Epidemiology of polymyalgia rheumatica

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ABSTRACT

Objective

To review the data on the epidemiology of polymyalgia rheumatica (PMR), in particular geographical and temporal differences in incidence and its risk factors including the actinic hypothesis.

Methods

Evaluation of the literature.

Results

Epidemiological data show that the incidence of PMR varies between 12.7/100,000 in Italy and 112.6/100,000 in Norway with a geographical gradient of increased frequency in the northern hemisphere. The incidence of PMR and giant cell arteritis (GCA) have increased in recent years. This observation may be related to a greater awareness of the disease but also to real epidemiological changes. Risk factors for PMR/GCA include infections, smoking, sun exposure, and nulliparity.

Conclusion

Epidemiological studies have helped to unravel the etiopathogenic factors at work in PMR/GCA. More data are needed on the correlation between the incidence of PMR/GCA and epidemics of infectious diseases and on environmental and biological risk factors.

Introduction

The epidemiology of polymyalgia rheumatica (PMR) and giant cell arteritis (GCA) has been extensively studied in the last years. In this review, we will consider data from descriptive epidemiology including the observation of geographical and temporal differences in incidence, the actinic hypothesis and other risk factors.

Incidence

The incidence of PMR has been investigated in several studies (1-7), which are summarized in Figure 1. In the population aged 50 years or older, it ranged between 12.7/100,000 in Italy (1) and 112.6/100,000 in Norway (7). Incidence varied as much as ten-fold in different areas, an observation that has been related to a geographical pattern. In fact, the incidence of PMR and GCA is higher in the northern hemisphere and in populations of Anglo-Saxon origin. Figure 2 shows the positive correlation between incidence and the latitude of the geographical area where the study was performed (Spearman's rank correlation = 0.66). This correlation is higher for GCA (0.78) than for PMR (0.57). Possible explanations for this trend, which is com-

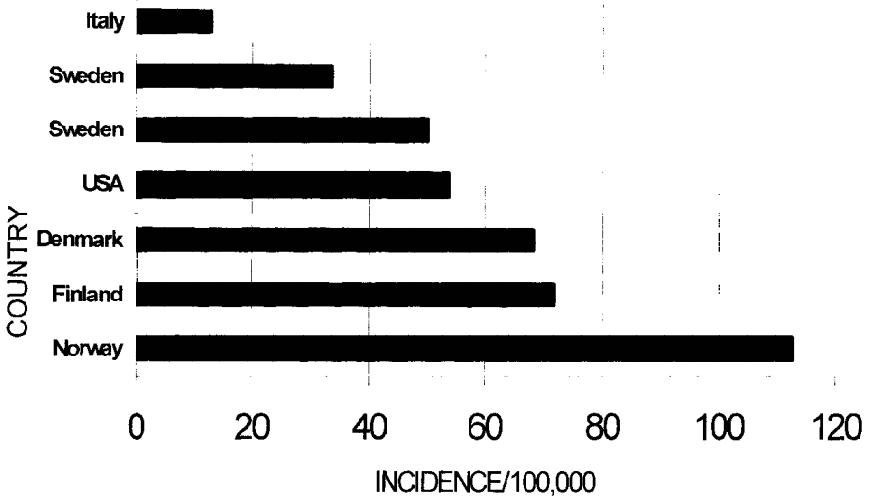

Fig. 1. Incidence of polymyalgia rheumatica in different countries. The data are obtained from references 1-7.

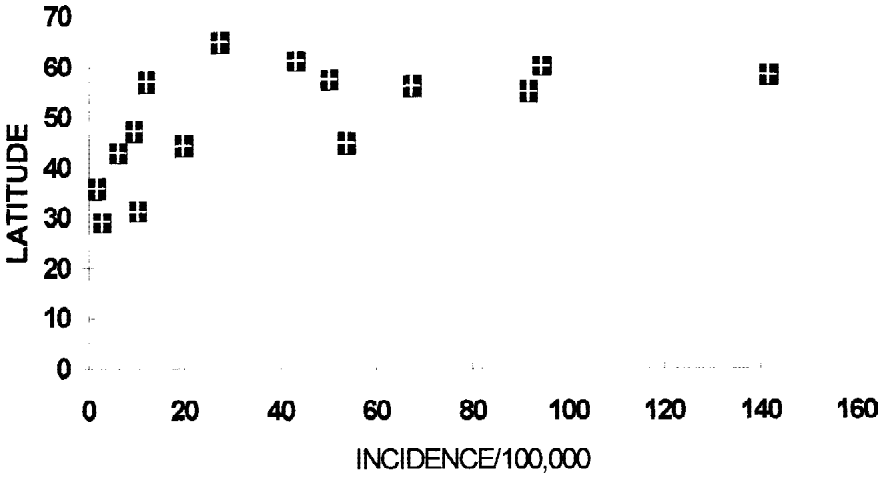

Fig. 2. Relationship between the incidence of polymyalgia rheumatica/giant cell arteritis and the latitude of the geographical area where the corresponding study was performed.

mon also to rheumatoid arthritis (8), include differences in genetic background, age distribution of the general population, and the prevalence of infections or other as yet unknown environmental factors. PMR/GCA is an HLA DRB1 associated disease in the US (9) and UK (10), although it is not completely clear if the rheumatoid epitope is involved. By contrast, Italian patients with PMR do not show any increased frequency of HLA DRB1 genes (11).

