SEMINARS IN BREAST DISEASE

Independent Consultative Review for Breast Disease: Implications for Quality, Cost, and Outcomes

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A pathology second opinion of breast biopsy material has many proponents, but is still infrequent in actual practice. Discrepancies between an initial and a review diagnosis vary in frequency between the type of review, cursory or comprehensive, and the specific type of lesion being examined. Among patients with microscopic proliferative lesions, the discrepancy rates can exceed 20%. Discrepancies with an initial diagnosis of atypical ductal hyperplasia and their potential impact on treatment costs are explored. The author's recent experience from a consult second opinion practice is reviewed and the types and frequency of discrepancies are discussed.

KEYWORDS breast pathology, consultations, discrepancies, costs, error rates, implications

A pathology second opinion, an independent evaluation of the histologic slide material for a patient with breast carcinoma, is often advocated but infrequently realized in actual practice. Commonly, patients seek a second opinion from therapists, surgical, medical, and radiation oncologists, but often the pathology slides and materials that form the basis of treatment decisions and from which prognosis is estimated are not reviewed independently. In these circumstances, therapy is based on the original written pathology report and addenda documenting biomarkers. A growing minority of hospitals require actual review of the outside pathology slides before a patient undergoes definitive treatment, but usually this is a cursory confirmation that carcinoma is present, not a comprehensive review. Such confirmatory reviews generally result in change in diagnosis in the order of 1.4% or less.[1] Concordance is much higher in situations in which there is a national policy of training and uniform standards for breast cancer diagnosis.[2]

Comprehensive reviews more commonly occur in interdisciplinary breast centers where formal treatment conferences review the clinical features, imaging, and pathology of a particular patient's breast cancer. Comprehensive review of the pathology slides may demonstrate more frequent errors or oversights in the initial report particularly for review of outside referrals.[3] Literature sources cite error rates of 7.8%[4] and 13.2%,[5] but services dedicated to breast pathology second opinion suggest an even larger error rate as recently cited in a Susan G. Komen Foundation White Paper.[6] Additionally, noncompliance with breast cancer pathology reporting guidelines can also result in both errors and significant omissions. Wilkinson and coworkers[7] note 23% of breast resections without inked margins, 75% without oriented margins, and 94% without Scarf-Bloom-Richardson grade/score.

Patient recognition and understanding of the role that proper pathologic evaluation plays in their treatment is generally poor, and, not infrequently, patients suppose erroneously that their surgeon created the report.

Certain classes of lesions generate a greater likelihood of discrepant and/or erroneous diagnoses. These are exemplified by proliferative and in situ neoplastic lesions of microscopic size, particularly in core biopsy material. Atypical hyperplasia is diagnosed in approximately 7–10% of core biopsies, the majority representing stereotactic procedures for microcalcification. An estimated 120,000 such biopsies occur in the United States each year. Formal review of diagnoses of ductal carcinoma in situ (DCIS) and atypical ductal hyperplasia (ADH) was the consensus recommendation of the Image-Detected Breast Cancer Consensus[8] and had been previously recommended by a joint American Cancer Society/National Cancer Institute informational guide for patients.

Diagnostic Discrepancies in ADH

Three studies have looked at the concordance between an initial diagnosis and the review diagnosis for core biopsy

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Table 1 Agreement Between an Initial Diagnosis of Atypical Hyperplasia and Review Diagnoses Based on Core Needle Biopsy

	N	Benign	Atypical Lobular Hyperplasia	ADH	DCIS	Invasive
Verkooijen et al.[9]	24	10	—	8	5	1
Collins et al.[10]	67	14	1	41	10	1
Jackman, et al.[11] and Lagios	101	26	7	51	15	2
Total *N*	192	50	8	100	30	4
%	100	26	4	52	16.5	2

