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Case Report

Primary mucinous cystadenocarcinoma of the breast coexisting with invasive ductal carcinoma: a case report and review of the literature

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Abstract: Mucinous cystadenocarcinoma (MCA) is an extremely rare variant of primary breast carcinoma that bears a striking resemblance to MCAs of the ovary and pancreas. A 58-year-old woman underwent mastectomy of the right breast with axillary lymph node dissection and received adjuvant chemotherapy and radiotherapy 11 years ago. Six months ago, she presented a nodule in the left breast. Histologically, the cystic areas are lined by tall columnar cells with an abundance of intracellular mucin, while part of tumor cells which presented with mild atypia displayed papillary structures and some exfoliated micro papillary floating in the mucinous lake. The tumor cells were highly expressed CK7, p53 and EGFR, and negative for p63, CK20, CDX2, Her-2, ER and PR. The patient was alive with no tumor recurrence or metastasis at a 6-month follow-up examination without further chemotherapy or radiotherapy. To date, the influence of MCA on patient prognosis remains controversial. Our case may provide further understanding of primary MCA of the breast.

Keywords: Breast, mucinous cystadenocarcinoma, treatment

Introduction

Primary mucinous cystadenocarcinoma (MCA) of the breast is an unusual neoplasm. Only 22 cases have been reported globally [1-18]. Mucinous carcinoma and carcinoma with signet ring cell differentiation were described in the World Health Organization (WHO) classification of breast tumors released in 2012 [19]. In MCA, multiple cystic spaces contain large amounts of mucinous. The cystic areas are lined by tall columnar cells with an abundance of intracellular mucin, while part of tumor cells which presented with mild atypia displayed papillary structures and some exfoliated micropapillary floating in the mucinous lake. Here, we report the first case of MCA in a 58-year-old woman, who had a history of invasive ductal carcinoma of right breast.

Case presentation

A 58-year-old Chinese woman was diagnosed with invasive breast cancer and 12/13 axillary lymphnodes from metastatic carcinoma in her right breast in 2005. She underwent mastectomy of the right breast with axillary lymph node dissection and received adjuvant chemotherapy and radiotherapy. The patient had neither recurrence nor metastasis during 11 years of follow-up.

Six months ago, she presented with a left breast lump. There was neither nipple discharge nor skin retraction. Breast ultrasonography displayed a well-circum scribed cystic-solid mass measuring 30 × 17 mm. No axillary lymph node involvement was noticed. Fine-needle aspiration biopsy identified mucinous adenocarcinoma (**Figure 1**).

A left-sided modified radical mastectomy was conducted after a frozen-section diagnosis of malignancy. On gross examination, the cut surface showed cystic-solid, irregular and white mass (45 × 30 × 20 mm). The cystic spaces were full of a tan gelatin-like material. Nothing abnormal detected in the rest of the breast. Microscopically, multiple cystic spaces contain large amounts of mucinous. The cystic areas

