Ductal Carcinoma In Situ

This interactive feature addresses the approach to a clinical case. A case vignette is followed by specific options, neither of which can be considered correct or incorrect. In short essays, experts in the field then argue for each of the options. Readers can participate in forming community opinion by choosing one of the options and, if they like, providing their reasons.

CASE VIGNETTE

A WOMAN WITH DUCTAL CARCINOMA IN SITU
Andrea L. Merrill, M.D.

Debbie is an otherwise generally healthy 54-year-old postmenopausal woman who presents to your breast surgery clinic one afternoon with a new diagnosis of ductal carcinoma in situ (DCIS) in her right breast. Her medical history is notable only for mild hypertension and hypothyroidism. Her current medications include hydrochlorothiazide, levothyroxine, and a multivitamin. She is an eighth-grade math teacher and is married, with two children. She has never smoked, and she drinks one or two glasses of wine per week. Her family history is notable for breast cancer in her mother at the age of 68 years.

She has undergone yearly screening mammography since she was 40 years of age. Last month, she had her annual screening and a small cluster of microcalcifications was found. A biopsy of the area revealed low-grade, estrogen- and progesterone-receptor–positive DCIS.

This new diagnosis of DCIS has caused marked anxiety for Debbie. She has spent time researching her condition on the Internet as well as speaking with friends and family. She tells you that she feels overwhelmed by the various treatment options. She states a strong preference to avoid mastectomy, if possible, and asks whether she needs radiation therapy. She also states that she read a recent article that suggested that she may not need any treatment. But this possibility scares her because she is worried that the DCIS might recur or turn into invasive cancer; she knows a neighbor who died from breast cancer after an initial diagnosis of DCIS.

Your physical examination finds no abnormalities of the breast or axilla. She has a body-mass index (BMI, the weight in kilograms divided by the square of the height in meters) of 28 and size 36C breasts without ptosis. After reviewing her mammogram, you see only a small 1-cm area of microcalcifications that would be amenable to a lumpectomy with needle localization of the lesion.

After completing your thorough review of Debbie’s history, physical examination, and imaging results, you sit down with her to discuss treatment options. What do you advise?

TREATMENT OPTIONS

Option 1: Recommend watchful waiting with close observation.
Option 2: Recommend lumpectomy with or without radiation.

To aid in your decision making, each of these approaches is defended in a short essay by an expert in the field. Given your knowledge of the patient and the points made by the experts, which option would you choose? Make your choice, vote, and offer your comments at NEJM.org.

TREATMENT OPTION 1

Recommend Watchful Waiting with Close Observation
Laura Esserman, M.D., M.B.A.

The first and most important message for Debbie is that her condition is not an emergency. The decision is about how to prevent a future breast cancer. Her recent biopsy results add information about her risk. Low grade DCIS is not a cancer, and her particular diagnosis is most similar to atypia.

I would explain to Debbie that breast cancer and DCIS are not one entity but a spectrum of...
conditions that range from indolent to aggressive. She is most likely to be at risk for an indolent cancer, which can be treated successfully at the time of diagnosis with lumpectomy and endocrine therapy, without radiation.\(^1\) Not surprisingly, evidence shows that radiation (after lumpectomy) for DCIS does not change mortality,\(^2\) and therefore the harms of radiation outweigh the benefits.\(^3\) The question is whether she can forgo lumpectomy and just choose active surveillance at this time.

In the majority of women with DCIS, invasive cancer will not develop. In fact, the chance of dying from breast cancer after a diagnosis of DCIS is similar to the risk in the average person without DCIS. Debbie's risk of breast cancer extends over 10 to 20 years, not the next few months. Therefore, a preventive approach is appropriate, including exercising 30 minutes a day, reducing her BMI to 25 or less, and initiating endocrine risk-reducing therapy. Endocrine therapy has been shown, in randomized trials, to decrease the chance of getting breast cancer by at least 50%.\(^4\)

