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Original Article

Secretory breast carcinoma: a clinicopathological and immunohistochemical study of 7 cases

Yunan Han[1], Qingfu Zhang[2], Bo Li[3], Nan Jiang[4], Zhen Qiao[1], Xinmiao Yu[1], Xiaoyun Mao[1], Xu Wang[1], Zhuo Li[1], Xueshan Qiu[2], Feng Jin[1]

[1]Department of Breast Surgery, The First Hospital of China Medical University, Shenyang 110001, China; [2]Department of Pathology, College of Basic Medical Sciences and The First Hospital of China Medical University, Shenyang 110001, China; [3]Department of Obstetrics and Gynecology, Shengjing Hospital of China Medical University, Shenyang 110004, China; [4]International Education School of China Medical University, Shenyang 110001, China

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Abstract: Secretory breast carcinoma (SBC) is a rare distinct subtype of invasive breast cancer with good prognosis. Due to the limited reported SBC cases, our aim was to discuss the clinicopathological features of a series of SBC cases. We accepted 7 cases of SBC from the First Affiliated Hospital of China Medical University between 2011 and 2015. Seven respective tissue slides were stained with hematoxylin and eosin and performed immunohistochemistry with antibodies against ER, PR, HER-2 and Ki-67. The age of the patients (all women) ranged from 25 to 61 years (median age, 50). The tumor sizes ranged from 1.70 cm to 3.04 cm in diameter (median size, 2.0 cm). None had positive axillary lymph nodes. Histologically, most cases showed mixed microcystic, solid and tubular patterns. All tumor cells showed intracellular and extracellular secretory materials and mild to moderate dysplasia. Immunohistochemically, most cases were negative for ER, PR, and HER2 and had a low Ki-67 LI. The median follow-up period was 39 months, and they did not have recurrence after surgery. One patient was not available for follow-up. One patient developed recurrence and metastasis 18 months after the initial surgery and died within 42 months of the surgery. This case had mixed patterns, moderate nucleus atypia, a prominent nucleolus, and high Ki-67. We suggested that solid and nested invasive growth patterns, higher nucleus grade, and high Ki-67 LI may be related to poor prognosis. However, the number of cases was not enough and more studies need to be researched in the future.

Keywords: Secretory breast carcinoma, breast cancer, immunohistochemistry

Introduction

Secretory breast carcinoma (SBC) is a rare type of breast cancer (less than 0.15% of all cases) [1]. SBC was first termed as "juvenile carcinoma" by McDivitt and Stewart in 1966, based on the fact that the average age of the seven female children was nine, with the ages ranging from three to fifteen years old [2]. Though subsequent research reported that this carcinoma was not limited to young adolescents and could occur in any age, the use of the term "juvenile carcinoma" lasted for ten more years. In 1980, Tavassoli and Norris proposed this disease could be renamed "secretory carcinoma" (2/3 of about 100 published SBC cases have been adults) [3]. SBC can occur both in females and males. SBC is a distinct variant of breast cancer and is distinguished by the characteristic of abundant extracellular and intracellular secretory materials, which is usually periodic acid-Schiff (PAS) positive eosinophilic secretions. In 1981, the World Health Organization officially listed SBC as a type of breast cancer [4].

SBC always occurs in the subareola but it may occur in any region of the breast. It usually presents as a mobile and well-described mass, sometimes resembling fibroadenoma [5]. In histology, SBC mainly includes solid, microcystic, and tubular patterns. Generally, SBC is negative for estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor (HER)-2/neu, and has a low proliferation index. This tumor has favorable prognosis and rare axillary lymph node metastases [6].

Table 1. Summary of clinical features of 7 patients with SBC

Case no	Age (y)	Sex	Site	Tumor size (cm)	Duration (mo)	Treatment	ALN involved	Recurrence (mo)	Follow-up (mo)
1	25	F	R	1.8×1.5×1	1	LE	NE	NA	NA
2	61	F	L	2×2×2	24	MRM + CT	None	None	Well, 23
3	51	F	R	2×2	12	MRM + CT	None	None	Well, 52
4	26	F	R	2.2×2×1.5	6	MRM + CT + RT	None	Yes, 18	Died, 42
5	48	F	L	2.6	1	SM + CT	NE	None	Well, 52
6	54	F	R	3.04×1.16	12	MRM + CT	None	None	Well, 39
7	50	F	R	1.7×1.5×1	3	NAC + MRM + CT + ET	None	None	Well, 39

Abbreviations: ALN, Axillary lymph nodes; CT, chemotherapy; ET, endocrinotherapy; F, female; L, left; LE, local excision; mo, months; MRM, modified radical mastectomy; NA, not available; NE, not examined; R, right; RT, radiotherapy; SM, simple mastectomy; y, years old; NAC, neoadjuvant chemotherapy.

