ORIGINAL ARTICLE

Audit of fibroepithelial tumors of the breast in a Nigerian tertiary institution

AO Daramola, OA Oguntunde[1], NA Awolola

Department of Anatomic and Molecular Pathology, Lagos University Teaching Hospital/College of Medicine University of Lagos, [1]Department of Anatomic and Molecular Pathology, Lagos University Teaching Hospital, Lagos, Nigeria

Abstract

Background and Objectives: Fibroepithelial lesions are the most common lesions of the breast seen in our laboratory consisting of fibroadenomas (FAs) and phyllodes tumors (PT). The aim of the study was to audit all fibroepithelial lesions and to reclassify all confirmed cases of PTs seen in the study period according to standard criteria.
Methodology: Records and slides of fibroepithelial lesions of the breast received at the department between January 2008 and December 2013 were retrieved and reviewed by the authors.
Results: Out of the 1242 fibroepithelial lesions of the breast retrieved, all but 19 were FAs. The 19 were initially reported as PT: 11 benign, 2 borderlines, 2 malignant, and 4 not classified; however, only 16 of these 19, PTs (84%) met the WHO criteria on review. The remaining 3 (16%) turned out to be FAs based on the absence of stroma overgrowth and hypercellularity. The PTs were reclassified into benign PT, borderline PT, and malignant PT accounting for 75% (12/16), 18.7% (3/16), and 6.3% (1/16), respectively. All of the PTs previously not classified turned out benign on review. One of the borderline PTs was originally reported as malignant PT. All cases initially diagnosed as FAs did not change on review.
Conclusion: These results show that FAs are rarely misdiagnosed. The three cases misdiagnosed as phyllodes may have been prevented if standard data sets were in use. Cases simply referred to as PT without further classification, limit the patients' access to appropriate management as accurate classification helps in the overall management and prognostication.

Key words: Fibroadenoma, fibroepithelial tumor audit, phyllodes tumor grade

Date of Acceptance: 15-Jan-2016

Introduction

Fibroepithelial lesions of the breast include basically fibroadenoma (FA) and phyllodes tumor (PT). They are neoplasms with dual proliferation of the epithelial and stromal component. FA which is by far more common accounts for the vast majority of benign breast tumor especially in the young.[1]

PT, on the other hand, is a rare fibroepithelial breast neoplasm that resembles FA but has a totally different clinical course and management. It accounts for 0.3–0.9% of all primary breast tumors.[2,3]

PT was originally described in 1838 by Muller, who believed the lesion to be benign but called it cystosarcoma because

Address for correspondence:
Dr. AO Daramola,
Department of Anatomic and Molecular Pathology,
Lagos University Teaching Hospital/College of Medicine
University of Lagos, Lagos, Nigeria.
E-mail: detoladaramola@gmail.com

Access this article online

Quick Response Code:

Website: www.njcponline.com

DOI: 10.4103/1119-3077.183251

How to cite this article: Daramola AO, Oguntunde OA, Awolola NA. Audit of fibroepithelial tumors of the breast in a Nigerian tertiary institution. Niger J Clin Pract 2016;19:645-8.

of its cystic change and fleshy cut surface cited by Bumpers 2015.[4] This tumor has a variable but usually benign course with a propensity to locally recur and to metastasize.

Histologically, PTs of the breast are biphasic fibroepithelial tumors composed of epithelial elements arranged in cleft-like ducts surrounded by a predominant connective tissue stroma typically organized in leaf-like structures. This mesenchymal component shows morphologic patterns that range from fibroadenoma-like to frankly sarcomatous.[5,6]

These rare fibroepithelial lesions are classified as benign, borderline, and malignant based on cellular pleomorphism, stromal hypercellularity, mitotic activity, stromal overgrowth, and margins.[5,7]

The standard treatment for PT is wide surgical excision with a clear margin of more than 1 cm as breast conservation is important to most women. However; mastectomy becomes necessary when the tumor cannot be removed with adequate clearance.[8,9]

Methodology

This is a hospital-based retrospective study of all fibroepithelial lesions of the breast received at the department between January 2008 and December 2013. All the slides of FA and PT made between the study periods were retrieved alongside their histopathology reports. They were reviewed simultaneously by two pathologists with specialty interest in breast and a 3rd-year senior resident; no recuts were performed.

