Lipid-rich histology in a basal-type immuno-profile breast carcinoma: a clinicopathological histochemical and immunohistochemical analysis of a case

Serena Russo,[1] Diana Coppola,[2] Paola Vinaccia,[2] Antonella Siciliano,[2] Francesca Baldassarre,[2] Giovanni Battista,[2] Giuseppe Pisani,[3] Joseph Sepe,[4] Francesco M. Maiello[2]

[1]ASL NA3 Sud, Maresca Hospital, Torre del Greco, Naples, Italy; [2]ASL NA1, Pellegrini Hospital, Division of Pathology, Naples, Italy; [3]ASLNA1, Pellegrini Hospital, Breast Unit, Naples, Italy.

[4]University of Maryland University College, USA

Abstract

We describe the clinicopathological and morphological features of an unusual breast carcinoma classifiable as a lipid-rich variant of ductal invasive carcinoma, with a basal-type immunohistochemical profile. Basal-type breast cancers show no hormonal receptor expression, rarely over-express HER-2 but exhibit molecular high weight cytokeratins, EGFR and c-kit positivity. Special stains and histochemistry tests were used to elucidate the nature of vescicles in the neoplastic cells. Sudan IV was performed on formalin-fixed tissue. Commercially available antibodies tested were: ER, PgR, EGFR, HER2, c-kit, high molecular weight cytokeratins. Cytoplasmic lipids were highlighted as red-orange droplets on Sudan IV staining. As for immunohistochemistry, the tumor showed no reactivity to ER, PgR and HER2 (triple negative), and diffuse and strong positivity to high weight cytokeratins, EGFR and c-kit, such as a basal-type breast carcinoma. A basaloid phenotype in a lipid-rich carcinoma has not been previously reported.

Introduction

Breast cancer represents a heterogeneous group of tumoral entities, associated with specific morphological changes and immunohistochemical features: the clinical presentation and molecular alterations make it a highly diverse disease. That is why patients with the same tumor types and staging respond differently to treatment and do not share the same prognosis. Lipid-rich invasive breast cancer is a rare enigmatic entity among special types of infiltrating duct carcinoma, with difficult diagnosis.[1]

Only a few cases are reported in the literature.[2] Tumor cells contain abundant intracytoplasmatic lipids.[3]

Lipid-rich carcinoma was first described in women by Aboumrad *et al.*[4] These authors thought that the lipid droplets were produced and secreted by the tumor cells instead of being the result of regressive degeneration because lipid droplets existed uniformly in metastasized lymph nodes and in tumor cells undergoing mitosis.[5]

Since there was great heterogeneity in clinical outcome for estrogen positive tumors compared to the uniform behavior of hormone negative tumors,[6] researchers have invested in molecular aspects of breast cancer by investigating biological markers.[7]

Recent literature[8] suggests a new classification of breast cancer, based on its biological features and categorizes tumors according their immunophenotype in a luminal and a basal-type,[9] corresponding to two distinct types of epithelial cells found in the normal mammary gland.

Basal-type breast tumors show no hormonal receptor expression, rarely over-express HER-2 (triple negative) but show high-molecular weight cytokeratins, EGFR and c-kit positivity.

It was suggested[10] that the heterogeneity of breast cancer may be derived from the diversity of the original cells for neoplastic transformation, which is thought to exist in the terminal duct lobular unit of the mammary gland.

The cells in the terminal duct lobular unit consist of glandular, basal and myoepithelial cells. This heterogeneous population of epithelial cells arises from a common progenitor but they each express unique markers and perform unique functions.

The paradigm that breast cancer is a heterogeneous disease shifts to the new one that breast cancer is at least two different diseases with age-specific incidence. Estrogen-negative tumors usually consist of high-grade, aggressive tumors or rare histoypes (adenoid cystic, metaplastic). The basal-like subtype has an interval presentation and it is not usually detected during a mammographic screening.[11]

We describe the clinicopathological and morphological features of an unusual breast carcinoma classifiable as a "lipid-rich" variant of ductal invasive carcinoma and correlate it with a basal immunohistochemical profile.

