# LOW-GRADE MALIGNANT PHILOID TUMOR ASSOCIATED WITH DUCTAL CARCINOMA IN SITU: A CLINICAL CASE REPORT

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**ABSTRACT**

Phyllodes tumors are rare in the breast, ranging from benign to malignant, rarely associated with carcinomas, especially ductal carcinoma in situ.
OBJECTIVE: To describe a clinical case of low-grade malignant phyllodes tumor associated with ductal carcinoma in situ GN2.
CASE REPORT: Patient E.R.A., 53 years old, presented with a rapidly growing nodule in the left breast in the upper lateral quadrant. Physical examination revealed a well-defined, hardened, and painless nodule. Mammography showed a dense, well-defined, 20 cm nodular lesion in the same location. Following a Fine Needle Aspiration Biopsy (FNAB) with negative cytology and clinically negative axillary nodes, the patient underwent a quadrantectomy to remove the tumor with clear margins. Pathological evaluation confirmed a low-grade malignant phyllodes tumor associated with ductal carcinoma in situ, displaying moderate cellular atypia and high expansibility. The diagnosis was confirmed through immunohistochemical analysis, showing positivity for specific markers.
DISCUSSION: Phyllodes tumors (PT) are more common in the 4th to 5th decades, especially among Asian and Latina women. They are typically painless, large, firm, and rarely associated with carcinomas. Considerable growth (up to 41 cm) is common, and axillary involvement is rare. Diagnosis is challenging due to unclear imaging findings. Surgical resection with clear margins is the preferred treatment.
CONCLUSION: Epidemiological studies are essential for standardizing phyllodes tumor management, and due to the lack of data, complete resection with clear margins is the best approach.

**KEYWORDS: NON-INFILTRATING INTRADUCTAL CARCINOMA; BREAST NEOPLASMS; PHYLLODES TUMOR**

## INTRODUCTION

Phyllodes tumors (PT) are a rare condition, accounting for 0.3% to 1% of breast neoplasms, making comprehensive studies on this lesion and its prognosis challenging. In histopathology, a fibroepithelial tissue with a foliaceous structural pattern is observed, featuring clefts lined with epithelial cells and hypercellularized stroma, justifying the name PT (ZHANG; KLEER, 2016). According to the World Health Organization (WHO), the malignant or benign nature is determined based on characteristics identified through microscopy, considering factors such as cellular features, stromal tissue cellularity, presence or absence of nuclear atypia, mitotic rates, among others (TAN et al, 2012). The histological features of the PT and fibroadenomas can overlap, with lobular duct involvement and stromal cellularity being compatible with PT (TAN et al., 2012). In the literature, it is recognized that malignant PT have a lower prevalence compared to benign tumors, and when malignancy is present, distant metastases occur in approximately 22% of patients (TAN et al., 2012; PAPAS et al., 2020).

In the worldwide literature, data on PT is scarce; however, it is known that the first report of malignancy occurred in 1931 after the identification of tumor metastasis to the lung (LEE; PACK, 1931). Thus, it can be observed that recurrences do not occur in the majority of patients, and abnormal growth, exceeding 10 cm, is not uncommon in these cases, referred to as giant PT (PAPAS et al., 2020). Epidemiologically, these tumors are more frequently diagnosed in patients with an average age of 45 years, with a predilection for the upper outer quadrant of the breast (PAPAS, et al., 2020). These aspects should be considered, as PT can be confused with fibroadenoma lesions, and the combination of histological and clinical factors can aid in the differential diagnosis (TAN et al., 2012).

The concomitant occurrence of Phyllodes Tumors (PT) with other lesions is uncommon and poorly reported, especially in carcinomas, and when present, in situ lesions show higher recurrence rates (OZZELLO; GUMP, 1985). The relationship between these two lesions is not clear, despite various existing theories attempting to provide a possible explanation. One of these theories suggests the

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sudden transformation of the epithelium into carcinoma cells or that the transformation of these cells occurs randomly (NISHIMURA et al., 1998). Additionally, the search for molecular markers that could correlate the two diseases does not contribute to explaining the potential associations (TSE et al., 2002).

The aim of the present study is to report a clinical case of a 20 cm low-grade malignant phyllodes tumor associated with ductal carcinoma in situ in a 53-year-old patient.

