

Mammography Reveals a 2-mm Intraductal Breast Carcinoma

Macaulay A.C. Onuigbo, MD, MSc

Margaret E. Cuffy-Hallam, MD

Nathan A. Dunsmore, MD

Eva S. Zinreich, MD

The American Cancer Society estimated in 1999 that 176,300 cases of breast cancer would be diagnosed in the United States in that year, of which 175,000 would occur in women and 1,300 in men.¹ In the same report, it was estimated that breast cancer would account for 43,700 deaths in 1999, with 43,300 (99.1%) of these deaths occurring in women.¹ Ductal carcinoma in situ (DCIS) comprised 3.1% of all breast cancers in 1985. The percentage of diagnosed breast cancer accounted for by DCIS increased to 7.9% by 1995 and apparently continues to increase as the use of screening mammography programs increases.²⁻⁴

In all cancers, the primary tumor size is generally a major determinant of outcome. Since the advent of widespread and routine use of mammography for breast cancer screening in women aged 40 years and above, the incidence of DCIS has been increasing.^{3,4} With mammography, even very small masses can be detected early, typically resulting in better treatment outcomes. In several studies, mortality from breast cancer has been significantly reduced in association with breast cancer screening programs, especially in women in the 50- to 74-year age group.⁵⁻⁷ This article describes a patient who was diagnosed with a small intraductal carcinoma that was identified on mammography. The diagnosis and management of DCIS are discussed.

CASE PRESENTATION

Patient Presentation

In November of 1998, a 54-year-old postmenopausal woman was referred to our radiation oncology unit following a breast excisional biopsy positive for DCIS.

History of Presenting Illness

In 1995, a routine mammogram exhibited clustered microcalcifications in the patient's left breast. As a result of this finding, the patient underwent follow-up

mammography at 6-month intervals. The microcalcifications remained stable until September of 1998, when her mammogram exhibited the previously observed microcalcifications, 2 cm deep to the nipple, but magnification revealed that the number of microcalcifications had increased. The microcalcifications were arranged in a tight cluster of fine opacities, measuring approximately 2 mm in diameter. The patient reported that she had been in otherwise normal health.

The patient exhibited no signs or symptoms of breast cancer throughout this period. There was no history of breast lump during this time, nor was there a history of breast skin changes or nipple discharge.

Subsequent to the September 1998 mammogram, the patient underwent needle localization and excision of a 3.5 cm × 2.1 cm × 0.6 cm piece of tissue, which was irregular, fibrofatty, and red-yellow in color. The specimen radiograph revealed the tight cluster of fine opacities identical to the mammogram picture. Sectioning through the specimen revealed a fragmented guidewire, which at the tip was remarkable for a 2-mm, indistinct nodule located more than 2 mm from the closest margin. The indistinct nodule corresponded to the specimen radiograph.

Microscopic examination of the biopsied tissue revealed a small intraductal papillary carcinoma, with a maximum tumor diameter of only 2 mm, with a 1.5-mm margin. The surrounding breast tissue shows fibrocystic

Dr. Onuigbo is an Assistant Instructor and Clinical Fellow, Division of Nephrology, University of Maryland School of Medicine, Baltimore, MD. Dr. Cuffy-Hallam is a Senior Resident in Internal Medicine, Department of Internal Medicine, and Dr. Dunsmore is an Associate Pathologist, Department of Pathology, Greater Baltimore Medical Center, Baltimore, MD. Dr. Zinreich is an Assistant Professor of Medicine, Department of Medicine, Johns Hopkins Hospital, and a Radiation Oncologist, Department of Radiation Oncology, Greater Baltimore Medical Center, Baltimore, MD.

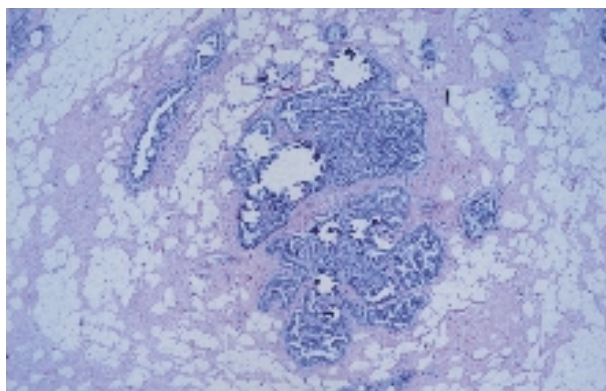


Figure 1. Ductal carcinoma in situ from breast excision biopsy of the case patient. Maximum tumor diameter, 2 mm. (Magnification, 40x.)