Correspondence: Serena Russo, Via Epomeo 72, 80126 Napoli, Italy. E-mail: qubmur@tin.it

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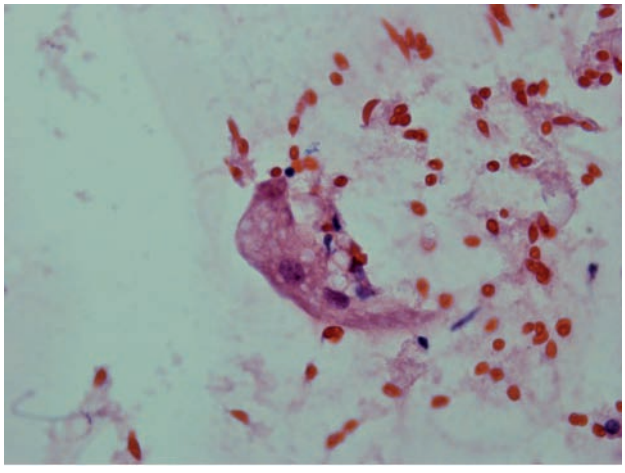

Figure 1. Fine needle aspiration cytology: Large, vacuolized cells. 400X.

Materials and Methods

A 73-year old woman, previously in good health, in menopause since she was 38 years old, presented with a sudden breast mass. Mammography performed 10 months earlier was negative.

Imaging studies further evaluated the extent of the disease: CT scan revealed no evidence of metastatic disease.

The patient was treated at the Breast Unit of Pellegrini Hospital (Naples, Italy). She underwent a modified radical mastectomy with axillary lymphadenectomy after a fine needle aspiration cytologic diagnosis of carcinoma (Figures 1 and 2).

All available paraffin blocks or unstained sections were retrieved and the original hematoxylin and eosin-stained sections were reviewed. After gross examination, the specimen was serially sectioned into 3 mm thick slices and formalin-fixed.

In addition, 9 invasive ductal carcinomas, not otherwise specified were used as a control group for histological and immunohistochemical correlations. Whole tissue sections (5 μm) were cut and used for histochemistry and immunohistochemistry.

The immunohistochemical stains were performed using Ventana® Benchmark™ Automated Immunostainer on formalin-fixed paraffin-embedded specimens. Commercially available antibodies tested were: ER, PgR, EGFR, HER2, c-kit (Ventana, Tucson, AZ, USA), high molecular weight cytokeratins (clone 34βE12-ORG-8735, Novocastra) all prediluted according to the manufacturers' instructions.

Peroxidase activity was visualized with diaminobenzidine chromogen as per routine protocol to obtain a brown-black end product. Appropriate internal and external positive controls were used. In an effort to elucidate the nature of the vescicles, special stains and histochemistry tests were performed. Sudan IV (modified by Coppola) method for fat: after fixation in 10% buffered neutral formalin, the specimen was rinsed in water for 24 hours to remove the excess. Then 10 micron frozen sections were cut, collected in distilled water and stained in a Sudan IV solution (Sudan was dissolved in 70% alcohol). After that we mounted slides with glycerin jelly (Figure 3). We chose alcohol instead of Herxheimer solution, made of alcohol and acetone, to avoid an excessive extraction since we dealed with previous formalin that is a fat solvent.

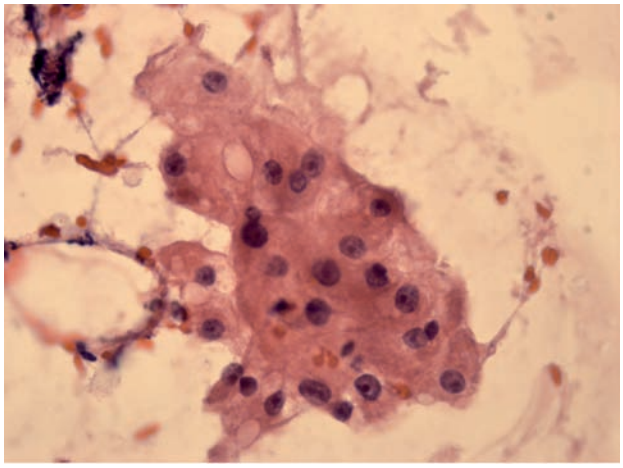

Figure 2. Fine needle aspiration cytology. E.E. 400X.

