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Spontaneous breast cancer remission: A case report

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ABSTRACT

INTRODUCTION: Spontaneous breast cancer remission is a rare phenomenon. We report the disappearance from the remaining breast of a new primary carcinoma that had been confirmed through cytology of a pathological specimen, in a case that is strongly suspected to be spontaneous remission.

PRESENTATION OF CASE: A 44-year-old woman underwent breast-conserving surgery for a tumor located on the border between the upper-outer and lower-outer quadrants of the left breast (T2, N1, M0; Stage IIB). Eleven years after surgery, computed tomography indicated a mass in the upper-inner quadrant of the left breast. Excisional biopsy was initially planned for treatment following the definitive diagnosis because cytology revealed malignancy. The patient had noticed tumor regression one month after fine-needle aspiration and repeat ultrasonography performed the day before excisional biopsy confirmed the tumor reduction. On pathological examination, no tumor cells were observed in the mass.

DISCUSSION: There was a discrepancy between FNA cytology and pathological diagnosis in our patient. The cytological findings indicated malignancy, but the pathological findings did not. When a tumor's pathological diagnosis is not malignant even though its FNA cytology diagnosis was malignant, sampling error, cytological over-diagnosis or some other error may have occurred. In this case, however, these were not detected. Because fibrosis was visible on pathological examination, we believe that these events corresponded to spontaneous remission.

CONCLUSION: We report a rare case of spontaneous remission in which the cancer disappeared on pathological examination although the cytological diagnosis had been malignant.

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1. Introduction

Spontaneous cancer remission is a rare phenomenon in which a cancer is reduced or disappears without treatment [1,2]. In breast cancer, a healing phenomenon has been reported where intraductal lesions are completely replaced by fibrous components. In one study, this healing phenomenon was confirmed in 7% of specimens obtained during breast cancer surgeries, suggesting that spontaneous breast cancer healing might occur more frequently than expected [3].

We report the disappearance from the remaining breast of a new primary carcinoma that was confirmed through cytology of a pathological specimen, which is strongly suspected to be spontaneous remission.

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2. Case presentation

A 44-year-old woman underwent lumpectomy and axillary lymph node dissection for a tumor located on the border between the upper-outer and lower-outer quadrants of her left breast in 2002. Pathological findings at that time were as follows: the papillotubular carcinoma, 15 × 14 × 15 mm in size, had infiltrated the fibro-adipose tissue; no lymphatic invasion and nuclear grade 3; negative margins; axillary lymph node metastasis in 3 of 24 nodes; estrogen receptor (ER) positive and progesterone receptor (PgR) negative. Adjuvant therapy included administration of cyclophosphamide, doxorubicin and 5-fluorouracil followed by docetaxel (CAF-T regimen) and a luteinizing hormone-releasing hormone (LH-RH) agonist in combination with tamoxifen for three years. Radiation therapy to the breast was also performed. The patient was followed-up for 10 years and three months after the initial surgery, without any findings of recurrence or metastasis. Mammography and ultrasonography revealed no abnormal findings in the breast. At the patient's request, fat injection for lateral volume loss was performed twice in the plastic surgery department

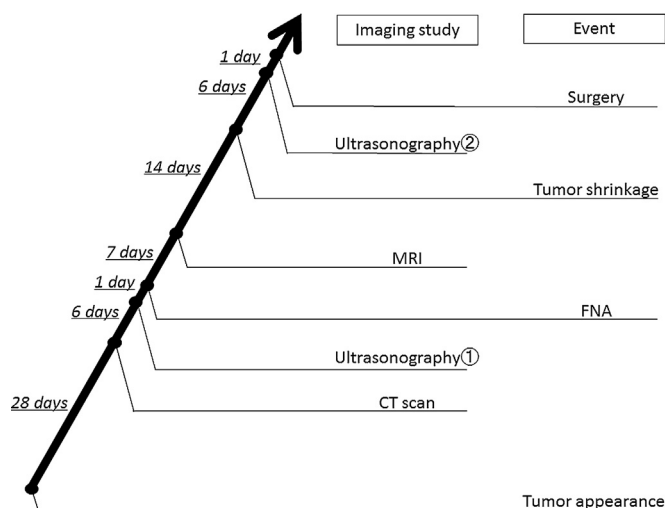


Fig. 1. Time course. Tests and episodes that occurred between the mass discovery and surgery.

