Conjunctival and corneal changes in renal failure

Influence of renal transplantation

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Secondary calcareous degeneration of the conjunctiva or cornea may follow such pathological conditions of the eye as spring catarrh, erysipelas of the lids, leucomata, uveitis, trauma, etc. On the other hand, primary calcareous degeneration is rare (Duke-Elder and Leigh, 1965); the corneal deposits occur on Bowman's membrane and the superficial layers of the stroma, acting as foreign bodies and causing irritation.

In otherwise normal eyes, conjunctival and corneal calcium deposits may be found in conditions involving hypercalcaemia, especially hyperparathyroidism, sarcoidosis, and vitamin D intoxication. Reports from Walsh and Howard (1947) and Cogan, Albright, and Bartter (1948) describe lesions observed in hyperparathyroidism. Changes in cases of sarcoidosis have also been reported by Friedman (1951), Cogan and Henneman (1957), and by Crick, Hoyle, and Smellie (1961). Patients receiving large amounts of vitamin D and exhibiting calcium deposits were described by Frost, Sunderman, and Leopold (1947), Walsh and Howard (1947), Cogan and others (1948), Gifford and Maguire (1954), Leira (1954), Gartner and Rubner (1955), and Smith (1957); in most of these patients the vitamin D had been given for rheumatoid arthritis.

Roentgenologic examination of the anterior portion of the eyeball may reveal calcification (Fleischner and Shalek, 1949; Gartner and Rubner, 1955).

Cogan and others (1948) observed calcium deposits in eight patients with severe renal damage, five of them with a history of high calcium and high alkali intake. In two other cases there was prolonged vomiting with chronic alkalosis. All had high serum levels of non-protein nitrogen and phosphorus. The calcium level was high in all but one case.

Berlyne and Shaw (1967) reported fifteen patients with severe renal failure, either acute or chronic, high serum inorganic phosphate, normal or low serum calcium, mean serum calcium $\times$ phosphorus product greater than 70, red eyes, and calcium deposits in the conjunctiva and cornea. Further evidence of conjunctival calcification in renal failure was offered by Berlyne (1968).

The present paper reports the findings in a group of five patients with chronic renal failure in whom red eyes became gradually manifest.

Methods

A group of five patients in the terminal stages of renal failure who were seen at the University Hospital exhibited signs of conjunctival reddening and irritation. Serial determinations of serum levels of calcium, phosphorus, alkaline phosphatase, creatinine, and urea were carried out. Peritoneal dialyses were performed several times at various intervals.

Presented at the 15th Brazilian Congress of Ophthalmology, Porto Alegre, April 27 to May 2, 1969.

Received for publication October 2, 1969

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Only three patients received a kidney transplant. In two a kidney from a living donor was used, and in the third from a cadaver. In all three the kidney was placed in the right iliac fossa.

Only one patient was examined with the slit lamp before and after surgery. A piece of bulbar conjunctiva of the right eye was surgically removed and studied under the microscope before the transplantation of a cadaver kidney. This patient was followed up for 20 weeks and biomicroscopy was carried out from time to time.

Results

The clinical and biochemical findings of the five patients with conjunctival congestion are presented in Table I, with later observations on the same patients when no redness was noticed, either in the earlier phase of renal failure or after they had undergone repeated peritoneal dialysis, followed in some cases by kidney transplantation.

Table I *Clinical and laboratory findings in five patients with renal failure with and without conjunctival congestion.*

Conjunctival congestion	Case no.	Age (yrs)	Sex	Diagnosis	Serum calcium (mg./100 ml.)	Serum inorganic phosphorus (mg./100 ml.)	Serum Ca × P	Serum alkaline phosphatase (KA units/100 ml.)	Serum creatinine (mg./100 ml.)	Blood urea (mg./100 ml.)	Comment
Present	1	34	F	P	7.2	13.4	96.48	10.9	26.0	300	
	2	25	M	G	8.1	16.9	136.89	4.0	28.0	288	
	3	27	M	G	8.8	17.0	149.60	3.6	25.0	330	
	4	28	F	G	7.8	16.5	128.70	2.2	20.0	206	
	5	35	M	G	7.6	16.3	123.88	7.4	22.0	243	
	Mean	29			7.9	16.0	126.40	5.6	24.2	273.4	
Absent	1	34	F	P	9.2	4.7	43.24	—	—	98	After repeated dialyses
	2	25	M	G	9.6	7.7	73.92	4.0	24.0	234	In steady state of renal failure
	3	27	M	G	8.5	2.7	22.95	—	1.2	50	After renal transplantation
	4	28	F	G	7.2	14.7	105.84	5.3	7.5	80	After repeated dialyses Aluminium hydroxide by mouth
	5	35	M	G	8.8	2.6	22.88	2.1	1.55	60	After renal transplantation
	Mean	29			8.6	6.4	55.04	3.8	8.56	104	

