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Hypercalcemia in Metaplastic Squamous Cell Carcinoma of the Breast

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Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Conflict of interest: None declared

Patient: Female, 71
Final Diagnosis: Metaplastic squamous cell carcinoma of the breast
Symptoms: Altered mental status • necrotic breast mass
Medication: —
Clinical Procedure: Mastectomy
Specialty: Oncology

Objective: Rare co-existence of disease or pathology
Background: Metaplastic breast carcinoma is a rare entity characterized by rapid growth and heterogeneous histological features. It comprises less than 1% of all breast cancers, and no definitive treatment has yet been identified.
Case Report: We describe here a patient who presented with acute hypercalcemia and was found to have a large ulcerated breast mass. Once the patient's hypercalcemia was stabilized, she underwent complete surgical resection that revealed a large, cavitary, necrotic mass measuring over 11 cm. The final surgical pathology revealed metaplastic carcinoma with extensive squamous differentiation and ductal carcinoma *in situ*. At the request of her family, no additional treatment was pursued.
Conclusions: While there is not a significant body of data on the pathogenesis of metaplastic breast carcinoma, it is typically hormone receptor negative and has a variable response to chemotherapy. Surgical excision is the most commonly pursued treatment.

MeSH Keywords: Breast • Carcinoma, Squamous Cell • Metaplasia

Full-text PDF: <https://www.amjcaserep.com/abstract/index/idArt/912427>

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Background

Metaplastic breast carcinoma (MBC) is a rare disease comprising less than 1% of all breast tumors [1]. The literature on MBC is limited to case studies and retrospective observational studies, and due to its variable pathology and low incidence, there is no consensus regarding treatment [2]. Recently revised National Comprehensive Cancer Network (NCCN) guidelines identified metaplastic histology as a negative prognostic factor when it accounts for >10% of a tumor. However, specific treatment guidelines are not provided, so common therapy modalities have historically paralleled those utilized for invasive ductal carcinoma (IDC) [3,4]. Despite this common approach, MBC is generally regarded as more aggressive than IDC due to its rapid growth and propensity to spread hematogenously [4]. In the past, there have also been reports of chemoresistance, but recent literature has shown that multimodal treatment is associated with improved outcomes [4].

Case Report

A 71-year-old female with a past medical history of dementia, hypertension, and hyperlipidemia presented to the emergency department with a 4-day history of progressive altered mental status accompanied by polyuria and polydipsia. She had mild hypotension, was unable to open her eyes, and responded only to painful stimuli. On further physical examination, she was found to have a large, firm, right retroareolar breast mass which was suspicious for a neoplasm. The mass had associated skin dimpling, nipple retraction, and bloody nipple discharge but with no evidence of axillary or supraclavicular lymphadenopathy.

The patient's family accompanied her and reported that her last mammogram 6 years prior showed no abnormalities. While her family discovered the breast mass approximately 2 weeks before admission, the patient was unable to communicate when the mass was initially noticed. She had no previous surgeries or family history of malignancy. Medications included hydrochlorothiazide, carvedilol, losartan, atorvastatin, and mirtazapine.

Laboratory work revealed a marked leukocytosis of 29.3 K/uL with neutrophil predominance, calcium of 15.3 mg/dL, potassium of 3.0 mmol/L, ionized calcium of 1.9 mmol/L, parathyroid hormone (PTH) level of 13.6 pg/mL, and PTH related-peptide of 31 pg/mL. Electrocardiogram showed a decreased QTc interval. A computerized tomography (CT) of her head was negative for any acute changes, but chest CT showed peripherally enhancing necrotic nodules in the right breast without signs of axillary lymphadenopathy. Both urinalysis and urine culture confirmed the presence of an *Escherichia coli* urinary tract infection which was treated with ceftriaxone.

The patient's mental status improved with intravenous fluids, zoledronic acid, and treatment of her urinary tract infection. Hydrochlorothiazide was also discontinued and replaced with losartan, as thiazides can cause hypercalcemia. After one week of treatment, both her calcium and ionized calcium down trended to 7.1 mg/dL and 1.2 mmol/L, respectively. During this time, head CT was repeated with intravenous contrast and bone scan was performed confirming no evidence of metastatic disease.

Once the patient was medically stable, a multidisciplinary discussion was held with the patient, her family, the surgical oncology team, and the medical oncology team to develop a treatment plan for her likely breast cancer. Considering the patient's age, dementia, and prior wishes, the family initially elected for isolated drainage of the mass rather than definitive surgical excision.

The initial operation revealed a necrotic mass draining serosanguinous fluid which was debrided from the surrounding breast tissue. The incision was left open and treated with a wet-to-dry dressing. Initial pathology showed a hormone-receptor negative invasive carcinoma with extensive squamous differentiation and necrosis, and ductal carcinoma *in-situ* (DCIS). The pathology was discussed with the patient and her family several days later and because of difficulties in wound care and the clear evidence of cancer, the decision for complete right mastectomy for wound palliation was reached. Final surgical pathology after mastectomy revealed metaplastic carcinoma with extensive squamous differentiation and DCIS. Per the wishes of the patient and her family, no further treatment was pursued.

The gross specimen was a large, ulcerative, cavitory, necrotic mass measuring 11.3×11×10.2 centimeters. The edges of the ulcer were indurated, and the nipple was ulcerated as well. The cut surfaces showed a white and tan infiltrative, nodular, ulcerative mass with irregular borders and finger-like projections in the breast extending all the way underneath the area of the nipple.