of our hospital 11 years after the surgery. When a chest computed tomography (CT) scan was performed to confirm the fat engraftment, a mass was identified in the upper-inner quadrant of the left breast (Fig. 1), and the patient was referred to our department. The patient reported having noticed the mass four weeks prior to the CT examination. Ultrasonography revealed an irregular hypoechoic mass (13 × 9 × 12 mm) with a rough surface and internal heterogeneity. An echogenic halo was observed in the surrounding tissue (Fig. 2a). These findings indicated invasive ductal carcinoma. Fine-needle aspiration (FNA) was performed on the following day. Material was aspirated from the lesion using a 21-gauge needle and a smear of the aspirate was fixed in 95% alcohol and stained using Papanicolaou stain. The smear revealed a cluster showing an aggregated arrangement in a straight line with discohesiveness under low-power magnification, and cellular pleomorphism and mitotic figures were observed under high-power magnification. Cells with an intracytoplasmic lumen were also identified. Given these findings, an invasive ductal carcinoma was suspected and we diagnosed malignant as per the Japanese breast cancer society [4] (Fig. 3). Fourteen days after CT examination, magnetic resonance imaging (MRI) was performed. The MRI revealed a mass lesion adjacent to the chest wall in the upper inner quadrant (low intensity on

T1-weighted imaging, high intensity on T2-weighted imaging and high intensity on diffusion-weighted imaging), which was thought to be a malignant mass or inflammation (Fig. 4). Unfortunately, the MRI was discontinued due to the patient's claustrophobia before a contrast-enhancing examination could be performed.

Based on the imaging and cytological findings, the patient was diagnosed with ipsilateral de novo primary breast cancer after breast conservation surgery. In general, core biopsy is performed as a definitive examination and biological markers are evaluated before an operation. However, in this case, we planned excisional biopsy as a diagnostic therapy. Before the excisional biopsy, the patient noticed that the mass had decreased in size 35 days after CT (28 days after FNA). Forty-seven days post-CT, a pre-operative ultrasound revealed tumor shrinkage (10 × 7 × 4 mm; Fig. 2b), and no symptoms of inflammation such as heat, swelling, pain or redness were noted on clinical examination. The next day (48 days after CT), excisional biopsy was performed for the purpose of definitive diagnosis and treatment. On pathological examination, no tumor cells were observed in the mass, and fibrosis and lymphocytic infiltrations were detected in an area of approximately 10 × 10 mm. Coagulative necrosis was observed in the center of the specimen (Fig. 5).

The patient was kept under observation without additional postoperative treatment because of the lack of known biological markers, and because the CAF-T regimen followed by LH-RH agonist with tamoxifen had previously been administered along with radiation therapy after the first operation.

3. Discussion

Spontaneous cancer remission without treatment is a known phenomenon, and has been previously reported in several patients with various types of cancer. This phenomenon has previously been confirmed to occur in specific cancers such as neuroblastomas, renal cell carcinomas, melanomas and lymphomas [1,2]. Muir et al. [5] reported the first case of spontaneous breast cancer remission in 1934; in 1999, Larsen [6] reported on 32 patients who had experienced spontaneous breast cancer remission. The authors concluded that this is a rare phenomenon, considering that breast cancer is a relatively common malignancy. A comparison between screened and non-screened groups in the Norwegian Breast Cancer Screening Program showed that the non-screening group had a lower proportion of invasive breast cancer than originally thought [7]. Therefore, the authors concluded that spontaneous remission of