## CASE REPORT

The patient, E. R. A., 53 years old, sought medical attention complaining of a painless, rapidly growing tumor mass in a large part of the left breast. On physical examination, a palpable nodule was noticed in the upper lateral quadrant (ULQ), with relatively well-defined borders, hardened consistency, and painless character. Additionally, no palpable lymph nodes were detected in the axillary or supraclavicular fossa. The mammography revealed a dense nodular image, rounded in shape, with well-defined contours, measuring 20 cm, located in ULQ (Figure 1).

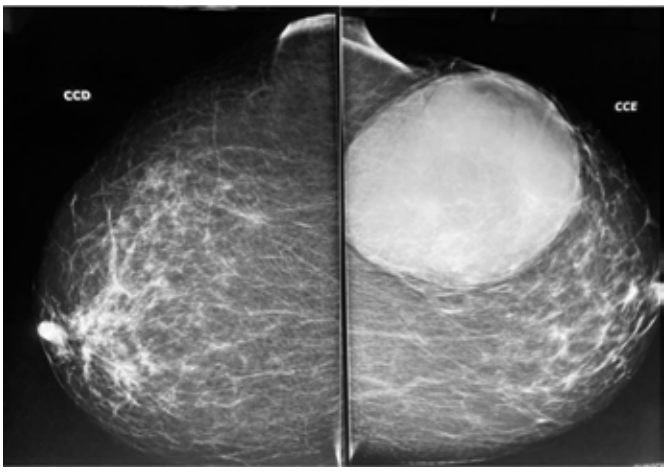


**Figure 1 - Mammography revealing a well-defined border tumor mass in the left breast with a diameter of 20 cm.**

Fine Needle Aspiration (FNA) was performed, and the cytology results were negative. Axillary staging was not detected. The patient was, therefore, subjected to surgical treatment through Quadrantectomy for tumor removal, with safety margins along the resection (Figure 2). An anatomopathological evaluation confirmed a lesion compatible with phyllodes tumor associated with low-grade ductal carcinoma in situ, moderate cellular atypias, and a high expansibility grade (Figure 3).

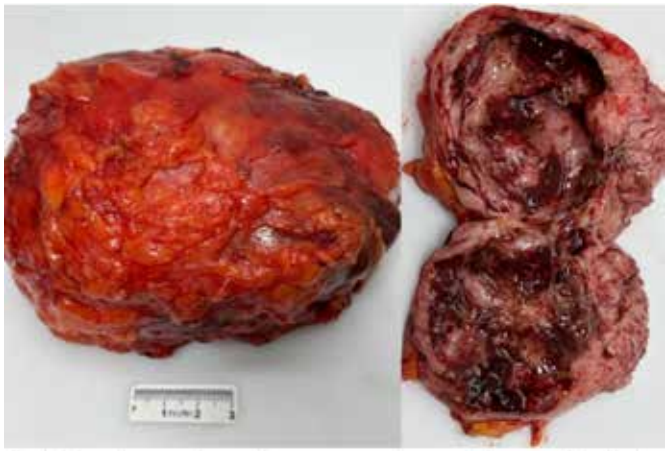

**Figure 2 - Lesion removed with safety margins, showing the internal and external aspects, with brown-red coloration, solid, and well-defined.**

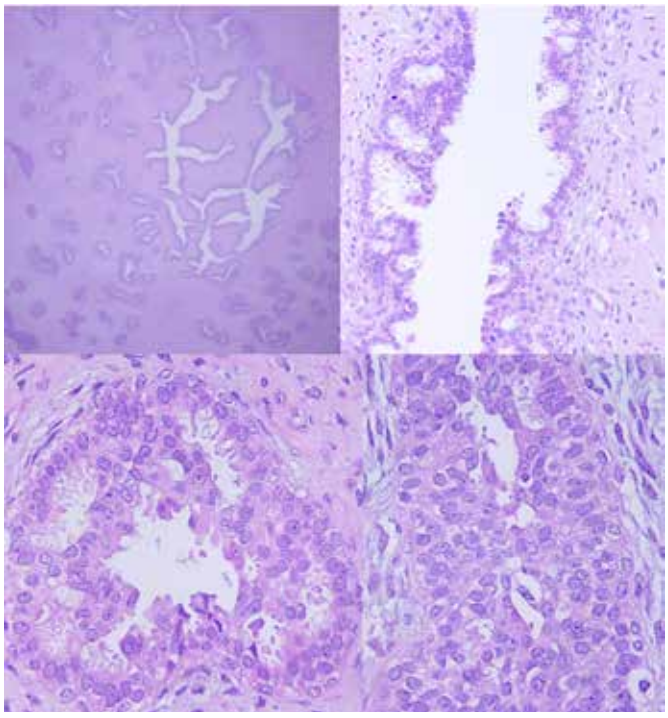

**Figure 3 - Microscopic aspect of the TF lesion in the upper photos, observing the foliaceous appearance. In the lower photos, carcinoma in situ.**

The diagnostic definition occurred with an immunohistochemical study that showed basal cell positivity for p63 protein, 5% expression in the portion affected by carcinoma in situ for the Ki-67 marker, and 10% for stromal cells, ER+, PR- (Figure 4).

