Journal of Cancer Research and Practice

journal homepage: https://journals.lww.com/jcrp

Review Article

# Myoepithelial Carcinoma of the Breast - A Case Report and Review of 72 Cases Reported in Literature

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## Abstract

**Objective:** Myoepithelial carcinoma of the breast is an extremely rare malignancy. A study of all reported cases was undertaken to understand the behavior of this disease entity and the response to different treatment modalities. **Data Sources:** Databases, like Pubmed, Scopus, Web of Science, etc. were searched using the keywords myoepithelial carcinoma breast and adenomyoepithelial carcinoma breast from 1984-2022. A total of 1551 results were reviewed. **Study Selection:** Studies reporting a diagnosis of myoepithelial carcinoma on histopathology and immunohistochemistry were selected. Seventy-one cases of myoepithelial carcinoma of the breast were identified and found to be suitable for our review. The individual data of these cases and our patient were then compiled and evaluated. **Results:** The median age at presentation was 57 years, and there was no side preponderance. The average tumor size at presentation was 2.6 cm – most patients presented with a lump in the breast. Surgery remained the mainstay of treatment, with wide local excision and mastectomy performed in 50% and 30% of the patients, respectively. The benefits of radiotherapy and chemotherapy could not be ascertained, and most patients had a poor response to both. Of the patients in whom follow-up data were available, 28.3% and 13.1% were alive at 2 and 5 years, respectively. Locoregional recurrence was reported in 18 (25%) patients, and distant metastases were reported in 17 (23.6%) patients. **Conclusion:** Myoepithelial carcinoma of the breast is a rare and aggressive cancer. Surgery with negative margins is the primary treatment.

**Keywords:** Adenomyoepithelioma, breast, epithelial–myoepithelial lesion, myoepithelial carcinoma

## Introduction

Myoepithelial carcinomas of the breast are a very rare malignancy. To date, 72[1-51] cases of myoepithelial carcinoma of the breast have been reported in the literature, including ours. Myoepithelial cells form a layer between the luminal epithelial cells and the basement membrane. The pathological features of this malignancy overlap considerably with several other conditions of the breast, such as spindle cell tumors, metaplastic carcinoma, squamous cell carcinoma, and benign lesions such as adenomyoepithelioma and myoepitheliosis. Thus, establishing a diagnosis is difficult. Due to the rarity of these tumors, diagnostic and management guidelines need to be

**Submitted:** 28-Nov-2023 **Revised:** 18-Jan-2024
**Accepted:** 19-Feb-2024 **Published:** 17-Sep-2024

Access this article online

Quick Response Code:

Website: https://journals.lww.com/jcrp

DOI: 10.4103/ejcrp.eJCRP-D-23-00053

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**How to cite this article:** Singh K, Negi RR, Thakur PS, Negi A. Myoepithelial carcinoma of the breast - A Case report and review of 72 cases reported in literature. J Cancer Res Pract 2024;11:93-9.

defined. Here, we report a case of malignant myoepithelioma of the breast and review all previous cases reported in the literature to determine clinicopathologic behavior, patterns of care, and treatment outcomes.

## Case Report and Review of the Literature

A 39-year-old woman presented to our department due to concerns about a lump in her left breast for 2½ months. She was premenopausal with two healthy children. There was no other significant history. On examination, a mobile, nontender, 4 cm × 4 cm lump was noted in the lower outer quadrant of the left breast. The overlying skin was normal, and there was no axillary lymphadenopathy. Tru-cut biopsy showed linear epithelial cells with high nucleo-cytoplasmic ratio, round-to-oval nuclei, fine chromatin, and prominent nucleoli, suggesting poorly differentiated carcinoma. Immunohistochemistry (IHC) was done on the specimen, and the findings were as follows: SOX-10 positive in most tumor cells (4+), CD56, S-100 positive in many tumor cells (3+) [Figure 1]; CD99, epithelial membrane antigen, smooth muscle actin (SMA) and cytokeratin positive in some tumor cells (2+); INI-1 retained in tumor cells; CD138 positive in a few tumor cells (1+); CD20, CD3, synaptophysin, TdT, CD45, CD30, desmin, CD43, CD45 RO, CD34, P63, CGA, INSM-1 were all negative. Ki67 was immunoreactive in 85%–90% of cells. Estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2/neu) were negative [Figure 1].