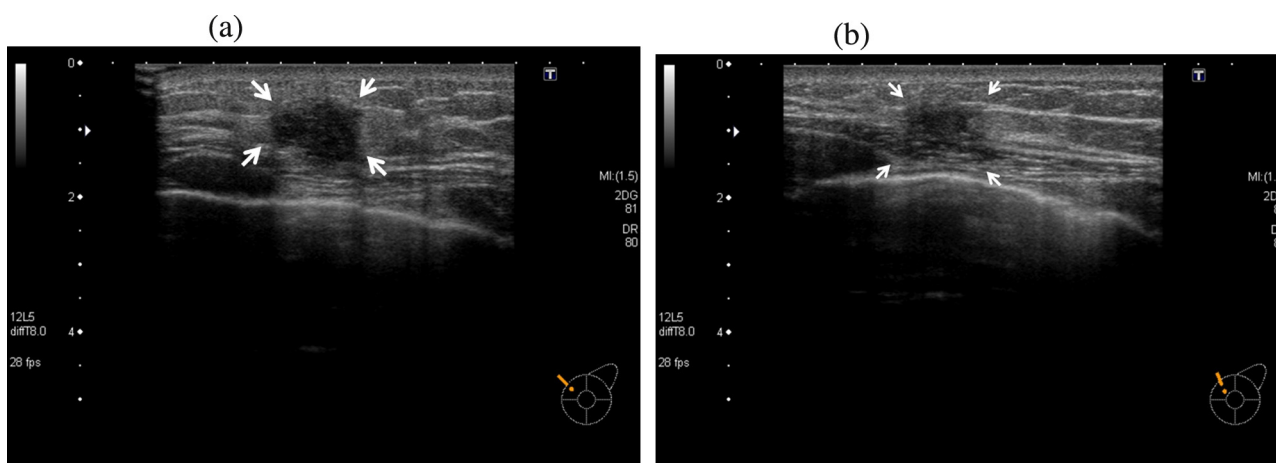


Fig. 2. (a) Ultrasonography at the initial diagnosis. A morphologically irregular (13 × 9 × 12 mm) and sharply demarcated hypoechoic mass with a rough surface and internal heterogeneity was found in the left upper-inner quadrant (arrow). Posterior ultrasonography was unchanged. There was no lateral shadow. A hyperechoic area was observed in the tumor border. A papillotubular carcinoma with scirrhous invasion was suspected. (b) Ultrasonography immediately before surgery. The identified mass had reduced to 10 × 7 × 4 mm (arrow).

