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Case Report

Oncocytic Breast Papilloma

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Summary. A rare case of an intracystic oncocytic papilloma of the breast in a 34 year old woman is described. The light and electron microscopic differences between oncocytic and apocrine epithelial cells and the problem of oncocytic meta- or neoplasia are discussed.

Key words: Breast – Papilloma – Oncocytic – Metaplasia

Introduction

Tumours of the breast with a histological structure similar to tumours of the salivary glands, for example pleomorphic adenoma (Sheth et al. 1978), adenoid cystic carcinoma (Anthony and James 1975) or adenomyothelioma (Hamperl 1970) are rare. Oncocytic neoplasia and metaplasia occur in salivary glands (Askew et al. 1971; Balogh and Sandford 1965; Gray et al. 1976; Hamperl 1936, 1962), the tyroid (Hamperl 1936, 1950) and the kidneys (Hamperl 1936, 1950), whereas the occurrence of oncocytes in cases of breast disease is uncommon. A breast tumour completely dominated by oncocytes has to the best of my knowledge never previously been described.

Case History

A 34 year old woman had a symptom-free tumour in the right breast, which had not increased in size for the last eight years. Mammography showed an approximately 3 cm diameter cyst situated superficially in the upper lateral quadrant towards the nipple; this was drained. Microscopy of the fluid showed no malignant or oncocytic cells. The tumour was removed four weeks later due to recurrence. There had been nor relapse $1\frac{1}{2}$ years after operation.

Pathology

Macroscopic examination showed an irregular 2.5 cm tissue specimen with a greyish fibrous surface on cutting, which contained several cystic lumina up to a maximum of 0.75 cm in size. One of these contained a papillomatous structure.

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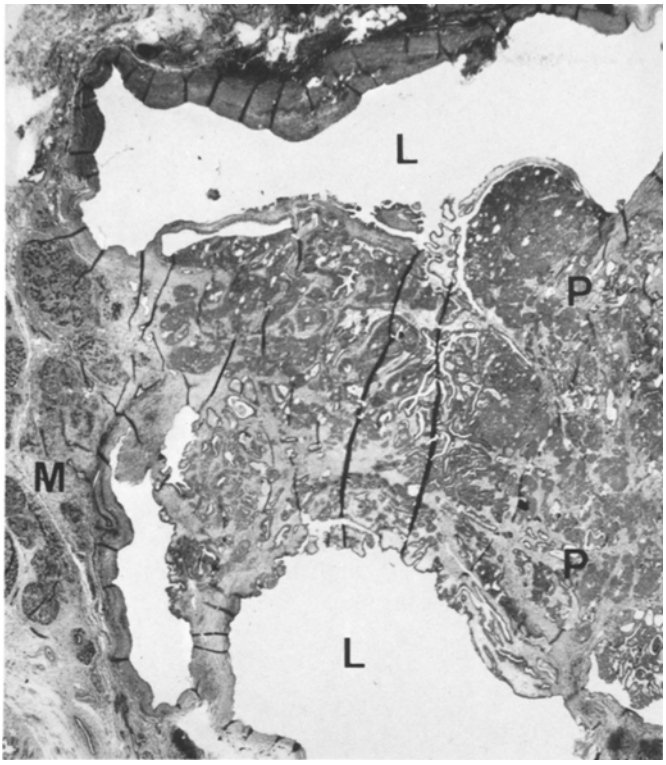

Fig. 1. Breast tissue surrounding a cystic lumen containing a papilloma (*P*). *L* lumen, *M* breast tissue (HE ×6)

