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Histologic Variants of Lipid-Secreting Carcinoma of the Breast

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Summary. Ten new cases of so-called lipid-secreting carcinomas of the breast are presented. Histopathologic analysis suggests three different microscopical patterns which are all characterized by abundant intracytoplasmic neutral fat deposits. Review of the literature yielded only 15 well-documented cases. Diagnostic problems are emphasized, with special regard to the secretory differentiation of normal and neoplastic mammary cells.

Key words: Breast – Cancer – Secretion – Lipids.

Introduction

The normal breast is unique since mammary epithelial cells are able to synthesize glucids, lipids and protids (Vorherr, 1974). Differentiation towards a secretory pattern is one of the criteria which are used in methods of histologic grading of adenocarcinomas (Hamlin, 1968). Many breast cancers are known to form secretory products like mucosubstances, the best examples being colloid (Cooper, 1974) and adenoid cystic carcinomas (van Bogaert et al., 1975). In other instances mucin secretion is evident from the presence of signet-ring cells (Steinbrecher and Silverberg, 1976), and Fisher et al. (1975) called attention to the high percentage of glycogen producing breast cancers. Other breast cancers, less frequently observed, exhibit neutral lipids in the cytoplasm of tumor cells. A few reports (Aboumrad et al., 1963; Hamperl, 1977; Hood et al., 1973; Ramos and Taylor, 1974) have appeared in the literature dealing with this special type of breast cancer. Our study adds 10 new cases to the 15 published cases, and suggests the existence of three distinct histopathologic patterns.

Material and Methods

All breast cancers on file in our laboratory during the past 3 years were reviewed. From a total 600 cases, ten (an incidence of 1.6%) were selected as fulfilling the criterion of positive staining by the neutral fat stain oil red 0. The staining procedure was performed on frozen sections of wet tissues. Additional stains consisted of P.A.S. and mucicarmine.

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At the time of diagnosis the patients ranged from 33 to 76 years, with a median age of 51.7 years. The tumor involved the left breast in 4 patients, the right in 6. No quadrant predominance was apparent. Grossly, the mean diameter was 2.0 cm, with a range of 1.2 to 3.5 cm. All the tumors were deeply located, without any skin connection or invasion. In 3 out of the 10 cases axillary lymph nodes were involved at the time of primary treatment.

Results

Three distinct basic histopathologic patterns were identified.

1. Histiocytoid Type

The histiocytoid type is illustrated on Figure 1. The epithelial components were comprised of large clear cells with a foamy cytoplasm, positive for neutral lipids (Fig. 2). This pattern was encountered in 5 out of the 10 cases. The general appearance and the cellular morphology was similar to that reported by others (Aboumrad et al., 1963; Hood et al., 1973; Ramos and Taylor, 1974). On H & E stained slides the appearance could be related to the presence of intracytoplasmic glycogen, as emphasized by Fisher (1976); however, the P.A.S. reaction was negative. In some areas of H & E sections the diagnosis of a so-called apocrine or sweat-gland carcinoma was suggested. However, in oncocytic carcinoma (Fig. 3) papillary and glandular patterns are prominent (Hamperl, 1977). In lipid-secreting carcinomas gland-like spaces are not a constant finding, moreover, oncocytic carcinomas are stainable by the P.A.S. method (Hamperl, 1977) while lipidcell carcinomas are not (Aboumrad et al., 1963).

Different architectural patterns may be encountered in the histiocytoid type of lipid-secreting carcinomas. The first pattern is a solid one; it was found in 3 instances. In another case the same foamy or histiocytoid cells appeared lining large dilated ducts (Fig. 4). Sometimes central necrosis occurred, suggesting a comedocarcinoma. However, unlike comedocarcinoma there was no nuclear pleomorphism; the abundant foamy cytoplasm stained heavily with oil red 0. An intermediate architectural pattern between the solid type and the large duct type was seen in the fifth case (Fig. 5). The common finding in these five cases was the appearance of the basic histiocytoid cell component. The intermediate architectural pattern suggests that they are all of the same basic origin.

