

CASE REPORT

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Acinic cell-like carcinoma of the breast

Received: 5 January 1996 / Accepted: 22 April 1996

Abstract A case of infiltrating carcinoma of the breast with features similar to those seen in acinic cell carcinoma of the parotid gland is described in a 42-year-old woman. The neoplastic cells were immunoreactive with anti-lysozyme- and anti-salivary-type amylase antisera and contained electron-dense cytoplasmic globules similar to those seen in acinic cell carcinoma of salivary glands. One lymph node out of 18 was found to contain a metastatic deposit. The patient is alive and well 1 year after mastectomy. This appears to be the first case of carcinoma with acinic cell-like features reported in the breast.

Key words Acinic cell carcinoma · Breast · Lysozyme · Amylase

Introduction

Acinic cell carcinoma (AC) of salivary glands is a well-known entity, which usually has a low malignant potential [6, 24]. Histologically, ACs display several architectural features, including solid, microcystic, papillary-cystic and follicular patterns [1, 4, 5, 24]. These are sometimes observed in combinations, but the solid type is the most frequent [5].

Primary breast tumours similar, if not identical, to those encountered in salivary glands are occasionally observed. These rare lesions include adenoid-cystic carcinoma [16, 21], mucoepidermoid carcinoma [15, 20], pleomorphic adenoma [17, 25] and adenomyoepithelioma [8, 13]. Nevertheless, to the best of our knowledge, cases with features of AC have never been described.

We now describe a primary carcinoma of the breast with morphological, ultrastructural and immunocytochemical features of a solid AC similar to those seen in salivary glands.

Clinical history

A 42-year-old woman was admitted to the Ljubljana Cancer Hospital because of a palpable lump in the upper outer quadrant of the right breast. The lesion had been present for a few months and had increased rapidly in size over the preceding month. The nipple and the skin overlying the lump were normal. Mammographically, the lesion showed well-defined margins and contained scattered granular calcifications. An enlarged axillary lymph node was also found. A diagnosis of invasive carcinoma was made, and the patient underwent radical mastectomy with lymph node dissection. Of 18 axillary lymph-nodes dissected, 1 contained metastatic deposits. The patient is alive and well 1 year after surgery, and no metastases are present.

Materials and methods

Tissue was fixed in 10% buffered formalin and processed normally. Standard haematoxylin-eosin (HE) and PAS staining with and without diastase pre-digestion was performed. Immunocytochemistry (ICC) was carried out using the ABC/peroxidase method [11]. The antisera used and their sources are reported in Table 1.

Electron microscopy (EM) was carried out on tissue fixed in 10% buffered neutral formalin. Tissue was washed in phosphate buffer at pH 7.2, post-fixed in buffered osmium tetroxide and embedded in Epon LX-112. Thin sections were stained with uranyl-acetate and lead citrate and examined with an Opton 9 electron microscope.

To investigate the presence of lysozyme and salivary-type amylase in breast cancer cells, a series of 30 consecutive cases of infiltrating carcinoma of the breast was retrieved from the files of the Institute of Pathology of the University of Bologna, at Bellaria Hospital and studied with ICC.

Pathological findings

Macroscopically, the lesion was a grey-pinkish, sharply circumscribed nodule, which measured 3 cm in its greatest axis. It showed a fleshy cut surface.

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Table 1 Antisera used for immunocytochemistry (*M* monoclonal, *P* polyclonal)

Antisera	Source	Dilution	Clone
Anti-low-molecular-weight cytokeratin	Dako, Calif., USA (M)	1:100	MNF116
Anti-epithelial membrane antigen	Dako, (M)	1:200	E29
Anti-lysozyme	Dako (P)	1:1000	–
Anti-salivary-type amylase	Biogenex, Calif., USA (P)	1:1000	–
Anti-pancreatic-type amylase	Biogenex (M)	1:1000	6105
Anti-oestrogen receptor	Dako (M)	1:100	1D5
Anti-progesterone receptor	YLEM, Italy (M)	1:50	MGR202
Anti-GCDFP-15	Signet, Mass., USA (M)	1:500	D6
Anti-chromogranin	Ortho, Italy (M)	1:200	PHE5
Anti-synaptophysin	Biogenex	1:200	SY38
Anti-S 100 protein	Dako (P)	1:1500	–
Anti-vimentin	Dako (M)	1:200	V9
Anti-alpha smooth muscle actin	Dako (M)	1:100	1A4
Anti-PG-M1 (CD68)	Dako (M)	1:100	PG-M1

