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Enhanced Modified Burow's Flap Reconstruction Following Oncoplastic Excision of a Giant Atypical Adenomyoepithelioma Mimicking Breast Cancer

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SUMMARY

Adenomyoepithelioma (AME) is an uncommon breast tumor that can develop from epithelial, myoepithelial, or both cell types.

Atypical AME may exhibit an infiltrative pattern and necrosis, mimicking invasive mammary carcinoma, underscoring the importance of clinical correlation and a multidisciplinary approach for accurate diagnosis. AME requires surgical excision with a wide margin. However, they are frequently large and located peripherally in the breast, creating a great challenge to avoid mastectomy. Here we describe a successful wide local excision of a 10cm AME and reconstruction using a modified Burow's flap, supercharged with a lateral thoracic artery perforator.

BACKGROUND

Myoepithelial cells are typically seen in the glandular epithelium of sweat glands, salivary glands, and the mammary duct system. These cells are frequently noticed in benign breast lesions such as intraductal papilloma, tubular adenoma, ductal hyperplasia, and sclerosing adenosis (1).

Adenomyoepithelioma (AME), initially identified by Hamperl in 1970 (1), is a tumor composed of two types of cells: ductal and myoepithelial cells. According to Hamperl, this tumor may exhibit a diverse pattern due to the variable proliferation of epithelial and myoepithelial cells. Most tumors exhibit papillary architecture, hence AME is regarded as a variant of intraductal papilloma (2,3).

The World Health Organization (WHO) classifies AME into two main categories: a benign form,

which has a favorable prognosis, and a malignant form, which features atypia or malignant transformation in either the epithelium and/or myoepithelial component (4).

Classical benign AME consists of epithelial and myoepithelial cells in variable ratios within and between tumors (5). Atypical AME is distinguished by epithelial or myoepithelial overgrowth, mild to moderate cytological atypia, enhanced mitotic activity (> 3 per 10 HPF), which could sometimes be associated with an infiltrative growth pattern, and focal necrosis (6).

Discerning between atypical and malignant AME from benign can be challenging, as the clinical and radiological manifestations can be misleading. (7).

Furthermore, malignant AME has demonstrated significant capacity for local recurrence and metastasis to remote locations, such as the lung, thyroid, bone, and brain. (8–10) Thus, the accurate diagnosis of atypical/malignant AME is essential for proper management and follow-up.

Since the morphological characteristics of a malignant AME have not been clearly identified, tumors that appear benign may potentially become malignant either when they first start to enlarge or after a prolonged time of stability (11). Hence, Surgical excision with adequate margin is the mainstay of treatment. For large tumors, standard breast-conserving surgery (BCS) may be challenging and result in large defects and breast deformity. Oncoplastic BCS is the optimal surgical technique to avoid mastectomy in such cases.

CASE PRESENTATION

A medically-free, 80-year-old post-menopausal woman presented to the breast surgery clinic with a complaint of a right breast mass that appeared 3 years ago. It was gradually increasing in size, recently became fixed, and was associated with redness of the overlying skin. There was no history of any other lesion, no nipple retraction or discharge, and no history of trauma, breast infection, or constitutional symptoms. She denied any family history of breast cancer.

On examination, her breast size was C with grade 3 ptosis. The mass was located in the central and upper inner quadrant (UIQ) of the right breast, 9 cm from the nipple, and measured approximately 10 x 9 cm in size, crossing the meridian of the breast into the center. The mass was well circumscribed with no ulceration or fungation, yet attached to the underlying muscle. The skin over the mass was very thin and erythematous. There were two small satellite skin lesions adjacent to the index mass. However, the remaining breast, skin, and nipple were normal. Examination of the right axilla revealed an enlarged, mobile axillary lymph node. The left breast and axilla were unremarkable. No supraclavicular lymphadenopathy. Fig 1.