Recently, studies have found that SBC has a characteristic balanced chromosome translocation t (12; 15), which creates an ETV6-NTRK3 fusion gene that encodes a chimeric tyrosine kinase [7].

Nevertheless, there are very few case series that reports this rare aggressive neoplasia. In this paper, we reported 7 cases of SBC in Chinese women and investigated a clinicopathological characteristic of SBC.

Materials and methods

Case selection

We reviewed the slides of SBC patients between 2011 and 2015 retrospectively from the First Affiliated Hospital of China Medical University. After a second diagnosis confirmed by two pathologists, 7 cases of SBC were accepted. Additional clinical and pathological information was obtained from pathological reports and hospital records. In accordance with the Declaration of Helsinki, written informed consent was obtained from all participants.

Immunohistochemistry

All the specimens had been formalin fixed and paraffin embedded (FFPE) routinely. 4 μm thickness tissue sections from FFPE blocks were stained with hematoxylin and eosin (H&E). Immunohistochemical staining was performed in all cases by the avidin-biotin-peroxidase complex method for the following antibodies (MaiXin Inc, China, prediluted): ER, PR, HER2, S-100 protein and Ki-67. After xylene deparaffinization and a series of graded concentrations of ethanol dehydration, the sections were pretreated with an autoclave by boiling in 0.01 M citrate buffer (pH 6.0) for 2 min. The sections were first incubated with hydrogen peroxide (0.3%) and normal goat serum, and then incubated with the primary antibody at 4°C overnight. Biotinylated goat anti-mouse serum IgG was applied as a secondary antibody the following day. After washing the slides, they were incubated with the streptavidin-peroxidase complex and visualized using 3,3'-diaminobenzidine tetrahydrochloride. Counterstaining with hematoxylin was performed, and the sections were dehydrated in ethanol before mounting.

Immunohistochemical evaluation

Two independent and blinded investigators randomly evaluated all the slides. ER and PR are considered positive if positive nuclear staining is at least 1% [8]. HER2 staining was defined as follows [9]: IHC staining of 3+ (>30% uniform, intense membrane staining of tumor cells); 2+ (at least 10% complete membranous staining, either weak or uniform staining of tumor cells); 1+ (<10% weak incomplete membranous staining of tumor cells); 0 (no immunostaining). IHC staining of 0 to 1+ were deemed as negative. S-100 protein was considered positive if the antigen was expressed in the nucleus or the cytoplasm, with nuclear expression being more dominant. Ki-67 was considered positive when nuclear staining presented with any intensity. The Ki-67 labeling index (LI) was determined by counting the number of Ki-67-positive tumor cell nuclei in 1000 invasive tumor cells in the hot spots. At least three high-power (×40 objective) fields were selected randomly, including the most densely Ki-67 staining areas, which were called "hot spots".