2. Sebaceous Type

The sebaceous-like form was seen in three instances. These three tumors showed microscopic features similar to that reported in salivary glands under the heading "sebaceous carcinoma" by Evans and Cruickshank (1970). Two main differences were noted, allowing distinction from the histocytoid type: the cells exhibited a prominent nuclear pleomorphism and large, irregular, bubbly vacuoles (Fig. 6).

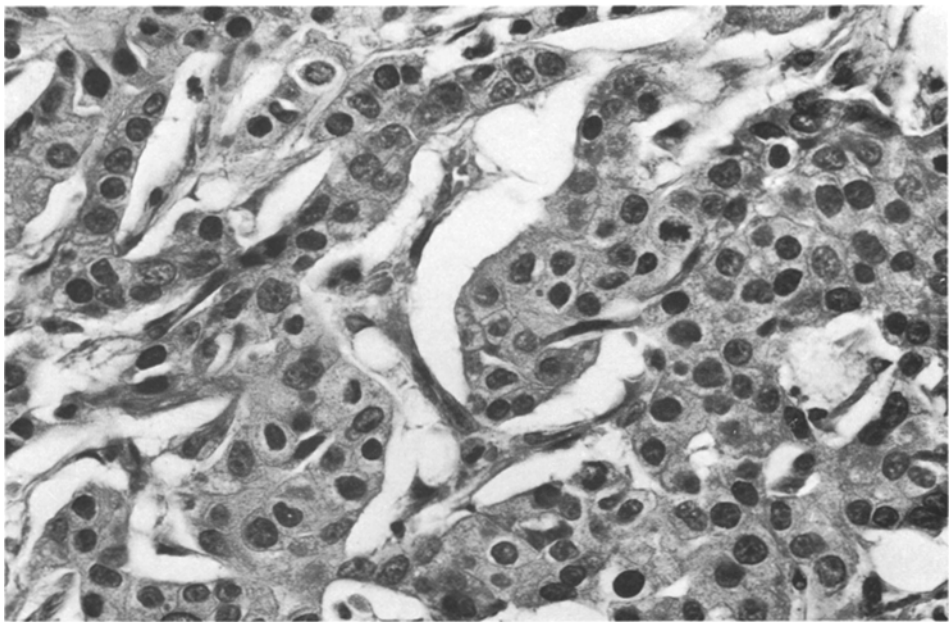

Fig. 1. Histiocytoid carcinoma: solid type (clear areas are retraction artefacts). Cytoplasms appear abundant and finely granular (H&E, ×400)

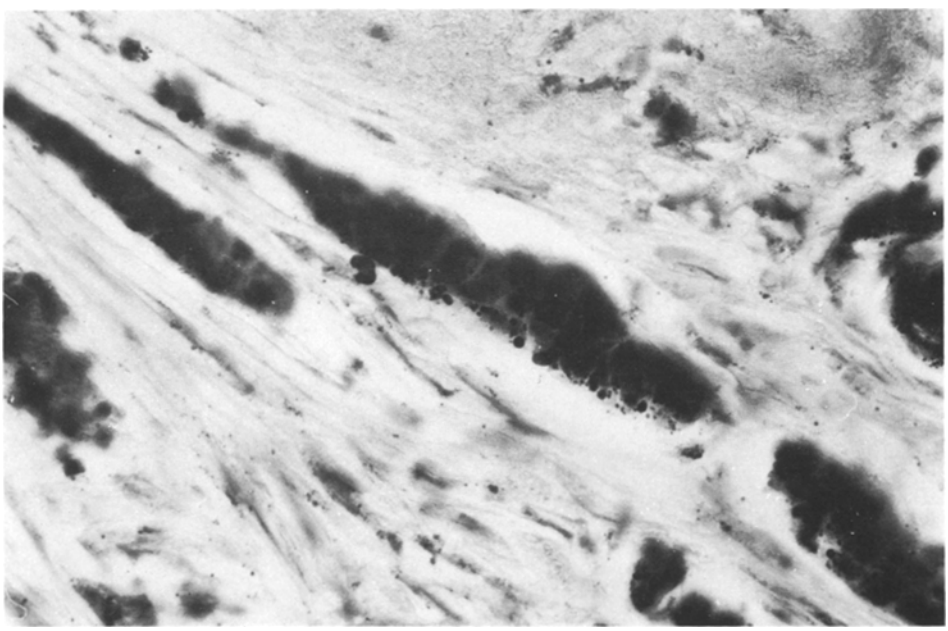

Fig. 2. Same specimen of solid type histiocytoid lipid-secreting carcinoma. Neoplastic cells are almost totally obscured by neutral lipids (oil Red 0, ×400)

