Serotype 6B Pneumococcal Meningitis in an Immunocompetent Infant Immunized with Heptavalent Pneumococcal Conjugated Vaccine

Sir—Little information is available on the risk of clinical failure of heptavalent pneumococcal conjugated vaccination among infants <6 months of age [1, 2]. We report a case of vaccination failure in a 5-month-old girl. The child was hospitalized in December 2003 for meningitis. CSF culture yielded 10^7 cfu/mL of Streptococcus pneumoniae serotype 6B that was sensitive to penicillin (MIC, <0.1 µg/mL). Bacteriologic eradication was obtained 48 h after the beginning of treatment with cefotaxime and vancomycin. The duration of treatment was 15 days with cefotaxime and 3 days with vancomycin.

The infant had received 1 injection each of combination diphtheria, tetanus, acellular pertussis, inactivated polio, Haemophilus influenzae type b (DTaP-IPV-Hib) vaccine and heptavalent pneumococcal conjugated vaccine (PCV7) at age 2 months and again at age 3 months. The third injections of DTaP-IPV-Hib vaccine and PCV7, which national health guidelines recommend to be received at age 4 months, were postponed because the patient had acute bronchiolitis.

Meningitis due to S. pneumoniae serotype 6B occurred on day 54 after receipt of the second injection of PCV7, which raised the possibility of an immune deficiency. The levels of immunoglobulins (IgG, IgA, and IgM), the complement fractions, the lymphocyte subpopulations, and the titers of antibodies to tetanus, Haemophilus influenzae type b, diphtheria, poliovirus, and pertussis vaccine antigens were within normal ranges. The results of lymphocyte proliferation tests were strong in response to mitogens and antigens (i.e., tetanus toxoid) at age 7 months.

Initial measurement, by ELISA (Wyeth-Lederle), of antibodies to the different pneumococcal strains contained in PCV7 showed that the titer of antibodies to serotype 6B (0.06 µg/mL) was far below the protective threshold (0.15 to 0.5 µg/mL) [1, 3]. In contrast, titers of antibodies to the other serotypes contained in PCV7 (23F, 14, 18C, 19F, 9V, and 4) were all >0.5 µg/mL.

Vaccination with PCV7—a total of 3 injections, at ages 2 months, 4 months, and 6 months, with a booster vaccination 12 months later—has been shown to reduce the risk of invasive pneumococcal infection due to the 7 serotypes contained in the vaccine [1, 2, 4]. It has also been shown that up to 30% of cases of pneumococcal meningitis occur in infants aged <6 months [5].

The failure of vaccination in infants <6 months of age has not previously been reported, to our knowledge. Although the infant we describe had received only 2 injections of PCV7, the antibody response to all the vaccine serotypes except serotype 6B was satisfactory. A lower vaccine response to this serotype has previously been reported, with the protective threshold for antibodies to this serotype (and to serotype 23F) being reached only after the third injection [6]. Invasive infections due to pneumococcal serotypes contained in the vaccine have been reported after both the complete and incomplete vaccination, but the vaccine response to the serotype involved has not been assessed [1, 2, 4].

S. pneumoniae serotype 6B frequently causes invasive infection in children <2 years of age [7, 8]. The estimated prevalence of such infections in this population before the advent of PCV7 was 10.6%–21.9% [7, 8]. This case points to the possible existence of a subset of young infants who are inadequately protected against serotype 6B pneumococci. This finding confirms the importance of giving the first 3 injections of PCV7 before the age of 6 months if optimal protection is to be achieved, especially against serotype 6B. Large-scale monitoring of pneumococcal vaccine failure is required to study the underlying mechanisms.

References

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Reinfection Versus Relapse in Urinary Tract Infection

Sir—The much-needed trial by Dow et al. [1] regarding treatment duration for urinary tract infection (UTI) in patients with spinal cord injury and the accompanying editorial commentary [2] raise questions regarding the determination of whether isolates from recurrent (posttherapy) episodes of UTI represent relapse or reinfection and determination of the possible sources of such infections. First, although various methods can be used to classify isolates from recurrent episodes of UTI as the same strain or a different strain than the pretherapy isolate, even isolates of the same strain can represent reinfection if there is a persisting external reservoir from which the organism can be reintroduced into the host’s urinary tract. Thus, whereas isolates of different strains almost certainly represent reinfection, isolates of the same strain are ambiguous with respect to whether they represent reinfection or relapse. This ambiguity can lead to overestimation of relapse rates.

Second, because of the relatively high prevalence of Klebsiella species, Enterococcus species, and Escherichia coli among pretherapy isolates from urine in the study of Dow et al. [1], an inference that a posttherapy isolate of the same species represents the same strain as the pretherapy isolate may be erroneous. Subspecies typing methods, such as PFGE, are needed here. It is unclear why Dow et al. [1] reserved PFGE analysis for only selected same-species posttherapy isolates. Third, even PFGE analysis may not provide unambiguous results. For example, it is statistically improbable that a patient whose pretherapy urine sample yielded Acinetobacter anitratus would have recurrent UTI due to an unrelated strain of A. anitratus, given that the overall prevalence of infection by Acinetobacter species in the study population was 10%, and only a subset of those infections, presumably, was due to A. anitratus [1]. It is perhaps as likely that the PFGE results in this instance were in error, or that the strain, while residing in the patient (or in a patient-associated reservoir), underwent genetic rearrangements that produced the observed PFGE profile alterations, which led to a false assessment that this was a different strain from the pretherapy isolate.

Finally, 70% of the study subjects were men [1]. Because the prostate gland is a common source for relapsing UTI in men [3] and is usually involved in cases of febrile UTI in men, despite the absence of localizing symptoms [4], it may be that some of the relapses observed by Dow et al. [1] derived from a persistently infected prostate rather than the upper urinary tract, as was proposed. The tenacity of prostatic infection [3] would be consistent with the superior microbiological efficacy of the longer treatment course that was observed by Dow et al. [1].

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References


Reply to Johnson

Sir—We thank Dr. Johnson [1] for his interest in and comments on our study. To determine outcomes of relapse or reinfection we used definitions commonly applied in clinical trials of urinary tract infection (UTI). We agree that isolation of the same species after therapy may possibly result from reinfection with the same strain from an external source. This has been well documented for young women with acute uncomplicated UTI [2], although similar observations for complicated UTI have not been reported, to our knowledge. Despite this, reinfection rates identified with the study definitions were similar for both treatment arms, whereas relapse occurred only in the 3-day treatment arm. Surveillance cultures of sites of colonization, the likely source of same-strain reinfection, did not reveal persistent colonization in either arm after treatment. These observations support the conclusion that outcomes classified as relapse did represent relapse rather than reinfection.

PFGE typing was only performed for organisms associated with late relapse. The expectation was that relapse would usually be identified early after therapy, so late relapse, of which there were only 2 occurrences, would more likely represent reinfection. The majority of study subjects were inpatients on the spinal cord injury unit and exposed to nosocomial pathogens, and Acinetobacter species are well recognized causal organisms in this situation. Thus, reinfection with Acinetobacter