P = Chronic pyelonephritis

G = Chronic glomerulonephritis

For the sake of comparison, the clinical and laboratory findings in eleven patients (Cases 6 to 16) with chronic renal failure but no redness of the eyes are presented in Table II (opposite).

Case 4 was examined with the slit lamp and had a piece of bulbar conjunctiva removed for microscopic examination.

Case report (Table I, Case 4)

A married woman aged 28 was admitted on March 5, 1968, with a history of cloudy urine for the last 10 years. During her first pregnancy, 5 years before, oedema, high blood pressure, dysuria, frequency of micturition, and proteinuria were noticed. The oedema persisted after the delivery of a premature stillborn infant. Three subsequent pregnancies followed the same pattern. Nausea, vomiting, paleness, and headaches were recorded for the last 3 months before admission. She was

Table II *Clinical and laboratory findings in eleven patients with renal failure and no conjunctival congestion.*

Case no.	Age (yrs)	Sex	Diagnosis	Serum calcium (mg./100 ml.)	Serum inorganic phosphorus (mg./100 ml.)	Serum Ca $\times$ P	Serum alkaline phosphatase (KA units/100 ml.)	Serum creatinine (mg./100 ml.)	Blood urea (mg./100 ml.)
6	41	M	G	7.1	7.0	49.70	—	16.0	201
7	31	M	G	8.1	5.9	47.79	3.9	9.0	225
8	22	F	G	5.4	4.1	22.14	6.6	—	190
9	26	M	G	7.9	9.1	71.89	—	14.0	237
10	15	F	P	6.4	12.2	78.08	3.6	16.0	172
11	31	M	G	7.3	12.9	94.17	—	—	404
12	23	M	P	6.9	9.0	72.10	4.1	25.5	294
13	42	F	P	9.5	10.3	97.85	10.7	13.0	256
14	36	M	G	8.1	15.0	121.50	6.2	15.0	394
15	36	M	G	8.2	10.1	82.82	5.8	16.0	270
16	27	F	G	4.9	10.0	49.00	6.8	16.0	240
Mean	30	—	—	7.2	9.6	69.12	5.9	15.6	263

G = Chronic glomerulonephritis

P = Chronic pyelonephritis

admitted with cardiac tamponade caused by haemopericardium; this was successfully treated by surgery. The blood urea was 440/mg./100 ml. Peritoneal dialysis was performed at intervals of approximately 20 days and she was put on a low protein diet.

She complained of soreness of the eyes, which were congested. She was given aluminium hydroxide by mouth and peritoneal dialysis carried out at 10-day intervals. The eye symptoms improved temporarily (Table I) but later reappeared.

Examination

On April 16, 1968 a slit-lamp examination showed nasal and temporal pingueculae in both eyes and hyperaemia on the bulbar conjunctiva extending to the canthi. In the interpalpebral area both conjunctival and corneal changes were noticed. In the bulbar conjunctiva, both temporal and nasal, and above and below the pingueculae, delicate chalk-white structures were seen. They were either punctate or striate, appearing as peaks of light superficial to the vessels. The cornea showed hazy greyish superficial deposits running concentrically with the limbus, on both sides of the interpalpebral area. This zone was separated from the limbus by a narrow, less dense zone and faded off gradually toward the centre of the cornea (Fig. 1).

FIG. 1 *Photograph of slit-lamp painting of temporal aspect of right eye, showing pinguecula and calcium deposits in conjunctiva and cornea*

Biopsy

On April 18 a piece of bulbar conjunctiva was surgically removed from the right eye, immediately above the temporal pinguecula and adjacent to the limbus. The temporal pinguecula was removed separately. The material was preserved in 10 per cent. formalin, imbedded in paraffin, sectioned, and stained with haematoxylin and eosin.

Microscopical examination showed irregular thickness of the epithelium differentiated from the substantia propria. Many vessels, some of them dilated, and zones of basophilic degeneration were seen. Between the epithelium and the substantia propria there was a ribbon-like deposit of calcium salts. In the deeper layers of the substantia propria there were minute calcium deposits (Figs 2 and 3).

