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## ***Streptococcus pneumoniae* as an Unusual Aetiology of Meningitis Sepsis in a 72 Hours Newborn: A Case Report**

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### Abstract

We report a case of pneumococcal neonatal meningitis in an Italian girl, occurred 3 days after birth. CSF microscopic examination revealed the presence of Gram Positive diplococci, identified as *S. pneumoniae* after detection of pneumococcal capsular antigen. Tests for Group B Streptococcus on mother and child were both negative. The case was peculiar because in industrialized countries the most common agents responsible of neonatal meningitis are GBS, *E. coli* and *Listeria monocytogenes*, where pneumococcal meningitis in the neonatal period is quite uncommon: It is then necessary to consider that, in any case of early onset neonatal meningitis, *S. pneumoniae* is a possible yet uncommon causative agent, and that the microbiological profile of early onset neonatal meningitis in industrialized countries might change substantially because of migratory streams and the subsequent diffusion of emerging microorganisms, which are unusual at the present time.

**Keywords:** Pneumoniae; *E. coli*; Meningitis; Neonatal

### Introduction

We talk of neonatal meningitis when a microorganism is isolated in CSF during the first month of extra uterine life. Clinically, this infection is usually presents as a septic condition associated to neurological signs such as irritability, seizures, muscle hyper tony, vomiting, sharp cry, hyperpyrexia and pulsing anterior fontanelle. In pediatric population mortality rates vary from 20% to 40% with a 20% risk of CNS sequelae and permanent acoustic dysfunctions, particularly related to pneumococcal infection [1]. The most frequent cause of neonatal meningitis is Group B *Streptococcus* (GBS), with

vertical transmission. Pneumococcal infection can be transmitted through contact with infected subjects or asymptomatic carriers, while vertical transmission is a rare yet possible occurrence. The incubation period may vary from 1 to 3 days. This case report is aimed to be an addition to the existing literature regarding cases of neonatal meningitis, considered that in industrialized countries this infection still is, along with sepsis and pneumonia, the first cause of death of the newborn in the first 60 days of life, advancements in antibiotic therapy notwithstanding [2].

### Case Description

The patient was given birth at 41 weeks and 2 days, after labor was induced because of oligohydramnios; no other complications occurred during pregnancy and maternal serologic tests for Group B *Streptococcus* were negative. At birth, the patient showed good adaptation to extra uterine life (APGAR 10/10 at 1 and 5 minutes) and both anthropometric measurements and weight were within normal range. At day 3 after birth, because of the onset of hyperpyrexia, trunk and limb rigidity and sunset eyes, blood tests were carried out, showing an increase in inflammatory markers (PCR 10.9 mg/dl). At the same time blood culture was found positive for *S. Aureus* and *S. Warneri*, while urine culture was found positive for *Serratia Marcescens* (>100.000 CFU/ml), for this reason empirical antibiotic therapy with intravenous Ampicilline and Metilmicine was initiated. The patient was then transferred to neonatal ICU after her clinical condition worsened, with hypo reactivity, axial hypo tony, limb hyper tony, absence of the reflex of Moro, shrill cry, pallor and mild jaundice. A lumbar puncture was then performed because of the suspicion of CNS involvement: the turbid appearance of the CSF sample suggested continuing antibiotic therapy with Ampicilline, Sulbactam and Amikacine. CSF laboratory examination showed an elevated protein concentration and WBC count, while microscopic examination revealed the presence of Gram

positive diplococci, further confirmed when PCR detected the presence of *S. pneumoniae* capsular antigen; no viral DNA was found. Blood tests showed an elevated WBC count (13210 mm<sup>3</sup>) and a further raise in PCR (177mg/dl); the subsequent blood culture was positive for Methicillin resistant strains of *S. Aureus* and *S. Epidermidis*, which forced to replace Amikacine with Vancomicine. Such therapy was continued until day 14.

In order to further investigate the patient's neurological condition, diagnostic imaging procedures were carried out: serial brain echography evidenced a marked oedema without signs of active hemorrhagic foci. Hemi cranial electroencephalography detected nonspecifically anomalies in the front cerebral regions and subsequent MRI showed no signs of hemorrhagic, ischemic or expansive lesions. Serum levels of immunoglobulins and complement factors were then investigated because an immunodeficiency condition was suspected, but no abnormalities were found. Other blood tests were carried out during the following period of hospitalization, showing a progressive decrease in both inflammatory and infection markers, until their complete normalization at day 26, after which the patient was discharged with a final diagnosis of *S. pneumoniae* meningitis. At discharge, physical examination showed no abnormalities, the patient fed well with both maternal and artificial milk, with a weight gain of 850 g. Neurologic and auditory follow up exams were then programmed.

