

Systemic reaction to pneumococcal vaccine: How common in pediatrics?

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ABSTRACT

The 23-valent-polysaccharide pneumococcal vaccine (PPV23) is currently recommended for patients at high risk for invasive disease from Streptococcus pneumoniae. It is also frequently used in the evaluation of patients with suspected immunodeficiency. Reports of systemic adverse reactions are rare. Our objective is to describe a patient with an apparent systemic reaction to PPV23 and review our hospital's 2-year experience with pneumococcal vaccine. Chart review of 173 patients given PPV23 between January 1, 2004 and December 31, 2005 revealed five who had significant adverse reactions, including local cellulitis, fever, and vomiting. Variables considered included age at immunization, indication for PPV23, and prior pneumococcal vaccines. The mean age of all patients given PPV23 during the defined time period was 8.6 years, and the most common indication for vaccination was recurrent infection. Of those patients who had adverse reactions, the mean age was 6.5 years. The time from prior pneumococcal vaccination was a mean of 20 months in children who did not have an adverse reaction. None of the patients who had an adverse reaction had documentation of receiving PPV23 before. Local reactions to PPV23 occur in ~50% of recipients, and revaccination of immunocompetent individuals increases the risk for local reaction. Systemic reactions are less common and only occur in ~1% of recipients. Our patient had no identifiable risk factors for development of an adverse reaction. Additional studies are indicated to determine whether there are identifiable risk factors for the development of adverse reactions to PPV23.

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Streptococcus pneumoniae is a significant cause of serious disease among young children and the elderly. Two vaccines have been developed in an effort to prevent invasive disease by *S. pneumoniae* in high-risk individuals. There have been few reported cases of systemic adverse reactions to these vaccines. Local reactions after immunization with the 23-valent vaccine and the hepta-valent vaccine occur in ~30–50% of recipients and are reported more frequently with repeated dosing.¹

As part of the work-up of individuals with suspected immunodeficiency, specific antibodies are frequently measured to determine response to common childhood vaccines. These antibodies typically include those representative of protein antigens (i.e., diphtheria and tetanus) and of polysaccharide antigens (i.e., pneumococcus). If the antibody titers are not protective, patients are given a booster immunization, and the titers are repeated to document presence or lack of response.

Here, we report a case of a child who developed significant local and systemic reactions after being administered the 23-valent-polysaccharide pneumococcal vaccine (PPV23) as part of an evaluation for possible immunodeficiency.

METHODS

Case Report

A 5-year-old Caucasian male was seen initially in the outpatient allergy and immunology clinic for evaluation of recurrent otitis media and chronic rhinitis. His medical history was significant for patent ductus arteriosus, facial dysmorphism, undescended testes, and chromosome 6q deletion (as determined by an evaluation by a geneticist). He had been followed by otolaryngology for the recurrent otitis media associated with conductive hearing loss and speech delay. His family history was remarkable for asthma and environmental allergies but there were no known immunodeficiencies or unexplained deaths. Skin-prick testing was negative to a panel of common aeroallergens. Screening immunology studies, including complete blood count with differential and quantitative immunoglobulins, were significant only for a slightly low absolute lymphocyte count (ALC) of 1500. On subsequent visits, the ALC was followed and remained at this level.

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At follow-up 4 months later, the child continued to have recurrent otitis media and had begun to have recurrent sinus infections as well. Further investigation of his immune function was initiated, including titers to diphtheria, tetanus, and pneumococcus, and a lymphocyte enumeration panel. His lymphocyte enumeration panel results revealed normal percentages and absolute numbers for CD3, CD4, CD8, CD16+56 and CD19 cells. In addition, he had protective titers to diphtheria and tetanus. However, he was found to have protective titers to only one of seven pneumococcal serotypes tested. Therefore, he was given the 23-valent Pneumovax (Merck & Co., Inc., Whitehouse Station, NJ) vaccination and was instructed to have the titers repeated three weeks after the vaccination.

Approximately 24 hours after the Pneumovax 23 injection, the child developed erythema, pain, and swelling at the injection site on the right upper arm. Over the following 2 days, he developed spreading erythema, fever to a maximum temperature of 103°F, vomiting, and diarrhea. Ultimately, he was evaluated in the emergency department of a children's hospital and admitted for i.v. antibiotic therapy for cellulitis of the right arm. Pertinent laboratory values upon admission included a white blood cell count of 19.6×10^3 cells/mm³ (89% neutrophils, ALC 1600), erythrocyte sedimentation rate of 110 mm/hour, and C-reactive protein of 23.7 mg/dL. The remaining complete blood count values were within their respective reference ranges. A peripheral blood culture was also collected prior to initiation of antibiotic therapy. During the hospital stay, the erythema continued to spread distally.

When the erythema failed to improve, an ultrasound of the upper extremity was done that revealed no evidence of abscess. However, the child remained febrile with minimal improvement in erythema and pain through 5 days of antibiotic treatment. The orthopedics team then performed an incision and drainage of a right elbow abscess. Cultures were collected, which ultimately grew coagulase-negative *Staphylococcus*, which was felt to be a contaminant. His blood culture showed no growth after observation for 5 days. After the incision and drainage, the patient showed rapid improvement with resolution of fever and decreasing erythema and pain with increasing range of motion. He was discharged to home on oral antibiotics. He made a full recovery from this illness and has resumed full, unlimited use of his right upper extremity. Postpneumococcal vaccine antibody titers were obtained approximately 2 months after the initial Pneumovax 23 injection and the hospitalization. At that point, he had protective titers to eight of the twelve serotypes tested.

