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# A Case of Metaplastic Squamous Cell Carcinoma of the Breast that Showed a Pathological Complete Response After Neoadjuvant Chemotherapy with Weekly Paclitaxel

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Statistical Analysis C  
Data Interpretation D  
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**Patient:** Female, 40-year-old  
**Final Diagnosis:** Squamous cell carcinoma of the breast  
**Symptoms:** A palpable tumor of the right breast  
**Medication:** —  
**Clinical Procedure:** Core needle biopsy  
**Specialty:** Oncology

**Objective:** Unusual or unexpected effect of treatment

**Background:** Primary squamous cell carcinoma of the breast is a rare type of metaplastic breast carcinoma, characterized by resistance to conventional chemotherapy agents. We report a case of metaplastic squamous cell carcinoma of the breast in which a pathological complete response was achieved after neoadjuvant chemotherapy with weekly paclitaxel and in which the patient remained disease free for 15 years and 7 months.

**Case Report:** A 40-year-old woman had a palpable 5-cm-diameter tumor in the right breast that was diagnosed as metaplastic squamous cell carcinoma of the breast based on core needle biopsy. The patient was initially treated with an adjuvant chemotherapy (AC) regimen consisting of doxorubicin (60 mg/m<sup>2</sup>) and cyclophosphamide (600 mg/m<sup>2</sup>) as neoadjuvant chemotherapy. Because the tumor grew rapidly and the skin redness increased after 1 cycle of the AC regimen, 12 cycles of weekly paclitaxel 80 mg/m<sup>2</sup> were subsequently administered. The tumor responded dramatically to paclitaxel. The patient underwent mastectomy with level II axillary lymph node dissection. No residual tumor cells were found, which indicated pathological complete response. The patient is currently disease free at 15 years and 7 months after the operation.

**Conclusions:** To our knowledge, there are no previous reports of metaplastic squamous cell carcinoma of the breast in which pathological complete response was achieved by treatment with neoadjuvant chemotherapy with weekly paclitaxel (80 mg/m<sup>2</sup>).

**Keywords:** Breast • Carcinoma, Squamous Cell • Neoadjuvant Therapy • Paclitaxel

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## Background

Metaplastic squamous cell carcinoma (SCC) of the breast, which is classified as a subtype of metaplastic carcinoma by the World Health Organization [1], is a rare type of breast carcinoma that accounts for less than 0.1% of all invasive breast carcinomas [2-5]. Some authors have suggested that it originates from squamous metaplasia observed in the epithelium of cysts, fibroadenomas, phyllodes tumors, duct hyperplasia, and papilloma [3,4,6] and in association with implants [7]. It has also been found in inflammatory lesions, such as abscesses [4,8]. The tumor is often accompanied by necrotic foci, hemorrhagic foci, inflammatory changes, and cyst formation, because of the rapid growth [9]. The majority of SCCs of the breast are generally negative for the expression of hormone receptors and HER2/neu [2-5,10], displaying a triple-negative immunophenotype. A few cases showing HER2 overexpression have been reported [11,12]. Most published studies report that the tumor tends to grow rapidly, be relatively larger when found in comparison with other histological types, be associated with frequent relapse, and result in death [2-5,10]. Hennessy et al [5] reported that the 5-year relapse-free survival rate of patients without metastatic disease at the time of diagnosis was 26%. Other authors reported that the 5-year overall survival rate ranged from 40% to 67.2% [2-5,10,13].

Thus, because SCC of the breast is an extremely aggressive disease, it might require more aggressive or additional systemic therapy. However, the optimal chemotherapy regimen for SCC of the breast is still unclear. We herein report a case of SCC of the breast in which a pathological complete response (pCR) was achieved after neoadjuvant chemotherapy (NAC) with weekly paclitaxel and in which the patient remained disease free for 15 years and 7 months.

