A 61-year-old white woman noted a slowly growing lesion within the right breast that had been present for at least 2 years. During that period, the mass increased in size and ulcerated through the skin. The patient’s mother had breast cancer at the age of 69 years. A computed tomographic scan revealed a large mass in the central portion of the breast abutting the anterior chest wall. Ipsilateral axillary lymphadenopathy was also present. The patient presented to our cancer prevention center for a second opinion regarding the management and treatment of this locally advanced disease. Physical examination revealed a large, fungating mass, which almost entirely replaced the central aspect of the right breast with a 5.0-cm open defect in the overlying skin. The computed tomographic scan of the abdomen demonstrated a metastatic liver lesion and the chest radiograph showed bilateral pulmonary nodules suspicious for metastatic disease. The bone scan revealed multiple osteolytic lesions consistent with metastases in the sternum and the right lateral tenth rib. A fine-needle aspiration biopsy of the breast mass was performed and showed moderately cellular smears with rare single cells and groups of cells arranged in loose three-dimensional clusters in a background of proteinaceous material. The majority of cells had abundant, granular, and vacuolated cytoplasm. The nuclei varied in size from intermediate to large and had mildly irregular nuclear contours and infrequent prominent nucleoli (Figure 1). The patient underwent diagnostic core needle biopsy (not shown), followed by preoperative chemotherapy. After completion of 4 courses of neoadjuvant chemotherapy with only minimal clinical response, the patient underwent palliative surgical intervention, which consisted of a 21.0 × 14.0 × 5.0-cm right modified mastectomy specimen. Grossly, a well-demarcated mass measuring 8.0 × 7.0 × 1.5 cm, with lobulated margins extending into the overlying skin and nipple/areolar complex, was present. The cut surface of tumor was white, and firm with focal areas of gray-tan necrosis, with the tumor extending closely to multiple resection margins (Figure 2). On microscopic examination of hematoxylin-eosin–stained sections, a diffuse population of tumor cells with abundant pale-to-pink or amphophilic cytoplasm; irregular, vesicular nuclei of varying sizes; and prominent nucleoli was noted (Figure 3, inset, higher magnification). The tumor cells, glands, and microcystic spaces contained abundant periodic acid-Schiff–positive vacuolated “bubbly” secretions (Figure 4). Ductal carcinoma in situ with secretory changes was focally present at the tumor periphery. Immunohistochemical analyses for estrogen and progesterone receptors and fluorescence in situ hybridization to detect HER-2/neu gene overexpression were negative. Tumor cells were strongly diffusely immunoreactive for gross cystic disease fluid protein-15 (not shown). All ipsilateral lymph nodes were completely replaced by metastatic carcinoma, and extranodal extension was present. After the surgery, the patient underwent postoperative radiation therapy. At her 3-month follow-up examination, the patient presented with a new finding of contralateral metastases in left axillary lymph nodes, and at her 7-month follow-up, she presented with moderate progression of metastatic disease in other sites. The patient is presently undergoing additional experimental chemotherapy.

What is your diagnosis?
Pathologic Diagnosis: Secretory Carcinoma With Apocrine Differentiation

Abstract

We describe here an unusual example of secretory carcinoma with apocrine differentiation that presented as a large mass, had an aggressive clinical course, metastasized to ipsilateral axillary lymph nodes, and presented with distant metastases. No clinical and pathologic response to systemic neoadjuvant therapy was observed, and the disease progressed after surgery. The gross features, microscopic characteristics, immunohistochemical findings, molecular data, differential diagnosis, and outcome studies of this entity are discussed.

Secretory carcinoma of the breast, originally called juvenile carcinoma, was first described in 1966 as a rare neoplasm by McDivitt and Stewart in a report on 7 patients ranging in age from 3 to 15 years. Since then, cases have been reported in all age groups, ranging in age from 3 to 87 years (mean age, 25 years), in both sexes. The typical clinical presentation is a painless, well-circumscribed, mobile mass, which can be located in any part of the breast. Patients with subareolar lesions may present with nipple discharge.

On mammography, secretory carcinoma usually appears as a discrete, solitary mass with irregular borders. Sonographic findings are nonspecific, typically mimicking a hypoechoic mass, often mimicking a juvenile fibroadenoma.

The most distinctive gross feature of secretory carcinoma is circumscription of the mass, which may be lobulated, and may show infiltrating margins. The tumor is typically very firm, and grayish white to tan or yellow. The size ranges from 0.6 to 12 cm, with a median size of 3.0 cm, and the largest tumors are reported in adults. Cytologically, the tumor cells are distributed as single cells or loose “grapelike” clusters and have abundant vacuolated, granular cytoplasm and many intracytoplasmic lumina. The nuclei are small and round, with a low-grade appearance and, occasionally, signet ring–like cells may also be present. Microscopically, secretory carcinoma is characterized by dense amphophilic secretions in the tumor cells, glands, and microcystic spaces. Several histologic patterns, including microcystic, glandular, tubular, and solid, may be present in variable proportions within a single tumor. Secretory carcinomas typically contain cells with small, round nuclei of low-to-intermediate grade. In some instances, a part or most of the lesion may have more granular or eosinophilic cytoplasm, apocrine differentiation, and higher nuclear grade. The main differential diagnosis includes apocrine carcinoma, especially when obscured by apocrine cytology, pregnancy-like change, and juvenile papillomatosis with apocrine metaplasia.

Secretory carcinoma has been reported to be strongly positive with periodic acid–Schiff with and without diastase, mucicarmine, α-lactalbumin, S100 protein, and polyclonal carcinoembryonic antigen. Immunohistochemical reactivity for estrogen and progesterone receptors was negative in most cases, and HER2/Neu is typically not overexpressed. The translocation t(12;15)(p13;q25), in which the ETV6 gene from chromosome 12 is rearranged with the NTRK3 gene from chromosome 15, was recently identified in secretory breast carcinoma in 12 of 13 cases. It has been suggested that the ETV6-NTRK3 fusion gene, which leads to the expression of a chimeric protein tyrosine kinase that has potent transforming activity, may be a specific genetic alteration that leads to secretory carcinoma and could be a useful tool for studying this disease in the future.

Secretory carcinoma usually has an indolent clinical course, hence, it has a more favorable prognosis in patients younger than 20 years of age. However, in older age groups, its course more closely follows invasive ductal carcinoma. Axillary metastases have been described, and finding multiple involved lymph nodes may indicate systemic metastases. Distant metastatic disease at clinical presentation is relatively uncommon, but usually fatal; of 4 such cases reported in the literature, 3 resulted in the patient’s death by metastatic disease. The fourth patient was treated for metastatic secretory carcinoma to the lung 12 years after the original diagnosis. She did not respond to multiple courses of combination chemotherapy and remained alive for 2 years after presentation with metastatic disease and 1 year after cessation of all chemotherapy.

References