The pinguecula specimen showed no particular characteristics.

FIG. 2 Conjunctival biopsy specimen, showing ribbon-like deposition of calcium between epithelium and substantia propria. Haematoxylin and eosin. $\times 60$

FIG. 3 Higher magnification of part of Fig. 2. $\times 240$

Operation

On May 26 a cadaver kidney was transplanted.

Ocular progress

A slit-lamp examination was afterwards performed at regular intervals. At the first examination on June 6, both eyes showed a few conjunctival deposits temporally but none nasally; corneal deposits were seen both nasally and temporally but were inconspicuous.

On June 26 the right eye was unchanged but the conjunctival deposits in the left had disappeared and the corneal deposits had diminished.

On July 10 the conjunctival deposits in the right eye had diminished temporally and disappeared nasally; in the cornea they were unchanged temporally and less conspicuous nasally. In the left eye the pathological appearance of the cornea was less marked nasally and unchanged temporally.

On August 14 the aspect of both eyes was the same.

On September 13 the bulbar conjunctiva of the right eye was unchanged temporally but two deposits had reappeared nasally; the cornea was normal temporally and unchanged nasally. The left eye was normal, except for a slight loss of transparency of Descemet's membrane temporally.

On October 3rd the bulbar conjunctiva of the right eye was normal temporally but the two nasal deposits were still seen; the superficial cornea was unchanged but a small opacity in Descemet's membrane was seen inferiorly. In the left eye only one conjunctival deposit was observed temporally; in the cornea there was one deposit nasally and one temporally.

Termination

The patient died on October 12 from gastrointestinal haemorrhage. The postoperative course had been complicated by diabetes, infection with *E. coli*, and rejection of the transplant. The patient succumbed after nearly 5 months' heroic treatment.

Discussion

Red eyes in normocalcaemic or hypocalcaemic patients with renal failure, described by Berlyne and Shaw (1967), were considered to be early manifestations of small deposits of calcium in the vicinity of the limbus.

Berlyne (1968) found superficial conjunctival deposition of calcium in almost every patient with advanced renal failure who had a high calcium $\times$ phosphorus product (above 70) caused by a high plasma-inorganic-phosphate-level. These calcium deposits may be regarded as diagnostic.

The predilection for calcium deposition in the interpalpebral portion of the cornea and conjunctiva would be explained by loss of carbon dioxide to the atmosphere during the waking hours, with a fall in the $p\text{CO}_2$ of the superficial ocular tissues and consequent rise in the pH. The low pH of the plasma exhibiting a high calcium $\times$ phosphorus product, and a higher pH of both the aqueous humour and the superficial tissues would create favourable conditions for the deposition of calcium-phosphate salts.

Berlyne and Shaw (1967) suggested that the redness was a reaction to this deposition, the crystals being of such a size as to cause the inflammatory reaction.

The conjunctival lesions consist of reddening and calcification plaques. In the cornea an arc-shaped deposit of a whitish material concentric with the limbus is the outstanding finding. The presence of red eyes in the absence of infection or uveal inflammation should alert the physician to the possibility of renal failure. A slit-lamp examination will elucidate the picture.

In our patient the initial ocular findings were typical. After renal transplantation increased diuresis and lowering of the blood urea were observed. When the first post-operative slit-lamp examination was performed, 11 days after transplantation, the conjunctival deposits in both eyes had disappeared nasally and were greatly reduced temporally. The corneal deposits were still present but much reduced.

During subsequent weeks the eyes gradually cleared although two crises of rejection were detected and fought. The corneal deposits regressed more slowly than the conjunctival deposits.

When signs of renal failure occurred again a few conjunctival deposits reappeared and remained until the patient's death. A slight loss of transparency of Descemet's membrane at the periphery was observed in both eyes.

The information gathered from this single case suggests that the conjunctival and corneal deposits in renal failure are reversible, tending to disappear when the renal function improves.

Summary

The conjunctival and corneal changes in renal failure are described. One patient who received a kidney transplant was examined with the slit lamp at regular intervals. The conjunctival and corneal deposits tended to disappear, the first more readily than the second. A few conjunctival deposits reappeared when the renal function deteriorated.

We should like to thank Dr. Affonso Krug Filho for the microscopical report on the conjunctival specimen. We are indebted to Mrs. Lúcia Oliveira for the drawing (Fig. 1).

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