

CASE REPORTS

Corneal ulceration in a patient with α_1 antitrypsin deficiency

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α_1 Antitrypsin is an α_1 globulin protease inhibitor (Pi) produced by the liver, which controls the proteolytic action of several enzymes including elastase, collagenase, and trypsin. There are 30 genetic variants of α_1 antitrypsin which are inherited as autosomal dominant alleles, the normal being PiM. The allele PiZ causes difficulty in secretion of the protein following its synthesis. Homozygous individuals (PiZZ) produce only 15% of normal amounts of α_1 antitrypsin and show hepatic damage in up to 20% of patients. They also develop emphysema due to the unopposed action of proteases produced by lung phagocytes resulting in destruction of elastic tissue. Normal serum electrophoresis separates an α_1 band which consists almost entirely of α_1 antitrypsin. This band is reduced or absent in α_1 antitrypsin deficiency.

Case report

A 5-year-old girl had been investigated for lobar pneumonia a year previously and found to have α_1 antitrypsin deficiency (PiZZ). She presented to the ophthalmology department with a history of recurrent styes of both lower lids. On attendance there were no active styes, but she was found to have multiple, large superficial scars in the lower half of each cornea with no overlying epithelial defects (Figs 1 and 2). Unaided visual acuity was 6/9 in each eye. No other ocular abnormality was detected.

Tear samples were collected from the patient using capillary tubes placed in the lower fornix. Reflex stimulation of tear production was minimised by avoiding contact with the cornea. α_1 Antitrypsin levels were measured by high sensitivity radioimmunoassay. Serum levels of α_1 antitrypsin had already been determined at the time of her original diagnosis. Tear and serum samples were also collected from three healthy women aged 27, 31, and 32 years and α_1 antitrypsin levels were measured in each specimen.

Tear and serum levels of α_1 antitrypsin are shown in Table 1. The patient had a low serum α_1 antitrypsin level of 0.8 g/l (normal range 1.1-2.2 g/l) and a correspondingly low level in tears, 0.68 mg/l. The controls had serum levels of α_1 antitrypsin within the normal range and levels in tears ranging from 9.7 mg/l to 14 mg/l.

Comment

The pathogenesis of corneal ulceration is thought to involve enzymatic degradation of

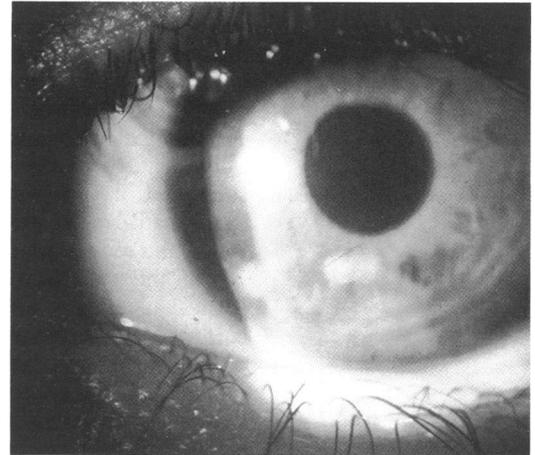


Figure 1 Superficial corneal scars in the right eye of a patient with α_1 antitrypsin deficiency.

collagen and proteoglycans.¹ Cells producing these destructive enzymes include keratocytes² and polymorphonuclear leucocytes.³ Many serum proteins inhibit the action of these enzymes, including α_1 antitrypsin, α_2 macroglobulin and α_1 antichymotrypsin. These anti-

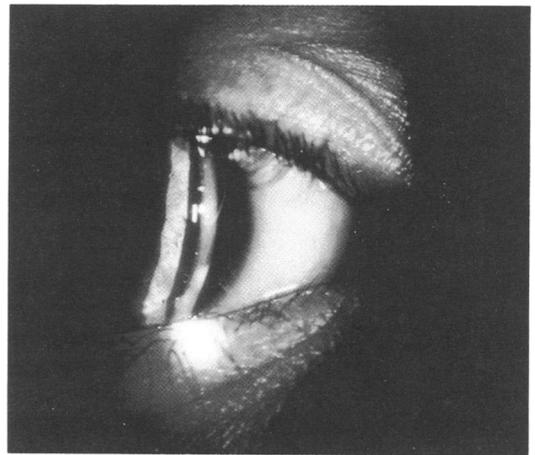


Figure 2 Superficial scars in temporal aspect of the left cornea of a patient with α_1 antitrypsin deficiency.