## Case Report

In April 2004, a 40-year-old woman was referred to our hospital with a palpable tumor of the right breast. The tumor was suspected to be SCC based on the fine-needle aspiration cytology. She had no coexisting diseases, was not taking any medications, and had no habit of drinking alcohol or smoking. She had no family history of breast cancer.

A physical examination revealed a 5-cm-diameter tumor with skin erythema, which was located in the upper portion of the right breast. The axillary lymph nodes were not swollen. Mammography showed an indistinct, high-density mass with a pleomorphic calcification in the upper portion of the right breast (Figure 1A). Ultrasonography revealed an irregularly shaped hypoechoic lesion with cystic components, measuring more than 7 cm (data not shown). Dynamic magnetic resonance

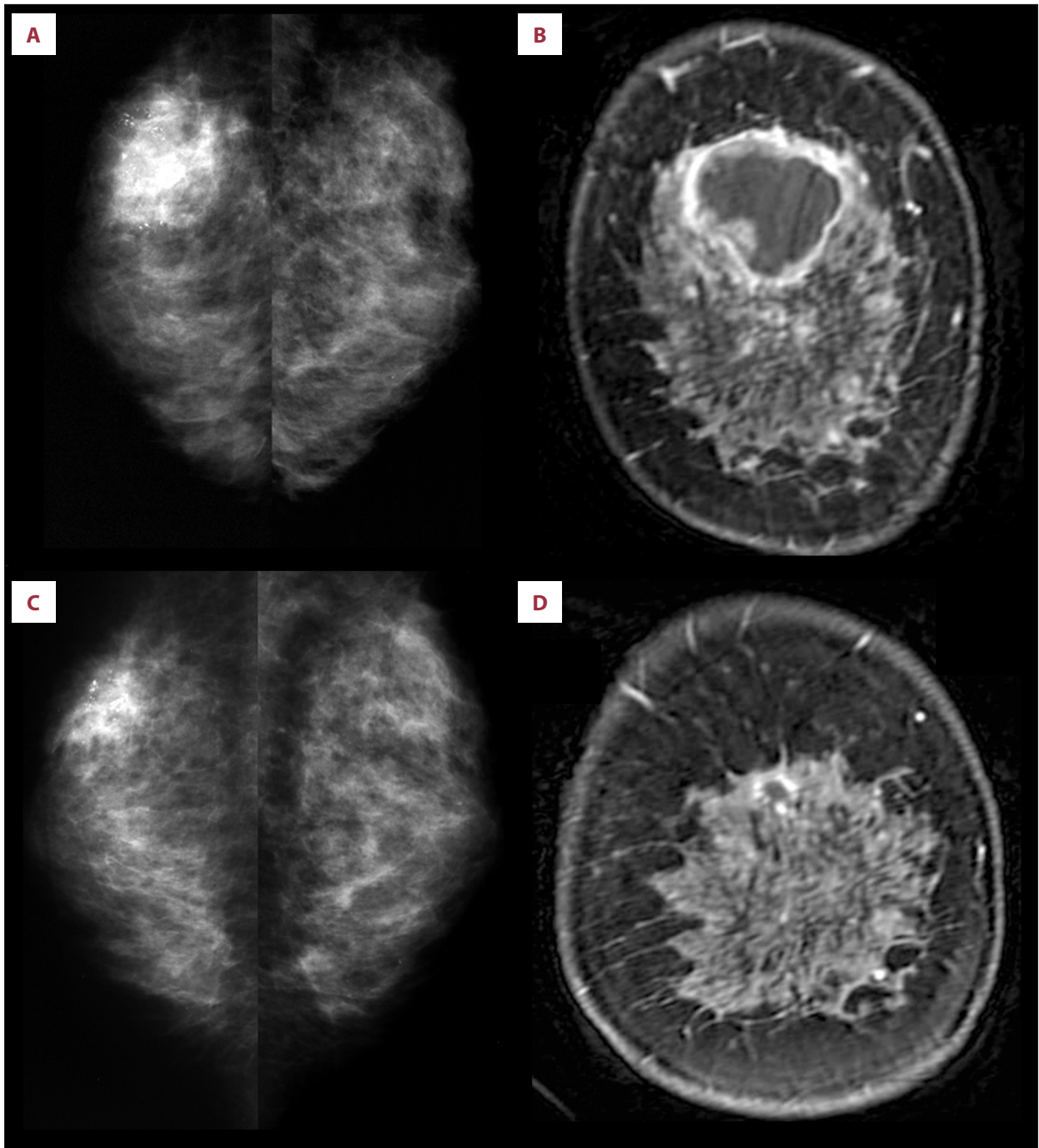
imaging (MRI) demonstrated a large cystic tumor in the upper portion of the right breast. The wall of the tumor was markedly enhanced. The papillary projection was formed from the wall to the lumen (Figure 1B). T2-weighted imaging showed a high-intensity tumor with a cystic lesion. Core needle biopsy revealed metaplastic squamous cell carcinoma (Figure 2). Immunohistochemical analysis was negative for estrogen and progesterone receptors and HER2/neu. The serum levels of tumor markers related to breast cancer, carcinoembryonic antigen, cancer antigen 15-3, and NCC-ST439, were within normal limits.