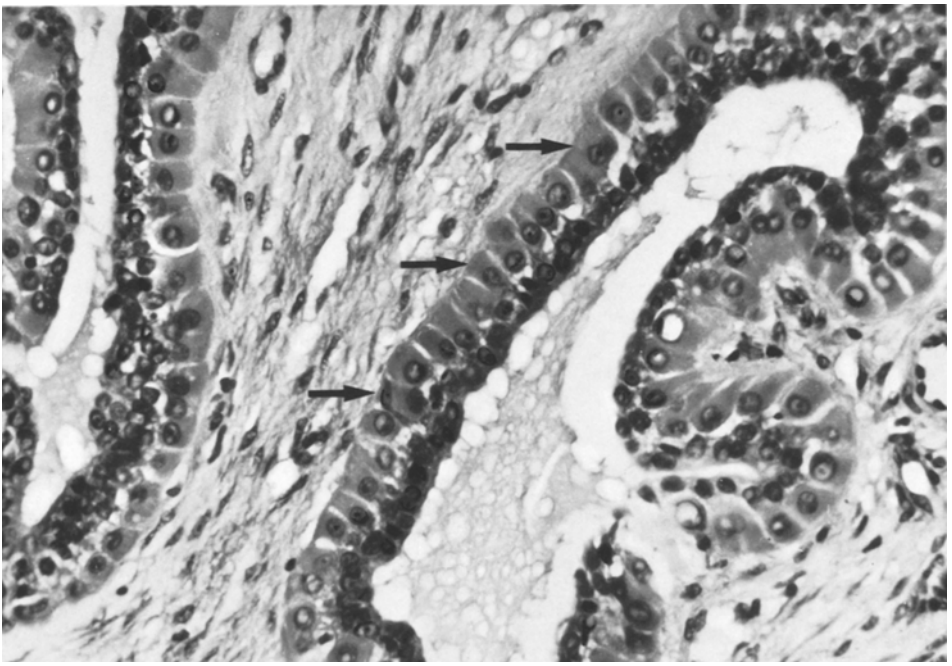

Fig. 2. Gland formation with an outer layer of oncocytes (*arrows*) (HE ×400)

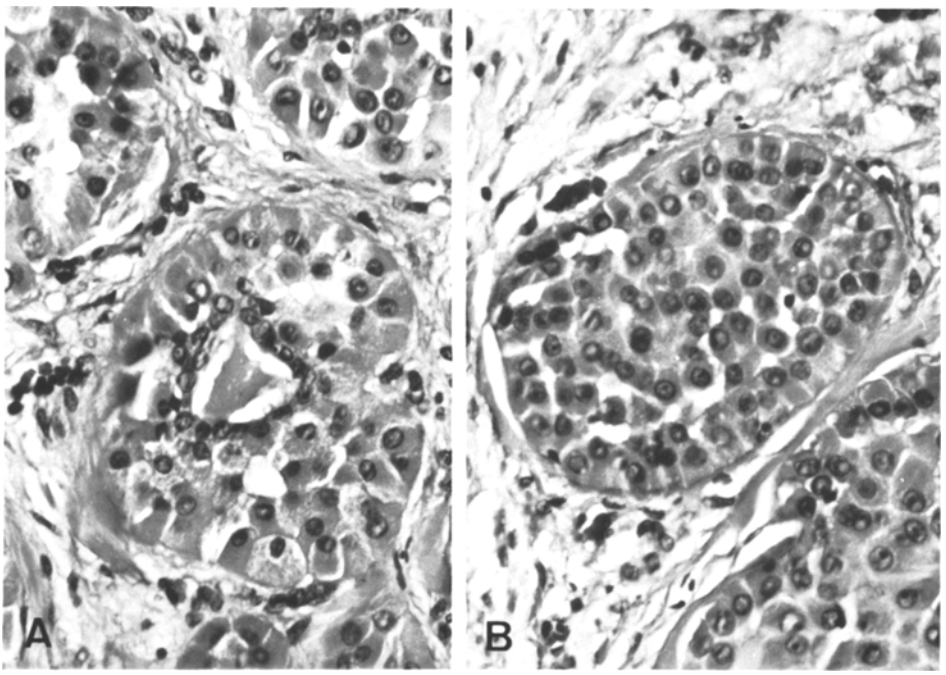

Fig. 3A, B. Increasing thickness of the oncocytic layer (**A**, **B**). B shows the luminal epithelium lost and the lumen obliterated (HE ×400).

Table 1. Some differences between apocrine cells and oncocytes which may be used in the differential diagnosis.