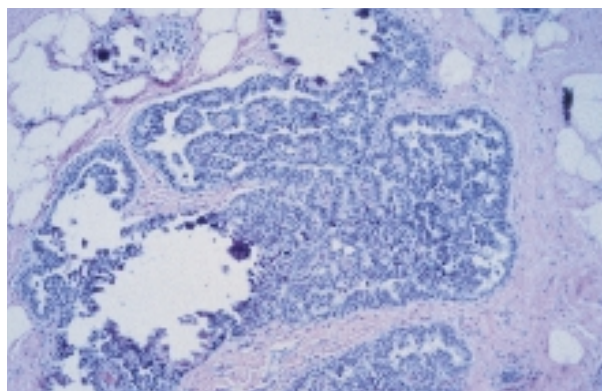


Figure 2. Greater histologic detail of the tumor shown in Figure 1. No microinvasion is visible. The surrounding breast tissue shows fibrocystic changes, including papillomatosis and duct epithelial hyperplasia without atypia. (Magnification, 100x.)

changes including papillomatosis and duct epithelial hyperplasia without atypia (**Figures 1 and 2**). No microinvasion was detected, and the biopsy margins were clear.

Following the biopsy diagnosis of DCIS, the patient's primary care physician started her on tamoxifen.

Other Medical History

The patient had 2 negative biopsies of the right breast in the 1980s for breast lumps suspicious for malignancy. Other relevant past medical history included controlled hypertension and in 1996, deep venous thrombosis in the left leg.

She experienced menarche at age 13 years, had a regular, 5/28 menstrual cycle, had a full-term pregnancy in 1985 and a miscarriage subsequently. She did not breast-feed her baby. She reported a bee sting on the left breast in 1994.

The patient used birth control pills in her 20s and 30s and had been on estrogen-progesterone hormone replacement therapy (HRT) since menopause at age 42 years. The HRT pills were discontinued following the diagnosis of breast cancer.

The patient reported allergy to sulfonamides, and current medications included hydrochlorothiazide, potassium chloride, and the tamoxifen therapy that had been recently initiated. The tamoxifen was discontinued when our evaluation revealed that the patient had experienced an episode of right lower extremity thrombophlebitis earlier in 1998.

The patient smoked for 20 years but quit smoking in 1994. She drank alcohol only occasionally.

Family History

The patient was separated and lived with her teen-aged daughter. Her family history was pertinent for

2 great aunts with breast cancer diagnosed when they were in their 70s, a grandmother with colon cancer, and a grandfather with lung cancer.

Physical Examination and Laboratory Evaluation

The patient was evaluated in our radiation oncology unit 6 weeks after the biopsy. Physical examination at this time revealed a well-developed, well-nourished African American woman. Head, ear, eye, and neck examination was unremarkable with no peripheral lymphadenopathy. Vital signs were normal. The right breast was unremarkable except for a well-healed old surgical scar. The left breast revealed a recent surgical scar around the periareolar area from the recent biopsy, but was otherwise normal. There was no evidence of nipple retraction, nipple discharge, or palpable hematoma. Results of the rest of the physical examination were normal.

Results of the complete blood count, urinalysis, and liver function tests were normal, as were serum levels of electrolytes, urea nitrogen, creatinine, and glucose. Sedimentation rate was 20 mm/hour (Wintrobe method).

Radiation Treatment

The patient was scheduled for definitive local radiation therapy consisting of 50.4 Gy to the whole breast in 28 treatments, and 10 Gy to the tumor bed in 5 treatments. The radiation treatment was well tolerated.

DISCUSSION

The patient in this case study was diagnosed with an extremely small (2 mm) intraductal carcinoma in the left breast following repeated follow-up mammographies for previously stable microcalcifications. DCIS of less than

2-mm maximum tumor diameter have been very rarely reported.^{3,8} Primary breast tumors of this small size are nearly always diagnosed through the use of screening mammography.³ These tumors are asymptomatic and typically do not exhibit multicentricity, nipple involvement, nodal involvement, or occult invasion.⁸ Recurrence following excision of these tumors is rare.⁸

Prognostic Signs in Breast Cancer

In a 10-year follow-up study of breast cancer patients in the National Surgical Adjuvant Breast Project (NSABP) protocol B-06, which included patients with DCIS, survival rates of patients with node-negative breast cancer were favorable in patients of white rather than black race; good rather than poor tumor grade; certain tumor types such as tubular, mucous, and papillary, rather than lobular or classic medullary; as well as a positive progesterone-receptor status.⁹ For node-positive patients, on the other hand, the number of nodal metastases, the degree of tumor elastosis, the patient's age, and the tumor nuclear grade were prognostically significant.⁹ Interestingly, unlike the previous NSABP protocol B-04 study, which showed that tumor size was related to survival, tumor size in the NSABP B-06 study—in which only tumors greater than 4 cm were enrolled—did not appear to be an important prognosticator.⁹ Breast tumors that are smaller than 2.5 cm, especially when they are unifocal and without occult invasion, generally demonstrate no multicentricity, have no nipple or nodal involvement, and portend an improved prognosis.⁸