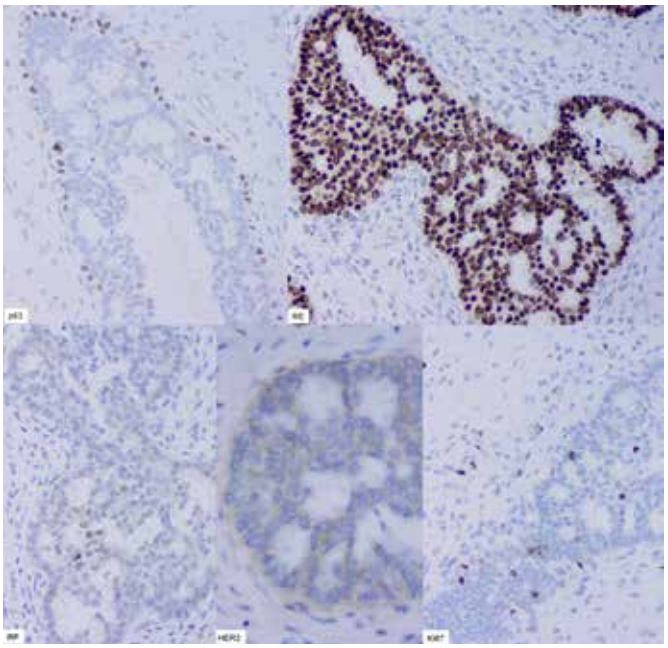

**Figure 4 - Immunohistochemistry showing positivity for p63 protein, ER+, and Ki67.**

## DISCUSSION

The present study is characterized as a case report aiming to describe the diagnostic and therapeutic process for the treatment of a patient with Phyllodes Tumor (PT). According to worldwide literature, the occurrence of these lesions is more prevalent between the 4th and 5th decades of life (PAPAS et al., 2020). In a recent systematic literature review, the authors found that patients were typically between 35 to 55 years old (YU; HUANG; TAM, 2022). Additionally, it is known that palpable axillary lymphadenopathy is not routine in the presence of PT, and the preference for the upper lateral quadrant of the breast occurs in 35% of cases (GULLET; RIZZO; JOHNSTONE, 2009). In this study, the patient was diagnosed at the age of 53, with a tumor in the upper lateral quadrant of the breast and without lymph node involvement, characteristics that are consistent with the reported data.

The tumor's growth occurs in two phases, with the initial phase characterized by slow growth, and in advanced phases, the lesions commonly can reach 10 cm or more (TAN et al., 2012). Recent data indicate that the average size of tumors at the time of diagnosis can range from 2 to 10 cm (YU; HUANG; TAM, 2022). However, in other studies, authors identified that sizes can be extremely variable, ranging from 1 to 41 cm, with an average of 4 to 7 (FERNÁNDEZ-FERREIRA et al., 2021). Despite this, tumors larger than 10 cm in diameter represent a minority of cases, accounting for 10% of lesions (LIANG et al., 2008). Thus, the patient in the presented case corresponds to this minority group as her diagnosis occurred when the tumor measured 20 cm. This demonstrates how delayed the seeking of professional help was.

The use of imaging exams can be helpful in diagnosis; however, clinical and radiographic data should be combined, especially for differential diagnosis from fibroadenoma (FERNÁNDEZ-FERREIRA et al., 2021). Although there is a similarity in appearance, the large size and rapid growth are suggestive of PT. Additionally, mammography shows the tumor as a smooth, multilobulated mass, and on ultrasound, the lesions are hypoechoic, solid, with partially circumscribed indistinction (GULLET; RIZZO; JOHNSTONE, 2009).

Despite the limited existing data, it is known that surgical treatment with complete excision is still the best form of treatment, with safety margins greater than 1 cm recommended (FERNÁNDEZ-FERREIRA et al., 2021). Additionally, the use of radiotherapy is only necessary when applying safety margins is not possible, as the risk of recurrence increases in such cases (BARTH et al., 2009). The scarcity of data does not allow for definitive conclusions regarding the use of chemotherapy in PT, and its indication is still limited (FERNÁNDEZ-FERREIRA et al., 2021).

