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Case Report

Acinic Cell Adenocarcinoma Arising in the Breast of a Young Male: A Clinicopathological, Immunohistochemical and Ultrastructural Study

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A 23-year-old man with acinic cell adenocarcinoma of the breast is reported. He presented with a 4.8×4.2 cm mass in his left breast, and excisional biopsy was performed. Under the light microscope, tumor cells had abundant periodic acid-Schiff-positive secretory granules and eosinophilic cytoplasms. Electron microscopy revealed the granules to have various electron densities, a finding characteristic of acinic cell adenocarcinoma. Immunohistochemically, the tumor cells were stained with salivary-type amylase. Electron microscopic and immunohistochemical investigation greatly facilitated the diagnosis of this acinic cell adenocarcinoma, which was in an unusual location. We believe this is the first case report of acinic cell adenocarcinoma of the mammary gland studied utilizing light microscopic, ultrastructural and immunohistochemical techniques.
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Key words: Acinic cell adenocarcinoma, Breast, Immunohistochemistry, Ultrastructure, Salivary-type amylase

Acinic cell adenocarcinoma, previously called acinic cell tumor in the first World Health Organization classification (1972) is usually observed in salivary glands or the pancreas. A primary acinic cell adenocarcinoma arising in the mammary gland, as in the present case, is extremely rare. Such a case has not previously, to our knowledge, been reported in the literature. We present herein a case of acinic cell adenocarcinoma arising in the left mammary gland, of a young male, which had the characteristics of a salivary type tumor. Immunohistochemical and ultrastructural methods were employed to make the diagnosis.

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Abbreviations:
GCDFP-15, Gross cystic disease fluid protein-15; EMA, Epithelial membrane antigen

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Case Report

Clinical History

A 23-year-old Japanese man was referred to Tokyo Women's Medical College Daini Hospital in September, 1994, with a left breast lump. He had been aware of the presence of the breast lump for two years. Tumor growth had been slow, but a recent increase in size and occasional pain in the left breast had been noticed.

Clinical examination revealed the tumor to be 4.8 by 4.2 cm in diameter, located in the lateral area of the left breast, and to have a clear margin, smooth surface and elastic softness. Depression of the overlying nipple was apparent. Mammary ultrasonography revealed a clear marginal cystic mass composed of hypoechoic intracystic fluid and a hyperechoic intracystic tumor. An excisional biopsy of the mass was performed, and the tumor was initially diagnosed as intracystic apocrine carcinoma. After review of hematoxylin-eosin (HE) slide and immunohistochemical and ultrastructural study, the tumor was diagnosed as acinic cell adenocarcinoma of the breast and left total mastectomy was recommended to remove any

residual tumor tissue and to dissect axillary lymph nodes. Neither residual tumor tissue in the mastectomy specimen nor lymph node metastasis was found. The whole body CT and MRI revealed no lesions in other organs. Following the surgical procedures, there has been no evidence of metastasis or local recurrence during two years and ten months.

Pathological Findings

Gross Findings: The tumor was 4.8 by 4.2 cm in diameter. The cystic mass had a smooth surface, and was well-circumscribed, encapsulated and composed of serous bloody fluid and intracystic tumor elements. The wall of the cyst was 3 to 5 mm thick. Partitions and crumbly atheromatous intracystic tumor element were observed within the cystic cavity (Fig 1).

Light Microscopic Findings: The surgical specimens were fixed in buffered 10% formalin dehydrated, and embedded in paraffin. The sections were stained with HE and periodic acid-Schiff (PAS) with and without diastase digestion.

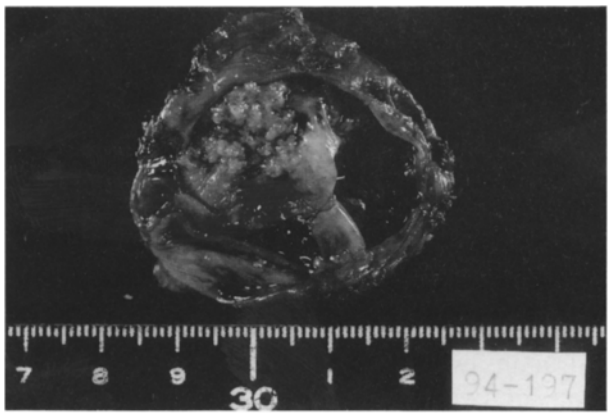

Fig 1. Cut surface of the left breast tumor. An atheromatous mass is observed in the cystic cavity.

