



Mucoepidermoid carcinoma—a rare salivary gland-type tumor of the breast: are we dealing with primary or secondary?—a case report and literature review

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Background: Salivary gland-like tumors are extremely unusual in the breast, and their histology is very similar to primary salivary gland neoplasms. Mucoepidermoid carcinoma (MEC), a common salivary gland tumor, displays an infrequent occurrence in the breast, accounting for a mere 0.2–0.3% incidence. Given its rarity, it is critical to accurately distinguish it from metastatic cases before diagnosing it as a primary breast MEC for appropriate treatment. Currently, there is no consensus on the treatment of MEC, and there is a paucity of literature highlighting the ideal treatment modality, especially for estrogen receptor (ER)-positive cancers. Therefore, the aim of our case report was to underscore the diagnostic process, surgical and adjunctive treatments for our patient with ER-positive, progesterone receptor (PR)-negative and human epidermal growth factor receptor 2 (HER2)-negative MEC while also conducting a literature review to contribute to the limited existing data.

Case Description: A 67-year-old African American woman presented with a lobulated 3.1-cm left breast mass on mammography, for which she underwent ultrasound-guided core needle biopsy that revealed invasive carcinoma with squamous differentiation. The carcinoma was ER-positive, PR-negative and HER2-negative. Subsequently, she underwent a lumpectomy with sentinel lymph node biopsy. Her final pathology revealed an intermediate-grade MEC with negative lymph nodes. She had a past medical history of benign salivary gland tumor, as well as a family history of BReast CAncer gene 1 (*BRCA1*)-associated breast cancer in her daughter.

Conclusions: MEC of the breast is a rare tumor with a relatively favorable overall prognosis. The early and precise diagnosis of this condition plays a pivotal role in formulating effective treatment strategies and ensuring positive survival rates. Nonetheless, future studies are recommended to further explore the role of surgical approaches and adjuvant therapy to improve treatment outcomes.

Keywords: Breast cancer; mucoepidermoid carcinoma (MEC); pathologic morphology; case report

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Introduction

Mucoepidermoid carcinoma (MEC) is an invasive tumor of the breast that histologically resembles its salivary gland counterpart (1). Since its initial documentation in 1979, approximately 47 cases have been reported in the English literature to date (2,3). The estimated incidence of MEC accounts for 0.2–0.3% of all breast tumors; however, some authors believe that the true incidence may be higher due to the potential misclassification of cases as carcinomas with squamous differentiation (4,5). Furthermore, despite being most frequently detected in the salivary gland, MEC has been reported to occur in a variety of organs, including the lungs, bronchus, esophagus, and thyroid (6). Regardless of location, the morphology of this tumor is characterized by a mixture of mucinous, squamous, and intermediate neoplastic cells arranged in solid and cystic patterns (1,6). Based on the tumor's histomorphology, MEC can be categorized into low, intermediate, or high grades (7). Regardless of the grade, the cell composition is similar. Low-grade MEC tend to be more cystic, while high-grade MEC is more solid with a high nuclear grade, necrosis, and brisk mitotic figures (8,9). To identify these aforementioned cell types observed in MEC, several immunohistochemical stains are utilized. CK14 stains basaloid cells, p63 stains epidermoid cells, and CK7 delineates mucous cells (9). Moreover, using GATA3 and mammaglobin expression, these stains help distinguish MEC of the breast from MEC of the salivary, where the

former will be expressed in breast MEC and negative in the latter (3).

While most documented cases in the literature emphasize MEC as a prevalent form of triple-negative breast cancer, these cases generally exhibit low invasiveness and a favorable prognosis (10). In fact, tumor grade has been identified as the most important predictor of long-term prognosis in MEC patients. Currently, there is no consensus or standard therapeutic guideline for the treatment of MEC. Prior studies have suggested that high-grade MEC is typically managed through mastectomy and axillary lymph node dissection, while breast conservation and sentinel node biopsy may be options for tumors of low and intermediate grade. However, a significant portion of these studies did not account for the hormone receptor status of patients, and those that did reported a prevalence of triple-negative breast cancer phenotypes. Consequently, there exists a scarcity of literature that examines the role of hormone receptor status on treatment outcomes (3,11). Thus, our case report aimed to underscore the diagnostic process, surgical and adjunctive treatments for our patient with estrogen receptor (ER)-positive, progesterone receptor (PR)-negative, human epidermal growth factor receptor 2 (HER2)-negative MEC, while also conducting a literature review to contribute to the limited existing data. We present this case in accordance with the CARE reporting checklist (available at <https://gs.amegroups.com/article/view/10.21037/gS-23-372/rc>).

