

Case Reports

Primary Signet Ring Cell Carcinoma of the Breast

Jalil Ali Al-Hariri

The University Institute of Pathology, Odense Hospital, DK-5000 Odense C, Denmark

Summary. Light microscopic (LM), histochemical, and electron microscopic (EM) investigations of a case of signet ring cell carcinoma (SRC) of the breast indicate that SRC is a variant of mucin-producing carcinoma and that in this particular case, it is of ductal origin.

Key words: Breast carcinoma – Colloid carcinoma of the breast – Signet ring carcinoma of the breast.

Introduction

Primary breast carcinoma with intracellular accumulation of mucin and the formation of typical signet ring cells is rare. Since there is some disagreement as to whether signet ring cell carcinoma (SRC) is of ductal (Harris et al. 1978a; Harris et al. 1978; Saphir 1941) or of lobular (Steinbrecher and Silverberg 1976; Gad and Azzopardi 1975; Martinez and Azzopardi 1979) origin it seemed of interest to report the present case in which light microscopy (LM), histochemistry, and electron microscopy (EM) indicated a ductal origin.

Case Report

A woman aged 56 with a history of conization in 1973 and later hysterectomy for severe cervical epithelial dysplasia. Present disease: In October 1978 surgery for a tumour of the left breast detected by the patient herself about 2 months prior to the operation. The tumour, freely movable and measuring about 2×2 cm, was in the upper lateral quadrant. The nipple was flattened, but without ulceration. The resected tumour was not sharply demarcated, $2 \times 2 \times 2$ cm, firm, and greyish white on cut surface. Total mastectomy with removal of the axillary tail and axillary fat was performed after frozen section had revealed carcinoma. The paraffin sections showed signet ring cell carcinoma as described below. The operation specimen was a $13 \times 12 \times 2$ cm breast, with a small remnant of intraductal carcinoma in the wall of the biopsy cavity. No changes in the nipple. The axillary fat included 2 lymph nodes, both with metastases. No tumour infiltration or lymph nodes in the axillary tail. Postoperative radiotherapy was given. In January 1979 an operation for a right-sided

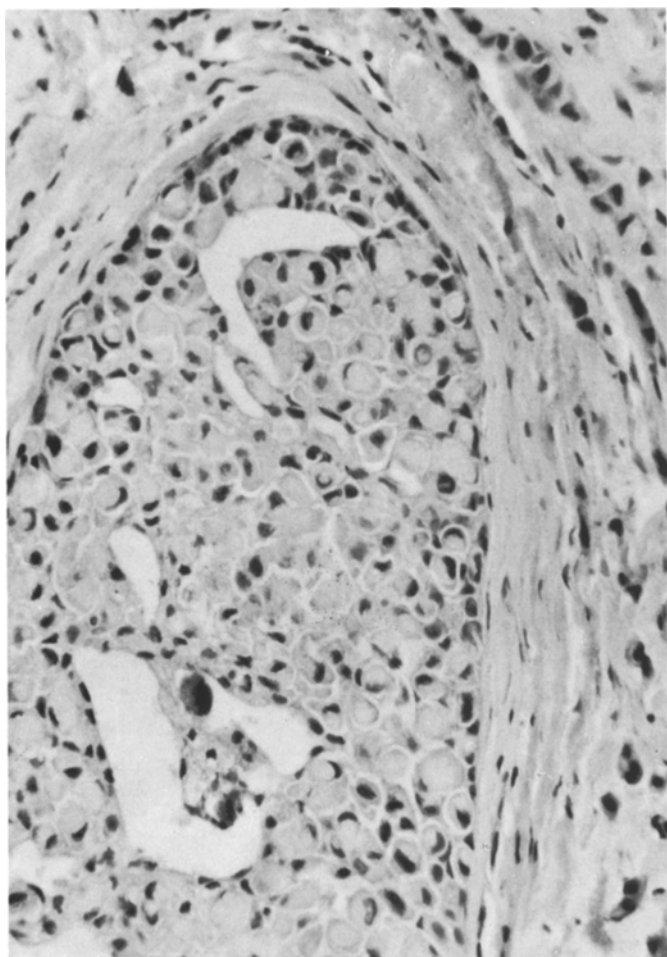


Fig. 1. Numerous signet ring cells in the intraductal component. HE $\times 200$

breast tumour was performed, this proved to be an infiltrating duct carcinoma without signet ring cells or foci of in situ lobular carcinoma. No lymph node metastases. Since then, no local recurrence or further metastases has occurred.

