CASE REPORT
(CC BY-SA)

UDC: 618.19-006-08
https://doi.org/10.2298/VSP180126143I

Secretory breast carcinoma in adulthood – A case report with literature review

Sekretorni karcinom dojke u odraslom dobu

Tatjana Ivković Kapicl*†, Ferenc Vicko*†, Lazar Popović*†, Dragana Djilas*†, Tanja Lakić†‡

***The Institute of Oncology of Vojvodina, Sremska Kamenica, Serbia; University of Novi Sad, †Faculty of Medicine, Novi Sad, Serbia; ‡Clinical Center of Vojvodina, Novi Sad, Serbia**

Abstract

Introduction. Secretory breast carcinoma is rare subtype of breast carcinoma which occurs primarily in children and young adults, so in the past it was called juvenile carcinoma. **Case report.** A 67-year-old female patient presented with mass of the right breast since one month. After physical, routine laboratory examination and mammography, core needle biopsy was performed and histopathological examination confirmed invasive carcinoma. Immunohistochemically, estrogen-receptors (ER) and progesteron-receptors (PR) showed weak positive reaction in 10% of tumor cells, while human epidermal growth factor receptor-2 (HER-2) was without expression. After an adequate preoperative preparation, operation was done – quadrantectomy with sentinel lymph node biopsy. Postoperatively, the patient was treated with 6 cycles of cyclophosphamide, methotrexate and fluorouracil (CMF) combination, radiotherapy (60 Gy) and tamoxifen. After 5-year follow-up the patient had no signs of the disease. **Conclusion.** Secretory breast cancer is a rare subtype of invasive breast carcinoma with wide age range of occurrence and good prognosis despite its triple-negative immunophenotype. Although the therapeutic management is non-consensual for this breast cancer special type, surgery is considered the mainstay of the treatment as well as the adjuvant chemotherapy and radiation.

Key words:
breast neoplasms; secretory breast carcinoma; triple negative breast neoplasms; diagnosis; mastectomy, segmental; adult.

Apstrakt

Uvod. Sekretorni karcinom dojke je redak tip karcinoma dojke koji se prvenstveno javlja kod dece i mlađih odraslih osoba, zbog čega se u prošlosti nazivao juvenilnim karcinomom. **Prikaz bolesnika.** Žena, starosti 67 godina, javila se zbog palpabilne, bezbolne mase u desnoj dojci, koja se javila mesec dana pre prijema. Nakon fizikalnog pregleda, rutinskih laboratorijskih analiza i mamografije, načinjena je iglena biopsija i patohistološkom analizom dijagnostikovan je invazivni karcinom dojke. Imunohistohemijski, 10% tumorskih ćelija je pokazalo slabu pozitivnost na estrogenske i progesteronske receptore, dok je receptor humanog epidermalnog faktora rasta-2 (HER-2) bio negativan. Posle adekvatne preoperativne pripreme, izvršen je opertivni zahvat – kvadrantektomija sa biopsijom limfnog čvora stražara. Postoperativno, bolesnik je tertiran kombinacijom ciklofosfamid/metrotreksat/fluorouracil (6 ciklusa), radioterapijom (60 Gy) i tamoksifenom. Petogodišnjim praćenjem bolesnice nisu ustanovljeni znaci bolesti. **Zaključak.** Sekretorni karcinom dojke je redak tip karcinoma dojke, koji zahvata sve starosne grupe i ima dobru prognozu bez obzira na karakteristični tripl-negativni fenotip. Iako ne postoji standardizovan protokol lečenja, hirurška resekcija uz adjuvantnu hemoterapiju i zračnu terapiju su glavni terapijski postupci za ovaj tip karcinoma dojke.

Ključne reči:
dojka, neoplazme; dojka, sekretorni karcinom; dojka, neoplazme, tripl negativne; dijagnoza; mastektomija, segmentalna; odrasle osobe.