Table 1 α_1 Antitrypsin levels in tear fluid and serum in three normal individuals and a subject with α_1 antitrypsin deficiency (genotype PiZZ)

	Serum concentration (g/l)	Tear fluid concentration (mg/l)
Female, age 27	2.20	10.7
Female, age 31	1.67	9.7
Female, age 32	1.98	14.0
Female, age 5 (PiZZ)	0.8	0.68
Normal reference range	1.1-2.1	-

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proteases may have a regulatory role in the destructive processes which can occur in the cornea following infection, inflammation, and trauma. The levels of antiproteases in tears are found to rise dramatically in patients with corneal ulceration and they are thought to leak from inflamed conjunctival vessels.^{4,5} This is supported by the fact that the level of serum albumin in tear fluid rises together with α_1 antitrypsin in conditions involving conjunctival inflammation. The ratio of serum albumin to α_1 antitrypsin is 20:1 in serum but can be up to 3:1 in tears of inflamed eyes. This relative increase in tear fluid α_1 antitrypsin may simply reflect the fact that the molecule is smaller than albumin and can thus leak from blood vessels more easily.⁶ However, the tear fluid concentration of α_1 antitrypsin decreases at a slower rate than other serum antiproteases following resolution of conjunctival or corneal pathology, and the possibility of its local release or production has been suggested.³

Berman *et al*⁶ found one patient with genotype PiMZ and measured α_1 antitrypsin levels in both serum and tear fluid of an eye with extensive corneal ulceration. Both levels were low when compared with other patients with similar ocular pathology. They found no patient with corneal ulceration who had genotype PiZZ. Our patient was known to have low serum α_1 antitrypsin and was found to have a very low level of α_1 antitrypsin in tear fluid when compared with our normal controls. Sen *et al*⁵ found levels of α_1 antitrypsin to be independent of age and sex and thus we ignored the age difference between our subject and controls. The α_1 antitrypsin level in tears in our patient was also low when compared with other published values in normal healthy individuals without ocular pathology (Table 2).

Table 2 Previously published values of α_1 antitrypsin concentration in tears of normal healthy subjects without ocular pathology

Author	Tear fluid (mg/l)		
	Normal (SD)	No of subjects	99% Confidence interval
Prause ³	3.5 (2.2)	14	1.73-4.77
Gupta <i>et al</i> ⁴	4.2 (2.2)	76	2.92-5.48
Sen <i>et al</i> ⁵	4.0 (3.34)	81	3.01-4.99

We suggest that insufficient levels of α_1 antitrypsin in serum in our patient who was homozygous PiZZ, resulted in low tear fluid α_1 antitrypsin levels during an acute infective episode of the adjacent conjunctiva and lid margin. This enabled protease activity on the cornea to proceed without one of the normal regulatory processes, resulting in extensive corneal ulceration and subsequent scarring. This complication of α_1 antitrypsin has not previously been reported.

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Progressive corneal vascularisation as a previously unreported complication of neonatal herpes simplex infection

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Bilateral, widespread progressive corneal vascularisation as a result of neonatal herpes simplex infection has not been reported previously. The child presented, one of the first treated with systemic acyclovir, demonstrates the morbidity associated with herpes simplex infection.

Case report

JP was born in January 1982 at 33 weeks'

gestation by caesarean section 5 days after spontaneous rupture of membranes with an antepartum haemorrhage. She was initially well, but on day 3 suffered three apnoeic attacks requiring ventilation, and developed bilateral purulent conjunctivitis. On day 5 she developed an erythematous desquamating rash over her scalp which became generalised (Fig 1), mouth vesicles, and pneumonia. Cultures grew herpes simplex type II virus and a diagnosis of dissemi-