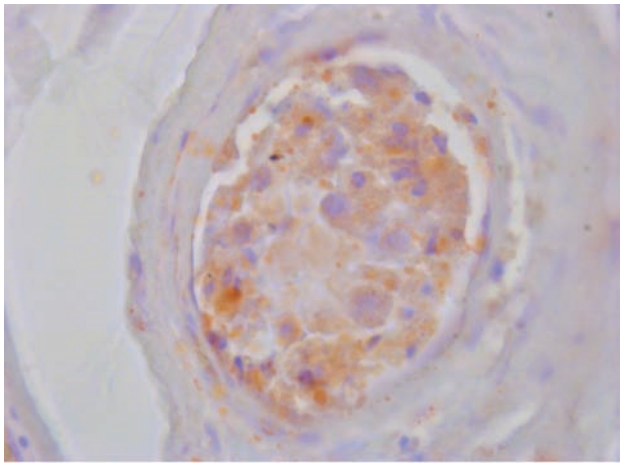

Figure 3. Sudan IV. 250X.

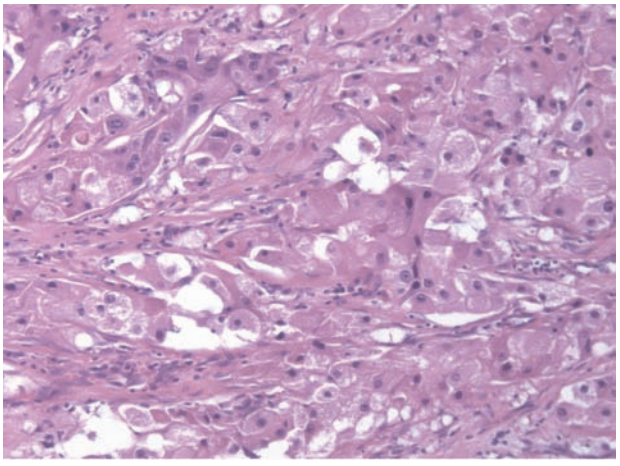

Figure 4. Hematoxylin-Eosin. 250X.

Results

On gross examination the tumor was firm and whitish with ill defined margins and measured 2.2 cm in diameter. On morphological grounds it was a high-grade invasive ductal carcinoma with an 80% histiocyte-like neoplastic component and a 15% *in situ* ductal carcinoma component .

The neoplastic cells, arranged in nests and cords were medium-sized, with a small round, dark, nucleolatus nucleus and a large foamy clear cytoplasm (Figure 4). There were perineural invasion, peritumoral neoplastic embolization and columnar alteration with prominent apical snouts and secretion (CAPSS) in uninvolved parenchima.

All the axillary lymphnodes (fourteen) were negative. We also observed some calcifications and a mild chronic intra and peritumoral inflammation. No reaction with Periodic Acid–Schiff, Alcian and PAS-D histochemical technique was observed within tumor cells. Cytoplasmic lipids were highlighted as red-orange droplets at the Sudan IV staining. In agreement with the current morphological description of human and canine tumors, the cells we examined with large vacuoles of neu-

tral lipids were consistent with lipid-rich carcinoma, a rare and distinct variant of infiltrative ductal breast carcinoma (lipid-rich invasive ductal carcinoma according to WHO classification, 2003). As for immunohistochemistry, the tumor showed no reactivity to ER, PgR and HER2 (triple negative), and diffuse and strong positivity to high weight cytokeratins,[12] EGFR (Figures 5 and 6) and c-kit (Figure 7), such as a basal-type breast carcinoma.