Based on the above characteristics, the patient's diagnosis was locally advanced (T3N0M0 Stage IIB) triple-negative breast cancer. The patient was treated with an AC regimen consisting of doxorubicin (60 mg/m<sup>2</sup>) and cyclophosphamide (600 mg/m<sup>2</sup>) as NAC starting in May 2004. After 1 cycle of the AC regimen, the tumor grew rapidly to 8 cm in diameter and the skin redness increased. We judged that the AC regimen was ineffective based on physical examination. Because the tumor was too big to be resected completely, we changed the treatment to weekly paclitaxel (80 mg/m<sup>2</sup>). The ultrasonography image before the administration of paclitaxel is shown in Figure 3A. Following the regimen of weekly paclitaxel, the tumor constantly regressed. There were no remarkable adverse events due to this therapy, and the tumor size dramatically decreased from 8 to 2 cm after 12 cycles. Imaging examinations were repeated to evaluate the effect of the chemotherapy.

Mammography showed a reduction of the mass size (Figure 1C). Ultrasonography similarly revealed that the size of the tumor was significantly decreased after chemotherapy (Figure 3B). MRI revealed that the diameter of the enhanced tumor had decreased from 37 to 11 mm (Figure 1D).

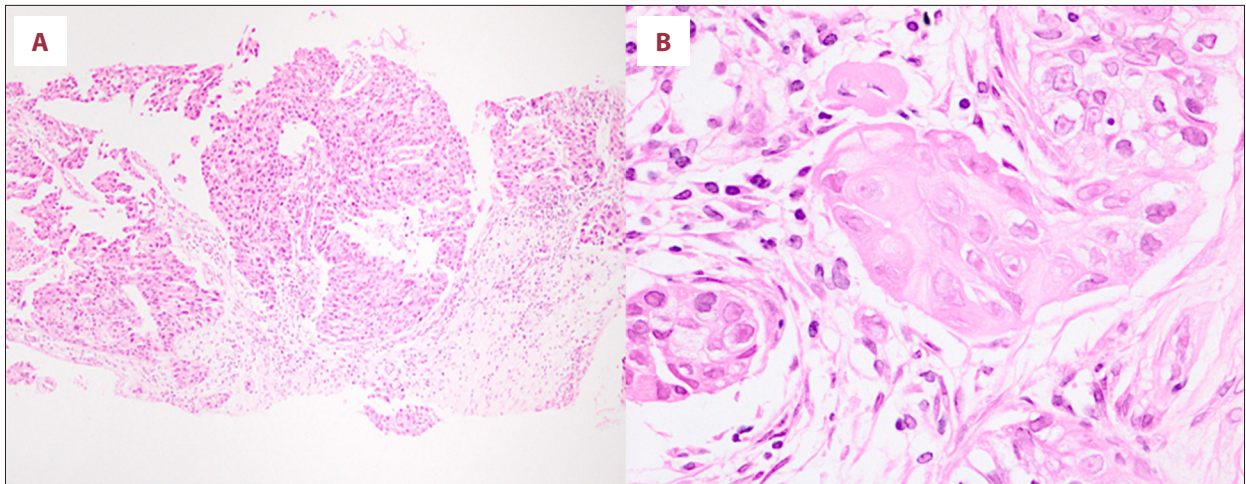
After chemotherapy, the tumor was down-staged to ycT1c-NOMO Stage I. Mastectomy with level II axillary lymph node dissection was performed in September 2004, after chemotherapy. We created a pathological specimen of the entire area in which the tumor was considered to have originally spread. Macroscopically, the resected specimen showed a cystic structure.