A contrast-enhanced computed tomography scan of the chest showed a 3.4 cm × 3.2 cm mass in the lower quadrant of the left breast. Her metastatic workup was negative, and she was scheduled for modified radical mastectomy (MRM). The final histopathology report was then used to determine further treatment.

## Review of the Literature

### Methods

We searched PubMed, Scopus, and Web of Science using the keywords myoepithelial carcinoma breast and adenomyoepithelial carcinoma breast from 1984 to 2022. A total of 1551 results were reviewed, and 34 reports and case series were identified. A citation search of these articles was done, and a further 18 reports were identified, of which 16 were found to be suitable for our review [Figure 2].

Eligibility criteria for inclusion included a diagnosis of myoepithelial carcinoma on histopathology and IHC. Consequently, 71 cases of myoepithelial carcinoma of the breast were identified and found to be suitable for our review. The individual data of these cases and our patient were then compiled and evaluated.

## Results

Most of the patients presented between the ages of 50 and 70 years (56.9%), and the median age was 57 years. Most patients presented with complaints of a mass in the breast (81.9%). A significant family history of breast cancer was documented in three patients; in most other patients, family history was unavailable – much of the data on menstrual, obstetric, and personal history was unavailable.

The size of the tumor ranged from 0.6 cm to 23.3 cm (median 2.6 cm; standard deviation [SD] ± 4.4 cm). The exact pathological nodal status could not be determined in almost 50% of the patients, as axillary lymph nodes were surgically addressed in only 50%. Among the patients who underwent nodal dissection, 78.8% were node negative (36.1% of all patients). All of the patients except one who did not undergo axillary lymph node dissection (ALND) were clinically node negative. On combining clinical and pathological nodal findings, approximately 85%–90% of the patients were node negative.

Regarding the composite pathological stage among those in whom it could be ascertained, the majority were Stage II (66%, 30.5% of all patients), Stage I (21.2%, 9.7% of all patients), Stage III (9%, 4.2% of all patients), and Stage IV (3%, 1.4% of all patients). The patient characteristics are summarized in Table 1.

### Pathology

The diagnosis of myoepithelial carcinoma in all studies was established by light microscopy and IHC findings. On light microscopy, myoepithelial carcinomas have atypical, plump spindle cells with prominent mitotic figures and intense eosinophilic cytoplasm. Epithelial components may also be present. Identifying malignant cells originating from the

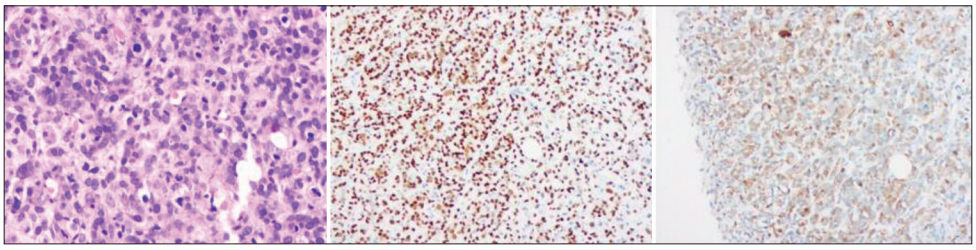

**Figure 1:** HPE and immunohistochemistry images of the patient. Left: H and E showing spindle-shaped cells with high N: C ratio and prominent nucleoli. Center: Tumor cells showing diffuse staining with SOX-10. Right: Tumor cells showing staining with S-100. IHC: Immunohistochemistry, HPE: Histopathological Examination

