Clinical Case Report

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Mucoepidermoid carcinoma of the breast

Four case reports and review of the literature

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Abstract

Rationale: Mucoepidermoid carcinoma (MEC) of the breast is a rare entity comprising specific morphological and immunohistochemical features, and has been previously only reported in 33 cases.

Patient concerns: Four cases of MEC of the breast are reported in this study. All patients were women with ages ranging from 39 to 66 years. The lesions consisted of neoplastic solid nests and cystic spaces sometimes filled with mucoid material.

Diagnoses: At high power, the tumors were composed of various proportions of basaloid, intermediate, epidermoid, and mucinous cells in different cases. All cases were classified as low-grade MEC of the breast. Tumor cells exhibited low levels of hormonal receptor expression in two cases (cases 1 and 3), and immunonegativity in one case (case 2). On the contrary, estrogen receptors (ER) were positively expressed in 60% of tumor cells in case 4. Tumor cells did not express human epidermal growth factor receptor 2 (HER-2)/neu protein in all the cases.

Interventions: Modified radical mastectomy (Auchincloss) was performed in the first two cases, while the remaining two patients underwent mastectomy plus sentinel lymph node biopsy.

Outcomes: All patients were alive and well without evidence of recurrent disease after a period ranging from 4 months to 156 months.

Lessons: MEC of the breast is a rare primary carcinoma that is difficult to diagnose. Multiple tissue blocks are necessary before obtaining all cell types. Special stains for mucin and electron microscopy would be helpful in suspected cases. Hormonal factors might have an impact on the biological behavior of tumors, but further studies are needed to draw conclusions.

Abbreviations: AB = alcian blue, CK = cytokeratin, ER = estrogen receptor, HER-2 = human epidermal growth factor receptor 2, HPF = high-power field, MEC = Mucoepidermoid carcinoma, PR = progesterone receptor, TNBC = triple negative breast cancer.

Keywords: breast, hormonal factors, immunohistochemistry, mucoepidermoid carcinoma, prognosis

1. Introduction

Mucoepidermoid carcinoma (MEC) is a common malignant tumor of the minor salivary glands with standard grading criteria and prognostic features. MEC of the breast shares similar morphologic features with MEC of the salivary gland. However, the former is a rare entity with an incidence of 0.2% to 0.3%.[1] Only 33 cases have been reported to date. Patchefsky et al[2] were the first to present 2 cases of low-grade MEC of the breast.

Salivary gland-like tumors of the breast have been divided into 2 categories: tumors with myoepithelial differentiation (myoepithelioma, pleomorphic adenoma, adenoid cystic carcinoma, adenomyoepithelioma) and tumors with scanty myoepithelial differentiation (acinic cell carcinoma, oncocytic carcinoma, mucoepidermoid carcinoma).[3] Histologically, MECs are composed of 4 cell types in varying proportions. These are basaloid, intermediate, epidermoid, and mucinous cells. Clinical features, therapeutic strategies, and the prognosis of MEC are related to its histological grading and the accuracy of existing literature.

In this study, we report 4 cases of MEC of the breast and present a review of the literature.

2. Methods

Data from 4 cases of MEC of the breast were retrieved from the consultation files of the Breast Center of the Fourth Hospital of Hebei Medical University between 2004 and 2016. All the patients were confirmed by histopathology and underwent surgeries after diagnosis.

The postoperative specimens were fixed in 10% formalin, routinely processed, and embedded in paraffin. Selected blocks were serially cut and stained with hematoxylin and eosin and Alcian blue (AB) (pH 2.5) after diastase digestion. For immunohistochemistry, a routine EnVison method was used.[4] The tumors were graded according to the Elston–Ellis grading system for breast carcinoma.[5] All procedures were supervised and approved by the Ethics Committee of Fourth Hospital of Hebei Medical University (No. SCXK2017-0025).

3. Results

3.1. Clinical findings

Clinical data are summarized in Table 1. All patients were females with ages ranging from 39 to 66 years. The first 3 patients presented with short medical histories of not more than 3 months,

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Table 1

Clinical findings of the herein reported cases.

