CASE REPORT

Streptococcus pneumoniae Neonatal Early-Onset Sepsis: Case Report

Joana Sousa Martins, Bruno Sanches, António Gomes, Anselmo Costa

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Abstract

Streptococcus pneumoniae is an uncommon cause of neonatal sepsis, but it is frequently associated with an aggressive clinical course. A full-term newborn with an uneventful pregnancy presented in the first hours of life with worsening general condition and seizures. Blood testing was suggestive of infection, and cerebrospinal fluid was consistent with meningitis. There was progressive deterioration with refractory hypotension, intravascular disseminated coagulopathy, and oliguria. He was pronounced dead on the 6th day of life. Blood culture was positive for *Streptococcus pneumoniae*. After birth, the mother presented with sepsis with the same agent being isolated in the blood cultures. Pneumococcal serotyping identified the serotype 3 in both the newborn and mother samples. Although uncommon, *Streptococcus pneumoniae* can cause clinically significant disease in newborns, with higher mortality compared with the common agents of early onset neonatal sepsis. Maternal bacteriemia is associated with a worse prognosis.

Keywords: Age of Onset; Infant, Newborn; Infectious Disease Transmission, Vertical; Neonatal Sepsis/etiology; Streptococcus pneumoniae

Introduction

Streptococcus pneumoniae is recognized as an important cause of morbidity and mortality in childhood, but there are rather few reported cases of neonatal sepsis, with incidences described between 1% and 11%.[1-8] *Streptococcus pneumoniae* early-onset sepsis is clinically indistinguishable from other etiologies, but often has a very aggressive clinical course, with a high mortality rate (up to 50%).[5-9] Colonization of the genitourinary tract by *Streptococcus pneumoniae* is very rare (approximately 0.03%)[4] and usually transitory. It has been described in cases of pelvic infections, after gynecological surgery, in the presence of a foreign body in the genitourinary tract, after a recent delivery or in association with pneumonia. Concomitant maternal bacteremia is uncommon in *Streptococcus pneumoniae* neonatal sepsis cases, being associated with a worse prognosis in the newborn.[3,5,9]

In this article, we report a case of *Streptococcus pneumoniae* early-onset neonatal sepsis with a fatal outcome, associated with maternal bacteremia to the same agent.

Case Report

Full-term male newborn, with birth weight appropriate for gestational age (39 weeks and 3 days, 3090 g), delivered by vacuum extraction followed by forceps, after an uneventful pregnancy, at a level 2 hospital. Group B *Streptococcus* screening in the vaginal and rectal exudate was negative, the rupture of membranes was spontaneous two hours before delivery and there was no record of intrapartum fever. The Apgar score was 7 at the first minute and 8 at the fifth minute.

At 10 hours of life, he started intermittent grunting and was put under close clinical surveillance. At 34 hours of life, there was clinical worsening with persistent grunting, global hypotonia, skin pallor, and increased capillary reperfusion time. Blood pressure and heart rate were normal. The laboratory evaluation carried out showed hemoglobin 12.6 g/dL, leukocytes 1 x 10^9 cells/L with 73.2% neutrophils, platelets 103,000 cells/µL, C reactive protein 15.7 mg/dL, and lactates 70 mg/dL. A chest X-ray showed bilateral interstitial infiltrate, with no signs of consolidation or other changes. Empirical antibiotic therapy was started with ampicillin (200 mg/kg/day) and gentamicin (5 mg/kg/day). At 40 hours of life, he started clonus of the four limbs, which motivated the start of therapy with phenobarbital and invasive ventilatory support. Lumbar puncture was performed, with a yellow-citrus liquid, 23 cells (98% polymorphonucleate), proteins 498 mg/dL and glucose

