Red eyes in renal failure

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Abstract

Of 57 patients with chronic renal failure who all had deposition of calcium salts in the conjunctival and corneal tissue two developed a brief episode of painful irritation and redness of the conjunctiva and subconjunctiva. This hyperaemia was adjacent to erosions of the corneal epithelium of the eye as a consequence of exfoliation of calcium concretions from the superficial corneal epithelium. Eight patients showed inflammatory reactions of the conjunctivae that were clinically identical to inflamed pingueculae. Three patients showed an inflammatory reaction of the eye that was characterised by a waxy red, more or less diffuse, episcleral and conjunctival hyperaemia extending beyond the palpebral fissure. The average value of the serum calcium concentration in these patients was particularly high and statistically significantly higher than in patients with calcification but without inflammatory signs and also higher than in patients who showed pingueculitis. We propose to reserve the term 'red eye of renal failure' for the latter group of patients.

In 1966 Abrams¹ drew attention to the association of irritable red eyes and renal failure in a patient with calcific deposits in the corneas close to the limbus. These deposits were extremely superficial and some had flaked off leaving small eroded areas which stained with fluorescein. The conjunctiva opposite the erosions was hyperaemic. The symptoms and signs were soon relieved by padding of the eye.

One year later Berlyne and Shaw² reported on 15 patients with red eyes and severe renal failure associated with raised serum inorganic phosphate and normal or low serum calcium. The illustration of a typical case showed bilateral temporal conjunctival hyperaemia in the interpalpebral area extending from the corneal limbus to the canthi. Their illustration gave the impression of a small elevated focus in the centre of the temporal conjunctiva.

In 1968 Berlyne³ described another 13 patients with renal failure (three of whom showed conjunctival irritation and injection) who were also associated with high serum inorganic phosphate levels and normal or even low serum calcium levels. There was no further description of the conjunctival hyperaemia. The authors suggested that there was a relationship between the conjunctival redness and conjunctival calcium phosphate salts deposited as microcrystals.

Subsequent studies of Caldeira *et al*,⁴ Ehlers *et al*⁵ and de Graaf *et al*⁶ identified the redness of the conjunctiva in patients with severe renal failure either by description or by diagnosis as conjunctival inflammatory reactions associated with pingueculae. It seems therefore that there are at

least two types of red eyes in renal failure; but what is the red eye of renal failure?

Patients and methods

During a 6 year period a total of 57 patients with terminal kidney insufficiency and on regular haemodialysis were followed for the occurrence of inflammatory complications of the anterior surface of the eye. There were 36 males ranging in age from 23 to 66 years and 21 females ranging in age from 33 to 68 years.

The age distribution of the patients is shown in Figure 1. The average age was 49 years and the average weight was 69.5 kg. In all patients a complete routine ophthalmic examination was carried out and repeated at periodic intervals. The corneoconjunctival depositions were graded according to the criteria of Porter and Crombie.⁷

Levels of serum calcium and inorganic phosphate were measured every 3 months in each patient and at the beginning of the development of inflammatory reactions of the outer surface of the eye. Fifty healthy persons, matched in sex and comparable in age and weight, were used as controls. As a parameter of kidney function the creatinine clearance was calculated in every patient on the basis of the level of serum creatinine and weight with the formula of Cockcroft and Gault.⁸ The statistical test used was analysis of variance.

Results

TYPES OF RED EYES

Three distinct types of inflammatory reactions were observed in the patients during this period. In two patients irritation and local hyperaemia

Figure 1 Cumulative frequency distribution of age in 57 patients with chronic renal failure.

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Figure 2 Localised hyperaemia around a raised greyish area of the bulbar conjunctiva in chronic renal failure. Clinically these lesions are indistinguishable from inflamed pingueculae.

