Intraepithelial carcinoma ("Bowen's disease") of the cornea

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Pre-invasive carcinoma of the skin epithelium was first described by Bowen (1912) under the name of precancerous dermatosis; 30 years later McGavic (1942) reported five cases of a similar disorder affecting the corneal and limbal epithelium of the eye. Since then many more ocular cases have been recorded. In the belief, however, that a terminology based on the pathology of a lesion is preferable to an eponymous nomenclature, it would seem proper, in describing pre-invasive neoplasia of the epibulbar epithelium, to abandon the commonly applied ascription 'Bowen's disease' in favour of the more explicit term 'intraepithelial squamous cell carcinoma.'

The clinical features of the disorder are characteristically described as those of an ill-defined, slightly elevated, vascularized lesion with a gelatinous appearance, the condition occurring predominantly in elderly patients and in males more often than in females (Reese, 1963). Not infrequently there is a history of previous corneal injury or inflammation. Several reports have stressed the relatively benign behaviour of the majority of such cases regardless of the degree of malignancy indicated by histological appearances (Ash and Wilder, 1942; Ash, 1950; Irvine, 1963).

Though there are at present two reports of the ultrastructure of invasive carcinoma of the corneal epithelium (Tanabe and Tanabe, 1965; Radnot and Lapis, 1970), the fine structure of preinvasive carcinoma in this situation has not been described. In this combined clinical, histological, and electron microscopical study of such a case, emphasis is placed on the clinical aspects, a detailed analysis of the ultrastructure being provided elsewhere (Tripathi and Garner, 1972).

Case report

CLINICAL FEATURES

An 80-year-old man was first seen in the Corneal Clinic at the Croydon Eye Unit on May 4, 1970. He complained of impaired vision in both eyes of 3 years' duration. Neither he nor his relatives had noticed any other abnormality and his general health was good. The visual acuity with correction was 6/18 in the right and 6/12 in the left, and he was found to have bilateral senile cortical lens opacities. The right cornea showed a flat opalescent cauliflower-shaped lesion extending from the pupillary margin to the limbus between the 12 and 3 o'clock meridians. The lesion was avascular apart from a narrow zone at the limbus and was sharply demarcated from the otherwise normal corneal tissue. Slit-lamp biomicroscopical examination suggested that the lesion was entirely
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confined to the epithelial layer (Fig. 1). The fundi were normal and routine investigations all gave negative results. A provisional diagnosis of intraepithelial carcinoma was made and a partial lamellar keratectomy was performed on July 14. Post-operative progress has been satisfactory but it is proposed to keep the patient under observation.

**PATHOLOGICAL FINDINGS**

*Light microscopy* showed a disordered epithelium, in which the cells were pleomorphic and disorientated (Fig. 2), covering all but the edges of the specimen. The nucleo-cytoplasmic ratio was increased while the nucleoli were invariably enlarged and frequently multiple. Giant cells were not uncommon most of them containing multilobulated or even several nuclei. Mitotic activity was increased and was not confined to the basal cell layer. The thickness of the epithelium, though in places marginally increased, was commonly within normal limits. At the periphery of the lesion the

**FIG. 1** Clinical and slit-lamp appearances of the epithelial lesion

**FIG. 2(a)** Section of the abnormal epithelium, showing loss of polarity, nuclear enlargement with occasional multilobulation and giant cell formation (arrowed), prominent multiple nucleoli, and (on the right of the picture) a dyskeratotic cell encircled by non-keratinized cells

Araldite sections, toluidine blue. x440

**FIG. 2(b)** An epithelial cell, showing advanced dyskeratosis, is present in the basal cell zone

Araldite sections, toluidine blue. x440
junction between disordered and normal epithelium was clearly defined, with a tendency for the abnormal tissue to over-ride the surface of the healthy epithelium (Fig. 3).

Some red blood cells were present on the surface of the cornea and were occasionally trapped between the epithelium and an intact basement membrane. There was, however, no vascularization of the stroma, except for a restricted zone near the limbus, and it seems probable that the subepithelial incarceration of blood cells was an artefact incurred at operation. No abnormality was observed in Bowman's membrane or the superficial stroma.

Electron microscopy generally amplified the histological findings, the multilobulate morphology of occasional giant nuclei being particularly well demonstrated (Fig. 4, opposite). In addition, there were several features not apparent by light microscopy. Thus, a marked finding was a reduction in junctional complexes and interdigitations between individual epithelial cells, although such desmosomes as were present appeared to be normally formed. Also, while many cells showed a pronounced perinuclear arrangement of tonofilaments bound into bundles (Fig. 5), occasional cells showed more advanced signs of dyskeratosis (or individual cell keratinization) in the form of even more marked condensation of tonofilaments with either pyknosis or dispersion of the nucleus (Fig. 6); in late stages of this process the whole cell content was reduced to an homogeneous electron dense mass. Such cells were sometimes engulfed or "cannibalized" by neighbouring non-keratinized cells.

Comment
In that the histological and ultrastructural changes in this lesion are essentially the same as those that have been described in frank carcinoma of the corneal epithelium, there would seem reasonable to regard the appearances as being diagnostic of carcinoma in-situ. As such it is a pre-invasive carcinoma and rather more than a pre-cancerous disorder. Nevertheless, the lack of basement membrane disruption and the abrupt transition from abnormal to healthy epithelium is strongly in favour of conservative treatment in the form of local resection, such as was undertaken in this case. Even frank carcinoma is rarely associated with significant invasion of the corneo-scleral stroma and a similar conservative approach to therapy has been advocated on several occasions (Ash and Wilder, 1942; Irvine, 1963; Zimmerman, 1969). The propensity for intraepithelial carcinoma to recur after simple excision is possibly somewhat in excess of 10 per cent. according to Irvine's figures but regrettably from a prognostic standpoint, according to the same author, the likelihood of this occurring is not closely related to the degree of histological disturbance (Irvine, 1963).
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**Fig. 4** Electron micrograph of a giant epithelial cell containing a multilobular nucleus

n = nucleoli, T = tonofilaments, BM = basement membrane, BW = Bowman's zone of the stroma. × 9,000
FIG. 5 Electron micrograph of an epithelial cell, showing perinuclear arrangement of the tonofilaments (T)
N = nucleus, D = desmosomes.  ×18,000
**Fig. 6** Electron micrograph of part of the dyskeratotic cell depicted in Fig. 2(b), showing a dense aggregation of tonofilaments admixed with degenerate and dispersed nuclear components (NC).

N = Intact nucleus of an adjacent non-keratinized cell. ×24,000
In several respects the clinical appearances of the present case were unusual. Thus, in most reported instances, the underlying stroma is vascularized and moderately infiltrated with chronic inflammatory cells, whereas the present case showed only a few vessels limited to the periphery of the cornea and no inflammation. Again, in the present case, there was in general no significant elevation of the corneal surface in contrast to the usual description of a slightly raised lesion. Possibly these departures from the typical findings are indicative of an early lesion. It should be stressed, however, that while the diagnosis may be suspected on clinical grounds, proof is dependent on histological examination.

Summary

A case is presented of intraepithelial squamous cell carcinoma (Bowen's disease) of the cornea together with light and electron microscope findings.

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