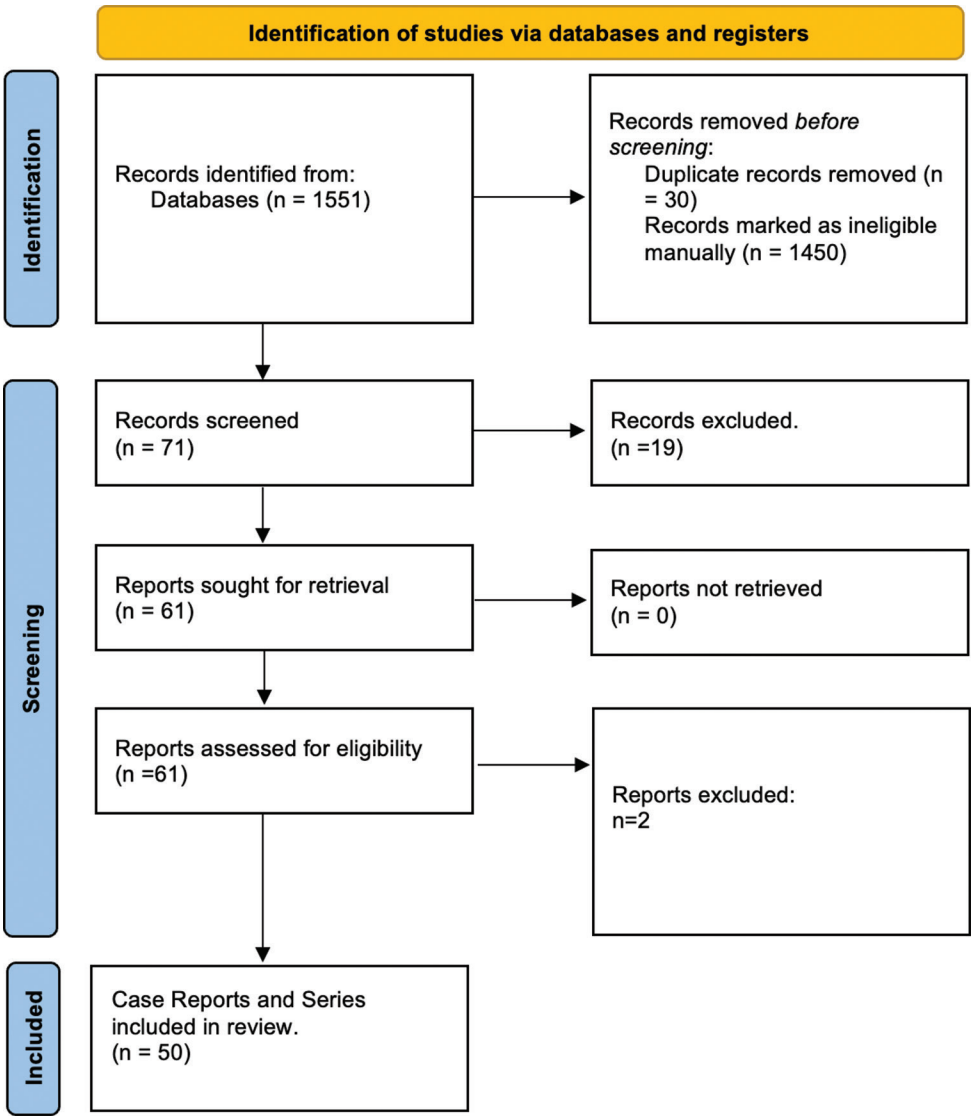


**Figure 2:** PRISMA flow diagram of the study

myoepithelial layer of preexisting ducts or the myoepithelial component of an epithelial–myoepithelial lesion supports the diagnosis of myoepithelial carcinoma.[13,19] Other features that have been reported on light microscopy include the presence of rhabdoid cells,[20] clear cells,[12,24,41,46] intraductal growth,[5] and interlobular growth.[11] Myoepithelial carcinoma of the breast was classified as a subtype of metaplastic carcinoma of the breast according to the WHO classification 5th edition.[52] Metaplastic carcinomas of the breast are a heterogeneous group with monophasic epithelial only, monophasic sarcomatoid, and biphasic types with both epithelial and mesenchymal components. Myoepithelial carcinomas are comprised of almost entirely malignant spindle cells with myoepithelial differentiation without epithelial or mesenchymal components. Spindle cell carcinoma variants, on the other hand, have monophasic sarcomatoid differentiation of the neoplastic epithelial cells.

On IHC, myoepithelial carcinomas stain positive for S-100, myoepithelial markers such as SMA, muscle-specific actin, smooth muscle myosin heavy chain, caldesmon, and calponin. Heavy-weight keratins and nuclear phosphoprotein p63 are also frequently present.[53] These tumors are typically negative for ER, PR, and HER2/neu. Spindle cell carcinomas are differentiated by the absence of myoepithelial markers on IHC.

Electron microscopy studies[1,2,4,6,7,9] have reported spindle-shaped cells with oval-to-elongated nuclei. Distinct desmosomes have also been reported, along with indented nuclear membranes with peripheral nucleoli and cytoplasm-containing microfilaments and abundant rough endoplasmic reticulum. Keratin filaments have also been shown to be present in many cells.