Treatment of DCIS

The Van Nuys Prognostic Index (VNPI) is a scoring system designed to aid the rather complex treatment selection process required in the management of patients with DCIS.¹⁰ This scoring system combines 3 significant predictors of local recurrence: tumor size, margin width, and pathologic classification. Scores of 1 (best) to 3 (worst) are assigned for each of the 3 predictors and totaled to give an overall VNPI score ranging from 3 to 9.¹⁰ In an 8-year follow-up study of 333 DCIS patients treated with excision or excision and radiation, patients with VNPI scores of 3 or 4 had a low rate of local recurrence, with no difference between patients who had lumpectomy alone and those who had lumpectomy and radiation treatment.¹⁰ In patients with VNPI scores of 5 to 7, there was a 17% local recurrence-free interval benefit for patients in the radiation treatment group. In patients with VNPI scores of 8 or 9, local recurrence rates in excess of 60% were observed, although the rate of local recurrence was lower with

radiation treatment.¹⁰ It was therefore concluded that for patients with VNPI scores of 3 or 4, treatment with tumor excision alone may be considered.¹⁰ For patients with VNPI scores of 5, 6, or 7, lumpectomy and radiation treatment is recommended. For patients with VNPI scores of 8 or 9, the high local recurrence rate regardless of radiation treatment warrants consideration of mastectomy.¹⁰

The importance of wide tumor-free margins was emphasized in a recent study of local recurrence in the breast-conserving management of DCIS.¹¹ This study further validated the clinical validity and usefulness of the VNPI scoring system in assessing the appropriate treatment modality for DCIS.

A decade ago, excision alone (“lumpectomy”) followed by surveillance was thought to be adequate treatment for selected women with DCIS.¹² However, as evidenced by several subsequent randomized studies, lumpectomy plus radiation therapy is now acknowledged to give better outcomes in terms of overall survival, event-free survival, ipsilateral breast cancer recurrence, and freedom from distant metastases.^{13–15} In the NSABP protocol B-17 study, 623 patients with DCIS were randomized into 2 treatment groups, lumpectomy alone and lumpectomy followed by radiation treatment.¹⁵ Radiation treatment following lumpectomy reduced the subsequent incidence of ipsilateral breast tumor recurrence from 31% to 13%.¹⁵ Factors identified in this study as predictive for ipsilateral breast tumor recurrence included moderate to marked comedo necrosis, solid tumor type, moderate to marked lymphoid infiltration, and multifocality.¹⁵

Treatment of the Case Patient

The patient described in the case presentation had a VNPI score of 4. Based on the better outcomes of DCIS patients who receive radiation treatment following lumpectomy, the case patient received post-lumpectomy radiation treatment.

Genetic screening for breast cancer susceptibility gene mutations are now available.^{16,17} Genetic screening has been recommended for women with a family history of breast cancer in a female relative younger than 50 years, the presence of 2 first-degree relatives with breast cancer, a male relative with breast cancer, or a family history of ovarian cancer in a relative younger than 50 years.¹⁶ The patient in the case presentation does not meet this criteria and did not undergo genetic screening.

Tamoxifen for Patients with DCIS

The results of a large randomized control trial of

1804 female patients with intraductal breast cancer randomized to lumpectomy and radiation treatment alone vs lumpectomy, radiation treatment, and 20 mg daily oral tamoxifen clearly demonstrated benefit for the tamoxifen-treated group.¹⁸ Over a 74-month median follow-up period, there were fewer breast cancer events in the tamoxifen group (8.2% vs 13.4%, $P = 0.0009$).¹⁸ The cumulative incidence of invasive breast cancer in the tamoxifen group was 1.8% compared to 2.35% in the other group.¹⁸ Notably, there was a higher incidence of deep venous thrombosis and pulmonary embolism in the tamoxifen group (< 1% vs 0.4%) as well as an increased incidence of endometrial cancer in the tamoxifen group (1.5 vs 0.45 per 1000 patients per year).¹⁸ Thus, the use of tamoxifen for chemoprevention of breast cancer in the case patient was contraindicated by the recent history of lower extremity thrombophlebitis.

CONCLUSION

The widespread adoption of mammography screening programs for breast cancer in the United States over the past 2 decades has led to a substantial increase in the number of cases of DCIS diagnosed each year. Very small intraductal carcinomas, such as that found in the case patient, generally carry an excellent prognosis. The recommended treatment for most cases of DCIS consists of lumpectomy with wide surgical margins, followed by radiation therapy. Mammography will continue to play a key role in the fight to reduce the incidence and mortality associated with breast cancer in women.

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