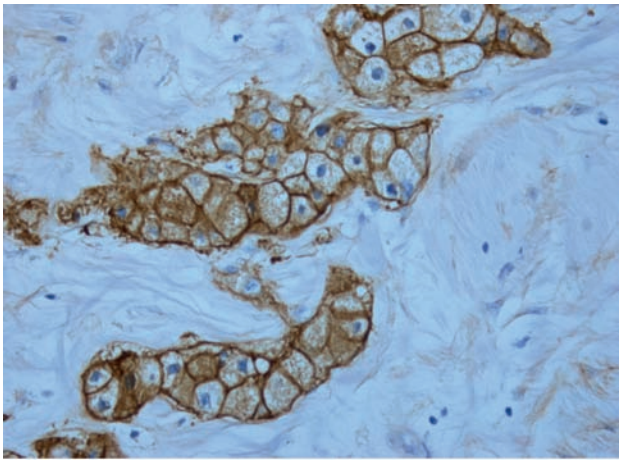

Figure 5. EGFR. 250X.

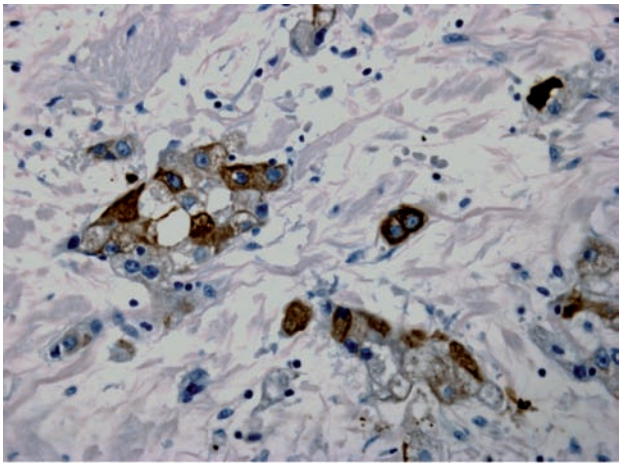

Figure 6. High molecu-lar weight cytokeratins. 250X.

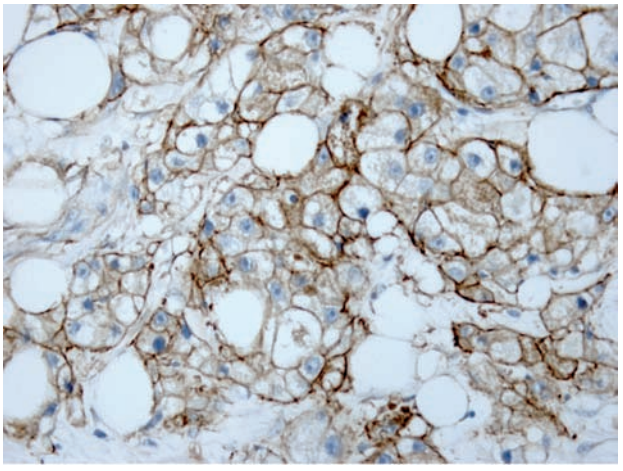

Figure 7. c-kit. 250X.

Discussion

The foregoing data suggest that breast cancers show great diversity in their morphologies, clinical histories and responsiveness to chemiotherapy. This wide diversity poses a challenge to provide accurate diagnostic, prognostic and predictive information and effective treatment. Traditional therapies targeting the estrogen-receptors or HER2 oncogene would not be expected to be effective on basal-like breast cancers because this subtype expresses neither of these proteins.

"Breast cancer can no longer be viewed as one biologic entity. If breast cancer overall consists of at least two main types, we need a stratified rather than a unified approach to breast cancer research, prevention and treatment".[13] Some investigators have previously suggested that basal-like carcinoma may consist of components of invasive ductal carcinoma, not otherwise specified, metaplastic carcinoma, and medullary carcinoma.[14]

This is the first report of a lipid-rich breast carcinoma with a basaloid phenotype.

Even if, based on one case, definitive conclusions about pathogenic implications cannot be reached, it is peculiar that we observed carcinoma secreting cells showing a basaloid immunoprofile, since the secretory function usually belongs to luminal cells.

It is reasonable to conclude that this paper may raise new questions, but it cannot give ultimate results.

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