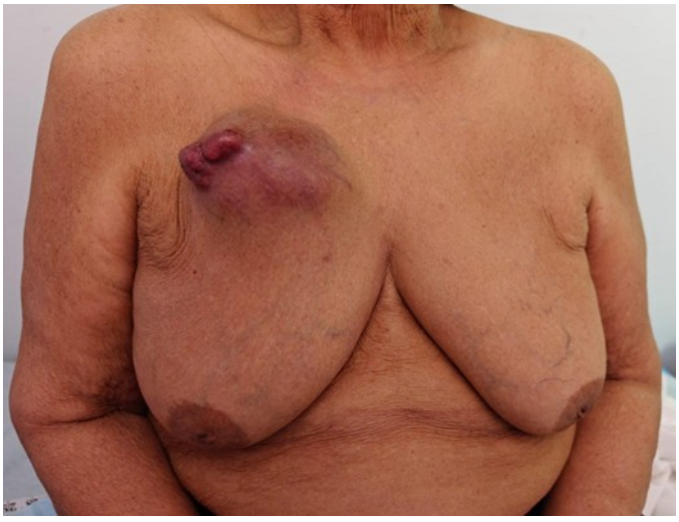

Fig 1: 1st presentation showing the mass at the upper inner quadrant of the right breast, in addition to erythematous skin and 2 skin lesions.

A breast mammogram revealed type B density according to the ACR classification. The mass was located in the posterior central and upper inner quadrants, measured 10 x 8 x 6.3 cm, and was 9 cm from the nipple. Arising from the central mass were two sub-dermal nodules.

There were no associated suspicious microcalcifications, architectural distortion, skin thickening, or skin or nipple retraction. Fig2

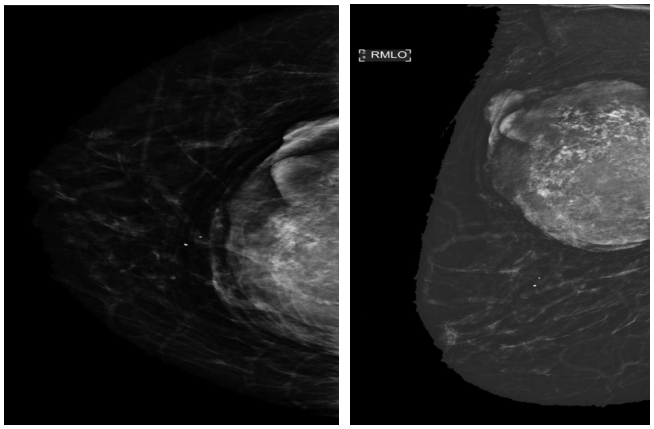

Fig 2: Right breast mammogram showing partially visible round circumscribed high-density mass, measuring 10 x 6.3 cm, at 7 cm from the nipple, with internal macrocalcifications.

The breast ultrasound showed a BIRAD 5 well-circumscribed complex mass with central cystic changes, suggestive of necrosis, an indistinct margin, and posterior acoustic enhancement. It was measuring 10 x 7.5 x 7.2 cm. The nipple and retroareolar complex were unremarkable. The right axilla shows an abnormal lymph node with a thick cortex, measuring 0.5 cm. However, the fatty hilum was preserved. Fig 3

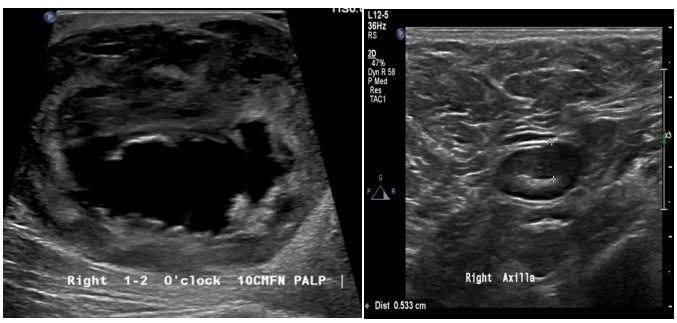

Fig 3:

A: Right breast ultrasound showing oval circumscribed complex cystic and solid mass, measuring 10 x 7.5 x 7.2 cm, with posterior acoustic enhancement, but no significant internal vascularity.

B: Right axilla ultrasound showing an indeterminate axillary lymph node with a thick cortex, measuring 0.5 cm, and a preserved fatty hilum.