Histology

The tumour was mostly circumscribed by a thick fibrous pseudocapsule, and where this was absent the margins were infiltrative. The lesion was composed of nests of neoplastic cells delimited by a thin network of connective tissue rich in capillaries (Fig. 1). Some nests showed central necrosis reminiscent of a comedo necrotic pattern (Fig. 2). Occasionally, neoplastic glandular structures with a lumen filled with eosinophilic material were also seen.

Cytologically, the tumour was made up predominantly of a monotonous proliferation of large polygonal cells showing distinct cytoplasmic borders and finely granular cytoplasm. Nuclei were round to ovoid with coarse and dispersed chromatin and with one or two nucleoli (Fig. 3). Occasional neoplastic cells presented abundant cytoplasm containing large vacuoles (Fig. 4). Some neoplastic cells contained eosinophilic globules within the cytoplasm. These varied in number from one to several in different cells. Neither perineural infiltration nor permeation of vessels was found. Irregular mitoses were numerous, averaging 13XHPF ($\times 400$). Scattered intratumour calcifications were also found throughout the lesion.

The fine cytoplasmic granularity seen in most of the cells stained with PAS before diastase digestion. This stain failed after diastase digestion. These same cells were negative with the Grimelius method. In contrast, the globules were PAS-diastase resistant. The lymph node metastasis showed features identical to those seen in the primary tumour.

Immunocytochemistry

Most of the neoplastic elements reacted with low-molecular-weight cytokeratin, anti-epithelial membrane antigen (EMA), and anti-lysozyme and anti-salivary-type amylase antisera (Figs. 5, 6). The neoplastic population was negative with the other antisera used, including anti-pancreatic-type amylase (Table 1). In the 30 consecutive cases of infiltrating carcinoma of the breast tested, anti-

lysozyme antiserum stained occasional cells in 4 cases, while anti-salivary-type amylase decorated rare cells in 1 case.

Electron microscopy

The tumour was composed of acinar and tubular structures bordering the central lumina (Fig. 7A). Cytoplasm contained numerous mitochondria and abundant granular endoplasmic reticulum. In addition, numerous cytoplasmic secretory granules, mostly with an homogeneous electron-dense appearance, were also seen (Fig. 7B). Their size ranged from 0.08 to 0.9 μm . Occasional granules were less electron-dense than those described above. A limiting single membrane was visible only in small and immature granules, which were of medium electron density.

Discussion

The present lesion showed a predominantly solid pattern composed mostly of polygonal neoplastic cells with finely granular cytoplasm. The majority of these same cells reacted with anti-low weight cytokeratin, anti-EMA, anti-lysozyme and anti-salivary-type amylase antisera. Electron-dense cytoplasmic granules resembling those of the zymogen present in salivary gland tumours were also observed on EM [6]. All these features were consistent with those seen in the solid type of AC of parotid gland [1, 5, 24, 26]. In addition, cells showing clear cytoplasm as well as necrosis and focal calcifications are further features observed in salivary gland AC [1]. Immunocytochemistry was confirmatory, as lysozyme and amylase are constituents of salivary gland AC [26].

