Mucinous breast carcinoma with tall columnar cells

N Tsoukalas^{1,2*}, M Kiakou^{1*}, M Tolia³, ID Kostakis⁴, M Galanopoulos¹, G Nakos⁵,
D Tryfonopoulos², G Kyrgias³, G Koumakis²

¹Department of Oncology, 401 General Military Hospital, Athens, Greece

²Second Department of Medical Oncology, Agios Savvas Anticancer Hospital, Athens, Greece

³Department of Radiotherapy, University of Thessaly, Medical School, Larissa, Greece

⁴Second Department of Propedeutic Surgery, Laiko General Hospital, National and Kapodistrian University of Athens, Medical School, Athens, Greece

⁵Department of Pathology, 401 General Military Hospital, Athens, Greece

*Contributed equally

ABSTRACT

Mucinous carcinoma of the breast represents 1%–4% of all breast cancers. The World Health Organization classification divides this type of tumour into three different subtypes: mucinous carcinoma, mucinous carcinoma with tall columnar cells (mucinous cystadenocarcinoma and columnar cell mucinous carcinoma) and signet ring cell carcinoma. A 74-year-old woman presented a tumour with inflammatory features in the upper outer quadrant of her left breast, 7 cm in diameter. The core biopsy showed infiltrating ductal carcinoma of no specific type. The tumour-node-metastasis clinical staging was T4cN3M0 (Stage IIIC). She received neoadjuvant chemotherapy, underwent left mastectomy with radical axillary resection and subsequently received radiotherapy and chemotherapy. The histological examination of the surgical specimen revealed two solid tumors in the tail of Spence, which corresponded to adenocarcinoma with high columnar cells. The patient died 16 months after the diagnosis, suffering from pulmonary metastases and anterior chest wall infiltration. A review of the literature revealed only 21 reports of mucinous carcinoma of the breast with tall columnar cells, including our case. This is only the third time that the specific histological type of columnar cell mucinous carcinoma has been reported in the literature.

KEYWORDS

Breast cancer – Columnar cell mucinous carcinoma – Mucinous breast carcinoma – Mucinous cystadenocarcinoma – Tall columnar cells

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CORRESPONDENCE TO

Nikolaos Tsoukalas, E: tsoukn@yahoo.gr

Introduction

Breast cancer is one of the most common neoplasms, corresponding to approximately one quarter of all cancers among women.¹ Apart from the prevailing types of breast cancer, ductal and lobular carcinomas, there are some rare histological types. In particular, mucinous cystadenocarcinoma (MCA) and columnar cell mucinous carcinoma (CCMC) of the breast are extremely rare tumours, both of which are categorised as mucinous carcinomas according to the last World Health Organization (WHO) classification.¹ While their histological findings are the same, the gross appearance is different. They look like the ovarian and pancreatic MCA, sometimes giving the impression that the tumour is a metastasis of malignant tumours originating from these organs. Here, we present an interesting case of CCMC and a comprehensive review of all the cases of mucinous breast carcinoma with tall columnar cells that

have been published in the literature. This is the third time that a CCMC has been reported in the literature.

Case report

A 74-year-old woman presented a tumour with inflammatory features (*peau d'orange*) in the upper outer quadrant of her left breast, 7 cm in diameter. There was no nipple discharge from either breast but there were enlarged lymph nodes in the left axilla. Mammography and sonography of the left breast revealed two big circumscribed lesions and many enlarged axillary lymph nodes.

The core biopsy revealed the presence of invasive ductal carcinoma of no specific type (grade II, estrogen receptor negative, progesterone receptor negative and C-erb-B2 negative; triple negative; Fig 1). After an extensive workup, the tumour-node-metastasis clinical stage was T4cN3M0 (stage IIIC). The patient was treated with neoadjuvant

chemotherapy initially (4 cycles of doxorubicin and cyclophosphamide followed by weekly paclitaxel), showing minimal response, and she afterwards underwent a left modified radical mastectomy. The histopathological examination showed two solid tumours in the tail of Spence, 4.1 cm and 2.6 cm in diameter, respectively, which corresponded to a grade II adenocarcinoma with high columnar cells (Figs 2 and 3). There were foci of mucous production and extended necrosis, as well as rare foci of ductal carcinoma in situ (DCIS) and IDC NST. In addition, there was infiltration of 10 of the 25 axillary lymph nodes which were removed in total. The tumour was positive for cytokeratin-7 (CK-7) and carcinoembryonic antigen (CEA), focally positive for cytokeratin-20 (CK-20) and negative for vimentin, CA19-9, CA125, estrogen receptor, progesterone receptor, C-erb-B2, gross cystic disease fluid protein 15 (GCDFF-15) and thyroid transcription factor 1 (TTF-1).