The core criteria used for the distinction of PT from FA were prominent fronds or leaf-like pattern and increased stromal cellularity.[10] The 2012 World Health Organization criteria for PT diagnosis was used in this review.[5] Classification into benign, borderline, and malignant categories relied on the degree of stromal hypercellularity, cellular pleomorphism, mitotic activity, stromal overgrowth, and nature of the margins using the portion with the highest cellular activity and most florid architectural pattern.[7] Cellular pleomorphism was designated little, modest, or marked, whereas stromal hypercellularity was categorized as modest or marked.[5] Stromal mitotic activity was quantified per 10 high-power fields (hpf) of the microscope objective (×40 objective and ×10 eyepiece) in the most mitotically active areas of the stroma.[5] Stromal overgrowth defined as a low-power field (×4 microscope objective and ×10 eyepiece) that comprised only stroma without epithelial elements was labeled absent or present.[5] A benign PT was diagnosed when the lesion showed well-circumscribed margins, modest stromal hypercellularity, little or moderate cellular pleomorphism, occasional mitoses that numbered up to 4/10 hpf, and no stromal overgrowth.[10] A malignant tumor was defined by marked stromal hypercellularity and cellular pleomorphism, presence of stromal overgrowth, brisk mitotic activity (≥10/10 hpf), and invasive margins;[5] the finding of a malignant heterologous element classifies the tumor as malignant.[10] Borderline PT showed some but not all characteristics observed in malignant lesions. All diagnoses made on core biopsy were excluded from the study.

Ethical approval for this study was obtained from the Health and Research Committee of the Institution.

Results

Out of the 1242 fibroepithelial lesions of the breast retrieved all but 19 were FAs. The 19 were initially reported as PT: 11 benign, 2 borderline, 2 malignant, and 4 unclassified. However, only 16 of these 19 PTs (84%) met the criteria on review accounting for approximately 0.8% of all breast tumors and 1.3% of fibroepithelial lesion diagnosed within the study period. The remaining 3 (16%) turned out to be FA based on the architecture, absence of stromal overgrowth, and hypercellularity. The PTs were reclassified into benign PT, borderline PT, and malignant PT accounting for 75% (12/16), 18.7% (3/16), and 6.3% (1/16), respectively. All of the PTs previously unclassified turned out benign. Nearly 100% (12/12) of the benign PTs had stromal overgrowth [Figure 1a], modest stromal hypercellularity, minimal cellular pleomorphism, uniform stroma distribution, without mitotic figures; 92% (11/12) had well-circumscribed margins, whereas the remaining 8% had inaccessible margins. All borderline PTs showed marked stromal overgrowth and hypercellularity [Figure 1b], moderate cellular pleomorphism, heterogenous stromal distribution with mitotic counts of 5–9/10 hpf. One of the borderline PTs was originally reported as malignant PT. The malignant PTs showed all of the latter features in addition to increased mitotic counts of >10/10 hpf, marked stroma

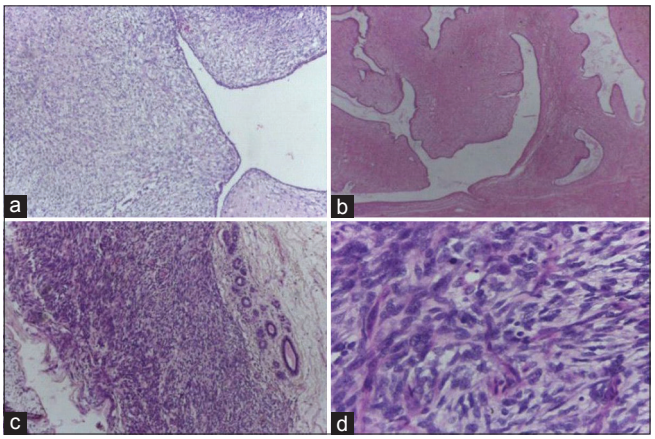

Figure 1: Some morphologic features of benign, intermediate, and borderline phyllodes tumors. Stromal overgrowth in benign phyllodes tumor. (a) Borderline phyllodes tumor (H and E, ×100), (b) marked stromal cellularity (H and E, ×40), (c) marked cellular pleomorphism (H and E, ×40), (d) malignant phyllodes tumor (H and E, ×400)

overgrowth as well as pleomorphism and infiltrative tumor margins [Figure 1c and d]. Tumor margins of two borderline PTs were poorly circumscribed but not infiltrative, the margin of the remaining one was inaccessible. All cases initially diagnosed as FAs did not change on review.

Discussion

FA and PT are two separate lesions with different clinical behaviors. Despite their histologic resemblance, standard criteria are available to distinctly distinguish these entities.