Pediatrics Department, Hospital Garcia de Orta, Almada, Portugal
Corresponding Author
Joana Sousa Martins
https://orcid.org/0000-0002-3636-8857
joanam1@campus.ul.pt
Hospital Garcia de Orta, Avenida Torrado da Silva, 2805-267 Almada, Portugal
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< 2 mg/dL. Given these results, compatible with the diagnosis of meningitis, cefotaxime (100 mg/kg/day) was added. On the second day of admission, hemorrhagic suffusions of the limbs appeared with progressive worsening (Fig. 1). A transfontanellar ultrasound showed evidence of cerebral edema, without hemorrhage. Due to hypotension, gradual inotropic support was started with dopamine (maximum dose of 20 µg/kg/min), dobutamine (maximum dose of 15 µg/kg/min), and noradrenaline (maximum dose of 5.3 µg/kg/min). Echocardiography showed right ventricular dysfunction, left ventricular systolic function at the lower limit of normal (ejection fraction of 25.4%), and moderate secondary pulmonary hypertension. Successive transfusions of fresh frozen plasma, fibrinogen, erythrocyte, and platelet concentrates were necessary. The convulsive condition became refractory, which led to an infusion of midazolam and therapy with phenytoin. He maintained progressive clinical deterioration, developing oligoanuria and anasarca on the 5th day of life. On this date, the result of the blood culture was known, with *Streptococcus pneumoniae* growth, sensitive to penicillin. Bacteriological examination of the cerebrospinal fluid was sterile. On the 6th day of life, fixed mydriasis was observed and a transfontanellar ultrasound revealed an extensive frontal-parietal-occipital hemorrhagic stroke. The newborn was shortly thereafter pronounced dead.

On the fourth day after birth, the mother developed a fever and worsening general condition. The laboratory evaluation revealed a C reactive protein of 34 mg/dL and the three blood cultures drawn also identified *Streptococcus pneumoniae*. The vaginal exudate was negative. She completed 14 days of intravenous penicillin with complete recovery. Subsequently, *Streptococcus pneumoniae* serotyping was performed, and serotype 3 was identified in the blood cultures of the mother and the newborn.

Discussion

There are no recent published national data on the frequency of *Streptococcus pneumoniae* early-onset neonatal sepsis. We are aware of two cases in the last five years, one case isolated from blood culture (serotype 23A) and one case isolated from cerebrospinal fluid culture (serotype 8).

In the present case, as previously reported in some cases of *Streptococcus pneumoniae* early-onset sepsis,[7] the classic risk factors for early-onset sepsis were not present. The most frequent way of transmission is vertical, through the colonization of the maternal genital tract. Although this colonization is uncommon (approximately 0.03%),[4] several articles suggest high rates of neonatal infection, in contrast to what happens with group B *Streptococcus.*[1,6] There are reports of rare cases of placental transmission of *Streptococcus pneumoniae*[3,5] and, when associated with concomitant maternal bacteremia, the newborn usually presents

