Pathologic Quiz Case

A 93-Year-Old Woman With an Enlarged and Tender Left Breast

Jorge S. Reis-Filho, MD; Laura G. Fulford, MBBS; Alex Freeman, MD; Sunil R. Lakhani, MD, FRCPath

A 93-year-old woman presented with a gradual onset of an enlarging, tender, and erythematous left breast. She had no other relevant history. Clinical examination suggested an inflammatory carcinoma, along with an area of diffuse thickening in the upper outer quadrant. She underwent mammography, the results of which were unremarkable, followed by a core biopsy of the thickened area. Following this, she underwent a left mastectomy with axillary dissection. Macroscopically, the specimen comprised a disk of fibrofatty breast tissue, 150 × 80 × 50 mm, covered by a nipple-bearing ellipse of skin measuring 130 × 80 mm. On sectioning, the entire breast was diffusely pale and firm, with a more distinct irregular, firm area that measured 30 × 20 × 50 mm in the upper outer quadrant, close to the deep margin.

Histologic examination revealed an extensive tumor, involving the entire breast, measuring 150 mm in maximum size, and extending to the medial and lateral margins, the dermis of the nipple skin, and within 1 mm of the deep margin. The tumor was composed of single files of large cells with focal targetoid growth around the normal breast structures (Figure, A). The neoplastic cells contained abundant foamy or finely granular pale pink cytoplasm (Figure, A, inset, and Figure, B), with occasional intracytoplasmic lumina identified (Figure, B, inset). The nuclei were uniform and round to oval; they had a fine chromatin pattern and a single prominent nucleolus. Mitotic figures were 4 per 10 high-power fields. Neoplastic cells were seen diffusely infiltrating through adipose tissue in scattered areas, mimicking the appearances of fat necrosis (Figure, C). Foci of lobular carcinoma in situ (LCIS) (Figure, A, arrows, and Figure, D, inset) admixed with the invasive tumor and in surrounding breast parenchyma were observed. No lymphovascular invasion was seen. Three of 12 lymph nodes examined contained metastatic carcinoma with morphologic findings similar to the primary tumor. Immunostaining for estrogen and progesterone receptors was negative. Immunostaining for HER-2 was strongly and diffusely (3+) positive. Gross cystic disease fluid protein 15 (GCDFP-15) (Figure, C, inset) and androgen receptor were positive, whereas E-cadherin (Figure, D, and D inset), S100 protein, calretinin, α-inhibin, and CD68 were negative in neoplastic cells.

What is your diagnosis?

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From The Breakthrough Toby Robins Breast Cancer Research Centre, Institute of Cancer Research, London, England (Drs Reis-Filho, Fulford, and Lakhani); Life and Health Sciences Research Institute, School of Health Sciences, University of Minho, Braga, Portugal (Dr Reis-Filho); The Ludwig Institute for Cancer Research, London, England (Drs Fulford and Lakhani); and Department of Histopathology, The Royal Marsden Hospital, London, England (Drs Freeman and Lakhani).

Corresponding author: Sunil R. Lakhani, MD, FRCPath, The Breakthrough Tony Robins Breast Cancer Research Center, Institute of Cancer Research, Chester Beatty Laboratories, Fulham Road, SW3 6JB London, United Kingdom (e-mail: lakhani@icr.ac.uk).

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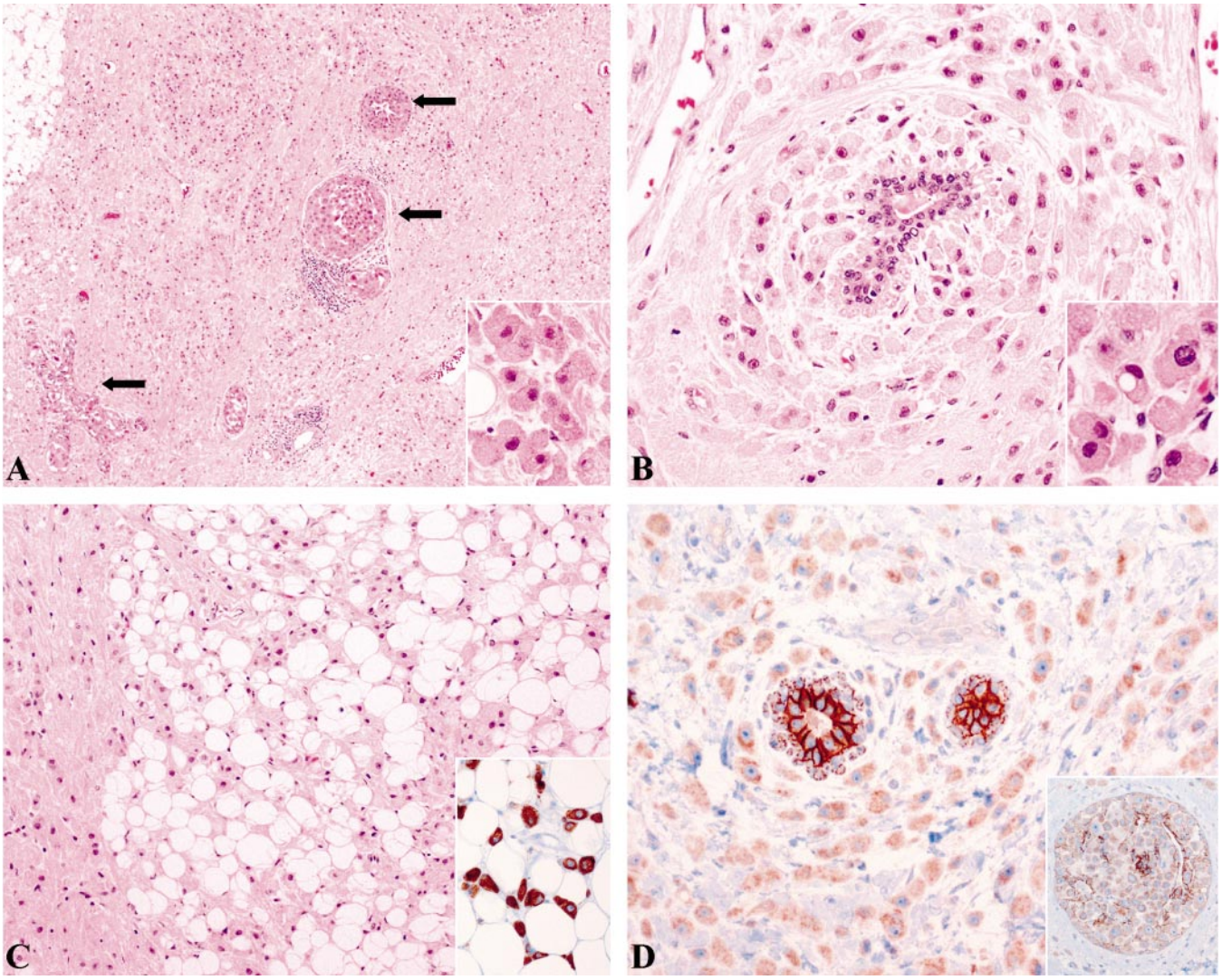
A
B
C
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Pathologic Diagnosis: Histiocytoid Variant of Lobular Breast Carcinoma

