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Benign Human Mammary Myoepithelioma

József Tóth

Research Institute of Oncopathology, H-1122 Budapest, Ráth Gy.-u. 7–9, Hungary

Summary. A leiomyoma-like, multifocal tumour developed from intraductal papillomatosis in the breast of a 42 year old woman. The spindle-shaped tumour cells were examined by light, electron and polarizing microscopy, which revealed that they originated from immature "precursor" myoepithelial cells. The author suggests that the tumour be called "myoepithelioma". From the morphological characteristics of the tumour the myoepithelial cells appear to be capable of producing leiomyoma-like benign or malignant tumours. The role that has been attributed by some to the myoepithelial cell in the production of epithelial tumours is problematical, in the light of the present finding.

Key words: Myoepithel – Mammary tumours – Leiomyoma – Myofilamentum.

Introduction

50 years ago it was already supposed that the myoepithel cells (m.e.) of the mammary gland might transform into a certain type of leiomyoma (Peyron et al., 1926). This mesenchymal differentiation capacity of m.e. cells has also been accepted by Hamperl (1970). In the human mammary gland descriptions of adenomyoepitheliomas, mixed tumours and tumours belonging to the group of carcino-sarcomas have been published in which one of the cellular components of the mesenchyme was considered to be of m.e. character (Melnick, 1932; Fink et al., 1968; Mackenzie, 1968; Hamperl, 1970).

Hübner et al. (1969) also reported m.e. like tumour cells in human salivary duct carcinomas and Donath et al. (1972) described a clear fine-structurally myoepithelial tumour cell type present in the intercalated duct carcinoma of salivary gland.

A myoepithelial tumour component was frequently encountered in the mixed tumours of the mammary gland of bitch (Bomhard and Sandersleben, 1973,

1974, 1975; Pulley, 1973). Recently, Schlotke (1975) found malignant myoepitheliomas in the mammary gland of bitch.

In mixed tumours of the human mammary gland where there is an m.e. component one can only speculate on the origin of the tumour, since the typical myofibrillar bundles cannot be identified either by light or electron microscopic examinations. Our case is reported because no tumour composed entirely of m.e. cells has been described to date. The report also calls attention to the fact that, apart from their contractile functions, m.e. cells may take part in the morpho-histogenesis of mammary gland tumours and be the origin of purely m.e. tumours.

Case Report

S.M., a 42 year old woman, complained of a painful hard nodule in the right breast. A circumscribed knot unattached to the skin, was palpated in the upper outer quadrant and removed "in toto" under local anaesthesia. There were no postoperative complications and the patient is now symptom free.