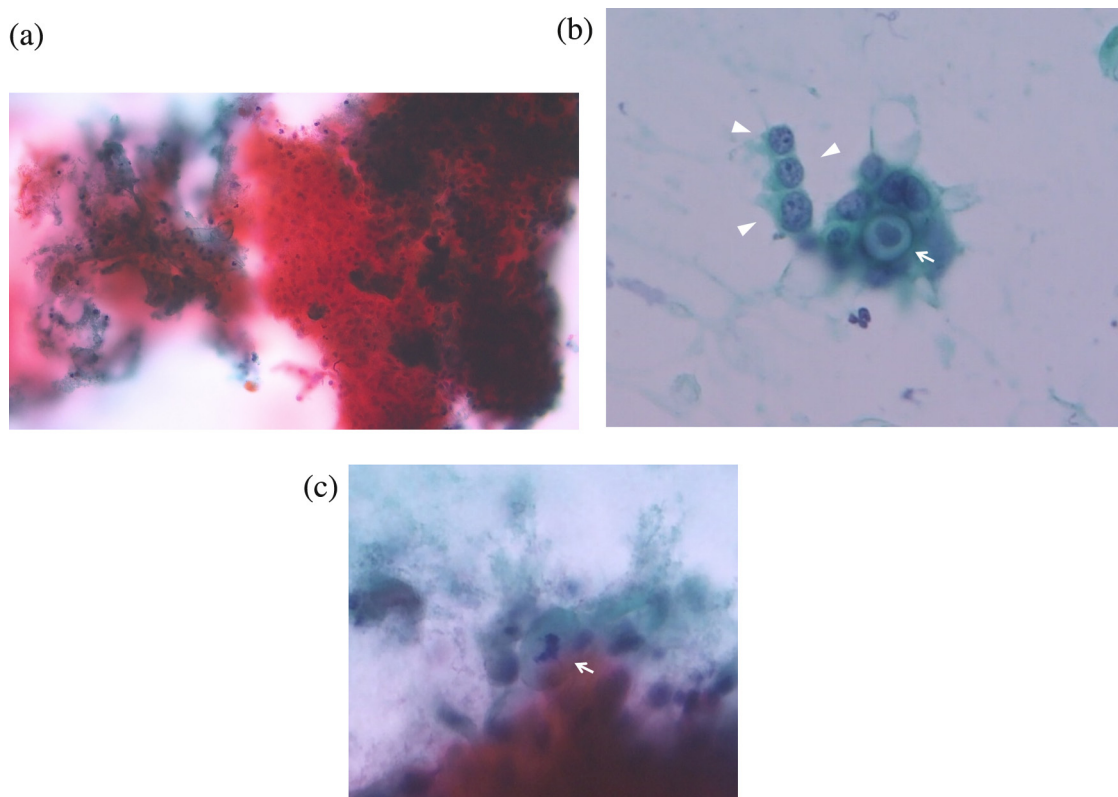


Fig. 3. (a) FNA: $\times 200$ magnification. A cluster with an aggregated arrangement and a loss of adhesion was observed. (b) FNA: $\times 400$ magnification. A small agglomeration, ICL (arrow) and a restiform arrangement (arrowhead) were observed. (c) FNA: $\times 400$ magnification. A typical cells and mitoses (arrow) were observed.

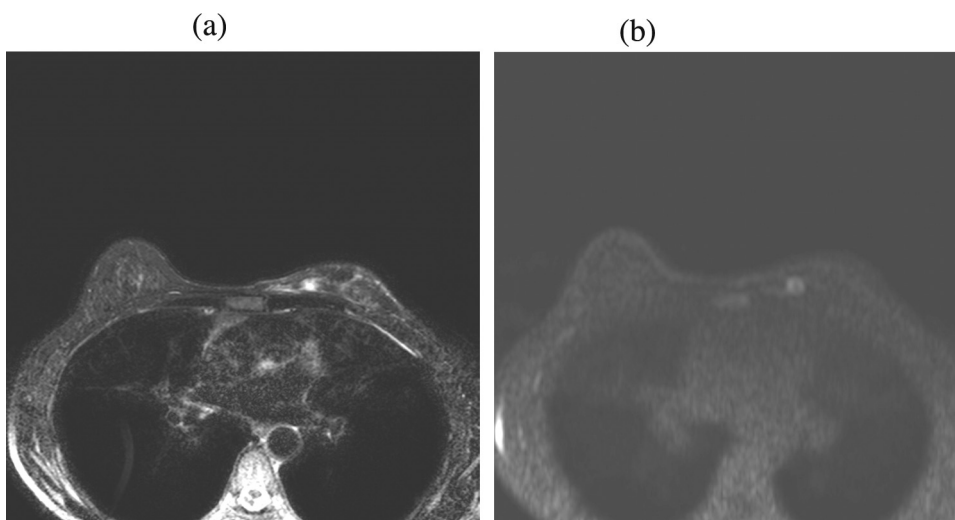


Fig. 4. (a) Non-contrast MRI: T2WI. High intensity was observed at the center of the tumor. (b) Non-contrast MRI: DWI. Accumulation at the center of the tumor suggested inflammation or a malignant component.

breast cancer without treatment occurs at a measurable rate. In 2005, Horii et al. [3] reported that the main pathological feature of the healing phenomenon in breast cancer is a high nuclear grade, especially in comedo/solid type ductal lesions.

Possible mechanisms of spontaneous cancer remission include immune system or hormonal mediation, tumor inhibition by growth factors/cytokines, induction of differentiation, elimination of a carcinogen, tumor necrosis/angiogenesis inhibition, psychological factors, apoptosis and epigenetic mechanisms [1,2]. It has also been speculated that this phenomenon is possibly related to trauma

[8]. Moreover, spontaneously induced T cell-mediated immunological responses have recently received attention in multidisciplinary cancer treatment [9,10]. In the present case, the patient could not remember any traumatic events to the site. FNA, which was performed 41 days before the surgery, was also a possible mechanism, yet the typical effects of FNA such as hematoma and swelling were not present.