The chest computed tomography (CT) scan revealed a mass compressing the pectoralis muscle, with no evidence of muscle invasion. Level I axillary lymph nodes were enlarged. No pulmonary nodules or internal mammary, supraclavicular, or mediastinal lymphadenopathy. Abdomen and pelvic CT scan did not show any signs of distant metastases. Fig4

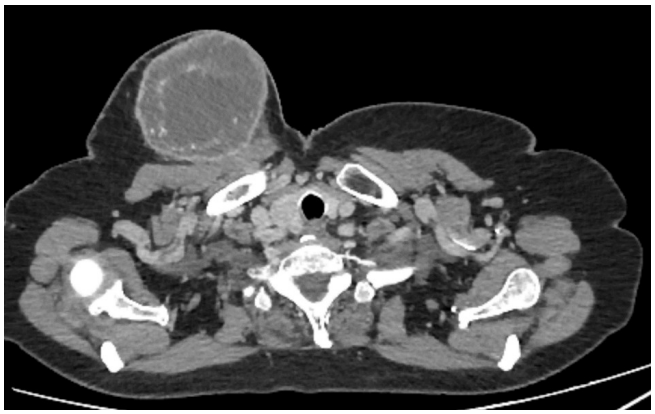

Fig 4: Chest computed tomography (CT) scan showing the right breast mass compressing the pectoralis muscle with no evidence of direct invasion.

True cut biopsy of the right breast mass revealed a focus of infiltrative glands, highly suggestive of invasive mammary carcinoma. A core biopsy of the axillary lymph node showed reactive tissue, negative for malignancy. The biopsy result was discordant with the image finding, and surgical excision was recommended.

Due to the discrepancy between the physical examination and the biopsy finding, and the lack of immunohistochemistry stains at our hospital, biopsy slides were sent to a tertiary cancer center for a second opinion. The review of the biopsy revealed a biphasic glandular lesion composed of both epithelial and myoepithelial cells lining compact, round glands separated by hyalinised stromal bands. No pleomorphism, atypia, or mitoses are seen; however, areas of necrosis are identified. Fig5. The IHC study showed the MSM stain highlighting the myoepithelial cells. Fig. 6.

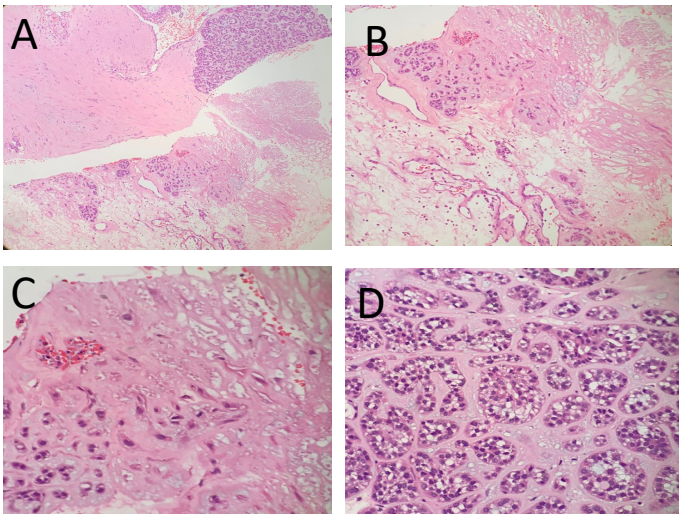

Fig5 : Core Biopsy

A: (4X H&E) compact nests in the upper right corner and scattered single cells in the center, and extensive necrosis.

B: (10X H&E) nests and single cells within a fibrotic stroma.

C: (40X H&E) Individual cells infiltrating the stroma with moderate eosinophilic cytoplasm.

D: (40X H&E) higher view shows irregular and variably sized nests with cytoplasmic clearing.