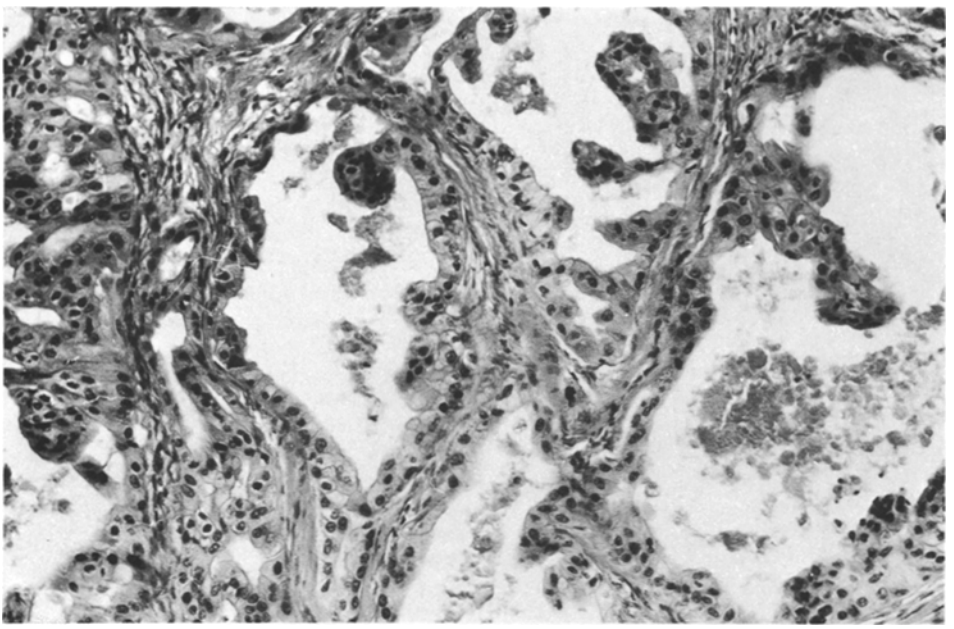

Fig. 3. True oncocytic (so-called apocrine or sweat-gland) carcinoma with an obvious glandular and papillary pattern. (H&E, ×100)

