Hypersecretory Hyperplasia with Atypia, Atypical Ductal Hyperplasia (ADH), and Ductal Carcinoma In Situ (DCIS)

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A special and uncommon group of breast lesions with cytoplasmic and luminal features of secretion constitutes a minor butimportant group(1). The cells are characterized by bubbly cytoplasm with irregular apical cytoplasmic and nuclear protrusions as well as by secretions.

Lesions characterized by hypersecretory changes and atypia were first described by Rosen (2) and Guerry et al. (3). Althoughthe latter paper by Guerry accepted an atypical hyperplasia category apart from the designation of DCIS, guidelines for segregation are not clearly available. We have attempted the following approach for segregation using our recent experiences as described in this paper. At the most benign end of secretion is the solitary lactational unit, at the other end of obvious ductal carcinoma in situ (DCIS) associated with hypersecretory changes (DCIS-HS). Frequent features of nuclear hyperplasia and/or bizarre nuclei are not proven to have direct clinical significance. Many lobulocentric changes associated with lactational cytoplasmic features may present without the clearcut diagnostic patterns of the most common atypical hyperplasia and low grade DCIS.

We accept (Kasami, M, et al, unpublished) four categories for these changes; one: hypersecretory changes without atypia (HS). Two: hypersecretory hyperplasia with atypia (HHA). The nuclei are often large and pleomorphic. These changes may be regarded as analogous to hypersecretory changes seen in the endometrium and usually referred to eponymously as Arias-Stella changes (4). HHA were characterized by nuclear atypia only (1). When specific features of atypical ductal hyperplasia (ADH)[which have been linked to clinically demonstrated increased breast cancer risk, and have histologic features of low grade DCIS in limited space, usually within a lobular unit] or DCIS are recognized (5-8), then a diagnosis of ADH or DCIS is rendered. Therefore, the third category is ADH associated with hypersecretory changes (ADH-HS), and the fourth is DCIS associated with hypersecretory changes (DCIS-HS). Hypersecretory lesions (HS, HHA, ADH-HS, and CIS-HS) are largely lobular-based, and frequently associated with microcalcifications that are related to the secretory material.

Lactational changes are often present in a limited number of lobular units without the nuclear protrusions, hyperchromatic and large nuclei, loss of polarity and proliferation that occur in HHA. When these lactational changes are present without HHA, they are diagnosed as such and have no known clinical significance by themselves. Lactational changes in many lobular units have been seen in association with hyperprolactinemia.

Cystic changes may occur in more than 30 % of HS. Usually the cystic changes were microscopic and making enlarged lobules. Occasionally, the cysts are large and cystic hyperplasia or carcinoma was diagnosed(2.3).

Similar changes to HHA have been reported by Fraser et al. (10), and found to have an association with formal atypical alterations in the setting of limited core needle biopsies. Similar observations linking columnar alteration of lobules with atypical lobular hyperplasia and tubular carcinoma have been made by Rosen (11) and Goldstein et al (12).

Thus, in this case the diagnostic focus for the most significant lesion is on the true ducts and the presence of micropapillaryatypia/DCIS. A wide excision as a quandrantectomy was performed and minimal ductal atypia was present at the margins of acompletely embedded specimen. Several blocks from the center had extensive (more than three ducts) involved with micropapillary DCIS. Close mammographic followup for reappearance of calcifications is being instituted.

General Agreement in diagnosis and ADH (Atypical ductal hyperplasia) Most biopsies have general agreement in general categories, but there may be variation in interpretation with regard to availability of re-excision, etc.

A recent concern has been lesions without hyperplasia, that tend to be lobular-based and have some nuclear atypia and columnar alteration.

These bear some similarity to lobular based lesions with hypersecretory activity. We believe that these lesions may be associated with formally defined patterns of atypical hyperplasia, but do not have any proven indication other than appearing adjacent to some low grade malignant lesions, usually ductal carcinoma in situ.