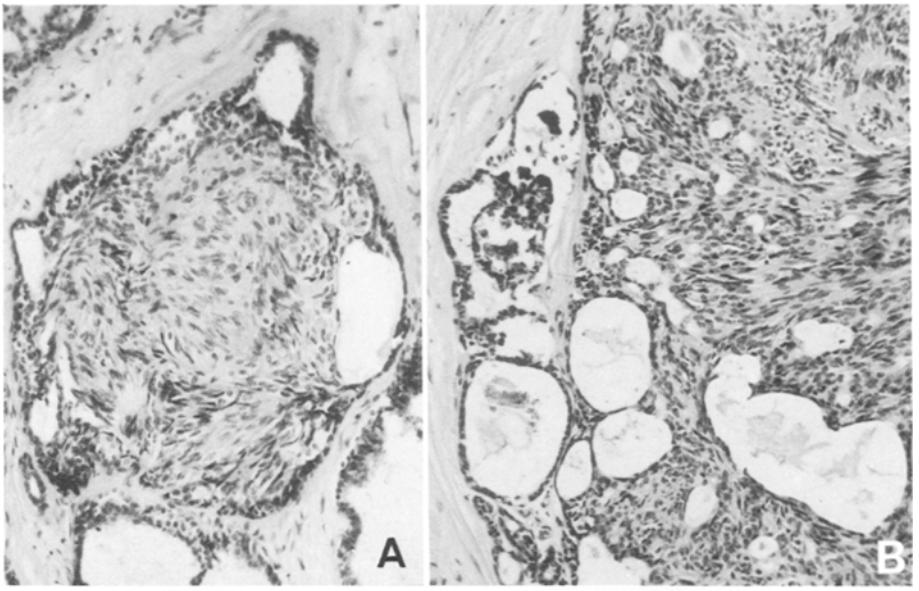
Material and Methods

The surgical specimen (Pathohistological register No. 16199/1973) consisted of two nodules measuring $2.3 \times 1.6 \times 1.4$ cm and $1.8 \times 1.0 \times 0.8$ cm, respectively. They appeared to be greyishwhite, dense and were covered by fat. No capsule was visible. On the greyish-white homogenous cut surface some small cysts and light red nodules were observed. The tumour was fixed in 4% formalin and embedded in paraffin. Sections were stained with haematoxylin-eosin, van Gieson stain, Gömöri's silver impregnation, iron haematoxylin (Heidenhain) and PAS reaction. For polarizing microscopic studies the sections were covered with a mixture of aniline oil and Canada balsam (1:1) in the same measure (Aniline reaction of Orbán and Romhányi, 1962).

From the rest of the specimen (fixed for 48 h in formalin) pieces between 1 mm^3 were cut. Washing was followed by post fixation in 4.5% glutar-aldehyde and 1% osmium-tetroxide. Embedding in Durcupan was then carried out. Semi-thin sections were stained with toluidine blue, ultrathin sections were contrasted with uranyl acetate and lead citrate. Electron micrographs were taken with a JEM-6 C electron microscope.

Histological Observations

Sections of both pieces of tissue showed dilated cystic ducts and groups of mammary glands in the cytopenic, hyaline connective tissue. The cysts were filled with cellular adenomatous intraductal papillomas. Beneath the glandular epithelium and stroma of some papillomas, m.e. cells accumulated. These spindle-shaped cells formed bundles that partly surrounded, partly compressed the glands. The proliferating m.e. elements almost filled the ducts and the remnants of papillomas could only be recognized in the peripheral parts (Figs. 1A, B, 2A). The efferent ducts of some of the cystic, dilated glands were almost completely filled with leiomyoma-like tumours, the spindle cells of which formed either bundles or whorl-like patterns. The nuclei of the tumour cells were elongated, rounded or oval, occasionally arranged in palisade-like rows (Figs. 1A,



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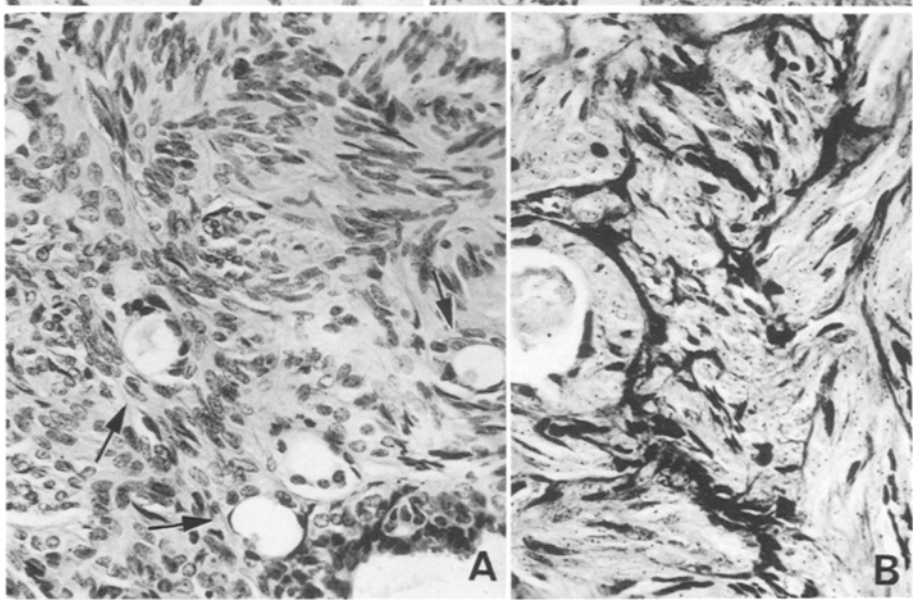

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Fig. 1. A The lumen of some dilated cystic ducts is filled with bundles of spindle-shaped tumour cells. H.E. ×125. **B** In the distinct papillomas different degrees of proliferation of spindle shaped tumour cells are detectable. H.E. ×125

