CASE REPORT

Breakthrough *Streptococcus pneumoniae* type 6B infection after adrenocorticotropic hormone therapy in a child vaccinated with pneumococcal conjugate vaccine

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Received 12 June 2009; received in revised form 11 August 2009; accepted 13 October 2009

**KEYWORDS**

*Streptococcus pneumoniae*; conjugate vaccine; vaccine failure; adrenocorticotropic hormone

Despite proven good efficacy of pneumococcal conjugated vaccine in preventing invasive pneumococcal disease, breakthrough infections remain a noticeable problem with significant morbidity and mortality, especially in selected high-risk groups. We present a 2-year-old girl with infantile spasm, who was treated with antiepileptic drugs and adrenocorticotropic hormone (ACTH). Vaccination with three doses 7-valent pneumococcal conjugate vaccine had been completed one month before ACTH therapy. Two months after ACTH therapy, she suffered from fever, cough, and decreased activity. *Streptococcus pneumoniae*, serotype 6B, was detected in blood culture. Vaccine failure could be possibly due to ACTH therapy. Copyright © 2012, Elsevier Taiwan LLC & Formosan Medical Association. All rights reserved.

**Introduction**

*Streptococcus pneumoniae* is a leading cause of serious illness among children worldwide.\(^1\) Following widespread use, the 7-valent pneumococcal conjugate vaccine (PCV7) has led to remarkable decline in the incidence of invasive pneumococcal disease (IPD) in the United States\(^2\) and
elsewhere. A report from the US Centers for Disease Control and Prevention (CDC) showed that overall IPD rates among children aged 5 years or less in 2005 were 77% lower compared with the years preceding vaccine introduction (1998–1999). However, because the protective efficacy of the vaccine is not 100%, a small proportion of vaccinated children will still get invasive pneumococcal infections. Underlying diseases such as malignancies and immunodeficiencies may or may not exist in vaccinated children with breakthrough pneumococcal infections. Here, we present a case of PCV7 failure in a 2-year-old girl who received adrenocorticotropic hormone (ACTH) therapy for infantile spasm.

Case report

A girl aged 2 years and 4 months was hospitalized because of fever for 3 days. During this time, mild cough and a running nose were noted.

The patient was born at 36 weeks of gestation with a birth weight of 2094 g (below the 10th percentile). The Apgar scores were 7 and 9 at 1 minute and 5 minutes, respectively. Results of newborn screening tests were normal. Neonatal seizure and brain atrophy were found at the age of 2 weeks. She was diagnosed as and treated for infantile spasm. Antiepileptic drugs including vigabatrin, lamotrigine, phenobarbital, and oxcarbazepine were used. The first course of ACTH therapy (tetracosactide hexaacetate 0.025 mg/kg/dose per day for 2 weeks, tapered to half frequency every 2 weeks for a total of 8 weeks) was administered intramuscularly at the age of 1 year and 1 month. A second course of ACTH therapy (tetracosactide hexaacetate 0.025 mg/kg/dose per day for 2 weeks and 0.025 mg/kg/dose every 2nd day for a week) was administered at the age of 2 years and 2 months, but was discontinued due to hospitalization for bronchopneumonia. There was no recent trauma, unusual ingestion, travel, or exposure to animals. However, she had contact with persons, including her parents, who had upper respiratory tract infections. The child had attended well-child visits and received routine immunizations. She also received three doses of PCV7, at the age of 9 months, 10 months, and 12 months.

On examination, the patient’s weight was 11.5 kg (about the 25th percentile) and her height was 86 cm (about the 25th percentile). Her temperature was 36.6°C, blood pressure 118/54 mmHg, pulse 138/minute, and respiratory rate 34/minute. Her throat was hyperemic and a coarse breathing sound was heard. As for neurologic development, she had poor head control, could only stand with aid, and only spoke a few words.