Introduction

Secretory breast carcinoma (SBC) is rare subtype of breast carcinoma (< 0.1%). This subtype of breast carcinoma occurs primarily in children and young adults, though persons of any age may be affected. Grossly, it is well-circumscribed tumor, which is microscopically composed of glands and solid nests with microacini and cysts containing

Correspondence to: Tanja Lakić, Clinical Center of Vojvodina, Hajduk Veljkova 3, 21 000 Novi Sad, Serbia.
E-mail: tanja.lakic@mf.uns.ac.rs

eosinophilic, periodic acid Schiff (PAS) positive secretions. Tumor cells have pale granular or vacuolated cytoplasm, low nuclear grade and are estrogen receptor (ER) negative. SBC has a favorable prognosis in children and adolescents, although it may recur locally or even metastasize, particularly in older women [1, 2].

Case report

A 67-year-old female patient presented with mass of the right breast since one month. After physical and routine laboratory examination, mammography was done. It showed presence of shadow in down right lateral area of the right breast measured 2 × 1.8 cm. Core needle biopsy was performed and histopathological (HP) examination confirmed an invasive carcinoma, probably of no special type. After an adequate preoperative preparation, operation was done – quadrantectomy with sentinel lymph node (SN) biopsy. Gross examination revealed presence of lobulated node diameter of 1.9 × 1.5 cm which was 1.5 cm to the closest resection margin. On the routine hematoxylin and eosin (HE) staining, the tumor showed pushing margin. The invasive tumor component was composed of solid areas of atypical tumor cells with granular cytoplasm as well as cells with signet-ring features. Also, there was a plenty of microcystic formations full of abundant eosinophilic material which was present in tumor cells as well (Figure 1).

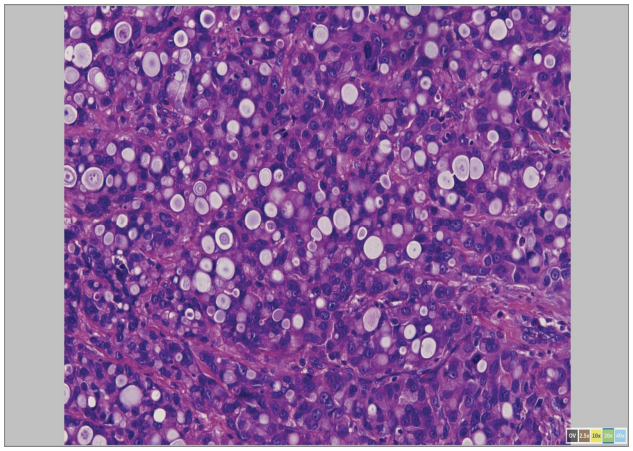

Fig. 1 – Microcystic and solid areas of atypical tumor cells with granular cytoplasm and signet-ring features [hematoxylin and eosin (HE), 200×].

The nuclei of the tumor cells were small, round and low grade cytologically. The secretory material was clearly PAS and PAS-diastase positive (Figure 2). Immunohistochemically, ER and progesteron receptors (PR) showed weak positive reaction in 10% of tumor cells (Figure 3, 4), while human epidermal growth factor receptor-2 (HER-2) was without expression. SN and lymphovascular spaces were negative for the presence of the tumor. Postoperatively, the patient was treated with chemotherapy – 6 cycles of cyclophosphamide, methotrexate and fluorouracil (CMF), radiotherapy (60 Gray) and tamoxifen, also. After 5-year follow-up the patient had no signs of the disease.

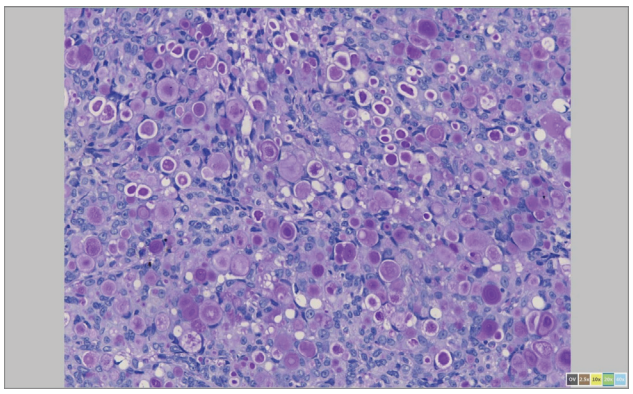

Fig. 2 – The secretory eosinophilic material [periodic acid Schiff (PAS), 200×].