## Treatment

Surgery was the mainstay of treatment in 69 patients (95.8%). Wide local excision (WLE) was performed in 36 (50%) patients, f/b simple mastectomy in 13 (18%), and MRM in 13 (18%). One patient could not undergo surgery due to advanced disease stage. Nodal dissection was done in 36 (50%)

**Table 1: Patient characteristics**

| Characters | *n* (%) |
|---|---|
| Age | |
| 30–40 | 5 (6.9) |
| 41–50 | 12 (16.6) |
| 51–60 | 23 (31.9) |
| 61–70 | 18 (25) |
| 71–80 | 12 (16.6) |
| 81–85 | 2 (2.8) |
| Side | |
| Left | 31 (43) |
| Right | 27 (37.5) |
| NA | 14 (19.4) |
| Presentation | |
| Mass | 59 (81.9) |
| Breast discomfort | 2 (2.7) |
| Distortion of shape | 2 (2.7) |
| Incidental | 2 (2.7) |
| NA | 7 (9.7) |
| Medical history | Documented in 17% |
| Benign breast disease | 8 (47) |
| Hormone replacement therapy | 2 (11.7) |
| Hypertension | 1 (5.8) |
| Diabetes mellitus + hypertension | 1 (5.8) |
| Diabetes mellitus + rheumatoid arthritis | 1 (5.8) |
| Endometrioid carcinoma | 1 (5.8) |
| ESRD | 1 (5.8) |
| Coronary artery disease | 1 (5.8) |
| Not significant | 2 (11.7) |
| Pathological T stage | |
| T1 | 18 (25) |
| T2 | 32 (44.4) |
| T3 | 7 (9.7) |
| T4 | 6 (8.3) |
| NA | 9 (12.5) |
| Pathological N stage | |
| N0 | 26 (36.1) |
| N1 | 6 (8.3) |
| N2 | 0 |
| N3 | 1 (1.4) |
| Nx | 30 (41.6) |
| NA | 9 (12.5) |
| Composite stage | |
| I | 7 (9.7) |
| II | 22 (30.5) |
| III | 3 (4.16) |
| IV | 1 (1.4) |
| NA | 39 (54.1) |

NA: Not available, ESRD: End-stage renal disease

patients, of whom 33 (91.6%) underwent ALND and 3 (8.3%) underwent sentinel lymph node dissection.