Figure 3 More or less diffuse waxy red hyperaemia of the episcleral tissue and the conjunctiva over it extending beyond the palpebral fissure in patients with renal failure having strikingly high serum calcium concentration.

developed, with pain and photophobia, adjacent to erosions of the corneal epithelium which developed as a result of exfoliation of very superficially deposited calcium salts in the peripheral corneal epithelium in the palpebral fissure. These erosions stained with fluorescein. Signs and symptoms disappeared rapidly after dressing of the eye. These lesions were similar to those described by Abrams.¹

In eight patients a more or less localised redness of the conjunctival vessels of varying intensity, and occasionally mild congestion of the episcleral vessel was observed. This local hyperaemia of the conjunctival vessels developed gradually around a greyish triangular area situated in the bulbar conjunctiva in the interpalpebral fissure usually on either side of the cornea. The hyperaemia was characterised by exacerbations and remissions. Bacterial cultures were negative.

The greyish triangular lesions were studded with yellowish white spots that were occasionally confluent and more conspicuous at the periphery. In all patients both eyes were affected on the nasal as well as on the temporal side of the conjunctiva. The lesions in the latter localisation were more pronounced. All of them did fluoresce in ultraviolet light.⁹ Clinically these lesions are indistinguishable from inflamed pingueculae (Fig 2).

In three patients the hyperaemic inflammatory reaction was of a decidedly different nature. In these patients there was congestion of the vessels of the episcleral tissue and of the conjunctiva over it. The congestion presented as a more or less diffuse, episcleral, and conjunctivally somewhat waxy hyperaemia of the bulbar region extending beyond the palpebral fissure (Fig 3). Discharge if at all present was scanty. No pingueculae were observed. The symptoms, itching and burning, were mild. Bacterial cultures were negative. The inflammatory reaction subsided in 4 weeks on average.

GROUPS OF PATIENTS

From all patients four groups can be constructed. Group A consisted of 46 patients with calcium deposits but without any inflammatory reaction of the conjunctiva. This group included two patients with a brief episode of corneal erosions

and reflex irritation and hyperaemia of the conjunctiva. Group B consisted of eight patients with calcification and inflammatory reactions associated with pingueculae. Group C consisted of three patients with an inflammatory reaction resembling diffuse episcleritis and associated conjunctivitis. The three patients from the last group after the inflammatory reactions subsided were placed in group D.

CALCIUM DEPOSITS

In all patients a deposition of calcium salts in the subconjunctival tissue and/or cornea was present. The degree of the corneoconjunctival calcifications for the four groups is shown in Table 1. From this table it is apparent that patients who experienced one or the other type of inflammatory reaction had rather dense conjunctival and corneal calcium deposits.

SERUM CALCIUM CONCENTRATION

Table 2 shows the average values and standard deviations of serum calcium and serum phosphate and also the serum calcium and phosphate product in the control group. Data on serum calcium concentration in the several patient groups presented in Table 3 indicated that patients of groups A, B, and C had statistically significantly elevated serum calcium concentrations compared with the control group. This is graphically shown in Figure 4.

Table 1 The number of patients (expressed as a percentage) in each grade at their first visit according to the criteria of Porter and Crombie. In most patients the temporal side of each eye was more affected than the nasal side. In this table the more heavily affected temporal side of the conjunctiva is noted

Grade of calcification	0	1	2	3	4	5
Group A (n=46)	0	35	41	20	2	2
Group B (n=8)	0	37	25	25	13	0
Group C (n=3)	0	0	0	67	0	33

Table 2 The average values and standard deviations of serum calcium and serum phosphate and the serum calcium and phosphate product in 50 healthy persons

	Serum calcium (mmol/l)	Serum phosphate (mmol/l)	Serum calcium* serum phosphate
Average	2.4122	1.2950	3.1276
SD (n-1)	0.1004	0.1704	0.4568

Table 3 The blood concentration of calcium (mmol/l) and phosphate (mmol/l), and the calcium phosphate product (Ca*P). As a parameter of the kidney function, the creatinine clearance values (Cr Cl) are shown