Histopathologically, the cyst contained necrotic tissue and foamy histiocytes. The cyst wall was covered by foamy histiocytes and lymphocytic infiltration, including calcification and hemosiderin-laden macrophages. No tumor cells, including in situ components, were observed in the resected specimen (Figure 4). There was fibrosis, edema, and infiltration of histiocytes and lymphocytes in the other area, which suggested the disappearance of the tumor. Histopathologically, the efficacy of chemotherapy was judged to be Grade 3, indicating a pCR according to the histopathological response criteria of the Japanese Breast Cancer Society [14].

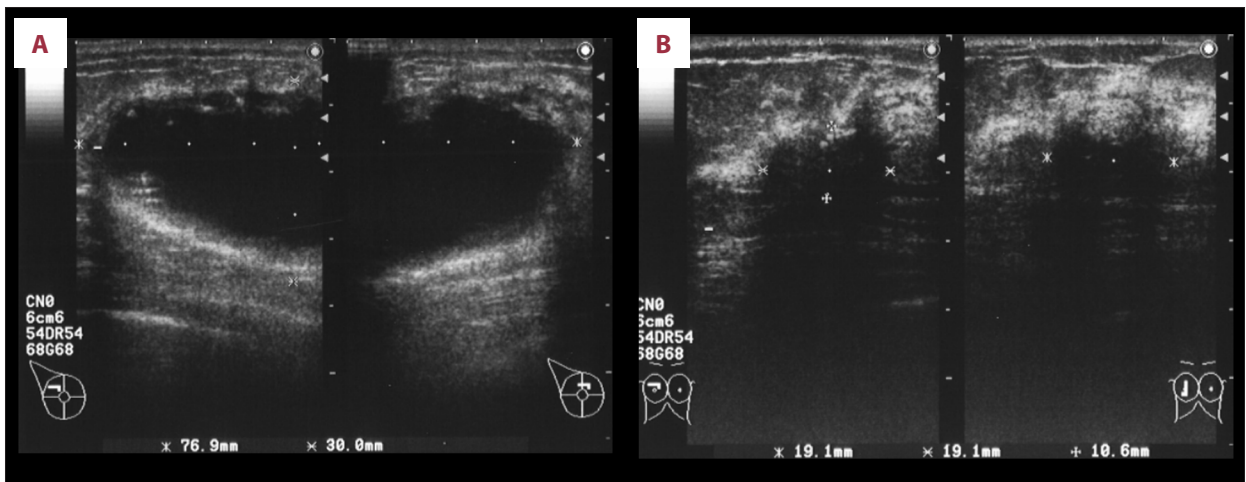


**Figure 1.** (A) Mammography performed before chemotherapy demonstrated an indistinct, high-density mass with pleomorphic calcification in the upper portion of the right breast. (B) Magnetic resonance imaging (MRI) before chemotherapy showed a lobulated mass with irregular margins and rapid enhancement during the early phase of the enhanced kinetics. The image demonstrated washout of the enhancement pattern during the delayed phase. (C) Mammography performed after chemotherapy showed the marked shrinkage of the mass with a microlobulated and partially irregular margin. (D) MRI after chemotherapy showed that the mass was considerably reduced.





