Primary Mucinous Cystadenocarcinoma of the Breast with Endocervical-Like Mucinous Epithelium

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Keywords

Breast cancer · Mucinous cystadenocarcinoma · Immunohistochemistry

Summary

Background: Primary mucinous cystadenocarcinoma of the breast is an extremely rare entity. To the best of our knowledge, only 17 patients have been described in the PubMed database. **Case Report:** Here, we report a primary breast mucinous cystadenocarcinoma with endocervical-like mucinous epithelium in a 62-year-old woman. The patient was followed for 5 months without any adjuvant treatment and she continues to be disease free. **Conclusions:** Primary breast mucinous cystadenocarcinoma usually displays unique pathologic and immunohistochemical characteristics simulating its ovarian counterparts; it seems to have a good prognosis after complete resection.

Schlüsselwörter

Mammakarzinom · Muzinöses Zystadenokarzinom · Immunhistochemie

Zusammenfassung

Hintergrund: Das primäre muzinöse Zystadenokarzinom der Brust ist ein extrem selten auftretender Tumor. Unseres Wissens sind nur 17 Patienten in der PubMed-Datenbank beschrieben worden. **Fallbericht:** Hier berichten wir über ein primäres muzinöses Zystadenokarzinom der Brust mit Gebärmutterhalsschleimhautartigem muzinösem Epithel bei einer 62-jährigen Frau. Die Patientin wurde 5 Monate lang nachuntersucht, ohne irgendeine adjuvante Behandlung zu erhalten, und sie ist weiterhin krankheitsfrei. **Schlussfolgerungen:** Das primäre muzinöse Zystadenokarzinom der Brust zeigt meist einzigartige pathologische und immunhistochemische Eigenschaften, die seinen ovariellen Pendant entsprechen. Nach kompletter Resektion scheint es eine gute Prognose zu haben.

Introduction

The primary mucinous cystadenocarcinoma of the breast is an extremely rare entity. In the World Health Organization (WHO) classification of breast tumors released in 2003, it belonged to the mucin-producing carcinomas. The latter included 4 variants: mucinous carcinoma, cystadenocarcinoma, columnar cell mucinous carcinoma, and signet ring cell carcinoma. The mucinous cystadenocarcinoma was defined as the carcinoma composed of generally tall, columnar cells with basally located bland nuclei and abundant intracytoplasmic mucin that appears cystic to the naked eye. There were only 4 recorded cases before 2003 when the third edition of the WHO classification was published, and based on these

reports, the tumor was thought to have similar clinical features as the common infiltrating ductal carcinoma [1]. Thereafter, a series of instances were described. However, the term was abandoned in the WHO classification of 2012 because of its rarity. Only 2 types of mucin-producing carcinomas were described in this edition: mucinous carcinoma and carcinomas with signet ring cell differentiation [2]. In the present study, we report a case of this rare tumor. To make further investigations, we performed a PubMed search using the terms 'breast' AND 'mucinous cystadenocarcinoma', and all articles written in English and cited by these reports were taken into account. A total of 17 cases were identified in 14 isolated papers (table 1). The aim of this study was to further investigate the clinicopathologic characteristics of this rare tumor.