On low power magnification, the tumor was localized within the cystically-dilated mammary duct, and it was characterized by a solid growth pattern. A few microcystic, acinar structures were recognized, in the solid area, some were filled with amorphous, eosinophilic materials and mitoses were occasionally seen (Fig 2, left). On higher magnification, the cells were large, round to polygonal in shape, and had abundant PAS-positive granular cytoplasm. A few of the smaller cells with light clear cytoplasm were also observed. Displacement of nuclei to the periphery was seen in the majority of cells, and the nuclei were round to oval, with striking nucleoli and coarsely stippled chromatin (Fig 2, right).

Ultrastructural Findings: An ultrastructural study was performed to examine cytoplasmic granules. For electron microscopy, tumor tissue fixed in formalin was refixed in 2.5% glutaraldehyde in phosphate buffer, pH 7.4 at 4°C, washed in the same buffer, postfixed in 1% OsO_4, dehydrated, and embedded in Epon. Ultrathin sections were stained with uranyl acetate and lead citrate and examined with an electron microscope (H-7000, Hitachi, Tokyo, Japan) .

A cohesive population of morphologically variable large cells with smooth surfaces displaying occasional short microvillus-like projections were observed. The cytoplasm was characterized by abundant, eccentrically placed, tightly packed, round, membrane-bound

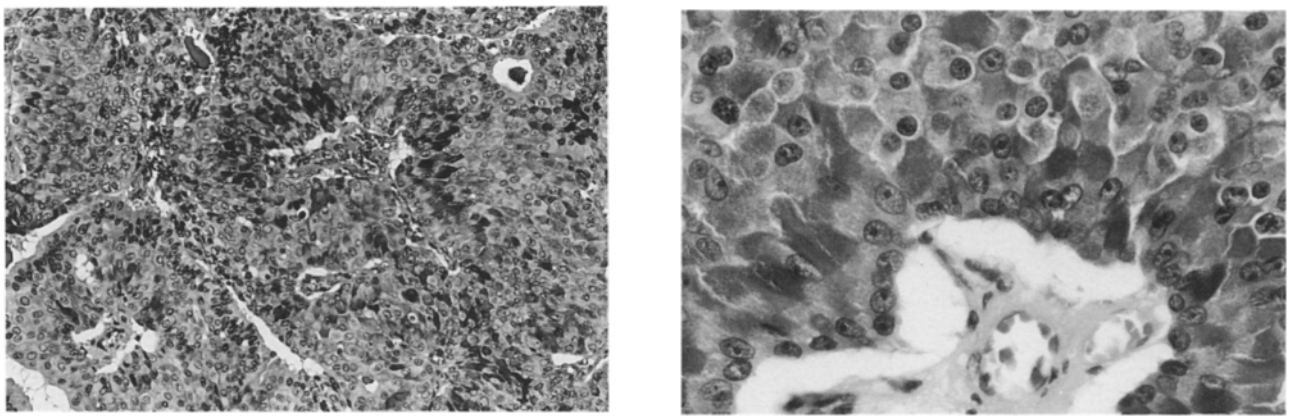

Fig 2. Left, Eosinophillic, dark-stained, granular cytoplasms and a few microcystic, acinar structures characterize the histology of acinic cell adenocarcinoma (×50). Right, Higher power view. Mostly these tumor cells consist of abundant granules which are PAS-positive (×200).

granules (Fig 3). These granules varied, from 10 nm to 20 nm in diameter, and were characterized by various electron densities, and thus strongly resembled secretory type granules known as zymogen granules. In addition, in the cytoplasm, well-developed rough endoplasmic reticulum, an occasional Golgi apparatus and mitochondria were observed . The nuclei were round to oval, mostly eccentrically placed and large, with peripheral condensation of chromatin. Some nuclei had one or more prominent nucleoli while others showed only coarsely stippled chromatin. A few smaller cells, of another type, with centrally placed nuclei and few granules, were also seen. Some nuclei had indentations in their membranes.