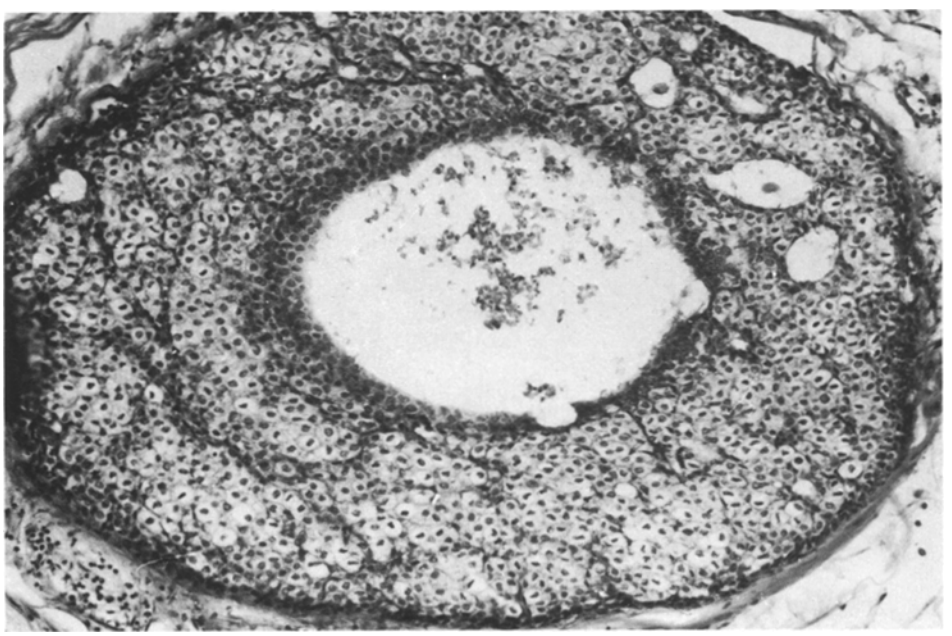

Fig. 4. Histiocytoid lipid-secreting carcinoma showing dilated ducts lined by several layers of foamy cells (H&E, ×200)

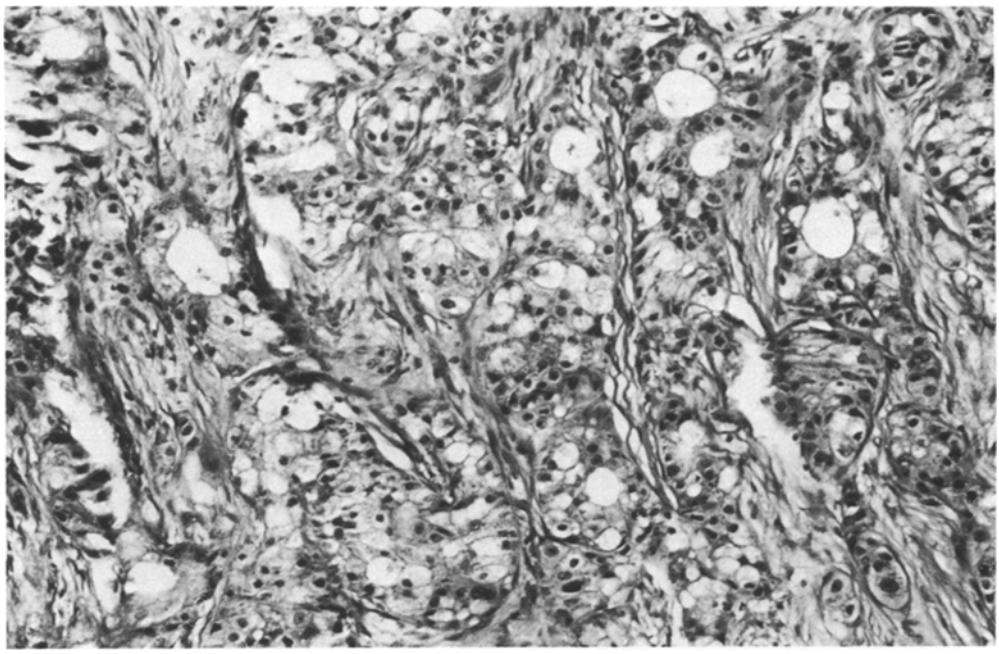

Fig. 5. Histiocytoid carcinoma: intermediate type. Compact areas alternate with neoplastic cell sheets with gland-like spaces. (H&E, ×100)

