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Photodamage of the conjunctiva in patients with porphyria cutanea tarda

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Abstract

Ninety two patients with porphyria cutanea tarda (PCT) were examined ophthalmically in a paired case control study. The incidence of pinguecula and of pterygium was 8 and 2 times higher respectively, in PCT patients than in the control group. The photodamage to the conjunctiva is considered to be a result of the photoactivity of uroporphyrin in the tissues.

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Porphyria cutanea tarda (PCT) is a chronic polyaetiological disorder in porphyrin biosynthesis, caused by a deficiency of uroporphyrinogen III decarboxylase in the liver cells, with typical skin and liver findings, as well as pronounced uroporphyrin excretion in the urine.[1] The skin manifestations are bullous erosive lesions triggered on the face and the backs of the hands by minor mechanical trauma, milia formation, melanosis, hypertrichosis in the eyebrows and the zygomatic area, chronic actinic skin changes, and pseudoscleroderma. The evidence suggests that the photoactivity of excess porphyrin in the plasma and/or tissues is involved in the cutaneous manifestations.

In the past few years, 92 patients with PCT have been examined ophthalmically. In this study the results of examinations of external ocular structures (lids, conjunctiva, corneas, and scleras) are reported.

Patients and methods

A paired case control study was performed.[2] For every patient with PCT, two controls were matched according to age (plus or minus 3 years was allowed) sex, and skin type on the basis of the tendency to burn and to tan[3]; furthermore, the members of the two groups worked in similar circumstances (indoor or outdoor). The frequencies of the pathological findings were compared by the χ^2 test.

PATIENTS

The study involved 92 patients with PCT (81 men and 11 women; mean age 47·3 (SD 4·8) years). The diagnosis was based on the porphyrin profiles (uroporphyrinuria and 7-carboxylporphyrinuria) and on the clinical manifestations.

CONTROL GROUP

The members of the control group suffered from psoriasis vulgaris, chronic venous insufficiency of the legs, eczema, urticaria, or allergic contact dermatitis.

Table 1 Clinical findings on external ocular structures in patients with porphyria cutanea tarda (PCT) and in a matched control group

Symptoms	Patients with PCT (n=92)	Control group (n=184)	
Hypertrichosis in the periorbital area	76	4	p<0·001
Solar elastosis in the temporal region	81	47	p<0·001
Favre-Racouchet disease	7	1	p<0·01
Erosive lesions on lids	9	0	p<0·001
Pinguecula	63	16	p<0·001
Pterygium	8	7	p>0·10

OPHTHALMIC EXAMINATIONS

Slit-lamp examination, ophthalmoscopy, visual field examination, tonometry, Schirmer test, corneal staining, and colour vision test were carried out in all patients and controls.

PORPHYRIN DETERMINATION

Urinary and faecal porphyrins were analysed by thin-layer chromatography.[4]

HISTOLOGY

The biopsy specimens were obtained from the involved conjunctiva of six patients with PCT. The tissues were fixed in formaldehyde solution (10% neutral formalin), embedded in paraffin, and sectioned in 5 μm thicknesses. The sections were stained with haematoxylin and eosin and resorcin and fuchsin.

Results

The incidence of clinical symptoms on the external ocular structures is given in Table 1.

In 68 male and eight female patients with PCT hypertrichosis was seen in the periorbital area. Frequently, diffuse solar elastosis in the temporal region and sometimes also solar elastosis with

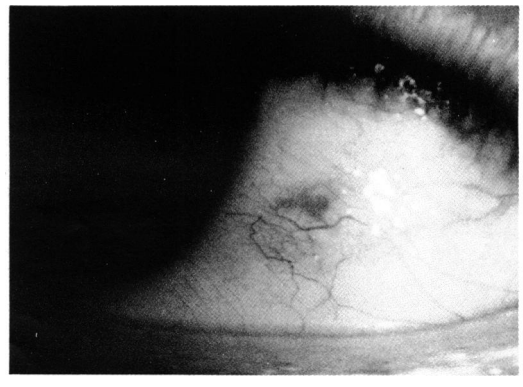

Figure 1 A nodule (yellow-brown in colour) on the temporal side of the cornea in the intrapalpebral portion of the bulbar conjunctiva.

