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Myofibroblast-like cells in human anterior capsular cataract

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Summary. In six cases of anterior capsular cataract, cells present in the subcapsular zone were investigated. In addition to organelles previously described, the cells were found to contain 7 nm and 15 nm filaments, suggestive of actin and myosin. The cells varied in shape from elongated or flat to rounded. Maculae adhaerentes, gap junctions and basement membranes were present. It is concluded that these cells closely resemble myofibroblasts, by virtue of their cytology and behaviour. The significance of this observation, concerning hypotheses on the genesis of anterior capsular cataract is discussed.

Key words: Anterior capsular cataract – Myofibroblasts – Wound healing

Lamb (1937) described the cells in the plaque of anterior capsular cataract as fibroblast-like in appearance, at the light microscopic level. Subsequent electron microscopical studies (Pau and Caesar 1967; Henkind and Prose 1967; Font and Brownstein 1974; Gosh and McCulloch 1975) have confirmed this opinion at the ultrastructural level, without, however, increasing our knowledge of the origin or role of these cells.

Since the first description of myofibroblasts in granulation tissue (Gabbiani et al. 1971), such cells have been reported from a number of normal tissues with moderate contractile properties (Böck et al. 1972; Güldner et al. 1972; Bressler 1973; Gorgas and Böck 1974; Kapanci et al. 1974). However, the major significance of these cells seems to lie in pathological states (Buntrock 1980; Balázs 1981; Schürch et al. 1981).

The purpose of the present communication is to report on the presence of myofibroblast-like cells in human anterior capsular cataract.

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Materials and methods

Six operatively extirpated lenses with anterior capsular cataract were investigated. The maturity of the cataracts ranged from two months to fourteen years. Fixation was effected with either 0.5% glutaraldehyde with 4% paraformaldehyde in 0.1 M phosphate buffer of pH 7.3 and subsequent postfixation in 6% glutaraldehyde in the same buffer, or directly in the latter fixative. All lenses were divided into numbered blocks and these were further postfixed for 1 h in 1% osmium tetroxide in the same phosphate buffer with addition of 0.1 M sucrose, or in 1% osmium tetroxide in veronal-acetate buffer.

Dehydration was performed with acetone and in some cases the blocks were contrasted with uranyl acetate and phosphotungstic acid. The embedding medium was either araldite (Durcopan, Fluka, Neu-Ulm, FRG) or Spurr's medium in the hard mixture. Most blocks were sectioned perpendicularly to the capsular surface, except in two cases, where unoriented blocks resulted in tangential sections. In all instances semithin sections were cut before and after thin sectioning and these were stained using 1% borax buffered toluidin blue.

Ultrathin sections were further contrasted with uranyl acetate and lead citrate and examined in a Zeiss EM9A or Hitachi H-600 electron microscope.

Results

The number of cells present in plaques of anterior capsular cataracts varies with maturity. In general, old plaques contain fewer cells, though the chronological correlation is not perfect (Table 1).

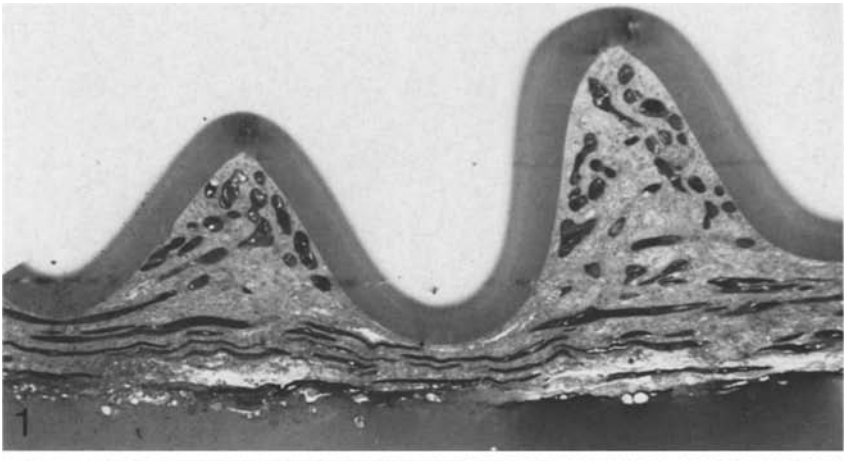
The cells range in shape from elongated to round. Since sections from different blocks and thus in different orientations, consistently show elongated cells in the basal portions of the cataract, there is reason to believe that such cells are in fact squamous. For the same reason the round cells near the capsule (especially in folds of the latter) are presumed to be spherical or ovoid (Fig. 1). At least some cells have processes. The elongated