Light Microscopic and Histochemical Findings

Formalin-fixed, paraffin-embedded sections from the left-sided breast tumour were stained with HE, PAS \pm diastase, mucicarmine, alcian blue (AB)/PAS-diastase, and aldehyde fuchsin (AF)/AB. These stainings showed ductal mammary carcinoma with intraductal as well as infiltrating components. About 50% of the cells in the intraductal component were irregularly distributed signet ring cells (Fig. 1) which had abundant intracellular accumulation of mucin and semilunar, peripheral nuclei. The infiltrating component contained some areas with small cells having no mucin content, often with single (Indian) filing, and other areas with many signet ring cells (Figs. 2 and 3). Mucin staining showed the signet ring cells to contain a homogeneous substance which was PAS-diastase positive, AB/PAS-diastase positive, and AF/AB positive, indicating a content

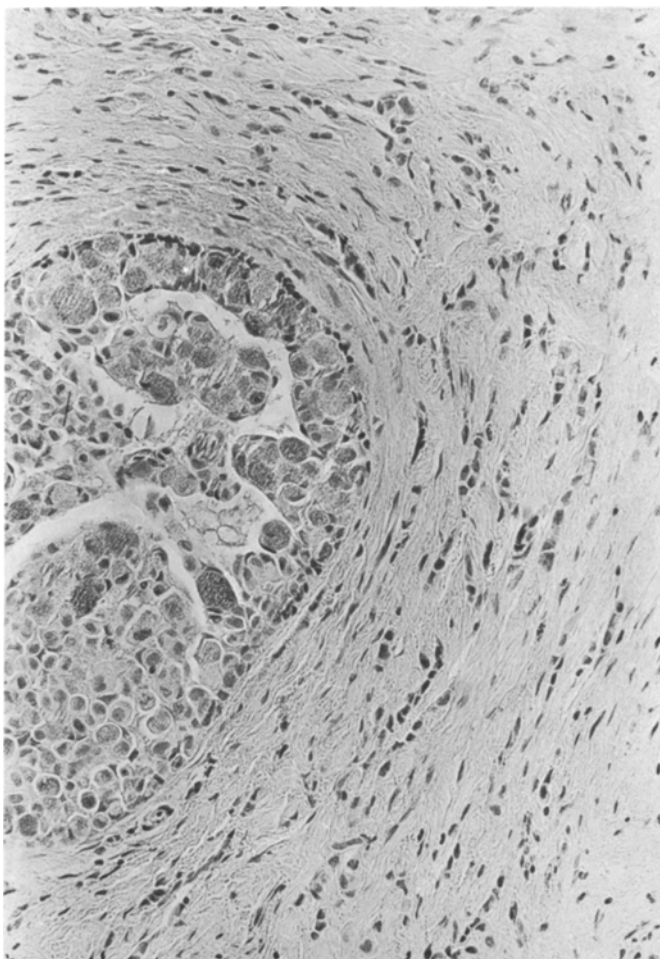


Fig. 2. Intraductal carcinoma with numerous signet ring cells and infiltrating carcinoma with single filing and a few signet ring cells. Mucicarmin $\times 80$

of sulphomucin. There was no extracellular mucin, in situ lobular carcinoma, or concentric rings of tumour cells around inactive lactiferous ducts (bull's eyes), but a few areas showed lobular involvement of ductal carcinoma with signet ring cells (Fig. 4). The two axillary lymph nodes exhibited focal tumour infiltrates, with and without signet ring cells, not typical of infiltrating lobular carcinoma. These signet ring cells had the same mucin content as those in the primary tumour.

