

Christopher Flynn¹, Donald R. Lannin², and Fattaneh A. Tavassoli¹

Department of ¹Pathology, Yale School of Medicine, and the Department of ²Surgery, Yale-New Haven Hospital, New Haven, CT

ABSTRACT

Introduction: Ductal Intraepithelial Neoplasia (DIN)/Ductal Carcinoma *In Situ* (DCIS) is a non-invasive process limited to the ducts and lobules of the breast. Nonetheless, as many as 9% of DIN cases have been reported to have lymph node (LN) involvement by “metastatic carcinoma.” Among the previously reported series, however, were cases suspicious for microinvasion. A large number of the reported cases were also treated by lumpectomy and consequently an occult infiltrating carcinoma may have gone undiagnosed. Confounding the issue, patients regularly have at least one if not multiple biopsies and/or aspirations before the final excision. To determine the frequency of LN involvement in cases of DIN/DCIS and the contribution of previous instrumentation, we evaluated all pure DIN/DCIS lesions treated by total mastectomy and sentinel lymph node (SLN) evaluation.

Design: At our institution, SLN assessment is routinely performed on all DIN/DCIS lesions treated by mastectomy. A total of 252 mastectomies with DIN/DCIS and a SLN evaluation from 2002-2012 were retrieved. All clinical and pathological data were reviewed. The clinicopathological features of the cases with any LN involvement were compared to those without LN involvement to determine if there was a correlation between any lesional or clinical characteristics (i.e. size or type of DIN/DCIS, number of procedures prior to mastectomy/sentinel lymph node biopsy, etc.) and the nodal status.

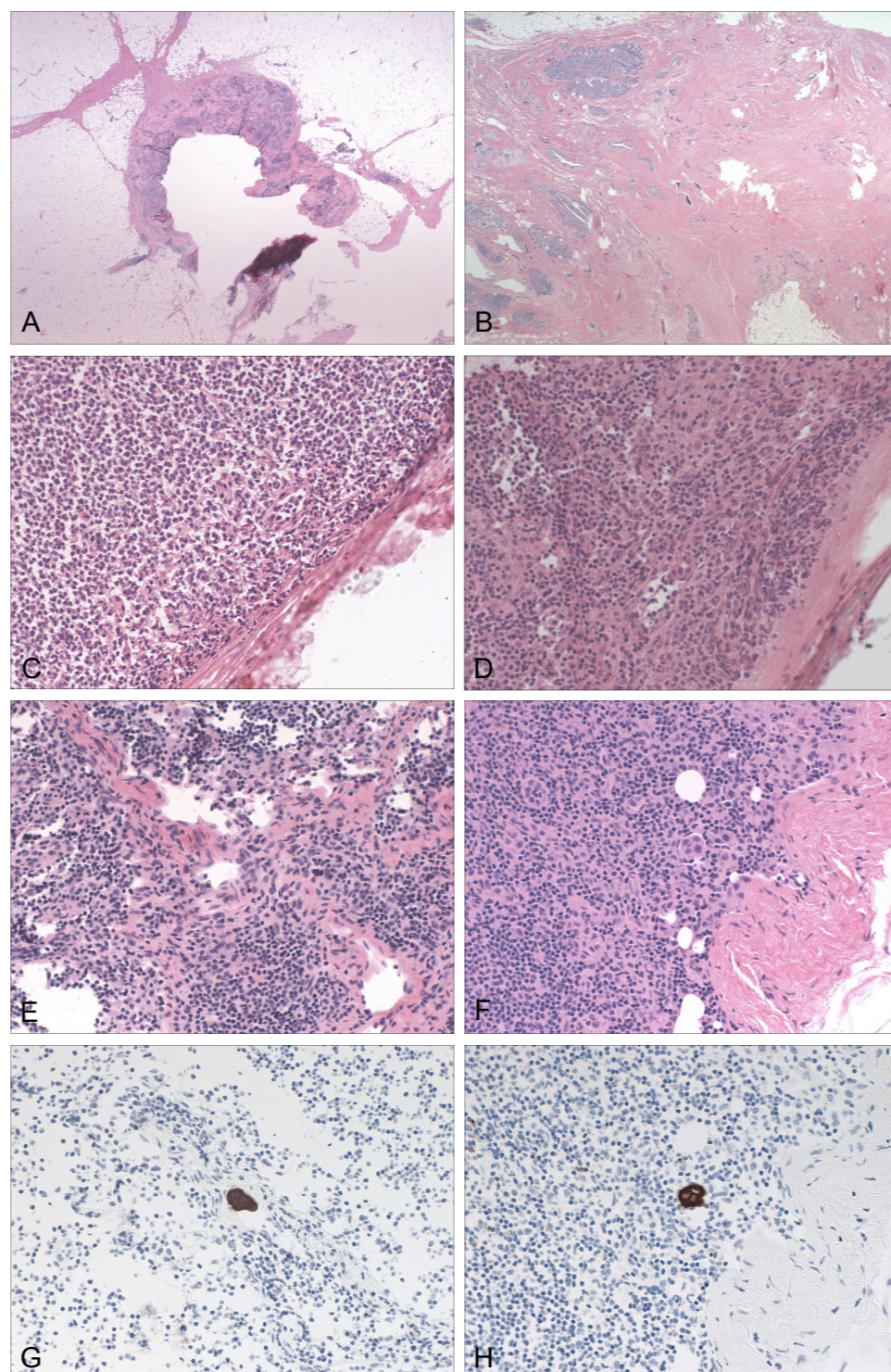
Results: Of the 252 cases evaluated, 9 (3.6%) had tumor cells in the SLN. All nine (100.0%) of these were isolated tumor cells (ITC) identified by immunohistochemistry only. Overall, the 9 patients with nodal involvement had, on average, 3.7 samplings prior to the mastectomy compared to 2.1 among those patients with no nodal involvement.