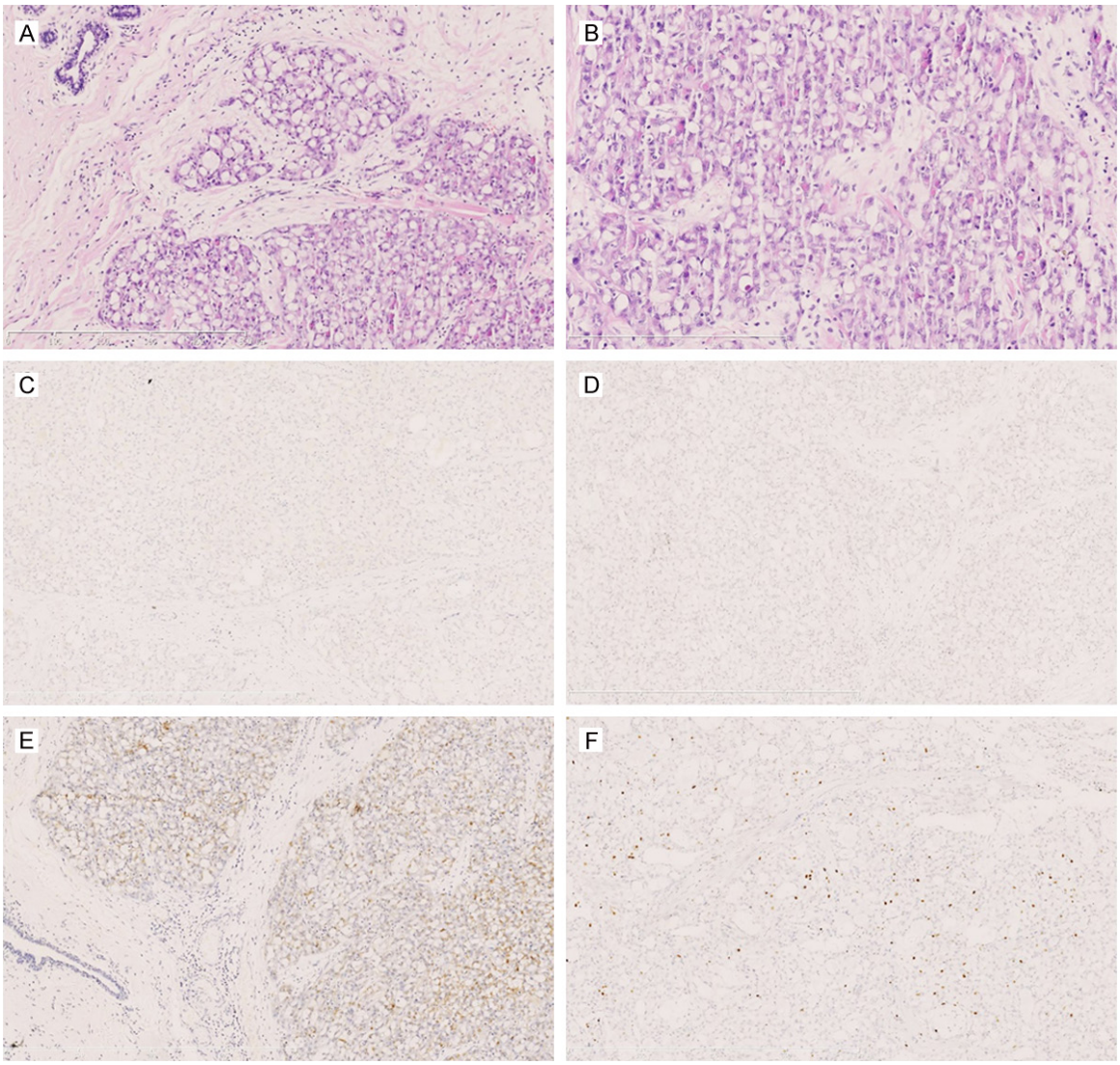

Figure 1. Case 3. A, B: H&E. C-F: Immunohistochemical staining. (Original magnification ×100). A. SBC tumor cells were arranged in microcystic pattern with aggressive growth. Secretory materials were seen in cysts. (Original magnification ×100). B. Tumor cells were arranged in microcystic pattern with cytoplasm eosinophilic secretory materials. (Original magnification ×200). C. Immunohistochemistry showed ER was negative. D. Immunohistochemistry showed PR was negative. E. Immunohistochemistry showed S-100 was weak positive in microcystic patterns, but normal breast duct epithelium was negative. F. Immunohistochemistry showed Ki-67 was about 3% positive.

Results

Clinical findings

The clinical features of the 7 patients with SBC are summarized in **Table 1**. The ages of the 7 patients (all women) ranged from 25 to 61 years (median age, 50). The tumor size ranged from 1.70 cm to 3.04 cm in diameter (median size, 2.0 cm). Of the 7 cases, 5 (71.4%) were in the right breast and 2 (28.6%) were in the left breast. All the patients went for clinical consultation after discovering a painless mass in the breast either by routine physical examination or by accidental self-examination. None had bleeding discharge from the nipple. The tumors had been growing slowly, and the mean duration from detection of the mass to treatment ranged from 1 to 24 months (median months, 6). In most of the cases, ultrasonography (**Figure 1**) and mammography (**Figure 2**) revealed a small, well-circumscribed, and solidary mass. No case suffered axillary lymph node infiltration. All 7 patients received surgery: 5 radical mastectomies, 1 simple excision, and 1 local excision. Excluding the patient who had local excision (case 1), the other six