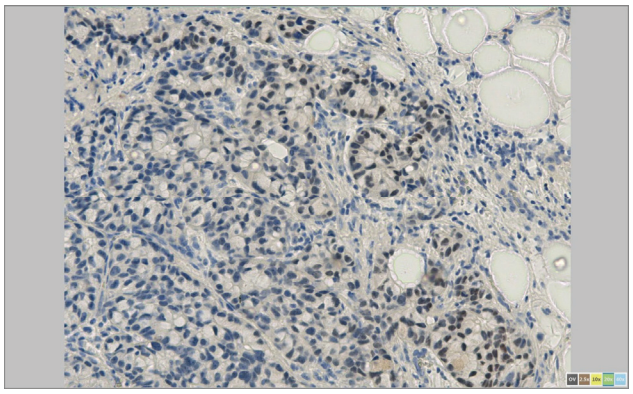

Fig. 3 – Weak estrogen receptor positivity in single tumor cells [immunohistochemistry (IHC), 200×].

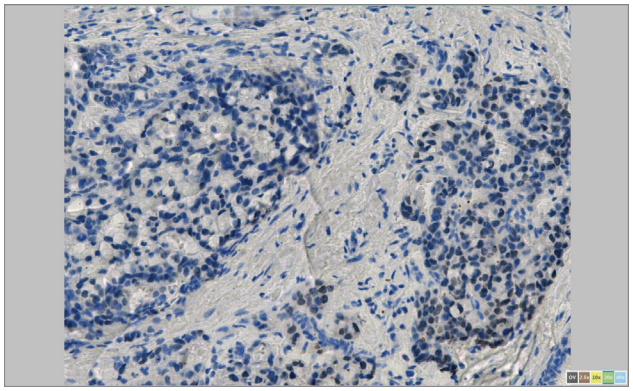

Fig. 4 – Weak progesteron receptor positivity in single tumor cells [immunohistochemistry (IHC), 200×].

Discussion

Secretory carcinoma is a very rare type of breast carcinoma, accounting for less than 0.1% of all infiltrating breast malignancies. It was first described in 1966 by McDivitt and Stewart [3] as juvenile carcinoma because they had 7 cases of this type of breast carcinoma without regional lymph node or distant metastases; patients ages ranged from 3 to 15 years, average 9 years SBC is most common under the age of 30, and it is the most common type of breast carcinoma in children. Although originally described in children, it is now known to occur in adults in both sexes, with male to female ratio 1:6. Reports suggest that the disease tends to be more

aggressive in males [4]. By 2003 there had been nearly 100 reported cases of SBC. Lamovec and Bracko [5] reported four cases of SBC among 7,038 breast carcinoma cases, and Botta et al. [6] found one case of SBC among 3,000 breast carcinoma cases. Li et al. [7] reported 15 SBC cases in their pathologic review of 10,000 breast carcinoma cases.

Clinically, the tumor usually presents as a mobile and palpable mass that is frequently subareolar but may occur in any part of the breast [8–10]. Tumor size ranges from 0.5 cm to 16 cm but it is usually between 1.5 cm and 3.0 cm, as in our case, and it tends to be larger in adults. Some authors consider that when larger than 2 cm it appeares to have increased malignant potential [11].

Radiographically, there are sparse descriptions of mammographic findings in the literature. SBC may be present as a discrete, lobulated, solitary mass with smooth or irregular borders which may mimic fibroadenoma. Because SBC occurs more frequently in young woman, mammography may have a diagnostic limitation because of the relatively high density of the breast tissue. A retroareolar dense mass is the usual finding in children as well as in male patients [12–14].

Ultrastructurally, the tumor consists of large number of membrane-bound intracytoplasmic secretory vacuoles containing abundant secretory material [4].

Grossly, it is often solitary, circumscribed, firm mass with grey, white or tan cut surface [15].

Secretory carcinoma is histologically special type of breast carcinoma which has two main features – abundant PAS positive intracellular and extracellular secretions and a granular eosinophilic cell cytoplasm [9]. The tumor has predominantly pushing margins, occasionally with focal areas of infiltration.

