EJGO European Journal of Gynaecological Oncology

Simultaneous bilateral invasive breast cancer with coexisting benign phyllodes tumor and lymph node metastasis

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Summary

Cases of coincidental phyllodes tumor (PT) of the breast and invasive breast cancer are extremely rare. This case report describes a 58-year-old women with simultaneous bilateral invasive breast cancer. On the left side, the carcinoma was associated with the epithelial component of a PT and presented with lymph node metastasis. To the best of the present authors' knowledge, this is the first report of a PT with simultaneous bilateral breast cancer and equilateral lymph node metastasis. Moreover, associated axillary lymph node metastasis with an invasive ductal carcinoma (IDC) arising from the epithelial component of a PT is extremely rare. In the absence of standardized treatment option, therapy recommendations should be tailored individually upon clinical presentation.

Key words: Phyllodes tumor; Breast tumor; Bilateral invasive ductal cancer; Collision tumor; Lymph node metastasis.

Introduction

Cases of coincidental phyllodes tumor (PT) of the breast and invasive breast cancer are extremely rare [1, 2]. Phyllodes tumors (PT) are rare fibroepithelial neoplasms deriving from intralobular or periductal stroma and ductal epithelium of the breast and most present with a benign phenotype [3]. Any PT that has recognizable epithelial elements may harbor ductal carcinoma in situ (DCIS), lobular neoplasia or their invasive counterparts, although this is an uncommon finding [4, 5]. An invasive ductal carcinoma (IDC) occurring within a PT has usually less aggressive clinical features, and association with lymph node metastasis is extremely rare [2, 6].

Case Report

A 58-year old women from Malaysia presented with a several-month history of growing mass in the left breast. She had no family history of breast or ovarian cancer, and her personal history revealed a diagnosis of thalassemia minor. On physical examination, a large irregular palpable mass was noticed extending to all quadrants of the left breast, associated with a significant asymmetry. Axillary lymph nodes were not enlarged. Ultrasound of the left breast showed an inhomogeneous, lobulated, partly cystic breast tumor approximately 12 cm in diameter. The right breast showed an architectural disturbance approximately 2 cm in diameter at 9 o'clock. Axillary lymph nodes were inconspicuous.

MRI revealed a large, inhomogeneous tumor with signs of hyperperfusion, involving nearly the entire left breast (Figure 1). On the right side a hyperperfused area, 2.3 cm in diameter was identified, accompanied with additional small foci, considered suspicious but without typical signs of malignancy (BI-RADS 4).

Core-needle biopsy was performed on both sides with the diagnosis of a benign PT on the left side and an intermediate-grade IDC, no special type, with a lobular pattern on the right side. The interdisciplinary tumor board recommended a bilateral mastectomy and sentinel lymph node (SLN) biopsies because of the very large size of the PT and a IDC, potentially multi-centric, on the right side. Surgery was performed accordingly.

SLN biopsies showed three incidental micrometastases on

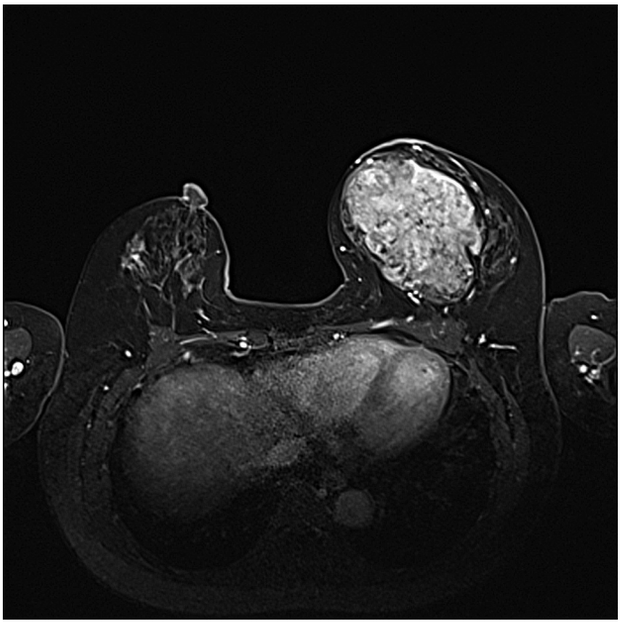

Figure 1. — MRI showing carcinoma of the right breast and PT of the left breast.