Highlight box

Key findings

- We report a rare case of estrogen-receptor positive mucoepidermoid carcinoma (MEC) of the breast in a patient with salivary gland tumor history.

What is known and what is new?

- MEC is a tumor most commonly occurring in the salivary glands. MEC of the breast is a rare, predominantly triple-negative breast cancer with a relatively favorable prognosis but little consensus on ideal treatment modality.
- No other cases of MEC of the breast in a patient with salivary gland tumor history have been reported. The current report highlights the importance of accurate diagnosis and appropriate surgical and adjuvant treatments.

What is the implication, and what should change now?

- The early and precise diagnosis of MEC of the breast, including evaluation of possible associated tumors, is crucial to formulating effective treatment strategies and ensuring positive survival rates.

Case presentation

A 67-year-old postmenopausal African American woman presented with a lobulated 3 cm left breast mass on screening mammogram. She denied any nipple inversion, nipple discharge or skin changes. Diagnostic mammogram and ultrasound demonstrated a 3.1 cm mass at 2:00 o'clock 9 cm from the nipple and an abnormal left axillary node with a thickened cortex. Subsequently, an ultrasound-guided core biopsy revealed carcinoma with squamous differentiation, ER-positive (51–60%), PR-negative, and HER2-negative by fluorescence in situ hybridization (FISH). Biopsy of the left axillary lymph node was benign. A follow-up magnetic resonance imaging (MRI) confirmed the tumor at 2:00 o'clock about 6.7 cm from the nipple measuring 2.1 cm × 2.9 cm × 2.8 cm with biopsy clip and no additional sites of disease. She had a past medical history significant for a 10-year history of a slowly enlarging right parotid mass, for which she underwent right deep lobe parotidectomy with

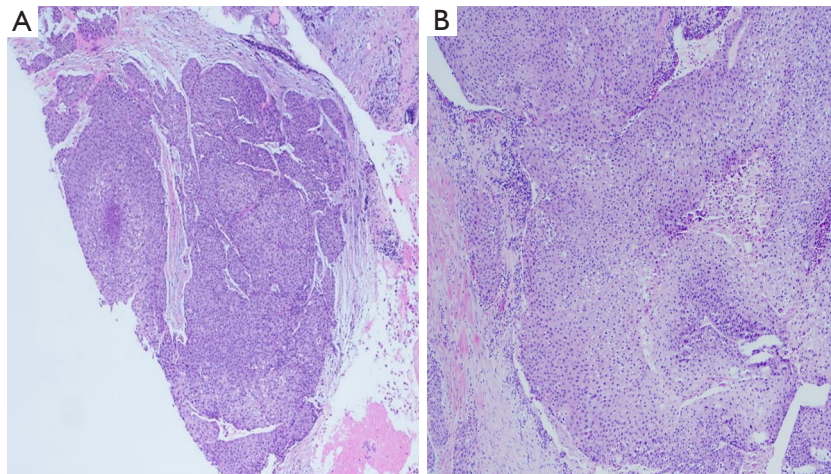


Figure 1 Histopathologic features of MEC of the breast. (A) 4× magnification of H&E-stained tumor showing a polypoid and solid growth with papillary configuration; (B) 10× magnification of H&E-stained section of eosinophilic cells with epidermoid appearance. H&E, hematoxylin and eosin; MEC, mucoepidermoid carcinoma.

facial nerve dissection and preservation at age 51. Pathology report of the excised mass revealed a 2.3-cm pleomorphic adenoma, with no features suggestive of malignant transformation. One intraparotid and two right neck lymph nodes were also negative. Her family history included breast cancer in her daughter, who was diagnosed in her late thirties and was found to have a pathogenic BReast CAncer gene 1 (*BRCA1*) variant. However, the patient's genetic testing results were negative.

The patient was presented at our institutional multidisciplinary tumor board with recommendations to undergo left breast lumpectomy and left sentinel lymph node biopsy.

