CASE REPORTS

LATE-ONSET NEONATAL SEPSIS CAUSED BY GROUP A STREPTOCOCCUS - AN UNLIKELY AGENT

SÉPSIS NEONATAL TARDIA A STREPTOCOCCUS DO GRUPO A - UM AGENTE IMPROVÁVEL

Ana Ventura¹, Catarina Rúbio⁴, Diogo Rodrigues⁴, Inês Silva⁴, Ana Peres⁴, Florbela Cunha⁴

ABSTRACT

Neonatal sepsis due to group A Streptococcus is rare and has a high associated mortality. The case of a 14-day-old female neonate who presented to the Emergency Department with feed refusal and hyporeactivity is reported. The girl was born at 36 weeks of gestation and had an unremarkable pregnancy and birth. Peripheral white blood cell count was 18.100/mm³ with 81% neutrophils, and C-reactive protein was 13.6 mg/dL. Urinalysis, cerebrospinal fluid cytochemical examination, and chest X-ray were normal. A multisensitive group A Streptococcus was isolated in the blood culture and ten-day course of ampicillin was completed. Urine and cerebrospinal fluid cultures were negative. All co-inhabitants were tested for the presence of group A Streptococcus antigen in the oropharynx, which was positive in a two-year-old cousin.

Group A Streptococcus is an uncommon neonatal sepsis agent. Transmission in the community through a carrier should be considered. This case highlights the importance of infection preventive measures for the newborn at home.

Keywords: neonatal sepsis; Streptococcus pyogenes; streptococcal M protein

RESUMO

Sépsis neonatal tardia por Streptococcus do grupo A é uma entidade rara, com mortalidade elevada. É descrito o caso de um recém-nascido do sexo feminino, com 14 dias de vida, que recorreu ao Serviço de Urgência por recusa alimentar e hipo-reatividade. Este tinha nascido às 36 semanas de gestação, tendo a gravidez, parto e período neonatal decorrido sem intercorrências. Entre os exames realizados destacam-se a contagem leucocitária de 18.100/mm³ com 81% de neutrófilos, proteína C-reativa de 13.6 mg/dL, e exame sumário de urina, exame citocitômico do líquor e radiografia torácica sem alterações. Por isolamento de Streptococcus do grupo A na hemocultura, o recém-nascido cumpriu dez dias de ampicilina. A cultura do líquor e urocultura foram negativas. Foi pesquisada a presença de antigênio de Streptococcus do grupo A na orofaringe em todos os conviventes, sendo positiva numa prima com dois anos.

O Streptococcus do grupo A raramente é descrito como agente de sépsis neonatal e a sua transmissão na comunidade através de um portador deve ser considerada. Com este caso, pretende reforçar-se a importância das medidas de prevenção da infeção nos cuidados de puericultura no domicílio.

Palavras-chave: proteína M estreptocócica; sépsis neonatal; Streptococcus pyogenes

¹. Pediatrics Department, Hospital de Santa Maria, Centro Hospitalar Universitário Lisboa Norte. 1649-035 Lisboa, Portugal. patriciaventura26@gmail.com
². Pediatrics Department, Hospital Vila Franca de Xira. 2600-009 Vila Franca de Xira, Portugal. catarinarubio@netcabo.pt; inesvazsilva83@gmail.com; anacrperes@gmail.com; flor.cunha@gmail.com
³. Women, Children and Adolescents Area, Centro Hospitalar Universitário de Lisboa Central. 1169-045 Lisboa, Portugal. goncalves_rodrigues88@hotmail.com

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INTRODUCTION

Sepsis substantially contributes to neonatal morbidity and mortality. When occurring after 72 hours of life, it is defined as late-onset neonatal sepsis (LOS). LOS has been well studied both in premature and hospitalized neonates. Immaturity, invasive interventions, failure of early breastfeeding, prolonged parenteral nutrition, and hospitalization are known risk factors.\(^1\)\(^2\) While early-onset neonatal sepsis (EOS) is usually associated with vertical transmission, microbiology of LOS can reflect the nosocomial or community environment, with the highest incidence observed between ten and 22 days of life.\(^1\)

The causative pathogens of LOS vary geographically and differ from EOS. Coagulase-negative Staphylococcus are the predominant pathogens of hospital-acquired LOS in industrialized countries, while Escherichia coli and group B Streptococcus are the main agents of community-acquired LOS.\(^1\)\(^2\)

With the advent of antibiotics, neonatal sepsis caused by Group A Streptococcus (GAS) became rare, but a high mortality rate is still observed.\(^4\)\(^5\) According to the World Health Organization, incidence of neonatal GAS bacteremia is 0.55 per 1000 live births.\(^6\)

Neonatal sepsis has nonspecific clinical signs and symptoms, such as grunting, temperature instability, respiratory distress, apnea, jaundice, feeding intolerance, bulging fontanelle, seizures, and skin lesions.\(^7\)

The spectrum of clinical presentations of invasive GAS infections is broad, with LOS most frequently associated with soft tissue infections and meningitis, and EOS with pneumonia/empyema, soft tissue infections, and toxic shock-like syndromes.\(^4\)

CLINICAL CASE

A 14-day-old female neonate was taken to the Emergency Department due to feeding refusal and hyporeactivity since the day before. She did not have a fever.