Fig. 2. A Remnants of the glandular elements of intraductal papilloma are partly surrounded by bundles of spindle shaped tumour cells (arrows). H.E. ×260. **B** Myofilaments in the form of brownish black bundles are visable in the cytoplasma of some of the tumour cells. Heidenhain's iron haematoxylin staining. ×260

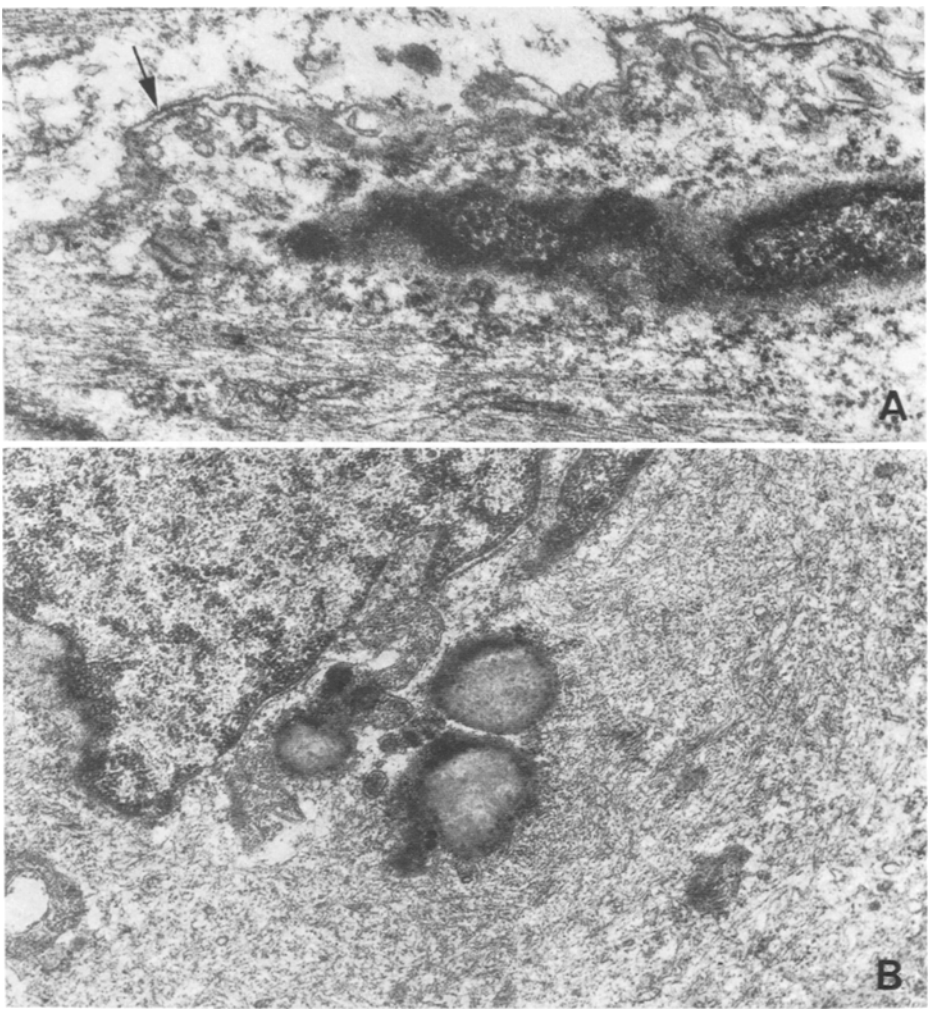

Fig. 3. A In the cytoplasm of every tumour cell there are myofilamentous bundles and elongated mitochondria. The cells are joined with poorly developed desmosomes (arrow). ×22,500. **B** Myoepithelial cell with large nucleus of bizarre appearance. There are lipid granules adjacent to the nucleus. The cytoplasm is almost completely filled with the network of actin like filaments. ×20,725

B, 2A). At high magnification, the cytoplasm had a clear appearance, the tumour cells stained yellow with Van Gieson stain and fine fibrous bundles became visible in the cytoplasm of some of the cells when iron-haematoxylin was applied (Fig. 2B). The cytoplasm contained a very few PAS positive fine granules. After Gömöri silver impregnation a fine fibrous network became visible around the spindle cells. Signs of cellular atypia and mitotic figures could not be seen. Following the aniline reaction, structures displaying positive brilliant birefingence appeared in the cytoplasm of the tumour cells. This phenomenon depended on the presence of oriented, intracytoplasmic fibers.