A left breast lumpectomy with margin assessment and sentinel lymph node biopsy was performed. The patient had four sentinel lymph nodes sent for final pathology. The surgery was successful, and the patient tolerated the procedure well. There were no intraoperative or postoperative complications. After an uneventful recovery, she was discharged the same day. Final pathology revealed the presence of 33 mm × 30 mm × 25 mm, grade-2 (as per salivary grading system) stage IIA MEC without angiolymphatic or perineural invasion that had been fully removed with clear margins. The tumor tested positive for ER but negative for PR and HER-2. Histologically, the tumor comprised of irregular nests of intermediate tumor cells with squamous differentiation (*Figure 1*) and mucous cells (*Figures 2,3*). It stained positive for GATA3 (diffuse, weak) (*Figure 4*) and ER. Additionally, as part

of her adjuvant treatment, the patient was referred to medical oncology and radiation oncology for adjuvant treatment recommendations. She underwent 15 fractions of external beam radiation (48 Gy) and was started on adjuvant aromatase inhibitor.

On follow-up, the patient was noted to have an enlarging neck mass for which she underwent a positron emission tomography (PET) scan and subsequent fine needle aspiration. While the PET scan showed increased focal uptake in the left inferior thyroid lobe, cytological test demonstrated numerous lymphoid cells and scattered oncocytic cells, negative for malignancy.

The total length of post-operative follow-up was 7 months. The patient is alive with no evidence of disease. No recurrence or metastasis were reported during the follow-up period.

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

Discussion

Primary MEC of the breast is a rare, atypical tumor, accounting for only 0.2–0.3% of all primary breast tumors (4).

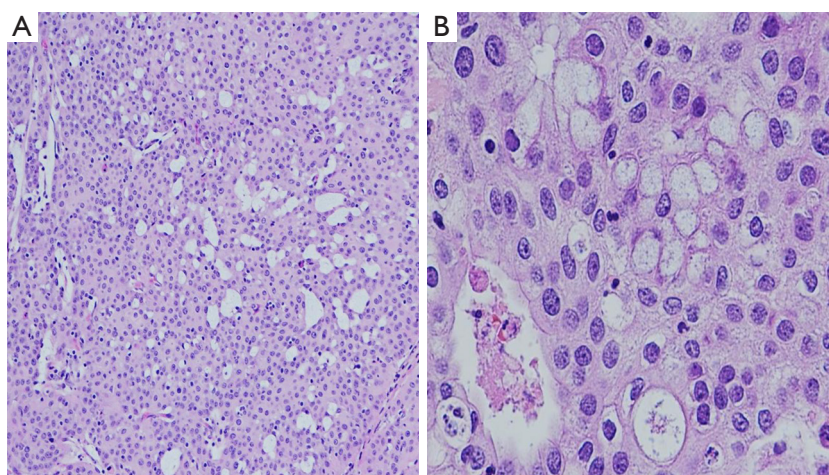


Figure 2 Histopathologic features of mucin-filled glandular cells of MEC of the breast. (A) Cystic spaces indicate mucin-filled glandular structures at 10× magnification stained with H&E; (B) 20× magnification of corresponding section (H&E). H&E, hematoxylin and eosin; MEC, mucoepidermoid carcinoma.

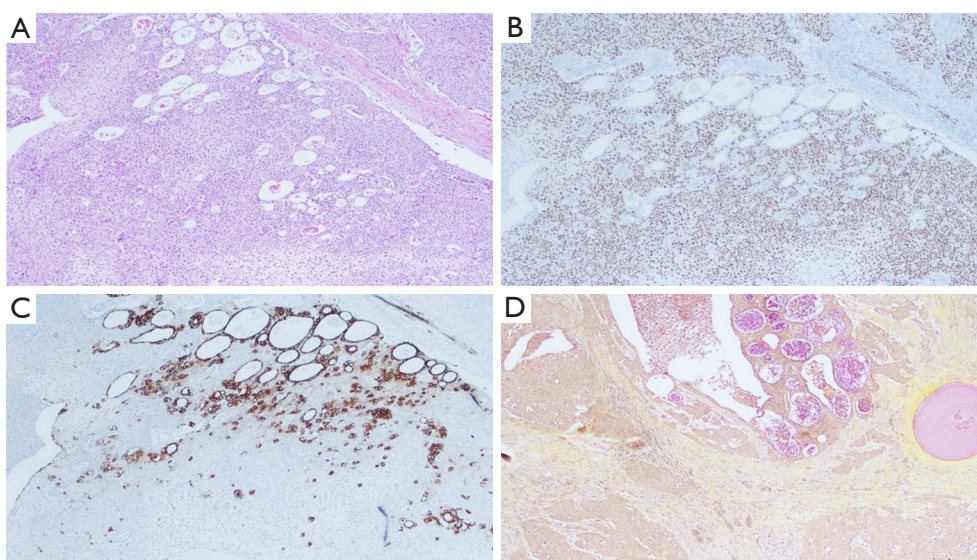


Figure 3 Immunohistochemistry of MEC of the breast. (A) H&E staining showing solid growth of eosinophilic epidermoid appearing cells merging with cystic spaces lined by mucous cells at 4× magnification; (B) IHC staining for P63 showing epidermoid cells at 4× magnification; (C) IHC staining for CK7 showing mucous cells at 4× magnification; (D) IHC staining for mucicarmine showing mucin in the cystic spaces at 4× magnification. MEC, mucoepidermoid carcinoma; IHC, immunohistochemical; H&E, hematoxylin and eosin.