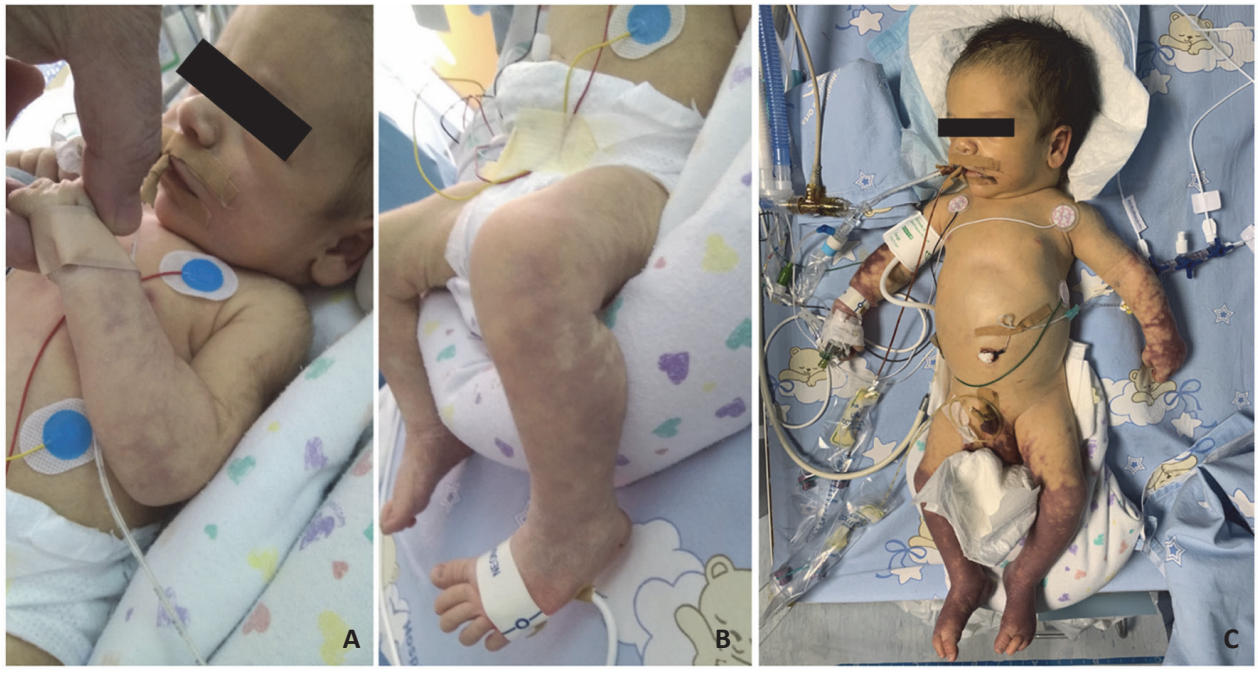

Figure 1. Progression of hemorrhagic suffusions of the extremities from the second (A, B) to fourth (C) day of admission.

with a more aggressive clinical course.[3,5,9] In this case, the source of maternal bacteremia was not identified, and the cultural exams of the maternal genital tract were negative. Thus, and since the isolated serotype in the mother was the same as the one found in the newborn, we admit that the transmission could have occurred through the transplacental route.

Regarding the clinical manifestations of *Streptococcus pneumoniae* early-onset neonatal sepsis, most newborns present with symptoms in the first 48 hours of life, indistinguishable from other agents such as group B *Streptococcus* or *Escherichia coli*, despite a more aggressive clinical course.[3,6,10] The majority is characterized by bacteremia, associated with meningitis and/or pneumonia, often manifesting with severe hypotension and leukopenia, as reported in this case.[1,2,5,10]

The recommended antibiotic therapy in these cases is the same as that used in the remaining cases of early-onset neonatal sepsis. There are some reports of cases with an aggressive clinical course associated with refractory hypotension in which oxygenation using an extracorporeal membrane was successfully used.[3,5] Regarding possible adjuvant therapies, despite some positive results with the use of intravenous immunoglobulin,[5,9] studies carried out so far have not shown superiority compared to isolated antibiotic therapy.[11]

Several clinical conditions are known to be associated with an increased risk of invasive *Streptococcus pneumoniae* infection, including some primary immunodeficiencies, specifically B cell changes, complement deficit, congenital asplenia, and changes in the Toll-like receptor pathway.[12-15] Although there are no well-defined guidelines for immunological assessment after a first case of invasive pneumococcal disease, many authors recommend that these patients undergo a screening evaluation for primary immunodeficiency allowing for timely diagnosis, early treatment and reduction of associated morbidity and mortality.[12-15] The newborn, if he would have survived, should have undergone this study.

The 13-valent pneumococcal polysaccharide conjugate vaccine (Prevenar 13®) is part of the Portuguese national vaccination program but does not include all of the serotypes of *Streptococcus pneumoniae* described as the cause of early-onset sepsis (1 to 12, 14, 17, 18, 19, 23, 27, 28, 31, and 39).[2,7,9,10] It is also important to emphasize that most women of childbearing age are currently not vaccinated, as was seen in this case. In the reported case, the identified serotype was serotype 3, included in Prevenar 13®.