Immunohistochemical Findings: Formalin-fixed, paraffin embedded tissue were immunohistochemically stained for S-100 protein, gross cystic disease fluid protein-15 (GCDFP-15), epithelial membrane antigen (EMA), cytokeratin, chromogranin A and amylase (of both salivary and pancreatic-types) by applying the labeled streptavidin-biotin-peroxidase method (K-680, LSAB kit, DAKO Japan Co, Kyoto, Japan). The antibodies used and their sources are listed in Table 1. The cytoplasm demonstrated immunoreactivity for S-100 protein, GCDFP-15, EMA and cytokeratin whereas chromogranin A was negative. In addition, staining for salivary-type amylase was strongly positive (Fig 4, left) while that for pancreatic-type one was negative (Fig 4, right), indicating a salivary-type acinic cell adenocarcinoma.

Discussion

Primary acinic cell adenocarcinoma of the mammary gland is extremely rare. A search of the literature failed to reveal any other case.

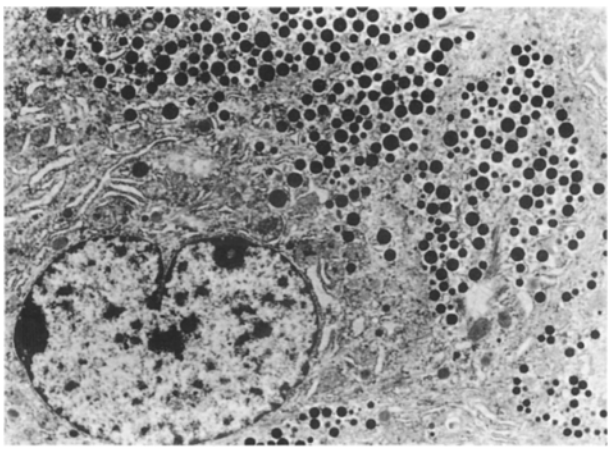

Fig 3. Morphologically variable large cells with variable electron density secretory granules resembling zymogen granules (×4000).

Table 1. Summary of Immunohistochemical Results

Antigen	Source	Dilution	Results
Cytokeratin	Immunotech	1:300	(+)
GCDFP-15	Signet Labo.	1:300	(+)
EMA	DAKO	1:400	(+)
S-100	DAKO	1:1200	(+)
S-100β	IBL	1:400	(–)
Chromogranin A	DAKO	1:100	(–)
Salivary-type amylase	Nordic Immunological Laboratories	1:100	(+)
Pancreas-type amylase	The Binding Site Limited	1:100	(–)
ER	Immunotech	1:50	(+)

GCDFP-15, Gross cystic disease fluid protein-15; EMA, Epithelial membrane antigen