	Oncocytes	Apocrine cells
Light microscope		
Limitation	Obvious, clefts	Obvious, snouts
Cytoplasm	Eosinophilic and granular	Eosinophilic
PAS	Positive granules, diffuse	Positive granules, apical
Inclusion stain cresyl violet	Diffuse red metachromasia	Apical red metachromasia
Electron microscope		
Cell membrane	Smooth	Many folds
Secretion granules	Few, dispersed	Many, apical
Mitochondria	Considerably increased in number, closely packed	Increased in number, dispersed
Other organelles	Few and inconspicuous	Well-represented

Light microscopic examination of a formalin-fixed, paraffin-embedded and haematoxilin-eosin stained specimen, showed breast tissue surrounding an intracystic papilloma (Fig. 1), built-up of branched, vascular and, in places, oedematous connective tissue stroma, containing closely packed irregular to circular glandular formations. A few of the glands were covered by a two-layered epithelium consisting of a basophilic cubical epithelium on the luminal aspect and a layer of oncocytes with eosinophilic granular cytoplasm, corresponding to the myothelial layer (Fig. 2). An eosinophilic substance was observed in the lumen. The majority of the glands were packed

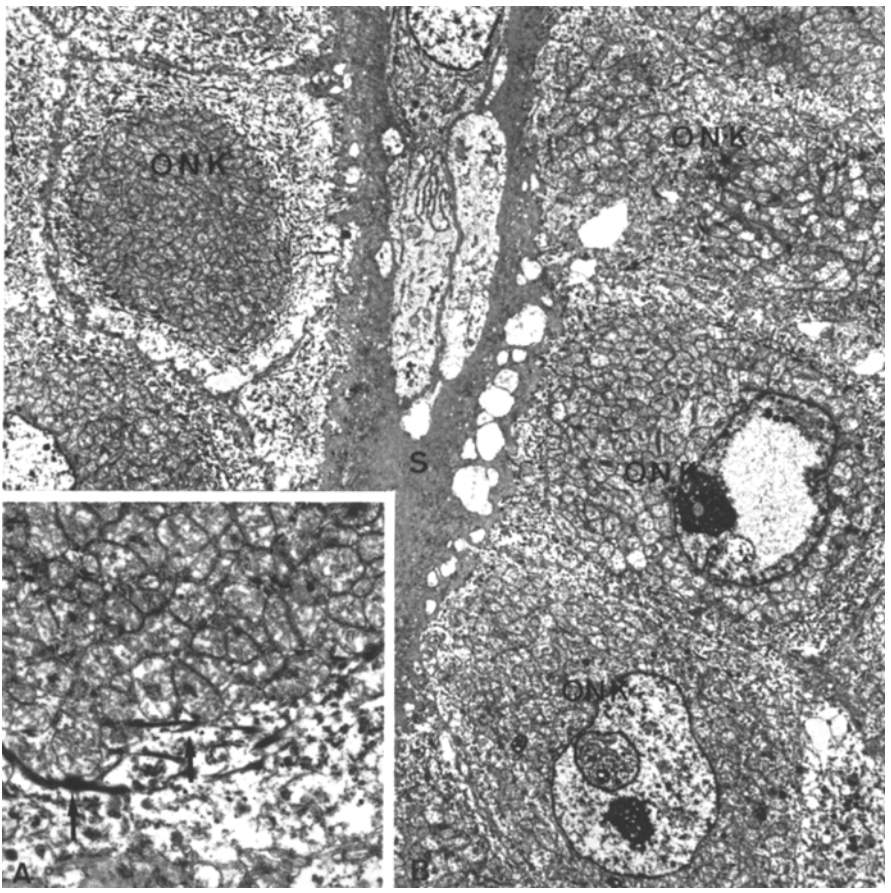

Fig. 4A, B. Closely packed oncocytes (**B**, onk) and the surrounding stroma (*S*). Enclosed (**A**), closely packed polymorphic mitochondria and peripherally situated actin-like filaments (*arrows*). Zinc uranyl acetate and lead citrate (**A**) ×13,500, (**B**) ×4,000

with oncocytes in varying quantities, so that the lumen was either completely or partially obliterated (Fig. 3). The cell borders were clearly visible with the formation of clefts between individual cells (Figs. 2 and 3). The cell nuclei were round and vesicular, with small, mainly peripherally situated nucleoli. No mitoses were observed and there were no signs of malignancy. PAS and PTAH staining showed red and blue diffuse granulation of the cytoplasm respectively (Table 1), and inclusion staining with cresyl violet demonstrated pale pink metachromasia.