The first cases were reported in 1979 by Patchefsky *et al.* (2) and since then 47 cases have been reported (2,7). MEC morphology can be heterogenous. Therefore, it is often confused with other benign and malignant neoplasms (6). All 47 reported cases have occurred in adult women with a wide age range of 29 to 80 years and a mean

age of 55.7. None of the previously reported cases reported presence of BRCA gene positivity, but of note, our patient reported a family history of *BRCA1* positivity in her daughter, who was diagnosed with breast cancer in her late thirties. Furthermore, our patient had a history of pleomorphic adenoma removal at age 51. The significance of this benign

salivary gland tumor history is unclear. Given MEC is a common salivary tumor with varying potential for aggressive behavior, there was suspicion to whether the patient's MEC tumor of the breast was a primary or secondary tumor (12,13). Since pleomorphic adenomas harbor a small risk of malignant transformation, it was determined the patient's MEC of the breast was likely a primary tumor.

Although the majority of MEC cases have been documented in the United States (11 cases) (2,4-6,14), followed by Italy (6 cases) (15,16), China (6 cases) (9,11,17), and Turkey (3 cases) (18-20), none have provided insights into the racial or ethnic backgrounds of their patients. To the best of our knowledge, we report the first case of MEC in an African American patient. Multiple studies have demonstrated that breast MEC presents as a triple-

negative cancer (7,9). Contrastingly, our patient showed positivity for ER (60%) and absence of PR and HER2. Moreover, in terms of receptor status, 12 studies were triple-negative (4,7,9,14,19,21-25). Six were ER⁻, PR⁻, and HER2 unspecified (26-30). In cases not classified as triple negative, three were ER⁺, PR⁻, and HER2⁻ including our case (8,11); two were ER⁺, PR⁺, HER2⁻. This has been further illustrated in *Figure 5*. Recent cases have shown an increasing incidence of non-triple negative breast cancers (6,8,21). The hypothesis that hormone receptor plays a role in prognosis was corroborated by Sherwell-Cabello *et al.* (21), who found favorable outcomes associated with lower hormone receptor expression. This finding suggests a potential hormone dependency of the disease and raises the possibility of considering endocrine therapy as a viable option.

Histological grade is an important prognostic factor in MEC of the breast (23). This type of tumor is graded using either the salivary gland grading system or the breast grading system, both yielding comparable outcomes. Among these grading frameworks, the Elston Ellis scoring system takes prominence. This system effectively categorizes tumors into low, intermediate, and high grades, factoring in components like cystic proportion, nerve invasion, necrosis, as well as the count of mitoses per 10 high-power fields (9,31). Patients diagnosed with high-grade MEC face a less favorable prognosis, often experiencing the development of distant metastases (9). Of the reported cases with low and intermediate grade, no deaths were reported which

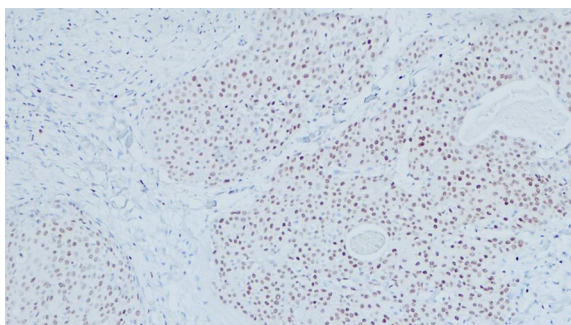


Figure 4 GATA3 staining weakly positive at 10x magnification (immunohistochemistry).