Possible strategies for preventing *Streptococcus pneumoniae* early-onset neonatal sepsis include testing for *Streptococcus pneumoniae* in vaginal exudate (with antibiotic prophylaxis during labor, if positive) and vaccinating pregnant women with pneumococcal vaccine 13-valent or 23-valent in the third trimester, to passively protect newborns through the transplacental transmission of antibodies.[2,6,9,10] A recent Cochrane library review on this subject reported that there was no evidence of an effect of pneumococcal vaccination during pregnancy in preventing neonatal infections. However, there were only a few trials reporting this outcome with an overall poor quality of evidence.[16] There is still insufficient scientific evidence for the implementation of such measures, so future studies on epidemiological surveillance and assessment of risk factors associated with neonatal *Streptococcus pneumoniae* sepsis are essential as well as the evaluation of these and other possible prevention strategies.

The reported case emphasizes the need to consider a wide range of microorganisms in the differential diagnosis of early-onset neonatal sepsis. Although uncommon, *Streptococcus pneumoniae* can cause clinically significant disease in newborns, with greater severity and mortality when compared with the most common agents of early-onset sepsis. In the absence of sufficient scientific evidence to implement specific preventive measures against early-onset sepsis for this agent, early and aggressive treatment of newborns remains the best therapeutic option.

WHAT THIS CASE REPORT ADDS

- Although an uncommon cause of early-onset neonatal sepsis, *Streptococcus pneumoniae* usually causes a severe disease with high associated mortality and should be kept in mind as a possible etiology of early-onset neonatal sepsis.
- Concomitant maternal bacteremia is uncommon in *Streptococcus pneumoniae* neonatal sepsis cases, being associated with a worse prognosis in the newborn.
- Testing for *Streptococcus pneumoniae* in vaginal exudate (with antibiotic prophylaxis during labor, if positive) and vaccinating pregnant women with pneumococcal vaccine 13-valent or 23-valent in the third trimester are possible future strategies for preventing *Streptococcus pneumoniae* early-onset sepsis.

Conflicts of Interest

The authors declare that there were no conflicts of interest in conducting this work.

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Confidentiality of data

The authors declare that they have followed the protocols of their work centre on the publication of patient data.

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Sepsis Neonatal de Início Precoce por *Streptococcus pneumoniae*: Caso Clínico

Resumo

O *Streptococcus pneumoniae* é uma causa rara de sepsis neonatal, mas associa-se frequentemente a uma evolução clínica muito agressiva. Um recém-nascido de termo, fruto de uma gravidez sem intercorrências, iniciou nas primeiras horas de vida agravamento do estado geral e convulsões. A avaliação laboratorial foi sugestiva de um quadro infecioso e o exame citoquímico do líquor foi compatível com meningite. Assistiu-se a agravamento progressivo com hipotensão refratária, coagulação intravascular disseminada e oligúria, acabando por falecer ao 6º dia de vida. Na hemocultura foi isolado *Streptococcus pneumoniae*. A mãe iniciou no pós-parto quadro compatível com sepsis, com isolamento do mesmo agente nas hemoculturas. A serotipagem identificou o serotipo 3 nas amostras da mãe e do recém-nascido. Apesar de pouco frequente, o *Streptococcus pneumoniae* pode causar doença clinicamente significativa no recém-nascido, com maior gravidade e mortalidade relativamente aos agentes habituais de sépsis neonatal precoce. A presença de bacteriemia materna está associada a pior prognóstico.

Palavras-Chave: Idade de Início; Recém-Nascido; Sepsis Neonatal/etiologia; Streptococcus pneumoniae; Transmissão Vertical de Doença Infeciosa