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cysts and comedones (Favre-Racouchot) were observed. These findings were significantly rarer in the control group.

In 63 patients, yellow-brown nodules were seen on either side of the cornea in the area of the lid fissure, which never extended onto the limbus (Fig 1). During slit-lamp examination we observed foamy-like degenerative changes on the surface of these nodules, which macroscopically resembled the structure of a pinguecula. Histologically, the epithelium was slightly thickened and hyperpigmentation was seen in the basal layer. The immediate subepithelial stroma contained amorphous, faintly basophilic staining material, and the stromal fibres were fragmented and partially coiled. The histological findings corresponded to the microscopic structure of pinguecula. In the control group typical pinguecula was observed in only 16 persons. Pterygium was seen in eight patients with PCT and in seven controls.

Ectropion, blepharochalasis, symblepharon, corneal and scleral abnormalities were not found in either the porphyric or the control group.

Discussion

The porphyrias are a group of diseases in which there are deficiencies of the metabolic pathway leading to the synthesis of haem. The error is recognised as lying either in the imperfect synthesis of enzymes having an aberrant structure or in the slowed synthesis of a perfect compound. The most important feature of the current classification of porphyrias is that the metabolic disorder can in all cases be localised to one specific enzyme within the haem biosynthetic pathway.

PCT is the most common form of porphyria. The basic biochemical defect is a reduced activity of uroporphyrinogen decarboxylase in the liver, which results in the overproduction and increased excretion of uroporphyrin and polycarboxylated porphyrins. The cause of the reduced enzyme activity is unclear, but appears to be a result of complex interactions of both genetic and acquired factors.[1]

In the present study, actinic damage of the periorbital skin was observed in 88 of the 92 PCT patients, with erosive lesions on the lids in nine. Pinguecula and pterygium were eight and two times, respectively, more frequent in the PCT group than in the matched controls (Table 1). Though other authors have described lid scars and ectropion,[5,6] we did not observe these in any of the patients, nor did we see those severe changes of the externed ocular structures (scleral ulceration and perforation, and symblepharon) observed in congenital porphyria.[7-9]

Sunlight-induced skin lesions are clinically characteristic of PCT. The evidence suggests that the phototoxic effect of porphyrins is involved in the cutaneous manifestations. The absorption of light with a wavelength of around 400 nm (which corresponds to the peak in the absorption spectrum of the porphyrins), and the more penetrating light of the subsidiary peaks between 500 and 600 nm, raises the porphyrin to its singlet or triplet excited state. Excited porphyrins can react directly with tissues and molecules within the cell, or they allow transfer of the excitation energy to molecular oxygen, thereby producing oxygen radicals and peroxides.[10] The exposure of porphyrins to 400–410 nm radiation results in complement activation[11] and the release of mediators from mast cells.[12] The biological effects of oxygen radicals, mast cell-derived mediators, and anaphylotoxin, generated as a consequence of complement activation, may account for the damage of the sunlight-exposed tissues.[13] Though the photoactivity of the porphyrins explains many aspects of the pathophysiology of tissue damage in porphyria, there are still many unanswered questions. For example, what accounts for hypertrichosis in the periorbital areas of patients with PCT?

Pterygium and pinguecula are consequences of the actinic damage of the conjunctiva.[14] This is indicated by the facts that they appear in every case in the interpalpebral fissure, their frequency increases in proportion to age, the time spent in sunlight and the intensity of the solar radiation, and their tissue structures are highly reminiscent of that of solar elastosis of the skin. We consider that their high incidence in PCT is a consequence of the phototoxic effect of the uroporphyrin accumulated in the tissues. We did not observe the previously reported serious effects of photodamage in porphyria – that is, ectropion, symblepheron, blepharochalasis, and scleromalacia. The explanation of this may be that a longer time is required for their emergence, but in our cases the treatment (phlebotomy and chloroquine) led to normalisation of the porphyrin excretion in 3–6 months.

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