**Figure 2.** Core needle biopsy specimen of the tumor. (A) A low-power view showed squamous cell carcinoma (HE, ×100). (B) A high-power view showed a nest of squamous cell carcinoma (HE, ×400). HE, hematoxylin and eosin.



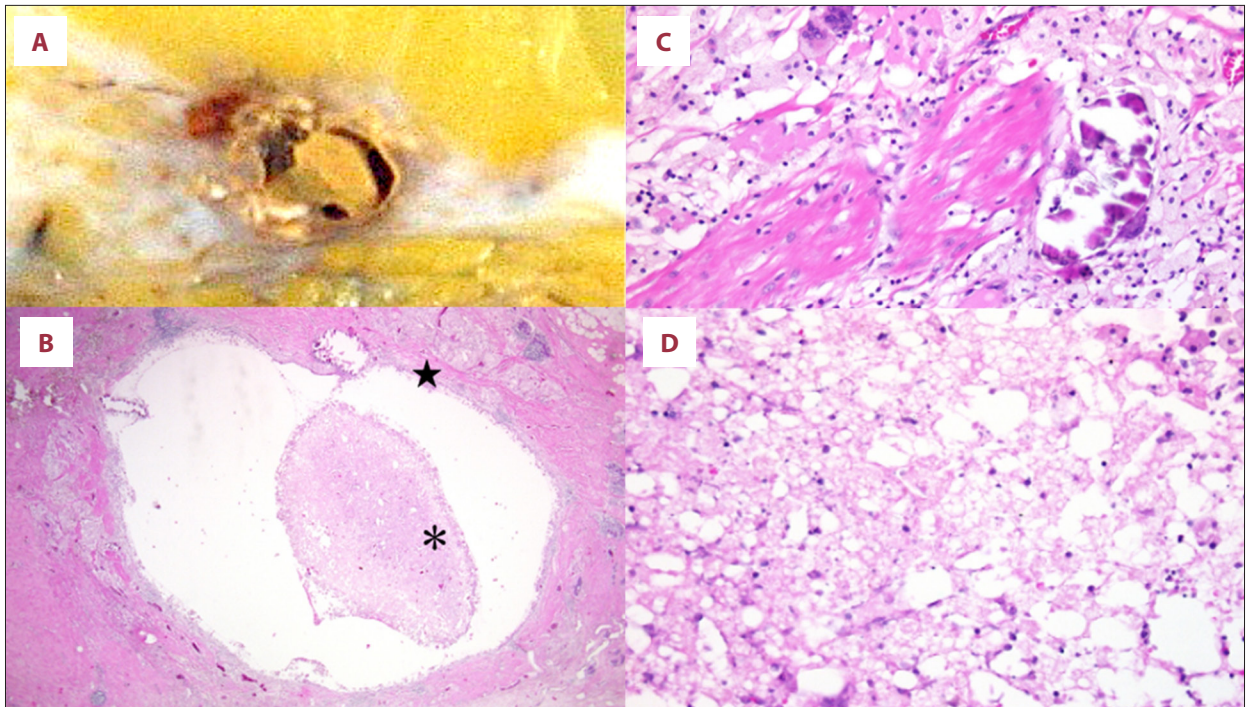
**Figure 3.** (A) Ultrasonography performed before the administration of weekly paclitaxel revealed a hypoechoic lesion with cystic components, measuring 7.7 cm. (B) Ultrasonography performed after chemotherapy showed that the size of the tumor was significantly decreased to 1.9 cm.

The patient was treated with postmastectomy radiotherapy to the right chest wall and supraclavicular lymph nodes from October to December 2004. A total radiation dose of 50 Gy was delivered. In April 2020, at the time of our last contact with the patient, she was very well and had remained disease free in the 15 years and 7 months after the operation.

## Discussion

The optimal chemotherapy regimen for SCC of the breast is still unclear. Adjuvant therapy for SCC has generally been carried out in the same way as therapy for more common types of breast cancer; however, it has been reported that anthracycline/taxane-based chemotherapy, which is used relatively frequently in breast cancer treatment, is ineffective for SCC of the breast [5].