Microscopically, this tumor is composed of polygonal cells with vacuolated pale-pink cytoplasm, granular eosinophilic or amphophilic cytoplasm and there is characteristic presence of large amounts of intracellular and extracellular secretory material which is variably reactive for mucin and PAS. Nuclei are small, round, bland with minimal atypia. Mitotic activity is low. Tumor cells are typically arranged into papillary, microcystic and glandular structures [4, 15]. Hyalinized fibrous tissue is frequently identified centrally. Sometimes, tumor cells may show prominent granular eosinophilic cytoplasm focally and higher nuclear grade, resembling apocrine carcinoma morphology [16]. Immunohistochemically, strong positive staining has been reported for S-100 protein, as well as α-lactalbumin and polyclonal carcinoembryonic antigen (CEA). No reactivity was observed for gross cystic disease fluid protein-15 (GCDFP-15). It has been reported that secretory carcinoma is negative for ER, PR and HER2, so called "triple negative" [2, 17]. Recent studies suggest that SBC espress basal-cell markers, including cytokeratins 5/6, 14 and 17, c-Kit (CD117), epidermal growth factor receptor and vimentin[17–19]. Also, there is consistently immunopositivity for S100 and α-lactalbumin [5] and for E-cadherin as expected in any subtype of ductal carcinoma. Proliferation index by MIB-1 ranges from 1% to 34% [20].

Cytogenetically, human SBC has been associated with balanced translocation t [12, 15] – associated ETV6-NTRK3 gene fusion as a dominantly acting oncogene in 12 of 13 cases [21] and it is the first demonstration of a balanced translocation in breast cancer. Also, some authors demonstrated that SBC with the ETV6-NTRK3 gene fusion belongs to the phenotypic spectrum of basal-like breast carcinomas [17].

Locoregional recurrence is rare, but some authors have reported that there is an increased rate of recurrence in those cases treated by local resection [11]. Rosen and Cranor [22] have suggested that local recurrence is related to incomplete resection of the tumor. Tavassoli and Norris [9] have reported that metastasis to axillary nodes is not shown in tumors smaller than 2 cm in diameter. Distant metastases are extremely rare, and only four cases have been reported [10].

Because of scarcity of reported cases, there is no published guidelines on the disease management. Surgical excision is the primary mode of the treatment for SBC with SN examination. In children, local excision with SN mapping is the preferred initial treatment with preservation of prepubertal breast tissue. In adults, because of the increased rate of recurrence, a simple mastectomy is recommended. Modified radical mastectomy has been favoured by some authors in cases with tumor size greater than 2 cm and poor gross circumscription [11]. Although there is no evidence to support, adjuvant chemotherapy and radiation have been tried for adults [10]. Recurrences may develop 6 and 8 years following both local excision and modified mastectomy, respectively. Distant metastases are extremely rare and were usually reported even after 20 years of a surgical treatment, so it is desirable to follow patients at least 20 years [23].

Conclusion

Secretory breast cancer is a rare subtype of invasive breast carcinoma with wide age range of occurrence and good prognosis despite its triple-negative immunophenotype. The histopathological diagnosis of this tumor is quite challenging although there is the specific morphologic pattern. SBC belongs to the phenotypic spectrum of basal-like breast carcinomas. Although the therapeutic management is nonconsensual for this breast cancer special type, surgery is considered the mainstay of treatment as well as the adjuvant chemotherapy and radiation. Future molecular analyses may help for making targeted therapy for this disease.

R E F E R E N C E S

1. *Arce C, Cortes-Padilla D, Huntsman DG, Miller MA, Dueñas-Gonzalez A, Alvarado A,* et al. 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.
2. *Costa NM, Rodrigues H, Pereira H, Pardal F, Matos E.* Secretory breast carcinoma - case report and review of the medical literature. Breast 2004; 13(4): 353–5.
3. *McDivitt RW, Stewart FW.* Breast carcinoma in children. JAMA. 1966; 195(5): 388–90.