The results of the histopathological and immunohistochemical examination were compatible with either metastatic cancer of ovarian or pancreatic origin or primary mucinous breast carcinoma consisted of columnar cells. The abdominal computed tomography did not show any pathology of the ovaries or the pancreas. Due to the results of the imaging studies and the presence of rare foci of DCIS and IDC NST, the diagnosis of metastatic tumour was ruled out. While the patient was under adjuvant radiotherapy, the tumour progressed by presenting cutaneous nodules and pulmonary metastasis. Unfortunately, the patient died 16 months after diagnosis, after having been treated with first line chemotherapy (6 cycles of carboplatin and docetaxel).

Discussion

Mucinous carcinoma of the breast represents 1–4% of all breast cancers. The WHO classification divides this type of

Figure 1 Core biopsy. Adenocarcinoma showing features of invasive ductal carcinoma of no specific type

Figure 2 Histologic features of mucinous carcinoma of columnar cells. The cysts are lined by a single layer of tall columnar mucinous cells with focal areas of micropapillary and small tufted structures, resembling those of the uterine endocervix

Figure 3 Cell morphology. The tumour cells showed mild atypia with basally located nuclei, increased nucleus to cytoplasm ratio and abundant intracytoplasmic mucin or mucin-depleted columnar cells with more pleomorphic nuclei

tumour into three different subtypes: mucinous carcinoma, mucinous carcinoma with tall columnar cells (MCA and CCMC) and signet ring cell carcinoma.² While mucinous carcinoma is relatively uncommon, even more rare is for a primary breast carcinoma to be composed of tall columnar cells with basally located bland nuclei and abundant intracytoplasmic mucin, a pattern which is identical to ovarian and pancreatic mucinous tumours.⁵ A review of the literature

revealed only 21 reports of this histological type.^{5–19} The carcinoma of this certain histological type is possible to appear to the naked eye either cystic, being characterised as MCA or solid, being characterised as CCMC.¹ Of the 21 cases, only 3 until now have been reported to belong to the solid columnar cell type and our case is one of them.^{5,16} Thus, the unique characteristic in this case is that the tumour, despite mucin production, appeared solid macroscopically. The clinicopathological features of all the 21 cases, including the present case, are summarised in Table 1.

The microscopic features of such tumours, especially the high columnar cells with abundant intracellular mucin, are unusual for primary breast carcinoma.^{1,20} As a result, metastatic mucinous carcinoma, particularly those originating from the ovaries or the pancreas, should be excluded before CCMC of the breast is diagnosed. Moreover, the immunohistochemical pattern of most primary breast carcinomas is CK7+/CK20–, exactly as in our case, whereas the majority of both ovarian and pancreatic mucinous carcinomas are CK7+/CK20+ and most gastrointestinal carcinomas are CK7–/CK20+.^{21,22} Thus, the immunohistochemical examination for CK7 and CK20 expression could be helpful in

distinguishing primary from metastatic mucinous tumours. On the other hand, ordinary mucinous carcinoma of the breast and signet ring cell carcinoma of the breast should also be included in the differential diagnosis. In contrast to CCMC, typical mucinous carcinomas of the breast are characterised by abundant lakes of extracellular mucin,²³ while signet ring cell carcinomas show classic signet ring cell morphology or have abundant extracellular mucin.²⁴

Regarding to the clinicopathological features, it seems that this special histological type tends to occur in elderly postmenopausal women.⁴ It seems that lymph node metastases are not directly associated with the size of the primary tumour but with a long history of primary tumour existence and they do not appear very often.^{5,4} As far as the clinical presentations and mammographic features of MCA and CCMC are concerned, they are similar to those of pure mucinous carcinomas, making the differential diagnosis almost impossible without taking histological findings into consideration.⁵

Even though pathogenesis and biological behaviour of mammary MCA and CCMC still remain unclear, it is now widely accepted that this histological type is in general triple

Table 1 Clinical and immunohistochemical features of mucinous cystadenocarcinomas and columnar cell carcinomas of the breast.