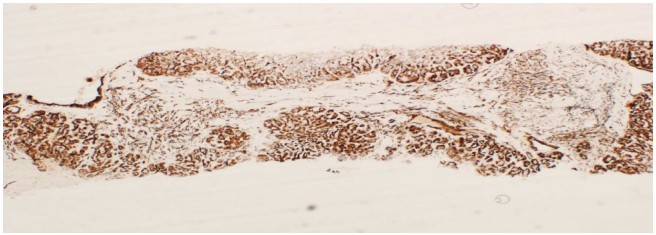

Fig. 6: Msm stain highlighting myoepithelial cells

TREATMENT

Extensive counselling was offered to the patient, including a differential diagnosis and a management plan. It was explained that complete surgical excision of the mass and excisional biopsy of the palpable and radiologically suspicious axillary lymph node were essential for accurate diagnoses. Whether it is AME or IMC, an adequate margin has to be achieved, which will result in a large defect and chest wall/breast deformity. The location of the tumour in the UIQ hinders mastectomy as an inappropriate option, as the remaining breast is healthy, and the lower mastectomy skin flap will not adequately cover the skin defect after excising the tumour. A skin graft may be required to cover the defect at the UIQ. Therefore, Oncoplastic BCS was the best surgical approach in this case. We offered the patient two options. The first procedure was a volume displacement therapeutic reduction mastopexy in a split reduction pattern, allowing for the excision of the skin overlying the lesion, as described by Silverstein (12). Here, the LIQ breast tissue would be rotated anticlockwise to replace the lost volume in the UIQ. This option would allow a large excision volume for oncological resection, as well as correction of the breast ptosis. However, it will require a contralateral balancing reduction mastopexy. The second option was a wide local excision with reconstruction using a volume replacement technique, involving an advancement myocutaneous flap (Burow's flap), which would allow for both oncological resection and reconstruction of the defect while maintaining the shape, ptosis, and symmetry of the breasts. However, due to the distant location of the defect from the base of the flap in the lateral chest wall, a modification of the standard flap will be necessary to maintain adequate perfusion to the distal end of the flap at the UIQ. This will be achieved by preserving the lateral chest wall perfo-

rator vessel within the boundaries of the mobilized Burrow's flap to enhance the blood supply of the flap. The patient opted for the second option to avoid contralateral symmetrizing surgery.

SURGICAL TECHNIQUE

Preoperative marking of the lateral dermo-cutaneous flap was done based on the Doppler identification of the lateral thoracic artery (LTAP) signal (Fig. 7). The mass was excised along with the overlying skin and a 2 cm circumferential safety margin, it weighed 500gm (Fig 8), Part of the pectoralis major muscle was excised at the posterior border of the tumour to secure the deep margin. The modified dermo-cutaneous flap was raised from the lateral chest wall while preserving the LTAP with the aid of intraoperative Doppler examination (Fig. 9). The technique was modified by keeping the LTAP attached to the lateral breast quadrants (the Burow's flap) to achieve greater skin coverage and double perfusion of the long flap, thereby avoiding necrosis of the distal end. The flap was rotated clockwise to cover the huge defect in the upper central and inner quadrants (Fig. 10). The flap appeared healthy and well perfused at the end of the procedure (Fig. 11). The palpable, firm right axillary lymph node was excised. Surgery was uneventful, and the patient was discharged from the hospital the next day, experiencing a smooth post-operative recovery.

Fig 7: The location of the Lateral thoracic artery was identified by the doppler signal and marked on the skin (green arrows) preoperatively.

Fig 8: The Tumor was excised with a 2cm wide margin, including the overlying skin and both skin nodules.

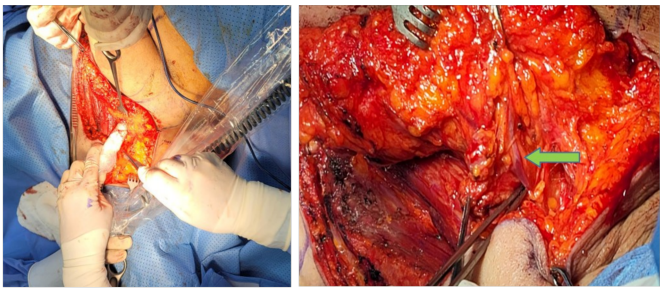

Fig 9: The LTAP vessel (green arrow) was identified intraoperatively by Doppler and preserved into the Burow's flap.

Fig10 and 11: The modified Burow's flap, enhanced by the LTAP vessel, was rotated clockwise to cover the defect at the upper central and inner quadrants.

