



Breast carcinoma with spontaneous regression after needle biopsy: a case report and literature review

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Background: Spontaneous regression (SR) of cancer is a rare condition in which the cancer partially or completely disappears without treatment. We report a case of breast cancer with tumor regression and spontaneously induced T-cell-mediated immunological responses in a surgical specimen obtained after core needle biopsy (CNB).

Case Description: A 52-year-old woman presented with a mass in the right breast. Mammography showed a high-density mass with fine serrated margins in the right lower outer quadrant. Breast ultrasonography showed an irregular hypoechoic mass with a maximum diameter of 22 mm. CNB was performed and revealed an invasive ductal carcinoma with negative estrogen receptors, positive progesterone receptors, and negative HER2 (1+). The Ki67 index was 70% to 80%. Luminal B cT2N1M0 stage IIB right breast cancer was diagnosed. Although preoperative chemotherapy was considered, surgery was selected because of her history of schizophrenia. She underwent right mastectomy and axillary lymph node dissection. A postoperative pathological analysis revealed a 20 mm × 10 mm × 10 mm mass. However, most areas of the mass regressed and appeared as necrotic tissue with no obvious invasive areas. Only intraductal extension was observed in one glandular duct. Axillary lymph node metastases were not observed. These results suggest that the tumor may have spontaneously regressed, possibly because of the CNB procedure. Follow-up without treatment was performed, and no recurrence occurred during 2 years after surgery.

Conclusions: Invasive ductal carcinoma may spontaneously regress after preoperative CNB.

Keywords: Breast cancer; case report; CD8-positive T cell; core needle biopsy; spontaneous regression after needle biopsy

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Introduction

Spontaneous regression (SR) of malignant tumors is a rare condition defined as the partial or complete disappearance of the tumor with no treatment or with treatment that is not expected to reduce the tumor size (1,2). It is a phenomenon that can be observed regardless of the type of carcinoma, and its causes include needle biopsy. Recently,

it was reported that immune responses occurring with cancer may be involved in the mechanisms of SR. We report a rare case of invasive ductal carcinoma of the breast that spontaneously regressed after core needle biopsy (CNB). We present this case in accordance with the CARE reporting checklist (available at <https://gs.amegroups.com/article/view/10.21037/gs-22-629/rc>).

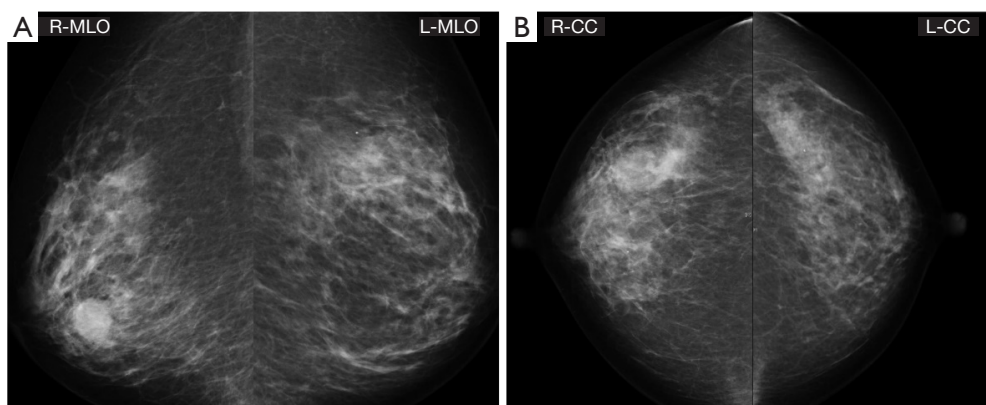


Figure 1 Preoperative mammogram findings. (A) MLO; (B) CC. A lobulated, marginal, micro-serrated, hyperdense mass was observed in the right breast. MLO, mediolateral oblique view; CC, craniocaudal view; R, right; L, left.

Case presentation

A 52-year-old woman presented to her primary physician because of a mass in the right breast. She had a history of schizophrenia and diabetes mellitus. She underwent hysterectomy for uterine cancer at age 51 years. She was using several medications, including ezetimibe, sitagliptin phosphate hydrate, metformin hydrochloride, glimepiride, perospirone hydrochloride, biperiden hydrochloride, mecobalamin, sultopride hydrochloride, and calcium sennoside A and B. Ultrasonography of the breast showed an irregular hypoechoic mass in the right breast, which was suspected to be breast cancer. The patient was referred to our department for further examination and treatment.

