

Case Report

Secretory breast cancer in a 7-year-old girl

Nanlin Li*, Meiling Huang*, Yuqing Yang, Rui Ling

*Department of Thyroid, Breast and Vascular Surgery, Xijing Hospital, Fourth Military Medical University, Xi'an, Shaanxi, China. *Equal contributors.*

Received January 17, 2017; Accepted March 18, 2017; Epub May 1, 2017; Published May 15, 2017

Abstract: Carcinoma of breast is rarely encountered in the juvenile population and no consensus has been reached on the optimal treatment modalities. Here, we present the case of a 7-year-old girl with secretory breast cancer. She had been seen by a surgeon elsewhere who considered the lesion was benign and performed surgical excision of tumor. Presently, considering the indeed young age, the patient was undergone segmental mastectomy, axillary lymphadenectomy and fascia tissue flap forming surgery. As no malignant cells were detected in lymph nodes and BRCA1-2 mutation examination was negative, further adjuvant chemotherapy or radiotherapy was not administered. Four months after operation, the patient remains well and had no evidence of recurrence.

Keywords: Secretory carcinoma, juvenile breast cancer, case report

Introduction

Breast cancer is the leading cancer and the leading cause of mortality among women throughout the world. The American Cancer Society provided an overview of female breast cancer statistics in the United States, indicating approximately 230,480 new cases of invasive breast cancer and 39,520 breast cancer deaths among US women in 2011 [1]. Similarly, the health burden of breast cancer is also increasing in Chinese women, accounting for 12.2% of all newly diagnosed breast cancers worldwide [2, 3]. Recently, breast cancer was most frequently diagnosed among adolescent and young adult (AYA) women. Nearly 1.8% of all breast cancers occur in women younger than 35 years of age [4]. Moreover, the risk of death rises by 5% for every 1-year reduction in age, highlighting the importance of studying breast cancer at an even younger age [5]. However, breast carcinoma is rarely encountered in the juvenile population [6]. Here we intend to report one case of breast cancer in a 7-year old girl to provide more clinical reference for the treatment of juvenile breast cancer.

Case report

A 7-year-old girl was considered primarily as right breast fibroadenoma in the local hospital

3 weeks ago and performed surgical excision of tumor (1.0 cm×1.0 cm). However, postoperative pathology was demonstrated malignant. She was admitted to our hospital for further treatment. After investigation, no prior or family history of malignancy was found, as well as radiation exposure. The patient's development was normal for her age but susceptible to cold, the temperature was up to 39 centigrade degree at first. Physical examination showed a transverse surgical scar close to the papilla on the right breast and healed well (**Figure 1**).

Ultrasonography revealed no obvious mass in bilateral breasts, except an enlarged axillary lymph node (1.0 cm in size) on the right and several enlarged cervical lymph nodes on the left, which was considered as reactive hyperplasia. Immunohistochemistry was also performed, revealing negative expression of estrogen receptor (ER), progesterone receptor (PR), human epidermal growth factor receptor-2 (HER-2), ALK, P53 and P63, as well as positive staining of 34BE12 (HCK), CK5/6, E-cadherin, CEA and P120. The proliferation ratio evaluated by Ki-67-MIB1 was estimated as 5% (**Figure 2**). A diagnosis of secretory breast cancer was then established. Furthermore, a mutational study of 40 susceptibility genes was performed by Anoroad Company (Beijing, China) via direct



Figure 1. Admission to our hospital after local excision of the lump.

sequencing analysis (**Table 1**). Results showed no related mutation.

Considering the diagnosis and indeed young age of patient, a segmental mastectomy, axillary lymphadenectomy and fascia tissue flap forming surgery was undergone (**Figure 3**). The margin was shown clear. Postoperative pathology displayed as granulomatous inflammation and all 16 lymph nodes were free of metastasis. Finally, adjuvant chemotherapy or radiotherapy was not administered. Four months after operation, the patient remains well with good life quality, except for the scar physique (**Figure 4**). No evidence of recurrence occurred so far.