Revised manuscript accepted for publication September 10, 2018

Eur. J. Gynaecol. Oncol. - ISSN: 0392-2936
XL, n. 5, 2019
doi: 10.12892/ejgo4839.2019

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Table 1. — *Publications of invasive ductal carcinoma associated with PT and equilateral lymph node metastasis.*

Size of carcinoma (mm)	Hormone receptors (HR) of IDC	Her2 status of IDC	Phyllodes (PT)	Size of PT (mm)	Lymph node metastasis	Therapy	Reference
Small focus	-	-	Borderline	30	1/21 (mi)	Mastectomy, chemo, Radiation	Wu D (2016) [12]
Foci	+	-	Benign	33	4/13	BCT, chemo, radiation, Tamoxifen	Parfitt R (2004) [13]
Small foci	+	n.p.	Malignant	160	2/12	Mastectomy, chemo, radiation, tamoxifen	Hennessy B (2008)[14]
25	+	-	Borderline	100	1/2	Mastectomy, chemo, tamoxifen	Yin-Ju Kuo (2010) [11]
25	n.p.	n.p.	Malignant	155	11/11	Mastectomy, chemo, radiation	Muthusamy (2017) [5]
30% of tumor mass	-	-	Malignant	240	16/16	Mastectomy, chemo, radiation	Shin Y D (2016) [16]

n.p. = not performed.