References

1)Page DL, Kasami M, Jensen RA: Hypersecretory hyperplasia with atypia in breast biopsies. Pathology Case Reviews 1:36-40,1996

2)Rosen PP, Scott M: Cystic hypersecretory duct carcinoma of the breast. Am J Surg Pathol 8:31-41, 1984

3)Guerry P, Erlandson RA, Rosen PP: Cystic hypersecretory hyperplasia and cystic hypersecretory duct carcinoma of the breast. Cancer 61:1611-1620,1988

4) Arias-Stella J: Abnormal endometrial changes associated with the presence of chorio nic tissue. Arch Pathol 58:112,1954

5) Page DL, Dupont WD, Rogers LW et al: Atypical hyperplastic lesions of the female breast: a long-term follow-up study. Cancer 55:2698-2708,1985

6) Page DL, Anderson TJ: Dagnostic Histopathology of the Breast. Churchill livingstone, Edinburgh, 1987p137

7) Scott MA, Laqios MD. Axelsson K et al. Ductal carcinoma in situ of the breast. Hum Pathol 28:967-73,1997

8) O'Malley FP, Page DL, NelsonEH et al. Ductal carcinoma in situ of the breast with apocrine cytology: definition of a borderline category. Hum Pathol 25:164-8,1994

9) Page DL, Rogers LW. Combined histologic and cytologic criteria for the diagnosis of mammary atypical ductal hyperplasia. Hum Pathol 3:1095-1097,1992

10)Fraser JL, Sughra R, Chorny K, et al: Columunar Alteration with prominent _ apical snouts and secretions. Am J Surg Pathol
22:1521-1527,1998

11) RosenPP: Columnar cell hyperplasia is associated with lobular carcinoma in situ and tubular carcinoma. Am J surg Pathol 23 :1561,1999

12) Goldstein NS, O'Malley BA: Cancerization of small ectatic ducts of the breast by ductal carcinoma in situ cells with apocrine snouts. Am J Clin Pathol 107:561-566,1997

13)Collins LC, Connolly JL, Page DL, Goulart RA, Pisano ED, Fajardo LL, Berg WA, Caudry DJ, McNeil BJ, Schnitt SJ. Diagnostic agreement in the evaluation of image-guided breast core needle biopsies: results from a randomized clinical trial. Am J Surg Pathol 28 (1): 126-31, 2004.

14) Dupont WD, Page DL. Risk factors for breast cancer in women with proliferative breast disease. N Engl J Med 312 (3): 146-51, 1985.

15) Dupont WD, Page DL, Parl FF, Plummer WD, Jr., Schuyler PA, Kasami M, Jensen RA. Estrogen replacement therapy in women with a history of proliferative breast disease. Cancer 85 (6): 1277-83, 1999.

16). Ely KA, Carter BA, Jensen RA, Simpson JF, Page DL. Core biopsy of the breast with atypical ductal hyperplasia: a probabilistic approach to reporting. Am J Surg Pathol 25 (8): 1017-21, 2001.

17) Jensen RA, Page DL. Ductal carcinoma in situ of the breast: impact of pathology on therapeutic decisions. Am J Surg Pathol 27 (6): 828-31, 2003.

18) Marshall LM, Hunter DJ, Connolly JL, Schnitt SJ, Byrne C, London SJ, Colditz GA. Risk of breast cancer associated with atypical hyperplasia of lobular and ductal types. Cancer Epidemiol Biomarkers Prev 6 (5): 297-301, 1997.

19) Page DL, Dupont WD, Rogers LW, Rados MS. Atypical hyperplastic lesions of the female breast. A long-term follow-up study. Cancer 55 (11): 2698-708, 1985.

20) Schnitt SJ. The diagnosis and management of pre-invasive breast disease: flat epithelial atypia--classification, pathologic features and clinical significance. Breast Cancer Res 5 (5): 263-8, 2003.

21) Schnitt SJ, Vincent-Salomon A. Columnar cell lesions of the breast. Adv Anat Pathol 10 (3): 113-24, 2003.

22) Sneige N, Lim SC, Whitman GJ, Krishnamurthy S, Sahin AA, Smith TL, Stelling CB. Atypical ductal hyperplasia diagnosis by directional vacuum-assisted stereotactic biopsy of breast microcalcifications. Considerations for surgical excision. Am J Clin Pathol 119 (2): 248-53, 2003.