ORIGINAL ARTICLE

Incidence of erythromelalgia: a population-based study in Olmsted County, Minnesota

KB Reed,† MDP Davis*‡

†Mayo Medical School, College of Medicine, ‡Department of Dermatology, Mayo Clinic, Rochester, MN, USA
*Correspondence: MDP Davis. E-mail: davis.mark2@mayo.edu

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 centre in Olmsted County, Minnesota (a rural county in the south-eastern 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, 95% CI) 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% CI) 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 three decades; overall incidence was 1.3 per 100 000 people per year, approximately 5 times higher than previously reported.

Received: 25 February 2008; Accepted 20 June 2008

Keywords

epidemiology, erythromelalgia, incidence, population-based study

Conflicts of interest

None declared

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 thrombocythemia.[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.

Mark D. P. Davis, MD had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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 centres, and most residents seek medical care with two 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 1 January 1976 through 31 December 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 leukaemia or thrombocythemia 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 (95% 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, NC). 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 age intervals are summarized in Fig. 1. The age-adjusted incidence rates are shown in Fig. 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.

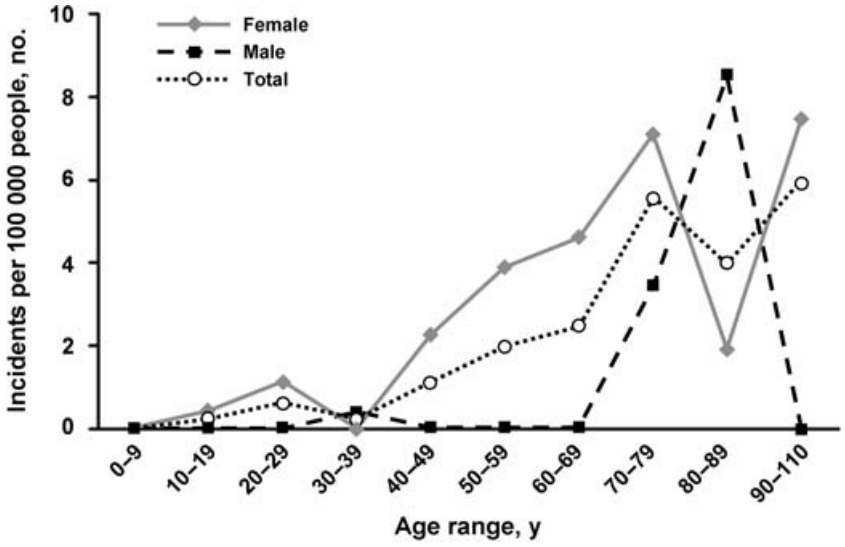

Figure 1 Incidence of ERYTHROMELALGIA in Olmsted County, Minnesota, 1976–2005. Rate was adjusted to the population structure of the US white population in 2000.

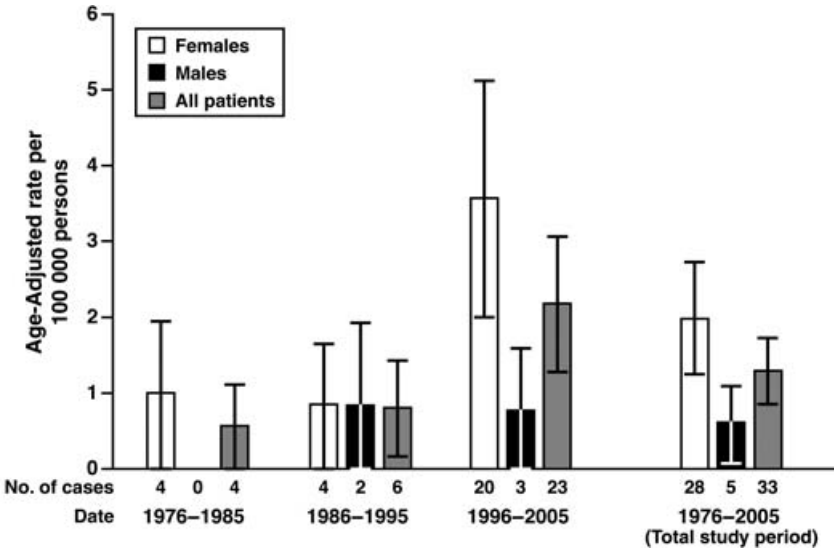

Figure 2 Age-Adjusted Incidence of Erythromelalgia in Olmsted County, 1976–2005. Plot whiskers indicate 95% CIs.

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 three 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 increases with each decade.

References

1 Babb RR, Alarcon-Segovia D, Fairbairn JF II. Erythermalgia: review of 51 cases. *Circulation* 1964; **29**: 136–141.
2 Mork C, Kvernebo K. Erythromelalgia: a mysterious condition? *Arch Dermatol* 2000; **136**: 406–409.
3 Davis MD, O'Fallon WM, Rogers RS III, Rooke TW. Natural history of erythromelalgia: presentation and outcome in 168 patients. *Arch Dermatol* 2000; **136**: 330–336.
4 Mork C. Erythromelalgia: studies on pathogenesis and therapy [thesis]. University of Oslo, Oslo (Norway), 2004.
5 Kvernebo K. Erythromelalgia: a condition caused by microvascular arteriovenous shunting. Chapter 4: incidence and prevalence. *VASA Suppl* 1998; **51**: 13.
6 Melton LJ III. History of the Rochester epidemiology project. *Mayo Clin Proc* 1996; **71**: 266–274.