Immunoassay of serum alpha-1 antitrypsin level in uveitis

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SUMMARY The serum alpha-1 antitrypsin level was measured in 60 patients with endogenous uveitis, 27 patients with phacoallergic endophthalmitis, 12 patients with phacolytic glaucoma, and 58 healthy subjects. Thirty-four patients with endogenous uveitis were also followed up for 6 months after treatment, and the serum alpha-1 antitrypsin level was measured again. There was a significant rise in the serum alpha-1 antitrypsin level in cases of endogenous uveitis and phacoallergic endophthalmitis but no alteration in cases of phacolytic glaucoma. Among the patients with endogenous uveitis the level was significantly raised in cases of anterior uveitis, but there was no change in cases of posterior uveitis. A significant rise was seen only in cases of acute anterior uveitis but not in chronic anterior uveitis. The serum alpha-1 antitrypsin level was unaltered in endogenous uveitis despite clinical improvement.

Inflammatory diseases of the eye may lead to severe impairment of vision and even complete loss of ocular function because of the development of secondary glaucoma, complicated cataract, cyclitic membrane, secondary retinal detachment, and phthisis bulbi.¹

Lens proteases liquefy the lens cortex to such a degree that lens material may escape through the capsule. Alpha-1 antitrypsin, a glycoprotein, is the major nonspecific protease inhibitor, synthesised by hepatocytes.² Serum alpha-1 antitrypsin (alpha-1 antiprotease) is frequently increased in malignancy,³ acute infections,⁴ corticosteroid therapy,⁵ rheumatoid arthritis,⁶ pregnancy,⁷ oral contraceptive administration,⁸ oestrogen therapy,⁹ sarcoidosis,¹⁰ and leprosy.¹¹ Serum immunoglobulins have been reported to be altered in uveitis.¹²⁻¹⁴ There is good evidence that alpha-1 antitrypsin is involved in the regulation of the immune system.¹⁵ In the present study the serum alpha-1 antitrypsin levels have been evaluated in patients with uveitis and the effect of therapy on its level have also been studied.

Material and methods

Sixty patients with endogenous uveitis, 27 with phacoallergic endophthalmitis, and 12 with phacolytic

glaucoma were studied for the immunoassay of serum alpha-1 antitrypsin level. The control group comprised 58 healthy subjects who had no evidence of ocular or systemic disease and attended the Eye Centre mainly for the purpose of refraction. The diagnosis of uveitis was established by detailed clinical examination, slit-lamp biomicroscopy, and direct and indirect ophthalmoscopy. Cases of uveitis, associated with hypermature cataract, exposure of lens matter into aqueous humour following trauma, needling, or extracapsular extraction were categorised as phacoallergic endophthalmitis clinically. They showed lid oedema, ciliary congestion, iris oedema, posterior synechiae, and numerous large keratic precipitates.

The age and sex distribution of all the subjects is given in Table 1. The sera samples were stored at -20°C until assayed. The alpha-1 antitrypsin level in serum was measured by a single radial immunodiffusion technique using monospecific goat anti-serum against human alpha-1 antitrypsin and the reference standard obtained from Meloy Laboratories, Virginia, USA.¹⁶ The alpha-1 antitrypsin level was calculated from the calibration curve constructed by incorporating 3 known concentrations of reference standard.

Thirty-four patients with endogenous uveitis were followed up for 6 months after treatment consisting of local and systemic steroids, oral phenylbutazone,

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Table 1 Age and sex distribution in healthy subjects and diseased states

	Age in years					Sex		Total no. of subjects
	10-20	21-40	41-60	61 and over	Mean $\pm$ SD	Male	Female	
Healthy subjects	3	37	16	2	34.6 $\pm$ 10.2	36	22	58
Endogenous uveitis	4	34	19	3	35.8 $\pm$ 12.4	34	26	60
Phacoallergic endophthalmitis	0	6	11	10	57.1 $\pm$ 18.2	19	8	27
Phacolytic glaucoma	0	0	11	1	56.8 $\pm$ 3.0	8	4	12

mydriatics, and cycloplegics. A repeat measurement of serum alpha-1 antitrypsin level was done on patients with endogenous uveitis after clinical improvement.

Results

The serum alpha-1 antitrypsin levels in the healthy subjects and in the patients with uveitis are given in Table 2. A significant rise in the level was observed in endogenous uveitis ($p < 0.001$) and phacoallergic endophthalmitis ($p < 0.001$). However, there was no significant change ($p > 0.5$) in its level in phacolytic glaucoma in comparison with the level in healthy subjects. Table 3 shows the serum alpha-1 antitrypsin level in the different subgroups of endogenous uveitis. The serum alpha-1 antitrypsin level was raised in the subgroup of anterior uveitis ($p < 0.001$). However, in the subgroup of posterior uveitis there was no significant change ($p > 0.3$). The patients with anterior uveitis were further subdivided into acute anterior and chronic anterior uveitis (Table 3). The serum alpha-1 antitrypsin level was significantly increased in acute anterior uveitis ($p < 0.001$) but unaltered ($p > 0.2$) in chronic anterior uveitis in comparison with the level in healthy subjects.

