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SHORT COMMUNICATION

Haemophilus influenzae type b meningitis in a vaccinated and immunocompetent child

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Abstract Invasive *Haemophilus influenzae* type b (Hib) disease decreased dramatically after the introduction of conjugate vaccine in routine immunization schedules.

We report a case of a fifteen-months-old girl, previously healthy and vaccinated, admitted in the emergency room with fever and vomiting. She was irritable and the Brudzinski's sign was positive. The cerebrospinal fluid (CSF) analysis showed pleocytosis and high protein level. Empiric intravenous antibiotics (ceftriaxone and vancomycin) were administered for suspected bacterial meningitis during 10 days. Serotyping of the *Haemophilus influenzae* strain found in CSF revealed a serotype b. After one year of follow-up no Hib meningitis sequelae were noted.

Despite vaccination compliance and absence of risk factors, invasive Hib disease can occur due to vaccine failure.

Efforts to keep the low incidence of invasive Hib disease should be directed to the maintenance of high vaccination coverage rates, combined with the notification and surveillance strategies already implemented in each country.

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Introduction

Haemophilus influenzae is a gram negative *coc-cobacillus* which can be capsulated or not. According to the capsule polysaccharide composition it is categorized into six serotypes (a–f) [1]. The serotype b (Hib) is the most virulent and the major cause of bacterial meningitis. Until the 1990s Hib was responsible for 3 million invasive infections, worldwide, which resulted in 386,000 deaths/year in children under five years [1–3].

After the introduction of Hib vaccines there was a dramatic decrease in the incidence (41/100 000 in 1987 to 0.11/100 000 in 2007) and mortality of invasive Hib disease in all ages [2,3]. This trend was also found in Portugal [4] since 2000, with the introduction of the vaccine in the routine immunisation schedule (RIS), at 2, 4, 6 and 18 months [5].

The European Union Invasive Bacterial Infections Surveillance defines true vaccine failure (VF) as the occurrence of invasive Hib disease at any time after 3 doses of vaccine administered during the first year of life; ≥ 2 weeks after one dose administered after 12 months, or ≥ 1 week after ≥ 2 doses administered before 1 year of life [6].

The incidence of vaccine failure is rare (0.2/100 000) and it is associated with the presence of comorbidities (44% of cases had clinical risk factors and/or deficit of immunoglobulins) [6–9]. Between 2002 and 2010, only five cases of Hib VF were reported in Portugal [4].

Case report

We describe a case, of a 15-months-old girl, born full term, previously healthy and vaccinated with 3 doses of a Hib vaccine (Pentavac[®], Sanofi Pasteur MSD) at 2, 4 and 6 months old.

She was admitted in the emergency room with fever (39 °C axillary temperature), food vomiting and progressive deterioration of general condition, during the previous 2 h.

On physical examination she was irritable and constantly whining, pale and dehydrated. Brudzinski's sign was positive. There were no rash or petechiae and the remaining exam was normal.

Analytical screening was performed: blood count with platelet and biochemistry showed no changes and C-reactive protein (CRP) was within the normal range (11 mg/L). The urinalysis was normal. A lumbar puncture was performed: cerebrospinal fluid (CSF) revealed pleocytosis (2900 cells/ μ L), with a predominance of polymorphonuclear neutrophils (83%), high protein levels (1.06 g/L) and normal CSF

Table 1 White blood cells count and C-reactive protein results.

Inpatient day	D1	D2	D7
Leukocytes ($\times 10^9$ /L)	6.0	21.4	16.7
Neutrophils (%)	53.8	79	26.7
CRP (mg/L)	11.0	194.1	8.9

CRP, C-reactive protein.

glucose (0.27 g/L). Blood, urine and CSF were sent for culture.

Suspicion of bacterial meningitis triggered hospital admission, droplet isolation and empiric intravenous antibiotics (ceftriaxone and vancomycin).

In the first 24 h inflammatory parameters increased: leukocytosis (21.4×10^9 /L) with neutrophilia (79%) and elevated CRP (194 mg/L).

The CSF gram stain showed a gram-negative *coc-cobacillus*, *Haemophilus influenzae* strain. Antimicrobial susceptibility testing showed no resistance to ceftriaxone and then vancomycin was stopped.

Bacteriological exams of blood and urine were both negative.

The serotyping of the *Haemophilus influenzae* strain was performed in the National Reference Laboratory for Bacterial Respiratory Infections by polymerase chain reaction [10] and revealed a serotype b.

Favourable clinical outcome was achieved and laboratory results returned to normal (Table 1).

After 10 days of intravenous ceftriaxone the patient was discharged home and referred to the General Pediatrics and Otolaryngology outpatient clinic.

Hib antibodies concentration was not measured during the acute phase of illness because recognition of this Hib strain was made only after discharge.

The child had the vaccine booster dose during the second year of life (at 18 months), according to the RIS. Only after that was Hib antibodies concentration measured, which was normal.

After one year of follow-up, an adequate psychomotor development and neurological examination as well as a normal immunological status (immunoglobulins and complement levels) were confirmed. The auditory evoked potentials were normal.

Discussion

This case typifies the most common form of Hib VF found in literature [6,8]. The majority of the described cases occurred in children with 3 doses

of vaccine before 12 months and 43% in children less than 2 years. The most common form of clinical presentation was meningitis (44%) [6].

It is recommended for all cases of Hib VF, to measure Hib antibodies concentration, in the disease convalescent period, especially in children under 18 months of age and/or with associated comorbidities. If convalescent antibodies concentration is low, a booster vaccine dose should be performed [6,9]. In this case report, vaccine booster was administered on a scheduled basis at 18 months, according to our RIS. Hib antibodies concentration was only measured afterwards and was normal.

All Hib VF survivors must be monitored, since 1 in 7 healthy children and more than 2/3 of children with morbidities, will develop at least one other serious infection, requiring hospital admission during childhood [11]. The girl described had no serious complications within one year after the acute event.

In order to maintain a low incidence of invasive Hib disease two different strategies have been described. First the administration of a vaccine booster dose during the second year of life and/or after an invasive Hib disease infection with low Hib antibodies concentration or without antibodies measurement available. The UK and Ireland introduced it at 13 month of age, since most children with Hib VF that received 3 doses of the vaccine before 6 months, developed disease at least 1 year after the last dose [6,8,12]. In Portugal the booster dose is administered at 18 months [5]. The second strategy considers that all Hib VF survivors should have an additional dose of vaccine a few years after infection, with the intent of enhancing the long-term immunity [9]. The implementation of this strategy will require additional studies to prove its benefit.

Despite vaccination compliance and absence of risk factors, invasive Hib disease can occur due to VF, which pathogenesis is not entirely clear [6].

With current global Hib vaccination programs, disease elimination can be conceivable, particularly in most developed settings. Nevertheless disease eradication is unlikely because of Hib nasal carriage in healthy population and VF.

Efforts should focus on keeping high vaccination coverage, ensuring good quality reporting and establishing a clear protocol for booster dose administration.

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Competing interests

None declared.

Ethical approval

Not required.

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