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ORIGINAL ARTICLE

The burden of epiglottitis among Japanese children before the *Haemophilus influenzae* type b vaccination era: an analysis using a nationwide administrative database

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Abstract Epiglottitis is a potentially life-threatening disease and is largely preventable by vaccination against *Haemophilus influenzae* type b (Hib). Little is known, however, about the epidemiology of childhood epiglottitis in Asian countries, including Japan. Using a nationwide inpatient database, this study aimed to determine the burden of childhood epiglottitis before the introduction of Hib vaccine into Japan. The study period was between July and December in 2007 and 2008, when Hib vaccine was not available. We found 102 cases with epiglottitis among children ≤5 years old. The annual incidence of epiglottitis in children ≤5 years old was estimated to be 3.2 per 100,000 population per year. Among the 102 patients, 31 (30.4 %) required respiratory support, including two cases with tracheotomy and one fatal case. Our study demonstrated the substantial burden of epiglottitis among Japanese children, highlighting that a routine Hib vaccination program is essential.

Keywords Epiglottitis · Epidemiology · Children · *Haemophilus influenzae* type b (Hib) · Vaccination

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Introduction

Epiglottitis is a rare but potentially life-threatening disease due to an acute onset of upper airway obstruction [1]. *Haemophilus influenzae* type b (Hib) is responsible for 75–90 % of epiglottitis in children [2], and the incidence of epiglottitis has been dramatically decreased in countries where universal Hib vaccination programs are available [1, 2]. In Asian countries, including Japan, data on childhood epiglottitis are scarce; a previous study, reviewing both English and non-English publications, reported that data were nearly absent [3]. In Japan, the Hib vaccine program was launched in December 2008 on a voluntary basis [4], and its coverage rate has yet to be examined. Active surveillance of epiglottitis is not currently performed in Japan. In this study, we used a Japanese nationwide administrative claims database to estimate the incidence and describe the clinical features of epiglottitis among Japanese children before the vaccination program was launched.

Patients and methods

Ethical consideration

This retrospective observational study was performed with the approval of the Institutional Review Board of the University of Tokyo. Informed consent of each patient was waived because of the anonymous nature of the data.

Nature of the database

The Diagnosis Procedure Combination (DPC) database includes administrative claims and discharge abstract data on inpatients discharged from 1 July to 31 December every

year [5, 6]. The database includes data on approximately 3 million inpatients from 926 hospitals in 2007 and 2.9 million from 855 hospitals in 2008, representing approximately 45 % of acute-care admissions in Japan. All 82 university hospitals are obliged to participate in the database, but the participation of community hospitals is voluntary. The database contains patient demographic data; diagnoses, complications and comorbidities coded with the *International Classification of Diseases, 10th revision* (ICD-10) codes and Japanese texts; medical procedures performed; and discharge status. The database does not include detailed clinical information such as clinical history, laboratory test results, and vaccination status.

Inclusion criteria of cases

We screened children ≤5 years old with a diagnosis of epiglottitis using the ICD-10 code (J05.1) and who were discharged between 1 July and 31 December 2007–2008. To improve the reliability of diagnosis in each case extracted from the database, we referred to the diagnosis provided in the Japanese text as well as ICD code. Patients who met one of the following criteria were defined as cases and were included for the subsequent analyses: (1) patients who had a primary diagnosis of epiglottitis, and (2) patients who had a primary diagnosis of respiratory failure or bacteremia/sepsis and a secondary diagnosis of epiglottis as a complication or comorbidity. After ascertaining each case, we investigated patients' demographics and clinical courses, including airway management.

Estimation of population-based incidence and statistical analysis

Although the DPC database covered 45 % of hospitalizations in Japan, patient sampling was not random, and it is uncertain whether the database proportionally retrieved epiglottitis cases. There is a potential bias in patient selection, as patients with severe conditions may tend to be admitted to large hospitals. To reduce the bias arising from hospital volume, we used the same approach as previously described for estimating the incidence of childhood intussusception in Japan [5]. First, we divided the DPC-participating hospitals and all hospitals in Japan into four strata ($i = 1, 2, 3, 4$) according to bed numbers: <400 ($i = 1$), 400–599 ($i = 2$), 600–799 ($i = 3$), and ≥800 beds ($i = 4$). Then, the annual number of cases [and 95 % confidence intervals (CI)] with childhood epiglottitis in each strata in all hospitals in Japan (Y_i) were calculated by applying the following equation:

$$Y_i/N_i = p \pm 1.96\sqrt{p(1-p)/n_i}, \quad p = 2X_i/n_i$$

where N_i indicates the bed numbers in all hospitals in Japan, X_i denotes the number of epiglottitis cases found in the DPC database, and n_i represents the bed numbers in DPC-participating hospitals. We assumed that there was no seasonality of the incidence of epiglottitis [7] and doubled the half-year number of cases (X_i) to obtain the whole-year number of cases. According to the Population Census data, the number of children ≤5 years old residing in Japan during the study period was 6,355,000. We used this figure as the denominator of the estimated population-based incidence of childhood epiglottitis. To compare continuous variables between two groups, we applied Student's t test using IBM SPSS version 19 (IBM Corp., Armonk, NY, USA). A P value of <0.05 was considered as statistically significant.

Results

Number and incidence of childhood epiglottitis cases

A total of 102 cases of epiglottis were identified from July to December 2007—2008. Table 1 shows the process of estimating the annual number of epiglottitis cases in children (≤5 years old) in Japan. As a result, the annual number was estimated to be 259–260 cases, and the estimated incidence was 3.2 per 100,000 population per year.

Patient characteristics and clinical course

Of the 102 patients, 71 (69.6 %) were boys. Mean age at admission was 2.3 ± 1.1 years. Figure 1 shows the age distribution. The mean length of hospital stay was 7.2 ± 4.4 days. Underlying infectious diseases were documented in 18 (17.6 %) cases. Among them, sepsis/bacteremia was the most common, which was found in 66.7 % (12/18) of cases; *H. influenzae* accounted for 41.7 % of sepsis/bacteremia cases (5/12). Other infectious diseases included *H. influenzae* infection ($n = 1$); pneumococcal pneumonia ($n = 1$); mycoplasma pneumonia ($n = 1$); and viruses that included the influenza A virus ($n = 1$), adenovirus ($n = 1$), respiratory syncytial virus ($n = 1$), and unspecified virus ($n = 1$). Thirty-one (30.4 %) patients required mechanical ventilation, including two with tracheotomy. The average age at admission was not significantly different between patients with and without respiratory support (2.2 vs. 2.6 years old, $P = 0.146$). The average duration of ventilation was 4.6 (range 1–12) days. Patients with mechanical ventilation stayed in hospital longer than those without airway management (10.6 vs. 5.6 days, $P < 0.001$). Among the 31 patients with ventilation, 30 (96.8 %) survived; one patient with a fatal