Electron-microscopic examination of formalin-fixed and later glutaraldehyde and osmium-fixed, epon embedded, and zinc uranyl acetate and lead citrate stained specimens showed polygonal oncocytes (Fig. 4B) surrounded by a smooth plasma membrane with many desmosomes (Fig. 5B). The peripherally situated oncocytes were surrounded by a basal membrane with few folds. The cytoplasm was filled with innumerable closely packed, enlarged and polymorphic mitochondria (Fig. 5A). These had closely packed and at times, club-shaped cristae. Several of the mitochondria had fibrillar or granular electron dense matrix (Fig. 5A, B). Numerous actin-like filaments could be observed, displaced peripherally in the cytoplasm and often lying parallel to the plasma membrane (Fig. 4A). Nearly all the cells contained electron dense lyzosomes, although these were not numerous in number. The nuclei were generally round to ovoid and contained dispersed chromatin condensations as well as a few nucleoli of normal structure, often situated in the periphery of the nucleus

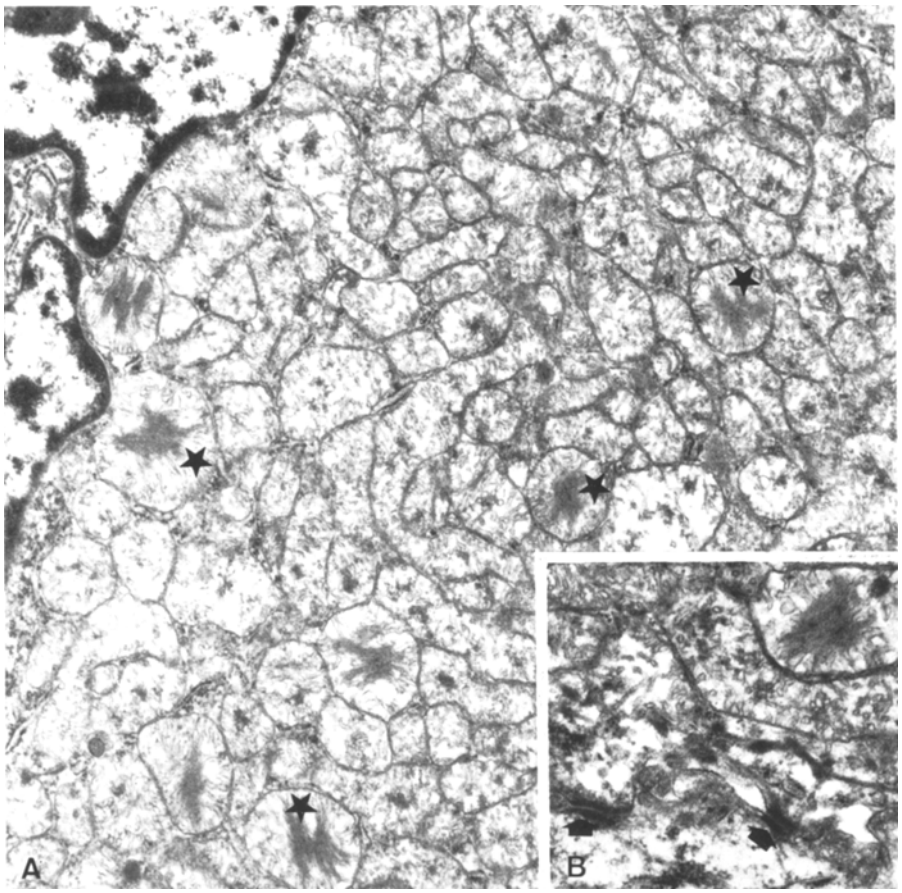

Fig. 5A, B. Closely lying, enlarged and polymorphic mitochondria (**A**). Several have electron dense fibrillar matrix (*stars*). **B** desmosomes along the plasma membrane (*arrows*). Zink uranyl acetate and lead citrate (**A**) ×10,000, (**B**) ×13,500

