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ORIGINAL ARTICLE

Antineutrophil cytoplasmic antibody-associated vasculitis in Taiwan: A hospital-based study with reference to the population-based National Health Insurance database

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Antineutrophil cytoplasmic antibody-associated vasculitis;
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Background: Antineutrophil cytoplasmic antibody-associated vasculitis (AAV), including granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), and Churg–Strauss syndrome (CSS), comprises a group of diseases with significant morbidity and mortality. The incidence and relative frequency of GPA/MPA/CSS are different all over the world. The epidemiology of AAV in Taiwan is still not clear.
Methods: The current study aimed to provide a population-based estimate of the annual incidence of GPA using the Taiwan National Health Insurance (NHI) research database and a single hospital-based estimate of the relative frequency of AAV in Taiwan.
Results: The annual incidence of GPA in Taiwan was 0.37 per million patient-years (95% Poisson rate confidence interval: 0.30–0.45) from 1997 to 2008, according to the NHI database. In our hospital, 24 patients were newly diagnosed with AAV between 2003 and 2011, including eight patients with GPA, 14 with MPA, and two with CSS. The ratio of the number of patients with GPA to that of MPA was 0.57.
Conclusion: The current results provide an estimate of the annual incidence of GPA and the relative frequency of AAV in the Chinese Han community in Taiwan. Such geoepidemiology

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information may help illuminate the interaction between ethnic background and environment in these autoimmune diseases.

Introduction

Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV), including granulomatosis with polyangiitis (GPA; previously known as Wegener's granulomatosis), microscopic polyangiitis (MPA), and Churg—Strauss syndrome (CSS), comprises a group of rare diseases associated with high morbidity and mortality. The timely diagnosis of any of these conditions is difficult due to their rare occurrence and variable clinical manifestations. The clinical diagnosis of AAV is facilitated by the recent availability of an enzyme-linked immunosorbent assay (ELISA) for ANCA, which has provided improved specificity compared with an indirect immunofluorescence assay.[1—3] The reported incidence of GPA, MPA, and CSS varies significantly all over the world. A north-to-south gradient of the GPA/MPA ratio is believed to exist according to the European data. For example, the incidence ratio of GPA/MPA is increased in Norway [incidence of GPA and MPA: 10.5 per million and 2.7 per million, respectively (ratio 3.9)] and decreased in Spain [incidence of GPA and MPA: 4.9 per million and 11.6 per million, respectively (ratio 0.42)].[4] Non-Caucasian epidemiological studies of AAV remain limited; a study in Japan showed that MPA comprises up to 83% of AAV.[5] Therefore, an examination of the incidence of AAV across ethnicities and geographic regions in Taiwan may help reveal the interaction between genetic and environmental components as contributing factors to these complex diseases.

There is a paucity of research examining AAV in Taiwan.[6,7] The Taiwan National Health Insurance (NHI), a single health insurance provider for citizens of Taiwan since 1995, is a good data source for the epidemiologic study of these rare diseases. The NHI Research Database uses the Ninth Revision of the International Classification of Diseases (ICD-9) for disease registry. At the time of data collection, only GPA had an ICD-9 code and data on the incidence of MPA or CSS were not available in the NHI database. The incidence of MPA or CSS may be estimated from the relative frequency of GPA, MPA, and CSS. This study aimed to estimate the incidence of GPA using the Taiwan NHI database analysis and to derive the relative incidence of AAV (GPA/MPA/CSS) as well as the clinical characteristics of these patients from a single-center experience.

Methods

National Health Insurance Research Database

The total number of patients with GPA and the annual incidence rate were derived from the NHI Research Database. In 2008, the NHI provided coverage for a population of nearly 23 million (approximately 99.5% of the population). The NHI research database includes all claim information of outpatients, inpatients, and emergency departments.[8] GPA (ICD-9 446.4) and end-stage renal disease (ESRD; ICD-9 585) that require renal replacement therapy are listed as catastrophic diseases in the NHI database. Patients with these severe diseases are exempt from a copayment at the time of care. In addition, the catastrophic disease registry is under the regulation of the NHI authority.

For the current study, the catastrophic illness file of the NHI claims data was used for analysis. We selected the patients who were diagnosed with GPA (ICD-9 446.4) between 1997 and 2008. The incident date was defined by the date of catastrophic illness certification. The annual incidence rate was defined as the number of new cases divided by the number of person-years observed during a given time period. Sex and age at diagnosis were obtained. The number of patients with ESRD and GPA, and the time interval between the diagnosis of ESRD and GPA were also calculated.

Generation of patient lists in the hospital-based study

Between October 2003 and October 2011, a list of patients diagnosed with AAV was generated from computerized databases of serology, pathology, electronic chart record system, and consultation records in the Far Eastern Memorial Hospital, New Taipei City, Taiwan. Patients with a creatinine clearance of less than 15 mL/minute were classified as having ESRD. All study protocols were approved by the Institutional Review Board of the Far Eastern Memorial Hospital (FEMH-IRB-100165-E).

Case ascertainment and classification

Complete chart reviews revealed patient demographic data, including sex, age at diagnosis, initial presentations, ANCA status, treatment, and prognosis. Clinical records of surrogate markers such as sinusitis, image studies of lung, urine analysis, and pathology reports were reviewed carefully. Proteinase 3 ANCA (PR3-ANCA) and myeloperoxidase ANCA (MPO-ANCA) were tested using commercial ELISA kits (EliA PR3 and EliA MPO; Phadia AB, Uppsala, Sweden). We followed the European Medicines Agency (EMEA) algorithm to avoid overlapping of cases and to ensure consistency of classification across studies.[9]

Statistical analysis

The annual incidences of GPA in each 3-year interval between 1997 and 2008 were calculated. The 95% confidence intervals of Poisson rate were calculated for each period using StatsDirect Version 2.7.9 (StatsDirect Ltd, Altrincham, UK).