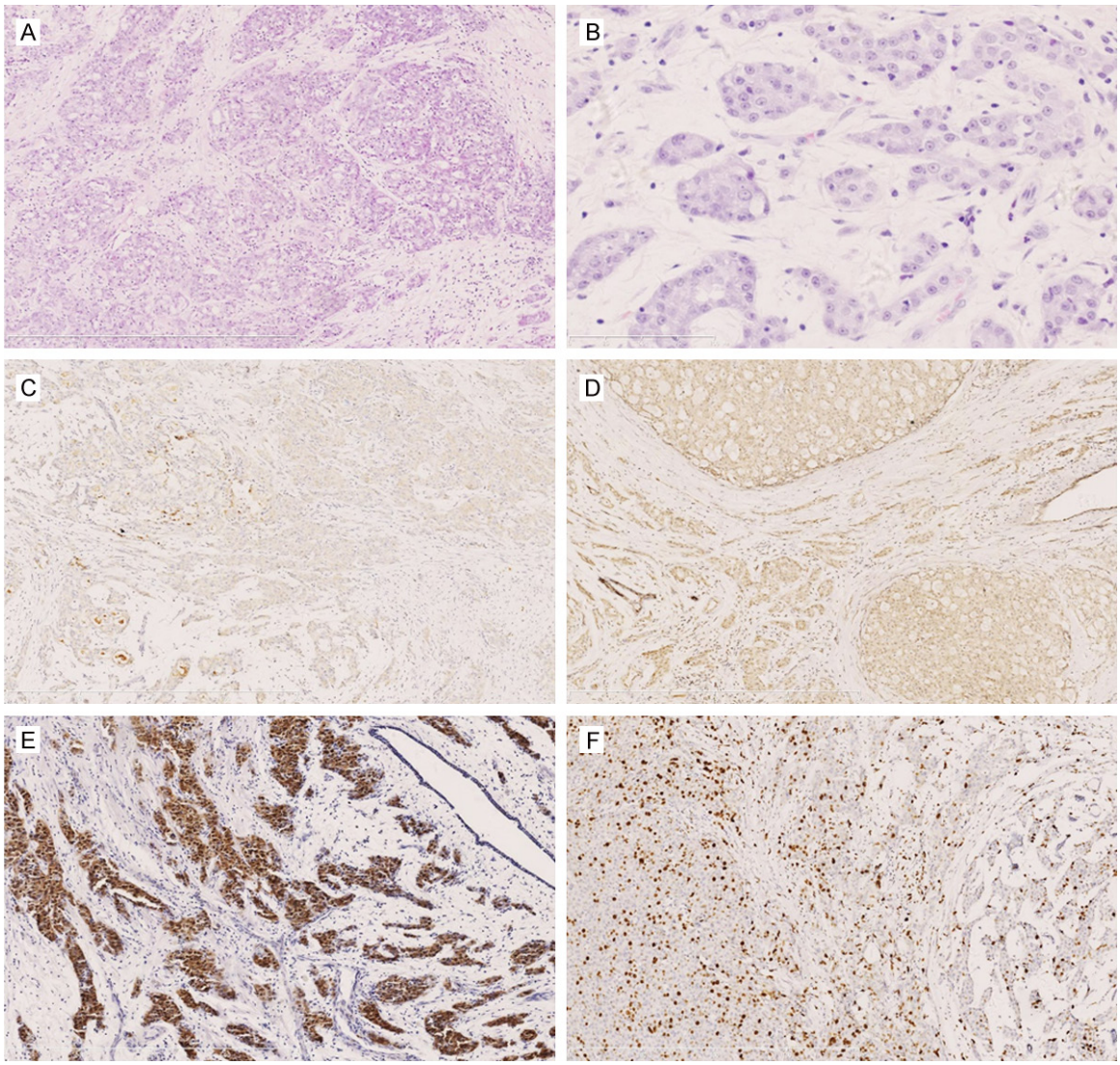

Figure 2. Case 4. A, B: H&E. C-F: Immunohistochemical staining. (Original magnification ×100). A. SBC tumor cells were arranged in microcystic pattern. (Original magnification ×100). B. SBC tumor cells were arranged in nested pattern with aggressive growth. Tumor cells were moderate in size, rich in granules cytoplasm with prominent nucleolus. (Original magnification ×400). C. Immunohistochemistry showed ER was negative. D. Immunohistochemistry showed PR was negative; normal breast duct was focal positive. E. Immunohistochemistry showed S-100 was positive; normal breast duct was negative. F. Immunohistochemistry showed Ki-67 was higher expressed in solid pattern (left regions) than nested pattern (right regions).