Case	Age	Size (mm)	TNM	Treatment	Follow up	ER	PR	cerbB2
13	54	190	T3N2M0	MRM/LND	Alive without disease (2 years)	N	N	N/A
23	67	23	T2N0M0	MRM/LND	Alive without disease (22 months)	N	N	N/A
33	49	85	T3N0M0	MRM/LND+Chm+RT	Alive without disease (11 months)	N	N	N/A
43	61	8	T1N0M0	Lumpectomy/LND	N/A	N	N	N/A
54	96	20	T2N2M0	Lumpectomy/LND	Died with other reason (46 months)	N	N	N
65	65	30	T2N0M0	MRM/LND	Alive without disease (8 months)	N	N	N
76	65	30	T2N0M0	PM/LND	Alive without disease (6 months)	N	N	N/A
87	52	100	T3N0M0	MRM+Tamoxifen	Alive without disease (24 months)	P	N	N
98	51	40	T2N0M0	Lumpectomy	N/A	N	N	N/A
109	52	65	T3N0M0	N/A	N/A	N	N	N
1110	59	9	T1N0M0	PM/LND+Chm	Alive without disease (3 months)	N	N	P
1211	79	60	T2N0M0	MRM	Died with other reason	N/A	N/A	N/A
1312	74	100	T3N0M0	MRM/LND	Alive without disease	N	N/A	N/A
1413	55	25	T2N0M0	Lumpectomy	Alive without disease (6 months)	N	N	N
1514	61	30	T2N0M0	MRM/LND	Alive without disease (6 months)	N	N	N
1615	73	45	T2N0M0	MRM/LND	N/A	N	N	P
1716	41	70, 50, 25	T3N1M0	MRM/LND	Alive without disease (24 months)	N	N	N
1817	62	56	T2N0M0	MRM	Alive without disease (5 months)	N	N	N
1918	55	20	T1N0M0	Lumpectomy+Chm+RT	Alive	N	N	P
2019	91	75	T3N0M0	MRM/LND+RT	Died (stroke)	N	N	N
Present case	74	80	T4cN3M0	MRM/LND+Chm+RT	Died (other reason)	N	N	N

Chm, chemotherapy; LND, lymph node dissection; MRM, modified radical mastectomy; N, negative; N/A, not available; P, positive; PM, partial mastectomy; RT, radiation therapy; TNM, tumour-node-metastasis.

negative (regarding estrogen receptor- α , progesterone receptor and c-erb-B2), suggesting that the tumour is developed independently of estrogenic stimulation. This may partly account for the higher average age at diagnosis in comparison with the more frequent invasive ductal carcinomas.⁴ On the contrary, mucinous metaplasia from ordinary ductal carcinoma has been suggested as the pathogenetic mechanism of mammary MCA and CCMC. The coexistence of ordinary DCIS and MCA in 6 of 21 cases, indicates that tumour cells of MCA might have been transformed from epithelial cells of ordinary DCIS via a process of metaplasia, accompanied by loss of expression of estrogen receptor and progesterone receptor.^{3,5,6,18,19} In two cases, both mucin-positive and mucin-negative tumour cells were found in the coexisting ordinary DCIS adjacent to the MCA. In some cases, this certain histological type of breast cancer seems to originate from the main mammary duct, next to the nipple, but the CCMC in the present case was quite far from the nipple.^{4,5,7}

Despite the invasive nature of mammary MCA and CCMC, both subtypes appear to be associated with a good prognosis.⁶ However, in none of the cases, the stage of the disease was so advanced as in our case (IIIC at diagnosis). Perhaps this fact suggests that if this certain type of tumour is allowed to progress locally and become larger and with nodal metastases, it follows an exponential growth with aggressive behaviour and resistance to treatment. As it has been mentioned before, patients with mucinous carcinoma of the breast with nodal metastases are significantly more likely to present recurrence of their disease.²⁵

In conclusion, mucinous breast carcinoma with tall columnar cells is a rare variant of breast cancer. Owing to its rarity, some cases may have been misclassified as mucinous carcinoma, cystic hypersecretory carcinoma or another histological subtype. Recognising the characteristic histopathological findings of this specific type of breast cancer is important, because it represents a malignant neoplasm with special clinicopathological features. Study of additional cases and longer surveillance are necessary to clarify of the nature and behaviour of mammary MCA and CCMC.