Table 1. Summary of the investigated cataracts, relating maturity of cataract to the frequency of occurrence of cells

Case	Age of patient in years	Maturity of cataract	Occurrence of cells
1	43	2 months	+ + + +
2	43	5 years	+ + +
3	28	9 years	+ +
4	78	10 years	+ +
5	27	12 years	+ + +
6	53	14 years	+

Fig. 1. Semithin section from cataract of 2 months maturity. The lens capsule, forming the upper boundary of the cataract, is folded. The lens itself appears as a homogeneous layer in the lower part of the figure. Note the elongated cells at the base of the cataract and the rounded or ovoid forms within the folds of the capsule. Magnification: × 320

Fig. 2. (Case 1) A cell from the apical portion of a capsular fold, possessing a prominent sublemmal layer of filaments [*f*], containing dense bodies [*d*]. Magnification: × 20,000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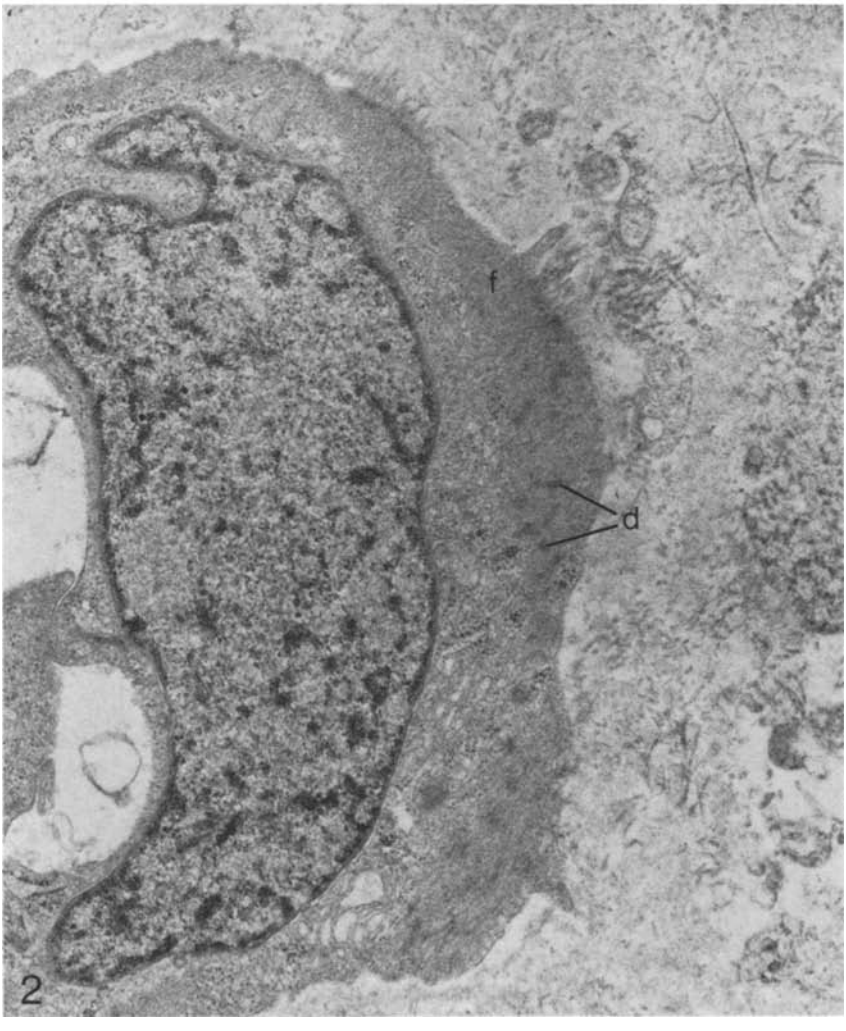
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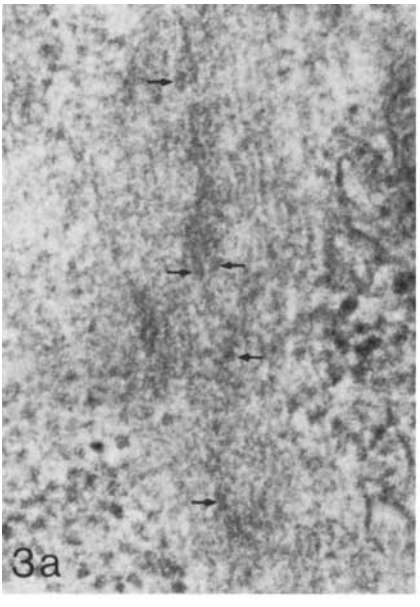
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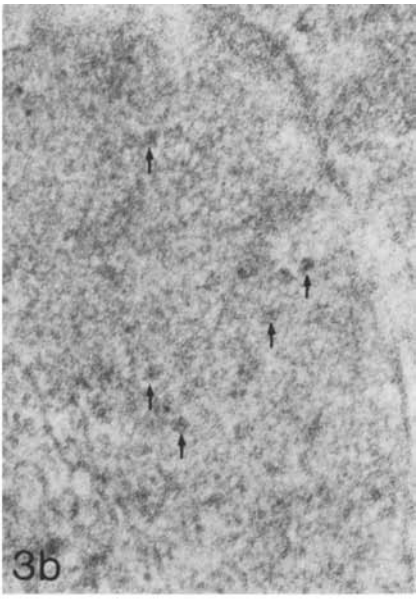
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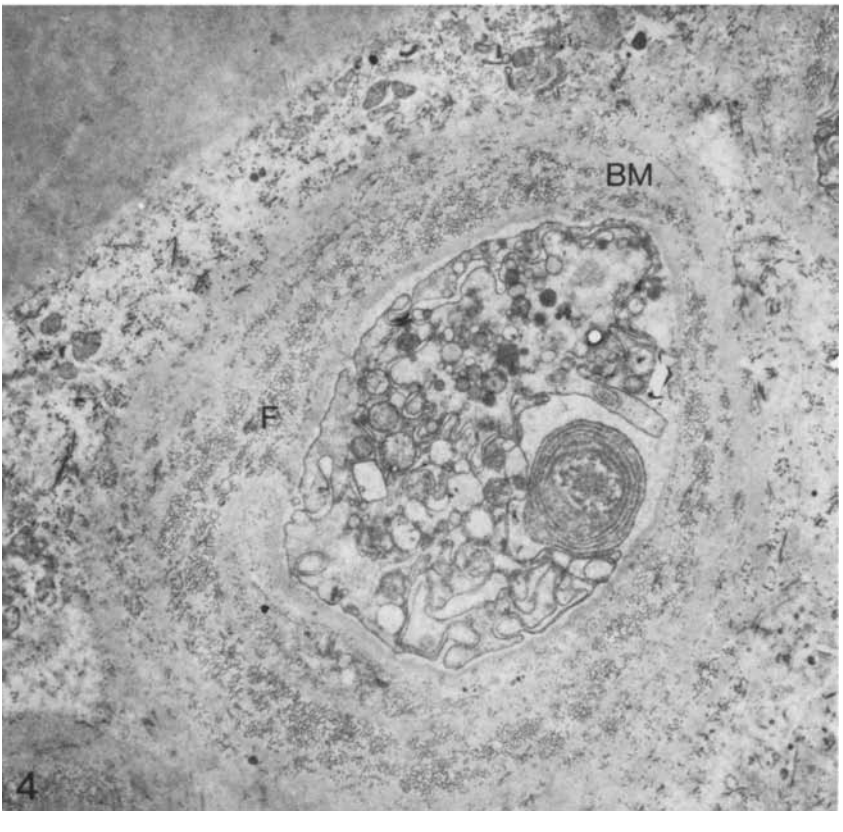