Although lysozyme is a normal component of human milk [14, 22], this enzyme is virtually absent in invasive carcinomas of the breast. Putative production of lysozyme has been reported in breast carcinomas in a study carried out using polyacrylamide gel electrophoresis on fluid obtained from the nipples of non-lactating women both with and without infiltrating carcinomas [23]. In ad-

Fig. 1 The tumour is made up of nests of neoplastic cells outlined by connective tissue. H&E, $\times 100$

Fig. 2 Central necrosis is occasionally seen in neoplastic nests. H&E, $\times 100$

Fig. 3 The neoplastic nests are composed of cells with distinct boundaries and finely granular cytoplasm. Nuclei are round to ovoid and show one to two nucleoli. Irregular mitoses are seen. H&E, $\times 400$

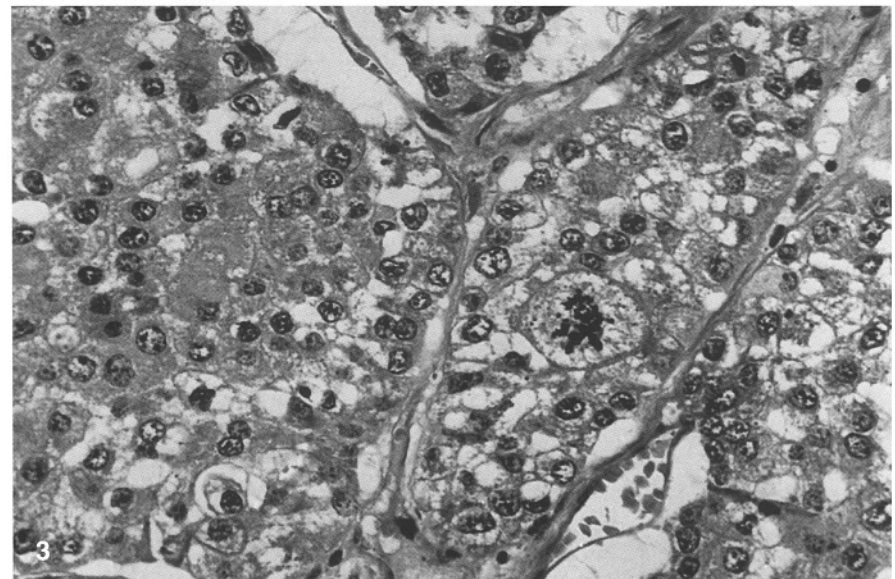
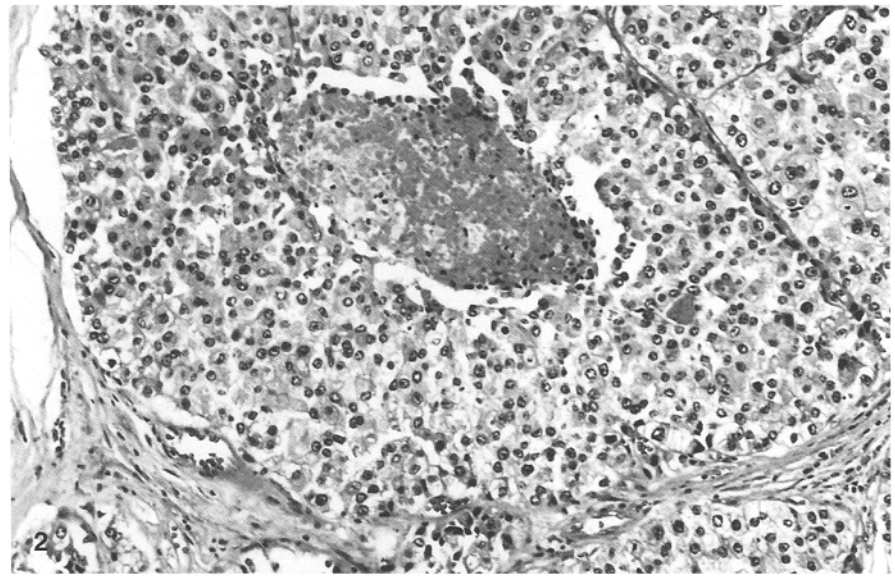
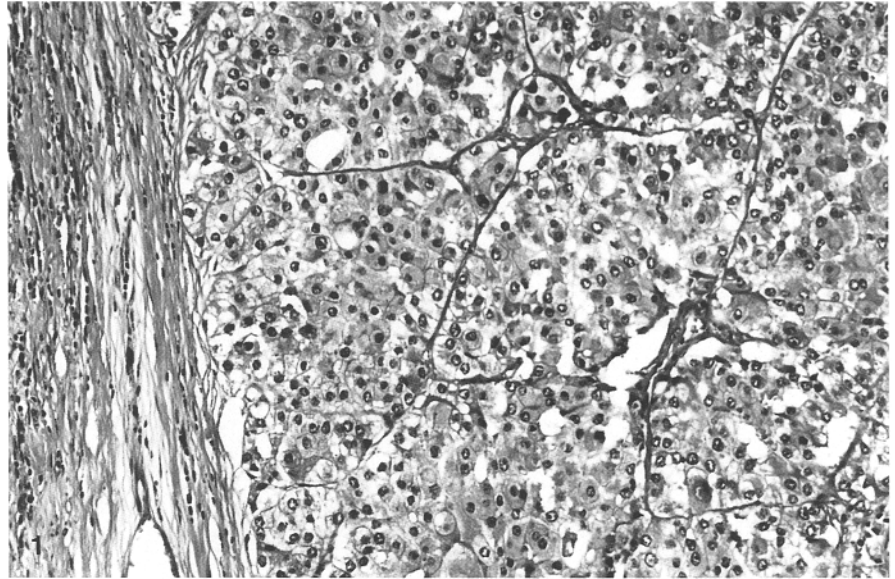
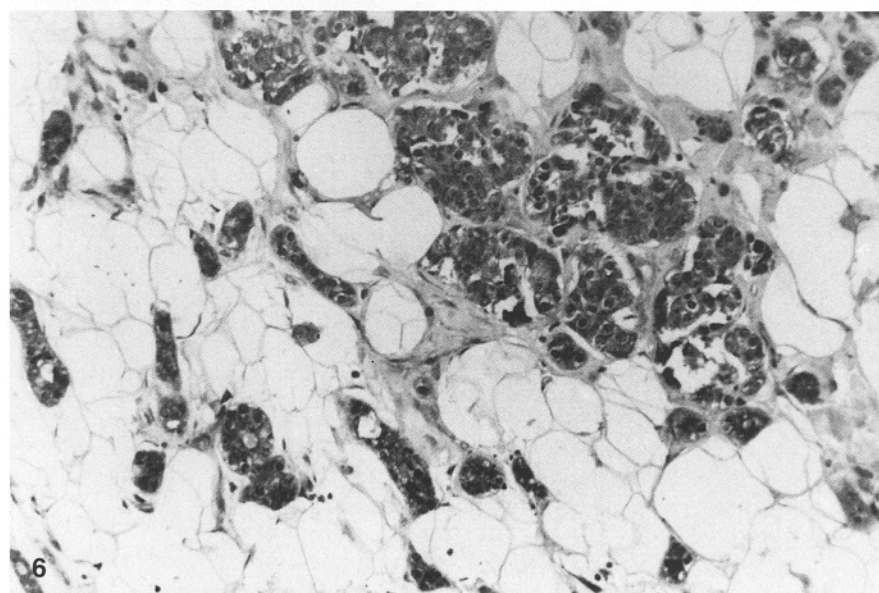
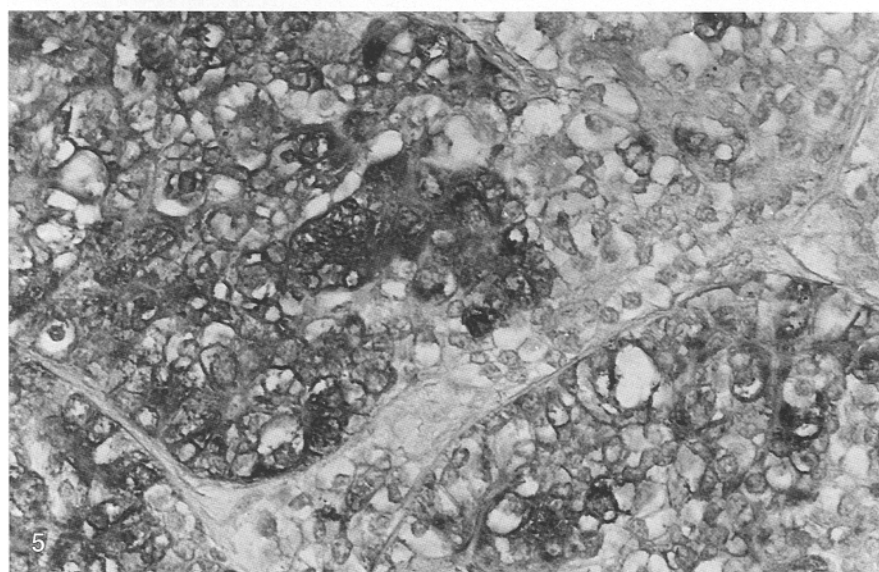
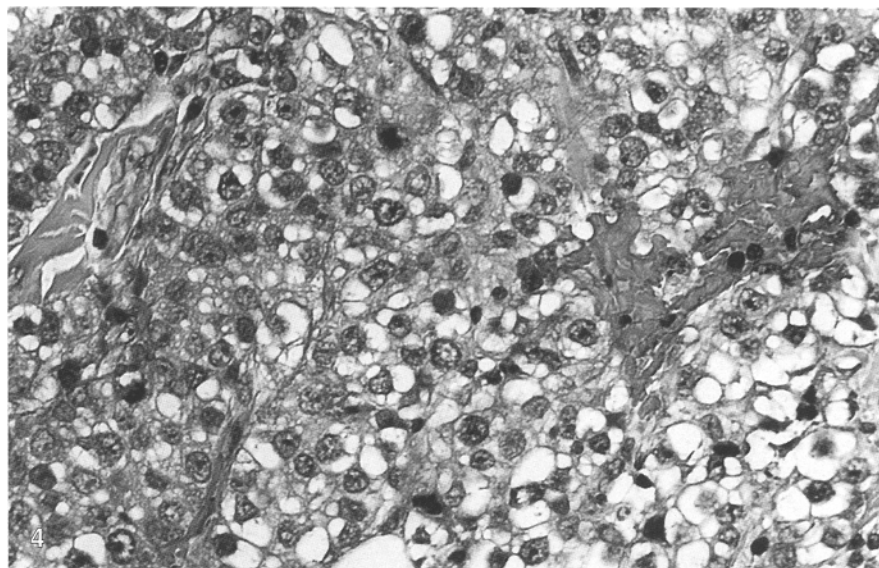