Discussion

Breast cancer was rarely seen in children. As reported by Murphy JJ et al, there only have 38 cases of primary breast cancer reported in children ranged from 3 to 19 years old before 2000 [7]. Since then, 18 cases of juvenile breast cancer were reported until July 2015, 11 of them was diagnosed as secretory breast cancer while 6 cases as ductal carcinoma, the remaining one case was locally advanced breast cancer [7-24]. These children usually present with a painless, firm, nontender, immobile, poorly circumscribed breast mass. Unfortunately, there is still no consensus of opinion as to how juvenile breast cancer should be treated.

Clinical evaluation is an essential component of complete assessment of pediatric breast complaints. The developing breast is vulnerable to injury, and the diagnostic and management approach emphasizes "first do no harm"

[25]. When necessary, ultra-sound is the primary imaging modality used, given its diagnostic specificity and lack of ionizing radiation. The cystic appearance secondary to the pseudocapsule may be a marker for secretory adenocarcinoma. Mammography is seldom used, but suitable to visualize the calcifications. Cross-sectional imaging modalities such as CT or MR are usually reserved for disease extent evaluation. Besides,

fine-needle aspiration (FNA), routinely used in adults, was evolved in children and may become a useful adjuvant tool. In addition, special attention should be focused on the young people with risk factors predisposing to breast cancer, such as strong family history, known extra-mammary malignancy, genetic mutations, or prior mantle irradiation. Biopsy is often required to exclude malignancy regardless of the imaging appearance of the breast lesion [25]. Moreover, genetic mutations exerted significant function to establish scientific treatment strategy in adult breast cancer, which is not yet determined in children breast cancer, such as estrogen and progesterone receptors, cytogenetics, BRCA1 and 2 [7].

Familial incidence has limited discussion in previously published cases. As reported in 2004, the maternal aunt of a 7.5-year-old boy with secretory breast cancer was operated for breast cancer at the age of 43 [9]. In 2012, a 13 year-old boy with invasive secretory breast cancer (pT1pN1M0) had an uncle with prostate cancer [21]. Meanwhile, an 18-year-old girl with medullary breast carcinoma also has a maternal aunt with breast carcinoma [20]. Yet, no association has been considered to be pure coincidence.

The pediatric breast cancer therapy remains controversial and inconsistent. Surgical treatment has ranged from local excision to radical mastectomy. Axillary node dissections have not been done consistently. In 2012, Tadesse A treated a 7-years- old girl with breast carcinoma by modified radical mastectomy with level II axillary dissection [13]. In 2015, a 6-year-old girl with secretory breast carcinoma was report-

