Increased risk of serious pneumococcal disease in patients with atopic conditions other than asthma

Ji A. Jung, MD, PhD,[a,c] Hirohito Kita, MD,[a] Barbara P. Yawn, MD, MSc,[d] Thomas G. Boyce, MD, MPH,[a] Kwang H. Yoo, MD, PhD,[e] Michaela E. McGree, BS,[b] Amy L. Weaver, MS,[b] Peter Wollan, PhD,[d] Robert M. Jacobson, MD,[a] and Young J. Juhn, MD, MPH[a] *Rochester, Minn, and Seoul, South Korea*

Background: We reported an increased risk of serious pneumococcal disease (SPD) among patients with asthma. It is not known whether this is true for patients with other atopic conditions.

Objective: To determine the relationship between atopic conditions other than asthma and SPD.

Methods: The study subjects were residents of Rochester, Minn, who developed SPD between 1964 and 1983 and their 2 sex-matched and age-matched controls. We used a population-based computer-linked medical diagnosis system to identify all individuals with potential SPD. All records were reviewed by using explicit predetermined criteria for SPD. All individuals with atopic conditions were identified by the physician diagnoses including atopic dermatitis or eczema, allergic rhinitis, and hay fever documented in medical records. The associations between these atopic conditions and SPD were assessed by using conditional logistic regression.

Results: A total of 3941 records were reviewed, and we identified 174 SPD cases. Of these 174 cases, 50.6% were male, and 94.3% were Caucasian. Twenty-six (14.9%) of the SPD cases and 29 (8.3%) of the controls had atopy. Atopic conditions other than asthma were associated with an increased risk of SPD (odds ratio, 2.13; 95% CI, 1.04-4.35; $P = .04$) after adjusting for smoking status, previous high-risk conditions for SPD, educational status, and ethnicity.

Conclusion: Like asthma, other atopic conditions, particularly atopic dermatitis, are associated with an increased risk of SPD. There may be a common immunogenetic mechanism underlying increased risk of SPD among individuals with either asthma or other atopic conditions. Our study findings need to be studied further. (J Allergy Clin Immunol 2010;125:217-21.)

Key words: *Atopic dermatitis, allergic rhinitis, serious pneumococcal disease, epidemiology, risk, pneumococcal pneumonia, Rochester Epidemiology Project*

Streptococcus pneumoniae presents a global threat of morbidity and mortality among children and adults. One million children younger than 5 years of age die from pneumonia and invasive pneumococcal disease (IPD) globally each year.[1] In the United States, the annual number of fatal pneumococcal infections is 40,000.[2] *S pneumoniae* is responsible for 6 million cases of otitis media per year; nasopharyngeal colonization among 20% to 50% of the population as a prelude to IPD; 100,000 cases of pneumonia; 60,000 cases of sepsis per year; and 3300 cases of meningitis per year in the United States. The case-fatality rate was 10% for all reported cases (1556 deaths/15,544 cases). Case-fatality rates increased from 1.4% among persons younger than 2 years to 20.6% among persons age 80 years or older.[3]

For the causes of IPD, the Advisory Committee on Immunization Practices (ACIP)–recommended pneumococcal vaccine–eligible conditions accounted for only 50.6% of IPD, but a large proportion of IPD cases occur among people without high-risk conditions for IPD.[3] Talbot et al[4] and Juhn et al[5] independently reported that patients with asthma were at a significantly increased risk of IPD. According to the results of these studies, the population-attributable risk percentage for asthma was 11% to 17%. The ACIP has recently issued a new recommendation that all adults with asthma (19-64 years) receive a single dose of 23-valent pneumococcal polysaccharide vaccine (PPV-23) to prevent IPD.[6]

Atopic conditions other than asthma such as atopic dermatitis or eczema, allergic rhinitis, or hay fever share the similar underlying immunologic mechanisms with asthma—that is, T_H2-predominant immune milieu[7-10]—and individuals with atopic dermatitis have been reported to have poor humoral and cell-mediated immune responses as well as innate immunity.[11-15] Currently, despite the shared immunologic mechanism among asthma and other atopic conditions, little is known about whether patients with atopic conditions other than asthma are associated with the risk of serious pneumococcal disease (SPD). No population-based study has been conducted to examine the relationship between atopic conditions other than asthma and SPD. To determine whether individuals with atopic dermatitis and/or allergic rhinitis have an increased risk of developing SPD, defined

From the Departments of [a]Pediatric and Adolescent Medicine and [b]Health Sciences Research, Mayo Clinic, Rochester; [c]the Department of Pediatric and Adolescent Medicine, Hallym University College of Medicine, Seoul; [d]the Department of Research, Olmsted Medical Center, Rochester; and [e]the Department of Internal Medicine, Konkuk University School of Medicine, Seoul, South Korea.

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Reprint requests: Young J. Juhn, MD, MPH, Division of Community Pediatric and Adolescent Medicine, Department of Pediatric and Adolescent Medicine, Mayo Clinic, 200 1st Street SW, Rochester, MN 55905. E-mail: juhn.young@mayo.edu.

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Abbreviations used
ACIP: Advisory Committee on Immunization Practices
IPD: Invasive pneumococcal disease
OR: Odds ratio
PPV-23: 23-Valent pneumococcal polysaccharide vaccine
SPD: Serious pneumococcal disease

as IPD and/or pneumococcal pneumonia, we conducted a population-based case-control study among the residents of Rochester, Minn, between 1964 and 1983.