Our study, in concordance with many other literatures, revealed FA as the undisputable most common fibroepithelial lesion.[1,11] The diagnosis of FA is relatively simple and easy except for the cellular variant, which has been reported among even breast pathologist as difficult to distinguish from benign PT.[12] All the FA reviewed in our study did not change which further highlights the unambiguity in the histopathologic diagnosis of simple FA. There were however three out of the previously diagnosed PT, which turned out as FA after the audit. These are believed to be cellular FA as they were encapsulated and maintained the biphasic architecture of FA.

In our study, PTs accounted for 0.8% of all primary breast tumors which parallels <1% incidence rates reported in the literature.[2,3,11] It also accounted for approximately 1.3% of fibroepithelial lesions. This is <2–3% quoted by a couple of authors.[1,13,14] This discrepancy could probably be due to the larger series studied by those authors.

Out of the remaining 16, PTs evaluated; our findings show that benign PT is significantly the most common, followed by borderline and malignant PT sequentially accounting for 75%, 18.7%, and 6.3%, respectively. This proportion is in considerable agreement with other studies showing approximately 40–75% benign tumors, 15–36% borderline, and 7–15% malignant tumors.[9,15,16]

Hundred percentage of the cases termed PT without a class turned out benign on review. This underscores the need for standard institutional datasets histologic diagnosis of this lesion. The clinical implication and surgical management of the three classes differ and as such bear varying prognostic tendencies. The local recurrence rate of PT has been estimated to be about 10–18% with negative and positive resection margins, respectively.[17] Some studies have also shown recurrence occurring in 8–10% of benign, 14–20% of borderline, and 20–59% of malignant.[18,19] It is also worthy of note that a benign variant can transform into a higher grade and recur as borderline or malignant.[1]

In our study, histologic parameters of stromal cellularity infiltrative margins and mitotic figures were largely adequate to classify PTs, and this has been found to be comparable to some literature findings.[3,20-22] There was no heterologous element in any of the PTs reviewed. Heterologous elements have been reported to be very uncommon among PT. Our study had a shortfall of inability to assess margins in two of the cases reviewed. This is probably because the tumor was excised piece-meal. Tumor margin is known to be an important element, especially in predicting local recurrence and has been found to be useful in resolving cases of ambiguity between benign and borderline. Lin *et al*. reported Ki-67 as a marker able to distinguish these two entities with high sensitivity, specificity, and accuracy among other immunohistochemistry panels.[23]

Other biologic markers such as vascular endothelial growth factor, p53, CD34, β-catenin, and IMP3 have been put forward as added diagnostic aids to either enhance sensitivity of distinguishing FA from PTs or in predicting and prognosticating PT.[23,24] Researches are ongoing in this regards and perhaps may be the possible future of accurate diagnosis and grading of fibroepithelial lesion of the breast.

Conclusion

These results show that FAs are rarely misdiagnosed. The three cases misdiagnosed as phyllodes may have been prevented if standard data sets were in use. Cases simply referred to as PT without further classification, limit the patients' access to appropriate management as accurate classification helps in the overall management and prognostication. In summary, morphologic criteria when applied in detail can conveniently diagnose fibroepithelial lesions and aid in the classification of PTs into its subtypes except in very few ambiguous conditions where immunohistochemistry may come in handy. It is therefore recommended that standard datasets should be routinely used in reporting these lesions.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

References

1. Yang X, Kandil D, Cosar EF, Khan A. Fibroepithelial tumors of the breast: Pathologic and immunohistochemical features and molecular mechanisms. Arch Pathol Lab Med 2014;138:25-36.
2. Dyer NH, Bridger JE, Taylor RS. Cystosarcoma phylloides. Br J Surg 1966;53:450-5.
3. Reinfuss M, Mitus J, Duda K, Stelmach A, Rys J, Smolak K. The treatment and prognosis of patients with phyllodes tumor of the breast: An analysis of 170 cases. Cancer 1996;77:910-6.
4. Bumpers HL, Tadros T, Gabram-Mendola S, Rizzo M, Martin M, Zaremba N, *et al*. Phyllodes tumors in African American women. The American Journal of Surgery 2015;210(1):74-9.
5. Tan PH, Tse G, Lee A, Simpson JF, Hanby AM. Fibroepithelial tumors. In: Lakhani SR, Ellis IO, Schnitt SJ, Tan PH, van de Vijver MJ, editors. World

