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Incidence of Erythromelalgia: A Population-Based Study in Olmsted County, Minnesota

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Abstract

Objective—To estimate the population-based incidence of erythromelalgia.

Background—Only one report describing the incidence of erythromelalgia has been published previously.

Study Design—A population-based analysis of data from the Rochester Epidemiology Project.

Setting—Tertiary care medical center in Olmsted County, Minnesota (a rural county in the southeastern portion of the state).

Patients—Thirty-three residents of Olmsted County with a diagnosis of erythromelalgia during the study period.

Methods—Age- and sex-specific incidence rates of erythromelalgia were determined.

Intervention—None.

Main Outcome—Population-based incidence rate.

Results—The overall age- and sex-adjusted incidence rate (95% confidence interval) was 1.3 (0.8–1.7) per 100,000 people per year. The incidence of primary and secondary erythromelalgia was 1.1 (0.7–1.5) and 0.2 (0.02–0.4) per 100,000 people per year, respectively. The age-adjusted incidence rates (95% confidence interval) were 2.0 (1.2–2.7) per 100,000 women and 0.6 (0.1–1.1) per 100,000 men. The study was limited by the small sample size and potential variability in recognition of erythromelalgia.

Conclusion—The population-based incidence of erythromelalgia has increased with each decade in Olmsted County over the past 3 decades; overall incidence was 1.3 per 100,000 people per year.

Keywords

epidemiology; erythromelalgia; incidence; population-based study

Introduction

Erythromelalgia is a clinical syndrome that is defined by the triad of erythema, increased temperature, and intermittent pain in the extremities (1,2). It typically has a chronic course and is associated with diminished quality of life and considerable disability (3). The disease may be primary or secondary; as a secondary disease, it most commonly is associated with myeloproliferative disorders such as polycythemia vera and thrombocytopenia (1,4).

The incidence of erythromelalgia has been estimated in a Norwegian population to be 0.25 to 0.33 per 100,000 people per year (5), but to our knowledge, no population-based study has been performed to date. To estimate the true incidence of this condition, we performed a population-based analysis of erythromelalgia in Olmsted County, Minnesota.

Methods

This study was approved by the Mayo Clinic Institutional Review Board. Olmsted County, Minnesota, is an ideal setting for population-based studies. The community is relatively isolated from urban centers, and most residents seek medical care with 2 providers, Mayo Clinic and Olmsted Medical Center. Through the Rochester Epidemiology Project (6), an extensive medical indexing system has been generated based on medical and surgical diagnoses from over 95% of patients in the county. This facilitates aggregation of medical information from all providers in the area. The patient records from all medical providers in Olmsted County were reviewed.

All potential subjects were identified by searching the Rochester Epidemiology Project database with diagnostic codes for “erythromelalgia,” “erythermalgia,” and “other peripheral vascular disease” from January 1, 1976, through December 31, 2005. A patient was considered to have erythromelalgia if a physician documented the clinical diagnosis of the condition or if the medical record reflected the triad of redness, burning pain, and bilateral increased temperature of the hands or feet (or both). Only patients who were residents of Olmsted County at the time of diagnosis and received a clinical diagnosis of erythromelalgia were included in the study. Patients were considered to have secondary erythromelalgia if they had a coexisting diagnosis of a myeloproliferative disorder such as polycythemia vera, chronic myelocytic leukemia, or thrombocytopenia at the time of diagnosis of erythromelalgia, if a myeloproliferative disorder was diagnosed within 2 years of the diagnosis of erythromelalgia, or if the erythromelalgia was thought to be attributable to another cause such as medications, human immunodeficiency virus, or mushroom poisoning.

Age- and sex-specific incidence rates were calculated with the assumption that the entire population of Olmsted County was at risk from 1976 through 2005. The numerator was the number of persons with the first occurrence of erythromelalgia within the study period. The denominator was obtained from decennial census data from 1976 through 2005, and linear interpolation was used between census years. Rates were age- and sex-adjusted to the population structure of US whites in 2000. The 95% confidence intervals (CIs) for the rates were calculated assuming a Poisson error distribution.