## Discussion

The causative agents of neonatal bacterial meningitis are different geographically. In most developed countries the main causative agents for neonatal bacterial meningitis isolated from cerebrospinal fluid (CSF) are Group B Streptococcus (GBS), *E. coli*, *Listeria monocytogenes* and at least *S. pneumoniae*. The Reasons for this may include genetic differences in immune response and possibly geographic differences in laboratory techniques for pathogen isolation and reporting and they are also influenced by maternal and infant risk factors, prevention and treatment strategies of the country [3]. Pneumococcal meningitis in the neonatal period is uncommon (only 28 cases reported in literature before 1945), however it's related to high mortality and morbidity rates, in particular neurological sequelae are a frequent occurrence. Neonatal and maternal risk factors for developing neonatal meningitis include low birth weight, prematurity, premature ruptures of membranes, maternal chorioamnionitis and low socioeconomic status. The newborn is particularly susceptible to infection as the immature immune system is deficient in humoral and cellular immune responses: for this reason the patient's immune state has been assessed, but test findings were normal. On the other hand, the importance of maternal infection was already highlighted by Berman and Banner in 1922, when they observed in their study that, in more than half of mothers with affected newborns, the same microorganism was isolated. The evidence that obstetrical complications increase the risk of infection, and that infection occurs within six days after birth, suggests that it is transmitted during childbirth, through placenta or birth canal [4]. However,

*S. pneumoniae* is not usually part of the vaginal flora, and it is present only in 0.03% to 0.75% of pregnant women [5]. Meningitis, as in the case here discussed, is accompanied by sepsis in 25% of cases, not necessarily caused by the same microorganism. This result in increased morbidity and mortality rates [6]. These elements lead to the following observations: if meningitis is suspected, it is necessary to initiate an aggressive empirical antibiotic treatment, which must extend to all the pathogen agents potentially involved: the combination of ampicillin with an aminoglycoside, or a third generation cephalosporin, is effective. However, it is necessary to consider that also *S. pneumoniae* is a possible etiological agent, which responds well to the administration of Vancomicine, and that such treatment must be initiated when microscopic confirmation is available: the finding of Gram positive diplococci in the blood smear is sufficient, as suggested by Yagmur Bas [6]. Moreover, considered that *S. pneumoniae* is an uncommon agent in neonatal meningitis, it is advisable to investigate the state of cellular immune response of the affected newborn, in order to rule out any immunodeficiency condition.

## Conclusion

A large scale world health organization (WHO) study conducted in various countries of meningitis belt has documented that *S. pneumoniae* being the most common organism. This lead us to the hypothesis that, in the next years, the microbiological profile of early-onset neonatal meningitis in industrialized countries will change substantially because of migratory streams and the subsequent diffusion of emerging microorganisms, which are unusual at the present time. Perhaps, new infective screening panels will be necessary during pregnancy, in order to carry out a highly effective antibiotic prophylaxis, rationally based on laboratory findings. In Spain, there are 16 published cases of neonatal pneumococcal disease: 14 with early-onset and 2 with late-onset.6 The administration of heptavalent pneumococcal vaccines over recent years, and most recently the 10- and 13-valent types (including the 7F, 3, and 6A serotypes, which are an important cause of invasive pneumococcal disease worldwide), has reduced the transmission of diseases due to pneumococcus in the general population (from 50-100 to 9 cases for every 100000 people) and, consequently, the incidence of neonatal invasive pneumococcal disease has decreased. Vaccination during the third trimester of gestation could be a measure to follow in the future, although there are no conclusive studies that currently confirm this. Cases such as the one here described demonstrate how molecular research, through the actuation of new diagnostic methods, is nowadays vital to reach an etiological diagnosis, in particular for those infections requiring prompt treatment in order to decrease morbidity and mortality rates. This case report allows highlighting that in medicine, paradigms are subject to continuous evolution and changes, which force clinicians to adopt new diagnostic and therapeutic strategies, especially in infectious field, where statistics show a constant evolution of etiological profiles of the main diseases which need, in the

neonatal period, prompt treatment with the appropriate instruments.

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