Corneal ulceration in a patient with $\alpha_1$ antitrypsin deficiency

R M Manners, M L Donaldson, C Low, P J Fenton

$\alpha_1$ Antitrypsin is an $\alpha_1$ 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 $\alpha_1$ 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 $\alpha_1$ 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 $\alpha_1$ band which consists almost entirely of $\alpha_1$ antitrypsin. This band is reduced or absent in $\alpha_1$ antitrypsin deficiency.

Case report
A 5-year-old girl had been investigated for lobar pneumonia a year previously and found to have $\alpha_1$ 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. $\alpha_1$ Antitrypsin levels were measured by high sensitivity radioimmunoassay. Serum levels of $\alpha_1$ 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 $\alpha_1$ antitrypsin levels were measured in each specimen.

Tear and serum levels of $\alpha_1$ antitrypsin are shown in Table 1. The patient had a low serum $\alpha_1$ 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 $\alpha_1$ 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 collagen and proteoglycans. Cells producing these destructive enzymes include keratocytes and polymorphonuclear leucocytes. Many serum proteins inhibit the action of these enzymes, including $\alpha_1$ antitrypsin, $\alpha_2$ macro- globulin and $\alpha_1$ antichymotrypsin. These antitrypsin variants genetic being proteolytic action of several enzymes including elastase, collagenase, and trypsin. There are 30 genetic variants of $\alpha_1$ 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 $\alpha_1$ 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 $\alpha_1$ band which consists almost entirely of $\alpha_1$ antitrypsin. This band is reduced or absent in $\alpha_1$ antitrypsin deficiency.

Figure 1 Superficial corneal scars in the right eye of a patient with $\alpha_1$ antitrypsin deficiency.

Figure 2 Superficial scars in temporal aspect of the left cornea of a patient with $\alpha_1$ antitrypsin deficiency.

Table 1 $\alpha_1$ Antitrypsin levels in tear fluid and serum in three normal individuals and a subject with $\alpha_1$ antitrypsin deficiency (genotype PiZZ)

<table>
<thead>
<tr>
<th>Serum concentration (g/l)</th>
<th>Tear fluid concentration (mg/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female, age 27</td>
<td>2.20</td>
</tr>
<tr>
<td>Female, age 31</td>
<td>1.67</td>
</tr>
<tr>
<td>Female, age 32</td>
<td>1.98</td>
</tr>
<tr>
<td>Female, age 5 (PiZZ)</td>
<td>0.80</td>
</tr>
<tr>
<td>Normal reference range</td>
<td>1.1–2.1</td>
</tr>
</tbody>
</table>
Progressive corneal vascularisation as a previously unreported complication of neonatal herpes simplex infection

Christopher J Hammond, Alec F Harden

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 disseminated...
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