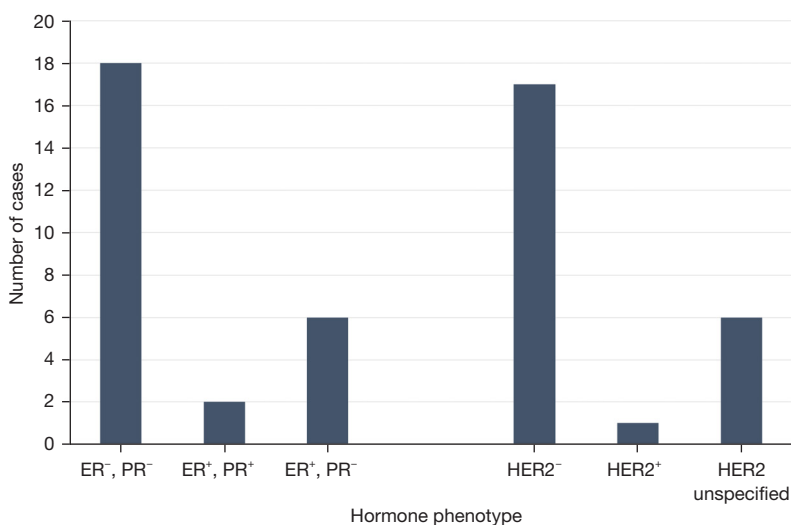


Figure 5 Hormone immunophenotype in reported cases of MEC of the breast. ER, estrogen receptor; PR, progesterone receptor; HER2, human epidermal growth factor receptor 2; MEC, mucoepidermoid carcinoma.

supported the hypothesis that low and intermediate grade MEC had a favorable clinical outcome (11,32). Low-grade MEC is non-aggressive, whereas high-grade MEC is aggressive, frequently leading to metastasis in axillary lymph nodes and distant organs (9,14,15).

To better understand the pathogenesis of MEC in salivary versus extra-salivary origins, researchers have compared the molecular profile of primary breast MECs with salivary and extra-salivary MECs (33). Primary MEC in the salivary gland and lung have been found to be associated with MAML2 fusion (34,35), however, the pathogenesis of primary thyroid MEC seems to be MAML2-independent (36). Among the reported cases of breast MEC that have been investigated for presence of MAML2 rearrangements, three have presented with the feature, suggesting a need for the classification of more tumors (1,14).

In the present literature, the standard surgical approach for MEC of the breast has not been well established because of its low incidence. Our patient underwent a lumpectomy for an intermediate-grade tumor measuring 2.9 cm. In cases documented prior to 2000, most patients underwent mastectomy or modified radical mastectomy (14 cases), regardless of tumor size or grade, while only three cases mentioned breast-conserving procedures such as

quadrantectomy, lumpectomy, or wide local excision. Post-2000, the majority of reported cases involved mastectomies or modified radical mastectomies (18 cases), with six cases reporting lumpectomies or local excisions, and three cases involving quadrantectomies (Table 1). This trend indicates a growing number of surgeons opting for breast-conserving surgery for removing breast MEC tumors, although mastectomies continue to be the preferred treatment option.

Lastly, there are no established guidelines for adjuvant therapy for treatment of MEC. Prior studies have documented a range of approaches, including chemotherapy, radiation, hormonal therapy, different combinations of these methods, or no additional treatment. Except for one patient who did not receive any adjuvant therapy and died due to unrelated causes, all patients who received adjuvant therapy survived until the end of the follow-up period. As noted earlier, the prognosis of breast MEC remains dependent on the pathological grade of the tumor, and the role of adjuvant therapy remains unclear. Therefore, future studies with a larger sample size are needed to explore the role of adjuvant therapy in MEC. Furthermore, additional studies are also required to better understand the significance of hormone receptor status in the context of MEC.

Table 1 Summary of treatment approaches in all cases

Case No.	Author (ref.)	Year	Surgical approach	Adjuvant therapy	Follow-up (mo.)	Status
Present case	Zhang <i>et al.</i>	2023	Lumpectomy + SLD	Radiation, hormonal	6	Alive
1	Gupta <i>et al.</i> (7)	2023	MRM	None	NA	Alive
2	Bak <i>et al.</i> (8)	2022	Lumpectomy + SLD	Chemotherapy, radiation, hormonal	37	Alive
3	Chen <i>et al.</i> (17)	2022	Excision	NA	6	Alive
4	Bui <i>et al.</i> (6)	2022	Lumpectomy + SLD	Radiation, hormonal	NA	Alive
5	Ye <i>et al.</i> (9)	2020	MRM	Chemotherapy	12	Alive
6	Yan <i>et al.</i> (14)	2020	Lumpectomy	NA	60	Alive
7	Burghel <i>et al.</i> (10)	2018	NA	None	NA	NA
8	Sherwell-Cabello <i>et al.</i> (21)	2017	MRM	None	3	Alive
9	Cheng <i>et al.</i> (11)	2017	MRM	NA	156	Alive
10			MRM	NA	41	Alive
11			Mastectomy + SLD	NA	9	Alive
12			Mastectomy + SLD	NA	4	Alive
13	Arun Kumar <i>et al.</i> (22)	2016	MRM	Chemotherapy, radiation, hormonal	24	Alive
14	Fujino <i>et al.</i> (23)	2016	Mastectomy + SLD	NA	NA	NA