Pregnancy was unremarkable and the female infant was born by normal delivery at 36 weeks of gestation, three hours after spontaneous membrane rupture. Group B streptococcus screening was not performed. The newborn was discharged on the third day of life.

On arrival to the emergency room, the newborn was hypotonic, with a weak cry, pallor, and signs of dehydration (dry mucous membranes, depressed anterior fontanelle, and weight loss). She was hemodynamically stable, without respiratory distress or groaning. There was no skin rash or signs of cutaneous inflammation.

Blood samples revealed a leukocyte count of 18.100/mm\(^3\), with 81% neutrophils; platelet count of 28.7000/mm\(^3\); C-reactive protein of 13.6 mg/dL (normal range <0.5 mg/dL); glucose of 48 mg/dL; sodium of 147 mEq/L; and normal renal function. Venous blood gas showed respiratory acidosis (pH 7.17; pCO\(_2\) 76.9 mmHg; base excess −3 mmol/L; HCO\(_3\) 27.9 mmol/L; lactates 4.08 mmol/L). Urinalysis, cerebrospinal fluid cytochemical examination, and chest radiograph were normal.

Sepsis was the main differential diagnosis and intravenous cefotaxime, ampicillin, and fluid therapy were started. The patient had a good clinical evolution, with no hemodynamic or respiratory instability, and no fever or cutaneous signs.

A multisensitive GAS (emm type STG7882) was isolated in the blood culture and ten-day treatment with ampicillin was completed. Cerebrospinal fluid and urine cultures were negative.

All six co-inhabitants were investigated for oropharynx GAS. GAS antigen positivity was only reported in a two-year old cousin (who presented amygdalin hypertrophy without hyperemia or exudates and no fever), who was treated.

DISCUSSION

GAS is an uncommon cause of neonatal sepsis. A nonspecific clinical presentation (hypotonia, weak cry, pallor, and dehydration) was observed in this case. Fever was not present in this patient, although it is a common sign in LOS associated with GAS and may reflect the neonate’s inability to respond to the pathogen.\(^4\) No typical rash or local soft tissue infection signs suggesting GAS infection were observed, namely impetigo, cellulitis, omphalitis, or paronychia.\(^6\)\(^9\)

Other focal infections – as pneumonia and meningitis – were excluded.

Pathophysiology of LOS due to GAS is poorly understood and does not seem to be related to perinatal factors. Transmission in the community through a carrier, usually the mother, should be considered.\(^6\)\(^9\) In this case, screening of all co-inhabitants was performed through rapid GAS antigen detection test in oropharyngeal secretions. This is a simple and very useful test in clinical practice. It has 85.6% sensitivity and 95.4% specificity, high enough to prevent unnecessary use of antibiotics.\(^10\)

The index case was potentially a two-year-old cousin of the neonate, who was identified as an asymptomatic carrier. The prevalence of GAS carrier status in children is 12%, varying with age. Carriers’ screening and treatment is recommended in some situations, such as outbreaks of invasive GAS disease.\(^11\)

Although molecular confirmatory study of the index case was not been performed, the carrier was treated to prevent
reinfection of the neonate.

The high rate of community-acquired resistant sepsis is a serious global public health concern, supporting empirical treatment with cefotaxime and ampicillin. For GAS infections, benzylpenicillin remains the antibiotic of choice, as resistance has not been described. Alternatively, ampicillin may be used, as all GAS reported are susceptible to both antibiotics. GAS has a high rate of resistance to gentamicin and increasing erythromycin resistance in some countries. Clindamycin-resistant strains are mainly associated with multi-resistant clones.

Several virulence factors contribute to the pathogenic complexity of GAS. One of the most important is M protein encoded by the emm gene. To date, more than 200 emm types and subtypes have been identified, which vary according to geographic location. Certain emm types are associated with specific manifestations, but few studies exist in pediatric populations. In Europe, emm types 1, 3, 4, 12, and 28 are the most prevalent in children. The emm type observed in this case (STG7882) is rare, and it can also be found in group G Streptococcus, supporting the interspecies genetic transfer of emm alleles. Recently, Seale et al described a case of invasive neonatal disease in Kenya with this emm type, with cutaneous and subcutaneous signs. Although molecular biology typing is possible, more studies are required to define its role in clinical practice.

This case highlights the importance of infection preventive measures directed at the newborn at home. In addition to basic hygiene measures, hand wash before picking up the baby should be routine, contact with poorly healthy persons should be restricted, and kissing the baby’s face should be avoided to prevent contagion.

Take-home messages:
- LOS caused by GAS is rare.
- Symptoms are usually nonspecific, but presence of soft tissue infection or toxic shock-like syndrome should make the clinician consider this agent.
- Rapid GAS antigen detection test can be used to determine the index case and avoid reinfection.
- Penicillin/ampicillin are the antibiotics of choice, since associated resistance has not been described.

REFERENCES


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CORRESPONDENCE TO

Ana Ventura
Pediatrics Department
Hospital de Santa Maria
Centro Hospitalar Universitário Lisboa Norte
Av. Prof. Egas Moniz s/n
1649-035 Lisboa
Email: patriciaventura26@gmail.com

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