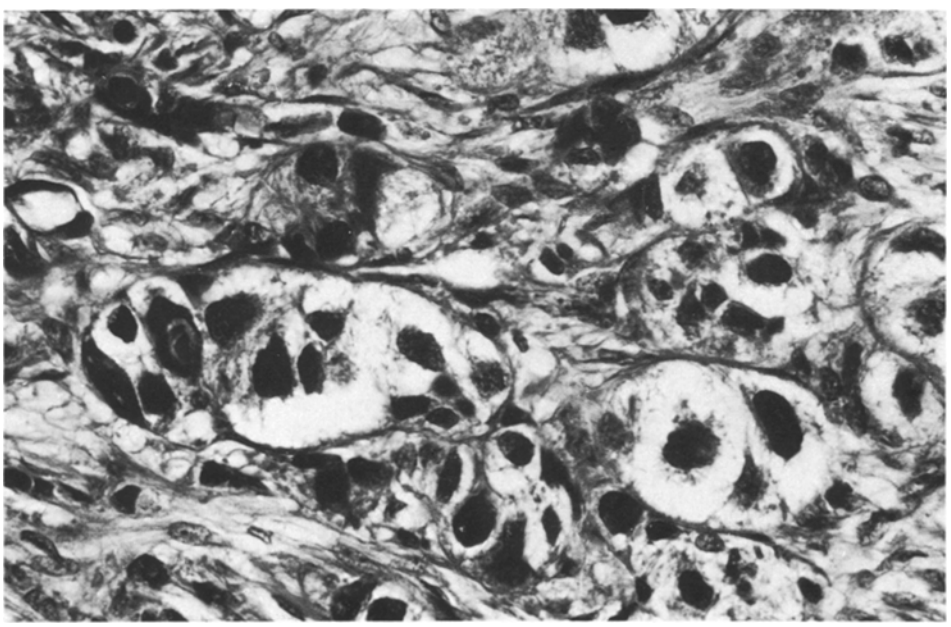

Fig. 6. Sebaceous-like lipid-secreting carcinoma of the breast. Nuclear pleomorphism is prominent; cytoplasms are grossly vacuolated (H&E, ×400)

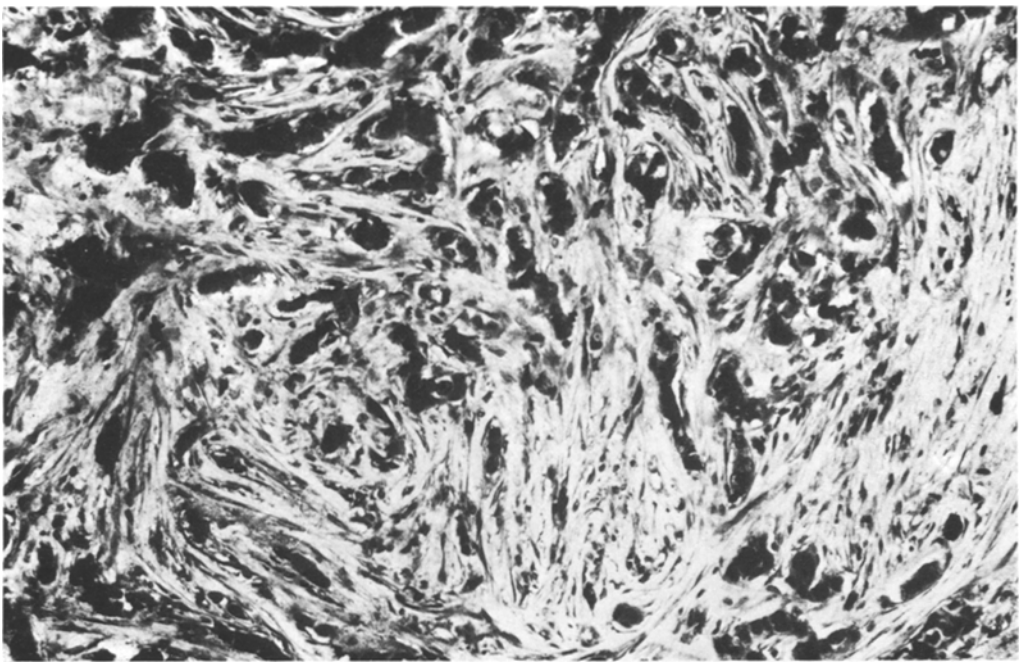

Fig. 7. Same specimen of sebaceous-like carcinoma showing neutral fats superimposed on neoplastic cells sheets (oil red 0 $\times 100$)