Table 1 (continued)

Table 1 (continued)

Case No.	Author (ref.)	Year	Surgical approach	Adjuvant therapy	Follow-up (mo.)	Status
15	Palermo <i>et al.</i> (24)	2013	NA	NA	NA	NA
16	Turk <i>et al.</i> (18)	2013	MRM	NA	5	Alive
17	Basbug <i>et al.</i> (19)	2011	MRM	Chemotherapy, radiation	12	Alive
18	Camelo-Piragua <i>et al.</i> (4)	2009	MRM	Chemotherapy	8	Alive
19	Hornychová <i>et al.</i> (25)	2007	SM + LND	Chemotherapy, radiation	18	Alive
20			MRM	Chemotherapy, radiation	60	Alive
21	Horii <i>et al.</i> (32)	2006	Mastectomy + LND	Hormonal	36	Alive
22	Gómez-Aracil <i>et al.</i> (37)	2006	MRM + LND	NA	54	Alive
23	Di Tommaso <i>et al.</i> (15)	2004	Excision	NA	5	Alive
24			Excision	NA	90	Alive
25			Quadrantectomy + LND	NA	13	Alive
26			Quadrantectomy + LND	NA	3	Alive
27			Quadrantectomy + LND	NA	18	Alive
28	Terzi <i>et al.</i> (20)	2004	MRM	NA	NA	NA
29	Tjalma <i>et al.</i> (30)	2002	RM	None	156	Alive
30	Berry <i>et al.</i> (38)	1998	Mastectomy + LND	NA	NA	NA
31	Markopoulos <i>et al.</i> (29)	1998	Wide local excision + LND	Chemotherapy, radiation, hormonal	60	Alive
32	Chang <i>et al.</i> (26)	1998	MRM	Chemotherapy	48	Alive
33	Lüchtrath and Moll (39)	1989	RM	NA	30	DOD
34	Pettinato <i>et al.</i> (16)	1989	MRM	NA	10	DOD
35	Hanna and Kahn (27)	1985	MRM	NA	8	Alive
36			MRM	NA	14	Alive
37	Hastrup and Sehested (28)	1985	RM	NA	25	DOD
38	Leong and Williams (40)	1985	SM	NA	7	DOD
39	Ratanarapee <i>et al.</i> (41)	1983	NA	NA	14	DOD
40	Fisher <i>et al.</i> (5)	1983	Lumpectomy	NA	60	Alive
41			MRM	NA	48	Alive
42			MRM	NA	120	Alive
43			RM	NA	108	Alive
44			SM	NA	48	Alive
45	Kovi <i>et al.</i> (42)	1981	MRM	NA	NA	NA
46	Patchefsky <i>et al.</i> (2)	1979	RM	None	94	DOR
47			Quadrantectomy	None	10	Alive

SLD, sentinel lymph node; MRM, modified radical mastectomy; NA, not applicable; SM, simple mastectomy; LND, lymph node dissection; RM, radical mastectomy; DOD, died of disease; DOR, died of other reasons.

A limitation of this case study is its short length of follow-up (6 months). Additionally, to our knowledge, this is the first and only case of MEC of the breast reported at our institution. Therefore, we are unable to comment on whether breast-conserving surgery and adjuvant therapy is the best approach to treatment. Nevertheless, MEC of the breast has relatively good prognosis, as none of the intermediate grade lesions, similar to the present study, led to distant metastasis or death (4,8,23).

Conclusions

MEC of the breast is a rare tumor with a relatively favorable overall prognosis. The early and precise diagnosis of this condition plays a pivotal role in formulating effective treatment strategies and ensuring positive survival rates. Nonetheless, future studies are recommended to further explore the role of surgical approaches and adjuvant therapy to improve treatment outcomes.

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Footnote

Reporting Checklist: The authors have completed the CARE reporting checklist. Available at <https://gs.amegroups.com/article/view/10.21037/gc-23-372/rc>

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <https://gs.amegroups.com/article/view/10.21037/gc-23-372/coif>). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review

by the editorial office of this journal.

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