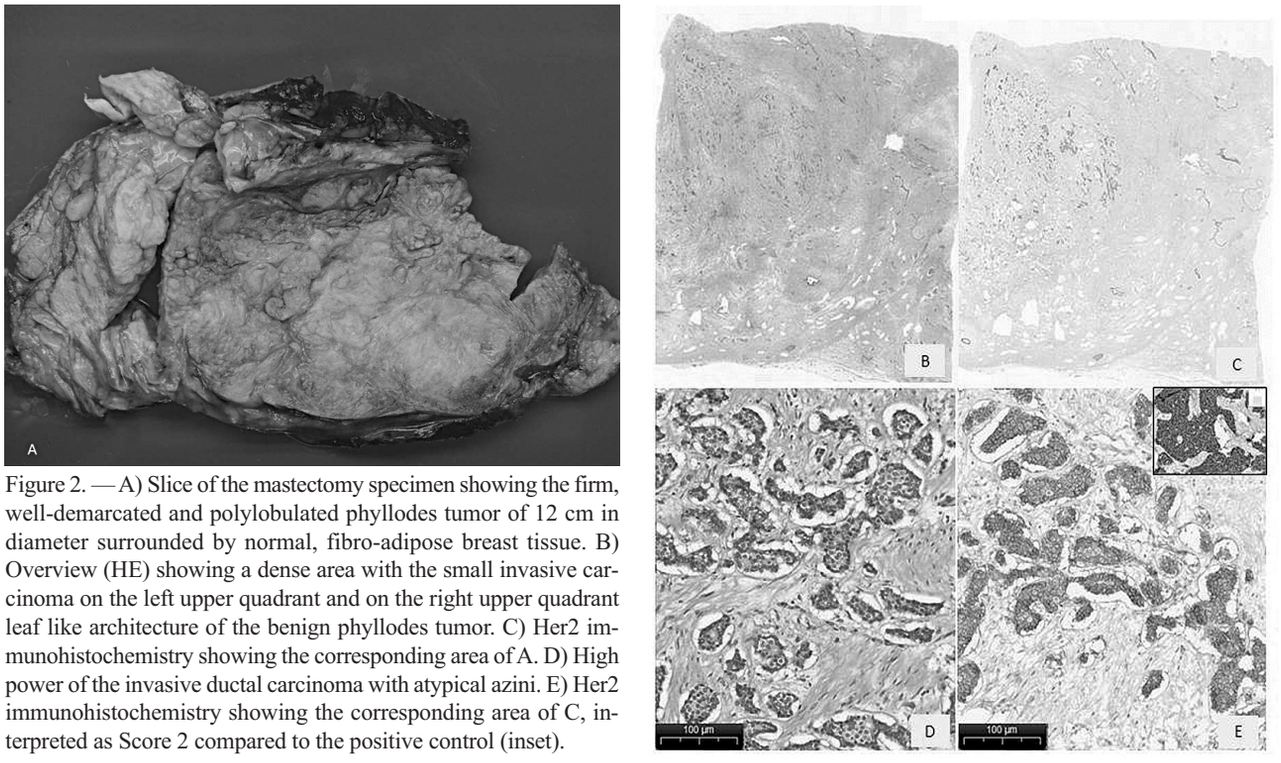

Figure 2. — A) Slice of the mastectomy specimen showing the firm, well-demarcated and polylobulated phyllodes tumor of 12 cm in diameter surrounded by normal, fibro-adipose breast tissue. B) Overview (HE) showing a dense area with the small invasive carcinoma on the left upper quadrant and on the right upper quadrant leaf like architecture of the benign phyllodes tumor. C) Her2 immunohistochemistry showing the corresponding area of A. D) High power of the invasive ductal carcinoma with atypical azini. E) Her2 immunohistochemistry showing the corresponding area of C, interpreted as Score 2 compared to the positive control (inset).

the left side and a negative SLN on the right side. Macroscopically, no suspicious areas were found within the PT. Extensive sampling of PT surgical specimen was performed and a focal, low-grade IDC, NST, 12 mm in diameter, associated with multifocal, intermediate-grade DCIS within a benign PT, 12 cm in diameter, was identified: pT1c pN1mi (sn)(3/3). Histologically, the right breast showed a multi-centric, intermediate-grade IDC, NST with lobular pattern, associated with low-grade DCIS of solid type: pT2 (m), pN0 (sn) (0/1). Both IDCs were estrogen receptor positive (100 and 80%), progesterone receptor positive (100 and 10%), Her2/neu negative, and proliferation rate Ki-67 was low (5% and 2%, respectively) (Figure 2).

A decentralized EndoPredict test performed on the collision cancer revealed a EPclin class of low risk with an estimated ten-year risk of distant metastasis of 10% if a five-year endocrine therapy is warranted. An endocrine therapy with aromatase inhibitor was initiated four weeks after surgery.

Discussion

PTs correspond to less than < 1% of breast neoplasms and show benign or borderline histology in about 70% of cases [4, 7]. Invasive carcinoma evolving from an epithelial component of a PT is a rare phenomenon, as malignant transformation mostly develops in the stromal

component, typically presenting with sarcomatous changes, and a rather hematogenous metastatic spread [8, 9]. Although a higher-grade epithelial transformation within a PT may be focal, extensive sampling of all PTs should be performed [4].

PTs harboring a carcinoma are usually benign or borderline tumors[10]. Carcinomas arising within a PT seem to show considerably less aggressive behavior than other carcinomas of the breast [10], and have to be distinguished from true collision tumors, lacking a transitional area between invasive carcinoma and PT [6]. In some cases, especially in a progressive tumor state, it might be unclear, whether the invasive carcinoma is a result of a malignant transformation process of the PT`s epithelial component or a rather coexisting collision lesion.

In the literature, approximately 40 cases of invasive ductal carcinoma (IDC) occurring within a PT have been documented, and in most cases the PT was classified as benign or borderline [11, 12]. Lymph node metastasis of carcinoma within a benign PT is so far described in only one single case [13]. Most reported cases regarding biphasic malignant PTs with carcinoma and lymph node metastasis could also be interpreted as metaplastic sarcomatoid carcinomas of the breast [14, 15] (Table 1). To the present authors' knowledge, the present case is the first with simultaneous bilateral invasive breast cancer in the presence of a PT and equilateral lymph node metastasis.

Surgical treatment with wide excision margins is the gold standard for PT. Because of insufficient data concerning malignant epithelial transformation within a PT, there is no recommendation concerning surgery of axillary lymph nodes. In most cases, there is no indication for axillary dissection, and sentinel node biopsy associated with low morbidity may be acceptable. Decisions concerning adjuvant treatment should be based on tumor biology and staging.

Conclusions

Malignant epithelial transformation within a PT is rare and may be focal. Clinical features are less aggressive, and axillary lymph node metastasis are extremely rare. As in the present case, imaging methods cannot sufficiently show heterogeneity of a PT [16], which has to be considered when planning a surgical treatment. Furthermore, even a benign PT with a carcinoma component can cause lymph node metastasis. Thus, SLN biopsy should be considered as a standard surgical procedure, especially in PTs of larger size.

References

[1] Quinlan-Davidson S., Hodgson N., Elavathil, L., Shangguo, T.: "Borderline phyllodes tumor with an incidental invasive tubular carcinoma and lobular carcinoma in situ component: a case report." *J. Breast Cancer*, 2011, *14*, 237.