Table 1. Reported instances of primary breast mucinous cystadenocarcinomas

Case no.	Age, years	Size, mm	Stage (pTNM)	ER	PR	c-erbB2	CK7	CK20	Ki-67, %	Treatment	Follow-up
1 [3]	79	60	T3N0M0	NA	NA	NA	NA	NA	NA	M,	DOR 2 years
2 [4]	54	190	T4N1M0	–	–	NA	+	–	40	M, LND	ANED 24 months
3 [4]	67	23	T2N0M0	–	–	NA	+	–	30	M, LND	ANED 22 months
4 [4]	49	85	T3N0M0	–	–	NA	+	–	70	M, LND, C, R	ANED 11 months
5 [4]	61	8	T1N0M0	–	–	NA	+	–	50	L, LND	NA
6 [5]	74	100	T3N0M0	–	NA	NA	+	–	21.8	M, LND	ANED
7 [6]	96	20	T2N2M0	–	–	–	NA	NA	35	L, LND	DOR 46 months
8 [7]	65	30	T2N0M0	–	–	–	+	focal+	20.5	M, LND, C	ANED 8 months
9 [8]	51	40	T2N0M0	–	–	NA	+	–	NA	L	NA
10 [9]	55	25	T2N0M0	–	–	–	+	–	90	L	ANED 6 months
11 [10]	52	100	T3N0M0	+	–	–	–	–	NA	M, LND	ANED 24 months
12 [11]	61	30	T2N0M0	–	–	–	NA	–	NA	M, LND	ANED 6 months
13 [12]	73	45	T2N0M0	–	–	2+	+	–	NA	M, LND	NA
14 [13]	65	30	T2N0M0	–	–	NA	+	–	NA	PM, LND	ANED 6 months
15 [14]	52	65	T3N0M0	–	–	–	+	–	10	NA	NA
16 [15]	41	70, 50, 25	T3N1M0	–	–	–	+	–	50	M, LND	ANED 24 months
17 [16]	59	9	T1N0M0	–	–	2+	+	–	5	PM, LND, C	ANED 3 months

ANED = Alive with no evidence of disease, C = chemotherapy, CK = cytokeratin, DOR = died with other reason, ER = estrogen receptor, L = lumpectomy, LND = with lymph node dissection, M = modified radical mastectomy, NA = not available, PM = partial mastectomy, PR = progesterone receptor, R = radiation therapy, TNM = tumor, node, metastasis.

Fig. 1. Imaging and histopathological features of the primary breast mucinous cystadenocarcinoma. **(a)** Ultrasonography showed a well-circumscribed and lobulated cystic-solid mass. **(b)** Computed tomography revealed a large non-homogeneous lobulated tumor mass in the right breast. **(c–e)** The tumor showed variably sized spaces lined by columnar neoplastic mucinous cells with intra/extracellular mucin, and mucinous micropapillae could be observed (hematoxylin-eosin staining; original magnifications: c, d, 100 ×; e, 20 ×). **(f–h)** The tumor cells were diffusely positive for p53 **(f)** and CK7 **(g)** and weakly positive for CK34βE12 **(h)** (immunohistochemistry; original magnifications: f, g, 100 ×; h, 200 ×).

Case Report

A 62-year-old woman visited the outpatient clinic, complaining of a firm painless lump in the right breast. She denied any history of tumors in other sites. Physical examination confirmed the tumor mass in the upper outer quadrant of the right breast. Breast ultrasonography showed a well-circumscribed and lobulated cystic-solid mass measuring 56 × 31 × 27 mm, within which 2 independent fluid sonolucent areas measuring 20 × 16 mm and 16 × 8 mm were detected (fig. 1a). The chest computed tomography revealed multiple non-homogeneous lobulated tumor masses in the right breast, of which the largest one was measured as 32.4 × 22.5 mm (fig. 1b). A right-sided modified radical mastectomy following a frozen-section diagnosis of malignancy was performed. Grossly, the tumor appeared to be well demarcated, solid and cystic, and contained mucoid material simulating an ovarian tumor. Microscopically, it showed variably sized spaces lined by columnar mucinous cells with intracellular mucin, and these neoplastic cystic spaces were in a hyaline background with extracellular mucin and surrounded by a dense basement membrane. The tumor cells presented with mild atypia and basally located nuclei. No typical ductal myoepithelial cells were observed below the mucinous epithelium. The intraluminal papillary structures and some exfoliated micropapillae floating in the mucinous lake could be observed (fig. 1c–e). Immunohistochemical staining showed that the tumor cells were diffusely positive for p53 and