On laboratory investigation, hemoglobin was 11.4 g/dL, leukocyte count was 40190/mm³, and platelet count was 388 × 10³/mm³. Levels of liver enzyme, creatinine, and sugar were all within normal limits except for a high C-reactive protein level (12.62 mg/dL). Chest X-ray showed focal consolidation in the right upper lung field. Both blood and urine cultures were done on the day of admission. Throat and rectal swabs were obtained for viral isolation. She was initially treated with ampicillin-sulbactam (ampicillin 150 mg/kg/day) for bronchopneumonia and antiepileptic drugs for infantile spasm. Fever resolved and activity improved after using antibiotics. No bacterium was isolated from urine and no virus was isolated from throat and rectal swabs. The blood culture yielded S. pneumoniae. The minimal inhibitory concentration was 1 μg/mL for penicillin. After treatment with 5 days ampicillin-sulbactam, then 4 days penicillin G (0.4 MU/kg/day), the girl was discharged. Serotyping for S. pneumoniae isolate was performed by the Quellung reaction with antisera from Statens Serum Institute, Copenhagen, Denmark. It revealed serotype 6B.

Discussion

Due to biologic variability, probably none of the current vaccines can achieve an absolute (100%) efficacy. In early clinical trials, the PCV7 was reported to have a 97.4% protective efficacy against invasive vaccine-type pneumococcal diseases. Early reports showing failures of PCV7 were frequently associated with incomplete vaccinations or underlying conditions such as HIV infections or chemotherapy for malignancies. Lower antibody concentration alone is not a sufficient factor for vaccine failure. Antibody concentration, functional activity, and avidity all play important roles. ACTH was used for treating infantile spasm since 1958 because conventional anticonvulsants were usually ineffective. ACTH stimulates the adrenal gland to release cortisol and, to a lesser extent, aldosterone and androgens. Reduced antibody response to polysaccharide vaccine was reported in patients on glucocorticoid therapy for nephrotic syndrome but not for asthma. The girl presented here received ACTH therapy about 1 month after the third PCV7 dose. The corticosteroid surge induced by ACTH might have compromised a proper immune response to the PCV7. As far as we know, this is the first report of PCV7 failure in a child receiving ACTH therapy for infantile spasm.

The current PCV7 contains 2 μg of protein-conjugated polysaccharide for 4, 9V, 14, 18C, 19F, 23F and 4 μg for 6B. 6B is less immunogenic and needs a higher content. An immunogenicity study of the PCV7 among 56 toddlers in Taiwan revealed that the post-booster antibody concentrations exceed 0.2 μg/mL for all serotypes except 6B.

Although we did not have a chance to determine the antibody titers against S. pneumoniae before the bacteremia in this case, we reckon suboptimal antibody response to 6B after ACTH therapy might have led to a breakthrough S. pneumoniae infection in this case.

Recommendations for immunization of children at high risk of pneumococcal disease were published in 2000. For children 23 months and younger, the PCV7 vaccine is administered at the age of 2 months, 4 months, 6 months, and 12–15 months. For children 24–59 months old who have received no previous doses, two doses of PCV7 are recommended. It should be given at an interval of 6–8 weeks, followed by a single dose of 23-valent polysaccharide vaccine no less than 6–8 weeks after the last dose of PCV7. An additional dose of 23-valent polysaccharide vaccine is recommended 3–5 years after the last dose. The catch-up dose(s) depends on the age and the
previous dose(s) that the host had received. The child we present here received three doses of PCV7, which is in line with the standard catch-up schedule for healthy infants of 6–12 months old. However, such a vaccination schedule might be inadequate for immunocompromised children. Additional doses of PCV7 or 23-valent polysaccharide vaccine is necessary if children with ACTH therapy are considered immunocompromised.

This case report highlights the problem of PCV7 catch-up vaccinations in infants receiving ACTH therapy. Vaccine failures may occur. Clinicians are encouraged to give children with ACTH therapy for infantile spasm complete failures may occur. Clinicians are encouraged to give children with ACTH therapy for infantile spasm complete pneumococcal vaccinations, including complete doses of PCV7 and a dose of 23-valent polysaccharide vaccine. Studies on immunogenicity of PCV7 in children under ACTH therapy may provide insights into the issue.

References