Epidemiological studies suggest that the incidence of PMR/GCA is increasing (2, 6, 13-15). Subsequent studies were performed in the same area and in the most recent survey the incidence was higher (Fig. 3). Possible reasons include changes in the classification criteria, an increase in the age of the general population, the shift from retrospective to prospective studies, an increased degree of medical attention, increased access to temporal artery biopsy, possible cyclic fluctuations in incidence that are discussed elsewhere in this issue of *Clinical and Experimental Rheumatology* (16), changes in possible environmental risk factors, and the birth cohort effect. This effect consists of subjects in a given population being at a higher risk for the disease based on their year of birth, if a potential environmental exposure occurred in that period.

Risk factors

With the exception of sex, age and certain HLA DR4 subtypes, risk factors associated with PMR/GCA have been only rarely studied. There is evidence that smoking and a history of arterial disease are independently associated with PMR/GCA, although only in women (17). A damaged arterial wall could cause exposure of new antigens or allow the localization of viral antigens that could elicit the inflammatory response (18). Former pregnancies hinder the development of PMR/GCA, probably through the associated hyperoestrogenic state which protects the arterial wall (19).

Data on environmental risk factors in PMR/GCA are scanty and mostly related to the effect of infections. Signs and symptoms of a previous infection are more frequent in PMR/GCA patients than in controls (20). Fessel *et al*. (21) described an association between bird-keeping and the occurrence of PMR, an observation that was not confirmed by other authors. The role of different microorganisms such as adenovirus, respiratory syncitial virus (22), *Mycoplasma pneumoniae* (5) and parainfluenza virus (23) in initiating the disease has been suggested, but not definitively proved.

Actinic hypothesis

The actinic hypothesis regards a specific environmental risk factor and was formulated after the observation of anecdotal cases of PMR/GCA following prolonged sun exposure (24) and of a clustering of disease onset during the summer months. To date, this latter observation has been confirmed in the UK (24), Italy (25), Israel (13) and, in preliminary form, in Slovenia. In addition, the duration of sun exposure seems to be a relevant risk factor for PMR/GCA (26).

Similarities between the histological appearance of the temporal artery in GCA and in actinic granuloma have been re-

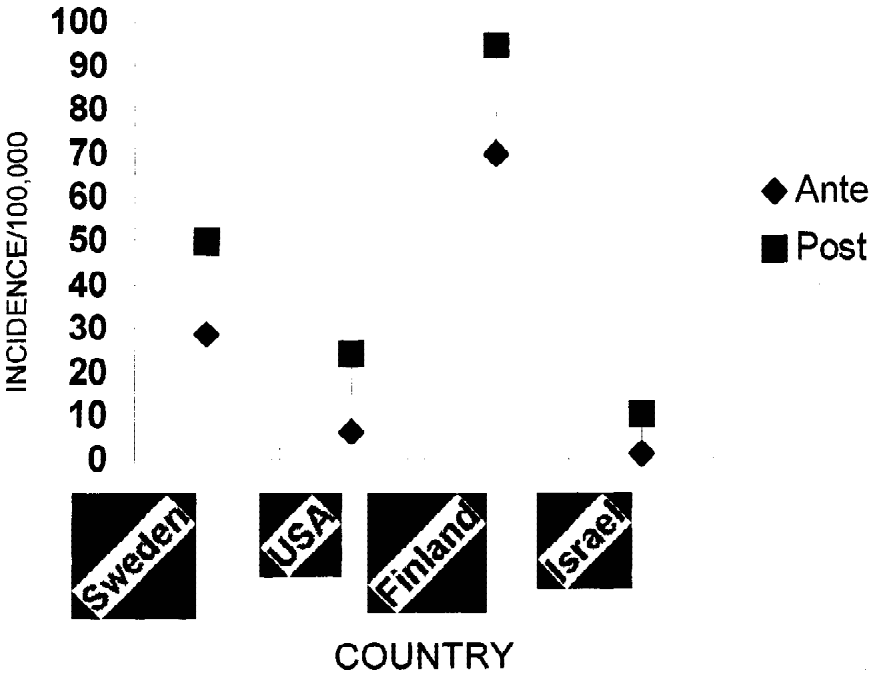

Fig. 3. Changes in the incidence of polymyalgia rheumatica/giant cell arteritis in subsequent studies performed in the same geographical area. The data are obtained from references 2, 6, and 13-15.

ported, suggesting that both conditions may be determined by sun exposure (27). More recently, actinic arteriopathy has been demonstrated in the posterior ciliary arteries of aged subjects, a location frequently affected by GCA (28). Taken together, these data suggest that degradation of the internal elastic lamina of superficial arteries by atherosclerosis and/or sun radiation may be the primary event in PMR/GCA. In a predisposed subject (e.g., elderly, female, and with a genetic predisposition), the arterial damage could allow exposure to new antigens or the localization of viral antigens that elicit the inflammatory response.
Nevertheless, the actinic hypothesis has been challenged by other studies that have not confirmed the seasonality of onset of PMR/GCA (29). The main objection, however, is that PMR/GCA is actually less frequent in areas where sun exposure is high. The possibility exists that sun exposure acts in combination with genetic predisposition and skin sensitivity, which is higher in people of Nordic origin, to modulate the effect of sun radiation on dermal arteries.

Conclusion

Epidemiological research has helped to unravel several of the pathogenetic mechanisms at work in PMR/GCA. In particular, advances have been made in our understanding of the genetic bases of the disease, on the relationship between PMR and GCA, and on the role of several risk factors. These findings need to be completed by further studies on the correlation between the incidence of PMR/GCA and epidemics of infectious diseases as well as on environmental and biological risk factors.

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