cytokeratin (CK)7, weakly positive for CK34βE12 (fig. 1f–h), and negative for estrogen receptor (ER), progesterone receptor (PR), c-erbB2, gross cystic disease fluid protein (GCDFP)-15, mammaglobin, thyroid transcription factor (TTF)-1, CK20, CK5/6, CK14, p63, CDX-2, and villin. The absence of myoepithelium was also demonstrated by the negativity of CK5/6, CK14, and p63. All axillary lymph nodes were free from metastasis. Further whole-body computed tomography and ultrasonography showed no abnormalities in the abdominal and pelvic organs. These imaging examinations demonstrated that the lung, the gastrointestinal tract, the pancreas, and the ovary were free of any tumor. As no other occupying lesion was found after careful retrieving, a diagnosis of primary mucinous cystadenocarcinoma was made. The patient was discharged 2 weeks after the operation, and she was uneventful without further chemotherapy or radiotherapy during the following 5-month postoperative period.

Discussion

Primary mucinous cystadenocarcinoma of the breast is an extremely rare entity. To the best of our knowledge, only 17 patients have been described in the PubMed database (table 1). When adding our report, the ages of all patients range from

41 to 96 years and the average age is 62 years. We found that most patients are in their 6th and 7th decades (12/18). The average onset age is similar to that of infiltrative breast carcinoma of no special type, being over 60 years, and onset is infrequent below the age of 40 years. The follow-up period was from 3 to 46 months and the prognosis seems to be good, even in patients suffering from lymph node metastasis, which occurred infrequently in the patients with this tumor, with only 3 reported cases [4, 6, 15]. No recurrence or distant metastasis was recorded in this cohort. 3 patients accepted chemotherapy and 1 accepted chemotherapy after tumor resection; however, whether the adjunctive treatment is necessary or not is still unclear. Usually, complete tumor resection is sufficient. We must acknowledge that the prognostic factors could not be analyzed because of the small sample and the short follow-up period.

Pathologically, the tumor resembles a mucinous tumor of the ovary with endocervical epithelium appearance. However, the mucinous epithelium is well differentiated with single or pseudostratified basal nuclei that present only mild or absent atypia, and the cystic spaces are lined by a single layer of predominantly bland appearing, columnar mucinous cells. Desmoplastic stroma could be observed. No obvious mitosis figures and necrosis were observed. It is rather difficult to exclude benign or borderline lesions and make a definite diagnosis of malignancy relying only on the cell morphology. Nevertheless, the mucinous glands were branched and crowded and showed back-to-back and complex papillary or budding architecture in some areas, suggesting malignancy. Moreover, 2 of the most important features, the absence of myoepithelium and the capability of metastasis, also represent distinct differences from other benign lesions.

To make a definite diagnosis, a metastatic mucinous cystadenocarcinoma originating from distant organs must be

excluded, especially from the ovary. This may depend only on careful inquiry after the clinical history and thorough imaging detection. Additionally, the immunohistochemistry results could also hardly lead to a differential diagnosis since they are often similar to those of an endocervical-like mucinous cystadenocarcinoma of the ovary, and the specific markers for breast cancer such as GCDPF-15 and mamoglobin may be completely negative. The most common immunophenotype reported previously was: ER-, PR-, c-erbB2-, CK7+, CK20-; however, the ER [10] or c-erbB2 [12, 16] may be positive. To make a further identification of the reported cases, we carefully re-reviewed all available images with hematoxylin-eosin staining. We found that the ER-positive and CK7-negative case reported by Rakici et al. [10] had morphological features different from all other cases, which showed a small glandular cavity and inapparent intracytoplasmic mucin. Only 1 c-erbB2-immunopositive case was demonstrated to harbor an amplification of the gene coding for the human epidermal growth factor receptor 2 (HER2) [12].

In conclusion, according to previous studies, the tumor usually occurs in older female patients, displays unique pathologic and immunohistochemical characteristics simulating its ovarian counterparts, and seems to have a good prognosis after complete resection. Nevertheless, in contrast to the infiltrating carcinoma of no specific type, the clinical and imaging features and the prognostic factors of the tumor are still poorly understood, and all published isolated case reports failed to draw a definite conclusion in this regard.

Disclosure Statement

The authors declare no conflicts of interest.

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