(Fig. 4B). Only a few of the nuclei showed irregular folds (Fig. 5A). The luminal cubical epithelial cells were found to have only sparse and small mitochondria on electron microscopy, and differed from the oncocytes in having well-represented cytoplasmic organelles and small plump microvilli on the surface. The nuclei were round and often without nucleoli. The connective tissue stroma displayed elongated fibroblastlike cells (Fig. 4B). The microscopic diagnosis was oncocytic breast papilloma.

Discussion

Carcinomas which consist wholely or partially of apocrine epithelium, are found to occur in up to 8% of malignant epithelial tumours of the breast (Mossler et al. 1981), while oncocytes have only been described in benign breast lesions (Hamperl 1972). In such benign conditions the differential diagnosis between apocrine epithelial cells, which occur frequently (Azzopardi 1979) and oncocytes, which are rare (Archer and Omar 1969; Schwartz and Feldman 1969; Zippel

1942), can be difficult, as both types of cell have plentiful eosinophilic cytoplasm. Oncocytes, as in the present case, have diffuse coarse granulation (Hamperl 1950, 1962; Askew et al. 1971), which can clearly be seen following PAS and PTAH staining (Schwartz and Feldman 1969), while the cytoplasm of apocrine cells is more homogeneous, has apical snouts and only apical granules after PAS staining (Azzopardi 1979; Bässler 1978). They show a more uneven and finer granulation with PTAH staining. Inclusion staining by cresyl violet (Hamperl 1950) gives oncocytes a metachromatic red colouration, while apocrine epithelium only displays a weak apical or no red metachromasia. The cells in the tumour described here clearly displayed red metachromasia (Table 1). Finally, oncocytes have, in contrast to apocrine epithelial cells, a tendency to form clefts between individual cells (Hamperl 1962). The difference between the two types of cell is more obvious in the electron microscope, as the characteristic closely packed, enlarged and polymorphic mitochondria and the blurred cytoplasmic organelles in the oncocytes (Askew et al. 1971; Balogh and Sandford 1965; Tandler 1966), clearly seen in this case, are not observed in metaplastic apocrine epithelium. Mossler et al. described apical secretory snouts and innumerable membrane bound osmophilic granules as being chracteristic of apocrine epithelial cells, but also mentioned the occurrence of a type of cell, different from apocrine cells, with eosinophilic granular cytoplasm and an increased number of mitochondria; however the authors did not name the cells, nor mention whether they occured in benign or malignant tumours. No reports have appeared on a transition between the two types of cells. Other electron microscopic differences are shown in Table 1. The oncocytes occurring in salivary glands, despite their appearence in the light microscope, can be either epithelial or myoepithelial in origin (Askew et al. 1971). Apocrine metaplasia in breast tissue is considered to be an epithelial metaplasia (Azzopardi 1979) and these cells always lie directly adjacent to the lumena of the gland, while the peripheral localization of oncocytes in glands with two-layer epithelium and the large number of actin-like filaments suggest a myoepithelial origin. The oncocytes described by Hamperl (Hamperl 1972) may be epithelial in origin, but the possibility that both myothelial and epithelial cells in breast tissue can undergo oncocytic metaplasia, does not necessarily mean that they have a common origin, as many other cells (Hamperl 1970) are subject to similar metaplasia. The histochemical characteristics and age-dependency of oncocytes have been described earlier (Balogh and Sandford 1965; Schwartz and Feldman 1969; Tandler 1966). The occurrence of oncocytes in a tumour can be an expression of metaplasia of the tumour cells or neoplasia of a previously metaplastic cell, in as much as oncocytic metaplasia does not decrease the ability of the cell to divide (Hamperl 1962). In the tumour described here, the presence of both oncocytes and epithelium of normal appearance would suggest oncocytic metaplasia (Hamperl 1962). No histological signs were present indicating malignancy.

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