Epidemiology of biopsy-positive giant cell arteritis: An overview

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ABSTRACT

Giant cell arteritis (GCA) is reported world-wide. However, the incidence varies greatly in different geographic regions with the highest incidence rates from Scandinavian countries and North American populations of the same descent.

The etiopathogenesis of GCA is incompletely understood. Although data on a positive correlation between the occurence of infection and the onset of GCA as well as rhythmic fluctuations in disease incidence have been reported, no statistically significant periodicity has so far been found regarding the annual incidence of GCA. Seasonal variations may indicate a role of infection or other environmental factors in the pathogenesis of GCA.

Introduction

Giant cell arteritis (GCA) is reported worldwide. The majority of studies on incidence rates reported in the literature are retrospective; prospective studies are so far few. The inclusion criteria and/or diagnostic criteria used may differ between studies and therefore a strict comparison of incidence rates may be inappropriate as in some reports only patients with a positive biopsy were included, while in others patients diagnosed on clinical grounds participated as well. In 1990 the ACR (American College of Rheumatology) (1) produced highly sensitive and specific criteria for the classification of GCA including clinical and/or biopsy data, yielding a basis for better conformity when evaluating patients in the future.

Mortality rate

Mortality rates among GCA patients have been found to be similar to that expected in the general population in most studies, although a fatal outcome during the first 4 months after diagnosis due to vascular disease has been reported (2). As GCA afflicts elderly people, vascular complications may be misinterpreted as ischemic vascular catastrophes caused by arteriosclerosis. The necropsy rate is low in many countries, and in most hospitals histologic examination of the coronary and cerebral arteries is not routinely performed in patients with fatal myocardial or cerebral infarctions. The aortic wall is not studied in detail in most patients with ruptured aneurysms. The real prevalence of fatal GCA thus is not known. Recent outcome studies have shown that although GCA has been considered a highly corticosteroid-responsive disorder and a self-limiting disease, the major underlying pathogenic mechanisms may continue despite an apparent clinical remission producing aortic aneurysms even in patients in clinical remission (3).

Incidence of GCA

The known incidence of biopsy-proven GCA is greatest in populations in Scandinavian countries (4-8) and in communities with a strong Scandinavian ethnic background (9-10). The incidence is lower in southern Europe (11) and GCA is rarely seen in blacks.

The disease is not uncommon. Recent epidemiologic studies performed in northern Europe and North America disclose an annual incidence rate of 18.6 to 27 cases per 100,000 in populations older than 50 years (4-8). The incidence increases with age and GCA is almost 10 times more common among subjects in their ninth decade than in people between 50 and 60 years of age. GCA is roughly twice as common among women as among men.

The incidence in Göteborg, Sweden during the periods 1973-1975 and 1983-1986 was studied by our group (5,7), including all cases of biopsy-verified GCA in Göteborg. Due to the retrospective nature of these studies, only patients with a biopsy diagnosis of GCA were included. Our incidence data should thus be regarded as minimum values.

It appears that the incidence of GCA is increasing with time in different countries, i.e. Minnesota (9), which is in accordance with our own studies from Göteborg, Sweden (5, 7). The average annual incidence of biopsy-verified GCA during the first years of the 1970s was estimated to 16.8 per 100,000 inhabitants aged 50 years or more (5). Interestingly, the reports from Minnesota showed almost identical results (17/100,000 > 50 years).

In the follow-up 1983-1986 study by our group (7) the number of women with biopsy-proven GCA almost doubled in Göteborg compared with the period from the early 1970s. The same increase was not found among men. No new diagnostic methods were introduced during that time, nor had the number of biopsies statistically changed. Furthermore, demographic changes in the population could not be the cause, since the relative number of women aged 50 years or older declined slightly between the two studies. Whether these observations indicate a true incidence increase or rather reflect an association with other factors in the community such as epidemics of infections resulting in a limited temporal incidence peak is an interesting issue.

Infection and GCA

The etiology and pathogenesis of GCA is incompletely understood. Although a possible antigen might be autologous such an antigen may also be of external origin. The role of infectious antigens in the pathogenisis of the disease has been repeatedly suggested (12, 13).

Russo and co-workers (13) investigated the correlation between infection and the onset of GCA in New Orleans, Louisiana. Medical records were retrospectively reviewed in a matched case-control study, including 100 patients with biopsy-proven GCA and 100 sex- and age-matched controls undergoing corrective surgery for hip fractures who did not have GCA. They checked the 2-4 month period preceeding the symptoms of GCA and found that the prevalence of infections was 3 times higher in GCA patients than in non-GCA patients, using pair odd ratios with a 95% confidence interval. The results were statistically significant. The authors suggested that their data strongly supported a correlation between the occurrence of infection and the onset of GCA, with the speculation that (bacterial) infections may act as trigger mechanisms in the pathogenesis of the aged temporal artery.

Rhythmic fluctuation in disease incidence may suggest an exogenous etiologic factor such as epidemic infections. In fact, Salvarani *et al.* (10) investigated the incidence rates over a 42-year period in a population-based study from Minnesota and reported apparent fluctuations in a cyclic pattern of the incidence rates, where incidence peaks occurred about every 7 years. However, the relatively small number of incidence cases produced a limited statistical power in that study. Elling and co-workers (12) found some fluctuations in a Danish cohort, which differed in periodicity from the Olmsted County series, including synchronous variations in the incidence of temporal arteritis and polymyalgia rheumatica associated with epidemics of *Mycoplasma pneumonia* infection. However, no statistical tests were made.

Challenged by the results from the Olmsted County, our group in Göteborg undertook another incidence study comprising all biopsy-positive GCA patients in Göteborg during a 20-year period (January 1, 1976 through December 31, 1995) and analysed the data with special reference to cyclic variations (14). We identified a total of 665 subjects with histologically verified GCA during the period. Although the incidence rate of positive biopsies varied considerly between different years during the period, no cyclic fluctuation was revealed, i.e. the annual fluctuations were random. Thus, no statistically significant rhythmic pattern has so far been found regarding the annual incidence of GCA.

The monthly assessments of our study, on the other hand, showed statistically significant fluctuations with peaks in late winter and autumn. This is in contrast to other studies (15, 16), where the greatest incidence was reported in the summer. One reason for this discrepancy might be that the present investigation focuses on the day of the biopsy, while the other authors based their statistics on the start of the symptoms. Seasonal variations may indicate a role of infection or other environmental factors in the pathogenesis of GCA. However, the pattern may be confused by other independent factors, such as seasonal variations of clinical activity as well as patient delays.

Concluding remarks

Although GCA has not been shown to be a truly infectious vasculitis, so far, it may be speculated that various infections (13) might act as triggers by activating the immune system in genetically susceptible patients with certain predisposing lesions in their arterial walls.

The incidence of GCA is increasing and may be even higher than reported today. This may partly be due to a longer life expectancy. Moreover, a better awareness of the atypical or less classic disease presentation forms may contribute to the increase in reported incidences. The findings of Östberg (17) are striking in this respect. She found in 1973 when studying consecutive autopsies, a post mortem prevalence for aortic GCA of 1.7%, the majority of which had escaped the correct diagnosis during life. This study clearly suggests, that GCA may be much more common than hitherto believed and is still underdiagnosed.

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