AUTO-ANTIBODIES IN THE HOSPITALISED ORIENTAL ELDERLY

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ABSTRACT

Aches and pains are a common problem in the elderly and often a positive auto-antibody result is difficult to interpret in the given clinical setting. We studied 96 unselected hospitalised Oriental elderly aged 65 years and above to determine the prevalence of auto-antibodies and their clinical significance. Anti-nuclear antibody (ANA) was positive in 33%; commonest titres were low (ie 1:40); commonest patterns were speckled and homogeneous; 44% had no known cause for a positive result apart from their age; 37% were taking drugs known to be associated with a positive ANA and 19% had both a disease and a drug known to be associated with a positive ANA.

Rheumatoid factor (RF) was positive in 16%; 47% had titres ≤40 IU/ml and 87% had no known cause of positive RF. Other auto-antibodies tested were negative. We conclude that the prevalence of auto-antibodies in the hospitalised Oriental elderly are common and of no clinical significance if accompanying features of an auto-immune disease are absent.

Keywords: auto-antibodies, hospitalised Oriental elderly, drug-related.

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INTRODUCTION

Ageing is associated with a decrease in antibody response to antigenic challenge which has often been purported to increase the elderly person's susceptibility to infections and neoplasia. Paradoxically, however, the elderly have higher levels of IgG and IgA which are manifested as anti-nuclear antibodies (ANA), anti-double stranded DNA antibodies, anti-thyroid antibodies, anti-cardiolipin antibodies and rheumatoid factor[1-10].

There have been no studies on the auto-antibody status of the hospitalised Oriental elderly in a Southeast Asian country. We therefore undertook to determine the prevalence of auto-antibodies and their clinical significance in 96 elderly patients warded in two general hospitals in Singapore.

METHOD

Ninety-six patients aged 65 years and above were randomly studied; the mean age was 77.6 years (range from 65 to 99 years) and the sex ratio was equal. Their medical diagnoses and current medications were obtained from their medical records. Ten millilitres (ml) of blood was drawn from each patient: 5 ml was sent for analysis for ANA (using Hep-2 substrate slide, Immunocept, Sacramento, USA) and RF (using latex agglutination); the remaining 5 ml was frozen at -70°C. If the first blood specimen was positive for ANA or RF, the second aliquot was then analysed for anti-double stranded DNA antibodies (anti-dsDNA) using radio-immunoassay; anti-Ro, anti-La, anti-Sm and anti-RNP using counter-immunoelectrophoresis. ANA was considered positive if the titre was ≥1:40 and RF positive if ⩾ 20 IU/ml.

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RESULTS

Anti-nuclear antibody

ANA was positive in 32 out of 96 (33%) patients and there was a slight preponderance in the females (Table I). Most had low titres ie. 1:40 (Fig 1). Only 5 out of 32 patients had a titre of 1:640.Out of these 5, one had miliary tuberculosis/ isoniazid, two had chronic renal failure of non-autoimmune cause, one had cerebrovascular accident of non-autoimmune cause and one had metastatic carcinoma/ampicillin.

Table I – Serology results

	No (%)	Male (No)	Female (No)
ANA negative	49 (51)	27	22
ANA positive	32 (33)	14	18
RF positive	15 (16)	7	8
Total	96 (100)	48	48

The commonest patterns were speckled or homogeneous (Fig 2). There was no relationship between the pattern of fluorescence and the disease state or drugs consumed by the patients.

None of them had any clinical evidence of an auto-immune disease except one who had rheumatoid arthritis. The majority of those positive for ANA had either no known cause or were taking drugs that could cause a positive result (Fig 3). Of the 6 who had both drugs and a non-autoimmune disease as putative causes for a positive ANA, 3 had active pulmonary tuberculosis/isoniazid, one had liver cirrhosis/ active pulmonary tuberculosis/isoniazid, one had rheumatoid arthritis/sulphasalazine and one had metastatic carcinoma/ ampicillin.

In the category of drugs known to cause a positive ANA, the main drugs ingested were the ß-lactam antibiotics and isoniazid (Table II).