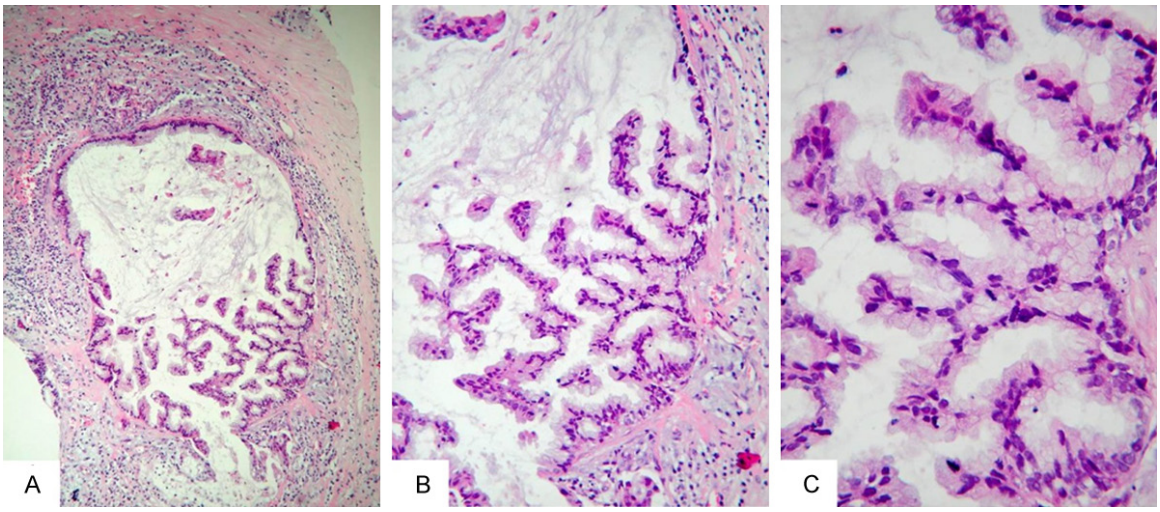

Figure 1. Fine-needle aspiration histology shows cystic tumor is lined with columnar mucinous cells with papillary structure and some exfoliated micropapillary floating in the mucinous lake (A: 40 ×, B: 100 ×, C: 200 ×).

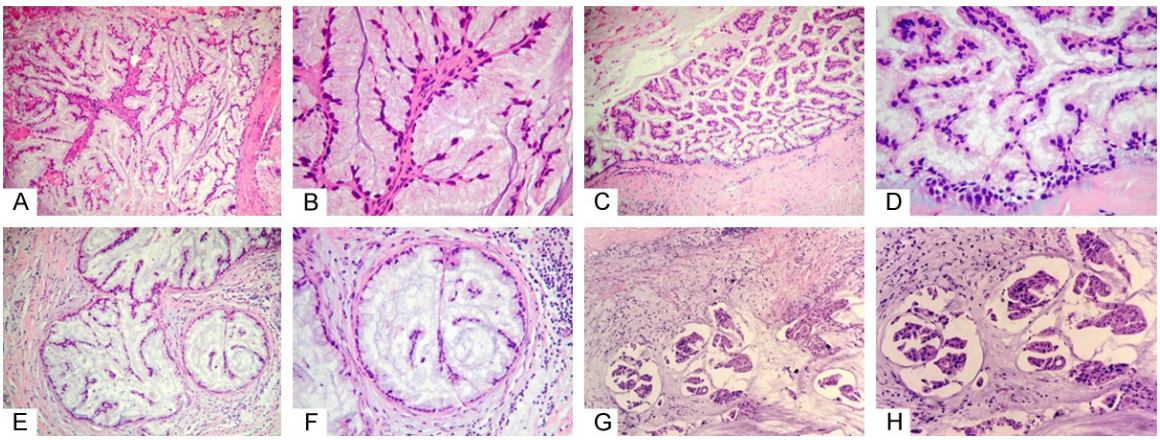

Figure 2. Histopathological features of the primary breast MCA. (A, B) The cystic areas are lined by tall columnar cells with an abundance of intracellular mucin. (C, D) Part of tumor cells which presented with mild atypia displayed papillary structures and some exfoliated micropapillary floating in the mucinous lake. (E, F) DCIS is also found in small cysts. The cysts are lined by monolayer tall columnar mucinous cells, and part of areas showed micropapillary structures. (G, H) The tumor cells floating in the mucinous lake show some degree of cellular pleomorphism displacing atypical nuclei to the periphery (A, C, E, G: 100 ×; B, D, F, H: 200 ×).

are lined by tall columnar cells with an abundance of intracellular mucin, while part of tumor cells which presented with mild atypia displayed papillary structures and some exfoliated micropapillary floating in the mucinous lake (**Figure 2**). Furthermore, a few cysts and ductal carcinoma *in situ* (DCIS) adjacent to the invasive ductal carcinoma (IDC) were also be detected.

Immunohistochemical (IHC) staining showed that the tumor cells were significantly expressed cytokeratin 7 (CK7), EGFR and p53, and negative for Her-2, estrogen receptor (ER), progesterone receptor (PR), grosscystic disease fluid protein (GCDFP)-15, p63, CDX-2, villin, CK20 and CK5/6. The proliferative index (based on Ki-67 staining) was high (approximately 80%) (**Figure 3**). There was no axillary lymph nodes metastasis (0/6). The patient had no history of a concurrent or subsequent ovarian or pancreatic carcinoma or an invasive malignancy at any other site. No other lesion was found after careful examination.