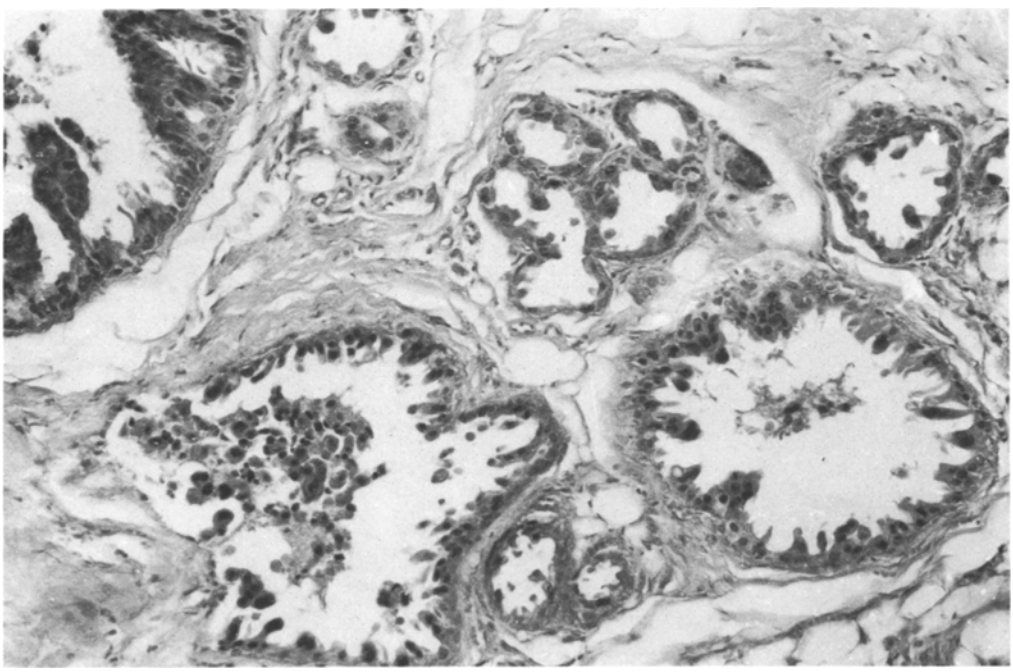

Fig. 8. Apocrine carcinoma of the breast with extrusion of nuclei. Epithelial tufts and desquamated cells are visible in the ducts (H&E, $\times 100$)

The malignant cells were irregularly or compactly arranged in nests, clusters or compact alveoli without lumen formation. They did not react with the P.A.S. and mucicarmine reagents; the lipid reaction was positive (Fig. 7).

3. Carcinoma with Apocrine Extrusion of Nuclei

Two cases fulfilled Hamperl's (1977) criteria for this peculiar type of lipid secreting breast carcinoma. Nipple secretions were cytologically highly suggestive of malignancy; clinical findings showed only an ill-defined lump in the breast. The pathologic specimen elicited dilated ducts lined by apocrine-like cells. Apical cell borders were round in outline; nuclear pleomorphism was evident. Epithelial tufts protruded into the lumens; desquamated cells occured frequently in the ducts (Fig. 8). Cytoplasms and lumens contained P.A.S. stainable mucopolysaccharids and oil red 0 neutral lipids, like in Hamperl's example.

Unlike other reports (Hamperl, 1977; Ramos and Taylor, 1974), all of our cases occured in a pure form and were not associated either with a lobular or a ductal carcinoma.

Discussion

Mammary cancer displaying extensive deposits of lipid are in large part ignored by present classifications. The Breast Cancer Task Force (1973) distinguishes a signet-ring cell (1B13) and a secretory carcinoma (1B14); this last is separated from the lipid-cell carcinoma (1C1). Since breast cancers may exhibit intracellular mucin, glycogen or lipid it is not clear what is meant by secretory carcinoma (1B14). Apparently the authors reserve a separate heading for lipid-cell carcinoma because lipids might be a storage or secretory product.

Hamperl (1975) reviewed extensively the mode of secretion of the human breast. Former studies generally believed the breast to have a mode of release of its products, that was intermediate between merocrine (without appreciable loss of cytoplasm) and holocrine (entire cell loss) secretion, which is the apocrine type. In fact, the amount of lost cytoplasm is far less than envisioned by the classical concept of apocrinia (Bloom and Fawcett, 1975). Salazar et al. (1975) called it micro-apocrine excretion; however, Pier et al. (1970) reported also merocrine, and Hamperl (1975) holocrine excretion in the breast.