Highlight box

Key findings

- We experienced a case of spontaneous regression due to stimulation of CNB and discussed the mechanism.

What is known and what is new?

- There have been several reports related to spontaneous regression of tumors, not only breast cancer, but the cause of spontaneous regression has not been elucidated.
- This report allowed us to discover a hypothesis regarding spontaneous tumor regression in breast cancer.

What is the implication, and what should change now?

- If the immune mechanisms involved in the spontaneous regression of tumors, as suggested in this study, are clarified in more detail, they may be useful for cancer prevention and new treatment methods.

Her body mass index was 30.8 kg/m². She had no family history of breast or ovarian cancer. The physical examination revealed an elastic hard mass in the lower outer quadrant of the right breast without dimpling. Tumor marker levels were within normal limits [carcinoembryonic antigen (CEA), 3.7 ng/mL; carbohydrate antigen 15-3 (CA15-3), 10.3 U/mL; breast cancer antigen 225 (BCA225), 52.8 U/mL]. The mammogram showed that the breasts were heterogeneously dense, and that there was a round high-density mass with microlobulated margins in the outer-lower quadrant of the right breast (*Figure 1*). Breast ultrasonography revealed a round hypoechoic 22 mm × 17 mm × 22 mm mass with internal vascularity in the outer-lower quadrant of the right breast (*Figure 2*). The CNB results showed invasive ductal carcinoma of no special type that was grade 3, estrogen receptor (ER)-negative, progesterone receptor (PgR)-positive, and human epidermal growth factor receptor 2 (HER2)-negative, with a Ki67 index of 70% to 80% (*Figure 3*).

Computed tomography was performed 13 days after CNB and showed an enhanced 22-mm mass in the right breast and an enlarged and enhanced lymph node in the right axilla. No other obvious distant metastases were observed (*Figure 4*).

Dynamic enhancement magnetic resonance imaging was performed 40 days after CNB and showed a homogeneously enhanced, round, irregular 22-mm mass in the outer-lower quadrant of the right breast. The time-intensity curve was fast-plateaued. No contralateral lesions were observed (*Figure 5*).

Based on these results, stage IIB breast cancer (cT2N1M0) was diagnosed. Although preoperative

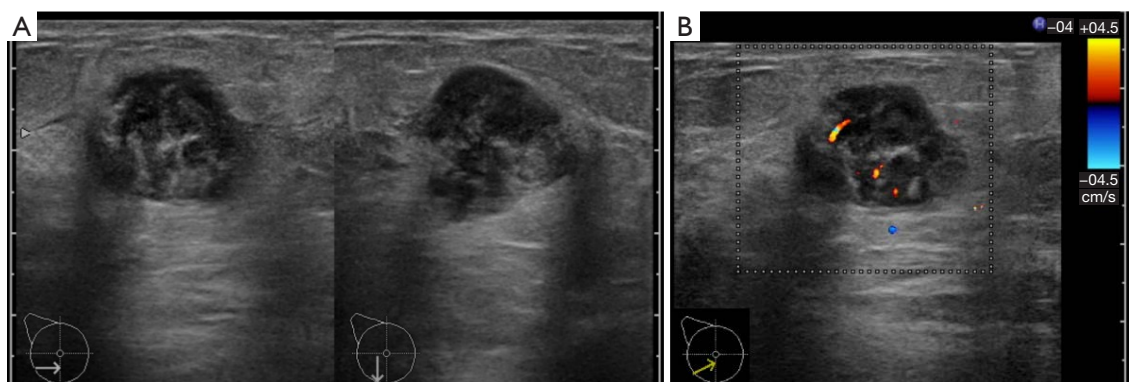


Figure 2 Preoperative ultrasonography findings. (A) Ultrasonography at presentation. (B) Color Doppler imaging. There was a lobulated, hypoechoic, 22 mm × 17 mm × 22 mm mass with blood flow in the right breast.