The association of PT with other lesions is rarely reported in the literature, with carcinoma in situ being the most frequent type of lesion (NOMURA et al., 2006). However, it is still unclear which factors may contribute to the concurrent occurrence of these lesions, and when it does occur, the secondary diagnosis often happens at the time of excision and histopathological analysis of the samples (NOMURA et al., 2006). Therefore, detailed handling of the tumor is essential, and, as in the present case, the evaluation of the association with carcinomas can be detected early.

## CONCLUSION

Epidemiological studies should be conducted to assist in standardizing approaches related to the management of PT, especially in cases of associations with other types of tumors. Due to the scarcity of data, complete excision of the lesion with adequate margins is currently the best way to control this neoplasm.

## REFERENCES

ADESOYE, T.; NEUMAN, H. B.; WILKE, L. G.; SCHUMACHER, J. R. et al. Current Trends in the Management of Phyllodes Tumors of the Breast. Ann Surg Oncol, 23, n. 10, p. 3199-3205, Oct 2016.

BARTH, R. J.; WELLS, W. A.; MITCHELL, S. E.; COLE, B. F. A prospective, multi-institutional study of adjuvant radiotherapy after resection of malignant phyllodes tumors. Ann Surg Oncol, 16, n. 8, p. 2288-2294, Aug 2009.

FERNÁNDEZ-FERREIRA, R.; ARROYAVE-RAMÍREZ, A.; MOTOLA-KUBA, D.; ALVARADO-LUNA, G. et al. Giant Benign Mammary Phyllodes Tumor: Report of a Case and Review of the Literature. Case Rep Oncol, 14, n. 1, p. 123-133, 2021.

GULLETT, N. P.; RIZZO, M.; JOHNSTONE, P. A. National surgical patterns of care for primary surgery and axillary staging of phyllodes tumors. Breast J, 15, n. 1, p. 41-44, 2009.

LEE, B. J.; PACK, G. T. Giant Intracanalicular Myxoma Of The Breast: The So-Called Cystosarcoma Phyllodes Mammae Of Johannes Muller. Ann Surg, 93, n. 1, p. 250-268, Jan 1931.

LIANG, M. I.; RAMASWAMY, B.; PATTERSON, C. C.; MCKELVEY, M. T. et al. Giant breast tumors: surgical management of phyllodes tumors, potential for reconstructive surgery and a review of literature. World J Surg Oncol, 6, p. 117, Nov 11 2008.

NISHIMURA, R.; HASEBE, T.; IMOTO, S.; MUKAI, K. Malignant phyllodes tumour with a noninvasive ductal carcinoma component. Virchows Arch, 432, n. 1, p. 89-93, Jan 1998.

NOMURA, M.; INOUE, Y.; FUJITA, S.; SAKAO, J. et al. A case of noninvasive ductal carcinoma arising in malignant phyllodes tumor. Breast Cancer, 13, n. 1, p. 89-94, 2006.

OZZELLO, L.; GUMP, F. E. The management of patients with carcinomas in fibroadenomatous tumors of the breast. Surg Gynecol Obstet, 160, n. 2, p. 99-104, Feb 1985.

PAPAS, Y.; ASMAR, A. E.; GHANDOUR, F.; HAJJ, I. Malignant phyllodes tumors of the breast: A comprehensive literature review. Breast J, 26, n. 2, p. 240-244, Feb 2020.

TAN, P. H.; ELLIS, I. O. Myoepithelial and epithelial-myoepithelial, mesenchymal and fibroepithelial breast lesions: updates from the WHO Classification of Tumours of the Breast 2012. J Clin Pathol, 66, n. 6, p. 465-470, Jun 2013.

TSE, G. M.; LEE, C. S.; KUNG, F. Y.; SCOLYER, R. A. et al. Hormonal receptors expression in epithelial cells of mammary phyllodes tumors correlates with pathologic grade of the tumor: a multicenter study of 143 cases. Am J Clin Pathol, 118, n. 4, p. 522-526, Oct 2002.

YU, C. Y.; HUANG, T. W.; TAM, K. W. Management of phyllodes tumor: A systematic review and meta-analysis of real-world evidence. Int J Surg, 107, p. 106969, Nov 2022.

ZHANG, Y.; KLEER, C. G. Phyllodes Tumor of the Breast: Histopathologic Features, Differential Diagnosis, and Molecular/Genetic Updates. Arch Pathol Lab Med, 140, n. 7, p. 665-671, Jul 2016.