Fig 1 - Antinuclear antibody titres

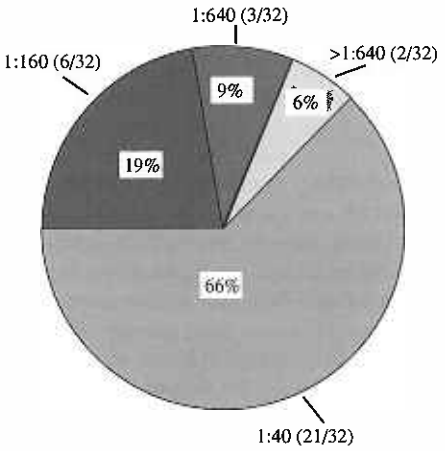


Fig 2 - Patterns of antinuclear antibody

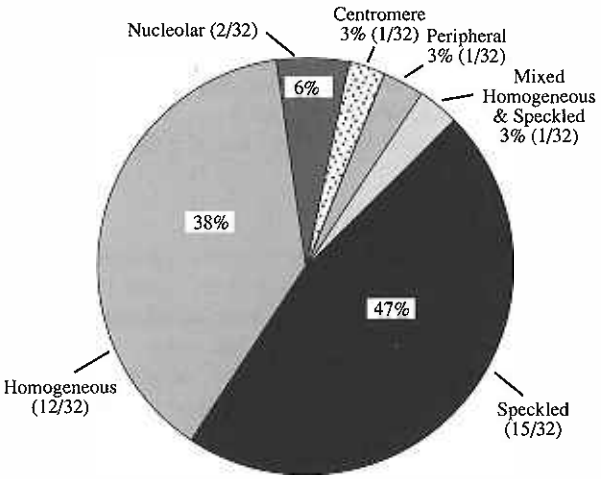


Fig 3 - Relationship between positive antinuclear antibody, drugs and disease

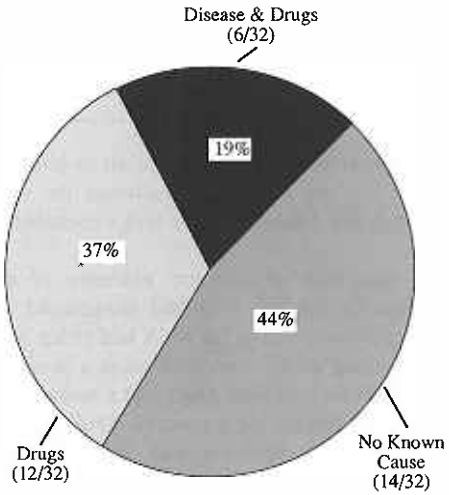


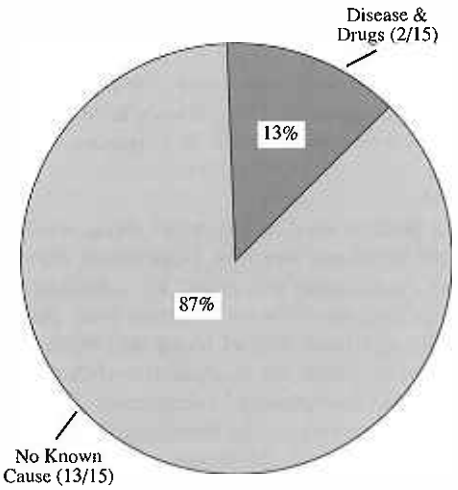
Table II - ANA prevalence in each drug group

Drug group	ANA+(No)	ANA-(No)	Total	%ANA +
ß-lactams	10	29	39	26
Isoniazid	4	3	7	57
Hydrallazine	1	2	3	33
Allopurinol	1	1	2	50
Methyldopa	1	0	1	100
Tetracycline	1	0	1	100
Phenytoin	0	4	4	0
Procainamide	0	1	1	0
Total	18	40	58	

Rheumatic factor

The prevalence of RF was lower compared to that of ANA and there was an almost equal distribution between the two sexes (Table I). The majority of positive RF had no known cause except their age; 2/15 (13%) had a disease known to cause a positive RF, namely rheumatoid arthritis and miliary tuberculosis (Fig 4). The majority had a titre of 80 IU/ml or less (Fig 5). Of the 3 patients with a titre of 320 IU/ml, one had multi-infarct dementia (ANA negative), one age-related osteoporosis and one pulmonary tuberculosis. The patient with rheumatoid arthritis had a titre of 80 IU/ml.

Fig 4 - Causes of positive rheumatoid factor



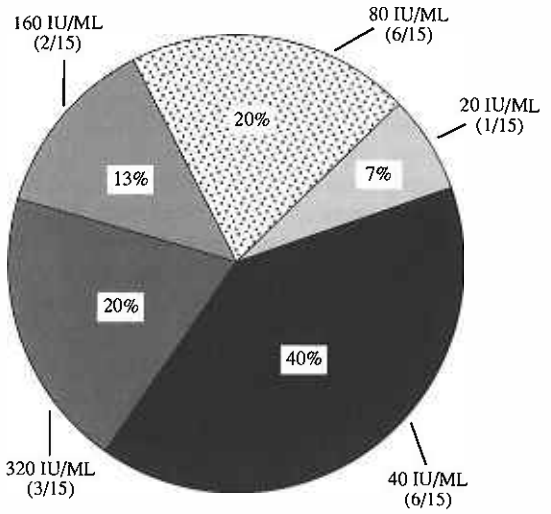
Other auto-antibodies

Anti-Ro, anti-La, anti-Sm, anti-RNP and anti-dsDNA were negative in the group that was positive for ANA. (Due to a logistic problem, anti-dsDNA was only analysed in 24/33 ANA responders)

DISCUSSION

Our study provides a good opportunity to compare prevalence rates of ANA and RF in the elderly of a Southeast Asian country with those of the West. Many large studies have been

Fig 5 - Rheumatoid factor titres



done on healthy Caucasian elderly who were not on medication. Goodwin[11] reported ANA positivity in 18% and RF positivity in 14% of healthy elderly subjects; Field[12] found ANA to be positive in 18.7% and RF 12.7% whilst Manoussakis[8] reported ANA to be positive in 31.3% and RF 14.1%. The first two studies used mouse and rat liver for the ANA assays whilst the last one used Hep-2 epithelial cells which is a far more sensitive assay. Our study which found ANA positive in 33% (also using Hep-2 epithelial cells) and RF positive in 16% is comparable to the figures in Manoussakis' study. However, if we consider the fact that our sample was hospitalised patients who were ill with several diseases and also that 56% of the positive ANA were attributable to drugs or a non-auto-immune disease, the actual prevalence rate for ANA and RF in the healthy Southeast Asian elderly may actually be lower than their Caucasian counterparts.

This study also illustrates the plethora of factors that confound the interpretation of a positive serologic result in the elderly. It is not uncommon for the doctor to run a panel of auto-immune tests for an elderly patient who presents with rheumatological complaints. It is prudent to correlate a positive result (in high or low titre) with the clinical features of auto-immune disease as positive serology simply indicates an immune abnormality and does not always reflect active clinical disease. Other causes of a positive result such as drugs or non-autoimmune illnesses should be excluded.

In conclusion, ANA and RF are commonly positive at low titres in hospitalised elderly patients in Singapore and it is probably not cost effective to run the whole battery of auto-immune markers if there are no consistent clinical features of the disease.

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