cases received postoperative chemotherapy, with one (case 4) receiving radiotherapy and one (case 7) receiving neoadjuvant therapy and endocrinotherapy. Clinical follow-up was available in 6 cases, and one patient (case 4) developed the evidence of recurrence and metastasis 18 months after the initial surgery and died after 42 months of the surgery. The follow-up period after the surgery of the 5 living cases ranged from 23 to 52 months (median months, 39), and they did not have recurrence after surgery.

Histopathological findings

The histological findings of the 7 patients with SBC are summarized in **Table 2**. H&E staining and immunohistochemical pictures of two cases are displayed in **Figures 1** and **2**. The border of tumors displayed pushed or infiltrated and tumor cells showed several histological patterns, such as microcystic (**Figures 1A** and **2A**), solid, and tubular patterns. Microcystic patterns were most frequent, but all three patterns can be mixed with varied proportions

Table 2. Histopathological and immunohistological findings of 7 cases of SBC

Case	Morphological patterns	Mitosis (/10 HPF)	Grade	ER	PR	HER2	Ki-67	S-100
1	Microcystic + solid	1	1	-	-	-	10%	+
2	Microcystic	1	1	-	-	1+	1%	+
3	Microcystic	1	1	-	-	NE	3%	+
4	Microcystic + nested + solid	2	2	-	-	-	40%	+
5	Microcystic + tubular	2	2	-	90%+	1+	10%	NE
6	Microcystic + solid + tubular	1	1	-	-	-	20%	NE
7	Microcystic + solid + tubular (calcification)	1	1	50%+	-	2+	40%	-

Abbreviations: ER, estrogen receptor; HER2, human epidermal growth factor receptor-2/neu; NE, not examined; PR, progesterone receptor.

among the cells. One case also displayed nested patterns (**Figure 2B**) mixed with microcystic (**Figure 2A**) and solid patterns. Most tumor cells had mild atypia without a prominent nucleus, but one case presented a prominent nucleus (**Figure 2B**). Mitotic activity was rare: two cases were in 2/10 HPF, and others were in 1/10 HPF. Two cases were grade 2, and other cases were grade 1. All tumor cells were round to polygonal in shape and observed secretory materials within tumor cells and extracellular lumens (**Figure 1B**) or a granular or vacuolated cytoplasm (**Figure 2B**).

Immunohistochemical findings

The immunohistochemical findings of the 7 patients with SBC are summarized in **Table 2**. The rate of negative expression of ER, PR, HER2 was 85.7% (6 of 7), 85.7% (6 of 7), and 83.3% (5 of 6, one not examined) respectively. The Ki-67 LI had a mean value of 17.71% and ranged from 1% to 40%.

Discussion

This SBC occurs mostly in young females, but middle-aged and older women can also be affected [10, 11]. In our cases, the median age of the patients was 50. This held that SBC could occur in older females. Additionally, occasional cases have been reported in men [12]. The tumor is usually a single mass and occurs in any quadrant of the breast, mostly under the mammary areola. SBC typically presents as a painless, mobile, well-circumscribed and slow-growing small mass. Bloody nipple discharge may manifest in some cases [13]. Breast ultrasound typically shows a solitary hypoecoic mass that resembles a benign lesion of the breast [14]. In our report, all patients were female with ages ranging between 25 to 61 years, and the tumor locations coincided with that of typical breast carcinomas. The tumor sizes were small, with most being less than 2.0 cm in diameter.