OUTCOME AND FOLLOW-UP

Surgical pathology: Histologically, the mass was a largely necrotic, fairly circumscribed, biphasic tumor. It was composed of nodules separated by

sclerosis and comprised of back-to-back glands lined by an inner epithelial and outer myoepithelial layer. There were numerous mitotic figures (5-6/10 HPF) in both epithelial and myoepithelial cells. The component cells also displayed moderate nuclear atypia. There was no overgrowth of either component, nor was there lymphovascular invasion. (Fig12)

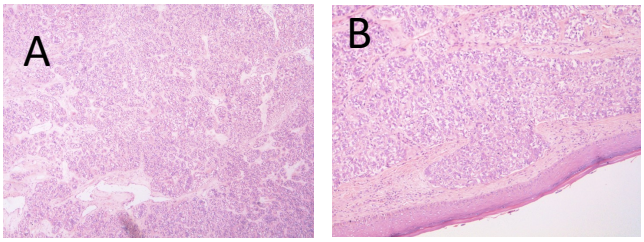

Fig 12

A:(10 X, H&E): Low power view depicting the lobulated architecture of the tumor.

B: (20X, H&E): The tumor has a lobulated architecture and is composed of glands lined by epithelial and myoepithelial cells. The tumor is focally infiltrative.

Immunohistochemistry revealed a biphasic pattern, characterized by CK7-positive epithelial cells and myoepithelial cells reactive for CK5/6, Muscle-Specific Myosin, and p63. Ki-67 was approximately 10%. The tumor, although fairly circumscribed, was focally seen to infiltrate the dermis as dispersed glands. (Fig 13) The background breast parenchyma features fibrocystic changes. The tumor was completely resected in the planes examined with an adequate surgical margin of at least 1 cm.

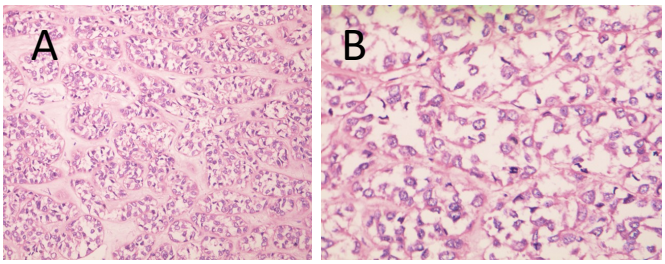

Fig 13: A: (40X, H&E). The glands are lined by an inner epithelial cells with eosinophilic cytoplasm and an outer myoepithelial cells evident with clear cytoplasm. There is mild to moderate nuclear atypia.

B. (40X, H&E) Numerous mitotic figures were identified. (An atypical mitotic figure within the circle)

The right axillary Lymph Node was negative for metastases.

The combined histological and immunohistochemical features were consistent with an "Atypical Adenomyoepithelioma", completely excised with adequate surgical margins. No malignant histological features were identified; therefore, no additional treatment modalities, such as radiation or systemic therapy, were offered to the patient.

The patient is currently on regular follow-up at the breast surgical clinic. The physical examination on the last visit, 3 months after surgery, revealed well-healed scars with a very satisfactory aesthetic outcome in terms of volume, shape, and symmetry. Fig. 14 The patient has a full range of motion of the right upper limb with no evidence of lymphedema.

Fig14:Three months post operative images showing healed surgical scars, nearly identical breasts, and full right upper limb mobility.

DISCUSSION

The occurrence of AME is infrequent, constituting less than 0.5% of breast tumors (11,13). It primarily affects elderly females, similar to our patient,

with rare reported cases in males. In a study conducted by Rakha et al, which reviewed a total of 55 individuals with AME (5), the majority of patients presented with a solitary breast lesion positioned centrally. The average age of AME with atypia was found to range between 40 and 93. Rosen et al. described 18 cases with a mass positioned at the periphery. It can be occasionally associated with nipple discharge (2,11)

The clinical presentation of AME is not specific and can mimic breast cancer. Zhai et al. reported two cases with the same age range and symptoms; one of them presented with bloody nipple discharge; the other case's core biopsy initially suggested breast cancer, so she underwent mastectomy and Sentinel Lymph Node biopsy, her final pathology confirmed malignant AME (11).

Histological examination of a core biopsy might not be sufficient to reach an accurate diagnosis. Immunohistochemistry (IHC) can be used to help differentiate between AME and IMC, as demonstrated in our case.

Assessing the outcome of AME is challenging due to its rarity. The optimal management for this disease is still a subject of controversy. Complete surgical excision is the treatment of choice for benign and atypical AME. However, malignant AME requires a more radical surgery since the risk of local recurrence increases, reaching 35% (11,14)

Unfortunately, there is a lack of definitive guidelines for adequate margin width. Petrozza et al. attempted a large local excision with a 2 cm margin for AME with focal malignant transformation, and reported no recurrence (5). Moro et al. reported a case of benign AME, where a lumpectomy was initially performed with negative margins. However, after 6 months, the mass recurred, prompting a mastectomy with SLNB. The final pathology revealed malignant AME, and the metastatic work-up revealed distant metastases (15).