METHODS

The study was approved by the Institutional Review Boards at both the Mayo Clinic and Olmsted Medical Center. This is a population-based retrospective case-control study designed to assess whether there was a higher prevalence of atopic conditions other than asthma before January 1, 1984, among the Rochester residents who developed SPD between 1964 and 1983, a primarily prepneumococcal vaccine era, compared with controls. SPD cases were identified through reviewing 3941 medical records, and atopic dermatitis and/or allergic rhinitis were ascertained by using documentation of the physician diagnosis of atopic dermatitis or eczema, allergic rhinitis, and/or hay fever in medical records.

Study setting and population

The study setting and population were previously described.[5] Rochester, Minn, is an excellent setting to conduct a retrospective case-control study such as this because medical care is virtually self-contained within the community, and the Rochester Epidemiology Project provides information on all Rochester residents who had received medical care from 2 primary medical centers in Rochester. The medical records for each site contain all inpatient and outpatient data. All diagnostic information has been indexed since 1935 by using Berkson codes even before International Classification of Diseases codes were available.[16] The incidence rate of asthma in Rochester was 238 per 100,000, which is comparable to those in other communities such as Tecumseh, Mich (250/100,000).[17]

Ascertainment of SPD cases

We reported the details for ascertainment of SPD cases previously.[5] Briefly, a total of 85 different medical index search codes (Berkson codes and International Classification of Diseases codes) were used to identify potential SPD cases, and each potential case was then confirmed by medical records review. We reviewed medical records of all 3941 persons and identified 174 SPD cases between 1964 and 1983. Case definition of SPD included isolation of *S pneumoniae* from a normally sterile site (such as blood or cerebrospinal fluid), and/or pneumococcal pneumonia requiring all 3 of the following criteria: (1) a physician diagnosis of pneumonia, (2) the isolation of pneumococcus from sputum gram-stain or culture, and (3) the documented pneumonia by chest radiograph. We defined the index date of onset of the SPD as the date of documented isolation of *S pneumoniae*.

Selection of controls

Selection of controls was previously described.[5] A list of potential controls was generated from the Rochester Epidemiology Project computerized database (almost 95% of community members), and the index date for controls was defined as the index date of SPD for the corresponding matched case. Two sex-matched and age-matched control individuals who had never developed SPD were randomly selected from the community. We applied the same eligibility and exclusion criteria of SPD cases to controls.

Exposure ascertainment (ie, atopy conditions other than asthma)

After we identified SPD cases and their age-matched and sex-matched controls, atopic conditions were ascertained by the presence of physician diagnoses of atopic dermatitis or eczema, allergic rhinitis, and/or hay fever in medical records. To identify the physician diagnoses of these atopic conditions, we conducted a comprehensive medical record review. The category of the physician diagnoses of atopic conditions in verbatim included atopic dermatitis, eczema, allergic rhinitis, or hay fever documented in the entire medical records of individual subjects (ie, prevalent cases of atopic conditions before 1964 and the incident cases of atopic dermatitis between 1964 and 1983).

Other variables

During data abstraction from medical records, we collected information including sociodemographic variables (age, sex, ethnicity, and educational status), high-risk conditions for SPD (on the basis of ACIP-recommended pneumococcal vaccine–eligible conditions) before the index date of SPD, smoking status at the time of index, pneumococcal vaccination status on the basis of medical records during the study period, and antibiotics use within 7 days before the index date of SPD.

Data analysis

Data analysis for the association between atopic conditions other than asthma and SPD followed that for the association between asthma and SPD as previously reported.[5] Briefly, conditional logistic regression for matched analysis was used to determine whether atopic conditions other than asthma were associated with the risk of SPD, adjusting for pertinent covariates or confounders. Associations were summarized using the odds ratios (ORs) and corresponding 95% CIs derived from the estimated parameters in the conditional logistic models. All calculated P values were 2-sided, and P values less than .05 were considered statistically significant. The analysis was conducted using the entire study cohort, and separately by age group (<18, ≥18 years of age). Analyses were performed by using the SAS version 9.1 software package (SAS Institute, Inc, Cary, NC).

RESULTS

Study subjects

The details of sociodemographic and clinical characteristics of study subjects are summarized in Table I. We reviewed a total of 3941 records and identified 174 SPD cases. Of these confirmed 174 SPD cases, 16% (n = 28), 22% (n = 38), and 62% (n = 108) had SPD, SPD with pneumococcal pneumonia, and pneumococcal pneumonia, respectively. Of the SPD cases, the age at index date was 57.0 (mean) ± 26.5 (SD) years old, 50.6% were male, and 94.3% were Caucasian. Only 21 cases (12%) were younger than 18 years. Fifty-one SPD cases (29.3%) and 18 controls (5.2%) had at least 1 high-risk condition for SPD before the index date of SPD. Twelve SPD cases (11 for 14-valent pneumococcal vaccine and 1 for 23-valent pneumococcal vaccines) had received a pneumococcal vaccine before the index date, whereas none of the controls had received a pneumococcal vaccine. Of these 12 SPD cases, 1 (58%) had pneumococcal vaccine–eligible conditions before the index date, whereas 5 (42%) did not have any pneumococcal vaccine–eligible conditions before the index date.

Atopic conditions and SPD

The results are summarized in Table II. Twenty-six (14.9%) of the SPD cases and 29 (8.3%) of the controls had atopic conditions other than asthma. In analysis with all subjects, the unadjusted OR