For electron microscopic study, we chose the parts of the tumour that showed the characteristics of m.e. proliferation. The glands within the tumor were lined with simple cuboidal or columnar epithelium. Between the basement membrane and epithelial cells there were groups of spindle cells of varying electron density. In their cytoplasm myofilamentous bundles of varying sizes could be seen, either at the periphery or in the vicinity of the cell nucleus. Focal proliferation of myofibrils within the bundles produced electron dense spots (Fig. 3A). The myofibrils cause some parts of the cellular membrane to appear serrated.

The tumour-cell nuclei contained finely scattered chromatin granules which were sometimes located at the periphery of the nucleus. In the cytoplasm a well developed Golgi apparatus, was seen with some mitochondria and a few strands of rough surfaced endoplasmic reticulum visible. Groups of lipid granules could also be seen and small membraneous indentations were present forming micropinocytotic vesicles, and a network of actin-like filaments (Fig. 3B). The groups of tumour cells were surrounded by fine electron dense fibrous tissue and a widened irregular basal lamina. This was probably connected in some way to the cytoplasm of tumour cells. In a few instances the cells were connected to one another by under-developed desmosomes and to the basal lamina by hemi-desmosomes (Fig. 3A).

Discussion

Myoepithelioma can be regarded as the final cellular form of a differentiation process. In breast ducts and acini, rounded or oval cells with clear cytoplasm have been observed among the columnar epithelial and m.e. cells. Typical mature m.e. cells take origin from these cells (Tandler, 1965; Murad and von Haam, 1968). Radnor (1972) followed the development of m.e. cells by electron microscopic examination and considered cells poor in organelles and with clear cytoplasm to be the immature or precursor m.e. type. In the development of m.e. tumours, these cells may have an important role since no atypical or mitotic forms have been found among mature m.e. cells. This suggests that they represent a highly differentiated cell form with contractile properties (Bässler et al., 1967) which is not capable of proliferation.

A tumour component of possible m.e. origin has been observed in the breast and in mixed tumours (fibromyoepithelioma, clear cell hidradenoma) (Peyron et al., 1926; Hamperl, 1970, 1971; Mackenzie, 1968; Fink, 1968). Areas composed of m.e. cells have frequently been encountered in the mixed tumours of the mammary gland of the bitch (v. Bomhard and v. Sandersleben, 1973, 1974, 1975; Pulley, 1973). Recently, Schlotke (1975) produced a well documented report of malignant myoepitheliomas found in bitch mammary glands, the first published report on malignant mammary tumours of pure m.e. origin. Histologic pictures of the metastases showed a similar picture to those of the primary tumour.

Neither benign nor malignant human mammary tumours of pure myoepithelial origin have been reported, although their existence might be inferred from

the presence of occasional myoepithelial-like areas in mixed tumours. Our own case and those of Schlotke are notable as they can be regarded as evidence for the direct neoplastic transformation of myoepithelial cells, or more correctly the myoepithelial "precursor" cells.

The microfibrillar bundles found in both benign and malignant epithelial tumour cells may be composed of actin and/or myosin-like proteins and are distinguishable from the thicker tonofilaments and m.e. myofilaments arranged in bundles (Schenk, 1974). Recently Feiner and Kaye (1976) reported that in granulomatous tissue fibroblasts can transform into myofibroblasts containing bundles of myofibrills. In regard to the histogenesis of the tumour therefore, the presence of cytoplasmic microfibrils made up of actin or myosin is not proof of myoepithelial origin. Electron microscopical criteria for benign m.e. tumours are, the presence of myofilamentous bundles of regular arrangement, micropinocytotic vesicles and occasionally, glycogen droplets and desmosomes. The possibility that neoplastic proliferation of m.e. precursor cells may produce typical leiomyoma or leiomyosarcoma cannot be excluded.

Schlotke's observations and our own findings contradict Murad's statement that certain types of breast cancer are derived from m.e. cells. Based on the study of 26 human fibrous breast cancer cases, Machinami (1976) is also unable to accept the m.e. origin of the human mammary carcinomas.

The m.e. origin of our intraductal leiomyoma-like tumour could be satisfactorily demonstrated even by light microscopy; its optical properties under the polarizing microscope and ultrastructural characteristics confirmed the m.e. nature of the tumour cells.

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