[2] Parfitt J.R., Armstrong C., O'Malley F., Ross J., Tuck A.B.: "In-situ and invasive carcinoma within a phyllodes tumor associated with lymph node metastases". *World J. Surg. Oncol.,* 2004, *2*, 46.

[3] Spitaleri G., Toesca A., Botteri E., Bottiglieri L., Rotmensz N., Boselli S., et al.: "Breast phyllodes tumor: A review of literature and a single center retrospective series analysis". *Crit. Rev. Oncol. Hematol.,* 2013, *88*, 427.

[4] Lakhani S.R., Ellis I.O., Schnitt S.J., Tan P.H., van de Vijver M.J.: "WHO Classification of Tumours of the Breast. Fourth Edition", 2012. Available at: http://apps.who.int/bookorders/anglais/detart1.jsp?codlan=1&codcol=70&codcch=4004

[5] Muthusamy R.K., Mehta S.S.: "Synchronous Malignant Phyllodes Tumor with Skin Ulceration and Invasive Carcinoma as Collision Tumor". *Indian J. Med. Paediatr. Oncol.,* 2017, *38*, 78.

[6] Shin Y.D., Lee S.K., Kim K.S., Park M.J, Kim J.H., Yim H.S., Choi Y.J.*:* "Collision tumor with inflammatory breast carcinoma and malignant phyllodes tumor: a case report and literature review". *World J. Surg. Oncol.*, 2014, *12*, 5.

[7] Moffat C.J., Pinder S.E., Dixon A.R., Elston C.W., Blamey R.W., Ellis I.O.: "Phyllodes tumours of the breast: a clinicopathological review of thirty-two cases". *Histopathology,* 1995, *27*, 205.

[8] Chopra S., Muralikrishnan V., Brotto M.: "Youngest case of ductal carcinoma in situ arising within a benign phyllodes tumour: a case report". *Int. J. Surg. Case Rep.,* 2016, *24*, 67.

[9] Ghosh P., Saha K.: "Ductal carcinoma in situ in a benign phyllodes tumor of breast: A rare presentation". *J. Nat. Sci. Biol. Med.,* 2014, *5*, 470.

[10] Co M., Tse G.M., Chen C., Wei J., Kwong A.: "Coexistence of Ductal Carcinoma Within Mammary Phyllodes Tumor: A Review of 557 Cases From a 20-year Region-wide Database in Hong Kong and Southern China". *Clin. Breast Cancer,* 2017, doi:10.1016/j.clbc.2017.06.001 (epub ahaed of print).

[11] Kuo Y.-J., Ho D. M.-T., Tsai Y.-F., Hsu C.-Y.: "Invasive Ductal Carcinoma Arising in Phyllodes Tumor with Isolated Tumor Cells in Sentinel Lymph Node". *J. Chin. Med. Assoc.,* 2010, *73*, 602.

[12] Wu D., Zhang H., Guo L., Yan X., Fan, Z. "Invasive ductal carcinoma within borderline phyllodes tumor with lymph node metastases: A case report and review of the literature". *Oncol. Lett.,* 2016, *11*, 2502.

[13] Parfitt J.R., Armstrong C., O'Malley F., Ross J., Tuck A.B.: "In-situ and invasive carcinoma within a phyllodes tumor associated with lymph node metastases". *World J. Surg. Oncol.,* 2004, *2*, 46.

[14] Hennessy B.T., Giordano S., Broglio K., Duan Z., Trent J., Buchholz T.A., *et al.:* "Biphasic metaplastic sarcomatoid carcinoma of the breast". *Ann. Oncol.*, 2006, *17*, 605.

[15] Gatta G., Iaselli F., Parlato V., Di Grezia G., Grassi R., Rotondo A., *et al.:* "Differential diagnosis between fibroadenoma, giant fibroadenoma and phyllodes tumour: sonographic features and core needle biopsy". *Radiol. Med. (Torino)*, 2011, *116*, 905.

[16] Shin Y.D., Lee S.K., Kim K.S., Park M.J., Kim J.H., Yim H.S., Choi Y.J.*:* "Collision tumor with inflammatory breast carcinoma and malignant phyllodes tumor: a case report and literature review". *World J. Surg. Oncol.*, 2014, *12*, 5.

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