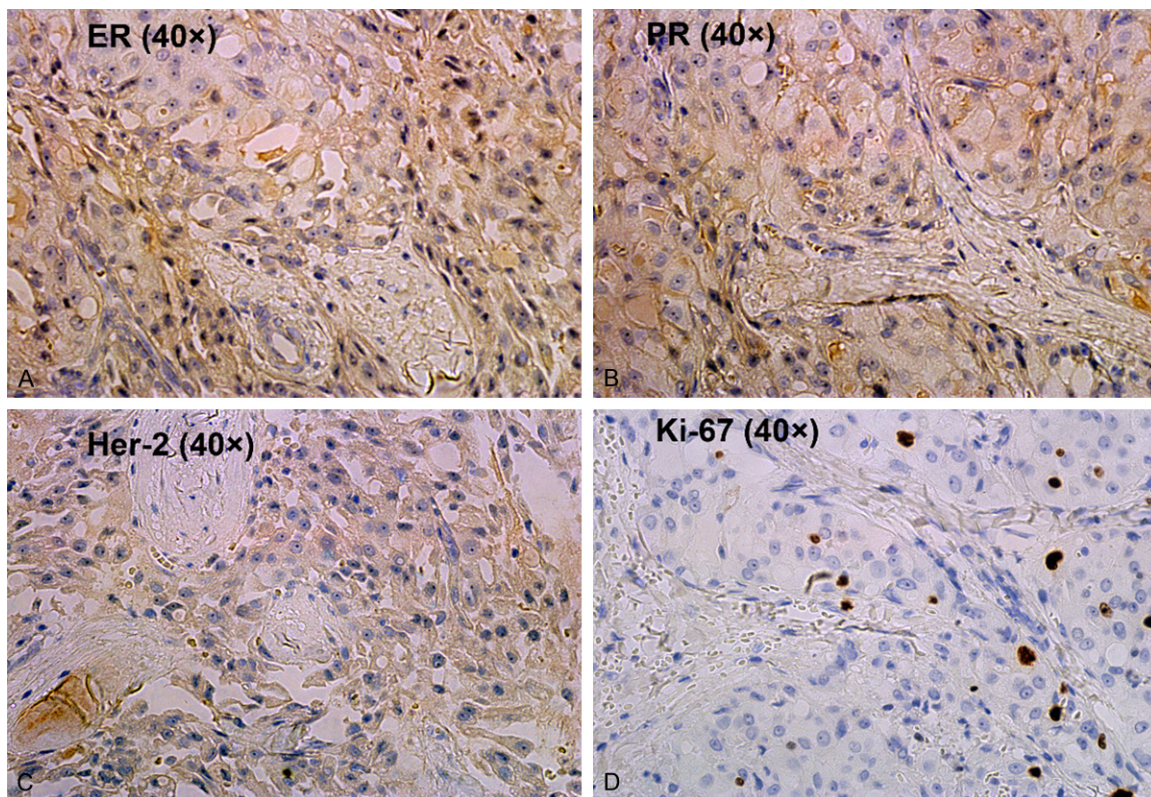


Figure 2. The histological and immunohistochemical figures of the cancer (40×). A: ER (-); B: PR (-); C: Her2 (-); D: Ki67 (10%+).

Table 1. The sequencing analysis of 40 susceptibility genes

No.	Gene	Mutation (Yes/No)	No.	Gene	Mutation (Yes/No)
1	BRCA1	No	21	MLH1	No
2	BRCA2	No	22	MRE11	No
3	AKT1	No	23	MRE11A	No
4	APC	No	24	MSH2	No
5	ATM	No	25	MSH6	No
6	BARD1	No	26	MUTYH	No
7	BR1P1	No	27	NBN	No
8	CDH1	No	28	NBS1	No
9	CHEK2	No	29	NQO2	No
10	CYP1A1	No	30	PALB2	No
11	ERBB2	No	31	PER1	No
12	FGFR2	No	32	PHB	No
13	HMMR	No	33	PIK3CA	No
14	PMS1	No	34	PPM1D	No
15	PMS2	No	35	PTEN	No
16	RB1	No	36	RAD50	No
17	TOX3	No	37	RAD51A	No
18	TP53	No	38	RAD51C	No
19	XRCC3	No	39	RAD51D	No
20	STK11	No	40	PPARG	No

ed to discuss the use of mastectomy with sentinel lymph node dissection [14]. Even for locally advanced breast cancer, a modified radical mastectomy was considered to be adequate treatment in an 11-year-old prepubertal girl [10]. Besides, breast-conserving therapy was gradually tried by clinicians. In 2014, breast-conserving therapy was carried out in a 12-year-old girl with secretory breast carcinoma [12].

