INVASIVE PNEUMOCOCCAL DISEASE IN HIGH RISK PATIENTS

Monica Luminos1,2, Anca Draganescu1, Magda Vasile1, Angelica Visan1,2, Cristina Negulescu3, Cornelia Dogaru1, Diana Slavu1, Anuta Bilasco1

1 National Institute for Infectious Diseases “Prof Dr Matei Bals” Bucharest
2 UMF “Carol Davila”, Bucharest

Abstract
Introduction. The clinical and epidemiological burden of Invasive Pneumococcal Disease (IPD) is still very increased. In the pathogenesis of Invasive Pneumococcal Disease there are three essential elements involved: nasopharyngeal colonization, the inflammatory response of the host and also the effect of viral and bacterial co-infections on pneumococcus virulence.

The highest susceptibility for IPD is found in children less than 5 years of age, especially in those under 2 years of age. Concerning the risk factors for IPD, the most important are congenital malformations or trauma of the skull with rhinoliquorrhea and otoliquorrhea, along with immunodeficiency and other chronic conditions.

Material and method: This paper highlights skull malformations with corticospinal fluid (CSF) fistula as a risk factor in developing IPD, like sepsis or recurrent bacterial meningitis. During 2014-2015 in our clinic there have been 3 cases of sepsis with meningitis with Streptococcus pneumoniae in children with CSF fistula. We report the case of a 4-year-old patient with sepsis and recurrent meningitis with Streptococcus pneumoniae serotype 6B, resistant to Penicillin, with repeated surgical interventions for naso-frontal CSF fistula with rhinoliquorrhea.

Conclusions: The diagnosis and treatment of these affections need considerable effort from a multidisciplinary medical team with the ultimate goal of making a quick recovery of the patient and avoidance of recurrence. During 2010-2013, ACIP (Advisory Committee on Immunization Practices) published new recommendations for vaccination with PCV13 and PPSV 23 regarding patients with high risk factors for IPD, highlighting the ongoing clinical burden of this affection.

Key words: CSF fistula, child, invasive pneumococcal disease, rhinoliquorrhea

Introduction
Streptococcus pneumoniae is a major cause of severe invasive infection like meningitis, bacteremia and pneumonia with bacteremia/empyema. Children less than 5 years of age, and especially less than 2 years of age, are most susceptible to pneumococcal infections, due to the immaturity of their immune system, frequent exposure and colonization with Streptococcus pneumoniae.1

Amongst the 93 different serotypes of Streptococcus pneumoniae (grouped in 46 serogroups) identified based on antigenic differences in the structure of the polysaccharide capsule, 10 serogroups are responsible for the majority of cases of invasive pneumococcal disease. The last serotype described was 11E,2,3,5 The most frequent serotypes involved in IPD in children are 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F,1,5,6 The incidence of invasive infections, due to these serotypes, varies significantly according to age of the population, ethnicity, seasonal and geographic distribution.1

Factors that increase the risk for invasive pneumococcal disease are chronic conditions (chronic heart disease, chronic lung disease, diabetes mellitus, chronic renal disease, nephrotic syndrome), congenital or acquired immunodeficiency, functional or anatomic asplenia, cochlear implant, CSF fistula and some specific ethnic groups.1

Case presentation
We report the case of a 4 year-old boy admitted to our intensive care unit for high fever (39 C), vomiting, headache and meningeal syndrome, symptoms which started on the day of admission. His personal medical history revealed one episode of pneumococcal meningitis at the age of 1 year, idiopathic intracranial hypertension syndrome diagnosed at the age of 2 years and CSF fistula with rhinoliquorrhea diagnosed at the age of 3 years. One surgical intervention was performed for the closure of the CSF fistula, but after 1 month rhinoliquorrhea reappeared.

At the time of past clinical presentations with intracranial hypertension syndrome, a differential diagnosis of intracranial hypertension was performed. We excluded, based on clinical examination, cerebral imaging and laboratory blood parameters, acute meningitis and encephalitis, intracranial tumors, thrombosis of the intracranial venous sinuses, hydrocephaly, hypothyroidism, hypocalcaemia, high blood pressure.