material classified as ADH[9-11] (Table 1). On review, a mean 26% were classified as benign and/or proliferative breast disease without atypia. An adequate concordant core biopsy diagnosis of proliferative breast disease does not require a subsequent open excision for definitive diagnosis or treatment. On average, 26% of such patients could have been spared the standard surgical recommendation of an open biopsy and the considerable cost and morbidity of such procedures. A substantial percentage of such patients also would be advised to take a selective estrogen receptor modulator (SERM; tamoxifen, raloxifene, etc.) or an aromatase inhibitor for chemoprevention. Such interventions, both surgical and hormonal, have no significant benefit for patients with proliferative breast disease, but all such patients would be at risk for the recognized complication of SERMs, including early menopause, thromboembolic events and bone loss, arthralgias and myalgias with aromatase inhibitors. In addition, there would be costs related to closer follow-up and surveillance, mammographic and potentially magnetic resonance imaging (MRI) staggered at 6-month intervals. Finally, there would be the unquantifiable costs of increased anxiety and dread among some of these patients, a fraction of which might elect bilateral prophylactic mastectomy as an alternative.

The aggregate costs for an open excision for the 26% of patients with an improper diagnosis of ADH can be estimated but will vary with the locale of the practice. However, in the San Francisco Bay area, an open surgical excision ranges from $4500 to $6500. Pathology charges for examination of the excision, including immunohistochemistries in some cases, run $400 to $500. Chemoprevention with tamoxifen for non-Medicare patients runs $500 year and an aromatase inhibitor $4980 year; total costs of $2500 to $25,000 for a 5-year course of treatment. Additional mammography and MRI might total $1500/year. These unnecessary interventions can result in an estimated minimal cost of $10,000 for the first 5 years for each misdiagnosed patient. These are direct costs and do not include the cost of treatment for complications, such as deep vein thromboses, pulmonary emboli, bone fractures secondary to osteoporosis, etc. Although some of these are one-time expenses, SERMs and aromatase inhibitors are scheduled for 5 years. The additional surveillance that may be predicated on a diagnosis of ADH could extend over the patient's remaining lifetime.

An additional 15–17% of core biopsies initially diagnosed as ADH actually represent DCIS, and of that number, 1–2% of the total were invasive. These patients might have been better served by a carefully planned oncological resection and sentinel node biopsy for invasive lesions when present rather than a limited diagnostic open biopsy.

Diagnostic Discrepancies in a Consult Practice

My consult practice primarily provides an independent review of pathology correlated with imaging for self-referred patients and oncologists. Most of the consults are not predicated on the basis of rare or challenging diagnostic problems submitted by pathologists. These are allegedly horses not zebras. Each case is prospectively classified at the time of review as concordant or discrepant, and a brief note specifies the particulars. For the calendar years 2007–2008, 597 reviews resulted in 141 in which either the diagnosis or imaging correlation was discrepant. These 24% were not all of equal weight in terms of their clinical consequences, although that can be debated.

Reclassification of DCIS accounts for 22% of the discrepant diagnoses, most of which represent diagnostic downgrades to columnar alteration with hyperplastic features (N13), ADH (N5), atypical lobular hyperplasia (N4), and one case reclassified as pleomorphic lobular carcinoma in situ with necrosis. Four cases of DCIS were reclassified as invasive carcinomas of T1mic and T1a size. Although most such patients reclassified as atypia would have received an open biopsy, none would be expected to undergo irradiation or additional surgery for margins for a benign diagnosis.

Reclassification of submitted diagnoses of ADH represents 16% of the discrepancies. The majority were downgraded to columnar alteration with hyperplastic features (N12), benign proliferative breast disease (N2), and in one case to postirradiation changes. Two cases of submitted ADH were reclassified as DCIS. These downgraded patients would also not be offered chemoprevention for a benign diagnosis.

Fifteen cases submitted with a diagnosis of high-grade DCIS were downgraded to intermediate grade (N14) and low grade (N1). This represents 10.6% of the discrepancies. In part, this reflects the persistent tendency to classify any DCIS with "comedo" (zonal) necrosis as high-grade regardless of nuclear morphology or architecture, rather than basing the classification on nuclear grade and the presence or absence of necrosis.[12] Reducing the grades of the DCIS will impact a patient's Van Nuys Prognostic Index score and can make the difference between re-excision or not and substantially alter the benefit of irradiation.