The term *histiocytoid breast carcinoma* (HBC) was first coined by Hood et al[1] in 1973. They described a group of breast carcinomas, showing a predilection for metastasis to the eyelid, composed of cells that resembled histiocytes with small ''inactive'' nuclei and abundant vacuolated cytoplasm. The neoplastic cells stained with Mayer mucicarmine and were negative for oil red O. In 5 of 8 cases in this series, the metastatic lesion presented before the primary carcinoma had been diagnosed. These lesions posed difficulties in the differential diagnosis with other benign lesions, such as xanthoma, xanthelasma, histiocytoma, and granular cell tumor.[1] Since this first report, several other case reports and small series of HBC have been reported, including a series of 13 cases under the heading *myoblastomatoid breast carcinoma*.[2]

Some authors regard HBC as a variant of apocrine carcinoma[2] or an apocrine variant of infiltrating lobular breast carcinoma[3–5] based on (1) the consistent expression of the apocrine marker GCDFP-15; (2) the association with foci of LCIS; (3) the presence of transitional areas between typical LCIS and histiocytoid/apocrine LCIS; and (4) the identification of areas with single-cell filling and targetoid growth pattern in bona fide cases of HBCs.[4–6] These features and the association of HBC with pleomorphic lobular carcinoma may suggest that HBC is a variant of pleomorphic lobular carcinoma.[6]

In contrast, several lines of evidence suggest that HBC is a morphological pattern that may be observed in ductal, apocrine, and lobular breast carcinomas rather than a specific type of breast carcinoma per se.[7] Recently, Gupta et al[7] described a series of 11 HBCs, in which 8 cases were associated with LCIS. In that series, 10 of the 11 cases were positive for the apocrine marker GCDFP-15, and 8 of these cases lacked E-cadherin expression. Based on these findings, the authors concluded that HBCs have an immunophenotypical profile consistent with both ductal and lobular differentiation and that the lack of specific and consistent clinical findings, morphologic features, or immunohistochemical profile warrants that histiocytoid carcinoma should not be considered a special type of breast cancer.

Despite the fact that it may not be a distinct entity, the term HBC is useful to remind pathologists that these tumors may be easily overlooked or misdiagnosed as benign or inflammatory processes, including xanthomatous lesions and granular cell tumors,[2] as well as other malignant neoplasms, such as histiocytosis, histiocytic sarcoma, and lipid-rich breast carcinoma. As noted in the present case, when HBC is infiltrating through adipose tissue, it may superficially simulate fat necrosis to the unwary.

Histiocytoid breast carcinoma may be distinguished from histiocytic lesions by the presence of nuclear atypia (albeit mild), the lack of histiocytic markers (CD68, HAM-56, lysozyme, CD1a, and S100 protein), and the consistent expression of markers of epithelial and apocrine differentiation,[2,4,6,7] namely, cytokeratins, epithelial membrane antigen, and GCDFP-15. In the case of the lobular variant, intracytoplasmic lumina and associated foci of LCIS in most cases are helpful features for diagnosis. Granular cell tumor may show a remarkable histologic similarity to HBC[2]; however, the former expresses S100 protein, calretinin, and α-inhibin[8,9] and is negative for epithelial markers and hormone receptors. Lipid-rich breast carcinoma is a special type of breast carcinoma characterized by nests, cords, and solid sheets of large polygonal cells, with abundant foamy or multivacuolated lipid-rich cytoplasm, which may confer a clear cell or lipoblast-like appearance to neoplastic cells.[10] These tumors may be differentiated from HBC by the distinctive morphologic features, lack of intracytoplasmic lumina and mucin in lipid-rich breast carcinomas, and lack of lipids in HBC cells.[1–6,10]

Owing to the small number of cases published to date and to the fact that HBC may not be a distinct entity, the prognostic implications of histiocytoid morphologic features in breast carcinomas remain unclear.

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