Hamperl has drawn the attention to the so-called apocrine or sweat-gland carcinoma of the breast, which has only morphological similarities with apocrine cells insufficient to justify this current appellation. He recognized two histologically well-characterized types: the oncocytic and the secreting (or carcinoma with apocrine extrusion of nuclei and fat accumulation) (Hamperl, 1977). In our cases of lipid-secreting carcinomas with an histiocytoid pattern some similarity with oncocytes was observed on H & E stained sections. The similarity between so-called apocrine like and lipid-cell carcinomas has already been emphasized by Fisher (1976); he found intramitochondrial material similar to that in lipid-rich carcinomas in an example of no otherwise specified ductal

carcinoma whose cells histologically were apocrine-like. However, oncocytic carcinomas are stainable by the P.A.S. method (Hamperl, 1977) while lipid-cell carcinomas are not (Aboumrad et al., 1963).

Hood et al. (1973) reported 13 cases of metastatic mammary carcinomas in the eyelid, with histiocytoid appearance. Some of their figures are very similar to our histiocytoid type of lipid-secreting carcinoma of the breast. However, the authors stated that the cells contained P.A.S., Alcian Blue and mucicarmine positive material. Moreover, oil red 0 stain failed to reveal any lipid material; notwithstanding this fact Hood et al. (1973) emphasized some similarity of their cases to the lipid-secreting type of mammary cancer.

In the published cases of lipid-cell carcinomas lipid stains which are indicators of triglycerides were used (Dustin, 1966). Lipid-storage, or steatosis, consists of an accumulation of triglycerids in the cytoplasm of cells which normally contain only traces, at the optic microscopic level. Fat synthesis in the lactating mammary gland occurs partly from triglycerides supplemented by the plasma (Vorherr, 1974). Ramos and Taylor (1974) have shown by electron microscopy of lipid-cell carcinoma of the breast, that these lipids are not a degenerative component, but a true secretory product of the neoplastic cells. Accordingly, it appears justified to call them lipid-secreting (Aboumrad et al., 1963) instead of lipid-cell or lipid-rich (Ramos and Taylor, 1973).

There are thus sufficient data to accept the existence of a particular form of secretory mammary cancer, i.e. the lipid-secreting variant. The 15 well-documented cases in the literature, which all stained with the neutral lipid stain oil red 0, exhibited an histiocytoid pattern, except for the case described by Hamperl (1977). We are not aware of other reports of the sebaceous type. Systematic staining of breast cancers by oil red 0 would be necessary for a more systematic search for lipid-secreting carcinomas.

Certain concepts, which seemed definitely established in the histopathologic recognition of human breast cancers, have recently been questioned. For instance, the classic "indian file" pattern (McDivitt et al., 1968) is actually considered as only one of the variants of infiltrating lobular carcinoma (Fechner, 1975). Other studies (Gad and Azzopardi, 1975; Steinbrecher and Silverberg, 1976) have illustrated a signet-ring or mucinous variant of infiltrating lobular carcinoma. Secretory changes have been considered as a useful prognostic factor in breast cancer (Fisher et al., 1975; Hamlin, 1968), but this widely accepted concept seems to need further consideration. Fisher et al (1975) reported that the presence of P.A.S. positive mucin was observed exclusively in tumors with high histologic malignancy. Lobular carcinoma, which is known to bear a poor prognosis (Fechner, 1975), may be encountered as a mucus-secreting tumor. Ramos and Taylor (1974) reported a 50 per cent mortality rate during the 2 years following the diagnosis of lipid-rich carcinoma. These data suggest a bad prognosis for certain secretory carcinomas.

In conclusion, mammary cells are obviously capable of secreting many substances and neutral lipids may be secreted by normal and neoplastic mammary cells. The oncocytic carcinoma shows some similarities with lipid-secreting cancers; differential diagnosis can only be made by proper stains, since some cytologic and even architectural patterns may be common to both types. Three

distinct histological patterns occur in lipid-secreting carcinomas, which have as their sole common property a positive reaction to neutral fat stains. Ten new cases are added to the 15 known cases in the literature. Their particular properties support their inclusion in breast cancer classifications.

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