Pathomorphology

According to the arrangement of tumor cells of SBC, Akhtar et al revealed that SBC mainly had solid, microcystic, and ductal histological patterns [15]. The solid pattern is characterized by the nodular structure of dense tumor cells, and the large clusters of the tumor cells are separated by variable thickness fibrous septa. Within the cytoplasm of the tumor cells, amounts of eosinophilic granules and small secretory vacuoles are present. In microcystic patterns, tumor cells consist of small cystic spaces which can combine into macro-cystic spaces. Among the tumor cells, there are unequal sizes of gland-like or cyst-like spaces containing eosinophilic secretions and lined by cuboidal epithelium cells. The ductal pattern consists of duct-like spaces with secretions [16]. Some tumor cells proliferate in the form of papillary projections [17]. In our cases, most cases were mixed with several usual patterns. We also found a patient (case 4) with nested growth pattern that had poor prognosis. SBC tumor cells consist with two subtypes and Tavassoli et al classified the SBC tumor cells into Type A and B according to the variations in the tumor cell cytoplasm and distribution of secretions [3]. Whether the SBC constituted mainly of Type A or Type B cells had no prognostic value. Our cases presented a mixture of these two types of cells with minimal cellular pleomorphism and mitoses.

Immunophenotype and molecular genetics

In the previous studies of IHC, most cases of SBC were ER, PR, and HER-2 negative (triple-negative), especially in children and adolescents [18-20], although a few cases have reported hormone receptors were positive [21]. Diallo et al reported 13 cases of SBC, the expression of ER, PR and HER-2 are low, and immune-positive rates were 31% (4/13), 15% (2/13) and 15% (2/13) respectively [22]. Our cases also showed low expression of hormone receptors and HER-2. Recently, studies have demonstrated that the immunohistological features of SBC belonged to the basal-like breast cancer phenotypic spectrum, including cytokeratins 5/6 (CK5/6), CK14, and KIT expression [23]. Initial gene spectrum analysis showed that all basal-like tumors have bad prognosis, but now researchers think the prognosis is different within variant subtypes. SBC is one of the basal-like tumors that has good prognosis and has significant heterogeneity with basal cell like carcinoma [23]. In molecular genetics, studies have found that SBC has a characteristic balanced chromosome translocation t (12; 15), which creates anETV6-NTRK3 fusion gene that encodes a chimeric tyrosine kinase [7]. In 2002, Tong et al first reported expression of the ETV6-NTRK3 fusion gene in SBC, and the fusion gene was confirmed in 12 of 13 (92%) SBC cases, but it was not expressed in other ductal cancers [7]. Nikita et al also confirmed that the ETV6-NTRK3 fusion gene is a characteristic genetic alteration in SBC [24].

Treatment and prognosis

SBC does not have consensus treatment guidelines, surgery is the primary treatment of SBC, but the method and extend of surgery remains controversial [25]. There is insufficient evidence to recommendation in chemotherapy and a metastatic SBC had been reported that it had no response to chemotherapy [26]. However, adjuvant chemotherapy is usually used, especially in patients with positive axillary lymph nodes [27]. Radiotherapy after the conservative surgery can be advised in adults, however it is not advised in children because of some negative effects such as pulmonary fibrosis, damage of the rib and asymmetry of the rib cage [28]. Recent research suggested PKC412, also named midostaurin, to be an inhibitor of the ETV6-NTRK3 fusion gene; this means it could serve as a therapeutic drug for SBC [29]. SBC has excellent prognosis, and axillary lymph node metastases or distant metastases events were rarely reported. Poor prognostic factors previously reported were masses greater than 2 cm in diameter and poor gross circumscription [30].

In our case, a 26-year-old woman (case 4) developed the evidence of recurrence and metastasis 18 months after the initial surgery and died after 42 months of the surgery. The tumor size was 2.2×2.0×1.5 cm, and she was treated with modified radical mastectomy in combination with chemotherapy and radiotherapy. In microscopy, the tumor patterns were mixed microcystic, nested and solid patterns, mitosis was 2/10 HPF, nucleus grade was 2, and the Ki-67 LI was 40%. The recurrence and poor prognosis in this patient suggested that solid and nested invasive growth patterns, higher nucleus grade, and high Ki-67 LI may be correlated with poor prognosis.

SBC is a rare type of breast cancer with indolent behavior and good prognosis. In our reports, we suggested that high grade tumors with a prominent nucleus and high Ki-67 LI may be related with poor prognosis. However, the number of cases was not enough to confirm this, and more studies are needed for further research.

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Disclosure of conflict of interest

None.