Electron microscopy showed signet ring cells with ample content of mucin granules in the cytoplasm. These granules had a varying electron density and were bounded by a thin smooth membrane. No intracytoplasmic lumina were seen (Fig. 5).

Discussion

Harris et al. (1978) have divided mucin-producing breast carcinomas into 4 groups:

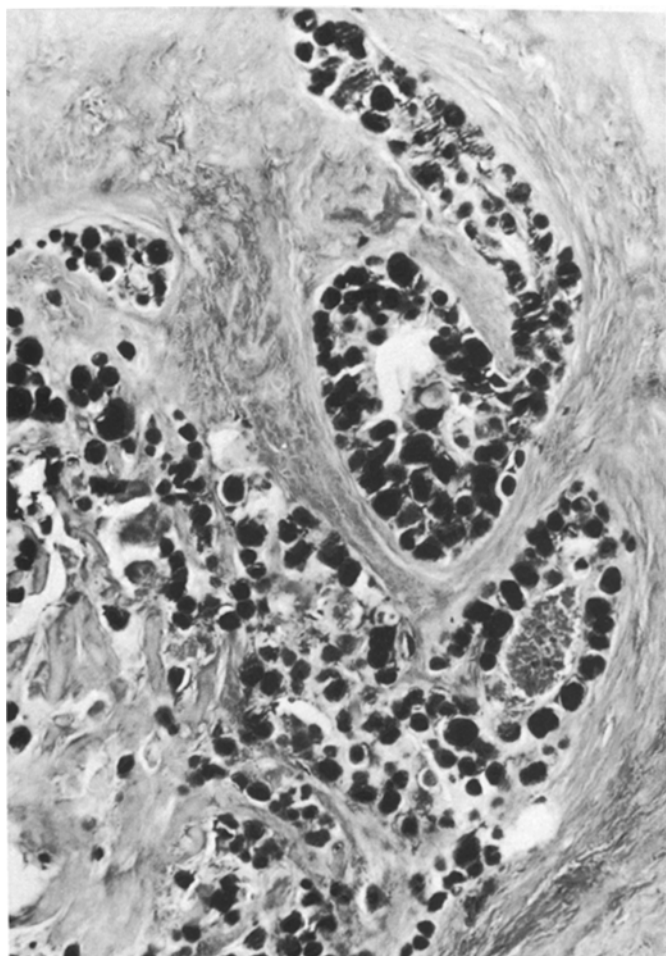


Fig. 3. Infiltrating ductal carcinoma with numerous signet ring cells. Aldehyde fuchsin/alcian blue $\times 200$

1. Typical mucoid carcinoma with abundant extracellular mucin.
2. Signet ring cell carcinoma.
3. Mucin-producing papillary carcinoma.
4. Infiltrating lobular carcinoma.

This classification, based upon EM, showed that the mucin-containing cells in infiltrating lobular carcinoma contain intracytoplasmic lumina with mucin vacuoles. The other three types contain abundantly granulated or reticular substance of variable electron density spread diffusely in the cytoplasm. Saphir (1941) has reported 3 cases and Harris et al. (1978) 2 cases of ductal carcinoma with an ample content of typical signet ring cells. In these 5 cases there was no in situ lobular carcinoma. Histochemical investigation of Harris et al.