On admission the child was febrile (38.5 C), pale, without cutaneous eruptions, with photophobia, somnolent but oriented to time and space, with a heart rate of 120 beats per minute and a normal respiratory rate and blood pressure. With the exception of meningeal syndrome, the rest of the clinical examination was within normal limits. Laboratory blood tests showed increased leukocyte count (32 000/mm3) with 93 % neutrophils, increased inflammatory syndrome markers (C
reactive protein=42.6 mg/l, Procalcitonin= 29.2 ng/dl) and a positive blood culture for Streptococcus pneumoniae, serotype 6B, resistant to Penicillin. The lumbar puncture revealed a turbid, raised pressure CSF, with 6400/mm³ cell count (out of which 87% Neutrophils), raised protein level and positive bacterial culture for S. pneumoniae serotype 6B.

The last brain magnetic resonance imaging, performed during this admission, showed asymmetry of the depth of the olfactory fossa (7mm on the right side and 4mm on the left side) and lateral right defect in the cribriform plate of 4mm, partially covered with dura mater, with fluid signal that prolonged to the rhynopharynx. This image is specific for a CSF fistula, active at the time of examination, with origins most probably in the lateral right cribriforme plate defect. (Fig. 1.) The CT examination also revealed the ethmoidal asymmetry. (Fig. 2.)

The patient received treatment with IV Meropenem 120mg/kg/day and Linezolid 30mg/kg/day for 21 days, IV mannitol and dexamethasone, acetazolamide orally, with favorable clinical and biological outcome. The patient underwent a second surgical intervention with resolution of the rhinoliquorrhea.

Discussions

CSF leakage commonly occurs secondary to head trauma or after skull base and endonasal sinus surgery. Spontaneous CSF leaks are caused mainly by occult malformations of the base of the skull, the majority of the sites of the fistulas being located at the cribriform plate and the ethmoidal roof, whereas the sphenoid bone and sinus being less involved. Intracranial hypertension syndrome in also recognized to have an important role in developing a CSF fistula.

In bacterial meningitis associated with cranial dural defects S. pneumoniae was found in 80% of cases, highlighting the fact that CSF fistula represents a high risk factor for invasive pneumococcal disease.

The diagnosis and treatment of these affections need considerable effort from a multidisciplinary medical team with the ultimate goal of making a quick recovery of the patient and avoidance of recurrence.

During 2010-2013, ACIP (Advisory Committee on Immunization Practices) published new recommendations for vaccination with PCV13 and PPSV 23 regarding patients with high risk factors for IPD, including those with a CSF fistula.

Conclusions

In this case, pneumococcal meningitis was associated with evident CSF fistula, clinically manifested with rhinoliquorrhea, in a child with idiopathic intracranial hypertension syndrome. Brain imaging showed clear evidence of recurrent rhinoliquorrhea and a second endonasal surgical repair was performed. The child received recommendation to vaccinate with both PCV 13 and pneumococcal polysaccharide 23-valent vaccine.

During 2014-2015 in our clinic there have been two other cases of sepsis with meningitis due to Streptococcus pneumoniae in children with CSF fistula; in one case we identified serotype 23F and the other was a nontypeable pneumococcus.

References

1. Tan T., Pediatric Invasive pneumococcal disease in USA in the Era of Pneumococcal Conjugate Vaccines, Clinical Microbiology reviews, July 2012, p 409-419
5. Mandell, Douglas, and Bennett’s *Principles and Practice of Infectious Diseases*, Part III, Section F, Chapter 200 streptococcus pneumoniae.
11. CDC. *Use of 13-Valent Pneumococcal Conjugate Vaccine and 23-Valent Pneumococcal Polysaccharide Vaccine Among Children Aged 6–18 Years with Immunocompromising Conditions:*

Correspondence to:
Monica Luminita Luminos, MD, PhD
Associate Professor
National Institute for Infectious Diseases "Prof. Dr. Matei Balș", Bucharest, Romania
1, Calistrat Grozovici street Bucharest
E-mail: monicaluminos@yahoo.com