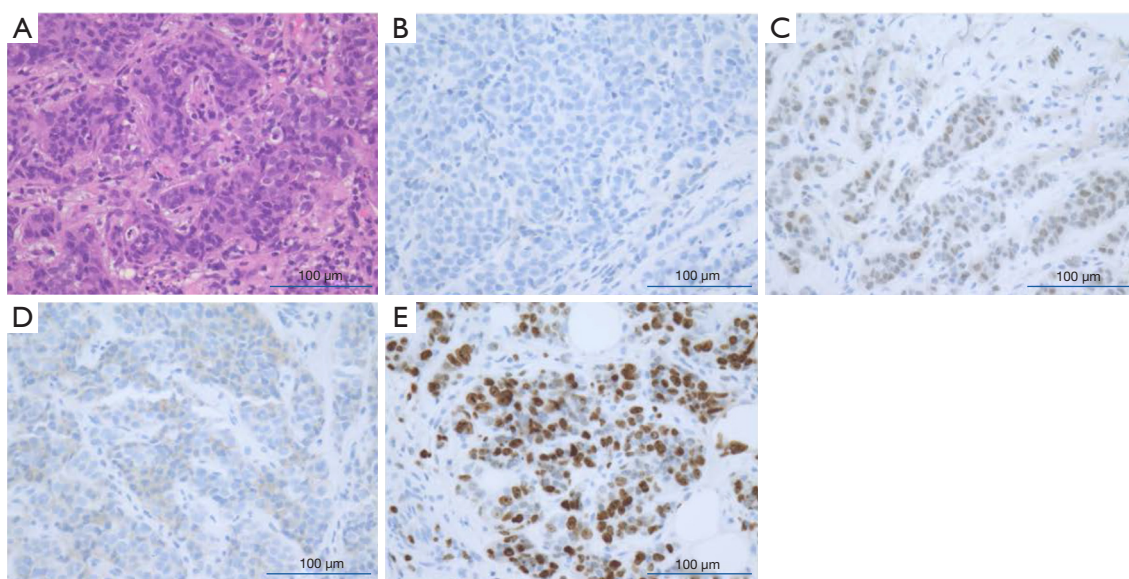


Figure 3 Preoperative pathological findings. Core needle biopsy was performed to determine the histopathological findings of the right breast. (A) Hematoxylin and eosin (magnification ×200). (B) Immunohistochemistry study of the estrogen receptor (magnification ×200). (C) Immunohistochemistry study of the progesterone receptor (magnification ×200). (D) Immunohistochemistry study of human epidermal growth factor receptor 2 (magnification ×200). (E) Immunohistochemical study of Ki67 (magnification ×200).

chemotherapy was considered as treatment, we decided to perform surgery because of her history of schizophrenia. She underwent right mastectomy and axillary lymph node dissection 48 days after CNB and was discharged on postoperative day 8.

Postoperative histopathology revealed that AE1/AE3-positive tumor cells did not observe in the region presumed to be the original tumor location; furthermore, tumor

cells were replaced with necrotic tissue and lymphocyte infiltration was observed in the surrounding area. Tumor cells in the CNB specimen were not present in the postoperative specimen, suggesting the possibility of SR. CD8-positive cells were present in aggregated lymphocytes (*Figure 6*). The patient has been alive for more than 2 years without recurrence. All procedures performed in this study were in accordance with the ethical standards

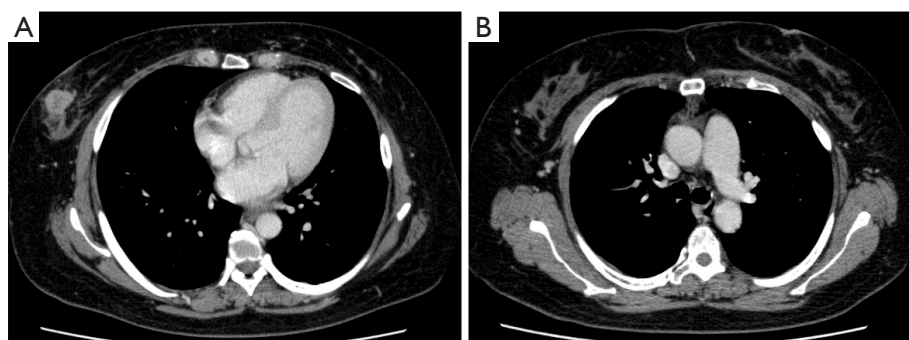


Figure 4 Preoperative CT findings. CT with enhancement. (A) The 22-mm enhanced mass was in the area of the right breast. (B) A nonspecific enlarged lymph node was in the right axilla. CT, computed tomography.