A RETROSPECTIVE REVIEW OF PATIENTS GIVEN PNEUMOVAX 23

The findings in this case led us to review the medical records of 173 patients in the Nemours health system who had been given PPV23 between January 2004 and December 2005. A total of five patients reported adverse reactions after receiving the vaccine.

Results of Review

The most common indication for vaccination was recurrent upper respiratory infection. Of those receiving the vaccine, adverse reactions were reported in five patients, including the patient described here (2%). Because the immunization was given by another department in two of these five patients, information about titers prior to immunization was not available. Pneumococcal titers were available for only one other patient who reported an adverse reaction. This patient had protective titers for one of twelve serotypes tested before vaccination and ten of twelve after the vaccination. The indications for Pneumovax in these patients were preparation for college, sickle cell anemia, low IgG and IgA, and recurrent infections. Three of the five patients who had reactions developed local swelling, fever, and emesis. The other two patients had local swelling only and low-grade fever. Previous vaccination records were available for 57 of the 173 patients and were reviewed for time between vaccinations. In children who had no adverse reaction, the mean time from last PPV23 was 20 months with a standard deviation of 11.7 months. These patients had received a mean of 1.1 prior PPV23 vaccinations. None of the patients who had an adverse reaction had received PPV23 before.

DISCUSSION

Streptococcus pneumoniae is the leading cause of bacteremia, sinusitis, pneumonia, and acute otitis media. It accounts for ~17,000 cases per year of invasive disease in the United States in children younger than 5 years.² In adults, it has been identified as the cause of 10–25% of all pneumonia and ~40,000 deaths annually.³ Because of the widespread occurrence of serious illness due to this bacteria, two vaccinations have been developed. The first was a 23-valent polysaccharide vaccine approved for use in individuals age 5 years and older in 1983. This vaccine contains the capsular polysaccharides from the 23 most virulent and common strains of pneumococcus. Because of the lack of protection in children younger than 2 years, the group with the highest rate of disease, a PCV7 vaccine (contains serotypes 4, 6B, 9V, 14, 18C, 19F, and 23F [all of which are in the 23-valent vaccine]) was recommended for use in this younger age group in 2000.² This newer vaccine currently is recommended for routine delivery at 2, 4,

6, and 12 months of age to infants 2–23 months of age. The original 23-valent vaccine is recommended for all individuals 65 years or older and for those 5–64 years of age with chronic medical conditions that place them at increased risk for infection.¹

The development of mild local reactions after vaccination with PPV23 is not uncommon. Approximately 50% of patients given this vaccine will report erythema and pain at the injection site.⁴ The risk for this is increased to around 60% with revaccination in immunocompetent individuals.^{5,6} The current recommendations for revaccination with PPV23 are 5 years after the first vaccination in adults and 3 years after the first vaccination in children younger than 10 years at the time of revaccination. The development of systemic symptoms is rare, although it has been reported in the literature.^{7,8,9} The symptoms are thought to be due to an arthus-like reaction with preformed antibody complexes inducing a local inflammatory response.^{1,6} These immune complexes are deposited in the blood vessels and lead to the activation of the complement pathway. In the patients for which we had prevaccination titers, however, these showed preformed antibodies to only one of seven or twelve serotypes tested, and neither had never received the PPV23 vaccine before.

Studies evaluating the safety of administration of PPV23 in children who have previously received PCV7 reported no increase of adverse events in these patients.² This led us to evaluate our patients for previous vaccination with PCV7. Those who did not have an adverse reaction had a mean of 2.4 PCV7 before receiving PPV23. The mean for children with an adverse reaction was 4.0 PCV7. The protective titer prevaccination in the patients with an adverse reaction was a PCV7 serotype in only one of the patients. In addition, the mean time from last PCV7 vaccination to PPV23 vaccination in patients without an adverse reaction was 39.8 months (standard deviation 15.3 months) versus 26.5 months (standard deviation 8.5 months) in patients with an adverse reaction. Therefore, this seems to support the findings that previous PCV7 vaccination does not increase risk of adverse reaction to PPV23.

Gherardi and Authier describe a macrophagic myofasciitis developing in patients after intramuscular injection of vaccines containing aluminum hydroxide as an adjuvant.¹⁰ This was further described by Rimaniol et al in 2004.¹¹ However, this condition appears to be a more chronic condition characterized by fatigue, central nervous system manifestations such as sleep and mood disturbance, diffuse myalgias, and elevated serum creatine-kinase concentration. It may present

months to years after the actual vaccination. Although this presents a possible explanation to adverse reactions to some vaccines, our patients do not seem to fit this description because they all achieved full recovery within a matter of days to a few weeks.

In summary, we presented the case of a systemic reaction to PPV23 in a child with no clear risk factors based on previous vaccination to pneumococcus. The cause of this severe reaction is unclear. Therefore, it is advisable to follow the current recommendations of the American Committee on Immunization Practices for time to revaccination to minimize the likelihood of developing an adverse reaction. This may be difficult, however, in the evaluation of a patient with suspected immunodeficiency when it is necessary to administer a polysaccharide vaccine and measure immune response. More studies are needed to determine whether there are identifiable risk factors for patients who will develop adverse reactions and to determine the etiology of such reactions in patients without significant prevaccination antibody titers.

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