Table 4 shows the comparative serum alpha-1 antitrypsin levels in patients with endogenous uveitis prior to treatment and after the treatment when there was clinical improvement. No significant change was seen in its level after treatment in any group.

Discussion

Several proteolytic enzymes are liberated in human serum during bacterial infections.¹⁷ The action of these proteases is modulated by various protease inhibitors like alpha-1 antitrypsin, alpha-1 antichymotrypsin, interalpha trypsin inhibitor, antithrombin-2, C-1 inactivator, and alpha-2 macroglobulin.¹⁸

The serum alpha-1 antitrypsin level in the healthy subjects (199.9 mg/dl) is lower than the values reported elsewhere from India, being 225 mg/dl¹¹ and

Table 2 Serum alpha-1 antitrypsin level in healthy subjects and diseased states

	No. of subjects	Alpha-1 antitrypsin level (mg/dl)
Healthy subjects	58	199.9 $\pm$ 54.9
Endogenous uveitis	60	233.2 $\pm$ 56.0
Phacoallergic endophthalmitis	27	241.8 $\pm$ 64.3
Phacolytic glaucoma	12	187.4 $\pm$ 49.6

SI conversion: mg/dl $\times$ 0.01 = g/l.

Table 3 Serum alpha-1 antitrypsin level in different subgroups of endogenous uveitis patients

	No. of subjects	Alpha-1 antitrypsin level (mg/dl)
Anterior uveitis	46	239.5 $\pm$ 55.4
Acute	29	241.8 $\pm$ 57.6
Chronic	17	220.2 $\pm$ 46.6
Posterior uveitis	14	221.8 $\pm$ 63.1

SI conversion: mg/dl $\times$ 0.01 = g/l.

266.4 mg/dl.¹⁹ In Western series, however, the serum alpha-1 antitrypsin level has been reported to vary between 180 and 400 mg/dl.²⁰⁻²² (SI conversion: mg/dl $\times$ 0.01 = g/l.)

There is a remarkable elevation of the serum alpha-1 antitrypsin level in endogenous uveitis and phacoallergic endophthalmitis. The rise in the level of serum alpha-1 antitrypsin was significant in acute anterior uveitis. However, cases of posterior uveitis and chronic anterior uveitis did not show any significant alteration in its level. The elevated serum alpha-1 antitrypsin level in patients with endogenous uveitis did not show any appreciable fall in spite of the clinical improvement. This could be explained by the fact that these patients were on systemic corticosteroids, which are known to increase the serum alpha-1 antitrypsin level,⁵ or it might be due to the persistence of subclinical activity of endogenous uveitis. It has been reported that there is no signifi-

Table 4 Serum alpha-1 antitrypsin level in endogenous uveitis patients before and after therapy

	No. of subjects	Alpha-1 antitrypsin level (mg/dl)		p Value
		Before therapy	After therapy	
Anterior uveitis	25	233.0±45.0	226.8±41.1	>0.7
Acute	16	239.5±47.5	227.5±37.8	>0.5
Chronic	9	221.4±40.0	225.6±48.8	>0.9
Posterior uveitis	9	220.0±33.6	218.3±45.9	>0.95
Total no. of patients	34	229.6±42.2	224.5±41.9	>0.7

SI conversion: mg/dl×0.01=g/l.

cant association of the alpha-1 antitrypsin phenotype variant MZ with uveitis.²³⁻²⁴

A few studies have been reported on the serum alpha-1 antitrypsin level in different eye diseases. It has been suggested that bacterial infections of the conjunctiva increase the level of alpha-1 antitrypsin in tears, and measurement of its level may be an effective help in the diagnosis of ocular inflammation.²⁵ The serum alpha-1 antitrypsin level has been reported to be low in cataract patients.²⁶ In patients with phacolytic glaucoma alteration in the serum alpha-1 antitrypsin level was not seen, which agrees with the lack of clinical and cellular inflammatory response seen in patients with phacolytic glaucoma. The serum and tear alpha-1 antitrypsin levels have been reported to be high in patients with corneal ulcer.²⁷ Alpha-1 antitrypsin acts like an acute-phase reactant and its level tends to rise in inflammatory conditions.²⁸ It has been observed that because of the acute reactant nature of this protein its serum concentrations may change dramatically in the presence of inflammatory processes and the growth of malignant tumours.² The protease inhibitors may also have a protective action.¹¹ During infections alpha-1 antitrypsin production increases to counteract endogenous or exogenous protease.^{29,30} It is possible that there is an excessive load of protease in circulation in uveitis, which may be counterbalanced by the release of alpha-1 antitrypsin.

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