Case	Age (y)	Clinical presentation	Location	Size (cm)	Medical history	Surgical treatment	LN metastasis	Follow-up (mo)
1	39	Nodule with obscure boundary	UIQ, right	1.5	3 mo	MRM	3/18	156A
2	49	Well circumscribed nodule	UIQ, left	1.5	20 d	MRM	0/17	41A
3	66	Nodule with obscure boundary	UIQ, left	1.3	3 d	Mastectomy plus SLND	0/6 (SLD)	9A
4	61	Solid-cystic mass	UOQ, left	3.0*	37 y	Mastectomy plus SLND	0/3 (SLD)	4A

A = alive, LN = lymph node metastasis at the time of primary diagnosis, MRM+ALND = modified radical mastectomy (Auchincloss), SLD = sentinel lymph node, SLND = sentinel lymph node biopsy, UIQ = upper inner quadrant, UOQ = upper outer quadrant.

* In this case only a few solid tissues were present.

while the fourth patient harbored a palpable mass in her left breast for nearly 37 years, which became enlarged with the time coursing.

In 3 cases, the lesion presented as a solid nodule, 2 of which had poorly defined boundaries (cases 1 and 3), while the other was well-circumscribed (case 2). The fourth patient harbored an irregular, solid, cystic mass in the breast. Computed tomography revealed only a few solid tissue masses within the septa-divided cystic spaces (Fig. 1). An ultrasound-guided core biopsy was performed during which purulent fluid was withdrawn. Cytological examination showed a small amount of proliferation of epithelial cells among a large number of blood cells. Excision biopsy revealed a circumscribed cyst measuring 30 mm in maximum diameter, and only a few solid tissue masses were present.

Modified radical mastectomy (Auchincloss) was performed in the first 2 cases, while the remaining 2 patients underwent mastectomy plus sentinel lymph node biopsy. Three of the 18 lymph nodes contained metastatic carcinoma in case 1, while no lymph node metastases were found in other cases.

Follow-up information was available for all the cases: patients were alive and well without evidence of recurrent disease after a period ranging from 4 months to 156 months.

3.2. Histopathological findings

The lesions comprised neoplastic solid nests and cystic spaces sometimes filled with mucoid material. At high power, the tumors were composed of various proportions of basaloid, intermediate, epidermoid, and mucinous cells in different cases. A prominent lymphocytic infiltrate was observed around the tumor lobules. AB stains showed numerous mucinous cells in the invasive component (Fig. 2A).

Tumor cells were plump with granular eosinophilic cytoplasm and eosinophilic secretory material. Scattered microcystic spaces, foamy cells, and vacuolated cells were also observed (Fig. 2B). The nuclei were large with mild chromatin clearing and prominent nucleoli (Fig. 2C). Cystic spaces were mainly lined by flat cells. The latter were devoid of cytoplasmic vacuoles, but their cytoplasm was stained with AB (Fig. 2D).

Mitoses were infrequent in 3 cases [1/10 high-power field (HPF) cases 2 and 4, 2/10 HPF case 3]. Case 1 showed a moderate number of mitoses (3/10 HPF) with mild cytological atypia, while no perineural or lymphovascular invasion was observed.

All the cases were classified as low-grade (grade 1), according to the Elston–Ellis grading system.[5]

3.3. Immunohistochemical findings

Immunohistochemical findings are summarized in Table 2. Most intermediate and epidermoid cells expressed cytokeratin (CK) 5/6 (Fig. 3A). CK 7 was mainly observed in the cells composing the central part of the neoplastic nests and in the cells lining glandular and cystic spaces (Fig. 3B). In addition, both basaloid and intermediate cells were positive for p63 (Fig. 3C). Tumor cells exhibited low levels of hormonal receptor expression in 2 cases (cases 1 and 3), and immunonegativity in 1 case (case 2). On the contrary, estrogen receptors (ERs) were positively expressed in 60% of tumor cells in case 4. Tumor cells did not express human epidermal growth factor receptor 2 (HER-2)/neu protein in all the cases.