Conclusions: The frequency of LN involvement in DIN/DCIS has been reported to be as high as 9%. The 3.6% in our study is substantially lower. This may reflect the more stringent criteria used in our study with the exclusion of any case with microinvasion and the limitation of our cases to mastectomy specimens. Given this low frequency and the fact that only ITC were found in the involved LNs, it would be reasonable to hypothesize that these patients are at no higher risk for subsequent metastasis or recurrence than patients with DIN and no nodal involvement. Also, the presence of neoplastic cells may well be secondary to prior sampling manipulations.

INTRODUCTION

- By definition, Ductal Intraepithelial Neoplasia (DIN)/ Ductal Carcinoma *In Situ* (DCIS), is in-general contained by myoepithelial cells and the basement membrane.
- Consequently, the neoplastic cells cannot access the lymphatics or subsequently the regional lymph nodes.
- Therefore, reports of approximately 9% of DIN/DCIS cases without accompanying infiltrating ductal carcinoma (IDC) having at least one positive lymph node appear contradictory.
- Part of the explanation may come from the design of the previous studies: 1. The majority of the cases reported had DIN diagnosed by FNA and lumpectomy and not mastectomy, 2. Cases suspicious for microinvasion were included in some of the studies.
- Due to the possibility of occult IDC in these situations the percent of positive lymph nodes in case of DIN may be exaggerated.

FIGURE 1



A-B. Biopsy/surgery site changes. C-H. Area of “metastatic” cells on frozen section (C-D), H&E (E-F), and AE1/AE3 immunostain (G-H).

METHODS & MATERIALS

- The pathology and surgery databases at our institution were searched for all cases of DIN/DCIS.
- All reports were reviewed and cases were excluded if they had prior or concurrent ipsilateral IDC, microinvasion, and/or did not have a mastectomy with a sentinel lymph node biopsy.
- Clinicopathologic characteristics (age, size of DIN/DCIS, type of DIN/DCIS, number of procedures performed prior to the mastectomy, etc.) were collected for each case.
- The cases were divided by their lymph node status (positive vs. negative).
- Statistical analysis was performed using Excel and Prism software. p-value < 0.05 was considered significant.

RESULTS

- A total of 252 cases of mastectomy with a sentinel lymph node biopsy for DIN/DCIS, without IDC or microinvasion, were identified.
- 9 cases (3.6%) had a “positive” lymph node.
- All 9 lymph nodes (100%) contained only isolated tumor cells.
- The 9 patients with a “positive” lymph node had, on average, 3.7 surgical procedures prior to the mastectomy compared to only 2.1 procedures in the patients who had negative lymph nodes.

CONCLUSIONS

- Compared to the current study, lymph node positivity in ~9% of DIN/DCIS cases in prior reports appears significantly elevated.
- One explanation for the difference in this study compared to previous studies is the elimination of any case that did not have a completion mastectomy along with the sentinel lymph node biopsy. The finding of ductal intraepithelial neoplasia (DIN/DCIS) in a core biopsy does not exclude the possibility of an occult infiltrating carcinoma remaining in the residual breast. By at least performing a thorough gross exam with appropriate sampling of the mastectomy specimen, one can have a greater degree of confidence that an occult invasive carcinoma is not present.
- Secondly, the elimination of cases with microinvasion, which by definition are no longer only intraepithelial disease, from the current study should also decrease the rate of positive lymph nodes.
- The relatively increased number of biopsies/procedures prior to the sentinel node assessment among patients with “positive” sentinel lymph nodes and those with completely negative lymph nodes suggests that the isolated tumor cells may not be true metastases, but rather iatrogenic. For example, prior to the final mastectomy, the patient whose specimen is pictured in Figure 1 B,D,F, and H underwent 20 passes of a 9 gauge needle at two different sites each with intraepithelial disease. The subsequent lumpectomy had positive initial margins with seven additional margins, one of which was also positive. Fragmentation, dislodgement, and benign transport could have resulted in pN0(i+) status.