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## CASE REPORT

### ***Streptococcus pneumoniae* serotype 19A meningitis in well-vaccinated immunocompetent 13-month-old child: a case of PCV13 failure**

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#### Introduction

The advent and implementation of conjugate antipneumococcal vaccines, 7-valent conjugate vaccine (PCV7) followed by 13-valent conjugate vaccine (PCV13), have led to a tremendous progress being achieved in both prevention and care of severe infections caused by the *Streptococcus pneumoniae* in the pediatric populations. In spite of this progress, severe infections due to *Streptococcus pneumoniae* still represent an important cause of both mortality and morbidity in children under the age of 5 years in industrialized countries [1, 2].

The generalization of the 7-valent conjugate vaccine in 2000 had, by itself, rapidly, led to 87% reduction in the incidence of severe infections in children aged <1 year, 58% in those aged <2 years, and 62% in children aged <5 years in the United States of America [3]. Concurrently, the PCV7 vaccine had also led to a significant reduction (by 38%) of otitis media as consequence to the reduction in pneumococcal ear, nose, and throat (ENT) infections.

#### Key Clinical Message

We report a 13-month-old immune-competent male child who was diagnosed with pneumococcal serotype 19A meningitis despite having received three PCV13 injections. Clinicians are reminded that bacterial meningitis can still occur, even in correctly vaccinated children. Investigations should include immune system screening along with abdominal ultrasound to exclude asplenia.

#### Keywords

Failure, meningitis, PCV13, *Streptococcus pneumoniae*, toddlers.

In 2010, although the Centre For Disease Control, Atlanta, confirmed the benefits of the new PCV7 vaccine in reducing both the resistance and carriage of pathologies due to *Streptococcus pneumoniae* serotypes contained in PCV7, it also expressed, however, a concern over the rise in the incidence of infections caused by the emerging strains not contained in the vaccine (serotypes 1, 19A, 3, 6A and 7F) [4]. Similar findings were to be reported, later, by other studies [5, 6].

In order to counter the changing epidemiology of *Streptococcus pneumoniae* infections and therefore, broaden the conjugate vaccine spectrum to cover the emerging serotypes (1, 3, 6A, 7F et 19A), the 13-valent conjugate vaccine (PCV13) was developed and commercialized in France, as early as June 2010.

Despite the fact that the benefits of this new vaccine are being universally recognized, some cases of vaccination failures have been reported, mostly in those immune-compromised and/or in children with underlying predisposing conditions [5, 7].

We report a case of a 13-month-old immune-competent male child, who was diagnosed with *Streptococcus pneumoniae* meningitis serotype 19A contained in the vaccine, despite having been correctly vaccinated with three doses of PCV13. Our aim is to remind clinicians that PCV13 vaccination failure is possible and therefore, a high level of suspicion is required in ill children, even in those correctly immunized.

## Case Report

A 13-month-old male child was referred to our emergency department, by his family doctor, with a 4-day history of fever (40°C), loss of appetite, loose stools, and vomiting. He was reported to have lost 8% of his usual body weight. Upon admission, his weight was 10.395 kg, height 90.5 cm, and BP 105/65 mm Hg, and his capillary refill time was prolonged (3 sec) despite being afebrile (36°C). The child's Glasgow Coma Scale score was 13/15; his neurologic and ENT examinations were both unremarkable, and his skin examination revealed no purpuric lesions or any other abnormalities. The personal past medical history was unremarkable: He was a term-born child following in vitro fertilization (IVF), with birth weight of 3.820 kg, birth Length of 52 cm, and head circumference of 36 cm; his vaccinations were up to date, according to the French immunization schedule, including three PCV13 injections (at 2, 4, and 12 months of age, respectively) and one *Neisseria meningitidis* group C (NeisVac<sup>®</sup>) vaccine. Laboratory screenings showed increased plasma C-reactive protein (170 mg/L). Lumbar puncture revealed abnormal cerebrospinal fluid (CSF) findings with elevated protein level at 1.7 g/L, chloride 120 mmol/L, and glucose 0.80 mmol/L. CSF cytology was positive, revealing an increased leukocytes count (1780/mm<sup>3</sup> with 75% polynuclear neutrophils, 24% monocytes, 1% lymphocytes, and RBCs 4/mm<sup>3</sup>). CSF soluble antigens were positive, and cultures grew numerous colonies of *Streptococcus pneumoniae* (19A serotype). Plasma white blood cell count, urea and electrolytes, and liver function tests were within normal limits.