Some reports suggested that cisplatin-based chemotherapy could achieve good control [15,16]. Others indicated that eribulin was effective for SCC [17]. However, most published data have indicated that SCC is refractory to the conventional chemotherapy [5,13,18]. Some authors have reported that SCC of the breast is significantly associated with no response to NAC [5,10,13,19]. Zhu et al [10] reported that the no-response rate to neoadjuvant chemotherapy was 20% for patients with SCC and 5.05% for patients with invasive ductal carcinoma. SCC was significantly associated with no response to NAC ( $P=0.019$ ) [10]. The poor response to chemotherapy suggested that NAC was not useful in the treatment of advanced SCC of the breast. It is generally recommended that patients diagnosed with triple-negative breast cancer receive NAC. However, if they are diagnosed with SCC of the breast, and if the case is considered operable, an operation followed by adjuvant therapy can



**Figure 4.** (A) Macroscopic finding of the tumor. A cystic area measuring approximately 8 mm was observed. (B) Histopathological findings of the cystic area (HE, ×20). (C) The cyst wall (★) was covered by foamy histiocytes and lymphocytic infiltration, including calcification and hemosiderin-laden macrophages (HE, ×100). (D) Only necrotic tissue and foamy histiocytes were observed inside the cyst (\*). No tumor cells were detected in the resected specimen (HE, ×100). HE, hematoxylin and eosin.

be selected. In our case, we chose NAC because we considered the case to be inoperable. However, some authors have reported that a pCR was achieved by NAC, even in patients with SCC of the breast.

Alan et al [20] showed a unique case of a patient with a triple-negative SCC tumor of 6.5 cm in diameter that showed complete pathological response after NAC with weekly paclitaxel followed by treatment with the combination of epirubicin and cyclophosphamide. This case was comparable to our case. Dejager et al [16] also showed that patients with SCC that was negative for the expression of hormone receptors achieved a pCR after neoadjuvant treatment with cisplatin and fluorouracil [16]. NAC may be effective even for cases of SCC.

The following points should be kept in mind. Some authors have reported that some triple-negative breast cancers show enlargement due to cystic changes inside the tumor due to the administration of NAC (rather than disease progression), which resulted in a reduction of the tumor burden [21,22]. In our case, our judgment that the first regimen was ineffective was based mainly on a physical examination. The response to NAC should be carefully based on imaging examinations when the tumor increases in size.

## Conclusions

SCC of the breast is an aggressive disease that tends to be associated with poor outcomes and a high risk of recurrence. Better systemic therapy is therefore needed to improve patient outcomes. We reported a very rare case of SCC of the breast in which a pCR was achieved after NAC with the weekly administration of paclitaxel (80 mg/m<sup>2</sup>) and in which long relapse-free survival and overall survival were achieved. The outcome in this case suggests that weekly paclitaxel therapy might be useful as a choice of chemotherapy for primary SCC of the breast. Our case paves the way for future studies to investigate treatment options of SCC of the breast with the aim of improving patient outcomes.

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## Declaration of Figures' Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