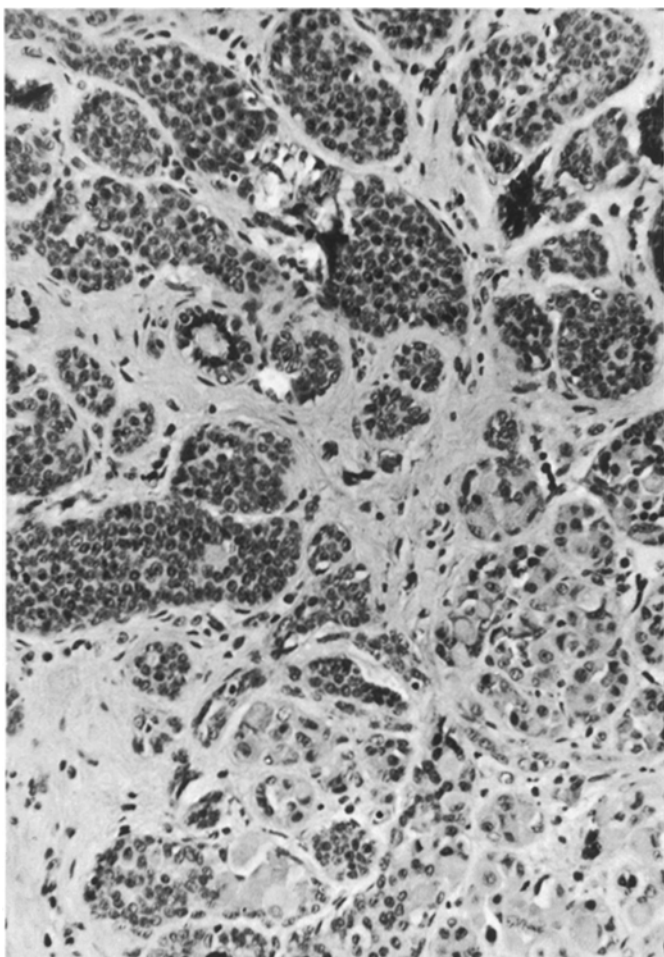


Fig. 4. Lobular spread of ductal carcinoma with signet ring cells. HE $\times 80$

cases showed the signet ring cells to contain sulphomucin. Our case exhibited the same light microscopic, histochemical, and electron microscopic findings as Harris et al. (1978).

Steinbrecher and Silverberg (1974) interpret SRC as a mucinous variant of infiltrating lobular carcinoma, finding in 3 out of 5 cases of breast carcinoma with varying quantities of mucin-containing "signet ring cells", foci of in situ lobular carcinoma, but no areas with intraductal carcinoma. In further support of a lobular origin they report also single (Indian) filing, that 2 cases were bilateral, and that the architecture of the lymph node metastases was typical of infiltrating lobular carcinoma.

To this hypothesis it may be objected that the authors found small quantities of extracellular mucin as in ordinary colloid carcinoma, that they demonstrated no signet ring cells in the in situ lobular carcinoma, and that single filing