Address correspondence to: Dr. Feng Jin, Department of Breast Surgery, The First Hospital of China Medical University, Shenyang 110001, China. E-mail: jinfeng@mail.cmu.edu.cn

References

[1] Nogales F TF. Pathology and genetics of tumors of the breast and female genital organs. Lyon: IARC Press; 2003.

[2] McDivitt RW and Stewart FW. Breast carcinoma in children. JAMA 1966; 195: 388-390.
[3] Tavassoli FA and Norris HJ. Secretory carcinoma of the breast. Cancer 1980; 45: 2404-2413.
[4] Arowolo OA, Njiaju UO, Ogundiran TO, Abidoye O, Lawal OO, Obajimi M, Adetiloye AV, Im HK, Akinkuolie AA, Oluwasola A, Adelusola K, Kayode AA, Agbakwuru AE, Oduntan H, Babalola CP, Fleming G, Olopade OC, Falusi AG, Durosinmi MA and Olopade OI. Neo-adjuvant capecitabine chemotherapy in women with newly diagnosed locally advanced breast cancer in a resource-poor setting (Nigeria): efficacy and safety in a phase II feasibility study. Breast J 2013; 19: 470-477.
[5] Costa NM, Rodrigues H, Pereira H, Pardal F and Matos E. Secretory breast carcinoma--case report and review of the medical literature. Breast 2004; 13: 353-355.
[6] Vasudev P and Onuma K. Secretory breast carcinoma: unique, triple-negative carcinoma with a favorable prognosis and characteristic molecular expression. Arch Pathol Lab Med 2011; 135: 1606-1610.
[7] Tognon C, Knezevich SR, Huntsman D, Roskelley CD, Melnyk N, Mathers JA, Becker L, Carneiro F, MacPherson N, Horsman D, Poremba C and Sorensen PH. Expression of the ETV6-NTRK3 gene fusion as a primary event in human secretory breast carcinoma. Cancer Cell 2002; 2: 367-376.
[8] Hammond ME, Hayes DF, Dowsett M, Allred DC, Hagerty KL, Badve S, Fitzgibbons PL, Francis G, Goldstein NS, Hayes M, Hicks DG, Lester S, Love R, Mangu PB, McShane L, Miller K, Osborne CK, Paik S, Perlmutter J, Rhodes A, Sasano H, Schwartz JN, Sweep FC, Taube S, Torlakovic EE, Valenstein P, Viale G, Visscher D, Wheeler T, Williams RB, Wittliff JL and Wolff AC. American Society of Clinical Oncology/College Of American Pathologists guideline recommendations for immunohistochemical testing of estrogen and progesterone receptors in breast cancer. J Clin Oncol 2010; 28: 2784-2795.
[9] Wolff AC, Hammond ME, Schwartz JN, Hagerty KL, Allred DC, Cote RJ, Dowsett M, Fitzgibbons PL, Hanna WM, Langer A, McShane LM, Paik S, Pegram MD, Perez EA, Press MF, Rhodes A, Sturgeon C, Taube SE, Tubbs R, Vance GH, van de Vijver M, Wheeler TM and Hayes DF. American Society of Clinical Oncology/College of American Pathologists guideline recommendations for human epidermal growth factor receptor 2 testing in breast cancer. J Clin Oncol 2007; 25: 118-145.
[10] Lee SG, Jung SP, Lee HY, Kim S, Kim HY, Kim I and Bae JW. Secretory breast carcinoma: A report of three cases and a review of the literature. Oncol Lett 2014; 8: 683-686.
[11] Yaqoob N, Kayani N and ul Hasan SH. Painless breast lump in an elderly woman. Secretory breast carcinoma in an elderly woman. Arch Pathol Lab Med 2006; 130: 1073-1074.
[12] Li G, Zhong X, Yao J, Chen J, Wang M, Liu H and Yang S. Secretory breast carcinoma in a 41-year-old man with long-term follow-up: a special report. Future Oncol 2015; 11: 1767-1773.
[13] Izumi J, Komaki K, Hirokawa M, Masuda E and Monden Y. Secretory carcinoma of the breast with a cystically dilated intraductal component: report of a case. Surg Today 2003; 33: 110-113.
[14] Paeng MH, Choi HY, Sung SH, Moon BI and Shim SS. Secretory carcinoma of the breast. J Clin Ultrasound 2003; 31: 425-429.
[15] Akhtar M, Robinson C, Ali MA and Godwin JT. Secretory carcinoma of the breast in adults. Light and electron microscopic study of three cases with review of the literature. Cancer 1983; 51: 2245-2254.
[16] Krausz T, Jenkins D, Grontoft O, Pollock DJ and Azzopardi JG. Secretory carcinoma of the breast in adults: emphasis on late recurrence and metastasis. Histopathology 1989; 14: 25-36.
[17] Din NU, Idrees R, Fatima S and Kayani N. Secretory carcinoma of breast: clinicopathologic study of 8 cases. Ann Diagn Pathol 2013; 17: 54-57.
[18] Soyer T, Yaman Bajin I, Orhan D, Yalcin B, Ozgen Kiratli P, Oguz B and Karnak I. Secretory breast carcinoma in a 6-year-old girl: mastectomy with sentinel lymph node dissection. Pediatr Surg Int 2015; 31: 677-681.
[19] Wang YQ, Wang Y, Zhang JH, Li YF, Li HM, Wang L and Yao Y. Secretory breast carcinoma in a 12-year-old girl: A case report. Oncol Lett 2014; 8: 1635-1637.
[20] Cabello C, Alvarenga M, Alvarenga CA, Duarte GM, Pereira PN and Marshall PS. Case report and review of the literature: secretory breast cancer in a 13-year-old boy--10 years of follow up. Breast Cancer Res Treat 2012; 133: 813-820.
[21] Yorozuya K, Takahashi E, Kousaka J, Mouri Y, Yoshida M, Fujii K, Akizuki M, Nakano S, Fukutomi T, Umemoto Y, Yokoi T and Imai H. A case of estrogen receptor positive secretory carcinoma in a 9-Year-old girl with ETV6-NTRK3 fusion gene. Jpn J Clin Oncol 2012; 42: 208-211.
[22] Diallo R, Schaefer KL, Bankfalvi A, Decker T, Ruhnke M, Wulfing P, Jackisch C, Luttges J, Sorensen PH, Singh M and Poremba C. Secretory carcinoma of the breast: a distinct variant of invasive ductal carcinoma assessed by com-