In consideration of no pronounced evidence demonstrates the significant efficacy of chemotherapy and/or radiotherapy, post-operative radiotherapy and/or chemotherapy was always not considered in juvenile breast cancer treatment, even for the metastatic and aggressive cancer. Nevertheless, Cabello C et al applied six cycles of adriamycin and cyclophosphamide to a boy with invasive secretory breast cancer in 2012 [21]. Similarly, four cycles of doxorubicin and cyclophosphamide followed by four cycles of docetaxel chemotherapeutic regimen was added to a 12-year-old girl with secretory breast carcinoma [12]. Moreover, Kim JY group select chemotherapy, in combination with radiotherapy strategy for a 14-year-old girl with

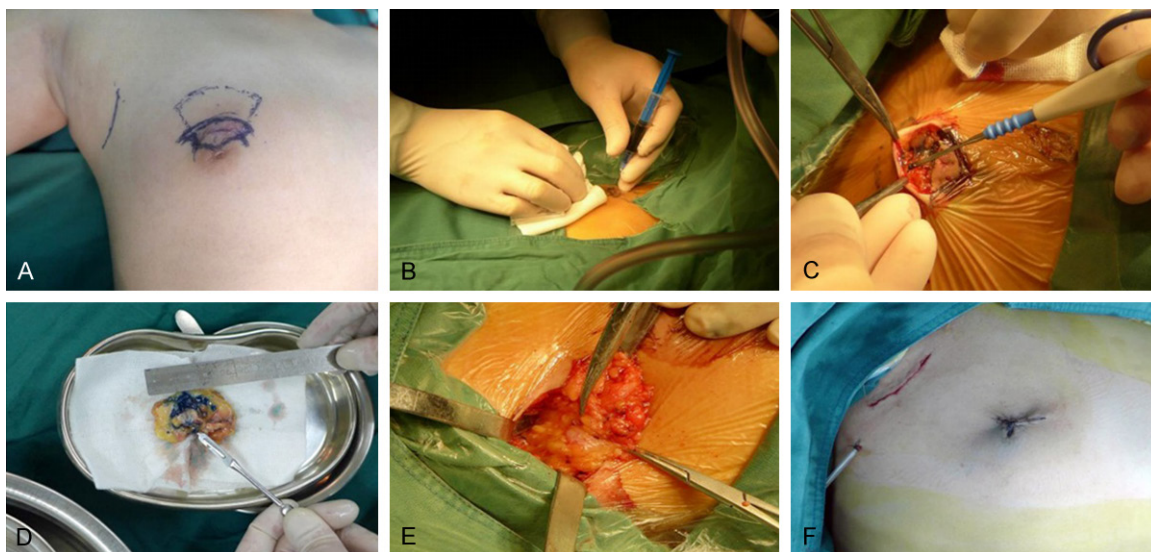


Figure 3. The process of operation. A: Designed fusiform incision, including the former surgical scar. B: Local injection of methylene blue. C, D: Remove part of the glands with electroton. E: Axillary lymph node dissection. F: Wound suture with assimilable thread.



Figure 4. Scars of the patient four months after surgery.

Disclosure of conflict of interest

None.

Address correspondence to: Rui Ling, Department of Thyroid, Breast and Vascular Surgery, Xijing Hospital, Fourth Military Medical University, Xi'an 710032, Shaanxi, China. Tel: 86+84775271; E-mail: lingruiaoxue@126.com

References

- [1] DeSantis C, Siegel R, Bandi P and Jemal A. Breast cancer statistics, 2011. *CA Cancer J Clin* 2011; 61: 409-418.
- [2] Fan L, Strasser-Weippl K, Li JJ, St Louis J, Finkelstein DM, Yu KD, Chen WQ, Shao ZM and Goss PE. Breast cancer in China. *Lancet Oncol* 2014; 15: e279-289.
- [3] Hong W and Dong E. The past, present and future of breast cancer research in China. *Cancer Lett* 2014; 351: 1-5.
- [4] Siegel R, Naishadham D and Jemal A. Cancer statistics, 2013. *CA Cancer J Clin* 2013; 63: 11-30.
- [5] de Deus Moura R, Carvalho FM and Bacchi CE. Breast cancer in very young women: clinico-pathological study of 149 patients ≤ 25 years old. *Breast* 2015; 24: 461-467.
- [6] Gewefel H and Salhia B. Breast cancer in adolescent and young adult women. *Clin Breast Cancer* 2014; 14: 390-395.

invasive ductal carcinoma in 2014 [16]. In my opinion, due to the possible secondary effects, such as fibrosis of the lung, rib damage and the consequent asymmetry of the rib cage, as well as a risk for future development of neoplasia, postoperative radiotherapy should not be advised for children. For the juvenile breast cancer patients with good prognosis, we agree with the “wait-and-see” policy presented by Szant J [9]. Further treatment will be given if it becomes necessary with the development of metastases.