Microscopically, the specimen showed invasive, poorly differentiated carcinoma composed of nests of large pleomorphic cells with large nuclei, abundant dense eosinophilic cytoplasm, and keratin pearls showing marked squamous differentiation (Figure 1). There were numerous mitotic figures, marked stromal desmoplasia, and large areas of necrosis. There was also a small focus of high grade *in situ* carcinoma (Figure 2). By immunohistochemistry, the tumor cells were negative for estrogen receptor (ER), progesterone receptor and human epidermal growth factor receptor type 2 (HER2/neu). The cells showed nuclear p63 staining consistent with squamous differentiation. The Ki-67 proliferation index was high and unfavorable at >20%.

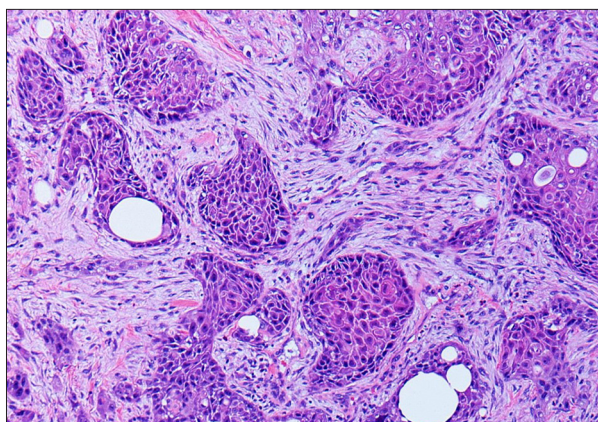


Figure 1. Microscopic examination showing invasive poorly differentiated carcinoma with keratin pearls and marked squamous differentiation.

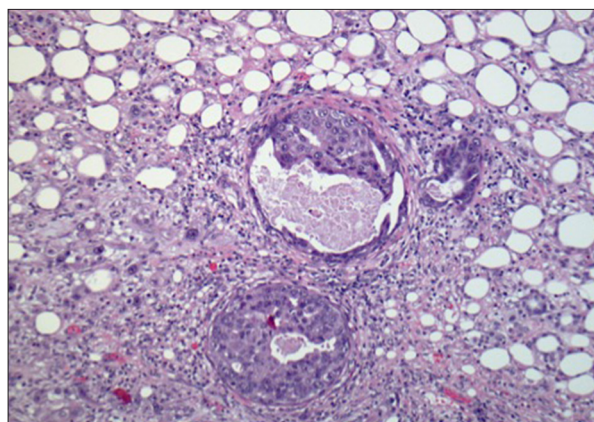


Figure 2. Microscopic examination showing a focus of high grade *in situ* carcinoma.

Discussion

Metaplastic breast carcinoma is a rare disease that was first recognized as a distinct pathologic entity in the 21st century. Wargotz and Norris developed a classification system that divides the disease into 5 subtypes: squamous cell, carcinosarcoma, spindle cell, matrix-producing, and MBC with osteoclastic giant cells [1]. The most common form identified thus far is the spindle cell subtype [2]. Data and research on MBC are limited due to its rarity and recent designation as a distinct pathological entity [4].

MBC commonly presents as a rapidly growing mass that is consistently larger than other breast cancers on initial examination [2]. Mean age at presentation is 53 to 61 years, and the majority of cases are hormone receptor negative [1,3,5]. In comparison to IDC, MBC typically presents as a more poorly differentiated tumor with less lymph node involvement [2,3]. Histology demonstrates infiltrating squamous carcinoma, eosinophilic cytoplasm, and some rare keratin pearl formation. The tumors are often cystic structures with lining composed of squamous cell carcinoma [1,2].

Imaging methods used to identify more common forms of breast cancer are also useful in identifying MBC. Magnetic resonance imaging (MRI) frequently shows an irregular mass with spiculated margins and T2 hyperintensity. Mammographic appearance is described as a high-density mass with irregular and/or spiculated margins. Sonographic appearance is described as complex echogenicity with solid and cystic components [2,6].

While treatment for MBC mirrors that of IDC, optimal treatment strategies have not been thoroughly researched. Options are usually limited to surgery and chemoradiation; however, traditional chemoradiation regimens used for IDC have had mixed results against MBC [4,7,8]. MBC does not preclude breast

conservation therapy (BCT), but the larger tumor size often requires mastectomy. BCT should be considered in appropriate patients, as there is no difference in disease-free survival when comparing BCT to mastectomy [7].

The American Joint Committee on Cancer's (AJCC) staging manual was recently updated to integrate HER2, PR, and ER status into the staging of breast cancer patients. These biomarkers must be included for case reporting in US cancer registries or the cancer is considered unstaged. While it is unclear exactly how the changes in staging criteria will affect treatment and outcomes, a preliminary study reported that 35% of women with stages I to III invasive breast cancer under the old AJCC staging guidelines would be restaged under the new criteria [9]. In the case of our patient, the tumor was T4bN0M0. Under the 7th edition AJCC staging guidelines, the tumor is stage IIIB, but under the 8th edition guidelines the tumor is stage IIIC. Although the increased stage suggests a decrease in overall survival, treatment was directed largely by the family's wishes and would not have changed [9].

Conclusions

This case highlights a rare form of breast cancer discovered in the setting of altered mental status due to hypercalcemia. Although there are no definitive treatment guidelines for MBC, a multidisciplinary approach must be developed by surgeons, medical oncologists, radiation oncologists, and the patient to best treat this disease. In this case, unique patient circumstances required a constant open dialogue between the patient, providers, and the patient's family. Further case reports, cases series, and prospective trials are needed to define treatment guidelines for this unique type of breast cancer.

Conflicts of interest

None.

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