He was started on antibiotics (Cefotaxime 300 mg/kg/day for 14 days associated with Dexamethasone 0.15 mg/kg 6 h for 2 days) and subsequently did well. The child's immune system screening was unremarkable (IgG 6.84 g/L; IgA 0.47 g/L; IgM 0.88 g/L; complement (C3 1.45 g/L [0.69–1.32]; C4 0.18 g/L)). Postvaccination antibody titers against *Streptococcus pneumoniae* showed normal level (IgG 12.4 mg/L [normal > 3.3 mg/L]). An abdominal ultrasound was performed and showed a normally located spleen.

## Comments

This report highlights the fact that severe infections due to *Streptococcus pneumoniae* are still a threat and may occur in well-vaccinated immunocompetent children with PCV13.

*Streptococcus pneumoniae* is a complex bacterium that contains over 90 known serotypes, all different from each other in prevalence and virulence [8]. PCV13 serotypes, therefore, represent only a minor part of the complex pathogen.

The earlier implementation of PCV7 vaccination had led to a tremendous reduction in severe pneumococcal infections worldwide [3–7]. In France, the 2007 EPIBAC study showed similar results after the introduction of PCV7 in national vaccination schedules [9]. The incidence of severe pneumococcal infections was reduced by 32% for acute meningitis and by 38% for bacteremia [9]. The same study additionally reported, however, a considerable rise in the incidence of both meningitis and severe bacteremia due to serotype 19A in toddlers, as reported by others [2, 4, 9, 10].

In another study by Bekri et al. [10], authors concluded that the impact of PCV7 was modest with regard to pneumococcal purulent pleuritis after reporting the highest incidence of serotypes 19A and 1 reaching around 50% of pneumococcal infections after the advent of PCV7 [11].

Essential of criticism formulated against PCV7 was, therefore, mainly related to the emergence of non vaccine serotypes, although cases of vaccination failures had also been reported in well or partially vaccinated children [12, 13].

The immunogenicity studies, performed after the introduction of PCV13 in immunization schedules, have shown that this conjugate vaccine was able to induce antibody production well above the recommended coverage level of  $\geq 0.35$   $\mu\text{g}/\text{mL}$  against the six additional serotypes, that caused concern with PCV7 (1,3,5,6A,7F and 19A), in 96.8–100% children who had received three injections [14, 15].

However, two cases of PCV13 failures (due to serotypes 19A and 19F) have been reported by Godot et al. [7]: One in a child aged 15.4 months at the time of diagnosis, who had received three PCV13 doses and had no underlying predisposing condition related to his vaccination failure. The second child, aged 57.1 months, had received three doses of PCV7 and a booster dose with PCV13; he, however, had a cochlear implant as the likely underlying condition.

Our patient with *Streptococcus pneumoniae* serotype 19A meningitis at the age of 13 months, after having been correctly vaccinated with three doses of PCV13,

around 35 days following the 3rd injection. It is a well-known fact that severe infections due to encapsulated bacteria are common in children with known underlying predisposing conditions such as asplenia, deficiency in the complement system, immunoglobulin deficiencies. Our patient was screened, but none of these factors was found.

Although we have no explanation as to why our patients whose postvaccinal antibody titer was within normal protective range presented with serotype 19A meningitis, the fact that we did not perform the opsonophagocytic assay may constitute a bias and temper our statement.

We speculate that PCV13 will contribute to further reduction in severe pneumococcal infections, but the likelihood of nonvaccine serotypes emergence cannot be excluded. Besides, failure cases remain relatively rare with regard to the extent of successful coverage in the large majority of children.

The occurrence of severe pneumococcal infection in a well-vaccinated child should lead to explore his immune system (complement system, immunoglobulin titer, opsonophagocytic assay, postvaccination antibody titer, etc.) and perform an abdominal ultrasound to exclude asplenia [16].

## Conclusion

This case illustrates the necessity for clinicians to remain alert and maintain high level of suspicion in children, especially those in “looks bad category” in pediatric emergency rooms. In spite of this rare failure, PCV13 remains a real medical progress and should strongly be recommended in children under the age of 5 years.

## Conflict of Interest

None declared.

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