The fear of close margin resection with traditional lumpectomy, and the risk of breast deformity with a wide margin resection, especially for large tumors or small breast size, may drive most surgeons to choose mastectomy. A better solution would be oncoplastic breast conserving surgery (OBCS), declared by the American Society of Breast Surgeons to increase satisfaction and psychosocial well-being in patients with breast cancer (16).

Many studies comparing traditional lumpectomy to OBCS in breast cancer have shown that OBCS is associated with larger resection volume, wider surgical margin, and lower re-excision rates, even in locally advanced or high-risk breast cancer(17–19). A meta-analysis of 13 studies comparing traditional lumpectomy to OBCS reported no difference in Locoregional recurrence, disease-free survival, or overall survival between the two groups, confirming the oncological safety of OBCS (20).

Different Oncoplastic techniques can be used to reconstruct the breast after the wide excision of AME, including volume displacement procedures described in the Atlas of oncoplastic breast surgery by Krishna Clough (21), or volume replacement procedures like chest wall perforator flap (CWPF) reconstruction, first described in 2004 by Hamdi et al. using a lateral intercostal artery perforator (LICAP) flap, to fill lateral breast defects because of its short pedicle. Hamdi also introduced the anterior intercostal artery (AICAP) flap to cover the lower quadrant defects (22). In 2015, McCulley et

al. described the lateral thoracic artery perforator (LTAP) flap, which is a larger flap size that allows greater mobilization than the LICAP (23). However, in patients with huge tumors similar to our case, LTAP alone does not provide adequate skin coverage, particularly for tumors far in the UIQ.

Burow's advancement flap is a reconstructive technique that is known for its utility in repairing fascial defects (24,25). Defects in the forehead, nose, or lips after excision of small tumors or skin lesions are usually small in size and require a small advancement dermocutaneous flap. The reconstruction of the breast defect after lumpectomy needed a modification of the flap to cover the larger defect. This has been previously described by El Dahshan and Elnemr, who have reported successful repair of upper and UIQ breast defects after oncoplastic lumpectomy in ten patients (26). The technique has demonstrated oncological safety and acceptable cosmetic outcomes in their case series. Another retrospective observational study has reported the use of a modified Burow's flap for oncoplastic excision and reconstruction of Breast tumors located in the superior quadrant or upper inner quadrant (27). The study analyzed patients submitted with an average initial tumor size was 5.9 cm, and a mean excised tumor weight of 117 g. None of the patients required nipple-areola complex or contralateral symmetrization. Only one patient had a minor wound dehiscence.

The choice of the appropriate flap depends on the location and size of the lumpectomy defect, the availability and size of the donor flap, the integrity of the supplying vessels, the surgeon's experience, and the patient's preference. The optimal flap for our patient was a modified Burow's advancement flap. To enhance the blood supply to the long flap and avoid necrosis of the distal end, we decided to preserve one of the CWPF vessels on the lateral aspect of the breast within the harvested flap during the dissection off the chest wall. The LTAP was the best option, due to its larger size and great mobility. The LICAP vessel would be too short to stretch with the rotation of the Burow's flap to the tumor bed defect. While the TDAP is another good option, it is better preserved as a plan B in case of tumor recurrence requiring mastectomy and LD flap reconstruction.

The risk of lymph node metastases is very low with Atypical AME; therefore, axillary lymph node dissection or sentinel lymph node biopsy (SLNB) is not recommended. On the other hand, the risk of lymph node metastasis from a malignant AME has been reported to reach 10% (5); therefore, biopsy of any suspicious axillary lymph node, or SLNB, is indicated in such cases.

In conclusion, clinical correlation, radiological concordance with biopsy result, as well as multidisciplinary discussion are crucial for accurate diagnosis of Atypical AME. The utilization of advanced oncoplastic techniques such as modified Burow's flap and CWPF can provide a wide excision and adequate surgical margins for large breast tumors, resulting in reduced recurrence risk and maintaining good cosmetic results while avoiding mastectomy.

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