## References:

1. Reis-Filho JS, Shin SJ, Gobbi H, et al. Metaplastic carcinoma. In: WHO Classification of Tumours Editorial Board, editors. WHO classification of tumours, breast tumours. 5<sup>th</sup> ed. Lyon: International Agency for Research on Cancer Press; 2019;134-38
2. Benoist P, Mureau A, Joueidi Y, et al. Management and prognosis of pure primary squamous cell carcinoma of the breast. *J Gynecol Obstet Hum Reprod.* 2018;47:275-80
3. Yadav S, Yadav D, Zakalik D. Squamous cell carcinoma of the breast in the United States: Incidence, demographics, tumor characteristics, and survival. *Breast Cancer Res Treat.* 2017;164:201-8
4. Grenier J, Soria JC, Mathieu MC, et al. Differential immunohistochemical and biological profile of squamous cell carcinoma of the breast. *Anticancer Res.* 2007;27:547-55
5. Hennessy BT, Krishnamurthy S, Giordano S, et al. Squamous cell carcinoma of the breast. *J Clin Oncol.* 2005;23:7827-35
6. Brogi E. Squamous carcinoma. In: Shaw R, editor. Rosen's breast pathology. 4<sup>th</sup> ed. Philadelphia: Lippincott Williams & Wilkins Press; 2014;599-610
7. Olsen DL, Keeney GL, Chen B, et al. Breast implant capsule-associated squamous cell carcinoma: A report of 2 cases. *Hum Pathol.* 2017;67:94-100
8. Kurpad V, Prabhu K C, Ramesh MK, Harindranath HR. Primary de novo squamous cell carcinoma breast masquerading as breast abscess. *Indian J Surg Oncol.* 2013;4(1):48-51
9. Yoneto T, Hasumi K, Yoshimoto T, et al. Case report: two cases of extremely rare primary pure squamous cell carcinoma of the breast. *Medicine (Baltimore).* 2018;97:e12340
10. Zhu L, Chen K. Clinicopathological features, treatment patterns, and prognosis of squamous cell carcinoma of the breast: an NCCDB analysis. *BMC Cancer.* 2019;19:26
11. Shui R, Li A, Yang F, et al. Primary squamous cell carcinoma of the breast with unusual basal-HER2 phenotype. *Int J Clin Exp Pathol.* 2014;7:5203-9
12. Cha N, Wang S, Lv M, et al. Breast metaplastic squamous cell carcinoma diagnosed with fine needle and core biopsy: a case study. *Am J Case Rep.* 2018;19:203-6
13. Zhang X, Zhang B, Zang F, et al. Clinical features and treatment of squamous cell carcinoma of the breast. *Onco Targets Ther.* 2016;9:3181-85
14. Japanese Breast Cancer Society (JP). General rules for clinical and pathological recording of breast cancer. 18<sup>th</sup> ed. Tokyo: The Institute; 2018 [in Japanese]
15. Tsung SH. Primary pure squamous cell carcinoma of the breast might be sensitive to cisplatin-based chemotherapy. *Case Rep Oncol.* 2012;5:561-65
16. DeJager D, Redlich PN, Dayer AM, Davis HL, Komorowski RA. Primary squamous cell carcinoma of the breast: Sensitivity to cisplatin-based chemotherapy. *J Surg Oncol.* 1995;59:199-203
17. Goto Y, Yoshida T, Kimura M. Higher efficacy and complete response with administration of eribulin for recurrent squamous cell breast carcinoma: A case report. *Mol Clin Oncol.* 2018;9:318-20
18. Takahashi T, Akashi-Tanaka S, Fukutomi T, et al. Two special types of breast cancer presenting as progressive disease after neoadjuvant chemotherapy with docetaxel plus doxorubicin. *Breast Cancer.* 2001;8:234-37
19. Al Sayed AD, Elshenawy MA, Tulbah A, et al. Complete response of chemorefractory metastatic metaplastic breast cancer to paclitaxel-immunotherapy combination. *Am J Case Rep.* 2019;20:1630-35
20. Alan O, Telli TA, Ercelep O, et al. A case of primary squamous cell carcinoma of the breast with pathologic complete response after neoadjuvant chemotherapy. *Curr Probl Cancer.* 2019;43:308-11
21. Nakagawa T, Horimoto Y, Arakawa A, et al. [Two breast cancer cases showing marked intra-tumor necrosis during primary systemic chemotherapy.] *Jpn J Breast Cancer.* 2009;24:657-62 [in Japanese]
22. Tanei T, Masuda N, Ishitobi M, et al. [The specific shrinkage pattern of neoadjuvant chemotherapy for locally advanced breast cancer: A case report.] *Jpn J Breast Cancer.* 2006;21:564-69 [in Japanese]