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CASE REPORT

Recurrence of occult pneumococcal bacteremia by an identical strain in an apparently healthy child

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Summary This is the first report to describe an apparently healthy girl, who developed recurrent occult bacteremia by the same *Streptococcus pneumoniae* strain, at 11 and 15 months of age. The two separately isolated organisms were demonstrated to have the identical serotype (type 6B), antibiotic susceptibility (intermediately penicillin-resistant), genotypes of penicillin-binding proteins, and patterns of pulse-field gel electrophoresis. The serum levels of anti-type 6B antibodies showed poor responses after both bacteremic episodes, but other immunological workups did not demonstrate any abnormalities. This case indicates that occult bacteremia may recur due to an identical pneumococcal strain in an immunocompetent infant, and that early introduction of pneumococcal conjugate vaccine is necessary in Japan.

Introduction

Occult bacteremia occurs in approximately 3–10% of relatively healthy appearing febrile children between 3 and 36 months of age.[1] The most frequent causative pathogen is *Streptococcus pneumoniae*, especially in the era of the *Haemophilus influenzae* type b vaccine.[2] Given the evidence that recurrent or relapsing episodes of invasive pneumococcal infections have been associated with underlying disease such as hypogammaglobulinemia, IgG subclass deficiency, human immunodeficiency virus (HIV) infection, complement deficiency, congenital disorders of hemoglobin, and asplenia,[3–8] such episodes are rare in immunocompetent children. Moreover, the majority of patients with recurrent pneumococcal invasive infections

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have an apparent focus of infection including pneumonia, meningitis, cellulitis, and otitis media[3–6,8–10] and demonstrated distinct pneumococcal serotypes.[5,7,11]

We report an otherwise healthy child, who developed two episodes of occult bacteremia by an identical pneumococcal strain, serotype 6B, approximately 4.5 months apart.

Case report

A previously healthy 11-month-old female was referred from a neighborhood physician because of tonic convulsion for 2 min and fever for 1 day. She has attended the day-care center since she was 10 months of age. On arrival, 5 h after the onset of the convulsion, her consciousness had become clear and she was active and playful. On admission, physical examination by the pediatrician and otolaryngologist did not demonstrate any abnormalities. Body temperature was 38.0 °C and pulse rate was 160/min. Laboratory data of peripheral blood showed that the white blood cell (WBC) was 203×10^9/l and C-reactive protein (CRP) was 7.7 mg/dl. Results of cerebrospinal fluid examination showed an absence of pleocytosis, normal range of glucose and protein levels, and negative culture. The patient was hospitalized and intravenous cefotaxime at 30 mg/kg every 8 h was begun. The following day the patient was afebrile and *S. pneumoniae* (minimal inhibitory concentration (MIC) for cefotaxime; 0.25 μg/ml) was isolated from blood culture obtained on admission. Urine and throat cultures on admission were negative. She was discharged after treatment with cefotaxime for 7 days.

One hundred and thirty-four days after discharge of the first episode of pneumococcal bacteremia, the patient (15 months of age) had another seizure associated with fever and was brought to the emergency room of our hospital. She was treated with a diazepam suppository. Laboratory data included WBC of 193×10^9/l and CRP of 1.5 mg/dl. One hour after arrival, the patient's consciousness became clear, and she returned home without any antimicrobial agents. Two days later she was readmitted to our hospital because of prolonged high fever. On examination the patient appeared well and in no apparent distress. The temperature was 40.0 °C and the pulse rate was 159/min. Physical examination did not demonstrate any abnormalities with an unremarkable focus of infection. Her WBC count was 206×10^9/l showing 5.5% bands and 55.0% segmented forms; CRP was 7.0 mg/dl. She was treated with parenteral meropenem 20 mg/kg every 8 h, which promptly decreased the fever. The next day, blood culture obtained on admission was found to be positive for *S. pneumoniae* (MIC for meropenem; 0.06 μg/ml). Throat swab culture grew non-typeable *H. influenzae*. Urine and stool cultures were negative. During hospitalization, we performed immunological workup to identify the reason for recurrence of bacteremia. Serum levels of total immunoglobulin (Ig)-G (1112 mg/dl), IgG1 (854.0 mg/dl), IgG2 (204.0 mg/dl), IgG3 (51.9 mg/dl), IgG4 (2.24 mg/dl), IgA (70 mg/dl), IgM (171 mg/dl), C3 (103 mg/dl), C4 (42 mg/dl), and CH50 (52.6 U/ml) were compatible with the normal range for her age. T cell (73%, positive for CD2) and B cell (14%, positive for CD20) subsets, and CD 4/8 ratio (1.7) in peripheral blood were normal. Serum IgG antibodies against previous vaccination including anti-tetanus toxoid antibody (6.16 IU/ml), anti-diphtheria toxoid antibody (1.61 IU/ml), anti-fragmentous hemagglutinin of pertussis antibody (18.0 EU/ml) were all normally responsive levels. The patient was discharged after a 7-day course of intravenous meropenem therapy. Culture of nasopharynx obtained 2 weeks after discharge did not yield any pathogens. She has remained well for more than 6 months after the second episode of occult bacteremia.

Both of the two separately isolated organisms, identified as serotype 6B, were intermediately resistant to penicillin (MIC; 0.25 μg/ml), and had the same gene alteration[11] of *penicillin-binding protein 2x*, and the same patterns in pulse-field gel electrophoresis (PFGE)[11] (Fig. 1). Based on

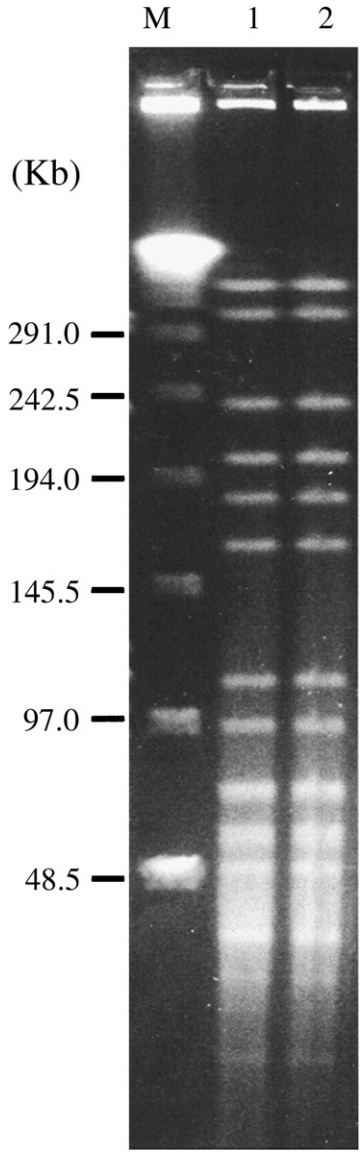

Figure 1 Pulse field gel electrophoresis of chromosome DNA from pneumococcal isolates on the first (lane 1) and second (lane 2) bacteremic episodes, after digestion with *Apa*1 restriction enzyme. Lane M indicates λ ladder molecular size marker. Note that the bandings of the two isolates show the same patterns.