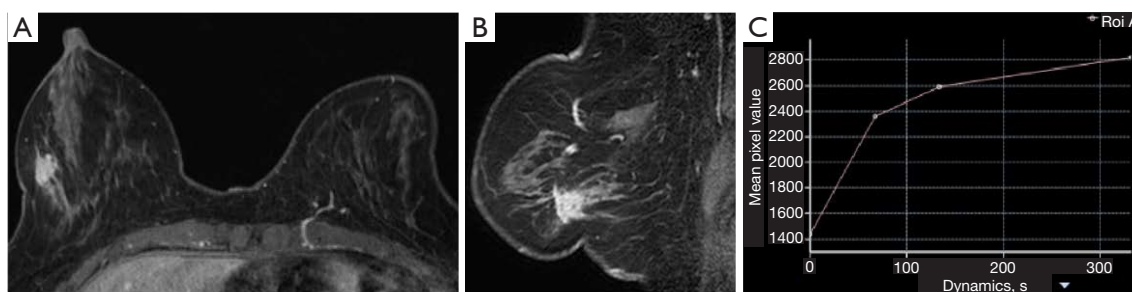


Figure 5 Preoperative MRI findings. (A) MRI with early gadolinium enhancement coronal section. (B) MRI with early gadolinium enhancement in the sagittal section. (C) Time-intensity curve. An enhanced 22-mm mass was observed in the right breast area. The time-intensity curve was fast-plateaued. MRI, magnetic resonance imaging; RoiA, region of interest analysis.

of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

Discussion

Breast cancer accounts for 43 (5.8%) of 741 cases of tumors with SR, which is relatively rare among carcinomas (3). Carcinomas that are prone to SR include renal cell carcinoma, neuroblastoma, malignant melanoma, hepatocellular carcinoma, and choriocarcinoma (4). These carcinomas are considered to have high immune activity, suggesting that immunological mechanisms are important factors in the mechanism of SR in cancer. Other mechanisms of SR in cancer have been assumed to include hormonal effects, tumor suppression by growth factors and cytokines, changes in the tumor growth environment, cell disruption,

disruption of nutrient vessels, and altered healing response traits after biopsy (1,2). It has been speculated that these phenomena are related to trauma or infection (1,5). It has been reported that 28% of gynecological malignancies with SR occur after prolonged fever, and that sepsis may activate the patient's immune response and enhance the immunity to the tumor (3,6). Our patient had no preoperative history of infection or trauma; however, lymphocytic infiltration and tumor necrosis were observed around the tumor, which was preoperatively treated with CNB. However, we found that CD8-positive cells were present in the postoperative specimen, which was undergone CNB. It is reported that surgical stimulation attracts immune cells and activate local immune responses (7). These attracted immune cells, especially anti-cancerous immune cells, induce the process of cancer cell killing, also known as "Immunogenic cell death (ICD)" (8). Given these mechanisms, we hypothesized that the stimulation of CNBs caused the SR in this case. Although ezetimibe, metformin, and glimepiride have been reported to have antitumor

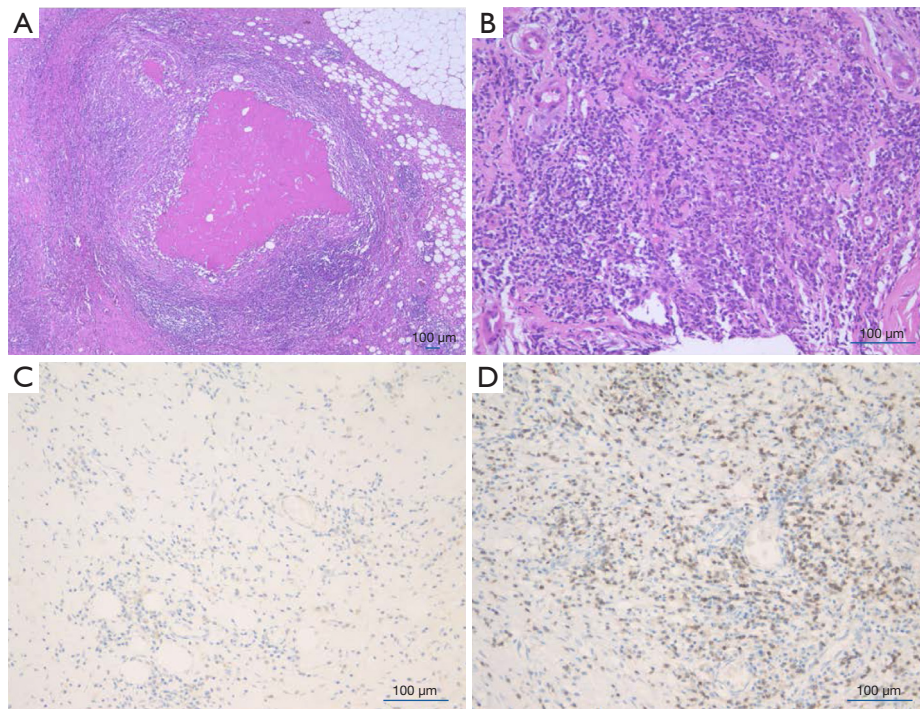


Figure 6 Postoperative histopathological findings of the resected breast tissue are shown. Tumors were replaced with vitrified and necrotic tissue. Lymphocyte infiltration was observed in the surrounding area. (A) HE staining (magnification $\times 40$). (B) HE staining (magnification $\times 200$). An immunohistochemical analysis of immunological surface markers was performed. (C) AE1/AE3 (magnification $\times 200$). (D) CD8 (magnification $\times 200$). HE, hematoxylin and eosin.

