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Original contribution

Lobulitis in nonneoplastic breast tissue from breast cancer patients: association with phenotypes that are common in hereditary breast cancer☆,☆☆

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Summary Lobular inflammation (lobulitis) has been demonstrated in benign breast tissue adjacent to in situ and invasive breast cancers and, more recently, in nonneoplastic tissue from prophylactic mastectomy specimens for hereditary high-risk breast carcinoma. The aim of this study is to investigate the incidence of lobulitis in benign breast tissue of patients with breast cancer and associated clinicopathologic features. We reviewed nonneoplastic breast tissue sections from 334 patients with invasive breast carcinoma to study lobulitis in normal breast tissue and to correlate its presence with clinicopathologic features of the associated tumor. Clinical information (age, menopausal status, and follow-up), tumor characteristics (type, grade, size, lymph node status, stage, estrogen and progesterone receptor, HER2), and survival were recorded. Characteristics of women with and without lobulitis were cross-classified with categories of clinical, pathologic, and histologic characteristics, and differences in distributions were tested in univariate and multivariate analysis. Lobulitis was found in 26 (8%) of 334 patients. The lymphocytic infiltrate was predominantly T-cell type. In a multivariate model, lobulitis in patients with breast cancer was significantly associated with younger age, triple (estrogen receptor, progesterone receptor, HER2)–negative cancers, and medullary phenotypes. Lobulitis in nonneoplastic breast tissue, away from tumor, is associated with clinicopathologic features more commonly seen in hereditary breast cancer.

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1. Introduction

Inflammatory infiltrates in the nonneoplastic lobules (lobulitis) have been described in patients with in situ and invasive cancers adjacent to tumors consisting predominantly of T cells [1-3]. Recently, lobulitis was found to be significantly more frequent in women with hereditary high risk of breast cancer undergoing prophylactic mastectomy compared with controls [4]. The inflammatory cells in these patients were predominantly T cells unlike B-lymphocyte infiltrate seen in diabetic mastopathy [5,6]. We hypothesized that lobulitis may be significantly associated with clinicopathologic features and survival in patients with breast cancer. We studied lobulitis in benign breast tissue away from in situ and invasive carcinoma and evaluated the clinicopathologic features of the associated tumors.

2. Materials and methods

2.1. Patient selection and data collection

After obtaining institutional review board approval, tissue samples were collected from a cohort of women diagnosed with invasive primary breast cancer, none of whom received neoadjuvant therapy before surgery. These patients, diagnosed between 1991 and 1996, were identified as a part of another study, which investigated potential effect of metabolizing enzyme polymorphisms on overall and disease-free survival in women who received chemotherapy and/or hormonal therapy. The original study included a total of 609 patients in the cohort. All slides were reviewed by 1 pathologist (H. E. G.) to confirm tumor characteristics. Of those patients, 334 had normal breast sections without in situ or invasive cancer on the same slide indicating normal breast tissue at least 0.3 cm from the tumor.

Lobulitis was defined as more than 50 mononuclear cells per lobule (50-100 cells per lobule: moderate; >100 cells per lobule: marked). Cases with "lobulitis" from the areas of in situ or invasive carcinoma were excluded as these may represent tumor-related/tumor-induced inflammation. Luteal phase changes, typically involving most of the lobules, characterized by stromal edema, myoepithelial vacuolization, and only a very small number of mononuclear inflammatory cells in the intralobular stroma were not scored as lobulitis either.

Clinical information (age, menopausal status, and follow-up) and tumor characteristics (type, grade, size, no. of positive lymph nodes, and stage) were recorded based on pathology reports and tumor registry data. Estrogen (ER) and progesterone (PR) receptors status, determined either by ligand binding assay or immunohistochemistry, were available in pathology reports. We have previously shown that there is good concordance between tissue microarrays (TMAs) and whole-section ER determination on the same patient population [7]. We repeated ER and PR immunohistochemical staining on 1-mm TMAs for uniformity of the type of test and the antibody used and for uniform interpretation of the test following current guidelines. None of the cases had had *HER2* status determined either by immunohistochemistry (IHC) or fluorescence in situ

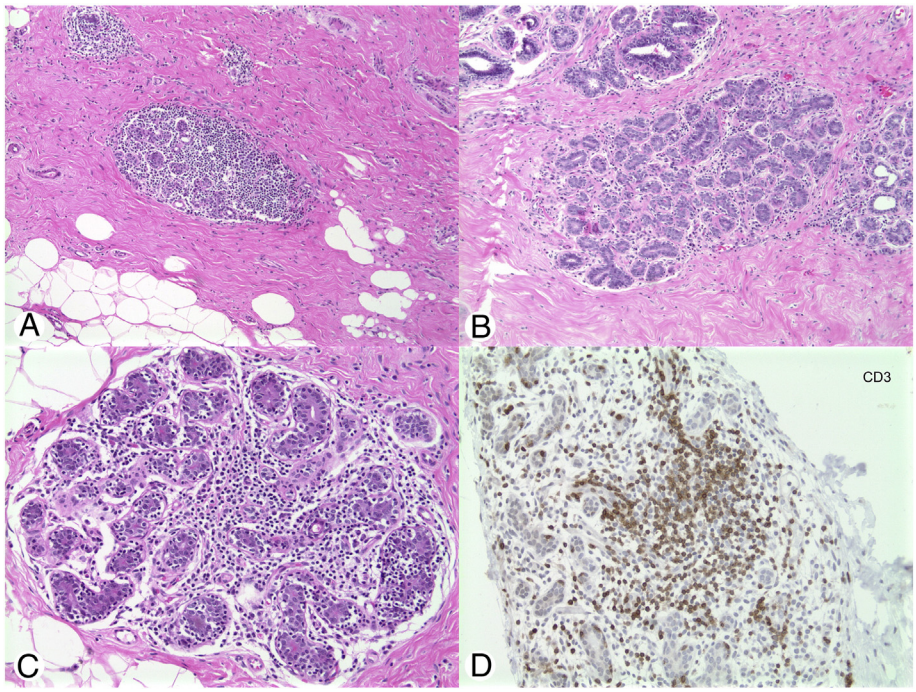

Fig. A, Lobulitis involved 25% or less lobules in more than half the cases. B, In some, the infiltrate was mild. C, Lobule with significant mononuclear infiltrate. D, Most of the lymphocytes were T cells. Hematoxylin and eosin, ×4 (A), ×10 (B), and ×20 (C); CD3, ×20 (D).