

PostScript

MATTERS ARISING

Presence of antinuclear antibodies and coronary heart disease

Recent reports have shown the importance of new risk factors for ischaemic stroke and myocardial infarction. An article by Grainger *et al* reports that antinuclear antibodies (ANA) are more prevalent in subjects with severe coronary atherosclerosis than in healthy subjects.¹

The authors' statement that the association is a potential indicator of increased risk of coronary heart disease is not fully supported by data obtained in our study. The authors affirm that ANA, determined by the immunofluorescent method in HEP-2000 cells, were detected at a titre of at least 1/40 in 28/40 (70%) subjects with severe stenoses of three main coronary arteries. In contrast ANA were detected in 5/30 (17%) subjects with no evidence of coronary atherosclerosis.

Our study mainly aimed at investigating the relationship between anticardiolipin antibodies (aCL), and β_2 -glycoprotein I antibodies (a- β_2 GPI), their association with increased risk of ischaemic stroke (IS) and myocardial infarction (MI), and the occurrence of clinical recurrence of ischaemic events as IS, MI, unstable angina or transient ischaemic attack (TIA). The study group comprised 139 consecutive patients (86 men, 53 women; mean (SD) age 64.8 (13.6) years), admitted to the department of medicine or to the intensive care unit of our hospital, with MI (n=50), IS (n=60), or TIA (n=29). The control group consisted of 50 sex matched healthy subjects (mean (SD) age 55.8 (16.9) years).

Furthermore, IgG aCL, IgM aCL, and a- β_2 GPI, other traditional risk factors, omocysteine, (data not shown), and ANA were also determined in the subjects examined. ANA were detected in HEP-2 cells (INOVA, San Diego, California) by indirect immunofluorescence. All the reported tests were performed in accordance with the manufacturer's instructions.

Preliminary data obtained have been partially published.² However, data relating to ANA have not been published so far. In our study, ANA at a titre of at least 1/40 were detected in 44/139 (32% (95% CI 23% to 41%)) patients with ischaemic events and in 13/50 (26% (95% CI 17% to 35%)) healthy subjects. The difference between detection of ANA between the study group and the control group was not significant (p=0.5). In detail, 22 serum samples from the ischaemic patients showed an ANA titre of 1/40, 15 sera showed an ANA titre of 1/80, three sera showed an ANA titre of 1/160, two sera showed an ANA titre of 1/320, and two sera showed an ANA titre of 1/640. In the control group six sera showed an ANA titre of 1/40, five sera showed an ANA titre of 1/80, and two sera showed an

ANA titre of 1/160. In the group of ischaemic patients 13 ANA positive sera were from subjects also affected by chronic hepatitis, three from subjects affected by connective tissue disease, and five from patients affected by viral or bacterial infections. The immunofluorescence pattern showed that only three sera had a nucleolar pattern.

Our data are not in agreement with those of Grainger *et al*. This may be because a different group were examined or because a different cell source of HEP-2 was used; in the latter case the discordance might be caused by the presence of the SSA/Ro antigen. In fact HEP-2000 cells are enriched with SSA/Ro. However, we think that additional data are required before considering ANA to be a useful marker of the increased risk of coronary heart disease.

I Brusca

Central Laboratory, "Buccheri La Ferla" F B F Hospital, Palermo, Italy

F M Sarullo

Division of Cardiology, "Buccheri La Ferla" F B F Hospital, Palermo, Italy

M Fazio

Division of Medicine, "Buccheri La Ferla" F B F Hospital, Palermo, Italy

Correspondence to: Dr I Brusca; ignbr@tin.it

References

- 1 Grainger DJ, Bethell HW. High titres of serum antinuclear antibodies, mostly direct against nucleolar antigens, are associated with the presence of coronary atherosclerosis. *Ann Rheum Dis* 2002;61:110-14.
- 2 Gristina T, Brusca I, Fazio M, Sarullo FM, *et al*. The beta(2)-glycoprotein 1-dependent anticardiolipin antibodies: their importance as risk factor for ischemic stroke and myocardial infarction. *Haematologica* 2002;87(suppl):96.

Author's reply

We recently published our results from a preliminary study of 70 subjects, in which we showed an association between the presence of antinuclear antibodies (ANA) and angiographically defined coronary artery disease. As a first investigation of this question, we deliberately studied extreme groups: people with severe disease (at least 50% stenosis of all three major coronary artery systems) were compared with subjects with no detectable disease in the coronary arterial tree. A comparison of such groups is likely to magnify the extent of any differences, allowing them to be detected in pilot scale studies.

Brusca and colleagues have made similar investigations on another small cohort of patients, using clinical rather than angiographic phenotype to classify their subjects. A crude analysis, grouping cardiovascular and cerebrovascular end points together failed to identify any link between ANA serostatus and cardiovascular disease. Unfortunately, no data are available on the extent of atherosclerosis

within these subjects, but it is likely that the severity of disease was considerably less than in our study, where angiography was used to classify the subjects. Furthermore, the impact of including 89/139 subjects with a cerebrovascular end point (which was not examined in our original study) is not considered. Considerably more information about the clinical characterisation of the cohort studied by Brusca *et al* is needed before robust conclusions can be drawn from their study.

Nevertheless, we agree with their suggestion that substantially larger numbers of well characterised subjects need to be examined before a robust conclusion about the relationship between systemic autoimmunity and atherosclerosis can be drawn. As we noted in our original paper, our study made use of the extreme groups available to us to catch a glimpse of what may turn out to be an important contributory mechanism in the pathogenesis of atherosclerosis. But a definitive answer to such questions must await a considerably larger study than either our study or that of Brusca *et al*.

D J Grainger

Department of Medicine, Addenbrooke's Hospital, Cambridge, CB2 2QQ, UK

Correspondence to: Dr D J Grainger; dig15@mole.bio.cam.ac.uk

NOTICE

Carol Nachman Award for Rheumatology 2003

The Carol Nachman Award, which is one of the oldest and most prestigious awards for rheumatology in the world, will again be granted in 2003 for outstanding, innovative research work in the field of clinical and experimental rheumatology and other related disciplines like orthopaedic surgery. The prize money is €38 000.

Previous award winners include Professors WJ van Venrooij, The Netherlands; P Lipsky, USA; B Hahn, USA; G Firestein and N Zvaifler, USA; RN Maini and M Feldmann, United Kingdom; JP Pelletier, Canada; S Gay, Switzerland; C Weyand, J Braun, and J Sieper, Germany; and other international well reputed clinicians and scientists.

Applicants should submit 12 copies of their scientific achievements within the past five years for nomination in 2003 together with a current CV by 15 December 2002 to the following address:

Professor JR Kalden
Director of the Department of Internal Medicine III and Institute for Clinical Immunology
Krankenhausstrasse 12,
91054 Erlangen, Germany
Tel: +49 (0)9131 853 9131
Fax: +49 (0)9131 853 4770
Email: joachim.kalden@med3.imed.uni-erlangen.de