Serum autoantibodies and uveitis

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SUMMARY The serum of 893 uveitis patients was examined for various non-ocular specific autoantibodies. Overall 40.8% of patients had detectable levels of autoantibodies in their sera. These comprised antibodies to smooth muscle (23.1%), nuclear material (12.7%), gastric parietal cell (3.0%), reticulin (1.8%), and mitochondria (0.2%). When the patients were distributed into nine selected categories of uveitis, only patients with one distinct clinical entity showed a statistically significant difference in the presence of the above serum autoantibodies as compared with healthy individuals. They were patients with uveitis associated with juvenile chronic arthritis, among whom antinuclear antibody was detected in 77% ($p < 0.001$). Testing for the presence of circulating non-ocular specific autoantibodies appears to be of little or no value in the routine screening of uveitis patients, but it may be helpful in the diagnosis and management of certain individual cases, such as juvenile chronic arthritis, or as a research tool to advance understanding of pathogenetic mechanisms.

Uveitis comprises a complex group of diseases, of which the aetiopathogenesis is often unknown. Although recent evidence reveals underlying immunological aberrations in a large number of patients,^{1,4} the exact relationship between non-ocular specific serum autoantibodies and uveitis is not clear, the literature^{5,6} being limited and contradictory.

In view of the puzzling nature of uveitis and that it may form part of a systemic disease process, many patients are frequently overinvestigated by being subjected to a vast battery of unnecessary tests.

A large patient population was examined, therefore, to determine whether circulating non-ocular specific autoantibodies have a significant role to play in the aetiopathogenesis of uveitis.

Materials and methods

This study involved 893 patients with uveitis seen at Moorfields Eye Hospital between July 1977 and December 1982. The patients were distributed into nine selected categories of uveitis: acute anterior, chronic anterior, pan, posterior, intermediate, heterochromic cyclitis, juvenile chronic arthritis, Behçet's disease and Vogt-Koyanagi-Harada syndrome. Criteria laid down by the International Uveitis Study Group⁷ were used for the classification.

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Circulation antibodies to nuclear material, smooth muscle, gastric parietal cells, reticulin, and mitochondria were detected by a standard indirect immunofluorescence technique using a Zeiss epifluorescence microscope equipped with the appropriate interference filters. Normal values were determined from 100 healthy individuals.

Statistical analysis was by the χ^2 method on 2×2 frequency tables with Yates's correction.

Results

Of the 893 patients studied the majority (53%) belonged to the acute anterior uveitis category (Table 1.)

Overall 40.8% of the patients had detectable levels of non-ocular specific autoantibodies (titre $< 1:50$) in

Table 1 Selected categories of uveitis in 893 patients

Classification	Number	Percentage
Acute anterior	469	53
Posterior	129	14
Pan	115	13
Chronic anterior	72	8
Intermediate	47	5
Heterochromic cyclitis	23	3
Behçet's disease	20	2
Juvenile chronic arthritis	13	1.5
Vogt-Koyanagi-Harada syndrome	5	0.5

Table 2 Serum autoantibodies in selected categories of uveitis

Classification	Autoantibody (titre <1:50)									
	ANA		ASMA		AGPCA		ARA		AMA	
	No.	%	No.	%	No.	%	No.	%	No.	%
Healthy individuals	15	15	16	16	3	3	2	2	0	0
Acute anterior	47	10	116	25†	19	4	7	1.5	1	0.2
Posterior	13	10	35	27‡	2	1.5	3	2	0	0
Pan	24	21	25	22§	3	2.6	3	2.6	1	0.9
Chronic anterior	7	10	12	17	2	3	1	1	0	0
Intermediate	4	8.5	8	17	0	0	2	4	0	0
Heterochromic cyclitis	5	22	4	17	1	4	0	0	0	0
Behçet's disease	3	15	4	20	0	0	0	0	0	0
Juvenile chronic arthritis	10	77*	1	8	0	0	0	0	0	0
Vogt-Koyanagi-Harada syndrome	0	0	1	20	0	0	0	0	0	0
Overall	113	12.7	206	23.1	27	3	16	1.8	2	0.2

ANA: antinuclear antibody. ASMA: antismooth muscle antibody. AGPCA: antigastrophic parietal cell antibody. ARA: antireticulin antibody. AMA: antimitochochondrial antibody.

*p<0.001.

†p>0.1 (NS).

‡p>0.05 (NS).

§p>0.1 (NS).

their serum. Although antismooth muscle antibody (ASMA) and antinuclear antibody (ANA) were the most frequently detected, 23.1% and 12.7% respectively, patients in only one of the uveitis categories showed a statistically, significant difference in the incidence of autoantibodies as compared with healthy persons. These were patients with uveitis associated with juvenile chronic arthritis; 77% had ANA in their serum (p<0.001) (Table 2).

Discussion

Uveitis may occur as an isolated event or as a manifestation of a systemic immuno-inflammatory disease process, for example, sarcoidosis and Behçet's disease. Intraocular inflammation can develop as a result of the breakdown of regulatory immune mechanisms, which may in some cases lead to autoimmune disease involving the production of circulating autoantibodies to ocular and non-ocular structures.

The results of this study are mostly in agreement with the findings of Kijlstra *et al.*,⁶ who were unable to show any association between non-ocular specific autoantibodies and various types of uveitis. Significant associations were reported, however, by Rahi *et al.*,⁵ but the numbers of their patients were so small they were unable to draw any firm conclusions from their study. The finding of ANA in the serum of 77% of patients with juvenile chronic arthritis (p<0.001) is in agreement with that of previous studies.^{8,9}

Recent work postulates that autoimmunity may be the result of anti-idiotypic antibodies (that is, to the

shape of the antigen binding regions) of viral antibodies,¹⁰ or occurring via mechanisms involving cross-reactive idiotypes¹¹—for example, micro-organisms or structures of a microbial agent. This may be relevant, as many infective agents have been implicated in the pathogenesis of uveitis; they include viruses,¹² chlamydia,¹³ and klebsiella.¹⁴

The two stages in the generation of autoimmune disease are, first, the initiation state (that is, the development of autoantibodies or autoreactive lymphocytes), then the development of tissue damage due to immune responses. Whether the initial induction of autoreactive B and T cells leads to autoimmune disease would depend on factors such as abnormalities of the suppressor T cell pathway reported to coexist with autoimmunity and necessary to induce autoimmune disease in mice.¹⁵ Defective suppressor T cells have been reported in acute anterior uveitis^{16,17} and heterochromic cyclitis,¹ and this defect may lead, via B cell overstimulation, not only to the production of autoreactive B and T cells but also to high levels of serum immunoglobulins and low affinity antibodies, which may be involved in immune-complex mediated inflammation. Raised levels of serum IgA¹⁸ and circulating immune complexes^{2,4} have been found in various types of uveitis. Autoantibodies to ocular structures have also been found in uveitis. These include antibodies to retinal 'S' photoreceptor antigen,² corneal epithelium,³ and lens crystallins (unpublished observation).

In conclusion, there seems little benefit in the routine screening of patients with uveitis for the presence of circulating non-ocular specific autoanti-

bodies. It may be of value in individual cases, as in the diagnosis and management of uveitis associated with juvenile chronic arthritis or for research purposes to advance understanding of immuno-pathogenetic mechanisms.

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