parative genomic hybridization and immunohistochemistry. Hum Pathol 2003; 34: 1299-1305.
[23] Lae M, Freneaux P, Sastre-Garau X, Chouchane O, Sigal-Zafrani B and Vincent-Salomon A. Secretory breast carcinomas with ETV6-NTRK3 fusion gene belong to the basal-like carcinoma spectrum. Mod Pathol 2009; 22: 291-298.
[24] Makretsov N, He M, Hayes M, Chia S, Horsman DE, Sorensen PH and Huntsman DG. A fluorescence in situ hybridization study of ETV6-NTRK3 fusion gene in secretory breast carcinoma. Genes Chromosomes Cancer 2004; 40: 152-157.
[25] Arce C, Cortes-Padilla D, Huntsman DG, Miller MA, Duennas-Gonzalez A, Alvarado A, Perez V, Gallardo-Rincon D and Lara-Medina F. Secretory carcinoma of the breast containing the ETV6-NTRK3 fusion gene in a male: case report and review of the literature. World J Surg Oncol 2005; 3: 35.
[26] Herz H, Cooke B and Goldstein D. Metastatic secretory breast cancer. Non-responsiveness to chemotherapy: case report and review of the literature. Ann Oncol 2000; 11: 1343-1347.
[27] Vieni S, Cabibi D, Cipolla C, Fricano S, Graceffa G and Latteri MA. Secretory breast carcinoma with metastatic sentinel lymph node. World J Surg Oncol 2006; 4: 88.
[28] Szanto J, Andras C, Tsakiris J, Gomba S, Szentirmay Z, Banlaki S, Szilagyi I, Kiss C, Antall P, Horvath A, Lengyel L and Castiglione-Gertsch M. Secretory breast cancer in a 7.5-year old boy. Breast 2004; 13: 439-442.
[29] Chi HT, Ly BT, Kano Y, Tojo A, Watanabe T and Sato Y. ETV6-NTRK3 as a therapeutic target of small molecule inhibitor PKC412. Biochem Biophys Res Commun 2012; 429: 87-92.
[30] Richard G, Hawk JC 3rd, Baker AS Jr and Austin RM. Multicentric adult secretory breast carcinoma: DNA flow cytometric findings, prognostic features, and review of the world literature. J Surg Oncol 1990; 44: 238-244.