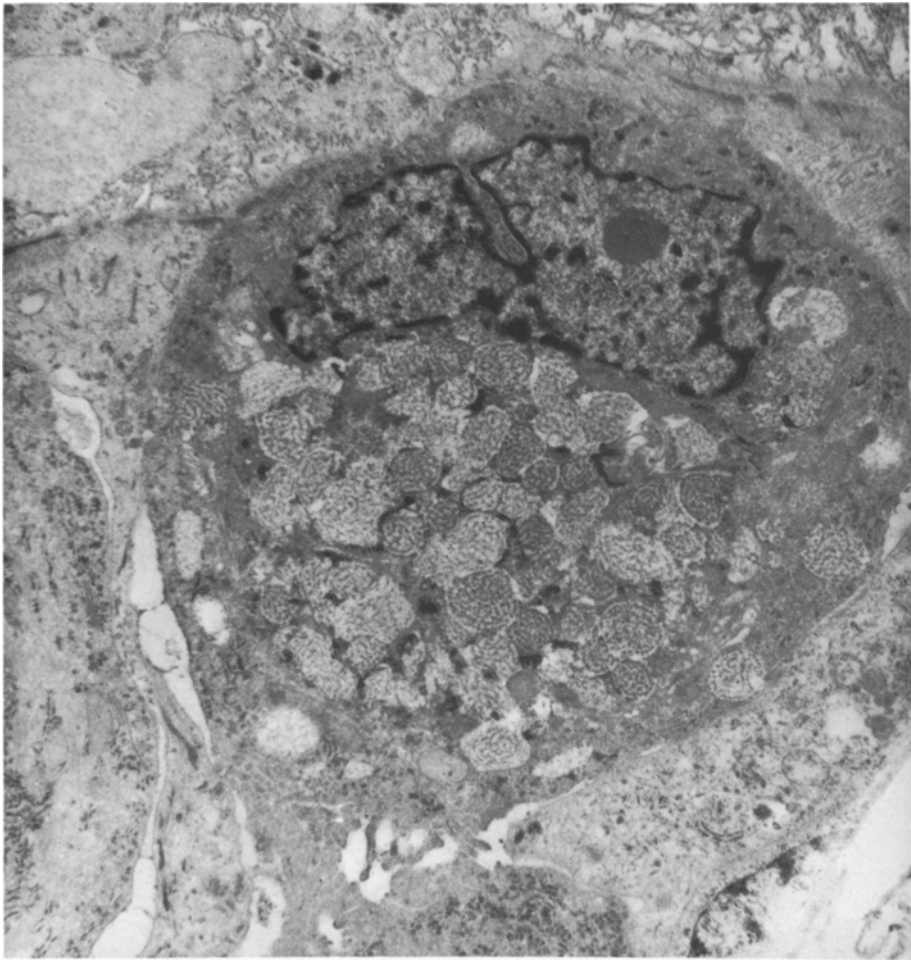


Fig. 5. Signet ring cells in which the cytoplasm is filled with mucin granules. $\times 12,000$

is often encountered in infiltrating ductal carcinoma (Richter et al. 1967). Besides, their EM is stated to be inconclusive, as intracytoplasmic lumina are present in a number of different malignant tumours of the breast and to a lesser extent in benign diseases of the breast and normal breasts (Battifora 1974; Tschubel and Helpap 1976). Further, bilateral cancer does not necessarily indicate a lobular origin, cf. the present case. Lobular carcinoma may also be found in combination with other mammary carcinomas (Fisher et al. 1975; Richter et al. 1967). The mucin-containing cells in Steinbrecher and Silverberg's (1974) cases were not morphologically typical signet ring cells, as also pointed out by Harris et al. (1978) and by Martinez and Azzopardi (1979).

Gad and Azzopardi (1975) assumed that SRC might be an extreme variant of infiltrating lobular carcinoma, because of focal signs of differentiation into signet ring cells, but in their cases the majority of the mucin-containing cells had a "target appearance", without the uniformly stainable cytoplasm seen

in Harris et al.'s (1978) and in our case. Martinez and Azzopardi (1979) found signet ring cells in 7 out of 28 infiltrating lobular carcinomas, generally focally, making up "5% or more of the neoplastic cells" against about 50% in our case. It may be added that EM appearances are not mentioned in Gad and Azzopardi's (1975) or in Martinez and Azzopardi's (1979) material.

Intracellular accumulation of mucin without the formation of typical signet ring cells has been described in various breast carcinomas (Breslow and Brancaccio 1976; Fisher et al. 1975; Tellum et al. 1966) and in benign states such as fibroadenomas and fibroadenomatosis (Tschubel and Helpap 1976). In such cases, however, the number of mucin-containing cells is relatively small, while signet ring cells have been the predominant type of cell in the cases of primary SRC of ductal origin reported so far. Secretory juvenile carcinoma (McDivitt and Stewart 1966) contains PAS positive intracellular material (secretion), but without the formation of signet ring cells.

The histogenesis of SRC seems to be complex, as also mentioned by Azzopardi (1979, p 305). Some cases are perhaps variants of infiltrating lobular carcinoma, while others appear to be variants of infiltrating ductal carcinoma. The LM, histochemical, and EM findings in our case indicated that it was of ductal origin.

SRC can and must be distinguished from other types of mucinous mammary carcinomas, as the prognosis of the various types differs (Harris et al. 1978; Saphir 1941).

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