References

1. Tavassoli FA, Devilee P. *World Health Organization Classification of Tumors, Tumors of the Breast and Female Genital Organs*, 2nd ed. Lyon: IARC Press 2003. pp. 31–32.
2. Yerushalmi R, Hayes MM, Gelmon KA. Breast carcinoma-rare types: review of the literature. *Ann Onc* 2009; **20**: 1,763–1,770.
3. Koenig C, Tavassoli FA. Mucinous cystadenocarcinoma of the breast. *Am J Surg Pathol* 1998; **22**: 698–703.
4. Honma N, Sakamoto G, Ikenaga M *et al*. Mucinous cystadenocarcinoma of the breast: a case report and review of the literature. *Arch Pathol Lab Med* 2003; **127**: 1,031–1,033.
5. Chen WY, Chen CS, Chen HC *et al*. Mucinous cystadenocarcinoma of the breast co-existing with infiltrating ductal carcinoma. *Pathol Int* 2004; **54**: 781–786.
6. Sentani K, Tashiro T, Uraoka N *et al*. Primary mammary mucinous cystadenocarcinoma: cytological and histological findings. *Diagn Cytopathol* 2012; **40**: 624–628.
7. Rakici S, Gonullu G, Gursel SB *et al*. Mucinous cystadenocarcinoma of the breast with estrogen receptor expression: a case report and review of the literature. *Case Rep Oncol* 2009; **2**: 210–216.
8. Coyne JD, Irion L. Mammary mucinous cystadenocarcinoma. *Histopathology* 2006; **49**: 659–660.
9. Li X, Peng J, Zhang Z, Zhang Y. Mammary mucinous cystadenocarcinoma. *Breast J* 2012; **18**: 282–283.
10. Kim SE, Park JH, Hong S *et al*. Primary mucinous cystadenocarcinoma of the breast: cytologic finding and expression of MUC5 are different from mucinous carcinoma. *Korean J Pathol* 2012; **46**: 611–616.
11. Rosen PP, Scott M. Cystic hypersecretory duct carcinoma of the breast. *Am J Surg Pathol* 1984; **8**: 31–41.
12. Domoto H, Terahata S, Yamazaki T *et al*. Mucinous cystadenocarcinoma of the breast showing sulfomucin production. *Histopathology* 2000; **36**: 567–569.
13. Lee SH, Chaung CR. Mucinous metaplasia of breast carcinoma with macrocystic transformation resembling ovarian mucinous cystadenocarcinoma in a case of synchronous bilateral infiltrating ductal carcinoma. *Pathol Int* 2008; **58**: 601–605.
14. Gulwani H, Bhalla S. Mucinous cystadenocarcinoma: a rare primary malignant tumor of the breast. *Indian J Pathol Microbiol* 2010; **53**: 200–202.
15. Petersson F, Pang B, Thamboo TP, Putti TC. Mucinous cystadenocarcinoma of the breast with amplification of the HER2-gene confirmed by FISH: the first case reported. *Hum Pathol* 2010; **41**: 910–913.
16. Deng Y, Xue D, Wang X *et al*. Mucinous cystadenocarcinoma of the breast with a basal-like immunophenotype. *Pathol Int* 2012; **62**: 429–432.
17. Lin DL, Hu JL, Shao SH *et al*. Primary mucinous cystadenocarcinoma of the breast with endocervical-like mucinous epithelium. *Breast Care (Basel)* 2013; **8**: 445–447.
18. Kucukzeybek BB, Yigit S, Sari AA *et al*. Primary mucinous cystadenocarcinoma of the breast with amplification of the HER2 gene confirmed by FISH: case report and review of the literature. *Pol J Pathol* 2014; **65**: 70–73.
19. Witherspoon LE, Oxenhandler RW. A rare tumor: mucinous cystadenocarcinoma of the breast. *Am Surg* 2015; **81**: E106–E108.
20. Rosen PP, Oberman HA. *Tumors of the Mammary Gland. Atlas of Tumor Pathology*, 3rd Series, Fascicle 7. Washington, DC: Armed Forces Institute of Pathology 1992. pp. 187–193.
21. Loy TS, Calaluze RD, Keeney GL. Cytokeratin immunostaining in differentiating primary ovarian carcinoma from metastatic colonic adenocarcinoma. *Mod Pathol* 1996; **9**: 1,040–1,044.
22. Wang NP, Zee S, Zarbo RJ. Coordinate expression of cytokeratins 7 and 20 defines unique subsets of carcinomas. *Appl Immunohistochem* 1995; **3**: 99–107.
23. Coady AT, Shousha S, Dawson PM *et al*. Mucinous carcinoma of the breast: further characterization of its three subtypes. *Histopathology* 1989; **15**: 617–626.
24. Harris M, Wells S, Vasudev KS. Primary signet ring cell carcinoma of the breast. *Histopathology* 1978; **2**: 171–176.
25. Vo T, Xing Y, Meric-Bernstam F *et al*. Long-term outcomes in patients with mucinous, medullary, tubular, and invasive ductal carcinomas after lumpectomy. *Am J Surg* 2007; **194**: 527–531.