Health Organization Classification of Tumors: Tumors of the Breast and Female Genital Organs. Lyon, France: IARC Press; 2012. p. 143-7.
6. Esposito NN, Mohan D, Brufsky A, Lin Y, Kapali M, Dabbs DJ. Phyllodes tumor: A clinicopathologic and immunohistochemical study of 30 cases. Arch Pathol Lab Med 2006;130:1516-21.
7. Moffat CJ, Pinder SE, Dixon AR, Elston CW, Blamey RW, Ellis IO. Phyllodes tumours of the breast: A clinicopathological review of thirty-two cases. Histopathology 1995;27:205-18.
8. de Roos WK, Kaye P, Dent DM. Factors leading to local recurrence or death after surgical resection of phyllodes tumours of the breast. Br J Surg 1999;86:396-9.
9. Guillot E, Couturaud B, Reyal F, Curnier A, Ravinet J, Laé M, *et al.* Management of phyllodes breast tumors. Breast J 2011;17:129-37.
10. Tan PH, Jayabaskar T, Chuah KL, Lee HY, Tan Y, Hilmy M, *et al.* Phyllodes tumors of the breast: The role of pathologic parameters. Am J Clin Pathol 2005;123:529-40.
11. Rosen PP, editor. Fibroepithelial neoplasms. In: Rosen's Breast Pathology. 2nd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2001. p. 163-200.
12. Lawton TJ, Acs G, Argani P, Farshid G, Gilcrease M, Goldstein N, *et al.* Interobserver variability by pathologists in the distinction between cellular fibroadenomas and phyllodes tumors. Int J Surg Pathol 2014;22:695-8.
13. Campagnaro EL, Woodside KJ, Xiao SY, Daller JA, Evers BM. Cystosarcoma phyllodes (phyllodes tumor) of the male breast. Surgery 2003;133:689-91.
14. Bernstein L, Deapen D, Ross RK. The descriptive epidemiology of malignant cystosarcoma phyllodes tumors of the breast. Cancer 1993;71:3020-4.
15. Karim RZ, Gerega SK, Yang YH, Spillane A, Carmalt H, Scolyer RA, *et al.* Phyllodes tumours of the breast: A clinicopathological analysis of 65 cases from a single institution. Breast 2009;18:165-70.
16. Tsang AK, Chan SK, Lam CC, Lui PC, Chau HH, Tan PH, *et al.* Phyllodes tumours of the breast – Differentiating features in core needle biopsy. Histopathology 2011;59:600-8.
17. Barrio AV, Clark BD, Goldberg JI, Hoque LW, Bernik SF, Flynn LW, *et al.* Clinicopathologic features and long-term outcomes of 293 phyllodes tumors of the breast. Ann Surg Oncol 2007;14:2961-70.
18. Tan PH, Thike AA, Tan WJ, Thu MM, Busmanis I, Li H, *et al.* Predicting clinical behaviour of breast phyllodes tumours: A nomogram based on histological criteria and surgical margins. J Clin Pathol 2012;65:69-76.
19. Lenhard MS, Kahlert S, Himsl I, Ditsch N, Untch M, Bauerfeind I. Phyllodes tumour of the breast: Clinical follow-up of 33 cases of this rare disease. Eur J Obstet Gynecol Reprod Biol 2008;138:217-21.
20. Chaney AW, Pollack A, McNeese MD, Zagars GK, Pisters PW, Pollock RE, *et al.* Primary treatment of cystosarcoma phyllodes of the breast. Cancer 2000;89:1502-11.
21. Cohn-Cedermark G, Rutqvist LE, Rosendahl I, Silfverswärd C. Prognostic factors in cystosarcoma phyllodes. A clinicopathologic study of 77 patients. Cancer 1991;68:2017-22.
22. Kleer CG, Giordano TJ, Braun T, Oberman HA. Pathologic, immunohistochemical, and molecular features of benign and malignant phyllodes tumors of the breast. Mod Pathol 2001;14:185-90.
23. Lin CK, Tsai WC, Lin YC, Yu JC. Biomarkers distinguishing mammary fibroepithelial neoplasms: A tissue microarray study. Appl Immunohistochem Mol Morphol 2014;22:433-41.
24. Ho SK, Thike AA, Cheok PY, Tse GM, Tan PH. Phyllodes tumours of the breast: The role of CD34, vascular endothelial growth factor and ß-catenin in histological grading and clinical outcome. Histopathology 2013;63:393-406.