Fig. 4 Some neoplastic cells show clear cytoplasm. H&E, $\times 400$

Fig. 5 Most of the neoplastic elements are reactive with anti-lysozyme antiserum. ABC/peroxidase, $\times 250$

Fig. 6 Neoplastic cells are decorated by anti-salivary-type isoamylase antiserum. ABC/peroxidase, $\times 100$



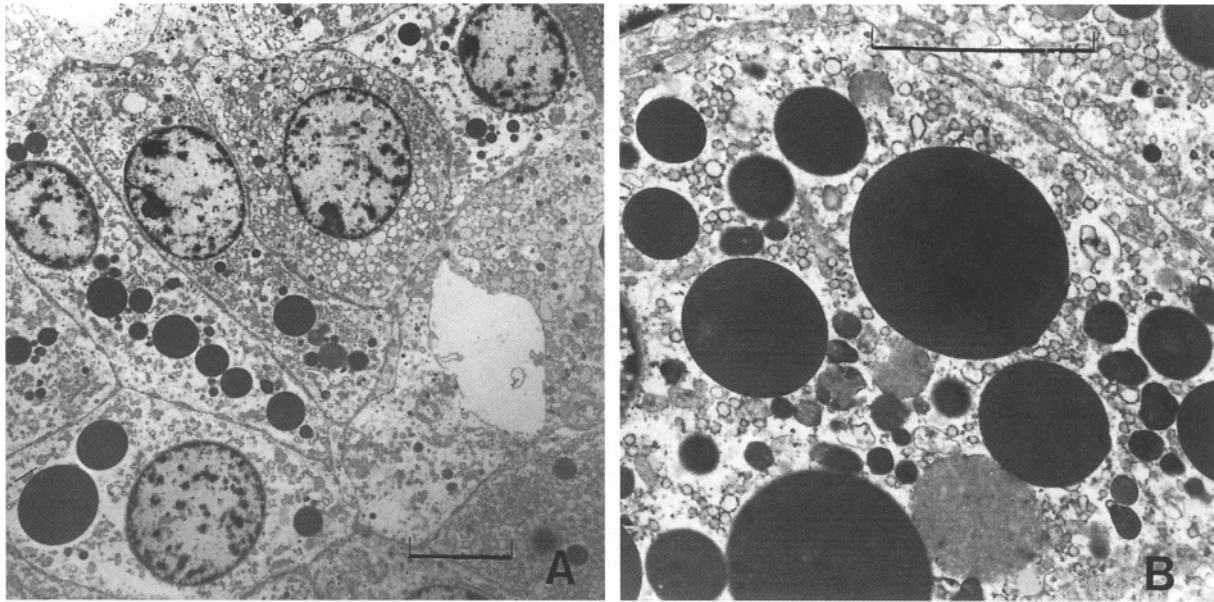


Fig. 7 **A** Acinar structures are easily seen at EM level. **B** Electron-dense granules show different sizes and stages of maturation. Bars 1 µm

dition, a case of invasive ductal carcinoma that immunoreacted with anti-lysozyme antiserum has been mentioned in a series of 14 cases of invasive carcinoma of the breast associated with Paget's disease [3]. Ectopic production of salivary-type amylase is also a very unusual feature in breast carcinomas, this having been reported previously in 1 case of invasive ductal carcinoma [12]. This latter case shares similarities with the lesion shown here: it was described as having a solid pattern and uniform cell morphology, and the electron-dense granules observed on EM were very similar to those seen in the present tumour. In contrast, neoplastic cells were PAS negative and occasional argyrophilic elements were revealed with the Grimelius stain [12]. The presence of pancreatic-type amylase is also a very rare finding in breast tumours; it has been found in only a single case of lipid-rich carcinoma [27]. Pancreatic amylase was absent in the present case.

In the 30 consecutive archival cases, both anti-lysozyme and anti-salivary amylase antisera stained only occasional cells, in 4 cases and 1 case respectively.

The present tumour shows histological similarities to apocrine carcinomas. It can be separated from these as the neoplastic cells lacked immunoreactivity with anti-GCDFP-15, which is a specific marker of apocrine differentiation [7, 18]. Glycogen-rich carcinomas of the breast are composed predominantly of cells showing clear cytoplasm lacking electron-dense granules [2, 9, 10]. The absence of immunoreactivity with anti-chromogranin A and anti-synaptophysin antisera in the present tumour excluded an invasive carcinoma with neuroendocrine differentiation [19]. The lack of immunoreactivity of neoplastic cell with anti-vimentin and anti-pancreatic amylase antisera allowed the exclusion of metastatic car-

cinoma from the kidney and pancreas respectively. The absence of primary tumours of parotid prompted us to exclude a metastatic AC and similarly, both metastatic renal cell carcinoma and pancreatic carcinoma were also definitively excluded, as no renal or pancreatic lesions were found despite extensive clinical investigation.

In conclusion, this case of invasive breast carcinoma with features reminiscent of AC of parotid gland extends the list of salivary gland-like tumours of the breast. Larger series are necessary to elucidate whether its clinical behaviour is similar to the indolent outcome seen in AC of the parotid gland.

Acknowledgements Thanks are due to Mr. A. Busi for photomicrographs. This work was financed by grants from MURST and CNR, PF project ACRO (40% and 60%).

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