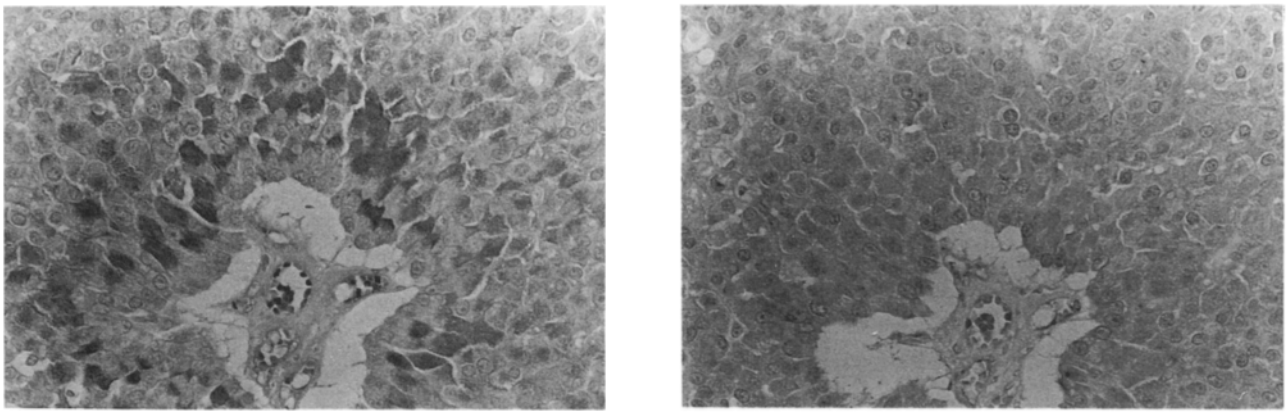

Fig 4. Salivary-type amylase (left) is positively stained, but the pancreatic-type (right) is negatively stained (×100).

Acinic cell adenocarcinomas are usually observed in salivary glands or the pancreas, the major salivary glands being the most common site. For minor salivary gland tumors, buccal mucosa, upper lip, and palate are the major sites of occurrence, though the tongue, oral cavity, larynx, and pharynx are also occasionally involved. Previously reported sites acinic cell adenocarcinoma other than a salivary gland or the pancreas were the lungs[1,2], the bronchial glands[3,4], the intrathoracic tracheae[5,6], the kidneies[7], and the lacrimal glands[8].

Based on amylase staining, our patient was considered to have a salivary-type acinic cell adenocarcinoma of the mammary gland, then we compared the characteristics of the tumor of this case with the salivary gland one. The tumor in our case most closely resembled an acinar cell-type acinic cell adenocarcinoma, though there were certain characteristics not consistent with this type of tumor. The morphological pattern was one of solid growth, as usually seen in acinar cell-type acinic cell adenocarcinomas. The cells of this tumor, which were large, round-to-polygonal in shape with dark-staining cytoplasmic granules and eccentrically placed nuclei, were also more compatible with acinar cell-type. However, microcystic structures were also seen in portions of the surgical specimen, a finding indicative of not only the acinar cell-type but also the vacuolated and intercalated duct-like types. Cytoplasmic staining with HE revealed eosinophilic cytoplasm characteristic of the intercalated duct-like type, whereas few smaller cells the cytoplasms of which failed to stain with HE had centrally placed nuclei, suggesting a clear cell tumor. Immunohistochemically, staining was positive for both S-100 protein and amylase, but not for S-100β. In the normal salivary gland, acinar cells show no immunoreactivity for S-100 protein though intercalated duct cells are occasionally positive. In addition, Dardick *et al*[9] described acinar cell-type tumors as being negative for both keratin and S-100 protein while intercalated duct-like tumors were positive for both. Some other groups[10-12] have detected immunoreactivity for S-100 protein in intercalated duct-like cells in acinic cell carcinoma. Although the tumor had arisen not in a salivary gland, but in the mammary gland in our case, the immunohistochemical as well as ultrastructural features in our case would be most consistent with that in a mixed acinar and an intercalated duct-like tumor. Many studies[13-19] have suggested that acinic cell adenocarcinoma develops from pluripotent duct cells. In light of the acinic cell adenocarcinoma having arisen in the mammary gland in our case, it is noteworthy that the tumor showed some of the features of an intercalated duct-like acinic cell adenocarcinoma.

Diagnosis of acinic cell adenocarcinoma located not in the salivary gland but in the mammary gland may be problematic and very difficult to prove. Eusebi *et al*[20] described a case of apocrine carcinoma which was strongly reminiscent of acinic cell adenocarcinoma. In fact, initial diagnosis of the present case was apocrine carcinoma in situ instead of acinic cell adenocarcinoma. In addition, Ellis and Auclair[21] reported that amylase immunostaining was not very useful because of the immunoreactivity in only a few salivary gland acinic cell adenocarcinomas when formalin-fixed and paraffin-embedded. Furthermore, the present tumor expressed GCDFP-15 which is also known as prolactin-inducible protein[20], and which is characteristically expressed in apocrine cells. Light microscopic features, including abundant PAS positive granular cytoplasm and microcystic structures, served as a reference. The numerous secretory-type granules, of variable electron densities, observed by electron microscopy were especially helpful in making the diagnosis.

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