Chemotherapy was administered in 16 (22.2%) patients, with paclitaxel and carboplatin in 7 patients. Other chemotherapy agents used were anthracyclines, platins, cyclophosphamide, ifosfamide, vinorelbine, capecitabine, and gemcitabine. The use of bevacizumab and prednisolone was also reported in one patient.[49] Hormone therapy was used with chemotherapy in two patients and as a single agent in one patient. The hormone therapy drugs used were tamoxifen, anastrozole, and raloxifene in one patient each.

Radiotherapy was performed in 18 (25%) patients. Of the 35 (48.6%) patients who underwent WLE, only 12 (34%) received radiotherapy (RT). Radiotherapy was administered in an adjuvant setting in 11 (15.3%) patients; for 2 radically treated patients, the RT dose was 50 Gy/25 fraction, 5 days a week. An electron boost was also used in one patient.[51] Palliative RT was administered in three patients, with a dose ranging from 20 to 36 Gy in 2.5–4 Gy/fraction. Three patients received RT for recurrence. The dose was 60 Gy/30# in one study, but it was not reported in the others. In a neoadjuvant setting, RT was used in one patient at a dose of 40 Gy. The treatment characteristics are summarized in Table 2.

## Outcomes

The outcomes at the last follow-up were available for 52 patients. The time to the last follow-up ranged from 2 to 79 months (median 13 months, SD ± 20.3). One patient died during treatment. Of the patients for whom follow-up data were available at 24 months, 15 (28.3%) were alive with no evidence of disease. At 5 years, only 5 (9.4%) patients were alive with no e/o disease, and 2 (3.7%) were alive with disease [Table 3].

Most cases of recurrence, both local and distant, occurred in the first 2 years. In addition, 64.7% (11) of the patients who developed distant metastases also had local recurrence, and 61% (11) of the patients who had local recurrence later developed metastasis, suggesting that locoregional recurrence may predispose patients to the development of distant metastases.

## Correlation with size

Among the patients with local recurrence, the average tumor size was 5.2 cm. In those with both local recurrence and distant recurrence, the average tumor size was 6.1 cm, and the tumor size in the only patient with distant recurrence was 6.3 cm. Among those who remained disease free, the mean size was 2.8 cm.

## Response to surgery

Among the 41 patients who underwent breast-conserving surgery (BCS), 4 (9.7%) experienced local relapse, 10 (24.3%) experienced distant recurrence, and 20 (48.8%) were alive without disease at the last follow-up. Of the 26 patients who underwent mastectomy with curative intent, 3 (25%) experienced local recurrence, 6 (23.1%) experienced distant metastases, 10 (38.4%) were alive with no e/o disease, and 1 (3.8%) was alive with disease.

## Response to radiotherapy

Twelve patients received RT with radical intent. Of the patients who underwent adjuvant RT, 6 (41.6%) had WLE, 3 (25%) had simple mastectomy, 2 (16.6%) had MRM, and 1 (8.3%) had radical mastectomy. Of the patients who received WLE + RT,

4 (66.6%) had no evidence of disease at the last follow-up. Of the patients who underwent mastectomy + RT, 3 (50%) were disease free at the last follow-up.

The treatment responses to surgery and RT are summarized in Table 4.

Of note, the patients undergoing BCS, or BCS with adjuvant RT, had less local recurrence, and more patients were alive at the last follow-up than those who underwent mastectomy and mastectomy plus RT, respectively. This paradox can be explained by the fact that the average size of the tumor in the patients who underwent BCS was 2.2 cm, and the average size in the patients who underwent curative mastectomy was 5.2 cm. Thus, the patients who underwent mastectomy were already at a higher risk of recurrence. In addition, among the patients who underwent BCS and MRM, adjuvant RT was offered to those with a larger tumor size; for the patients who were offered mastectomy alone, the tumor size was 4.6 cm, and for those who received mastectomy with adjuvant RT, the tumor size was 6.6 cm.