4. Discussion

MEC is a malignant tumor usually associated with the salivary glands. Primary MEC of the breast is extremely rare, having an incidence of 0.2% to 0.3%.[1] In our study, the incidence was 0.03% (4 cases of MEC of the breast out of 15,344 cases of breast cancer between 2004 and 2016), which is much lower than that reported previously. Fisher et al[1]suggested that the true frequency of MEC in the breast is higher than previously realized since MEC may masquerade under other diagnoses, such

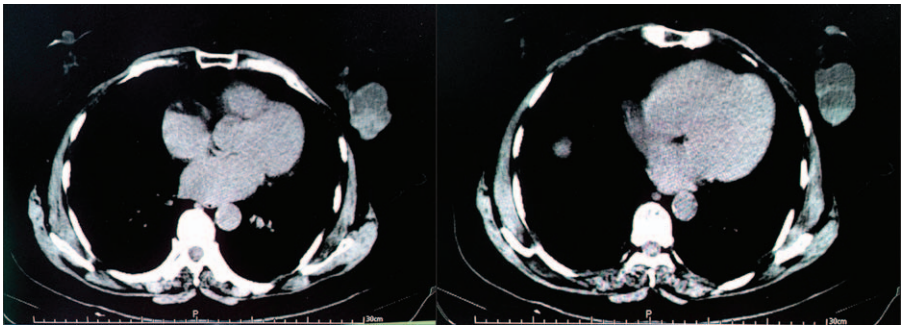

Figure 1. Computed tomography revealed only a few solid tissue masses within the septa-divided cystic spaces.

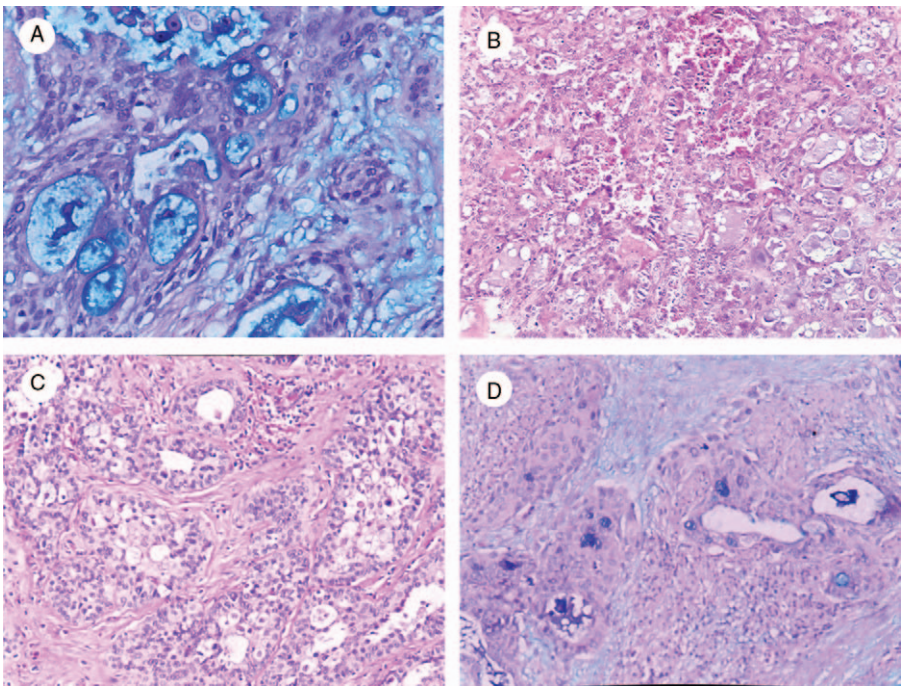

Figure 2. Histopathological features of mucoepidermoid carcinoma of the breast. A, Alcian blue stains showed numerous mucinous cells in the invasive component (Alcian blue stain, ×200). B, Scattered microcystic spaces, foamy cells, and vacuolated cells were also observed (HE, ×200). C, The nuclei were large with mild chromatin clearing and prominent nucleoli (HE, ×200). D, Cystic spaces were mainly lined by flat cells (Alcian blue stain, ×100).

as atypical squamous metaplasia. This possibility must be taken into consideration, especially when only 1 cell type is observed. Multiple tissue blocks are necessary before obtaining all cell types and their true ratio of constituents. Special stains for mucin and electron microscopy may be helpful in suspected cases. On the other hand, studies on the incidence of MEC of the breast in Asian populations are not available, so we cannot exclude population susceptibility factors.