BM
F
4

or flat cells tend to have smoothly contoured nuclei, while the nuclei of the ovoid cells are somewhat irregular and indented.

Besides the organelles such as distended rough endoplasmic reticulum, prominent Golgi apparatus and occasional lysosomes, previously described by other authors, numerous cells possess a prominent sublemmal layer of filaments, within which there are dense bodies (Fig. 2). More detailed examination reveals that the majority of filaments have a diameter of 5–7 nm, whereas within the dense bodies 15–17 nm filaments are also present (Fig. 3). Some cells contain 10 nm intermediate filaments.

Cells lie singly or in groups, each cell or cell group being surrounded by basement membrane-like material. Beyond this, collagen fibrils or filaments are to be found, frequently arrayed in alternation with further layers of basement membrane-like substance (Fig. 4). Where cells are numerous and contact each other maculae adhaerentes may be frequently found. Gap junctions are also present (Fig. 5). In the cataract of two months maturity intercellular junctions of unusual morphology are frequent (Fig. 5b). In view of the close apposition of the membranes these might be considered to be multilaminated gap junctions. Their significance is unknown.

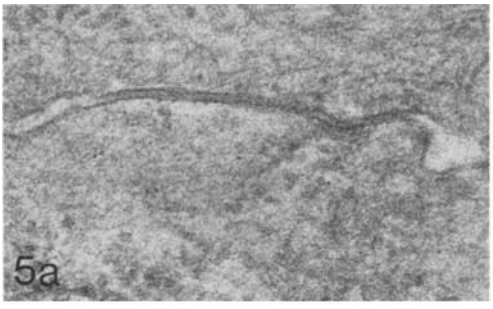
In all cases it is possible to distinguish cells of differing electron opacity. The paler cells (electron lucent) initially have the same range of organelles and inclusion to be found in the darker cells. However, with increasing electron lucency the cell organelles seem to disintegrate and the cells accumulate a variety of vesicles (Fig. 4). Finally, it is possible to find aggregations of such vesicles lying within areas of alternating layers of basement membrane-like material and collagenous fibrils, characteristically found also around intact cells (Fig. 6). Darker cells may also appear to lose their organelles and can become filled with an electron dense granular mass. The relationship to the extracellular components is similar.

Discussion

The cytological features of the cells found in anterior capsular cataract are identical with those of myofibroblasts, as described by Gabbiani and his co-workers (for a fuller survey see Gabbiani 1981), and those of modified myocytes (m-myocytes) present in diseased blood vessels (Parker and Odland 1966; Staubesand 1978 and 1980). Myofibroblasts and m-myocytes are considered to be identical (Staubesand 1983 – personal communication).

Fig. 3a, b. Detail of the filaments in the vicinity of the densities found within the cells in anterior capsular cataract. Arrows point to 15–17 nm filaments. **a** Longitudinal section; **b** cross section. Magnification: ×120,000

Fig. 4. (Case 5) Degenerating cell remains, within the typical border, consisting of alternating arrays of basement membrane-like material [*BM*] and collagenous filaments [*F*]. Magnification: ×7,500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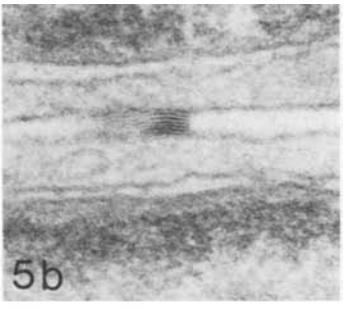
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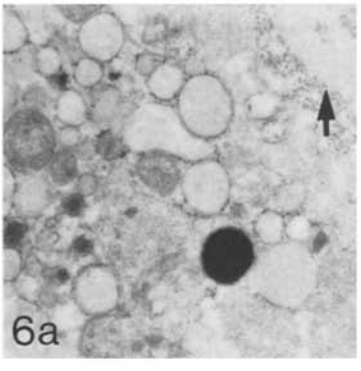
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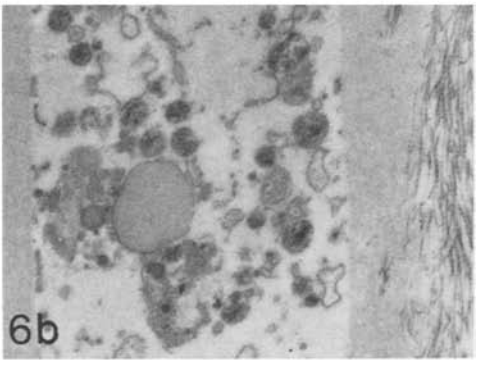
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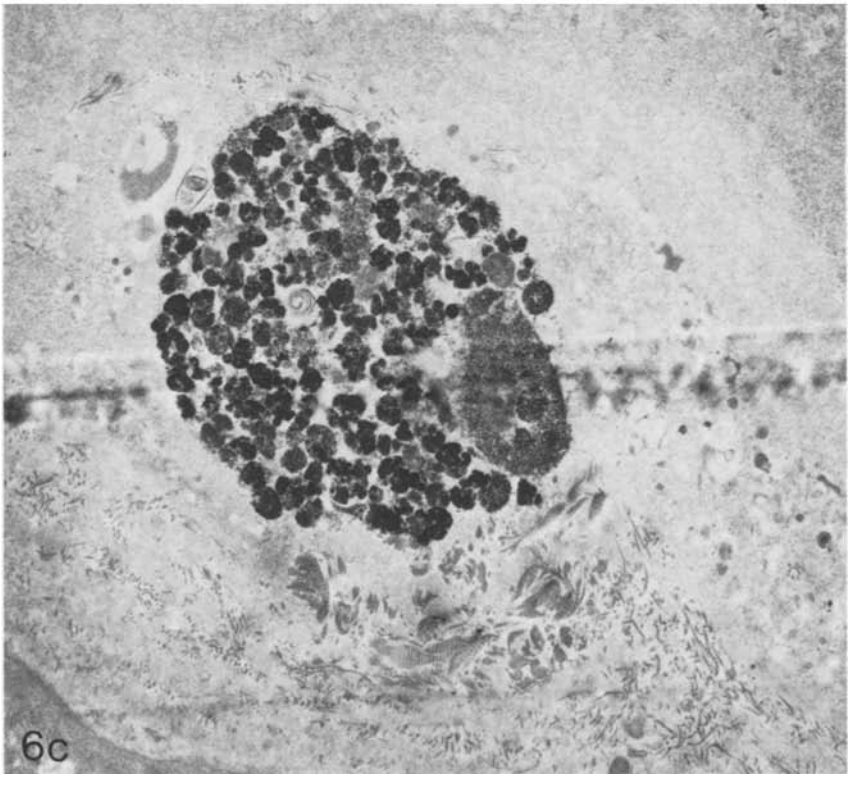
6c