Acknowledgements

This operation was funded by National Natural Science Foundation of China (No. 81572917 and No. 81472598).

- [7] Murphy JJ, Morzaria S, Gow KW and Magee JF. Breast cancer in a 6-year-old child. *J Pediatr Surg* 2000; 35: 765-767.
- [8] Lemoine C, Mayer SK, Beaunoyer M, Mongeau C and Ouimet A. Incidental finding of synchronous bilateral ductal carcinoma in situ associated with gynecomastia in a 15-year-old obese boy: case report and review of the literature. *J Pediatr Surg* 2011; 46: e17-20.
- [9] 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.
- [10] Ahmed ST, Singh SK, Mukherjee T and Banerjee M. Breast carcinoma in a prepubertal girl. *BMJ Case Rep* 2014; 2014.
- [11] Yorozya 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.
- [12] 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.
- [13] Tadesse A, Tesfaye W and Hailemariam B. Breast carcinoma in a 7-years-old girl. *Ethiop Med J* 2012; 50: 89-94.
- [14] 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.
- [15] Sedloev T, Bassarova A, Angelov K, Vasileva M and Asenov Y. Combination of juvenile papillomatosis, juvenile fibroadenoma and intraductal carcinoma of the breast in a 15-year-old girl. *Anticancer Res* 2015; 35: 5027-5029.
- [16] Kim JY, Kim YJ, Kim SH, Kang BJ and Song BJ. Invasive ductal carcinoma of the breast in a 14-year-old girl. *Pediatr Radiol* 2014; 44: 1446-1449.
- [17] Buchino JJ, Moore GD and Bond SJ. Secretory carcinoma in a 9-year-old girl. *Diagn Cytopathol* 2004; 31: 430-431.
- [18] Titus J, Sillar RW and Fenton LE. Secretory breast carcinoma in a 9-year-old boy. *Aust N Z J Surg* 2000; 70: 144-146.
- [19] Noh WC, Paik NS, Cho KJ, Chung JH, Kim MS and Moon NM. Breast mass in a 3-year-old girl: differentiation of secretory carcinoma versus abnormal thelarche by fine needle aspiration biopsy. *Surgery* 2005; 137: 109-110.
- [20] Galzerano A, Rocco N, Accurso A, Ciancia G, Campanile AC, Caccavello F and Fulciniti F. Medullary breast carcinoma in an 18-year-old female: report on one case diagnosed on fine-needle cytology sample. *Diagn Cytopathol* 2014; 42: 445-448.
- [21] 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.
- [22] Wadie GM, Banever GT, Moriarty KP, Courtney RA and Boyd T. Ductal carcinoma in situ in a 16-year-old adolescent boy with gynecomastia: a case report. *J Pediatr Surg* 2005; 40: 1349-1353.
- [23] Corroppolo M, Erculiani E, Zampieri N, Gobatto M, Camoglio FS and Giacomello L. Ductal carcinoma in situ in a 15-year-old boy with gynaeomastia: a case report. *Pediatr Surg Int* 2008; 24: 943-945.
- [24] Chang HL, Kish JB, Smith BL and Goldstein AM. A 16-year-old male with gynecomastia and ductal carcinoma in situ. *Pediatr Surg Int* 2008; 24: 1251-1253.
- [25] Gao Y, Saksena MA, Brachtel EF, terMeulen DC and Rafferty EA. How to approach breast lesions in children and adolescents. *Eur J Radiol* 2015; 84: 1350-1364.