

## Letters to the Editor

### Lack of association between altitude and incidence of giant cell arteritis in Northwest Spain

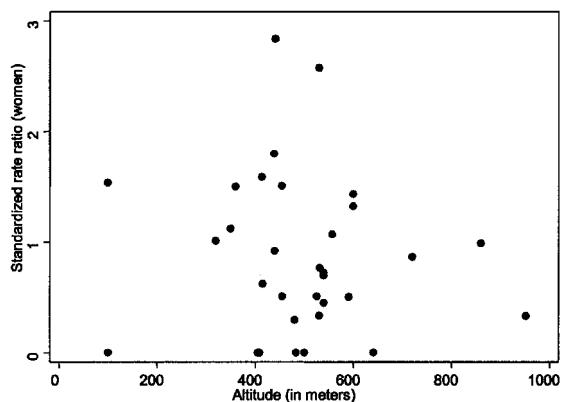
Sirs,

Giant cell arteritis (GCA) is a common vasculitis that involves the large and medium-sized blood vessels with predisposition to the cranial arteries in the elderly (1, 2). Both genetic implications (3) and a trend to increasing incidence with more northerly latitudes have been described (4). To further investigate the potential role of geographical factors, we assessed whether altitude may be associated with GCA susceptibility. We performed a retrospective study in biopsy-proven GCA patients (5), diagnosed at Hospital Xeral-Calde (Lugo, Northwest Spain) from 1981 to 2001. This is the only referral center for a mixed urban and rural population of almost 250,000 people (6). Population data by municipality were obtained from the Spanish National Institute for Statistics (INE). Since all biopsy-proven cases observed during the study period were older than 55 years at the time of diagnosis, we only considered for this analysis the population older than 55 of age. GCA incidence rates by municipality were standardized by age (indirect method) using the entire Lugo population as the reference. Results were expressed as Standardized Rate Ratios (SRR). They were obtained by dividing the number of cases observed in a municipality by the number of cases that should have been expected if this municipality had had the same age-specific rates as the reference population. We then estimated the linear correlation coefficient ( $r$ ) between SRR and altitude. For this purpose, the altitude of its main urban center was assigned to each municipality.

By municipality, the female population over 55 years of age ranged between 309 and 13,686 inhabitants and the male population ranged between 274 and 10,128 inhabitants. Altitude ranged between 100 and 952 meters. SRR ranged between 0 and 2.84 in women. Apart from a single municipality that had a SRR of 5.21, the remaining SRR in men ranged between 0 and 2.37. No correlation between SRR and altitude was observed in women ( $r = -0.097$ ;  $p = 0.596$ ) (Fig. 1) or men ( $r = -0.039$ ;  $p = 0.834$ ). This lack of association in men remained unchanged when the municipality with an SRR of 5.21 was excluded.

Neither genetic susceptibility nor the occurrence of some infections offers complete explanations as to why Scandinavians or North American subjects with a Scandinavian ethnic background are at increased risk of GCA(7). In this regard, although genetic

**Fig. 1.** GCA standardized rate ratio in women (Yaxis) and altitude of the place of residence in meters (X axis). No correlation was found ( $r = -0.097$ ;  $p = 0.596$ ).



GCA susceptibility in Lugo (Spain), Scandinavian countries and Rochester, Minnesota (USA) was in all cases associated with HLA-DRB1\*04 alleles (3,7), the incidence rates were very different.

Exogenous factors may be responsible for the variability in incidence. An attractive explanation associated with latitude may be linked to some environmental factors, in particular infectious agents, which could be responsible for peaks and seasonal variations in the disease incidence (1, 7). Regrettably, molecular-based studies have not confirmed the presence of bacterial or viral antigens in the temporal artery walls of biopsy-proved GCA patients (8).

In patients with intermittent vascular claudication due to peripheral artery occlusive disease, exposure to moderate altitudes has been associated with a marked decreased in tissue  $\text{pO}_2$  values in the diseased legs (9). Since atherosclerosis and vascular damage related to vasculitis share many immune inflammatory mechanisms, we tried to assess the potential influence of altitude in GCA susceptibility. Although our results do not support this hypothesis, two limitations, however, should be considered when interpreting the findings: first, although there was little migration in Lugo during the last two decades, we analyzed the site where the patient lived at the time of the study, and not where they had lived most of their lives; second, the range of altitude in Lugo is rather narrow. Additional studies in populations with a larger altitude range will be required to fully discount the potential role of altitude in susceptibility to GCA.

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### References

1. GONZALEZ-GAY MA, GARCIA-PORRUA C: Epidemiology of the vasculitides. *Rheum Dis Clin North Am* 2001; 27: 729-49.
2. SALVARANI C, CANTINI F, BOIARDI L, HUNDER GG: Polymyalgia rheumatica and giant-cell arteritis. *N Engl J Med* 2002; 347: 261-71.
3. GONZALEZ-GAY MA: Genetic epidemiology. Giant cell arteritis and polymyalgia rheumatica. *Arthritis Res* 2001; 3: 154-7.
4. WATTS RA, SCOTT DGI: Epidemiology of vasculitis. In BALL GV and BRIDGES SL JR (Eds.): *Vasculitis*, NY, Oxford University Press 2002: 211-6.
5. GONZALEZ-GAY MA, GARCIA-PORRUA C, VAZQUEZ-CARUNCHO M, DABABNEH A, HAJEER A, OLLIER WER: The spectrum of polymyalgia rheumatica in Northwestern Spain: Incidence and analysis of variables associated with relapse in a ten year-study. *J Rheumatol* 1999; 26: 1326-32.
6. GONZALEZ-GAY MA, GARCIA-PORRUA C, RIVAS MJ, RODRIGUEZ-LEDO P, LLORCA J: Epidemiology of biopsy proven giant cell arteritis in northwestern Spain: trend over an 18 year period. *Ann Rheum Dis* 2001; 60: 367-71.
7. GRANJT: Some thoughts about the etiopathogenesis of temporal arteritis – a review. *Scand J Rheumatol* 2002; 31: 1-5.
8. HELWEG-LARSEN J, TARP B, OBEL N, BAS-LUND B: No evidence of parvovirus B19, *Chlamydia pneumoniae* or human herpes virus infection in temporal artery biopsies in patients with giant cell arteritis. *Rheumatology (Oxford)* 2002; 41: 445-9.
9. LANDGRAF H, SCHULTE-HUERMANN D, VALLBRACHT C, EHRLY AM: Muscle tissue  $\text{PO}_2$  during moderate altitude exposure in patients with peripheral arterial occlusive disease. *Presse Med* 1994; 23: 164-8.