**Table 2: Treatment characteristics**

| Treatment Modality | *n* (%) |
|---|---|
| Surgery | |
| WLE | 36 (50) |
| Simple mastectomy | 12 (16.7) |
| Radical mastectomy | 1 (1.3) |
| Modified radical mastectomy | 13 (18) |
| Quadrantectomy | 5 (6.9) |
| Palliative mastectomy | 2 (2.7) |
| NA | 2 (2.7) |
| Surgery not done | 1 (1.3) |
| Axillary lymph node | |
| Not done | 32 (44.4) |
| ALND | 33 (45.8) |
| SLND | 3 (4.2) |
| NA | 4 (5.5) |
| Chemotherapy | |
| Yes | 16 (22.2) |
| No | 46 (63.8) |
| NA | 8 (11.1) |
| Hormone therapy | 3 (4.2) |
| Radiotherapy | |
| No | 47 (65.2) |
| Yes | 18 (25) |
| NA | 7 (9.7) |

WLE: Wide local excision, NA: Not available, ALND: Axillary lymph node dissection, SLND: Sentinel lymph node dissection

**Table 3: Long-term outcome of myoepithelial carcinoma breast**

| Time duration (years) | No evidence of disease, *n* (%) | Loco-regional recurrence/ progression, *n* (%) | Metastases, *n* (%) |
|---|---|---|---|
| 2 | 15 (28.3) | 15 (20.8) | 11 (15) |
| 5 | 5 (9.4) | 18 (25) | 17 (23.6) |

## Response to chemotherapy

Of the 17 patients treated with chemotherapy, only 1 who was treated with paclitaxel and carboplatin-based chemotherapy[35] reported a remarkable response with complete resolution of local disease. Two studies reported stable disease for a short duration,[17,49] and all of the other studies reported progression on chemotherapy.

# Discussion

Myoepithelial lesions of the breast were classified by Tavassoli[1] as myoepithelioma, adenomyoepithelioma, and malignant myoepithelioma, with the latter, as the name suggests, being the most aggressive. As a rare entity, little is known about the clinical behavior and appropriate management.

As shown in our review, surgery is the mainstay of treatment, with a slight predilection toward WLE compared to mastectomy. We found that the patients who underwent mastectomy had worse outcomes than those who underwent BCS, which could be explained by selection bias toward mastectomy in the patients with larger tumors. Nodal dissection was done in 50% of the patients, and low nodal positivity was observed, i.e. 10%–15%, indicating that, like sarcomas, the predominant mode of spread is hematogenous.

As for adjuvant treatment, adjuvant RT was performed in only 11 (15.3%) patients; one patient received neoadjuvant radiation. In the BCS patients who received RT, local recurrence was slightly lower than in those who did not (16.6% vs. 20%, respectively). However, distant recurrence was higher in the RT group, which could be explained by the larger tumor size in these patients. Of the patients who underwent mastectomy, those in the adjuvant RT arm had higher local recurrence and distant recurrence, and poorer long-term outcomes. In the patients who underwent mastectomy, RT was offered to those with a larger tumor size compared to those who were not offered RT, i.e. 6.6 cm versus 4.6 cm.

The tumor size seems to be a significant factor in determining recurrence rates and long-term outcomes. Behranwala *et al*.[29] reported that a size of >2 cm conferred a poor prognosis.

All of the patients except one who underwent chemotherapy had a dismal response to treatment. Paclitaxel with carboplatin was the most commonly used regimen, with a good response in one patient and stable disease in two patients. Thus, palliative chemotherapy with paclitaxel and carboplatin may be an option for patients who are not candidates for surgery. As these tumors are ER, PR, and HER2/neu negative, hormone therapy and anti-HER2/neu treatment have no role. Targeted agents have not been explored so far in the treatment of this disease entity.

The 2- and 5-year survival rates in our review were much lower than those reported previously, i.e. 28.3% and 13.1%, compared to 88% and 63% (30), respectively. Locoregional recurrence was reported in 18 (25%) patients, with one patient having axillary nodal recurrence; all the rest had chest wall recurrence. Except for one patient, most patients died of distant disease progression.