There was a discrepancy between FNA cytology and pathological diagnosis in our patient. The cytological findings, namely, high nuclear/cytoplasmic ratio, hyperchromasia, pleomorphism,

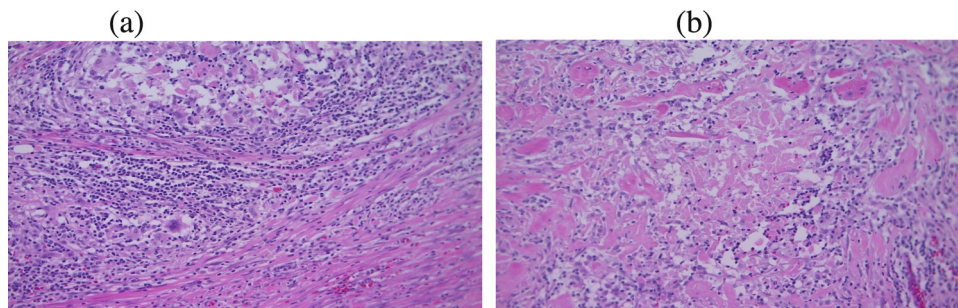


Fig. 5. (a) Surgical specimen: hematoxylin and eosin (H.E.), $\times 200$ magnification. Fibrosis and lymphocytic infiltration were observed in an area of approximately 10×10 mm. (b) Surgical specimen: H.E., $\times 400$ magnification. Coagulative necrosis was detected at the center of the tumor.

discohesiveness and necrosis, indicate malignancy [11]. FNA cytology for palpable breast masses has a high specificity, reported to be 78–100% [12–14]. When a tumor's pathological diagnosis is not malignant though the tumor was diagnosed as malignant through FNA cytology, sampling error, cytological over-diagnosis or some other type of error may have occurred [15]. Sampling error is not likely in this case because the tumor was a palpable lesion and its location was confirmed using ultrasonography. Over-diagnosis is possible, as there are reports of intraductal proliferating lesions, hyperplasia, fibrocystic changes, and breast masses during pregnancy or lactation having been misdiagnosed as malignancies [14,16]. The lesion ought to be compatible with the patient's pathological sample, but fibrosis and lymphocytic invasion were recognized in the pathological specimen. These changes are similar to those associated with inflammation. The findings are compatible with the healing phenomenon, in which a cancer disappears. These results are similar to those of other reports because they occurred in a ductal lesion with a high nuclear grade [3].

The results of the MRI, which was performed seven days after FNA, were retrospectively reviewed; high-intensity signals were detected on T2-weighted and diffusion-weighted imaging in the center of the mass compared with the margins, suggesting that inflammation may have occurred in the center of the tumor. Because fibrosis was visible on pathological examination, we believe that the MRI findings correspond to spontaneous remission which was ongoing during this period.

In each case of spontaneous breast cancer remission, the optimal chemotherapy drug or hormone replacement therapy regimen should be considered on an individual basis. In our patient, cancer was not detected in the pathological specimen and there were no known biological markers that could aid in a decision on adjuvant therapy. After discussing treatment options with the patient, we decided to place her under observation without further treatment. Because the cancer disappeared completely, we believe that this case will provide important information for the pathological diagnosis and future treatment of patients with similar cases.

4. Conclusion

We report a rare case of spontaneous breast cancer remission in which the cancer disappeared on pathological examination though the cytological diagnosis was malignant.

Conflict of interests

The authors declare no conflict of interests for this article.

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None.

Ethical approval

Written informed consent was obtained from the patients for publication of these case reports and accompanying images.

Consent

This patient was properly informed and gave consent for her clinical information to be included in an Elsevier publication.

Author contribution

Eisaku Ito contributed to all aspects of the manuscript, wrote the manuscript and is responsible for the information. Satoko Nakano contributed to all aspects of the manuscript and reviewed this manuscript. Masahiko Otsuka reviewed and contributed to all aspects of the manuscript. Akemi Mibu performed Ultrasonography and supported FNA cytology. Masahito Karikomi interpreted radiological examination. Toshinori Oinuma and Masahiro Yamamoto are responsible for histopathological examination. All authors read and approved the final manuscript.

Guarantor

Eisaku Ito is the guarantor of this paper.

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