4. *Ozguroglu M, Tascilar K, Ilvan S, Soybir G, Celik V*. Secretory carcinoma of the breast. Case report and review of the literature. Oncology 2005; 68(2–3): 263–8.
5. *Lamovec J, Bracko M*. Secretory carcinoma of the breast: light microscopical, immunohistochemical and flow cytometric study. Mod Pathol 1994; 7(4): 475–9.
6. *Botta G, Fessia L, Ghiringhello B*. Juvenile milk protein secreting carcinoma. Virch Arch Pathol Anat Histol 1982; 395(2): 145–52.
7. *Li D, Xiao X, Yang W, Shui R, Tu X, Lu H,* et al. Secretory breast carcinoma: a clinicopathological and immunophenotypic study of 15 cases with a review of the literature. Mod Pathol 2012; 25(4): 567–75.
8. *Gupta RK, Kenwright D, Naran S, Lallu S, Fauck R*. Fine needle aspiration cytodiagnosis of secretory carcinoma of the breast. Cytopathology 2000; 11(6): 496–502.
9. *Tavassoli FA, Norris HJ*. Secretory carcinoma of the breast. Cancer 1980; 45(9): 2404–13.
10. *Herz H, Cooke B, Goldstein D*. Metastatic secretory breast cancer. Non-responsiveness to chemotherapy: case report and review of the literature. Ann Oncol 2000; 11(10): 1343–7.
11. *Richard G, Hawk JC 3rd, Baker AS Jr, Austin RM*. Multicentric adult secretory breast carcinoma: DNA flow cytometric findings, prognostic features, and review of the world literature. J Surg Oncol 1990; 44(4): 238–44.
12. *Amott DH, Masters R, Moore S*. Secretory carcinoma of the breast. Breast J 2006; 12(2): 183.
13. *Longo OA, Mosto A, Moran JC, Mosto J, Rives LE, Sobral F*. Breast carcinoma in childhood and adolescence: case report and review of the literature. Breast J 1999; 5(1): 65–9.
14. *Milošević Z, Spasić N*. Magnetic resonance imaging of the breasts: Clinical practice and further development. Srp Arh Celok Lek 2004; 132(7–8): 260–6. (Serbian)
15. *Rosen PP*. Secretory carcinoma. In: *Rosen PP*, editor. Rosen's Breast Pathology. 3rd ed. Philadelphia, PA: Lippincott Williams and Wilkins; 2009. p. 563–70.
16. *Anderson P, Albarracin CT, Resetkova E*. A large, fungating breast mass: secretory carcinoma with apocrine differentiation. Arch Pathol Lab Med 2006; 130(4): e50–2.
17. *Lae´ M, Fréneaux P, Sastre-Garau X, Chouchane O, Sigal-Zafrani B, Vincent-Salomon A*. Secretory breast carcinomas with ETV6-NTRK3 fusion gene belong to the basal-like carcinoma spectrum. Mod Pathol 2009; 22(2): 291–8.
18. *Ivković-Kapicl T, Panjković M, Nikolić I, Đilas-Ivanović D, Knežević-Ušaj S*. Expression of cytokeratins 5/6 and cytokeratin 17 in invasive breast carcinoma. Vojnosanit Pregl 2012; 69(12): 1031–8. (Serbian)
19. *Lambros MB, Tan DS, Jones RL, Vatcheva R, Savage K, Tamber N,* et al. Genomic profile of a secretory breast cancer with an ETV6-NTRK3 duplication. J Clin Pathol 2009; 62(7):604–12.
20. *Diallo R, Schaefer KL, Bankfalvi A, Decker T, Ruhnke M, Wülfing P,* et al.. Secretory Carcinoma of the breast: a distinct variant of invasive ductal carcinoma assessed by comparative genomic hybridization and immunohistochemistry. Hum Pathol 2003; 34(12): 1299–305.
21. *Tognon C, Knezevich SR, Huntsman D, Roskelley CD, Melnyk N, Mathers JA*, et al. Expression of the ETV6-NTRK3 gene fusion as a primary event in human secretory breast carcinoma. Cancer Cell 2002; 2(5): 367–76.
22. *Rosen PP, Cranor ML*. Secretory carcinoma of the breast. Arch Pathol Lab Med 1991; 115(2): 141–4.
23. *Krausz T, Jenkins D, Grontoft O, Pollock DJ, Azzopardi JG*. Secretory carcinoma of the breast in adults: emphasis on late recurrence and metastasis. Histopathology 1989; 14(1): 25–36.

Received on January 26, 2018.
Accepted December 19, 2019.
Online First December, 2019.