**Table 4: Treatment response to surgery and radiotherapy**

| Treatment (number of patients) | Mean size of tumor (cm) | Local recurrence, *n* (%) | Distant recurrence, *n* (%) | NED, *n* (%) | AWD, *n* (%) | NA, *n* (%) |
|---|---|---|---|---|---|---|
| BCS total (41) | 2.2 | 4 (9.7) | 10 (24.3) | 20 (48.8) | 3 (7.3) | 8 (29.5) |
| Mastectomy with curative intent total (26) | 5.2 | 3 (11.5) | 6 (23.1) | 10 (38.4) | 1 (3.8) | 5 (19.2) |
| BCS without RT (25) | 2.16 | 5 (20) | 3 (12) | 16 (64) | 1 (4) | 5 (20) |
| BCS with RT (6) | 2.5 | 1 (16.6) | 1 (16.6) | 4 (66.6) | 1 (16.6) | 0 |
| Mastectomy without RT (17) | 4.6 | 3 (17.6) | 3 (17.6) | 7 (41.2) | 1 (5.8) | 5 (29.4) |
| Mastectomy with RT (6) | 6.6 | 3 (50) | 2 (33.3) | 3 (50) | 0 | 1 (16.6) |

BCS: Breast-conserving surgery, RT: Radiotherapy, NED: No evidence of disease, NA: Not available, AWD: Alive with disease

Distant metastases were reported in 17 (23.6%) patients. The predominant sites of metastasis were the lungs, bone, and brain. Other reported sites of metastases included the kidneys, parotid, heart, jaw, mediastinal nodal, scalp, and opposite breast, emphasizing the hematogenous pattern of spread and aggressive behavior of this malignancy. Recurrence as late as 5 years after the initial diagnosis has been reported, thus reiterating the need for long-term follow-up in these patients.

This review has several limitations, the most prominent of which is that it reviews case reports and case series. Due to a small number of patients and considerable missing data, subset analysis was not feasible. The outcomes of different treatment modalities could not be assessed effectively due to the small numbers and nonuniformity of surgical techniques, radiation techniques, and doses of radiation used. Moreover, current treatment outcomes may differ from earlier reports as the surgical, pathological, and RT techniques have evolved over time. However, due to the rarity of this disease, generating level I evidence is challenging. The aim of this review was to fill some of the many gaps in the knowledge of this elusive disease entity.

## Conclusion

In clinically node-negative smaller tumors, WLE without axillary node dissection or sentinel node dissection may be an appropriate surgical option. In patients with larger tumors, mastectomy should be offered upfront to obtain clear margins. As neoadjuvant chemotherapy has not been shown to be beneficial, it should not be offered to patients with larger tumors to achieve BCS. The benefit of RT remains ill-defined but may be offered to patients with a larger tumor size and higher-grade lesions as an adjuvant. Doses as high as 60 Gy have been used in the literature. The role of chemotherapy is limited primarily to palliative settings. If considered, paclitaxel plus carboplatin is the most effective regimen documented to date. Recurrence occurs in most patients in the first 2 years; however, recurrence as late as 5–6 years has been documented. Thus, regular long-term follow-up is warranted.

### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent form. In the form the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that her name and initial will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

### Acknowledgment

We would like to thank Dr. Chitresh, Associate Professor, Department of Endocrine Surgery, AIIMS, Bilaspur, H.P., India.

### Data availability statement

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

### Financial support and sponsorship

Nil.

### Conflicts of interest

Dr. Kaalindi Singh, Prof. R.R. Negi, Dr. Preyander Singh Thakur, Dr. Anup Negi certify that they have NO affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or nonfinancial interest (such as personal or professional relationships, affiliations, knowledge, or beliefs) in the subject matter or materials discussed in this manuscript.

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