Blood concentration	Group							
	A (n=46)		B (n=8)		C (n=3)		D (n=3)	
	Av	SD	Av	SD	Av	SD	Av	SD
Calcium	2.49	0.28	2.61	0.27	3.53	0.65	2.41	0.39
Phosphate	1.85	0.65	1.92	0.53	1.92	0.64	1.63	0.44
Ca*P	4.52	1.33	5.02	1.41	6.62	1.62	3.96	1.28
Cr Cl	5.63	1.59	5.70	1.91	5.61	0.54	6.78	2.05

In eight patients from group B with the localised type of redness associated with pingueculae the average serum calcium concentration was not significantly different from the average value of group A, who showed no inflammatory reaction of the conjunctiva. In the small group of patients presenting with a more or less diffuse type of episcleral hyperaemia there were strikingly high serum calcium concentrations in comparison with the other groups and these differences were statistically significant. Patients were treated with aluminium oxide hydrate in a dose of between 4.5 and 6 g daily and the systemic administration of dihydrotachysterol was discontinued. As soon as the serum calcium concentration returned to normal the inflammatory reaction subsided.

SERUM PHOSPHATE CONCENTRATION

In all groups the serum phosphate concentration was statistically significantly higher than in the control group (Fig 5). The serum phosphate concentration between groups A, B, and C however did not differ significantly statistically. The serum calcium and phosphate product was statistically significantly higher in group C and this was because of the markedly elevated serum calcium concentration.

Figure 4 The average serum calcium concentrations with the 95% confidence limits in the four groups and in the control group (CO). The average serum calcium value of groups A, B, and C were statistically significantly higher than that of the control group. The average serum calcium value of group C is markedly elevated and significantly higher than that of groups A and B. The average value of groups A and B did not differ significantly.

Figure 5 The average serum phosphate concentrations with the 95% confidence limits in the four groups and in the control group (CO). The average serum phosphate concentration in all groups was significantly higher than in the control group but statistically no difference was found between groups A, B, C, and D.

Discussion

The first case illustrating the association between irritable red eyes and renal failure was a patient in whom calcium salts deposited in the corneal epithelium had flaked off resulting in superficial corneal erosions causing painful irritable red eyes which were soon relieved by padding of the eye.¹ This case represented a reflex irritation and hyperaemia and therefore hardly qualifies as a specific ocular disease entity associated with renal failure.

The description of Berlyne and Shaw² and Berlyne³ on the type of the red eye, initially not having a slit-lamp available, was in rather general terms, such as ‘conjunctival hyperaemia’ and ‘conjunctival irritation’, and the illustration presented in a typical case seemed suggestive of inflamed pingueculae at the lateral aspects of the bulbus in both eyes. From the description and the illustration of Caldeira *et al*⁴ the red eye of renal failure seems identical to inflamed pingueculae, as were the lesions reported by Ehlers⁵ and de Graaf *et al*,⁶ and therefore cannot be considered a specific disease entity.

These inflamed swellings close to the limbus associated with renal failure cannot be differentiated clinically from inflamed pingueculae not associated with renal failure. The formation of pingueculae is essentially the result of a combination of an age change and of exposure due to the prominent position of the globe in the palpebral aperture. Ehlers considered pingueculae in patients with chronic renal failure as an accelerated age change, a view shared by others⁶; this is also our opinion.

Therefore we propose to reserve the term ‘red eyes of renal failure’ for those rare but specific inflammatory conditions of the anterior surface of the eyes which are characterised by a more or less diffuse waxy red episcleral and conjunctival hyperaemia extending beyond the palpebral fissure with little or no exudate. The lesion is

quite unlike the nodular episcleritis or diffuse localised episcleritis periodica fugax. This red eye of renal failure is associated with a disturbance of the calcium metabolism resulting in a high serum calcium concentration. Once the serum calcium concentration returns to normal the inflammatory reaction subsides.

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