The tumor was ultimately diagnosed as MCA of the breast coexisting with an invasive ductal carcinoma. The patient was discharged one

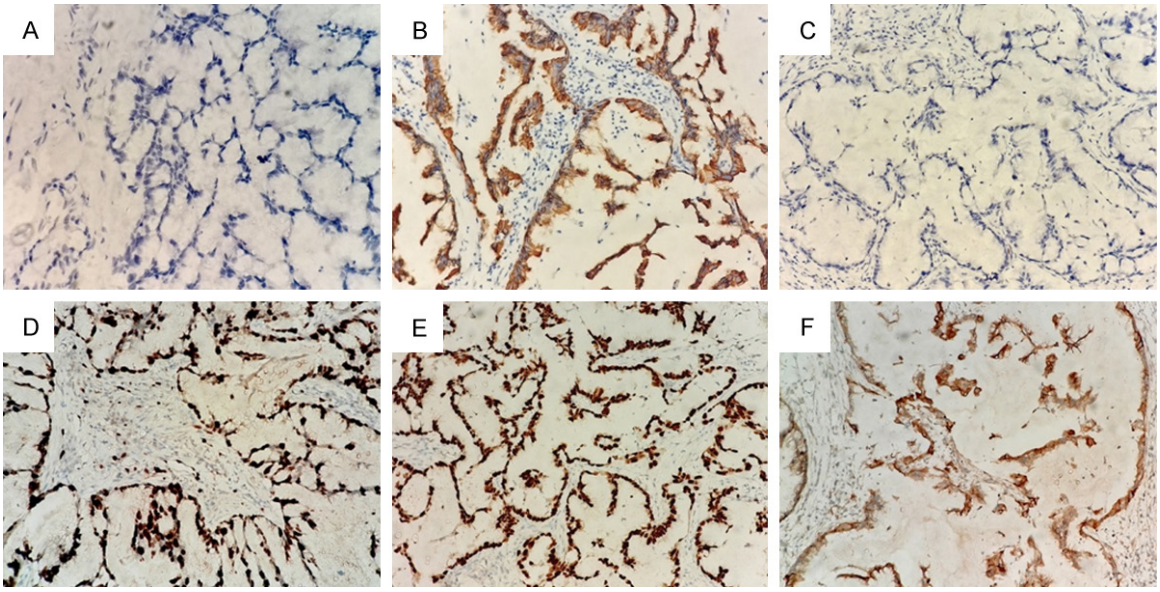

Figure 3. Immunohistochemical staining of MCA. The tumor cells are negative for p63 (A) and CK20 (C), and positive for CK7 (B), Ki-67 (D), p53 (E) and EGRF (F) (100 ×).

week after the operation without chemotherapy or radiotherapy and followed up six months.

Discussion

Primary MCAs of the breast were first reported by Koenig and Tavassoli in 1998 [2]. There were only 22 cases have been reported in the literature. The tumor is characterized by multiple cystic spaces which contain large amounts of mucinous material. The cystic areas are lined by tall columnar cells with an abundance of intracellular mucin. The clinicopathological features of MCA are summarized in 23 cases (**Table 1**). The patients were aged 41-96 years and the average age was 60 years. There were 15 patients aged ≥ 55 years (15/23). The follow-up period was from 6 to 46 months.

The diagnosis has to be made cautiously because of the rarity of mammary MCA. To make a definite diagnosis, a metastatic MCA must be excluded because of the possibility of metastatic MCA from the pancreas, ovary or gastrointestinal tract. This requires careful inquiry about the patient's detail clinical history and physical examination. Moreover, the IHC results could help to exclude the possibility of metastatic MCA. The tumor cells were negative of CK20, villin, and GCDFP-15. Her-2, ER and PR may also be negative. However, a review of the literature identified one case that was ER+ [8], three cases were Her-2+ [8, 12, 16] and one case was Her-3+ [18].

In our case, it is noteworthy that the patient who had history of right breast cancer. There was not reveal any tumor in other organs with detailed clinical examination and the presence of ordinary DCIS adjacent to the tumor. The tumor cells showed a p63-/CK7+/CK20-/CDX2-/villin-pattern, overexpression of p53 and EGFR, and 80% tumor cells expressed Ki-67. ER, PR, and Her-2 negative breast tumors are related with a poor prognosis [20]. In the literature, only four MCA patients presented with lymph node metastasis, and all of them were treated with surgery and lymph node dissection, but they did not receive chemotherapy (CT) or radiotherapy (RT) [2, 4, 11]. No disease was observed in these patients during a 6-46-month follow-up. However, it is insufficient to discussing only a few patients with good outcomes for these rare breast tumors. Furthermore, the patients were not affected by the lack of CT and RT. Although the nature of breast MCAs is invasive, patient prognosis appears to be good despite lymph node metastasis, which occurs in frequently in the patients with recurrence or distant metastasis [6]. In some cases, DCIS and/or IDC were also found in MCA surrounding the tumor [3, 5, 14]. In the present case, the patient will receive CT and/or RT because of the MCA coexisting with IDC.