The breast and major salivary glands are derived from the embryonal ectoderm and their basic tubuloalveolar structures, probably explaining the similar morphologic features of tumors arising at these different sites.[6] MEC is described in other organs besides the salivary gland and breast including the esophagus, pleura, forearm, penis, tonsils, thyroid, colon, lacrimal gland, and thymus.[7–14] The 4 current cases of MEC were all primary MEC of the breast.

All tumors located outside the salivary glands share the same morphological and even immunohistochemical features as MEC of the major salivary glands.[15–18] Histologically, MEC is composed of 4 cell types in varying proportions. These are basaloid, intermediate, epidermoid, and mucinous cells. The tumor in the fourth patient was initially considered to be a pure mucinous adenocarcinoma of the breast, but on further examination, the diagnosis was changed to MEC.

Table 2

Immunohistochemical findings of the herein-reported cases.

Antibody	1	2	3	4
ER	+	–	10%	60%
PR	+	–	–	2%
CK7	ND	+	ND	+
CK5/6	ND	+	ND	+
P63	ND	±	ND	+
HER2	–	–	–	–

CK = cytokeratin, ER = estrogen receptor, HER-2 = human epidermal growth factor receptor 2, ND = not detected, PR = progesterone receptor.

The parameters for the grading criteria are the relative proportion of cystic components, the presence of neural invasion and necrosis, mitotic rate, and anaplasia.[5,19] All 4 cases were classified as low-grade (grade 1), according to the Elston–Ellis grading system. Patients with high-grade tumors that are highly aggressive should be treated by radical surgery with lymph node sampling and dissection, and patients with low-grade tumors may be cured by complete resection as low-grade tumors are usually considered to be potentially curable. All the patients underwent surgery; the first 2 cases underwent modified radical mastectomy (Auchincloss), and the others underwent mastectomy with sentinel lymph node biopsy. Three of the 18 lymph nodes contained metastatic carcinoma in case 1, while no lymph node metastases were observed in the other 3 cases. All the patients were alive and well without evidence of recurrent disease, with follow-up ranging from 4 to 156 months.

Tumors with the basal cell phenotype represent 15% to 25% of invasive breast carcinomas. They are usually high-grade; comprise areas of necrosis; are often ER-, progesterone receptor (PR)-, and HER2/neu-negative (triple negative breast cancer, TNBC); and affected patients harbor BRCA1 mutations more frequently than other types of breast carcinoma.[20,21] Some studies have shown that most cases of MEC of the breast are characterized by negative expression for ER, PR, and HER2. However, unlike other TNBCs, they exhibit a relatively good prognosis.[3] The absence of the expression of hormonal receptors (estrogen and progesterone) is found in the literature for most metaplastic carcinomas, including MEC.[22] According to previous reports, hormonal receptor status was studied in only 11 cases (Table 3).[6,18,22–28] Of these, 4 patients expressed ERs, while the other 7 cases were ER-negative. PRs were

