mg/dl	N	N	N	N
Iron	12 mcg/dl				
Ionogram	Na↓	N	N		N
Immunogram	IgA,IgG↓				
Albumin	↓	↓	↓	↓	
Bilirubin	IB ↑	IB, DB↑	N	N	

DISCUSSION

Sepsis due to *Neisseria meningitidis* is an infection that is rapidly progressive and life-threatening in infants and young children. This bacterium indeed causes meningococcal meningitis and sepsis, two of the most severe infections of the pediatric population. Clinical manifestations can escalate very fast, leading to shock, failure of organs, and neurological complications that are serious. As in the case of the 2-month-old infant presented, early diagnosis and early aggressive treatment are critical. The clinical deterioration in the form of tonic seizures, anisocoria, and subdural hygroma points toward the continuous monitoring and a multidisciplinary approach such patients need.

The diagnosis of meningococcal sepsis is an integrated analysis of clinical suspicion, laboratory tests, and imaging studies. Blood cultures, as in the case presented, are a very important part in the recognition of the pathogen, while imaging techniques such as cranial CT and MRI are really necessary in the assessment for neurological complications like brain edema or subdural fluid collections. The development of evolving neurological symptoms in the patient, such as anisocoria and ptosis, further underlines the seriousness of the infection with its long-term sequelae of cognitive and motor impairments (10). Antibiotic treatment should be given according to the antibiotic susceptibility profile of *Neisseria meningitidis* to control the infection. In this case, the stepwise escalation from ceftriaxone to meropenem and linezolid, with a return to ceftriaxone once the pathogen was confirmed, represents an approach to optimization.

As common with sepsis induced by *Neisseria meningitidis*, DIC often follows in suit, and indeed, this case exhibited similar trends. This was a serious complication characterized by widespread clotting and bleeding, resulting from an excessively activated coagulation system. This condition significantly contributed to the sudden clinical deterioration observed in this patient. Such conditions require careful management with anticoagulation as supportive therapy to counteract the hypercoagulable state, along with fluid resuscitation and transfusions to address clotting factor deficiencies and maintain hemodynamic stability during treatment (5). In pediatric cases, DIC is associated with a higher mortality rate, making early recognition

and treatment vital. This is consistent with the findings from several studies which demonstrate that early intervention in sepsis, particularly in infants, can significantly reduce mortality and long-term disability (1).

The role of vaccination in preventing *Neisseria meningitidis* infections is something that cannot be denied. Vaccination has clearly been the major driving factor for a reduction in invasive meningococcal disease in many countries. These have involved conjugate vaccines against serogroups A, C, W, and Y and a monovalent vaccine for serogroup B; the number of cases has drastically declined since then (6).

These vaccines stimulate the immune response to produce antibodies against these serogroups, thereby preventing primary infections and hence their serious complications. The very low incidence of meningococcal infection in the developed world illustrates the efficacy of vaccination programs in controlling disease burden and averting life-threatening conditions (8).

CONCLUSION

This case of an infant demonstrates the fulminant course of *Neisseria meningitidis* infection with rapid neurological and systemic complications, disseminated intravascular coagulation, including tonic seizures, subdural hygroma, ventricular asymmetry, and anemia. Successful management was performed based on a multidisciplinary approach: early diagnosis by paraclinical investigations, appropriate antibiotic therapy, anticonvulsant treatment, and supportive care. This again highlights early intervention and close follow-up as key factors to decrease complications and mortality, along with improving the long-term outcome in severe pediatric sepsis.

Abbreviations:

INR- international normalized ratio

PT-prothrombin time

APTT- activated partial thromboplastin time

ESR- erythrocyte sedimentation rate

LDH- lactate dehydrogenase

CK-creatine kinase

CT- computerized tomography scan

MRI- magnetic resonance imaging

DIC- disseminated intravascular coagulation

REFERENCES

1. *Ebbesen, M. S., et al. (2018). Sepsis and Disseminated Intravascular Coagulation in Pediatric Patients: A Comprehensive Review. Pediatric Blood & Cancer, 65(9), e27099.*
2. *Hollingshead S, Tang CM. An overview of Neisseria meningitidis. Methods Mol Biol. 2019;1969:1–16.*
3. *https://www.ecdc.europa.eu/sites/default/files/documents/MEN%20AER%202021.pdf*
4. *Kvalsvig A.J., Unsworth D.J. The immunopathogenesis of meningococcal disease. J Clin Pathol. 2003;56:417–422. doi: 10.1136/jcp.56.6.417.*
5. *Levin, J. L. (2012). Disseminated Intravascular Coagulation in Pediatric Sepsis: Pathophysiology and Management. Pediatric Critical Care Medicine, 13(2), 158-164.*
6. *MacLennan, J. M., et al. (2013). Vaccination and Prevention of Meningococcal Disease: A Global Perspective. Lancet Infectious Diseases, 13(3), 229-238.*
7. *McCarthy, P. C., Sharyan, A., & Sheikhi Moghaddam, L. (2018). Meningococcal Vaccines: Current Status and Emerging Strategies. Vaccines, 6(1), 12. https://doi.org/10.3390/vaccines6010012*
8. *Meningococcal Vaccine Study Group. (2019). Impact of Vaccination on the Incidence of Meningococcal Disease in Europe. Vaccine, 37(2), 290-295.*
9. *Olbrich KJ, Müller D, Schumacher S, Beck E, Meszaros K, Koerber F. Systematic review of invasive meningococcal disease: sequelae and quality of life impact on patients and their caregivers. Infect Dis Ther. 2018;7:421–38. doi:10.1007/s40121-018-0213-2.*
10. *Peltola, H., et al. (2006). Invasive Meningococcal Disease in Children: Pathogenesis, Treatment, and Prevention. Clinical Infectious Diseases, 43(10), 1299-1305.*
11. *Pelton SI. The global evolution of meningococcal epidemiology following the introduction of meningococcal vaccines. J Adolesc Health. 2016;59:S3–11. doi:10.1016/j.jadohealth.2016.04.012.*
12. *Rosenstein, N. E., Perkins, B. A., Stephens, D. S., Popovic, T., and Hughes, J. M.(2001). Meningococcal disease. N Engl. J. Med. 344 (18), 1378–1388. doi: 10.105nejm200105033441807*
13. *Stephens, D. S., Greenwood, B., and Brandtzaeg, P. (2007). Epidemic meningitis,meningococcaemia, and Neisseria meningitidis. Lancet 369 (9580), 2196–2210.doi: 10.1016/s0140-6736(07)61016-2*
14. *Thompson MJ, Ninis N, Perera R, Mayon-White R, Phillips C, Bailey L, Harnden A, Mant D, Levin M. Clinical recognition of meningococcal disease in children and adolescents. Lancet. 2006;367:397–403. doi:10.1016/S0140-6736(06)67932-4.*
15. *Wang B, Santoreneos R, Giles L, Haji Ali Afzali H, Marshall H. Case fatality rates of invasive meningococcal disease by serogroup and age: a systematic review and meta-analysis. Vaccine. 2019;37:2768–82. doi:10.1016/j.vaccine.2019.04.020.*