Table 1. Reported cases of primary breast mucinous cystadenocarcinomas

Case No.	Detail information	Age (years)	Size (mm)	Stage (pTNM)	ER	PR	c-erbB2	CK7	CK20	Ki-67 (%)	P53 (%)	Treatment	Follow-up
1 [1]	Rosen, 1984	79	60	T3N0M0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	M	DOR 24 m
2 [2]	Koenig, 1998	54	190	T4N1M0	-	-	N/A	+	-	40	N/A	M, LND	ANED 34 m
3 [2]	Koenig, 1998	67	23	T2N0M0	-	-	N/A	+	-	30	N/A	M, LND	ANED 22 m
4 [2]	Koenig, 1998	49	85	T3N0M0	-	-	N/A	+	-	70	N/A	M, LND, C, R	ANED 11 m
5 [2]	Koenig, 1998	61	8	T1N0M0	-	-	N/A		-	50	N/A	L, LND	N/A
6 [3]	Domoto, 2000	74	100	T3N0M0	-	N/A	N/A	+	-	21.8	-	M, LND	ANED
7 [4]	Honma, 2003	96	20	T2N2M0	-	-	-	N/A	N/A	35	5	L, LND	DOR 46 m
8 [5]	Chen, 2004	65	30	T2N0M0	-	-	-	+	Focal +	20.5	+	M, LND, C	ANED 8 m
9 [6]	Coyne, 2008	51	40	T2N0M0	-	-	N/A	+	-	N/A	N/A	L	N/A
10 [7]	Lee, 2008	55	25	T2N0M0	-	-	-	+	-	90	N/A	L	ANED 6 m
11 [8]	Rakıcı, 2009	52	100	T3N0M0	+	-	-	-	-	N/A	N/A	M, LND, TMX	ANED 24 m
12 [9]	Gulwani, 2010	61	30	T2N0M0	-	-	-	N/A	-	N/A	N/A	M, LND	ANED 6 m
13 [10]	Petersson, 2010	73	45	T2N0M0	-	-	2+	+	-	N/A	N/A	M, LND	N/A
14 [11]	Deng, 2012	41	70, 50, 25	T3N1M0	-	-	-	+	-	50	N/A	M, LND	ANED 24 m
15 [12]	Kim, 2012	59	9	T1N0M0	-	-	2+	+	-	5	5	PM, LND, C	ANED 12 m
16 [13]	Li, 2012	52	65	T3N0M0	-	-	-	+	-	10	N/A	N/A	N/A
17 [14]	Sentani, 2012	65	30	T2N0M0	-	-	N/A	+	-	N/A	N/A	PM, LND	ANED 6 m
18 [15]	Lin, 2013	62	56	T2N0M0	-	-	-	+	-	N/A	+	M, LND	ANED 15 m
19 [16]	Kucukzeybek, 2014	55	20	T3N1M0	-	-	2+	+	-	30	-	M, LND, C, R	ANED 10 m
20 [17]	Witherspoon, 2015	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
21 [18]	Seong, 2016	59	20	N/A	-	-	3+	N/A	N/A	N/A	N/A	N/A	N/A
22 [18]	Seong, 2016	50	22	N/A	-	-	-	N/A	N/A	N/A	N/A	N/A	N/A
Present case		58	45	T2N0M0	-	-	-	+	-	80	+	M, LND	ANED 6 m

ANED: Alive with no evidence of disease, C: Chemotherapy, CK7: Cytokeratin 7, CK20: Cytokeratin 20, DOR: Died with other reason, ER: Estrogen receptor, L: Lumpectomy, LND: With lymph node dissection, M: Modified radical mastectomy, N/A: Not acquired, PM: Partial mastectomy, PR: Progesterone receptor, R: Radiation therapy, TNM: Tumor, node, metastasis, TMX: Tamoxife.

MCA displays unique pathological histology and IHC characteristics, and patients show good prognosis after complete and detail resection. Nevertheless, the clinical and imaging features and the prognostic factors of MCA remain poorly understood in contrast to the IDC. Thus, more cases and longer follow-up will be necessary for understand the disease.

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Disclosure of conflict of interest

None.

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