The association between incidence rate and sex, age (10-year groups), and time period of diagnosis (10-year intervals) were assessed by fitting generalized linear models and assuming a Poisson error structure (SAS procedure GENMOD; SAS Institute Inc, Cary, North Carolina). Observations used for the regression analysis were the crude incidence counts for all combinations of sex, 10-year age groups, and 10-year intervals, which were offset by the natural logarithm of the number of persons. The significance of sex and linear

trends across age groups and time periods were each assessed with likelihood ratio statistics with 1 degree of freedom.

Results

We initially identified and reviewed records of 59 patients. Of these, 26 were excluded (17 lacked documentation of erythromelalgia, 5 were not residents at the time of diagnosis, and 4 declined authorization for use of their medical records for research). The median age at diagnosis was 61 years (range, 16-90 years).

The overall age- and sex-adjusted incidence rate of erythromelalgia was 1.3 (95% CI, 0.8-1.7) per 100,000 persons per year. The incidence of primary and secondary erythromelalgia was 1.1 (95% CI, 0.7-1.5) and 0.2 (95% CI, 0.02-0.4) per 100,000 people per year, respectively. The incidence rates by sex and 10-year intervals are summarized in Figure 1. The age-adjusted incidence rate is shown in Figure 2. No cases of hereditary erythromelalgia were identified.

Discussion

The Rochester Epidemiology Project (6) is an extensive medical indexing system that facilitates aggregation of medical information from all health care institutions in the area and provides a rare capability for population-based studies of diseases such as erythromelalgia.

The incidence of erythromelalgia in the present study (1.3 per 100,000 persons per year) was approximately 5 times greater than the incidence rate reported in Norway in 1998 (0.25 to 0.33 per 100,000 per year) (5). The Norwegian study is the only published report of erythromelalgia incidence to date. In that report, a different technique to calculate incidence was used: most subjects contacted the research group directly (without a doctor's referral) after learning of the researchers through a health program broadcast on national radio. The disease was mentioned in only one program that aired during working hours; one could assume that few potential erythromelalgia patients heard the program. The patients were examined prospectively by 3 physicians. Additionally, some patients in that study were identified because of increased awareness of this disease among Norwegian doctors. Approximately 50% of those who responded were considered to have erythromelalgia, and 40 subjects in a population of about 4 million were thus identified. The prevalence was estimated to be 1 per 100,000, and an educated estimate of 2 per 100,000 with moderate or severe erythromelalgia was made. In a calculation derived from this prevalence value, the incidence rate of moderate-to-severe erythromelalgia was shown to be 0.25 to 0.33 per 100,000 people per year (5). How can the different incidence rates be explained? Perhaps erythromelalgia truly is less prevalent in Norway or perhaps the technique for calculating the incidence of erythromelalgia underestimated the true rate.

The data from our study showed that the incidence of erythromelalgia is increasing with time. Does incidence increase because we are only now recognizing erythromelalgia? We do not think this is the case. We believe that the increased incidence is real because physicians in Olmsted County have been quite aware of this disease for several decades (1). Our data also showed that the incidence of erythromelalgia increased with age. This finding was consistent with a previous study (1).

Several limitations must be acknowledged in the interpretation of our results. The physician's ability to recognize the disease may vary among clinical settings and over time. Patients with mild disease may not present for evaluation to a medical provider. The estimates of incidence may be inaccurate because of the small sample size. Despite these

limitations, our study suggests that the incidence of erythromelalgia is higher than previously reported and is increasing with each decade.

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Abbreviation

CI confidence interval

Figure 1. Incidence of Erythromelalgia in Olmsted County, Minnesota, 1976-2005. Plot whiskers indicate 95% confidence intervals. Rate was adjusted to the population structure of the US white population in 2000.

Figure 2.
Age-Adjusted Incidence of Erythromelalgia in Olmsted County, 1976-2005.