effects against breast cancer (9,10), the cancer appeared while the patient was using these drugs. Therefore, it is unlikely that these drugs were involved in SR of this tumor.

A literature search of the PubMed database using the keywords “spontaneous regression”, “spontaneous remission”, “breast cancer”, and “breast carcinoma” between 1994 and 2022 revealed nine reported cases, including autologous cases (*Table 1*) (4,5,11-17).

Of the eight cases, excluding autopsy cases, seven SR cases were attributable to an immune response. Three of these studies have suggested the involvement of CD8-positive T cells. The mechanism by which cellular immunity acts against tumors is being elucidated, and tumor-infiltrating lymphocytes have been the focus of treatment, especially in breast cancer. Tumor cells express class I human leukocyte antigens on the cell membrane surface, which activate cytotoxic T cells to recognize tumor cells and exert antitumor effects (18). Furthermore, tumor-infiltrating lymphocyte activity is regulated by complex immune system activator and inhibitor pathways (19).

Regarding our case, the pathological analysis revealed vitalization, necrotic tissue, and infiltration of CD8-positive lymphocytes in the tumor area, suggesting that an immune response may be involved in SR of the tumor. However, further studies are required to elucidate these mechanisms.

Whether SR is associated with the prognosis has not been adequately studied, and there are no clear criteria, such as the follow-up period. No recurrence was mentioned in any of the reports of breast cancer with SR. Our patient has not experienced recurrence, and it was recommended that she should undergo follow-up including mammography and ultrasonography annually for the next 8 years.

Conclusions

This case showed that invasive ductal carcinoma of the breast can experience SR after preoperative CNB. The exact mechanism of SR in cancer should be elucidated because it may lead to the development of cancer treatment and prevention.

Table 1 Nine cases of breast cancer with SR

| References | Year | Age (years)/sex | Subtype | Suggested mechanism | Possible trigger | Regression | Pathologically verified SR |
|------------|------|-----------------|---------|--|------------------------------|---|----------------------------|
| (11) | 1994 | 46/F | – | Immunological response mediated by activated CD8 ⁺ T cells and NK cells | Treatment with dexamethasone | Regression of primary tumor and metastatic lesion | – |
| (5) | 2008 | 68/F | – | Immunological and local inflammatory response | Arm injury Needle biopsy | Complete regression of primary tumor | + |
| (4) | 2014 | 52/F | Luminal | Immunological response | Unclear | Nearly complete regression of primary tumor and complete regression of metastatic lymph nodes | + |
| (12) | 2016 | 44/F | Luminal | Immunological response | Needle biopsy | Complete regression of primary tumor | + |
| (13) | 2019 | 67/F | Luminal | Immunological response | Unclear | Nearly complete regression of primary tumor and complete regression of metastatic lymph nodes | + |
| (14) | 2019 | 72/F | TNBC | Immunological response mediated by activated CD8 ⁺ T cells | Unclear | Complete regression of primary tumor and metastatic lymph nodes | + |
| (15) | 2020 | 86/F | TNBC | Immunological response mediated by activated CD8 ⁺ T cells | Unclear | Regression of metastatic skin lesions | – |
| (16) | 2020 | 70/M | Luminal | Ischemia/infarction | Unclear | Regression of primary tumor followed by reappearance | – |
| (17) | 2021 | 59/F | TNBC | Immunological response | Unclear | Partial regression of primary tumor | + |
| Our case | 2023 | 52/F | Luminal | Immunological response mediated by activated CD8 ⁺ T cells | Unclear | Partial regression of primary tumor | + |

SR, spontaneous regression; NK, natural killer cells; TNBC, triple negative breast cancer.

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Footnote

Reporting Checklist: The authors have completed the CARE reporting checklist. Available at <https://gs.amegroups.com/article/view/10.21037/gS-22-629/rc>

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <https://gs.amegroups.com/article/view/10.21037/gS-22-629/coif>). AY serves as an unpaid editorial board member of *Gland Surgery* from April 2021 to March 2023. The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

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