Myofibroblasts are associated with dysplastic collagen and basement membrane in Dupuytren's contracture (Gabbiani and Majno 1972; Nemetschek et al. 1976). Dysplastic collagen fibrils are also found in the vicinity of m-myocytes in pathologically altered blood vessels (Pott and Staubesand 1977; Riede and Staubesand 1977). Similar aggregations of dysplastic collagen are found in anterior capsular cataract: Pau H, Novotny GEK, Arnold G (1984) Ultrastructural investigations on anterior capsular cataract. II. Extracellular structures (in preparation).

In view of these similarities between myofibroblasts and the cells of anterior capsular cataract, these may be regarded as, at least functionally, equivalent.

As in previous studies, the question arises, as to the origin of the collagen producing cells in the capsular cataract. The lenticular capsule may be regarded as a thick basement membrane. It is well known that cells can penetrate basement membranes. Hence, there is no a priori reason to assume that the cells in the cataract cannot enter from the outer surface of the lens. It cannot be excluded that mobile blood cells could enter the aqueous humour and from there penetrate the capsule. However, Gabbiani et al. (1972) discuss the possible origin of myofibroblasts without suggesting such an origin. Other studies (Krawczyk 1971; Gabbiani and Ryan 1974) have further demonstrated that epithelial cells can also develop mobility and contractile properties, as found in myofibroblasts. Furthermore, a study by Iwig et al. (1981) has shown that lenticular epithelial cells grown in culture can develop contractile properties, and Ireland and Maisel (1982) have found actin filaments in normal lens fibres. Therefore there are good reasons to suppose that lenticular epithelium can give rise to the myofibroblast-like cells present in the capsular cataract.

The ultrastructural findings of this and previous studies indicate that the cells of the capsular cataract produce collagen. As demonstrated by Bailey et al. (1975a and b), myofibroblasts of granulation tissue produce a high proportion of type III collagen. It is likely that the collagen found in anterior capsular cataract is also of this type, an hypothesis corroborated by the rather irregular arrangement of even normal appearing collagen fibrils in the cataract, which is equally true for collagen fibrils of reticular fibres. Type III collagen is characteristic during embryonic development, and

Fig. 5a, b. (Case 1) Junctions between cells. **a** Normal type of gap junction. Magnification: × 80,000. **b** Frequently encountered type of cell contact with a multilaminar aspect. Magnification: × 120,000

Fig. 6a–c. Vesicular structures representing remains of degenerated cells. **a** (Case 2) Membrane bound vesicles with varying contents in a field delimited by basement membrane-like material and collagenous filaments (*arrow*). Magnification: × 16,000. **b** (Case 3) Vesicles and non-membrane bound material resembling that found in vesicles within a region bounded by basement membrane-like material. Magnification: × 14,000. **c** (Case 5) An acumulation of small portions of granular material, not bounded by membranes. Note the dysplastic collagen in close proximity. Magnification: × 10,000

wound healing may be regarded as a reversion to an earlier developmental state, for the purpose of increased production of material. Similarly, the high incidence of desmosomes and gap junctions between myofibroblasts may be taken as a further indication of a reversion to the embryonic state (Gabbiani 1979). Anterior capsular cataract is frequently a sequel to blunt or perforating injuries of the eye, or in some cases a metabolic lesion. Thus, anterior capsular cataract may be presumed to be a reversion to an embryonic status, this time by lenticular epithelium, for the purpose of wound repair, which in this situation is inappropriate.

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