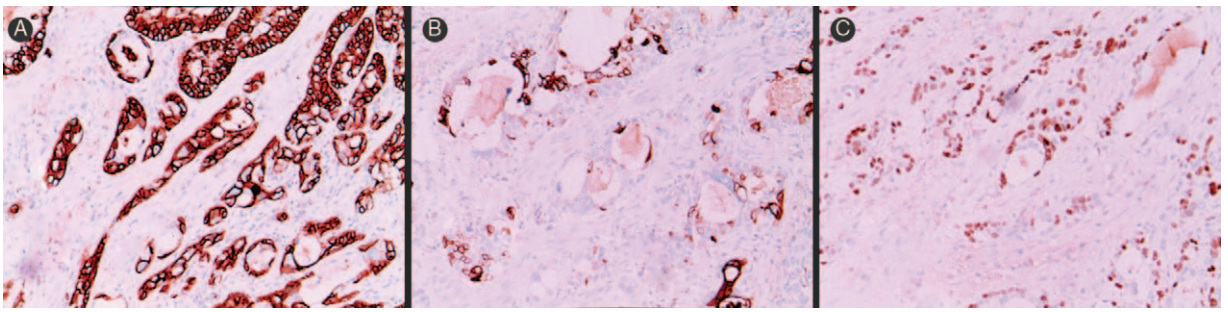

Figure 3. Immunohistochemical features of mucoepidermoid carcinoma of the breast. A, Most intermediate and epidermoid cells expressed CK 5/6 (immunohistochemistry reactions, ×200). B, CK 7 was mainly observed in the cells composing the central part of the neoplastic nests and in the cells lining glandular and cystic spaces (immunohistochemistry reactions, ×200). C, Both basaloid and intermediate cells were positive for p63 (immunohistochemistry reactions, ×200). CK = cytokeratin.

Table 3

Summary of previously reported cases of mucoepidermoid carcinoma of breast.

	Yr	Age	Tumor grade	ER	PR	HER2	LN metastasis	Distant metastasis	Follow-up (mo)
Hastrup and Sehested[22]	1985	59	HG	N	N	NS	0/4	Y	25DOD
Hanna and Kahn[18]	1985	51	NS	P	N	NS	0/NS	NS	8A
Hanna and Kahn[18]	1985	31	NS	P	N	NS	2/18	NS	14A
Horii et al[23]	2006	54	LG	P	N	N	0/NS	NS	36A
Gomez-Aracil et al[24]	2006	69	HG	P	N	NS	24/28	N	54A
Hornychová et al[6]	2007	30	LG	N	N	N	0/NS	N	60A
Hornychová et al[6]	2007	63	HG	N	N	N	0/17	N	18A
Camelo-Piragua et al[25]	2009	49	IG	N	N	N	1/3	N	12A
Murat Basbug et al[26]	2011	69	NS	N	N	N	0/NS	N	12A
Palermo et al [27]	2013	80	HG	N	N	NS	NS	NS	NS
Turk et al[28]	2013	40	NS	N	N	N	1/24	NS	5A

A = alive, DOD = died of disease, ER = estrogen receptor, HER-2 = human epidermal growth factor receptor 2, HG = high grade, IG = intermediate grade, LG = low grade, LN = lymph node metastasis at the time of primary diagnosis, N = negative, NS = not stated, P = positive, PR = progesterone receptor.

immunonegative in all the cases. In the cases reported herein, tumor cells exhibited low levels of hormonal receptor expression in 2 cases (cases 1 and 3), and immunonegativity in 1 case (case 2). No HER-2/neu protein was detected, but all the cases presented with good prognosis.

The effect of hormonal factor expression in MEC is controversial; a few studies have mentioned the role of hormonal factors. Liang et al[9] described a MEC located in the left forearm of a 39-year-old pregnant woman, in which tumor growth accelerated with increasing hormone levels, suggesting that hormonal factors might influence the biological behavior of tumors. In case 4, we observed strong ER immunopositivity; the patient was diagnosed with low-grade MEC and no metastasis was identified despite a 37-year medical history without treatment. Hormonal factors may influence the prognosis of MEC of the breast, although the number of cases is far too small to draw conclusions. Follow-up is necessary to determine the biological behavior.

5. Conclusion

MEC of the breast is a rare primary carcinoma that is difficult to diagnose. Multiple tissue blocks are necessary before obtaining all cell types. Special stains for mucin and electron microscopy may be helpful in suspected cases. Most cases of MEC of the breast are characterized by negative expression of ER, PR, and HER2. However, unlike other TNBCs, they exhibit a relatively good prognosis. Hormonal factors might influence the biological behavior of tumors, but further studies are needed to draw conclusions.

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