Debbie is anxious about doing too little but does not want a mastectomy. When a person embarks on a path that is less well traveled, joining a peer-reviewed clinical study can provide additional reassurance. The goal of surveillance and endocrine risk-reduction is to learn, over time, whether more treatment is needed. If she were at my institution, I would offer her participation in the Cancer and Leukemia Group B (CALGB) 40903 study (ClinicalTrials.gov number, NCT01439711), in which a patient first undergoes magnetic resonance imaging (MRI), to rule out invasive cancer and serve as a baseline scan, and then receives aromatase-inhibitor therapy. The lesion is then followed at two consecutive 3-month intervals with repeat MRIs to look for progression. If the lesion has largely resolved, excision can be avoided. This option allows us to understand the response that Debbie, in particular, has to the aromatase inhibitor. Another option is participation in a registry that is opening at the Athena Breast Health Network at the University of California, in which a molecular test (Oncotype DCIS) is used to reclassify low- or intermediate-grade DCIS as indolent lesions of epithelial origin (IDLES)\(^5\) or atypical lesions. This reclassification then allows more informed discussions about the range of treatment options, including observation, treatment with endocrine agents, or lumpectomy, as appropriate.

Many patients like Debbie, who are anxious about their disease, can be reassured that DCIS is not an emergency. There is time to see how their situation will evolve before they have to make a decision about surgery. Participating in trials and registries helps us all develop the best options going forward. Close follow-up should minimize any risk. Debbie has plenty of time to think about what treatment she wants, and starting with observation still leaves all options open in the future.

Disclosure forms provided by the author are available with the full text of this article at NEJM.org.

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TREATMENT OPTION 2

**Recommend Lumpectomy with or without Radiation**

Monica Morrow, M.D.

In a healthy 54-year-old woman who is concerned about future breast-cancer risk, watchful waiting is not the appropriate choice. A meta-analysis of 1385 women with low- or intermediate-grade DCIS diagnosed by core biopsy\(^6\) indicates that the likelihood that invasive carcinoma, not present in the needle-biopsy specimen, is present in her lesion is approximately 20%. The diagnosis of invasion would change therapy, and a 20% rate of delay in diagnosis of invasive cancer is too high to justify avoidance of lumpectomy, a brief outpatient operation with minimal complications.

Once the diagnosis of DCIS is certain, clear communication between surgeon and patient regarding the risks of recurrence and death is crucial, since patients with DCIS tend to greatly overestimate the risk of death from breast cancer.\(^7\) Debbie can be reassured that there is no necessity for mastectomy, and data from clinical trials will help to inform her decision regarding radiotherapy. In the subgroup of patients in the Eastern Cooperative Oncology Group (ECOG) 5194 study with 12 years of follow-up, excision alone for low-to-intermediate-grade DCIS less than 2.5 cm in size was associated with a 14.4% incidence of local recurrence.\(^8\) In a trial specifi-
cally examining the benefit of radiotherapy in patients with low-risk DCIS (defined as low-to-intermediate grade, with a lesion less than 2.5 cm in size and a margin of 3 mm or greater), the use of radiotherapy reduced 7-year local recurrence rates from 6.7% to 0.9%; invasive recurrence was seen in 42% of the women in the no-radiotherapy group. Although studies have not shown a survival benefit with radiotherapy, invasive local recurrence is associated with an increased risk of death from breast cancer, and prevention of any recurrence is a major factor in the selection of therapy for many women with DCIS, even if it has no effect on survival.

In contrast to the body of evidence regarding outcomes of DCIS treated with excision, there are essentially no data on the outcome of DCIS managed with observation. Excellent outcomes with treatment do not necessarily translate into excellent outcomes without treatment. Evidence-based shared decision making is impossible owing to a lack of knowledge about the risk that invasive cancer will develop, the likelihood of growth of DCIS precluding breast-conserving surgery, and even appropriate imaging methods and intervals for follow-up. The ongoing Low Risk DCIS (LORIS) trial (Current Controlled Trials number, ISRCTN27544579) in the United Kingdom (comparing surgery with active monitoring for low-risk DCIS) will provide critical data to inform this discussion. This study will randomly assign women 46 years of age or older with screening-detected calcifications diagnosed as non–high-grade DCIS to surgery or observation with annual mammography; the end point will be the development of invasive cancer at 5 years.

In the absence of such information, observation of DCIS without excision in women who are not at high risk for death from other causes cannot be considered an appropriate approach outside the setting of a clinical trial.

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