Hospital Practice

The value of screening for autoantibodies in patients with non-specific symptoms

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Summary: An autoantibody screen is often requested in patients with non-specific symptoms such as pyrexia of unknown origin. However, in a survey of 100 consecutive requests for this investigation in such patients only one patient was encountered in whom the investigation led to a positive diagnosis at an estimated cost of £2500. These requests accounted for 5% of the total workload. These observations reaffirm that this should remain a second line investigation and should be deferred until more likely diagnoses have been excluded.

Introduction

The investigation and management of patients with non-specific symptoms such as pyrexia of unknown origin (PUO) and 'general malaise' can be very difficult, as the differential diagnosis is very extensive (Petersdorf & Beeson, 1962; Molavi & Weinstein, 1970). It is recognized that one diagnostic possibility in these patients is some form of autoimmune disease (Jacoby & Swartz, 1973), and as a result an autoantibody screen is often sought early in the disease course. The aim of this report is to evaluate the value of performing such a screen in this group of patients.

Patients and methods

Patients for study were identified from consecutive request cards submitted to the laboratory for the investigation. Case notes were then reviewed for confirmation of the reason for referral and for details of presenting features, final diagnosis, treatment and outcome. From these the relevance of the autoimmune profile was assessed. Thus, the study included all patients for whom the request card stated the words 'fever of unknown origin' or 'general malaise' or words to that effect. Patients with a specific note of any other condition at the time of the request were excluded. Follow-up period was at least 1 year.

The following antibodies are included in the autoimmune profile in Southampton: thyroid

microsome, thyroglobulin, gastric parietal cell, antimitochondrial, skeletal, smooth muscle, renal glomerular, rheumatoid factor, reticulin and antinuclear. Where the latter is positive, a DNA-binding is performed. If the rheumatoid screening test is positive, a SCAT titre is obtained and only if greater than 1 in 32 is reported positive. Patients with thyroid antibodies have routine thyroid function tests performed (Tanner *et al.*, 1982).

Results

Sixty consecutive patients with general malaise and 40 with PUO were identified. Seventy five per cent of all patients were in-patients. These accounted for approximately 5% of the total referrals. Forty-two were male, 58 female. Age range was 13 to 87 y with a mean of 55 y. Final diagnosis was: hypercalcaemia 4, arteritis/vasculitis 9, systemic lupus erythematosus 1, malignancy 5, subacute bacterial endocarditis 2 and Dressler's syndrome 3. In 46 patients the final diagnosis was assumed to be an infection, although a definite organism was confirmed in only 14. Identified infections were treated with the relevant antibiotic, and nine patients received steroids. No specific diagnosis was made in the remaining 30 patients. There were 26 patients with positive antibody screen, as shown in Table I. Seventy-four patients had a completely normal autoimmune profile. The term 'insignificant abnormality' was used to describe those patients with either autoantibodies which were not considered to be

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Table I Results of autoimmune profile screening in 100 patients

Normal	74
Significant abnormalities	
thyroid antibodies (with proven abnormal thyroid function)	2
ANF + ve, DNA-binding + ve	1
Insignificant abnormalities	
gastric parietal cell antibodies	7
thyroid antibodies (normal thyroid function)	7
ANF (low titre c normal DNA-binding)	5
rheumatoid factor (SCAT < 1 in 32)	5
smooth muscle antibody (low titre)	3

ANF = antinuclear factor; SCAT = sheep cell agglutinin titre

related to the illness or those in whom the titre of autoantibodies was below that level defined by the laboratory as a true positive. In only one patient was it considered that the autoimmune profile had aided the diagnosis (a patient with SLE presenting with a PUO). A further 2 of the 9 patients with thyroid antibodies were found to have mild hypothyroidism, although in neither case was this considered to be the cause of the non-specific symptoms.

Discussion

This study shows that in patients with non-specific symptoms such as general malaise or pyrexia of unknown origin the diagnostic yield of an antibody

screen is very limited. An estimate of the cost of a single profile is about £25, and thus in our series it is estimated that the cost of making one diagnosis in this group of patients from the autoimmune profile was about £2500. This observation is compatible with a recent series of patients with PUO which emphasized that 'autoimmune disease' is a rare cause of these symptoms (Larson *et al.*, 1982). The investigation of these patients often included a series of progressively more invasive investigations. These were frequently negative and in the majority symptoms remitted spontaneously without a final diagnosis being confirmed or specific treatment given. The term PUO should strictly be limited to those with symptoms which have defied investigations for a period of 4–6 weeks (Petersdorf & Beeson, 1961). However, from our study it is clear that, as far as the request forms were concerned, patients with shortlived symptoms were included, an observation compatible with our conclusion that the investigation is presently being requested too early in the disease course. Similarly, the nature of the final diagnoses in those patients referred with general malaise also suggest that, had the request for the investigation been deferred for a few days, diagnosis would have become obvious. The early request may well result from the ease of access to the investigation in Southampton. The most economical use of an autoantibody screen remains to be defined but clinicians should be aware of the low diagnostic yields from such an investigation in this group of patients. Thus, in the absence of specific or severe symptoms, we suggest that this survey indicates that the autoimmune profile should be a second line investigation, to be obtained only when more likely diagnoses have been excluded.

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